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Key personalities in the development and popularization of the transsphenoidal approach to pituitary tumors: an historical overview

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Like many other technologic or scientific advances, the events that led to the development and widespread acceptance of the transsphenoidal approach to lesions of the sellar region are the result of an evolutionary rather than a revolutionary process. The perfection of the transsphenoidal approach as we know it today has been the result of many contributions from different pioneers. Yet, it is unequivocally accepted that a few key personalities played a critical role in the development and preservation of the technique and in its eventual popularization. These individuals share some of the characteristics typical of our neurosurgical heritage, namely, vision, courage, and incredible perseverance even in the face of apparently insurmountable obstacles.

Surgical approaches to the pituitary gland developed in parallel with technologic advances and increased understanding of its physiology and pathology. Serious interest in possible ways to approach the sellar region was triggered by a better understanding of the syndromes associated with mass lesions and their relation to tumors of the pituitary gland. Additionally, the introduction of the X-ray by Roentgen allowed for confirmation of clinical suspicion by demonstrating enlargement of the sella in many cases. It was in parallel with these advances that pioneer surgeons tried to develop avenues to reach the sella at the turn of the last century. Given the significant morbidity and mortality associated at that time with craniotomy, several of these visionaries concentrated on an approach through the paranasal sinuses. Most of these attempts, however, were associated with mutilating and cosmetically unacceptable scars. It was not until 1910 that Oskar Hirsch and Harvey Cushing, by putting together advances and technical minutiae introduced by other authors, eventually described and popularized the two major techniques (transnasal and sublabial) to approach the pituitary gland through the transsphenoidal approach.

Oskar Hirsch

The lateral endonasal approach to the pituitary gland that is used today was originally described by Oskar Hirsch while he was working in Vienna as a rhinologist. Early in his career, Hirsch developed an interest in the anatomy and pathology of the paranasal sinuses. Over time, he accumulated an impressive collection of pathologic specimens that formed the basis for a series of annual teaching seminars on this topic [1]. Hirsch originally described an endonasal approach to the sellar region based on the approach to the sphenoid sinus used by his teacher, Hajek, for the treatment of sphenoid sinusitis [2]. In 1909, Hirsch demonstrated his approach on a cadaver at a meeting of the *Gesellschaft der Aerzte* in Vienna [3]. The medical community was skeptical at first. Hajek himself considered it too dangerous and difficult [4]. In a subsequent dissection, to verify the safety of his approach, Hirsch asked an anatomopathologist to dissect the skull after he had performed a

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transnasal-transseptal approach in a cadaver specimen. The pathologist indeed verified that, as hoped, Hirsch had made "a large opening in the floor of the sella turcica without having injured any of the important neighboring organs (optic nerve, cavernous sinus, etc.)" [2].

In 1910, an encounter with a patient with a pituitary lesion and visual failure prompted Hirsch to perform his first endonasal approach to the pituitary in a living individual [2]. Surgical excision of the tumor was carried out in the following five stages: (1) removal of the middle turbinate, (2) removal of the ethmoid cells, (3) removal of the anterior wall of the sphenoid sinus, (4) removal of the floor of the sella, and (5) removal of the lesion. These different stages spanned a period of 5 weeks and were performed under local anesthesia. In describing the fourth stage, Hirsch stated, "After cocainizing the nose and the sphenoidal sinus with a 20 per cent cocain solution I placed on the hypophysial prominence a small chisel and by careful hammering made a transverse fissure in the bony envelope of the hypophysis tumor" [2]. After completion of the final stage, Hirsch observed that the patient was "so slightly disturbed by the operation that she was able to walk with a nurse from the operating room to her ward" [2]. Her vision subsequently improved [2].

Unhappy with the long interval necessary for a multistage procedure, Hirsch observed, "As it may be possible that the progressive symptoms of a case, especially the optic atrophy, will not allow so long a period of treatment, I searched for a method in which the operation of hypophysis tumor could be performed at one sitting" [2]. Influenced by Kocher's and Killian's methods of submucosal dissection of the septum, Hirsch eventually devised the procedure that is essentially the same used today, 90 years later. On June 4, 1910, he performed a transnasal approach with submucous resection of the septum [5]. The mucosal flaps were retracted laterally, and exposure was maintained with the use of an instrument well known to a rhinologist—a nasal speculum (Fig. 1). By coincidence, on that same day across the Atlantic, Harvey Cushing performed the first case in which he used a sublabial incision and submucosal resection of the septum [5]. After these pioneering attempts, Hirsch corresponded with Cushing about this latter experience with pituitary tumors (Fig. 2). Hirsch demonstrated his procedure for Cushing in Vienna in 1911 [1].

Hirsch's operation was designed to debulk the tumor and decompress the optic apparatus. No attempts were made at radical resection. Trying to obtain long-lasting tumor control, Hirsch soon started using local radiotherapy by means of a rudimentary apparatus attached to the teeth (Fig. 3) [6]. "By providing, at the end of the operation, a permanent access to the tumor remnants, I was able to make this radium application an office procedure" [7]. It took Hirsch almost 10 years between 1911 and 1921 to find the effective dose [7].

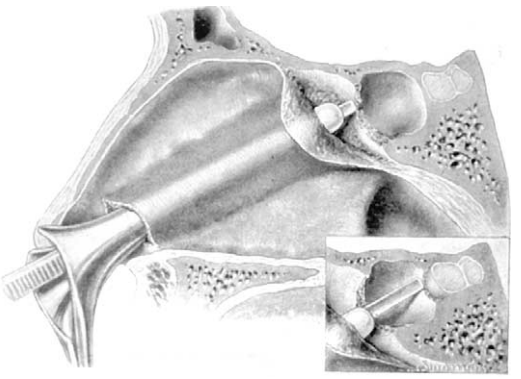


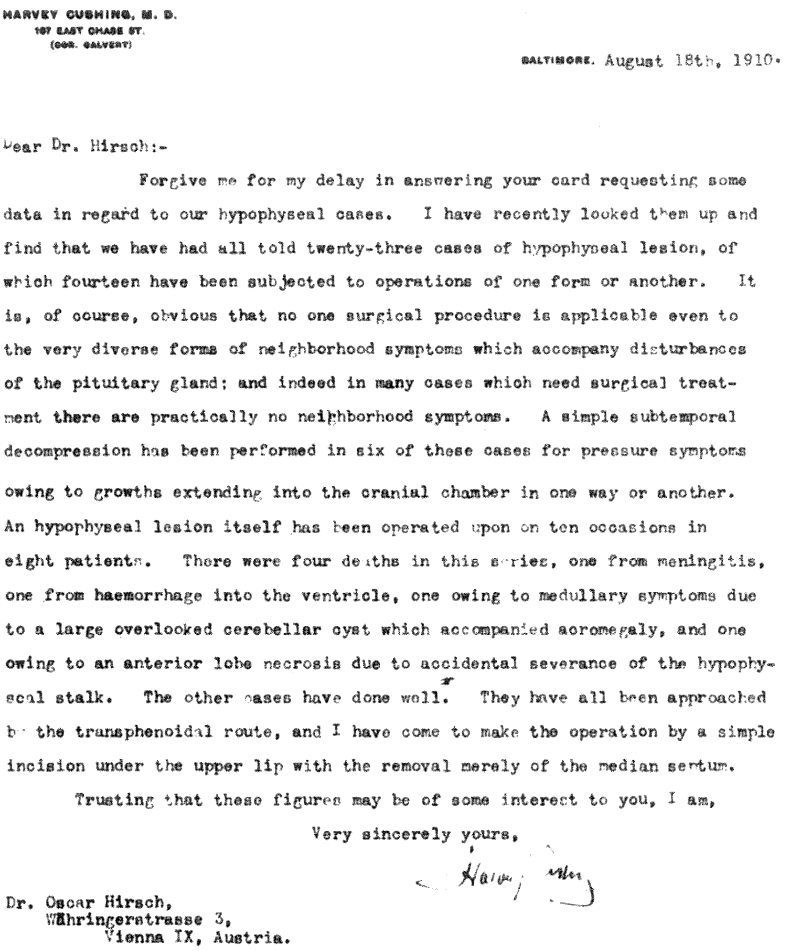
Fig. 1. Hirsch's endonasal, submucosal, transseptal approach to the sella turcica. A speculum is used to retract laterally the mucosal flaps and to maintain exposure.

In 1957, Hirsch summarized his career's results with 413 patients operated on through the transsphenoidal route [8]. In patients operated on before the availability of antibiotics (1919–1937), there was a mortality of 5.4% In those patients operated on after the "antibiotic era," there was a mortality of 1.4%. Long-lasting improvement was observed in 68% of patients who were followed 5 to 19 years after surgery. In his report, Hirsch stressed the importance of postoperative local irradiation in ensuring long-lasting benefits [8].

Because of the political turmoil in Europe in the late 1930s, Hirsch had to leave Vienna and moved to Boston. There, he continued to perform "his" operation in conjunction with a neurosurgeon, Hannibal Hamlin, (Fig. 4) at a time when everybody else in the United States, following Harvey Cushing's example, had abandoned the transsphenoidal approach in favor of the transcranial one. In doing so, he remained an "obscure voice in the wilderness" [9].

Harvey Cushing

Contemporary to Oskar Hirsch, Harvey Cushing developed the sublabial transsphenoidal approach. As Cushing recognized, "The performance itself has been much simplified since the ori-



HARVEY CUSHING, M. D.
107 EAST CHASE ST.
(COR. CALVERT)

BALTIMORE, August 18th, 1910.

Dear Dr. Hirsch:-

Forgive me for my delay in answering your card requesting some data in regard to our hypophyseal cases. I have recently looked them up and find that we have had all told twenty-three cases of hypophyseal lesion, of which fourteen have been subjected to operations of one form or another. It is, of course, obvious that no one surgical procedure is applicable even to the very diverse forms of neighborhood symptoms which accompany disturbances of the pituitary gland; and indeed in many cases which need surgical treatment there are practically no neighborhood symptoms. A simple subtemporal decompression has been performed in six of these cases for pressure symptoms owing to growths extending into the cranial chamber in one way or another. An hypophyseal lesion itself has been operated upon on ten occasions in eight patients. There were four deaths in this series, one from meningitis, one from haemorrhage into the ventricle, one owing to medullary symptoms due to a large overlooked cerebellar cyst which accompanied acromegaly, and one owing to an anterior lobe necrosis due to accidental severance of the hypophyseal stalk. The other cases have done well. They have all been approached by the transphenoidal route, and I have come to make the operation by a simple incision under the upper lip with the removal merely of the median sertum.

Trusting that these figures may be of some interest to you, I am,

Very sincerely yours,

Dr. Oscar Hirsch,
Währingerstrasse 3,
Vienna IX, Austria.

Fig. 2. Letter from Harvey Cushing to Oskar Hirsch dated August 18, 1910 (*from* Zervas NT, editor. Neurosurgery at the Massachusetts General Hospital, 1909–1983. A short history and alumni record. Boston: Massachusetts General Hospital; 1984; with permission.)

ginal transsphenoidal operation which Schloffler boldly originated. The procedure which I have come to employ is merely a composite of such modifications of the Schloffler operation, suggested by Kanavel, Halstead, Hirsch, and others, as are adapted to my own requirements. It therefore makes no claim for originality" [10]. He continued, explaining, "The operation combines all the advantages of the endonasal procedure of Hirsch, and for one who does not possess the practiced hand of the rhinologist it has the further advantage of affording almost double room that an operation through one nostril permits" [10]. The critical steps of Cushing's sublabial approach are shown in Figs. 5–8 through Max Brödel's original illustrations. As Cushing himself recognized, "Few words in description of the operation are needed to supplement Mr. Max Brödel's drawing which are reproduced, for, as is true of all his superb medical illustrations, they serve to make the context superfluous" [10].

In his early experience, Cushing definitively preferred the transsphenoidal route to the intracranial one: "It is fair to say that this experience while discouraging is slight, and I shall further pursue this matter as favorable circumstances arise, but certainly the cases for which a frontal operation is indicated cannot compare, either in number or on the ground of risk or of promised improvement, with those to be discussed under the following heading in which a transsphenoidal operation is suitable" [10]. Over time, however, he found himself performing more transcranial procedures. In 1921, he wrote [11]:

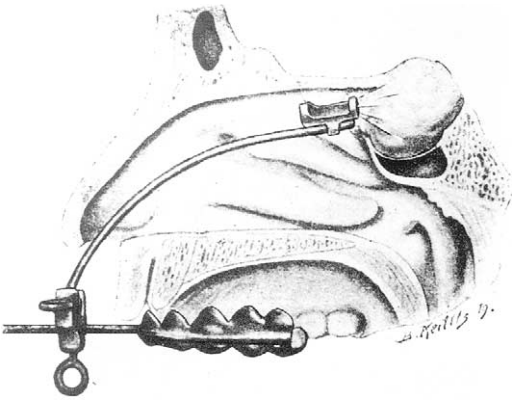


Fig. 3. Hirsch's method of delivering local postoperative radiation therapy. The device was secured to the superior teeth by an applicator and left in situ for a short period of time. (*From* Hirsch O. Ueber Radiumbehandlung der Hypophysentumoren. Arch Laryngol Rhinol 1921;34:135–43; with permission.)

> Surgeons have assailed it (the pituitary) from below through the nasal cavities, and from above through the skull elevating the frontal lobe either from in front or the side. It is certain that no method is applicable for all conditions of pituitary tumor and that for some no satisfactory procedure has been devised. Speaking for myself, I find that I am conducting proportionately fewer rather than more transsphenoidal operations, though in favorable cases with a large ballooned sella I believe the latter to be the simplest and easiest method, the one most free from risk and most certain to lead to a rapid restoration of vision. However, in increasing numbers, both in children and adults, suprasellar tumors giving secondary hyperphysical symptoms are being recognized, and if the sella is not enlarged an approach from above is necessitated.

Later, he completely abandoned the transsphenoidal approach in favor of the transcranial one, and from 1929 to 1932, he performed pituitary surgery only by the transfrontal route [12]. Cushing's rejection of the transsphenoidal approach was dramatized by the fact that his highly publicized two thousandth operation for a brain tumor was a transfrontal removal of an acidophilous adenoma [12]. The reasons behind this rejection are not entirely known. Most likely, several factors played an important role, including the improved

Fig. 4. Residents and faculty, Neurosurgery Department, Massachusetts General Hospital, 1958. Back row (*left to right*): Drs David Kline, Tony Monaco, John Mealey, Richard Rovit, Dagoberto Sosa, and Daniel Joly. Front row (*left to right*): Drs Louis Bakay, William Sweet, James White II, Thomas Ballantine, Jr., Merril C. Sosman, Oskar Hirsch, and Hannibal Hamlin. (*From* Zervas NT, editor. Neurosurgery at the Massachusetts General Hospital, 1909–1983. A short history and alumni record. Boston: Massachusetts General Hospital; 1984; with permission.)

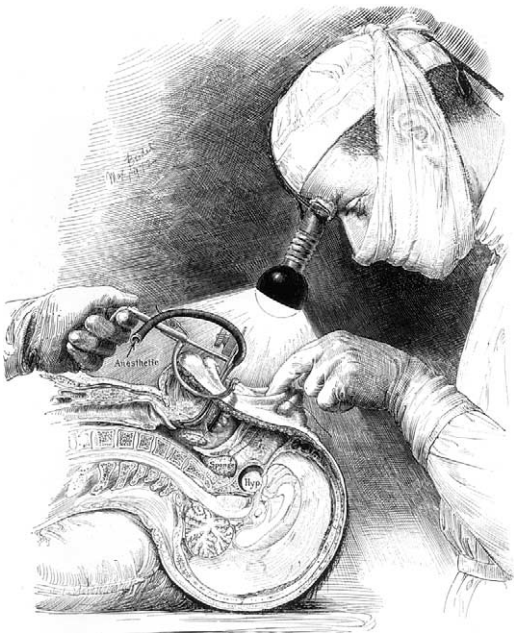


Fig. 5. Cushing's sublabial approach. Note the position of the patient relative to the surgeon. A tongue elevator is in place, and a sponge is in the retropharynx to prevent aspiration. The lip is being elevated in preparation for the sublabial incision. (*From* Cushing H. Disorders of the pituitary gland. Retrospective and prophetic. JAMA 1921;76:1721–6; with permission.)

safety of transcranial operations, the perceived notion that visual recovery was slightly better with the transcranial operation, and the fact that diagnostic "surprises" (ie, nonadenomatous tumors of the sellar region, such as craniopharyngiomas, meningiomas, and chordomas) were more easily dealt with from "above." Because Cushing influenced neurosurgery worldwide, his shift from the transsphenoidal approach to the transcranial route was to influence the destiny of pituitary surgery for many years to come. As a result, most surgeons embraced the transcranial operation, and the transsphenoidal approach was completely abandoned, except for a few exceptions.

Norman Dott

The lineage that kept the transsphenoidal procedure "alive" passed through Edinburgh, Scotland, and was the work of Norman Dott. Norman Dott was selected as a Rockefeller fellow to spend several fruitful months on Cushing's service at the Peter Bent Brigham Hospital (Fig. 9) [13]. A bold neurosurgeon (credited with having been the first one to plan a surgical attack on a ruptured aneurysm, which he wrapped in a nursing home) [14], Dott appreciated the merits of the transsphenoidal procedure during his stay in Boston from November 1923 to June 1924. Once back in Edinburgh, he continued to operate on pituitary tumors through the transsphenoidal route at a time when most other surgeons had followed Cushing's example and had abandoned it. Dott was also an experienced pediatric surgeon with expertise in the correction of complex facial defects, such as cleft palate. One wonders how much this expertise contributed to his level of comfort while working in a deep and dark field like the one afforded by the transsphenoidal route [15]. Over the years, Dott designed instruments specifically for the transsphenoidal procedure. Particularly successful was a speculum with lights attached to it. The difficulties encountered at that time in performing a transsphenoidal operation can be appreciated by reading this recount of Dott's operation [14]:

> Now watch Dott carrying out a typical pituitary operation. The patient, lying supine, is covered overall by surgical drapes; only the nose and the mouth are exposed. Dott leans over this area with a headlight on and every now and then adjusts the position of the long malleable light, held by the assistant. Anxiety lies in the narrowly exposed eye of his assistant who is responsible for maintaining the correct position of this light but can only fleetingly see the deep operation site as he peers first one way then another around Dott's neck and hands. Sister too looks anxious, especially when she sees the light start to flicker and go out, which test it as you may before the operation, seems unfailingly to occur at least once during the crucial period.
> How Dott would have appreciated the convenience of transaxial illumination of the operating microscope which was denied to him by a matter of years. Sister can see even less of the operating field than the assistant and the confident way she slaps the instruments into Dott's outstretched hand comes only from years of experience and the ability to deduce the stage of the operation from sound and hand movements. She too, in company with the small group of hopeful postgraduate students, hovering behind the assistant, seeing little but hanging eagerly on any word or gesture, would have appreciated the modern microscope, with its television facility; all would have been shown

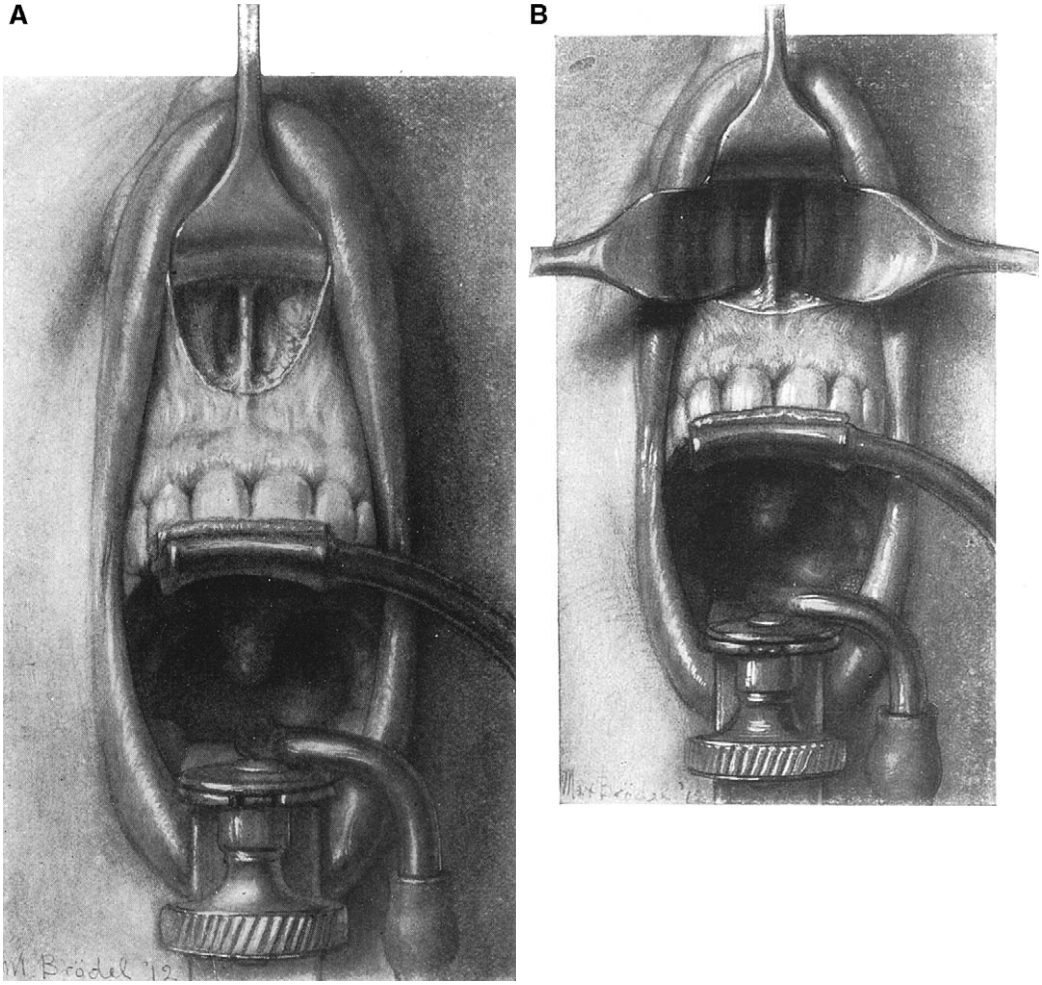


Fig. 6. Cushing's sublabial approach. (*A*) Exposure by blunt dissection of the lower edge of the cartilaginous septum. (*B*) Lateral retractors are introduced between the reflected mucous membrane and the denuded septum before removal of the septum is carried out. (*From* Cushing H. Disorders of the pituitary gland. Retrospective and prophetic. JAMA 1921;76:1721–6; with permission.)

> so clearly, on a nearby screen. So approximately ninety minutes pass to the noise of the sucker, or of instruments against bone, the silence of soft tissue, the occasional, sometimes testy, interjection. Then Dott packs the nose and strips off his gloves. His assistants have been privileged by an occasional fleeting glance of the vital areas.

Dott's results with the transsphenoidal procedure were eloquently illustrated by the personal story of one of his patients. Grace Allison was operated on by Dott during her childhood for a sellar lesion causing visual disturbances. She grew up to become a professional photographer and produced the best available photographic portraits of Dott (Fig. 10) [14].

Gerard Guiot

Gerard Guiot, a pupil of the legendary French neurosurgeon Clovis Vincent, was the Chief of the Hôpital Foch in Paris [16,17]. A pioneer in stereotactic and functional neurosurgery, he was also the first one to use cardiocirculatory arrest during a neurosurgery procedure for the resection of a complex intracranial arteriovenous malformation [17].

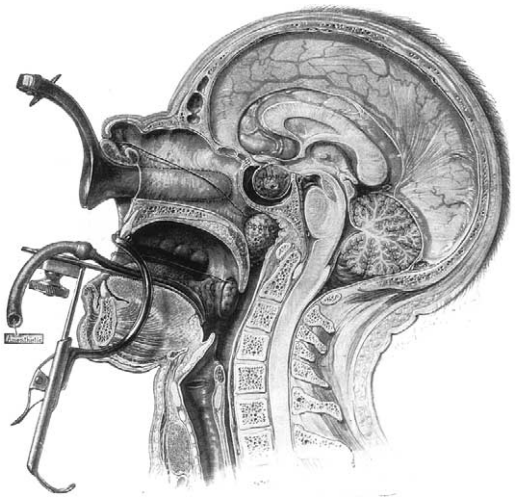


Fig. 7. Cushing's sublabial approach. Sagittal reconstruction after substitution of the two lateral retractors with a self-retaining bivalve speculum through which further steps are conducted. (*From* Cushing H. Disorders of the pituitary gland. Retrospective and prophetic. JAMA 1921;76:1721–6; with permission.)

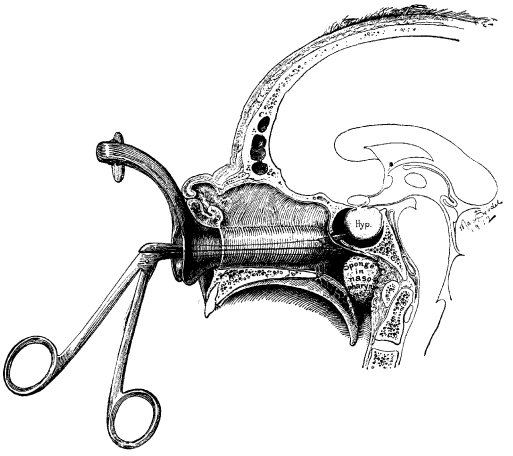


Fig. 8. Cushing's sublabial approach. Removal of the anterior wall of the sphenoid sinus with a rongeur. (*From* Cushing H. Disorders of the pituitary gland. Retrospective and prophetic. JAMA 1921;76:1721–6; with permission.)

Fig. 9. Photograph showing Cushing's team during Dott's stay in Boston. Dott is standing in the back row (last person on the right). Cushing is seated in the center of the front row. (*From* Rush C, Shaw JF. With sharp compassion. Norman Dott: Freeman Surgeon of Edinburgh. Aberdeen: Aberdeen University Press; 1990;130: with permission.)

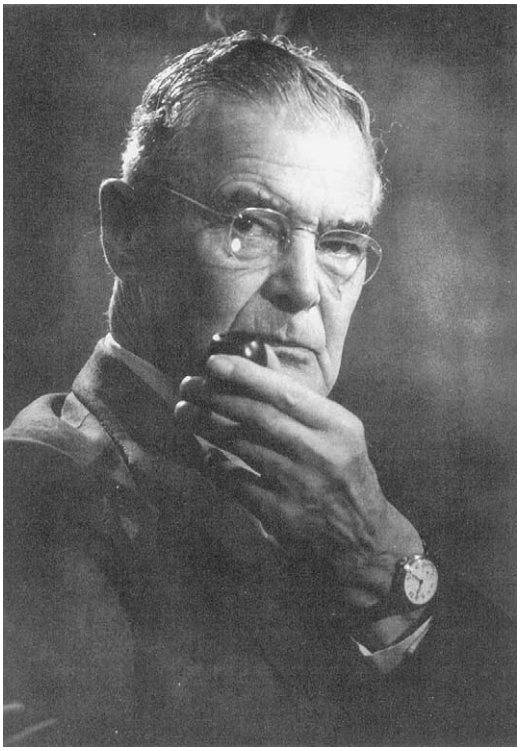


Fig. 10. Photographic portrait of Norman Dott by Grace Allison, a former patient who had been treated for a pituitary tumor as a child by Dott. (*From* Rush C, Shaw JF. With sharp compassion. Norman Dott: Freeman Surgeon of Edinburgh. Aberdeen: Aberdeen University Press; 1990;273; with permission.)

Guiot visited Norman Dott in 1956 and had the chance of observing the transsphenoidal operation. He later recalled, ''During those two weeks I saw Pr. Dott operating two pituitary tumors by transsphenoidal route. And I remember Pr. Dott telling me the day after: 'look at the postoperative campimetry! The patient is already improved'…He showed me his statistics: no mortality for the last 80 cases…I was convinced. Back to Paris I had to try the Dott instruments and I began to operate the year after… But N. Dott never published his results! I think it was by respect for the memory of his master, H. Cushing who had abandoned this route'' [12].

Guiot introduced intraoperative radiologic control during transsphenoidal surgery. He recalled: ''…I thought it was possible to have radioscopic control during the operation. So I changed the position of the patient (Pr. Dott was operating with the head of the patient between his knees—patient in 'decubitus dorsal') and I began to have the patient in the 'semi sitting position'…'' [12]. The introduction of intraoperative radiologic control was a progressive one. At the beginning, intraoperative fluoroscopy with a screen was not available. Instead, a huge complicated X-ray apparatus hung from the operating room ceiling. One of the assistants would look directly into the apparatus with binoculars and guide the instruments of the operator during the approach and the opening of the sellar floor. The eventual adjunct of the image intensifier was much appreciated by Guiot and his team (P. Derome, personal communication, 2001).

In 1958, Guiot presented his first few cases of pituitary adenoma operated on transsphenoidally in front of the French Society of Neurosurgery. This report was received rather coldly (P. Derome, personal communication, 2001). Despite this initial skepticism, Guiot and his group persevered. Eventually, the ''Foch group'' went on to perform approximately 5500 transsphenoidal surgeries from the introduction of the technique by Guiot in the 1950s until Patrick Derome retired in 1999 (P. Derome, personal communication, 2001). Professor Derome was Guiot's successor as Chairman of the department in 1982.

Jules Hardy

The comeback and eventual reaffirmation of the transsphenoidal procedure in North America was closely related to the work and vision of Jules Hardy. Dr. Hardy's interest in transsphenoidal surgery was serendipitous. After graduating from the University of Montreal, he spent a year studying basic neurophysiology under Herbert Jasper at the Montreal Neurological Institute [18]. As a fellow of the McLaughlin Foundation, he spent 1 year at the Hôpital Foch in Paris with Professor Guiot and was interested in his pioneering work in stereotactic and functional neurosurgery (Fig. 11). During the same period in Paris, Dr. Hardy was involved in the first cases of microelectrode recording from the human thalamus. This was completed by Guiot in collaboration with Professor Denise Abel-Fessard during stereotactic surgery for Parkinson's disease.

During his stay in France, Hardy was impressed by Guiot's transsphenoidal procedure for pituitary tumors and by the rapidity of visual improvement after successful operations. After returning to Montreal, where he was in charge of

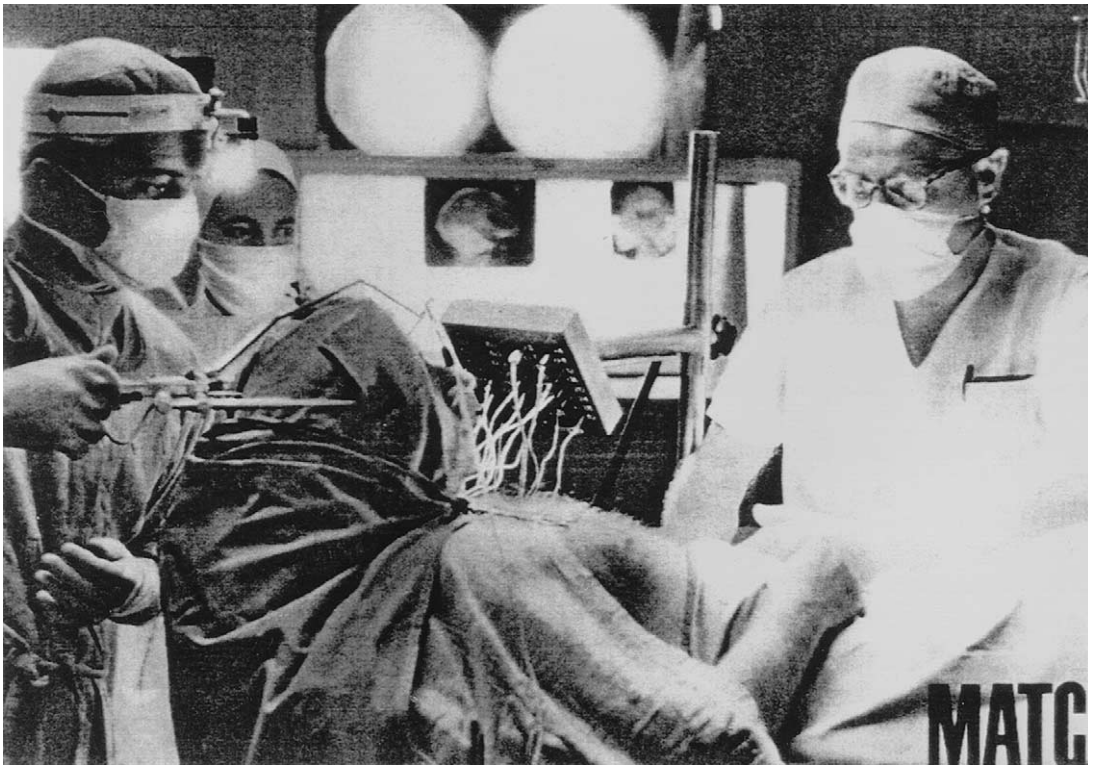


Fig. 11. Jules Hardy (*left*) performing a functional procedure under the close scrutiny of Gerard Guiot (*right*) during his stay in Paris. (*Courtesy of* Jules Hardy, MD.)

the neurosurgical patients at Notre-Dame Hospital, he introduced transsphenoidal surgery. In the same period, metastatic breast cancer was being treated with oophorectomy and hypophysectomy, a task much more demanding than simple debulking of a pituitary tumor. At that time, hypophysectomies were routinely done through a craniotomy. Hardy decided to try the transsphenoidal route. To be able to perform hypophysectomies in a dark, deep, and narrow field, he introduced the surgical microscope. The microscope allowed for proper illumination and magnification in the narrow field provided by the transsphenoidal procedure [19]. It proved to be an invaluable tool, critical to the eventual widespread acceptance of the transsphenoidal approach. Because Hardy was performing both tumor resections and hypophysectomies, he became aware of the possibility of identifying the normal pituitary gland within the abnormal tumor tissue. He later introduced the concept of microadenoma and demonstrated surgical cure to be possible in the case of small hyperfunctioning adenomas.

Like Hirsch's presentation in Vienna more than 50 years earlier, Hardy's innovations were encountered with skepticism. Hardy presented his preliminary results at the first meeting of the Montreal Neurosurgical Society. On this occasion, Bronson Ray from New York (who had mastered the transcranial approach to the pituitary gland) said, "We

Fig. 12. Gerard Guiot (*left*) with his pupil and friend, Jules Hardy (*right*), on the occasion of the celebration of the twenty-fifth anniversary of the introduction of transsphenoidal surgery in Montreal. (*Courtesy of* Jules Hardy, MD.)

should discourage any effort to revive this old ancient method of trans-sphenoid surgery which was abandoned by Cushing in 1929'' (B.A. Adaba, unpublished observation, 2000). Like his predecessors, Hardy persisted in the face of initial difficulties and skepticism. The rest is recent history, and the transsphenoidal procedure has become universally accepted in the treatment of pituitary lesions. Hardy celebrated the twenty-fifth anniversary of the introduction of the transsphenoidal procedure in Montreal in 1987. This occasion was also attended by his mentor and friend, Gerard Guiot (Fig. 12).

Summary

Although the transsphenoidal procedure, as we know it today, was devised at the beginning of the last century, its acceptance and eventual widespread affirmation have been a slow but relentless process. Like many technologic and scientific advances, several individuals contributed to the perfection of an idea whose time had come. Yet, it is unequivocally accepted that a few key figures played a critical role in the development, preservation, and eventual widespread popularization of transsphenoidal surgery. These pioneers were original thinkers and bold (albeit careful) surgeons. Their persistence in the face of incredible obstacles provides a source of continuous inspiration.

Acknowledgments

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