A neuropathologist’s perspective on the celebration of the 2000th operation of Harvey Cushing

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Dr. Harvey Cushing was one of the founding fathers of modern neurosurgery in the English speaking world along with William MacEwen and Victor Horsley. Of this triumvirate, Cushing had not only the most impact in neurosurgery, but he also exerted lasting influence upon all the clinical neurological sciences. I shall restrict my remarks to certain aspects of his creative personality, and more specifically to his great influence upon the field of neuropathology. I shall also briefly mention the clinical history and results of his 2000th operation, and finally I will relate a few enlightening anecdotes told me by his associates and colleagues after he joined Yale University in 1933 as Sterling Professor of Neurology.

Contributions on Brain Tumors

We can better appreciate Dr. Cushing’s contributions by temporarily placing ourselves in the beginning of this century. There were virtually no guidelines in neurosurgical operative techniques. Control of hemorrhage, prevention of infections, and prognosis for neurosurgical patients was essentially a guessing game, especially since the pathology of the tumors of the central nervous system was for all practical purposes unknown. Most pathologists used Virchow’s classification of brain tumors, which was based upon a combination of gross and microscopic observations. Virchow discriminated between soft, cellular, medullary, hard, fibrous, and teleangiectatic gliomas. In addition to the gliomas, he accepted the existence of myxomas and sarcomas of the brain. However, these terms had a totally different meaning than they do today as is evident by Virchow’s own descriptions. “If the network increases and accumulation of slime material occurs,” he stated, “so we have a transition of a soft glioma to a myxoma; if, however, the cells increase in number, so that the network becomes narrow, we are faced with the appearance of a true medullary glioma which in turn can be transformed into a medullary sarcoma.” Such ideas of Virchow dominated pathology, while Harvey Cushing was helping to create a new discipline, neurosurgery. Little attention was paid by the scientific community to a small paper published in 1910 by Ribbert on the derivation (Ableitung) of the neuroepithelium and glioma, in which the author discussed for the first time disturbances of the histogenesis of the neuroepithelial tissues. These humbly stated ideas culminated in an excellent paper by Ribbert in 1918 on spongioblastoma and glioma, in which the author takes into consideration histological as well as histogenetic factors. At the same time, Strauss and Globus published independently their own observations on fast-growing brain tumors, which they called spongioblastomas.

These papers, however, were two isolated instances of the progress in the understanding of brain tumors. The term “glioma” was a generic name in Dr. Cushing’s time, and indicated for all practical purposes merely “a brain tumor.” Cushing, however, had the insight to recognize the intellectual poverty of this classification and was very unhappy about this designation. He and Bailey stated “we are at a loss to know how it could be that a patient from whose cerebellum a large tumor diagnosed ‘glioma’ was removed as long ago as 1906, might prove to be living and well, and the father of a family and a wage earner 19 years later, whereas another patient from whom a ‘glioma’ happened to be removed in like fashion, supposedly in its totality, might survive for a scant six months before a rapid recurrence took place.”

The setting in Peter Bent Brigham Hospital was perfect to solve such questions. Cushing was a dynamic and tireless neurosurgeon with excellent and voluminous material, and was also totally dissatisfied and frustrated with surgical pathologists. He had by that time his own laboratory and attracted associates like Percival Bailey and Louise Eisenhardt, who helped him skillfully to unfold the pathology of the brain tumors, enabling prognosis to be made on a sound basis. In 1926, Bailey and Cushing published the monograph “A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of Prognosis.” This was one of the most fundamental monographs, since it represented the first serious attempt to classify brain tumors on a histological basis, and correlated the life history of each...
type of tumor. Research on brain tumors may be classified historically into two major periods, before and after this publication. Over 50 years have passed and one may have justifiable disagreements as to the importance of histogenesis in the delineation of the different types of gliomas. Yet the different groups of gliomas, such as astrocytomas, oligodendrogliomas, glioblastomas, and medulloblastomas, as classified by Bailey and Cushing, survived as operative entities. Additional classification has been proposed, yet these are but variations and modulations to the theme set up in Cushing's department.

There is still an ongoing debate about Cushing's real contribution to the monograph on the classification of the tumors of the glioma group, and doubts are still expressed, in all probability with some truth, whether Cushing was himself skillful with the microscope. It is important, however, to keep in mind that the excellent neurosurgical material was his as well as the meticulous postoperative observations, clinical follow-up reviews, and postoperative survivals. He was, in addition, very unhappy with the pathological generic diagnosis of "glioma," as already stated, and most certainly was not inhibited in clearly expressing his dissatisfaction and frustrations to all around him, clinicians as well as pathologists. That clarity of expression was related to me on numerous occasions by the late Louise Eisenhardt.

The monograph of Harvey Cushing with Louise Eisenhardt on Meningiomas: Their Classification, Regional Behavior, Life History, and Surgical End Results is correctly regarded as Dr. Cushing's greatest clinical monograph. This study was commenced in 1915 and it represents over 20 years of meticulous and scholastic work. In the foreword on meningiomas, Cushing wrote that his monograph on "the tumors of Nervus acousticus" was an outgrowth of the present work on meningiomas, since the eighth nerve tumors were thought at first to be of meningeal origin. On numerous occasions Louise Eisenhardt stated to me how much Cushing liked his investigations on meningiomas. Yet, he was very critical of his own favorite research subject. He stated that fine histological differences in the various types of meningiomas, although very important from an academic viewpoint, had little influence upon the clinical treatment.

Harvey Cushing was an innovator and in many aspects much ahead of his time. Very little is mentioned and few details are available on the introduction of tissue-culture techniques under the stimulus of Harvey Cushing in his laboratory for the investigation of brain tumors. Buckley, one of his associates in the late 1920's, reports that the tissue-culture method in Cushing's service was "part of the examination of each brain tumor." Yet Kredel, another associate, stated that one of Harvey Cushing's interests was to find out "whether the primitive medulloblast could undergo differentiation into both spongioblasts and neuroblasts." The technical difficulties in tissue culture at that time were immense and only short-term cultures were accomplished. Yet, for the first time, successful culturing of glioblastomas, medulloblastomas, astrocytomas, meningiomas, acoustic tumors, and metastatic tumors was reported from Cushing's laboratory. Thirty years later tissue cultures were reintroduced in the investigation of brain tumors, long-term lines of tissue cultures were established, and at the present time in major medical centers as Boston, New Haven, and San Francisco, tissue-culture techniques are used in the investigation of brain tumors. But it was in Harvey Cushing's service that these investigative approaches were initiated. These are but a few selected examples of the creative accomplishments undertaken under the aegis of Harvey Cushing and their impact upon neurological sciences.

Cushing's 2000th Operation

The film of Cushing's 2000th operation to be shown today was taken while he was operating on a 31-year-old woman who was admitted with the chief complaint of headaches, visual disturbances, and cessation of menstruation. On x-ray examination an enlarged sella turcica was found. In addition, the patient had acromegalic features. Cushing performed a right transfrontal exploration exposing a large, soft adenoma of the pituitary gland, which was radically extirpated by suction and subsequently verified by Louise Eisenhardt as a chromophile adenoma. The convalescence was not especially eventful, although the patient complained of various discomforts, and she was discharged on May 7, 1931; at this time she perceived full visual fields.

Cushing was very much interested in his patients and in the follow-up period of the patients operated upon by him. In the Brain Tumor Registry at Yale, Cushing's extensive correspondence with his patients and their physicians is attached to each individual case history. An example is the following letter written by Dr. Cushing regarding the case celebrated today:

Jan. 12, 1932

Dr. E.D. Friedman,
1197 Park Avenue
New York, N.Y.

Dear Dr. Friedman:

Your patient, I.H., has been back here for the 3rd time complaining bitterly of her headaches from which she was free for a period of 3 months after her operation.

It is quite possible that this may be due to an early recurrence of her chromophic adenoma and the fact that Dr. Sosman found the sella turcica slightly enlarged over his former measurements points in this direction. However, her fields of vision are now unimpaired whereas
The 2000th operation of Harvey Cushing

FIG. 1. Inscription from Plato’s Republic over the entrance to Yale Medical School.

at the time of her first admission she had a bitemporal hemianopsia and I have impressed upon her that for this at least she ought to be thankful even if her headaches are bad. She is a worthy soul but has come to complain so much of her headaches that I told her that if she ever mentioned the word to me again that I would have nothing more to do with her and that she must make the best of it because people with her malady often have bad headaches even when the trouble is quiescent. I hope this may give her a psychotherapeutic boost, if nothing else could.

Meanwhile I hope that you and Dr. Luther J. Warren, 220 Hicks St., Brooklyn, N.Y., will keep an eye on her and have her sent back here after a few months interval so that we can check up on her fields of vision and on the condition of the sella, for I may find that I shall have to reoperate upon her for an early recurrence though I hope this may not be necessary.

Sincerely yours,
Harvey Cushing, M.D.

In a letter written on October 12, 1936, to our Brain Tumor Registry, it is stated that the vision of patient I.H. is better and that she menstruates regularly; however, she has daily headaches. In another letter dated April 4, 1941, it is stated that this patient is doing very well, she does not have any complaints, and she had no headaches which may say something for the strength of Dr. Cushing’s character. The last communication we have with this lady is around 1968. She had retired in the meantime to Florida, was enjoying life, and she no longer complained about any headaches. Dr. Cushing, I am sure, would have been delighted if he knew that she did not complain any longer about headaches; he may have even characterized her not only as “a worthy soul” but a delightful and charming patient. Unfortunately the histological slides of this tumor were lost. Louise Eisenhardt used to show this case as an example of chromophile adenoma during neurosurgical boards to candidates and it may very well be that one person took the slides as a souvenir knowing that this was Cushing’s 2000th operation.

The Last Years

When Cushing arrived in New Haven at the end of 1932, his friend the chairman of surgery at that particular time, Dr. Sam Harvey, had arranged for a ward to be used by Cushing if he wanted to operate again. Cushing was very excited and he felt the offer to be very tempting. Unfortunately he started to have stomach problems, and at this particular time at Yale his symptoms were ascribed to cancer of the stomach; an exploratory laparotomy was contemplated. However, Dr. Sosman, a radiologist at Boston, disagreed with the diagnosis; he felt that the Chief had in all probability an ulcer of the stomach and no operation was performed. Subsequently Dr. Cushing started having circulatory disturbances in the lower extremities. He thereafter concentrated his time in New Haven on completing his monograph on meningiomas and in participating very actively in the sessions of the neurological study unit.

Dr. Cushing was very fond of medical students and house officers. The class of 1926 in Harvard Medical School dedicated their yearbook to Dr. Cushing. The foreword of this volume is written by Dr. Cushing who gave touching advice to medical students and ends with the saying “Learn as to live forever; live as to die tomorrow.” At Yale he was always available for the medical students and house officers with whom he had excellent relationships. On account of the circulatory disturbances in his lower extremities he developed gangrene of one of his toes and was operated upon under local anesthesia. During the operation Dr.
Cushing was making jokes and smoking cigarettes. It was his belief that his circulatory problems had nothing to do with his smoking habits. How correct he was became evident at Cushing's autopsy, performed by Dr. Harry M. Zimmerman, who found “organized and recent thrombi in the aorta (below renal arteries) and iliac arteries.” “Since little vascular disease was actually found below the femoral arteries, he evidently suffered small injury, as far as the vessels in his legs were concerned from this habit” (smoking).

After his operation while he was convalescing, he was driven to the medical school in the morning and it was the task of a medical student to bring Dr. Cushing in a wheel chair to his office where he was working on his monograph on meningiomas. One day shortly after Cushing's arrival, a patient in distress with flexion of his right knee was brought to the emergency room while Cushing and the medical student were watching. Cushing asked the medical student to make the clinical diagnosis. When the student was not able to do so, Cushing told him that obviously this was a case of acute appendicitis. The next day while the same student was bringing Cushing up to his office in his wheel chair, he asked him whether he was interested in a follow-up report of the case he had diagnosed the previous day as appendicitis. Yes, was his reply, “Well, Dr. Cushing,” replied the medical student, “the patient was diagnosed as having a brain tumor.”

It is appropriate for a person of Greek descent such as me to close his remarks by quoting Plato in a section from “The Republic” which ornaments the entrance of our Medical School at Yale (Fig. 1). The English translation is “those who have torches will pass them to others,” the torch being the symbol of knowledge. Dr. Cushing had many torches, and he passed them on to all of us in neurological sciences.

Acknowledgments

I was privileged to know and remember with fondness conversations I had on Harvey Cushing with the late Drs. Louise Eisenhardt, John Fulton, and Ernest Sachs. I am indebted to Drs. William German and L. M. Davey and Miss Madeline Stanton for the opportunity given to me over the years to converse on Harvey Cushing. In a recent meeting with Dr. Harry M. Zimmerman these beautiful memories were revived and additional information was brought to light.

References

3. Cushing H, Eisenhardt L: Meningiomas: Their Classification, Regional Behavior, Life History and Surgical End Results. Springfield, Ill: Charles C Thomas, 1938, 785 pp

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