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NEUROLOGICAL AND PHYSIOLOGICAL COMMENTS ON THE SECTION OF THE PITUITARY STALK IN HUMANS (MISCHOTOMY)

J. LE BEAU J. F. FONCIN S. NICOLAIDIS

Four years after the first hypophysectomy in a patient suffering from breast cancer 22 , 25 we started in november 1955 the section of the pituitary stalk 18 for three reasons:

(a) Surgical hypophysectomy was often proved to be incomplete when at post mortem one takes care to estimate the significance of the anterior lobe remnants through serial sections of the decalcified sella turcica 16 ;

(b) Furthermore if sella turcica, pituitary stalk and hypothalamus are removed together and included in the same block one observes the great regenerative ability of hypophyseal portal vessels towards anterior lobe remnants and of anterior lobe cells themselves. This was described both after hypophysectomy and after pituitary stalk section. On the other hand as hypophysectomy may be dangerous and difficult owing to diffuse bleeding in severely ill patients with multiple metastasis, we use pituitary stalk section when at operation hypophysectomy seems hazardous for local conditions (short optic nerves and/or a bulging tuberculum sellae). If pituitary section is adopted it is therefore imperative to find a way to interrupt permanently any vascular connexion between the hypothalamus and the anterior lobe, in agreement with the experimental work of Harris¹¹.

(c) Finally, the extent of pituitary tissue necrosis after mischotomy (*miskos*, stalk; *tomé*, section) is a significant though variable factor 24 .

We shall comment here some aspects of mischotomy under three headings: (1) Surgical technique and clinical results; (2) Anatomical and physiological observations; (3) Studies on normal pituitary tissue removed during the operation and examined by electron microscopy.

From the Laboratoire de Physiologie et de Psychologie Neuro-Chirurgicales de l'École Pratique des Hautes Études (Directeur: Prof. J. Le Beau), Service de Neurochirurgie de l'Hôpital de la Salpêtrière.

SURGICAL TECHNIQUE AND CLINICAL RESULTS

The main steps of the operation were detailed before 2^{0} , 2^{1} and are similar to other reports 4, 5. Since then only a few technical modifications are worth to be described. The usual stages are: (a) Bi-frontal scalp; (b) Unilateral bony flap which should be tangent to the medial line and no more than 2 or 3 cm above the eyebrow. It is indeed imperative to get a vertical view upon the optic chiasm; (c) Opening the dura mater as far as possible medially and anteriorly; (d) Retracting the frontal lobe either classically following the sphenoidal wing or, as advocated by Bronson and Pearson 3^{0} , backwards paramedially in order to reach the sella turcica directly.

Whatever the approach used frontal lobe retraction is greatly facilitated in patients with an excess of intraventricular or subarachnoideal cerebrospinal fluid. On the other hand cerebral oedema although a rare condition makes the operation more hazardous when one has to excise the anterior part of the frontal lobe to obtain a correct exposure.

(e) Then comes the main stage of the procedure, that is, the choice between hypophysectomy and pituitary stalk section: we choose hypophysectomy when the optic nerves are long, the tuberculum sellae small and the tendency to bleeding is moderate; we choose mischotomy when the optic nerves are short nearly touching the tuberculum sellae which then seems bulging.

Mischotomy itself is performed with long angled and thin scissors cutting as low as possible the pituitary stalk elevated by an angulated hook. There is usually no significant bleeding; if any, it is easily controlled by electrocoagulating the proximal end of the stalk. It is always necessary to take great care not to pull on this proximal end in order to prevent damage to the anterior hypothalamus. After the section we usually remove two small pieces of the anterior lobe for electronic and optic microscopical examinations. Thus, as will be seen later, it became possible to identify some functional types of anterior lobe cells.

(f) One of the most important steps of a successful mischotomy is the achievement of a permanent interruption of the hypothalamo-pituitary vascular connexions. At the beginning (1955-1957) a small piece of tantalum foil was placed between the proximal end of the stalk and the sellar diaphragm. This procedure has proved to be not enough and, in 1958, we adopted to set a piece of fresh plastic paste hardening in situ. Here again, as could be demonstrated by post mortem serial sections, the regeration ablity of the portal vessels was such that in some cases we were able to find conjunctivo-vascular pedicles coming from the hypothalamus going around the solid edges of the plastic plate and terminating into what was left of the anterior lobe. So later (1960) we started to use a polyethylene transparent film folded in two layers fixed by a Cushing clip and large enough to shut off the sellar diaphragm well over its limits. The main difficulty is to push it far backwards below the severed stalk which is kept elevated by an angulated blunt hook. Then gelfoam between the optic nerves presses upon the plastic film and keeps it firmly in place.

(g) The last steps of the operation are classical. After checking the base of the frontal lobe and especially the proximal end of the right olfactory nerve torn or divided surgically for any bleeding, as well as the olfactory bony groove, the dura mater is closed, bone flap replaced and scalp sutured.

Endocrine treatment is obviously necessary. On the average we give 100 mg of cortisone for two days before the operation, 200 mg the day of the operation, 100 mg the following day, then 50 mg on the fourth and fifth days. We switch to Delta-cortisone giving 5x5 mg orally, progressively diminishing the dose to 3x5 mg which the pacient should take every day and forever. Of course the doses should be augmented when cause of stress are foreseen. The treatment of diabetes insipidus usually needs, during the first week at least, daily injections of retropituitrin. Latter polyuria tends to abate and more so when cortisone is reduced. On the average patients live confortably with a urinary excretion of 3 to 4 liters, with or without pituitary powder sniffing. Again for the first 10 or 15 days patients must be rehydrated orally and/or intravenously; hydric and electrolytic balance are followed daily first, every '2 or 3 days later. It is not uncommon to observe accidents of acute dehydration which never should be lethal.

The operatory mortality of mischotomy is inferior to 10 percent. Fatalities occur nearly always in women with metastatic involvement of the liver or of the bone marrow. Preoperative laparoscopy, blood count and examination of the sternal marrow are therefore among the most important tests to be made before the operation. There is practically never a postoperative acute shock such as is observed sometimes after a difficult hypophysectomy.

The future of the mischotomized patients is probably a little less satisfactory than those in which hypophysectomy is made. We have had very encouraging results in 4 groups of cases: (a) extensive tumor of the breast with metastasis into the skin, instances in which we tend to resect the breast tumor at the same session as the mischotomy; (b) lung metastasis preferably without pleural involvement; (c) bone metastasis without bone marrow destruction; (d) and this is less known, in cases with brain metastasis. Just to illustrate this group we report one of our cases:

Mrs. D..., 51 years old, had an ablation of the left breast for an infiltrating carcinoma in 1963. In May 1965 she is sent to La Salpêtrière with signs of a right parietal expansive lesion (left hemiplegia, apraxia, left homonynous hemianopia) and "polyneuritis" of the lower limbs, the electrical examination showing to be due to peripheral neurogenic dysfunction. On June 23, after an arteriography confirming the right parietal tumor, a large cystic metastasis was partially excised for microscopical examination, then completely destroyed by two minutes refrigeration at minus 100° centigrades with the Cooper unit. The cytologic examination of the cystic fluid yielded numerous malignant cells and the histological examination of the tumor specimen showed a secreting cylindrical epithelioma. There was rapid regression of the left hemiplegia and on July 23 a pituitary stalk section

was performed with interposition of a polyethylene film between hypothalamus and pituitary gland. The recovery was uneventful and the patient left for convalescence on August 6th. Twenty months after the brain operation the neurological signs including the paraneoplasic polyneuritis have subsided and the patient seems entirely normal except for a moderate polyuria. The EEG showed still some slow waves on the right parietal region but less and less marked. The biological tests performed 18 months after the mischotomy have shown a flattening of the hyperglycemia curve, lowering of the 17-ceto and 17-CH steroids levels, a basal metabolism at -22 per cent and a very low thyroid fixation of Γ^{ia1} (the patient was using thyroid extract), a rate of FSH less than 5 mouse-units/24 hours. On April 1966 Mrs D, started again his previous occupation of telephonist doing it normally

Of course such a case report does not demostrate the benefical action of mischotomy on a metastatic brain lesion since it is well known the variable evolution of breast cancer metastasis. But at least it proves that a metastatic brain tumor is not a sufficient reason to give up mischotomy or hypophysectomy.

ANATOMICAL AND PHYSIOLOGICAL OBSERVATIONS

In our research program mischotomy was an application to human beings of experimental results obtained before 1955¹¹: the functional equivalence between anterior lobe ablation and permanent interruption of the portal system carrying the secretory materials from the hypothalamus to the pituitary gland, a variable part of which undergoes ischaemic necrosis. As in our earlier reports ^{16, 17}, the results presented here owe their significance to anatomo-histological study. Post mortem we remove "en bloc" the hypothalamus, the pituitary stalk and sella turcica which is then decalcified. Serial sections 150 μ thick of celloidin included block, imperative to describe the eventual vascular reconnexions, are selectively embedded in paraffin to obtain new cuts 5 μ thick for correct cytological study. The survival times ranged from 30 hours to 18 months.

Our observations and hypotheses are reported and discussed under 6 headings: (a) pituitary vascularisation; (b) portal regeneration; (c) anterior lobe regeneration; (d) releasing factors; (e) pars tuberalis; (f) peripheral endocrine gland. Since our first publications (1958, 1960, 1962) many of our findings were confirmed by others through human or animal studies ¹, ², ³, ¹², ¹³, ²³, ²⁶, ³³.

Pituitary vascularisation — The description of the hypophyseal portal system in man made by Xuereb et al.³⁴ is well known and perfectly valid. But after mischotomy normally unimportant vessels raise their functional status. The artery of the trabecula, branch of the superior hypophyseal artery, plays then a definite pituitary feeding part (Nicolaidis, 1962; Adams et al., 1966). It is plausible then to suspect a physiological role misunderstood until now: indeed not only the ischaemia of the glandular parenchyma does not involve the areas in the immediate neighbourhood of the artery of the trabecula, but both the vascular and the cellular regenerations radiate from this vascular bed. So it seems that quite a significant number of anterior lobe cells may receive their blood supply not through the portal

system but from the medial eminence. Furthermore there is another possible source of blcod supply: the capillaries developed in the membranes surrounding the pituitary gland which penetrate into the adjacent parenchyma. Thus, oxygen diffusion postulated by some authors ¹ is not necessary to explain the existence of living cells at the periphery of the ischaemic gland.

Portal regeneration — The extraordinary ability of vascular regeneration in humans is confirmed since 1958^{16} . Tropism is a convenient word to describe how the smallest channel even when covered with dura mater is used as a communicating line sometimes made of very large new vessels with thin walls. Once more it should be clearly understood that any assertion of "definitive" mischotomy is devoid of signification without serial histological sections. From another point of view we did not observe any case of regeneration of nervous fibers in relation to the posterior lobe.

Cellular regeneration — The possibility of cellular regeneration was discussed following our first cases and was demonstrated later ^{17, 24}. The area of necrotic ischaemia except for the trabecular zone is usually central and anterior, corresponding to the territory of the long portal vessels. But its extent, as explained above, is definitely lesser than it can be expected. Inside this large ischaemic area neocapillaries containing macrophages during the first days are in intimate contact with numerous indifferentiated cells which do not show orangeophile granules before the 17th day. Then there are two possibilities: (a) If the hypothalamo-pituitary interruption persists the whole functional glandular parenchyma is made of these Azan orangeophile cells analogous to prolactin cells¹⁵. Furthermore it is now proved in human beings that the isolated pituitary produces the mammotrophic factor in excess 12, 26, 27, as we suggested in 1962. (b) More often there is some portal regeneration towards the anterior lobe and then the pituitary cells show the variegated colorations which are a common occurance in the normal gland. Only in these cases of revascularisation castration cells can be observed ^{2, 24}. Thus it seems that hypothalamic structures are responsible for this evolution.

Releasing factors — In one of our patients with a 10 months survival castration was made before mischotomy. On serial sections a "lame porte-vaisseaux" made of a few very thin neocapillaries established a communication between the lower infundibular stem and the posterior tuber and many orangeophile cells (cells \mathcal{E} of Romeis) as well as many castration cells were found in the anterior lobe. Such observations lead us to infer that the prolactin inhibiting factor could come from the anterior hypothalamus whereas the developmental factor of castration cells would be related to the posterior tuber. These two hypotheses are in way to be confirmed by recent experimental studies ³, ⁶, ¹⁴, ²³, ³³.

It is also interesting to note that in at least another of our patients — in agreement with Ehni and Eckles cases 5 — lactation was observed although not persistently; post mortem, 6 months later, there was a marked revascularisation of the anterior lobe.

Pars tuberalis — A compensatory hypertrophy of the pars tuberalis is observed after mischotomy (Fig. 1) and is closely associated to vascular hypertrophy (after the 23rd day). Several layers of cells develop and at the same time there occur a cellular differentiation marked by numerous chromophile granulations contrasting with the normal chromophobe appearance of this region. Such modifications are probably of some functional significance.



Fig. 1 — Hypertrophy of the pars tuberalis (T), visible in front of the stalk stump and above the plastic paste (18 months survival).

Peripheral endocrine glands — Biological and histological explorations of endocrine glands show some differences between the post-effects of hypophysectomy and those of mischotomy. During the first weeks after mischotomy there is a marked fall of endocrine activity but not quite as definite as after total hypophysectomy ¹⁹. After the first month a general although weak reascension of biological tests is observed. But the FSH levels stay very low even when there is portal regeneration (with the exception of one out 8 of such cases); the LH and ACTH production becomes less diminished; on the contrary the TSH progressively comes back to normal or even higher and the more so when there is vascular regeneration Our conclusion, recently confirmed ², ¹², was that with the exception of prolactin the pituitary autonomy is at its maximum for the thyreostimulating hormone.

Our histological studies concerned mostly the adrenal glands ^{17, 42}; atrophy is a general findng principally noticeable at the fascicular zone. Nevertheless we observed in several cases figures of acute exhaustion directly related to a lethal stress. That lead us to propose a massive influx of pituitary stimulines. As there is never any nervous fiber regeneration one has to fall back on the humoral or portal transmission. But in two of our cases with such atrophic and exhausted adrenals the absence of any vascular portal reconnexion was very precisely checked. Perhaps then the cortico releasing factor itself is active ^{10, 29}.

ANTERIOR PITUITARY TISSUE STUDIES

The pituitary stalk section and hypophysectomy provided us with an opportunity to study biopsic specimens of normal hypophiseal tissue. We felt that a study of these specimens by electronic microscopy would be the most fruitful approach inasmuch, firstly, biopsic specimens are to date irreplaceable for such studies and, secondly, a purely morphologic description such as provided by the electron microscope appears to be a necessary basis for any further elaboration.

The failure of photomicroscopic histological studies of the human pituitary in trying to provide a coherent histophysiological concept of the anterior lobe is readily explained when one studies the electronic microscopic images with a comparatively low power. The polymorphism of cells is quite bewildering and the overall effect is quite different, for instance, from that seen in the mouse. In that latter form nearly 98 per cent of the cells can be classified into one of the classically recognised cellular types. In the human being the first impression is that there are more histological cell types than could be expected if to one type corresponded one hormone (STH, ACTH, LTH, FSH, LH, TSH, MSH).

Another difficulty is to ascribe any given function to a morphologically identified cell type in the absence of experimental material. Considerations about the physiological state of the pituitary gland at the time of operation (e. g. castration), comparison with secreting human tumors and cautious analogy with other mammals have nevertheless provided some clues. It must be borne in mind that the functional state of any cell type may be recognised only partly.

1) Somatotrophic (STH) cells are the only ones evident at first (Fig. 2). They are the most numerous and display prominent opaque 350 m_{μ} granules and differenciated ergastoplasm. They are quite similar to the STH cells of many mammalian forms and to cells in many acidophilic adenomas in patients with acromegaly ³².



Fig. 2 — Part of a STH cell with numerous granules (\times 24.000 reduced one third).

2) Corticotrophic (ACTH) cells were identified for the first time in the human with the aid of electron microscopy (Fig. 3) because all their cytoplasmic characters are beyond the resolving power of the light microscope³,



Fig. 3 — Part of an ACTH cell poorly granulated. Note contrast with granules of an adjoining STH cell (\times 24,000 reduced one third).

Our description was based mainly on the comparison with an adrenocorticotrophic tumor ⁷. The typical human corticotrophic cell is rather alongated with an oval nucleus. Its secretory granules are the smallest in the human pituitary measuring 90 to 130 m_{μ} ; they are mostly peripheral; the cytoplasm

is remarkably uniform with ribosomes, simples or in rosettes, and vesicles usually rounded and smooth. Cisternal ergastoplasm or Golgi zone are absent. These cytoplamic features are typical enough to characterize the corticotrophs even where they are mostly degranulated as it happens in some instances related to various stresses in the immediate history of the patient. In this way we ascribe corticotrophic function to follicular cells grouped around colloidal material, probably similar to those described in the rat by Farquhar in pionneer studies (Anat. Rec. 127: 291,1957).



Fig. 4 — Part of the cytoplasm of a FSH gonadotroph. Note the prominent Golgi cisterns apparently empty contrasting with the large ergastoplasmic cisterns with flaky material. Ajacent is part of an unidentified cell (LH gonadotroph?) (× 19.000 reduced one third).

3) FSH gonadotrophs were long identified in the human to the β cells of Romeis. Ultrastructural evidence lead us to a different conclusion⁹. Starting from the castration cells which we described with electron microscopy

in man we identified a new type of cells in the human pituitary, analogous to FSH cells described by others authors in various mammals. Such FSH gonadotrophs are large ovoid cells with large secretory granules (500 m μ aproximately). These are regularly rounded and far less dense on the average after osmic fixation than any other. Cisternal endoplasmic reticulum is prominent filled with relatively dense and flaky material; so is the Golgi apparatus with optically empty saccules (Fig. 4).



Fig. 5 — A LTH (prolactin) cell with two large granules and dense mitochondria. Ergastoplasm is visible at the opposite pole of the cell $(\times 7.400 \text{ reduced one third}).$

4) LTH (prolactin) cells are very rare in our material (no pregnant woman was operated upon during our study). A few were found only in the pituitary of a 66 years-old male patient submitted to stalk section for a metastatic hypernephroma. Tentatively, they are identified by a comparison with the prolactin cells cultivated in vitro by Pasteels and with comparable cells in

mammals, in the rat in particular; in some mouses LTH granules are smallest although general cytoplasmic landmarks are similar. Their granules are often very large (700 m_{μ}) but variable inside the same cell in size, shape and density. Lamellar ergastoplasm is often prominent. The mitochondria are rod-shaped; the density of their matrix is striking (Fig. 5).



Fig. 6 — A β (MSH^f) cell. A lipoid inclusion partially disolved by embedding is visible in the middle (× 24,000 reduced one third).

5) β (MSH?) cells. The identification of FSH cells (see above) is an indirect corroborative evidence for the attribution of secretion of MSH (intermedin) to the β cells of Romeis²⁸ β cells are readily seen in electron micrographies. They are often polygonal containing many granules and large inclusions probably lipoidic in nature which correspond to those stained with PAS. The granules are dense, rather diverse in size but usually between 160 and 200 m μ . The remainder of the cytoplasmic characters are remarkably similar to those of ACTH cells, with numerous vesicles and clusters of ribosomes; this similarity is perhaps related to the similarity of the hormones produced (Fig. 6).

SUMMARY

Our first hypophysectomy in a metastatic carcinoma of the breast was performed in November 1951 and the section of the pituitary stalk (mischotomy) for the same purpose was started in November 1955, the first results being published in 1956. When one succeeds in preventing the hypothalamohypophyseal vascular regeneration the general results of mischotomy are little different from those obtained with hypophysectomy. We adopt mischotomy when total pituitary removal seems to be a too great surgical risk.

Anatomo-physiological studies are being published since 1958, showing: (a) The variations of the anterior lobe necrosis which is neither total nor definite (pituitary regeneration) and the importance of the trabecular arteries in that respect; (b) The striking ability of vascular regeneration from the hypothalamus to the anterior lobe remnants thus creating a new anatomical and functional portal system; (c) After permanent pituitary isolation, the proliferation of prolactin (orangeophile) cells and the compensatory hypertrophy of pars tuberalis.

Removal of normal pituitary tissue obtained during the operation allowed us to describe for the first time in man the ACTH cells (1964) and the FSH cells (1966).

RESUMO

Comentários neurocirúrgicos e fisiológicos sôbre a secção da haste pituitária em seres humanos (miscotomia)

Nossa primeira hipofisectomia para tratamento de carcinoma metastático do seio foi feita em novembro de 1951 e a secção da haste pituitária (miscotomia) para o mesmo fim foi iniciada em novembro de 1956. Quando se consegue impedir a regeneração vascular hipotálamo-hipofisária os resultados gerais da miscotomia são pouco diferentes daqueles obtidos com a hipofisectomia. Empregamos a miscotomia sempre que, por condições locais ou gerais, a remoção total da hipófise parece constituir grande risco cirúrgico. Temos publicado estudos anatomo-fisiológicos desde 1958 mostrando: (a) as variações da necrose do lobo anterior da hipófise que não são totais nem definitivas (regeneração pituitária) e a importância das artérias trabeculares a êste respeito; b) a grande capacidade de regeneração vascular a partir do hipotálamo e dirigindo-se para a parte restante do lobo anterior da hipófise, o que constitui um nôvo sistema anatomo-funcional portal; c) após isolamento permanente da pituitária ocorre proliferação das células de prolactina (células orangeófilas) e hipertrofia compensadora da pars tuberalis.

A remoção cirúrgica de tecido hipofisário normal nos permitiu descrever, pela primeira vez no ser humano, as células ACTH (1964) e as células FSH (1966).

REFERENCES

- ADAMS, J. H.; DANIEL, P. M. & PRICHARD, M. M. L. Transection of the pituitary stalk in man: anatomical changes in the pituitary glands of 21 patients J. Neurol. Neurosurg. a. Psychiat. 29:545, 1966.
- ASSENMACHER, I. & TIXIER-VIDAL, A. Répercussion de la section des veines portes hypophysaires sur la préhypophyse du canard pékin mâle entier ou castré. Arch. Anat. Microsc. et Morphol. Exper. 53:83, 1964.
- DE VOE, W. F.; RAMIREZ, Z. E. & McKANN, S. M. Production of mammary secretion by hypothalamic lesion in male rats. Endocrinology 78:158, 1966.
- DUGGER, G. S.; VAN WYK, J. J. & NEWSOME, J. F. The effect of pituitary stalk section in thyroid function and gonadotrophic-hormone excretion in women with mammary carcinoma. J. Neurosurg. 19:589, 1962.
- EHNI, G. & ECKLES, N. E. Interruption of the pituitary stalk in the patient with mammary cancer. J. Neurosurg. 16:628, 1959.
- EVERETT, J. W. & KUINN, D. L. Differential hypothalamic mechanism inciting ovulation and pseudopregnancy in the rat. Endocrinology 78:141, 1966.
- FONCIN, J. F. & LE BEAU, J. Étude en microscopie optique et électronique d'un tumeur hypophysaire à fonction adrenocorticotrope. C. R. Soc. Biol. 157:249, 1963.
- FONCIN, J. F. & LE BEAU, J. Identification au microscope électronique des cellules adrénoorticotropes de l'hypophyse humaine. C. R. Soc. Biol. 158: 2276, 1966.
- FONCIN, J. F. & LE BEAU, J. Cellules de castration et cellules FSH dans l'hypophyse humaine vues au microscope électronique. J. Microscopie 5:523, 1966.
- GIROUD, C. J. P.; STACHENKO, I. & VENNING, E. H. Secretion of aldosterone by zona glomerulosa of rat adrenal glands incubated in vitro. Proc. Soc. Exper. Biol. Med. 92:855, 1956.
- 11. HARRIS, G. W. Neural Control of the Pituitary Gland. Edward Arnold, London, 1955.

- 12. HERLANT, M.; LINQUETTE, N.; LAINE, E.; FOSSATI, P.; MAY, J. P. & LEFEBURE, I. Adénome hypophysaire à cellules thyréotropes avec syndrome aménorrhée-galactorrhée chez une malade porteuse d'un myxoedème congénital par ectopie thyroidiènne. Endocrinology 27:57, 1966.
- 13. KORDON, C. Recherches sur le controle hypothalamique des fonctions gonadotropes femelles du rat. Thèse Sciences, Paris, 1966.
- 14. KORDON, C. -- Controle nerveux du cycle ovarien. Arch. Anat. Microscop. et Morph. Exper. 1967 (sous presse).
- LACOUR, F. Recherches sur la relation entre les cellules hypophysaires à granulations orangées (cellules epsilon de Romeis) et les phénomènes de lactation. C. R. Soc. Biol. Paris 144:248, 1950.
- LE BEAU, J. & FONCIN, J. F. Anatomical study of anterior pituitary remnants after stalk section and hypophysectomy. Acta Psychiat. et Neurol. Scandinavica 35:13, 1960.
- LE BEAU, J.; NICOLAIDIS, S. & FONCIN, J. F. Étude anatomique et biologique de 16 cas de mischotomie pour cancers hormonodépendents. Acta Endocrinol. 4ème Série: 227, 1963.
- LE BEAU, J.; PERRAULT, M. & TESTARD, E. A propos de l'hypophysectomie dans le traitement du cancer du sein. Bull. et Mém. des Hôp. de Paris 21, 22, 23:663, 1956.
- LE BEAU, J. Laboratory findings and clinical results of pituitary stalk section in the treatment of breast cancer. J. Neurol. Neurosurg. a. Psychiat. 23:81, 1960.
- LE BEAU, J. L'Hypophysectomie dans le Traitement du Cancer. Editions Doin, Paris, 1958.
- 21. LE BEAU, J. La section de la tige de l'hypophyse en particulier dans le traitement du cancer du sein. Neurochirurgie 6:128, 1960.
- LUFT, R. & OLIVECRONA, H. Experiences with hypophysectomy in man. J. Neurosurg. 10:301, 1953.
- MEITES, J. Control of prolactin secretion. Arch. Anat. Microse. et Morphol. Exper. 1967 (sous presse).
- NICOLAIDIS, S. Section de la Tige Pituitaire chez l'Homme. Étude anatomique et biologique. Thèse Médicine, Paris. Le Tendre, Caen, 1962.
- 25. PERRAULT, M.; LE BEAU, J.; KLOTZ, B.; SICARD, J. & CLAVEL, B. L'hypophysectomie totale dans le traitement du cancer du sein. Premier cas français. Avenir de la méthode. Thérapie 7:290, 1952.
- PASTEELS, J. L. Siège cellulaire de la secretion de prolactine par l'hypophyse humaine. IIe Réunion Europ. Anat., Bruxelles. Excerpta Medica, 70, 40:141, 1963.
- PASTEELS, J. L. Recherches morphologiques et expérimentales sur la sécrétion de prolactine. Arch. Biol. (Liège) 74:439, 1963.
- PURVES, H. D. & BASSET, E. G. The staining reactions of pars intermedia cells and their differenciation from pars anterior cells. *In* Cytologie de l'Adénohypophyse. C. N. R. S. Paris 1963, pág. 231.

- 29. RAUSKOLB, E. W. & FARREL, G. L. Evidence for diencephalic regulation of aidosterone secretion. Endocrinology 59:526, 1956.
- RAY, B. & PEARSON, O. Hypophysectomy in the treatment of an advanced cancer of the breast. Ann. Surgery 144:394, 1956.
- ROMEIS, B. Hypophyse. Hdb. Mikr. Anat. des Menschen (v. Müllendorf) II Teil, Springer Verlag, Berlin, 1940.
- SCHELIN, U. Chromophobe and acidophil adenomas of the human pituitary gland. A light and electron microscopic study. Acta Path. Microbiol. Scandinavica, Suppl. 158, 1962.
- 33. STUTINSKI, F. A quelles structures hypothalamiques peut-on attribuer l'origine des "releasing factors"? Rev. Europ. Endocrinol. 4, 1967 (sous presse).
- 34. XUEREB, G. P.; PRICHARD, M. M. L. & DANIEL, P. M. The hypophyseal portal system of vessels in man. Quart. J. Exp. Physiol. 39:199-217 and 219-230, 1954.
- Service de Neuro-chirurgie Hôpital de la Salpêtrière 47, Boulevard de l'Hôpital — Paris 13e, France.