Percival Bailey and the classification of brain tumors

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Throughout his illustrious career, Percival Bailey made numerous contributions to the fields of neurology, neuroanatomy, psychiatry, neuropathology, and, of course, neurosurgery. His expertise, his curiosity about the nervous system, and his desire to examine it from all angles were unique. With the exception of Harvey Cushing, Dr. Bailey made some of the greatest contributions in the area of neuro-oncology at the turn of the last century. In this essay the authors summarize the key episodes of Bailey’s life and discuss his impact on the classification and treatment of human brain tumors.

KEY WORDS • Percival Bailey • brain tumor • meningioma • glioma • tumor classification • neurosurgical history

Percival Bailey was born in 1892 in the southernmost part of Illinois, a rural area known as “Little Egypt.” He spoke warmly of his memories of childhood and growing up in this small town in his autobiography, _Up from Little Egypt._ Bailey’s early education took place in a one-room schoolhouse and then at Southern Illinois Normal University. He originally intended to become a school teacher, but with the death of his mother when he was 19 years old, his interest shifted to medicine. In 1912 Bailey transferred to the University of Chicago, and while taking a neuroanatomy course he became instantly enamored with the nervous system. In keeping with his newfound passion, after earning his undergraduate degree Bailey went on to complete his doctoral dissertation on the development of the choroid plexus. Indeed, his first publications were on this very topic. By teaching gross anatomy, Bailey was able to earn a medical education from Northwestern University in Evanston, Illinois. After graduating in 1918, he began a 9-month internship at Mercy Hospital in Chicago.

At the end of his internship, Bailey was positive that he wished to develop the field of neuroscience to a greater extent. Apparently, he was not particularly concerned whether his activities were in neurology, psychiatry, or neurosurgery. He wrote two letters, one to Adolf Meyer, a prominent psychiatrist at Johns Hopkins, and the other to Harvey Cushing in Boston, who was already recognized as a brilliant neurological surgeon. As fate would have it, Dr. Cushing replied first, and so Bailey arrived at the Peter Bent Brigham Hospital in 1919. It was under the tutelage of Cushing that Bailey flourished as a neurological surgeon and made some of his most impressive contributions to the scientific community.

Interestingly, Bailey’s first contribution was entirely accidental. Some of Cushing’s earlier research was dedicated to the study of hypophysectomy in dogs, and as his student, Bailey was assigned to these studies. During a routine dissection of the pituitary, Bailey unintentionally damaged the infundibular artery. At the time, Bailey thought his mistake was an incredible blunder. Nevertheless, the next morning he found a large pool of urine on the floor next to the dog. To his surprise, he realized that he had produced polyuria without exposing the pituitary gland. Bailey discussed his finding with a visiting neurologist from Brussels, Dr. Frederic Bremer. In further collaboration, the two found that without touching the pituitary, puncture of the hypothalamic infundibulum provoked adiposogenital dystrophy and diabetes insipidus, and they attributed this result to disturbance of hypothalamic innervations of the pituitary. This was a groundbreaking finding and a major contribution to the rising field of neuroendocrinology.

The partnership of Cushing and Bailey produced many breakthroughs in the field of neurosurgery. Specifically, their book _A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of Prognosis_ was published in 1926, formed the basis of modern-day neuro-oncology. Prior to the collaboration of these two pioneers, virtually all tumors of the brain were called gliomas. In 1867, Virchow was the first to put forward the idea that these tumors arose from interstitial brain tissue. Then, in 1875, Golgi showed that some brain tumors contain distinctive star-shaped neuroglial cells of the brain, and he distinguished soft and hard forms.

During this era, it was also known that some tumors could be either aggressive or benign. Nevertheless, the classification of brain tumors was in its infancy. Some, such as Cushing himself, considered the classification of glial tumors to be in a state of disarray. Bailey and Cushing believed that the existing classifications of gliomas were both inadequate and confusing. They also believed that the only way order could be attained was through the meticulous examination of a large series of tumor speci-
mens and medical records in cases that had been observed over a period of years, from the onset of symptoms to the death of the patient. With this in mind, they set out to understand the basis of the structural variability shown by gliomas and to determine whether these histological differences carried clinical implications. Furthermore, they aimed to refute the ubiquitous notion that microscopic examination of a specimen removed at operation could not serve to predict the clinical course of the disease. Fortunately, Cushing had an extensive collection of brain tumor specimens amassed from his surgical experiences and Bailey was more than happy to take on such an assignment. It seemed to be the ideal opportunity to apply his knowledge of neuropathology and neuroanatomy to neurosurgery.

This auspicious work began in 1922 when Bailey first began to classify the gliomas, working intermittently for the next 3 years. Bailey began by going through the specimens as they came into the laboratory and arranging them in groups according to length of the patient’s survival. Additionally, new methods such as impregnation allowed for the demonstration of both neuronal and interstitial aspects of the nervous system. All in all, Bailey exhaustively examined and classified the pathological material and records of a total of 414 cases of glioma in Cushing’s series and performed histological tissue studies in 254 of these. Based on the predominant cellular configuration, Bailey classified these tumors into 13 categories. This histological categorization was the first ever and formed the basis for all subsequent classification. The results of the glioma studies were first reported by Cushing in the Cameron Prize Lectures given at the University of Edinburgh in October of 1925. In 1926, the completed monograph by Bailey and Cushing, *A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of Prognosis*, was published. This book completely revolutionized the understanding of gliomas based on the tumor’s natural history and clinical course. This was, of course, an achievement of immense practical value and earned Bailey and Cushing worldwide recognition.

In 1927, Bailey simplified the glioma classification to 10 groups, and this new system correlated the tumor type with survival (Fig. 1). He also went on to publish a practical histological atlas of gliomas. Cumulatively, the work of Bailey and Cushing not only changed antiquated thinking by showing that the microscopic structure of a tumor is important for prognosis, but also completely revamped the understanding of these tumors. In fact, the histopathological basis of brain tumors in relation to patient survival and outcome still influences present-day neurosurgical thought.

The collaboration of Bailey and Cushing did not end with their classification system. In 1925, Bailey and Cushing published a significant paper on medulloblastomas titled *Medulloblastoma Cerebelli: a Common Type of Midderebellar Glioma of Childhood*. During their endeavor to classify gliomas, Bailey had isolated a peculiar tumor that occurred primarily in the cerebellum of children, for which he suggested the name medulloblastoma. He and Cushing had specimens of 31 of these intriguing tumors, each of which they scrutinized in detail in an attempt to determine its natural history. At that time, Bailey and Cushing formulated a theory on the origin of the medulloblastoma. As recounted in Kunschner, they postulated that this tumor was derived from embryonic undifferentiated cells in the ependymal lining of the fourth ventricle. Moreover, they described the characteristic gross and microscopic structure of this tumor; its reddish-gray color, extremely cellular nature, numerous mitotic figures, and the formation of pseudorosettes, as detailed later by Bailey. Additionally, Bailey observed the tendency of this tumor to spread to the leptomeninges, which proved valuable in terms of treatment considerations. Bailey and Cushing contributed not only to the description of this neoplasm but also to its treatment. At the time, the grim prognosis for patients with medulloblastomas was well documented. This fact encouraged Cushing to introduce radiotherapy in the postoperative care of patients with medulloblastomas. In 1928 and 1930, Bailey went further, publishing articles about the effects of radiotherapy on medulloblastomas. Interestingly enough, he was the first to explain the complications associated with this therapy, including brain edema. This work paved the way for the use of craniospinal radiation treatment in medulloblastomas.

Bailey and Cushing spent almost 10 years working together, both as clinicians and as researchers. In this time, they wrote a second monograph titled *Tumors Arising from Blood-Vessels of the Brain; Angiomatous Malformations and Hemangioblastomas*, in 1928. Although this book did not receive the recognition accorded to their earlier work on tumors of the glioma group, it was ahead of its time in its depiction of the microscopic structure of hemangioblastomas. In fact, it was Bailey and Cushing who introduced the term hemangioblastoma. Another noteworthy accomplishment of this pair was their establishment of the microscopic structure of pituitary adenomas. In 1928, they were the first to describe the condition known as fugitive acromegaly, in which patients may exhibit physical stigmata of acromegaly without biochemical evidence of the disease.

After a decade with Cushing, Bailey was ready to venture out on his own, and in 1928 he was selected to head the neurosurgery section at the University of Chicago. Bailey, delighted with this opportunity, left Cushing’s laboratory in Boston with his newly refined neurosurgical expertise. After Bailey accepted the associate professorship in 1929, he immediately endeavored to launch an Institute of the Neurosciences. He intended to recruit into his new department men with backgrounds in all aspects of the neurosciences, including neurochemistry and neurophysiology. He also started the Neurology Club at the University of Chicago, with the goal of encouraging a conducive atmosphere for the growth of inquisitive neuroscientists. In addition to administrative, clinical, and research responsibilities, Bailey was an exceptional teacher. During his period at the University of Chicago, Bailey trained William H. Sweet, who later became the head of neurosurgery at Harvard. Bailey also trained Paul Bucy, a rising neuropathologist, who later became the head of neurosurgery at Northwestern University and codiscover-
er of the Kluver–Bucy syndrome. Unfortunately, Bailey’s vision of creating a neuroscience institute did not materialize. It seemed that others in positions of power did not share his zeal, and a disheartened Bailey left the University of Chicago in 1939. Not only did the university lose one of its greatest minds but it also forfeited the chance to be a preeminent neuroscience center in the world.

During his time at the University of Chicago, Bailey continued to pursue his interest in brain tumors. The first tumor type he investigated was the oligodendroglioma. As early as 1924, in his paper titled *The Interstitial Tissues of the Central Nervous System,* Bailey proposed that, because oligodendrogliomas were so closely related, one could expect to find gliomas composed primarily of oligodendroglia. Nevertheless, due to a lack of laboratory technology, this theory could not be fully investigated. With the passage of years, the development of new laboratory methods, and the help of Bucy, Bailey was finally able to engage in an in-depth study of this matter. With the publication of their memorable paper *Oligodendrogliomas of the Brain* in 1929, these men were the first to confirm the existence of tumors that were, in fact, composed of oligodendroglia and to establish this type of glioma as a definite entity. Other works of Bailey and his pupil Bucy included *Astroblastomas of the Brain,* which was one of the first works to characterize the intricacies of this tumor; *Intracranial Tumors of Infancy and Childhood,* which was the first significant writing on this topic; and *The Origin and Nature of Meningeal Tumors.* In addition to research and teaching the aforementioned outstanding students, Bailey was active in teaching undergraduates, and he established the university clinics as an exceptional institution for the treatment of brain tumors.

Bailey’s writings on the subject of brain tumors are so extensive that it is impossible to do them all justice in a short treatise. It must be emphasized, however, that he made significant contributions to the study of meningiomas. In addition to his article titled *The Origin and Nature of Meningeal Tumors,* which he wrote with Bucy in 1931, Bailey also dedicated a large portion of his book *Intracranial Tumors* (Fig. 2) to the detailed analysis of the natural history, diagnosis, and treatment of meningiomas. From a neuropathological perspective, Bailey, with the aid of Bucy, contributed much to our knowledge of the structure of these tumors, as is evidenced by this passage from the aforementioned book: “The ordinary meningeval tumor is more or less a bulbous mass, separated from the nervous tissue by a capsule of connective tissue but adherent to the dura mater.” Furthermore, the descriptions of the microscopic findings provided by Bailey are still used in the teaching of medical students today: “the cells of these masses are somewhat elongated and wound around each...
other to form whorls. The central cells of the whorls undergo a hyaline transformation and then become calcified. They cause a gritty noise when the tumor is cut, hence their name of psammoma (sand-like) bodies.” Bailey also noted that the microscopic structure and distribution of these tumor cells resembled that of arachnoid granulations (Figs. 3 and 4). Finally, he taught us that these tumors regularly invade the brain but can at times affect the underlying bone, and reminds us that alterations in the cranium are characteristic of this tumor. These changes are characterized by both erosion and formation of bone (Fig. 5). In his book, Bailey’s approach to the discussion of meningiomas is through cases he encountered in clinical practice.

Fig. 2. Reproduction of the inside cover of Bailey’s book. *Intracranial Tumors* was one of the most significant academic accomplishments of his career. (Reprinted with permission from Bailey P: *Intracranial Tumors, ed 2.* Springfield, IL: Thomas, 1948.)

Fig. 3. Drawing showing the location of arachnoid granulations over the skull base. (Reprinted with permission from Bailey P: *Intracranial Tumors, ed 2.* Springfield, IL: Thomas, 1948.)

Fig. 4. Schematic drawings representing the distribution of meningiomas. (Reprinted with permission from Bailey P: *Intracranial Tumors, ed 2.* Springfield, IL: Thomas, 1948.)

Fig. 5. Schematic drawings based on two x-ray films of the parasagittal region demonstrating alterations of the cranium due to a meningioma. A: Erosion by parasagittal lacunae. B: Erosion and formation of bony spicules by a meningioma. (Reprinted with permission from Bailey P: *Intracranial Tumors, ed 2.* Springfield, IL: Thomas, 1948.)
intermixed with excerpts from current research articles on the subject, including some of his own, and his insights on diagnosis and treatment. Bailey describes four syndromes that typify meningeal tumors, specifically syndromes of the central region, the olfactory groove, the sphenoidal wing, and the sellar tubercle. Despite the fact that meningiomas in these various locations have some similarities, he thought that the manifestations were different enough to warrant individual attention.

According to Bailey, the parasagittal central region is a very common site of origin for meningiomas, hence the signs of it are of particular importance. He described a patient who suffered from epileptic seizures that began in his foot and subsequently involved his leg and face. Bailey explained that such a course of events is very characteristic of meningiomas in this region and is rarely caused by any other type of tumor. He also stressed that this neoplasm must be carefully distinguished from all other conditions that cause focal epilepsy.

Bailey taught us how to recognize the external clues of a meningioma, including the presence of visibly dilated, tortuous extracranial blood vessels and a prominent cranial protuberance (Fig. 6). Regarding meningiomas arising from the tuberculum sellae (Fig. 7 left), Bailey contended that this diagnosis can be suspected when a bitemporal visual defect develops in a middle-aged patient. On the other hand, in meningeal tumors arising along the sphenoidal bone, unilateral exophthalmos is the most prominent symptom. Additionally, the triad of anosmia, optic atrophy, and mental status change should lead one to suspect a meningioma of the olfactory groove (Fig. 7 right). Even though it was not his most famous work, Bailey’s contribution to our present understanding of meningiomas was quite significant.

In 1939 Bailey transferred to the University of Illinois and joined the faculty with the title of Distinguished Professor of Neurology and Neurological Surgery. He continued his clinical practice, taught neuropathology, and expanded his research to include neurophysiology. The change in the direction of his research proved to be very valuable to the neurosurgical community. It was at this time that Bailey began to use temporal lobectomy for the treatment of some forms of epilepsy. He also collaborated with Gerhardt von Bonin, a professor of neurology at the University of Illinois, to uncover the corticocortical connections in the brain and the functions of these connections in monkeys. Prior to this work, only Brodmann and Von Economo and Koskinas had published studies of the cerebral cytoarchitecture. Bailey and von Bonin wrote two books, *The Neocortex of Macaca Mulatta* in 1947, and *The Isocortex of Man* in 1951. These manuscripts were the first to define with precision the cytoarchitecture of the human cortex. Furthermore, in 1959 German neurologist Georg Schaltenbrand, along with

Fig. 6. Drawings of patients showing characteristic skull changes associated with meningiomas. (Reprinted with permission from Bailey P: *Intracranial Tumors, ed 2.* Springfield, IL: Thomas, 1948.)

Fig. 7. *Left:* Drawing showing a meningioma of the tuberculum sellae. *Right:* Drawing showing a meningioma of the cribriform region with invasion of the nasal cavity. (Reprinted with permission from Bailey P: *Intracranial Tumors, ed 2.* Springfield, IL: Thomas, 1948.)
Bailey, produced a stereotactic atlas of the human brain that became an instant classic because of the caliber and accuracy of the photographs of the brain. Despite the fact that his later research was not specifically directed at brain tumors, the practical applicability of this work to neurosurgical practice is clear.

When he suffered cataracts later in his life, Bailey was unable to continue to work in the laboratory, with the microscope, or in the operating theater. His interest in the nervous system did not cease with the end of his neurosurgical career. He had long been interested in the relationship between the brain and human behavior, so naturally his attention turned to psychiatry. This focus was quite fitting, in that it was the only neuroscientific field he had not yet conquered. In 1951 he was appointed director of the Illinois State Psychiatric Institute, and he dedicated the remainder of his career to cultivating this field.

With the death of Percival Bailey in 1973, the neurosurgical community lost an exceptional scientist. In his lifetime, he covered the full spectrum of neurological science, including neurology, neurosurgery, neuropathology, and psychiatry, to name just a few. During his career, Bailey truly revolutionized the study of the nervous system and was able to make numerous contributions to the diagnosis, treatment, and study of brain tumors. He is known and honored in the whole medical and scientific community. Bailey was president of the American Neurological Association and the Society of Neurological Surgeons, and he was awarded an honorary Doctor of Science degree by Southern Illinois University, the University of Chicago, and the University of Paris. He also held honorary memberships in approximately 25 foreign medical and scientific societies. To many, he may seem capricious about which field of medicine or academics he chose to pursue. Bailey’s feelings on the matter can be summed up in this statement: “It may look to some as though I have never been able to make up my mind. I do not feel that way about it. My interest had always been in the nervous system and how it works. This problem can be approached by many pathways.” Throughout the world, Bailey was acknowledged as having the most expansive understanding of the central nervous system. He truly lived up to the title of “Mr. Neurology.”

References


Manuscript received January 25, 2005. Accepted in final form March 14, 2005. Address reprint requests to: Maciej S. Lesniak, M.D., 5841 South Maryland Avenue, MC 3026, Chicago, Illinois 60637. email: mlesniak@surgery.bsd.uchicago.edu.

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