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Historical vignette

The evolution of Harvey Cushing's surgical approach to pituitary tumors from transsphenoidal to transfrontal

AARON A. COHEN-GADOL, M.D., EDWARD R. LAWS, M.D., DENNIS D. SPENCER, M.D., AND ANTONIO A. F. DE SALLES, M.D., PH.D.

Department of Neurologic Surgery, Mayo Clinic and Mayo Foundation, Rochester, Minnesota; Department of Neurological Surgery, University of Virginia Health System, Charlottesville, Virginia; Department of Neurosurgery, Yale University School of Medicine, New Haven, Connecticut; and Division of Neurosurgery, University of California at Los Angeles, California

The evolution of transsphenoidal surgery represents a special chapter in the progress of neurosurgery. Although Cushing initially advocated a transsphenoidal approach to pituitary tumors, he became disenchanted with this approach, ultimately favoring the subfrontal or "transfrontal" route late in his career. Other neurosurgeons followed Cushing's example, and the fate of transsphenoidal surgery entered a dark era in 1929. A review of Cushing's patients' records reveals that his abandonment of the transsphenoidal route was primarily related to the limitations of this approach in providing effective resection of large pituitary lesions—the symptomatic tumor recurrence rate after this procedure was substantial. Furthermore, given the preoperative uncertainty about the suprasellar extension of pituitary tumors prior to modern neuroimaging, the transfrontal route assured Cushing an adequate decompression of the optic chiasm. By 1927, Cushing's mastery of intracranial surgery was accompanied by the use of electrosurgical methods that enabled him to remove sellar lesions through the transfrontal route safely and with timely and effective restoration of visual loss. Transsphenoidal surgery remained relatively dormant, awaiting the efforts and enthusiasm of Norman Dott who bridged the gap between Cushing and Gerard Guiot, the surgeon who revitalized transsphenoidal adenomectomy for future generations of pituitary surgeons.

KEY WORDS • Harvey W. Cushing • transsphenoidal surgery • pituitary tumor • history of neurosurgery

We have become confronted of late years with new surgical problems relating to a group of patients with disorders which were unrecognized by our forebears, and hesitating as our steps may be in meeting these problems our operative experiences must from time to time be recorded in all their lights and shadows.

HARVEY W. CUSHING,[9] 1914

Surgeons have assailed it from below through the nasal cavities, and from above through the skull by 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 transphenoidal [sic] 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 hypophyseal symptoms are being recognized, and if the sella is not enlarged an approach from above is necessitated.[4]

DR. HARVEY W. CUSHING,[4] 1921

Cushing's surgical approach to pituitary adenomas evolved from palliative subtemporal decompression to transsphenoidal partial lesionectomy to subfrontal radical adenomectomy.[28] Early attempts at resection of parasellar lesions were associated with significant risks. Sir Victor Horsley[23] attempted the first recorded intracranial approach to a pituitary adenoma in 1889; the operation was unsuccessful due to forceful retraction of the frontal lobe. Caton and Paul[3] attempted resection of a pituitary tumor in 1893 by using a subtemporal approach that had been recommended by Horsley; the tumor was never exposed and the patient died 3 months later. In 1906 Schloffler[32] was the first surgeon to embark on resection of a pituitary lesion through extensive resection of the ethmoid and sphenoid sinuses through a lateral rhinotomy approach. This technique was simplified and improved by Kanavel and Kocher[25] in 1909[24] and by Halstead[15] and Hirsch[18] in 1910. Cushing perfected the sublabial transsphenoidal route, reporting on it in his large series in 1912,[8] 1914,[9] and 1922.[7]

Cushing, by publishing the sublabial technique, and Oskar Hirsch, by espousing the endonasal technique, together

popularized the transsphenoidal approach. Before 1922, based on his confidence in the transsphenoidal method, Cushing did not hesitate to elaborate on his approach to pituitary tumors in his operative notes. He referred to this route as his "customary transphenoidal [sic] route." Circa 1925, he questioned his commitment to the transsphenoidal method, expressed in his patients' notes: "I have kept him [the patient] waiting for some time not knowing just what was the correct procedure, whether to go at the gland from above or below."

By 1929, 3 years before his retirement as an active surgeon, Cushing gave up the transsphenoidal method and exclusively used the subfrontal route, which he referred to as the "transfrontal" method. While debating which of the two approaches to use, he noted in one of his operative reports in 1928: "I have reached the stage of thinking that each of these recent transfrontal exposures is more satisfactory and interesting than the last."

Cushing may have dramatized his support of the transfrontal approach by using this approach to resect a pituitary adenoma during his highly publicized 2000th brain tumor operation. He referred to this operation as an example of the great progress in intracranial surgery that had taken place in his lifetime.[31] Near the end of Cushing's surgical career in 1932, other neurosurgeons followed his example and transsphenoidal surgery was reduced to a minor role in the specialty. Nevertheless, Hirsch continued to advocate and report on the endonasal approach until the end of 1950s.[19,20]

What were the reasons for such a paradigm shift? Significant debate exists regarding the rationale behind Cushing's rejection of the transsphenoidal procedure in favor of the transfrontal route and the actual statistical validity of his findings.[1,14,26,31] Cushing never specifically discussed the reasons for his rejection of the transnasal route in 1929, but in 1932 he did allude to the patient's improved recovery of vision and the lower recurrence rate for tumors resected through the transfrontal approach.[6] From 1927 to 1929, there was an abrupt change in Cushing's policy[31] toward using the transfrontal route exclusively for all pituitary adenomas, despite enlargement of the sella turcica. In this review, we attempt to clarify the reasons behind Cushing's shift in preference. We do so by directly reviewing Cushing's patients' records, in order to examine details of operations he performed around the time he abandoned the transsphenoidal procedure. Understanding the reasons for such a revolution in technique may provide an improved insight into the development of modern transsphenoidal surgery.

Materials and Methods

The medical records of 1870 consecutive patients in whom Cushing performed tumor surgery at the Peter Bent Brigham Hospital between 1912 and 1932 have been reviewed and indexed according to demographic data at the Cushing Tumor Registry (housed at the Department of Neurosurgery at Yale University). Of these 1870 patients, 336 (18%) underwent surgery for a pathologically proven pituitary adenoma. This high proportion of patients reflects Cushing's strong interest in the treatment of these lesions. Based on this database, 89 patients underwent at least one operation for resection of a pituitary tumor between 1926 and 1929. Henderson[16] conducted a comprehensive review of Cushing's pituitary practice in 1939. He reported that 91 patients were surgically treated during this 4-year interval; two of these patients were not found in our database.

The medical record of each patient was reviewed to identify symptoms and signs at presentation, as recorded by Cushing's resident, and to examine Cushing's own evaluation notes, which include details of the operation, hand-drawn illustrations, and information regarding patient outcome. The operative reports contain rich details, often including personal reflections about the surgical procedure. More than 75% of the records for subfrontal cases and less than 10% of the records for transsphenoidal cases include detailed hand-drawn illustrations by Cushing for use in describing the operative findings. Cushing retained careful follow-up records by asking his patients to record their status in a letter on the anniversary of their operation. Introductory and concluding notes in each operative report include Cushing's observations on lessons learned from the operation and how these new observations modified previous surgical experience. A review of these detailed notes allowed us to investigate Cushing's decision-making process and the evolution of his choice of surgical technique from transsphenoidal to transfrontal.

Results

The 89 patients who underwent surgery for a pituitary adenoma most commonly presented with visual field deficits, endocrine abnormalities, and headache, and were also found to have optic atrophy with an enlarged sella turcica on further evaluation. A detailed visual field evaluation was performed before and after surgery. Skull x-ray studies were the only imaging modality used in these cases. Initially 69 patients underwent a transsphenoidal procedure and 20 patients a transfrontal procedure. We observed certain trends among these patients. Notably, 24 (35%) of the 69 patients who underwent a transsphenoidal operation later experienced a recurrence of preoperative symptoms and signs; of these 21 (30%) underwent a transfrontal operation for repeated resection of the tumor and three received only radiation therapy. Of the 20 patients who initially underwent a transfrontal procedure, only two (10%) required a repeated transfrontal operation for recurrent tumor. No patient underwent transsphenoidal surgery after a transfrontal exploration. All patients survived their operations.

Surgical complications occurred in four patients (5.8%) who suffered from meningitis after a transsphenoidal procedure and in two patients (10%) in whom a postoperative hematoma developed following a transfrontal operation. The latter two patients required a repeated operation to evacuate the hematoma. Visual recovery was more complete immediately after surgery in the patients who underwent a transfrontal operation than in those who underwent a transsphenoidal surgery. Seven (10%) of 69 patients who underwent transsphenoidal surgery and four (20%) of 20 patients (20%) who underwent a transfrontal procedure regained near-normal visual fields after surgery. Almost half of the patients who underwent either procedure experienced some relief in their visual field deficits postoperatively.

Discussion

Harvey Cushing played a pioneering role in the introduc-

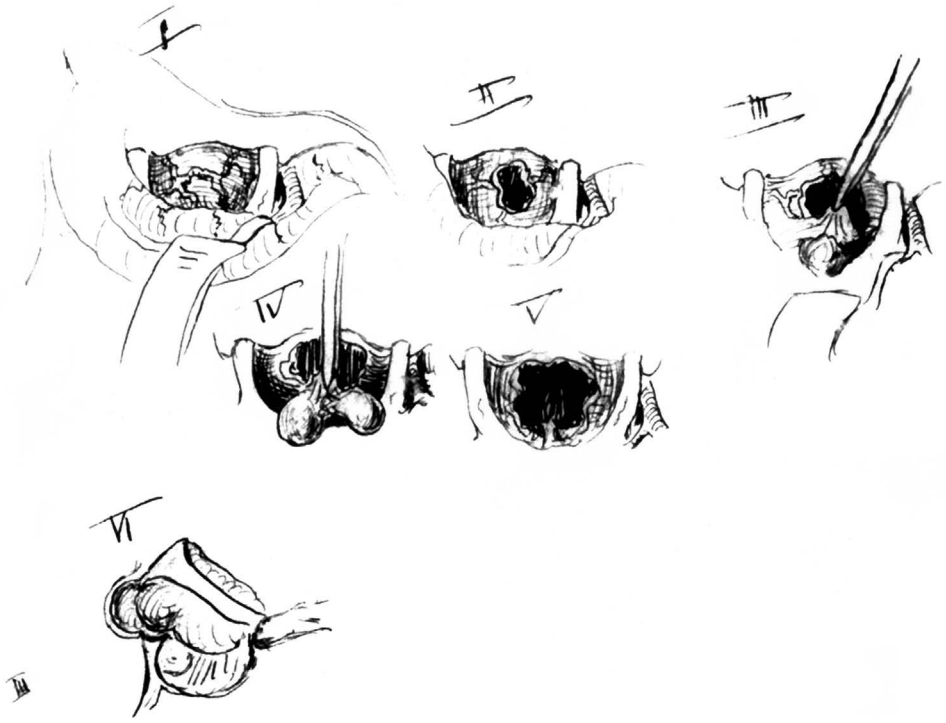

FIG. 1. Cushing's hand-drawn images demonstrating his exposure and techniques for the resection of pituitary tumors through the transfrontal route (I–V). The extension of the tumor is illustrated in a sagittal view (VI).

tion of transsphenoidal surgery to our discipline.[21,22,34] Although he advocated this approach throughout most of his career (1909–1927), his enthusiasm for the transsphenoidal route later diminished in favor of the transfrontal method. The suprasellar extension of pituitary tumors became further appreciated and Cushing's surgical techniques allowed a more radical decompression of the optic chiasm with a superior and more immediate restoration of visual fields. At the end of 1927, Cushing adopted the transfrontal approach (Fig. 1) for pituitary tumors,[2] and by 1929 he had completely abandoned the transsphenoidal procedure.

Throughout Cushing's career, because of a lack of adequate diagnostic modalities patients frequently presented with significant visual deficits (some had lost useful vision) and most likely harbored tumors with a sizable suprasellar extension (Fig. 2). As early as 1914, Cushing noted limitations of the transnasal route in allowing radical tumor resection and chiasmal decompression:

> . . . judging from the postmortem study of a number of these [transsphenoidal] cases, few if any of them could have been benefited by a partial removal of the growth and its total removal would have been out of the question.[9]

At this time, intracranial attempts by Cushing[2] and others including Frazier[12] (1913), Elsberg[11] (1914), Dandy[10] (1918), and Heuer[17] (1920), were associated with a 30 to 40% mortality rate, because a safe and adequate exposure of the optic chiasm through the intracranial chamber had not yet been fully developed. For many surgeons the transsphenoidal route, therefore, remained the most reasonable option for extirpation of pituitary tumors.

Our review of Cushing's personal notes revealed that in the 1927 patient subgroup, nine (38%) of 24 patients who previously had undergone an intranasal operation required a transfrontal reoperation to relieve their recurrent visual symptoms. In case records for these second operations, Cushing often included a note expressing his doubts regarding the potential of a transsphenoidal exposure to allow adequate decompression of the chiasm. Following transfrontal surgery, all nine patients experienced improvements in their visual deficits. At this time, Cushing's experiences with recurrent tumors clearly demonstrated to him the limitations of the transsphenoidal approach in resection of pituitary tumors. In a 1927 operative note for a patient with a pituitary adenoma Cushing wrote:

> The matter of discussion concerned the best way to approach the tumor, and whether or not the pressure against the nerves could be at all affected by a transphenoidal procedure. The operation is perhaps the best case I have ever seen in which there was perfect evidence why an extensive transphenoidal procedure would never relieve the pressure against the chiasm.

Hugh W. B. Cairns was Cushing's resident during 1926 to 1927.[27] He expressed his own thoughts on the shortcomings of the transsphenoidal route:

> By that method [transfrontal technique] the chiasm can be freed from pressure under direct vision and prompt recovery of sight is almost invariable. . . . Recovery of sight after transphenoidal [sic] operation . . . is typically delayed and slow. Little improvement has taken place by the time the patient leaves the hospital, and it is not surprising if those of us whose experience of this operation has been gained as hospital residents should have formed a poor opinion of it.[2]

Cairns believed that Cushing's experience in treating suprasellar meningiomas had led the eminent surgeon to recognize that there was a greater possibility of relieving chiasmal compression under direct vision through a transfrontal procedure.[2] Henderson's comprehensive review[16] of

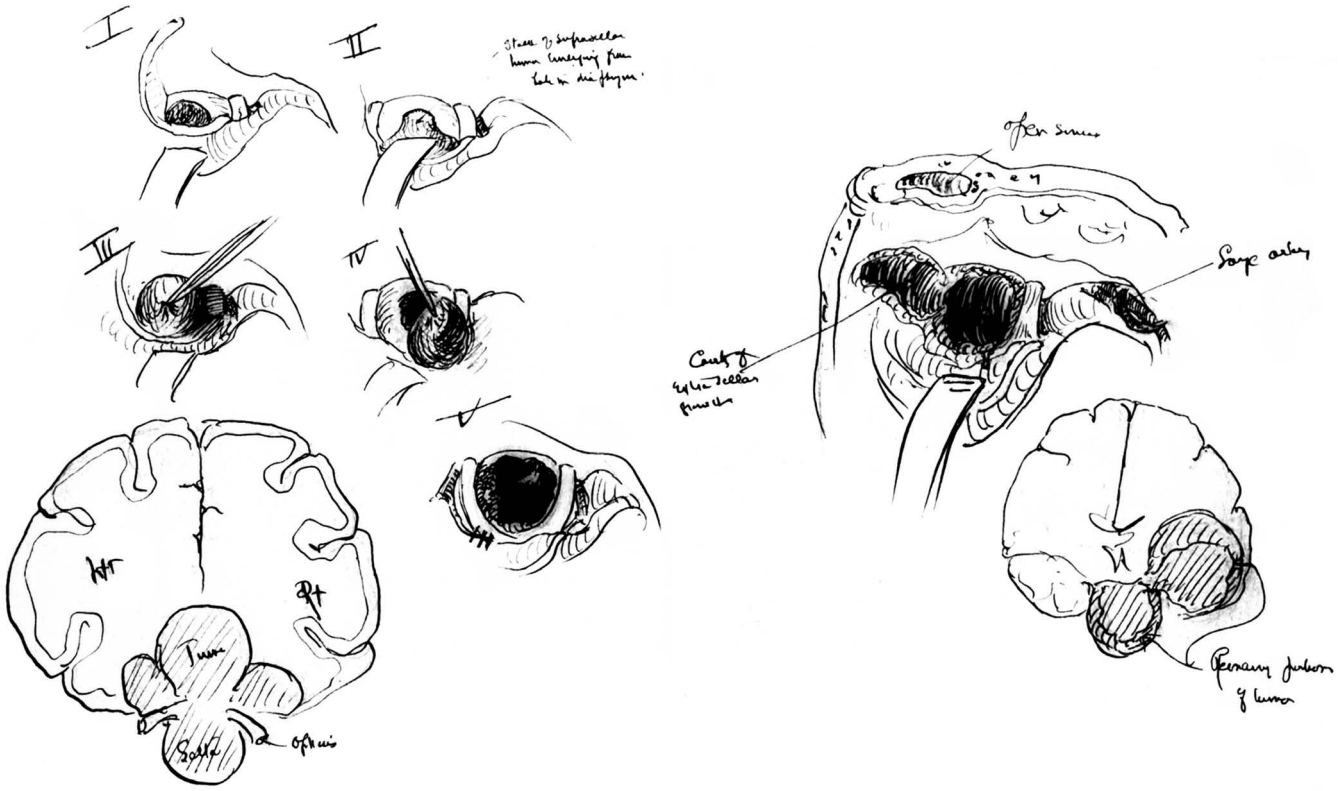

FIG. 2. Intraoperative drawings by Cushing. *Left:* Coronal drawing of the brain *(lower left corner)* demonstrating the large extension of a pituitary adenoma. *I–V:* Steps involved in the decompression of the chiasm. *Right:* Images emphasizing the large suprasellar components of the tumor in another patient.

Cushing's 1932 pituitary series[6] further supports the aforementioned findings. In Henderson's review, which he wrote in 1939, the author reported that the 5-year recurrence for chromophobe adenomas was 67% for patients who underwent a transsphenoidal operation and 42% for those who underwent a transfrontal procedure. Henderson also reported early restoration of vision in 21% of patients who had undergone transfrontal operations and in 9% of those who had undergone transsphenoidal surgery.

Cushing initially employed the transfrontal procedure for exploration of the optic chiasm in patients with "unexplained" bitemporal hemianopia and a nonenlarged sella turcica, many of whom harbored suprasellar meningiomas, craniopharyngiomas, and adenomas.[16] Through his experience with these cases, Cushing realized that pituitary tumors may occasionally present with a normal-size sella and a large suprasellar extension. Aided by the increasing safety of intracranial surgery, he pursued his curiosity to describe the relationship between patterns of visual field deficits and the anatomical deformation of the chiasm by suprasellar lesions as observed through a transfrontal approach.[30] More importantly, nonadenomatous sellar tumors were no longer a "surprise" finding during transsphenoidal surgery. Indeed, despite the lack of modern diagnostic modalities, Cushing's struggle with the preoperative differential diagnosis was no longer decisive for him in choosing whether to confront a lesion from "below" or "above," because the transfrontal approach was an all-purpose technique that allowed decompression of the optic apparatus regardless of the specific pathological condition. He mentioned in a 1926 operative note: "Of course a transfrontal operation would have settled either question and the procedure [transsphenoidal surgery] I carried out would only have settled the adenoma."

There were other reasons for Cushing's rejection of the transsphenoidal route. His expertise in intracranial surgery accelerated with the introduction of electrosurgical methods in 1926.[5] In a 1928 operative note Cushing stated:

> This young man has been rapidly getting blind from what was evidently a pituitary adenoma. The sella was completely wiped out and in days gone I would have satisfied myself by a transphenoidal procedure and have laid it to ill-chance that his vision did not subsequently improve. Encouraged by the possibility of electrosurgery for these cases I decided to tackle this lesion from above . . .

The limited exposure of the transsphenoidal procedure did not allow him to use a Bovie electrocautery to achieve a more complete tumor resection. Cushing's thoughts were often prescient and challenged the limitations of the instrumention available to him. It is intriguing that in one note written in 1928 on a patient who underwent transfrontal pituitary surgery, Cushing may have considered the idea of a bipolar electrosurgical tool (Fig. 3):

> . . . it was possible to catch the margins of the capsule with the pituitary rongeurs and to pull then outward, and then to coagulate through the rongeur, itself. This suggests that it would be an excellent thing if we could have a number of specially built instruments for purposes of this sort on an angle just like the pituitary rongeur, through which to shoot the current.

Cushing attained hemostasis through Zenker fixation of

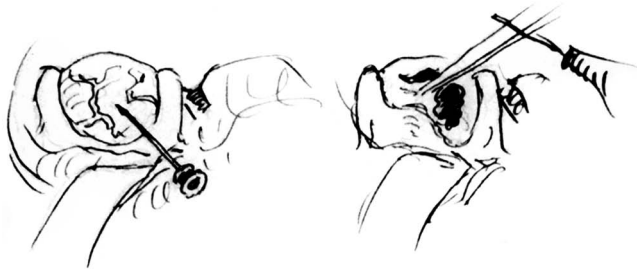

FIG. 3. Additional drawings by Cushing showing a cystic adenoma that was decompressed by needle aspiration *(left)*. Forceps and rongeurs are used to coagulate the tumor margins; the electrocautery needle is in contact with the instruments.

the cyst wall, electrical coagulation, and drainage. These modalities were only available to him through the transfrontal approach, a particularly safe procedure to use for recurrent tumors.[16] Cushing noted that in some of his transsphenoidal operations:

> . . . further progress was checked owing to bleeding from the surface of the tumor; in others it was inadvisable owing to a threatened leakage of cerebrospinal fluid: in still others impossible, for the reason that a flattened pituitary gland lay between the tumor and the operator.[9]

During 1927 and 1928, Cushing's reservation about whether to use the transsphenoidal route for removal of recurrent tumors became apparent. Some patients' operations were delayed for months despite progression of their visual field deficits, and some of these patients were left untreated. Such delays may explain the difficulties Cushing facerd in resection of recurrent large tumors in the transfrontal operations:

> One draw back to the transphenoidal procedure lay in the fact that many of the patients had previously been subjected to intranasal operations which added greatly to its difficulties; and for the same reason, as former patients began to return because of recurrence of their symptoms . . . Hence we have gradually swung away from the transphenoidal route and for the past few years it has been entirely superseded by what for a better name is called a unilateral, osteoplastic "transfrontal method" of approach, a procedure which has had various sponsors.[6]

Unlike the transnasal route, Cushing believed that the transfrontal operation could be repeated relatively more safely. After one transfrontal operation performed in 1927, Cushing wrote: "My success this morning makes me feel that it [the transfrontal approach] might be repeated indefinitely."

The complication rate was considered similar for the two procedures. Even though the incidence of postoperative hematoma after a transfrontal method was higher than meningitis in our subgroup sample, Henderson's review confirmed Cushing's belief that "this is a risk therefore which approximates the risk of meningitis by the old transphenoidal route."[6] Cushing used the transsphenoidal route between 1909 and 1925 with the remarkable mortality rate of 5.6%, despite the unavailability of antibiotic agents. Over the next decade, his surgical expertise reduced the mortality rate associated with intracranial operations to 4.6%.[6] Unlike earlier in his career, Cushing no longer had to base his selection of operation on differing mortality rates. Therefore, his enthusiasm for and commitment to intracranial surgery, accompanied by the aforementioned advantages of subfrontal exposure, led him to abandon the transsphenoidal route that he had treasured and taught for so many years as a younger neurosurgeon.

One of Cushing's last cases of transsphenoidal surgery may be considered a crucial defining experience in his decision to abandon this surgical technique. A 33-year-old man presented to Cushing on August 25, 1927 with a history of progressive acromeglic features and headaches. Hugh Cairns examined the patient and found no abnormality during the neurological examination, which included perimetric field, visual acuity, and ophthalmoscopic studies. Skull x-ray films disclosed an enlarged sella turcica with erosion of the clinoids. Cushing carried out a transsphenoidal procedure, which he considered "difficult." A large amount of colored fluid escaped and a cystic tumor collapsed. He terminated the operation before all the tumor could be resected because of excessive "oozing." The histological diagnosis was consistent with the presence of a chromophile adenoma.

The patient continued to complain of significant headaches. Cushing explored the surgical field 5 days later and evacuated "many old clots in the region of the [sphenoid] sinus." The patient remained hospitalized because his headaches continued to worsen and he suffered from "a bad attack with what was said to be Cheyne-Stokes respiration" on the 26th postoperative day. He remained afebrile during this time. Cushing noted:

> Yesterday afternoon I found him so rigid that I thought it [sic] really ought to see what could be done. I hoped that I might possibly find the old cyst refilled and yet I realized I would have difficulty in getting in again thru the nose after a 3-week interval.

Cushing reexplored the sella turcica by following the previous transsphenoidal route. In his notes he stated, "I did not succeed in getting definitely into the old opening in the sella and certainly found nothing which suggested the reformation of a cyst."

Five weeks after a third transsphenoidal exploration the patient continued to complain of severe headaches and began to experience a left abducent nerve palsy. This time Cushing explored the sella turcica through a transfrontal approach and found an abundant amount of "creamy pus," which was evacuated by suction. A sizable suprasellar extension of the tumor was found intact. Despite the unavailability of antibiotic agents at that time, this patient remarkably recovered from his infection and was discharged from the hospital weeks later in January 1928.

In December 1927, in an operative note on another patient with a pituitary adenoma Cushing noted:

> I was on the point of calling this man's operation off because I was not in the mood for transphenoidal procedures since the episode with [the name of the patient from the above case], who is still in the House and on whom I am wavering between abandoning him to his fate or doing a transfrontal operation.

Ironically, Cushing performed a transsphenoidal operation in this patient. Seventeen months later this man presented with recurrent visual field deficits and underwent a transfrontal operation resulting in remarkable restoration of his vision.

Following Cushing's shift to the transfrontal method, transsphenoidal surgery was almost eliminated from our

specialty, because other neurosurgeons followed Cushing's example and emphasized the intracranial method in their publications dealing with pituitary tumors. Indeed, Frazier[13] (1928), Vincent[33] (1932), Olivecrona[29] (1935), and others exclusively wrote about the latter technique. Norman Dott, who trained under Cushing during 1923 to 1924,[27] remained faithful to the transsphenoidal approach. Dott not only continued to perform this technique in Edinburgh but also convinced the French neurosurgeon Gerard Guiot of its potential. In the late 1950s, Guiot proved the effectiveness of transsphenoidal surgery in resection of pituitary tumors and therefore played an important role in reviving the popularity of this method. The later introduction of the operating microscope by Jules Hardy and the new use of bipolar electrocautery by Greenwood and Malis, complemented by imaging roadmaps, circumvented many of the difficulties that Cushing had faced in visualization of the operative field and obtaining hemostasis during transsphenoidal surgery. These pioneers paved the way for the development of the modern techniques that have shaped the current status of transsphenoidal surgery.

Conclusions

Transitions in Cushing's surgical treatment of pituitary tumors mirror the development of intracranial surgery throughout his career. As intracranial surgical techniques improved, the transfrontal approach replaced the transsphenoidal route for the decompression of the suprasellar portion of tumor and superior restoration of the visual field. The old principle of "adequate exposure" enabled Cushing to attain a more complete removal of the suprasellar components of pituitary adenomas. Further refinements in neuroimaging, bipolar electrocautery, and microsurgical techniques led to the rebirth and eventual acceptance of transsphenoidal surgery as a safe and effective primary approach to pituitary adenomas.

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Address reprint requests to: Aaron A. Cohen-Gadol, M.D., Department of Neurologic Surgery, Joseph 1-229, Saint Mary's Hospital, 1216 Second Street SW, Rochester, Minnesota 55902. email: cohengadol.aaron@mayo.edu.