200th Anniversary Commemoration

A Tale of Two Cities: Montreal and Boston

Emergence of the Public Hospital Systems and the Impact on Study of Diseases of the Nervous System

JOSEPH B. MARTIN, MD, PHD, OC

INTRODUCTION
1

CHAPTER ONE
The Founding of Two Cities and Two Hospitals
2

CHAPTER TWO
The Establishment of Academic Neurology in Montreal and Boston
11

CHAPTER THREE
1900–1950: Emergence of Neurological Centers of Excellence
15

CHAPTER FOUR
1950–2000: Emergence of Neurology-Based Neuroscience and Neurogenetics
23

INTRODUCTION

In 2021, we celebrate the 200th anniversary of the founding of two renowned hospitals in North America: Montreal General Hospital and Massachusetts General Hospital. The stories are remarkably similar; each was established as a charitable public institution for the care of the indigent, many of whom were homeless, recently arrived immigrants who had swarmed to North America after the conclusion of the War of 1812, principally from the British Isles and Ireland, and in the case of Montreal, from France.

Both developed innovative programs and new models for the education of physicians and nurses. Montreal General became the founding entity in the establishment of an esteemed institution of higher learning, McGill College, later University. In Boston, Massachusetts General became the first well-equipped hospital for general public benefit and for the further development of clinical teaching at Harvard Medical School, founded about 40 years before the hospital in 1782 at the end of the Revolutionary War. The medical school moved from Cambridge to Marlborough Street in Boston in 1810 and would later relocate to a site adjacent to where the hospital opened in 1821.

My personal involvement with the two hospitals began in 1970 when I joined Montreal General as an assistant neurologist and McGill University as an assistant professor of neurology, remaining on the faculty there until 1978, when I accepted a position at Harvard Medical School. I was recruited to Boston to head the neurology department at Massachusetts General, a position I held until 1989, when I moved to San Francisco as dean of the medical school at the University of California, San Francisco.

In 1997, I returned to Harvard to head the medical school, an appointment I held for 10 years, retiring in 2007 but remaining on the faculty until my emeritus appointment in 2016.

The impact that these two hospitals have had on the appreciation and understanding of diseases of the nervous system is the focus of this report. It is remarkable how many interactions and relationships have evolved between the hospitals over the years in neurological clinical research.

CHAPTER ONE

The Founding of Two Cities and Two Hospitals

Montreal: 1641

In the spring of 1641, three ships and 50-some passengers set sail from France to the New World to carry out the mission of the Société Notre-Dame de Montreal, namely the establishment of Ville-Marie, a Catholic Utopian community. Ville-Marie was led by Paul de Chomedey de Maisonneuve, the first governor of the nascent settlement that would go on to become Montreal. Among those who sailed with Maisonneuve was a 35-year-old nurse named Jeanne Mance, who left behind a large family of bourgeois importance to play a pivotal role in establishing the new colony. Prior to her journey and after her mother's death, Mance helped to raise a family of 11 siblings while active as a medical caretaker during the Thirty Years War and the plague. In Ville-Marie, she set about establishing the Hotel-Dieu Infirmary in 1642, recruiting and leading the nuns who would provide care, raising funds, and acting in an administrative capacity for more than two decades. Mance played an essential role in the initial development and organization of hospital-based care in Canada.

The settlers to Lower Canada (now Quebec) in the 17th and 18th centuries were predominantly of French background, introducing their language, Catholic religion, and laws. Immigrants arrived from France and other French-speaking regions of Europe. By 1800, Hotel-Dieu still contained just 30 beds and exclusively served the French-speaking population. A hospital and medical school that would serve the English-speaking community would not be established until Montreal General Hospital opened in 1822 and its teaching unit, the Montreal Medical Institution, cofounded by pioneer in medical education and former dean Dr. Andrew Holmes, was incorporated into McGill College as its first faculty in 1829. A French-language university, the University of Montreal (with faculties of theology, law, and medicine), did not open until 1878 as a satellite of Laval University, located in Quebec City.

English-speaking immigrants to Montreal in the 18th century came primarily from England, Scotland, and Ireland, and after the American Revolution, from the United States. Religious and educational differentiation developed along Catholic (French) and Protestant (English) lines. The exception was the Irish Catholic immigrant population that, as we shall see, had a significant impact on the development of Montreal General.

Montreal: 1759–1786

The Battle of Quebec on the Plains of Abraham near Quebec City in 1759 was won decisively by British forces, led by General James Wolfe, who died at the point of victory. Also mortally

wounded was his French counterpart, General Louis Montcalm, who succumbed to his injuries the following day. It was this definitive victory that led to the surrender in 1763 to British control of all French settlements in eastern North America.

In the aftermath of the war, immigration from the British Isles accelerated. Counted among the immigrants was the young John Molson, who left England in 1782 for Montreal, where he obtained a job in a brewery that he would purchase at auction two short years later. Recognizing the commercial value of producing beer for the growing population of English and Irish settlers, he returned to England to bring back grain seeds to provide malt for beer and ale, brewing the first ale in 1786. In 1816, he was joined in the business by his three sons, John, Jr., Thomas, and William, and the Molson family brewery became the leading liquor company in English-speaking Lower Canada. The founding of the brewery and its subsequent family management was to have a major role in the plans for an English hospital in the city. Together with other members of the Freemasons, John Molson provided an important and supportive role in the planning and fund-raising necessary to obtain approval from the fledgling government of Lower Canada to establish Montreal General.

Throughout the 19th and 20th centuries (and even today), the Molson family continued to serve as key members of the hospital's governing boards, providing leadership and generous philanthropy that sustained Montreal General during its periods of growth and expansion of services.

Boston: 1620–1782

In 1620, two decades before the founding of Ville-Marie, Boston's first Puritan settlers arrived aboard the double-mast Mayflower, 66 days after setting sail from Plymouth, England. They came ashore 40 miles south of the current-day city in what came to be known as Plymouth, Massachusetts. About one-third of the 102 passengers were of the Puritan sect, eager to establish a new world in the name of their religion. In 1630, the arrival of the John Winthrop fleet in Salem would bring additional Puritan families. Many would soon make their way to an area known as the Shawmut Peninsula, settled in 1629 by a lone Englishman named William Blaxton, near a spring on the north side of what would later be called Beacon Hill and not far from where Massachusetts General Hospital would open about 200 years later.

In 1630, Governor John Winthrop, after surveying the coastline between Salem and Plymouth and discussions with the indigenous peoples, proclaimed Boston as the capitol for the new settlers. Designated as a "City upon the Hill" (hence Beacon Hill), Boston quickly became the commercial, political, religious, and educational center of the New England region. The American Revolution erupted in Boston in 1775, with the British forced to evacuate the city on March 17, 1776. Prominent members of Boston society served in the war and one, Joseph Warren, died in the battle of Bunker Hill.

The Historic Green Dragon

In 1780, a group of Bostonian doctors and Harvard professors gathered at the Green Dragon Tavern to discuss the fee schedule for medical care in the city. The tavern, located within a short

distance of the Old North Church, where Paul Revere signaled the arrival of hostile British troops, was a common watering hole for the city's elite, including Paul Revere himself, John Hancock, and members of the professional and academic societies. It was also a common meeting place for the Freemasons of the region. The outcome of the meeting was the formation of the Boston Medical Society (not to be confused with the Massachusetts Medical Society, formed a year later).

At a subsequent meeting that same year, 14 doctors met at the tavern determined to start a new medical school. Recognizing they had no authority directly to do so, they composed a letter to the Harvard Corporation that included this reference to the Revolutionary War:

> *"Now that the recent hostilities have been concluded, we think it would be well for Harvard to pay attention to the health of the citizens of Boston."*

Among those attending these meetings was John Warren, a Harvard College graduate, physician, and surgeon recognized for having the largest medical practice in Boston. Dr. Warren was invited to deliver a series of lectures in anatomy and physiology using cadavers obtained from military sources. On one occasion, the audience included Harvard President Joseph Willard, who on May 16, 1782, at a meeting of the Fellows of Harvard College directed the medical group to develop a curriculum for a new medical school. In addition to meeting educational benchmarks, faculty of the new school were to be Protestant and of "strict morals." Further, with funds to pay faculty in short supply, it was decided that students would pay professors directly for each lecture attended.

With plans now in place, that November Willard named John Warren as the first professor of anatomy and surgery. A bitter rival, Benjamin Waterhouse, was appointed professor of the theory and practice of medicine to fill a position made possible by a prior donation to Harvard from Ezekiel Hersey, a physician and graduate of the school. (The chair still exists and is held by the chair of the Department of Medicine at Brigham and Women's Hospital.) Aaron Dexter was appointed to teach chemistry and materia medica (pharmacology). The three professors, Warren, Waterhouse, and Dexter, were to be the founding faculty. And so was established in 1782 the third medical school in the United States (after the University of Pennsylvania and Columbia).

Benjamin Waterhouse, whose portrait adorns the Waterhouse Room at Harvard Medical School, became a source of great agitation among the faculty over the distribution of the Jenner-derived smallpox vaccine, which he had received from Edward Jenner in 1800. Inoculating four of his own children and two servants and exposing them to smallpox, Waterhouse carried out studies that ultimately proved the vaccine worked. Warren and Dexter were outraged at these unorthodox experiments and Waterhouse's initial refusal to share the vaccine with local physicians, as well as his intent to benefit monetarily by forming a vaccine trust. While there is debate regarding whether his actions were in reality the result of a desire to ensure proper inoculation, these events and Waterhouse's prickly personality and proclivity for engaging in disagreements led to his discharge from the faculty in 1812, despite protestations from former President Thomas Jefferson.

Canada and the United States: 1776–1804

Post-War Northern Migration

After the Revolutionary War, tens of thousands of U.S. citizens crossed the border into British territory. These "British Empire Loyalists" settled primarily in Upper Canada (now Ontario) and in the maritime provinces of Nova Scotia and New Brunswick. Most who left the U.S. came from New York, Ohio, and northern portions of the New England States, eager to receive property for establishment of rural settlements. Conestoga wagons of Mennonites from Pennsylvania and Maryland also traveled North. Together with groups of Quakers and Dunkards, all pacifist religious followers, they accepted the generous offer of 200 acres of land and a promise that they would be spared conscription into the Upper and Lower Canada armed forces, an arrangement they had not succeeded in obtaining in the U.S. To this day, most refuse to serve in the military and eschew politics, including voting.

Many of those who left the U.S. during this time period, regardless of religious beliefs, settled in the strip of Upper Canada adjacent to and inland from Lake Erie, Detroit, and Niagara Falls into communities that gave rise, among others, to the twin cities of Kitchener and Waterloo, located about 65 miles west of present-day Toronto. A century on, renowned neurologist C. Miller Fisher (see page 21) would be born in Waterloo and grow up among their descendants.

The War of 1812 and Its Impact on Hospital Planning

As the 19th century opened, Montreal and Boston had remarkably similar socioeconomic footprints, with growing demands to address medical needs in each community. However, progress in establishing hospitals in both cities would not occur until after the War of 1812, a continuation of the U.S. versus Britain saga that led to the Revolutionary War. The War of 1812 was fueled by maritime embargoes and taxations, with ambitions on both sides to extend geographic boundaries. The confrontations that took place extended across a broad brush of eastern North America, from Lower Canada (now Quebec) to New Orleans and included direct attacks on Montreal that were successfully repelled by the British. Boston was the site of one major skirmish, the Battle of Boston Harbor, which resulted in the capture of an American frigate and a significant number of military fatalities and injuries. While the Treaty of Ghent officially ended the war in December of 1814, word did not reach hostile forces on either side in North America until two months later.

My Canadian friends have always considered that we won the War of 1812, whereas those in the U.S. say we've never lost any war!

Montreal—Early Plans for Montreal General Hospital

Following the War of 1812, and once the Atlantic Ocean was free from war-related embargoes, there was a surge of new immigration to Montreal. The major influx was of English-speaking immigrants from the British Isles and Ireland, most of whom arrived in Montreal without

accommodations. While French predominated in Lower Canada, nearly half of the population of Montreal was English-speaking, but of two differing religions, Irish Catholic and the largely Protestant British. Of the thousands who arrived from Ireland each year, most settled in Montreal, although farm settlements throughout the province were also common, particularly following the increase in immigration that followed the potato famine.

The health of the homeless population was a principal concern for the community. Montreal physicians in private practice were often unwilling to make charitable calls. Care was inadequate for many health issues, of which infectious diseases like smallpox, cholera, and dysentery were common and carried risk for the general population.

In 1817, the Female Benevolent Society of Montreal began soliciting interest to accommodate creation of a facility for care of English-speaking arrivals. With commitment from a few physicians to provide care in an institutional setting, the society sought to raise enough money to locate a facility. One year later, they rented a four-room house in a district outside the western wall of Ville-Marie. Provisions were obtained by a United Empire Loyalist, Isaac Winslow-Clarke, who had moved to the area from Boston after the Revolutionary War. As commissar general in charge of military stores, he was able to provide straw bedding, used clothing, and stoves. In 1819, patient treatment moved to a slightly larger home on Craig Street, the precursor to Montreal General, then in the planning stages. A formal proposal for the hospital was made to the Crown in late 1818 by the Duke of Richmond, the king's representative in Lower Canada. With no response received, John Molson agreed in 1819 to submit a more elaborate proposal to the legislature.

It might seem unlikely that the deal to establish a hospital for the indigent and growing immigrant population would be settled by a duel, and yet one did occur. Despite strong political and financial support from the Molson family, the bill placed before the legislature had been defeated by an Irish Roman Catholic legislator named Michael O'Sullivan. Mr. O'Sullivan took exception to this Protestant proposal, referring to the nuns' devotion to duty—no special training should be required—as a satisfactory method of dealing with the sick. O'Sullivan also objected to the idea that medical students would have access to patients in the hospital in the future, potentially subjecting them to experiments.

Outraged by this insinuation, an English-speaking physician, Dr. William Caldwell, wrote an unsigned rebuttal that was published in the *Canadian Current* in April 1819, calling O'Sullivan a coward. After insisting on ascertaining the identity of the author, O'Sullivan challenged the doctor to a duel that took place in an exchange of five volleys. Both duelists had long-lasting injuries—a shattered bone in Dr. Caldwell's arm prevented him from performing surgery, and O'Sullivan suffered from spinal pain for the remainder of his life.

The futility of the duel was proven later in 1819 when legislative approval was granted to establish Montreal General Hospital for the English-speaking community, with plans to open the facility in 1822. Not to be entirely overshadowed, O'Sullivan arranged the first St. Patrick's Day parade in Montreal in 1824. The Irish immigration expansion of the following decades would lead to rapid growth in the population of Montreal, with the majority receiving care in the "Protestant" hospital.

Another Historic Tavern

Once again, a tavern was key to an unfolding event. Freemasonry was prominent in Montreal and meetings were often held at the City Tavern on St. Paul Street. On June 6, 1821, the day of the ceremonial laying of the cornerstone, 200 or so marchers assembled at the tavern for a parade to the construction site on Dorchester Street. Participants included dignitaries of the government, the military, and local supporters, with procedural formalities carried out in the fashion characteristic of the Freemasons. Crowds lined the street. At the site, objects of the period were placed in a cavity of the cornerstone, which was sealed. After the event, guests convened again at the City Tavern for a sumptuous dinner.

Hospital construction took about a year, officially opening on May 3, 1822, with admission by transfer of the first eight patients.

As to the origin of McGill College, according to former McGill Medical School Dean Richard Cruess:

> *"In 1823, four Edinburgh-trained physicians working at the Montreal General established the "Montreal Medical Institution," a proprietary medical school. James McGill had wisely stipulated that his university must be functioning within 10 years of his death, or the property and money would revert to his wife's children. In 1829, the Montreal Medical Institution was incorporated into McGill College as the Faculty of Medicine, ensuring that the estate and endowment would remain intact for educational purposes. It became the first Faculty of Medicine in the country."*

One of these physicians was Andrew F. Holmes, who was born in Spain in 1797, after the ship he and his family were aboard was captured while sailing from the British Isles to British North America. After receiving his medical degree from the University of Edinburgh in 1819, he returned to Montreal, taking a position at Montreal General when it opened in 1822. He was there at the founding of the McGill University Faculty of Medicine in 1829. In 1843, he was appointed professor of the principles and practice of medicine to serve the school, a title that was later changed to dean. He died unexpectedly in 1860.

Boston—Early Plans for Massachusetts General Hospital

Prior to the Revolutionary War, citizens of the "province" of Massachusetts derived health care for their families largely through shared community and family responsibility, local services rendered within the structure of the town meeting organization, and church support. The dislocations after the War of Independence resulted in a growing need for the care of the homeless, those injured in the war, and former enslaved people who were seeking refuge in a perceived freer place. These requirements prompted state-mandated budget disbursements to assist in social welfare needs of the individual communities. The resulting necessity for fair distribution of such funds led to state-wide definitions of "pauper status" and to the development of almshouses to care for the general needs of such a population—physical, mental, and medical.

For over 100 years, the northeast edge of the Boston Common was the location of the Boston Almshouse (and a separate workhouse and prison), which provided some respite for the poor, (paupers) who were often single members of a family, displaced from their homes and frequently in need of medical care. They were about equally men and women, and by the turn of the 18th century approximately 4% to 5% were African American. Medical care was delivered through contracts with local physicians. By 1800, the condition of the almshouse was deplorable, and plans were made to build a new one near present-day Leverett Circle on the Charles River. The new facility opened in 1801; it served as a location where medical practitioners received stipends for medical care and for the teaching of medical students at Harvard when the school was still located in Cambridge. In 1808, the chaplain of the almshouse, Reverend John Bartlett, began discussions with medical practitioners and representatives of civic government to consider the possibility of building a much-needed public hospital. (In 1810, led by the efforts of Professors James Jackson and John Collins Warren, the medical school moved from Cambridge to Boston to a location on Marlborough Street, although the almshouse remained a teaching site of the medical school.)

Immigration to Boston flourished between 1815 and 1821 after the end of the War of 1812. Most medical care for the well-to-do in Cambridge and Boston was delivered at home for a fee by medical staff readily available to treat patients who could afford it. But concern grew for the immigrant and homeless population and led to a state initiative to provide a facility for their medical care. Very important to the subsequent planning was that patients who were likely to benefit were those needing short-term 24-hour care, with the assistance of a nursing staff. The intention was to support the health care of an emerging middle class (separate from the paupers, who were to continue to receive medical care in the almshouse).

The Puritan Influence

In Boston, the continuation of the Puritan influence and the emergence of the Boston elite (the term Brahmin was later coined by Oliver Wendell Holmes, dean of Harvard Medical School from 1846 to 1853) resulted in power struggles among the establishment, some of whom wanted the hospital placed in Cambridge while others felt it important to have it located in the midst of the growing city, which by this time had a population of about 43,000. Hospital planning was integrated with the medical school to accommodate an emerging academic structure, where most of the leading members of the professorial faculty came from a few prominent families that were often in competition with each other both in business and in health care.

On February 25, 1811, the Massachusetts Legislature granted a charter for the Massachusetts General Hospital. It gave James Bowdoin and 55 prominent Bostonians the “power to hold real and personal estate of the yearly value of $30,000.” The “Board of Visitors” would include the governor, lieutenant governor, president of the senate, and speaker of the house. The state would appoint four of the 12 trustees, a practice that has continued to the present time, although as of 2020 the total board now consists of 16 members. The provision of the charter, to include real estate, was to depend on the trustees raising an additional $100,000 within five years, a condition that was extended due to the War of 1812. The charter included a duty to formalize

and create a separate "insane asylum" for the care of the mentally ill, which was to be located across the river in Charlestown.

Immigration from Ireland, from areas of non-English-speaking Europe, and from other countries around the world led to growing societal and religious segregation. To the credit of the planning group, as noted in one history:

> *"Fund-raising efforts extended to a diverse contingent of religious groups, including Roman Catholic, Greek Orthodox, Lutheran, Calvinist, and Quaker: efforts supported by the public announcement that 'a donation to the hospital satisfied a personal responsibility to one's community and to God.' Thus, in a literal sense, the charter recognized Massachusetts General as a hospital to serve the good of the entire community."*

Charles Bullfinch, renowned for designing the U.S. Capitol and Massachusetts State House among other notable buildings, was selected as the architect. A site was chosen on the banks of the Charles River below Beacon Hill, with stones for construction of the hospital building shaped by convicts at the state prison in Charlestown. July 4, 1818 was selected for the ceremonial laying of the cornerstone. Once again, the celebratory details were assigned to the Freemasons, this time the Grand Lodge of Massachusetts.

The ceremonies that accompanied the laying of the cornerstone for the U.S. Capitol in Washington in September 1793 were similar to those later used for these two hospitals, embedded with the concepts of the Freemasons—brotherhood of all men, equal opportunity for all, and an embrace of integrity committed to doing the public good. The symbolism invoked by the items placed in the cornerstones during each of these ceremonies included tokens of the framework established by the Freemasons centuries before, which laid the groundwork for societal responsibility to the common good.

As more students were admitted, the medical school continued to relocate to larger facilities over the next 40 years. In 1816, a new building was built on Mason Street, just a block off the eastern edge of Boston Common. In 1846, it moved to a new brick building on North Grove Street adjacent to Massachusetts General, where it remained for 30 years.

Impact of Irish Immigration

The first Irish residents of Montreal were primarily former soldiers who were part of the conquering British Army in 1760. Irish Catholics started to appear on official city records in 1817, and there would be a contingent of sufficient size to hold Montreal's first St. Patrick's Day parade seven years later, organized as previously mentioned by duelist Michael O'Sullivan.

The religious separation of the English-speaking world of Montreal, formed by immigrants from Britain and Scotland and those of Irish Catholic descent, resulted in a number of issues. Language and religious affiliations contributed to the language separation of the two public

school systems: Catholic–French, and Protestant–English, which persists to this day. By 1867, after the exodus that followed the potato famine, the Irish were the second largest ethnic group in Canada (after the French), making up approximately 25 percent of Canada's population.

In Boston during the years of the Irish potato famine in the late 1840s and in its aftermath, Irish immigration resulted in their becoming the largest single ethnic group in the city. Between 1845 and 1855, 1.8 million Irish residents arrived in the U.S., many of them to the Boston region. Their arrival changed Boston from an Anglo-Saxon Protestant city to a more diverse community. Many of the immigrants found employment with the Yankee establishment but were considered socially separate because of customs and religion. One example of this segregation was the establishment in 1863 of the Jesuit Catholic Boston College, considered a rival to Harvard College. Prejudices were alleviated to an extent when members of the Irish community served side-by-side with others in the Civil War.

Fenian Raids

The growing number of Irish immigrants to Montreal and Boston shared a strong antipathy toward the British, based on their historic treatment in Ireland and the failure of Britain to provide resources to the poor, malnourished population during the famine that devastated the country. This was reflected in the emergence in 1866 in the northern United States of an armed guerrilla force of Irish descent that identified themselves as Fenians. They sought to antagonize the British and weaken British sovereignty in North America by carrying out a series of raids. Although a trivial part of history in most ways, the Fenian incursions resulted in unification efforts of several Canadian provinces that eventually resulted in the formation of the Dominion of Canada on July 1, 1867.

Conclusion

Like all institutions with long histories, there are many people and many stories that have propelled Montreal General and Massachusetts General to this moment. Both hospitals focused attention on the importance of clinical and pathological observations in the parsing of neurological conditions, which built importantly upon the development of neurology as a study of diseases complementary to the field of internal medicine.

CHAPTER TWO

The Establishment of Academic Neurology in Montreal and Boston

Looking back at a snapshot of the late 1860s, we find Montreal in the midst of a major historical event, the establishment of the Dominion of Canada. On July 1, 1867, after decades of planning, the British-North America Act formalized the union of Nova Scotia, New Brunswick, and Upper and Lower Canada. Across the border, Boston was part of a country struggling to reunite following the end of the Civil War in May 1865, and the political upheaval associated with the assassination of President Abraham Lincoln, a month earlier.

Like Canada, McGill was entering a new phase, galvanized by the work of William Osler, who had just entered medical school there. Osler would join the McGill faculty in 1874 and at Montreal General go on to show the power of autopsy examination in discerning medical diagnoses, including neurological disorders. In Boston, the soon-to-be head of neurology at Massachusetts General, James Jackson Putnam, had returned from travels to Europe, where he had explored new "electrotherapies," leading to his appointment in 1872 as "Electrician" at the hospital and lecturer at Harvard Medical School.

The contributions of Osler and Putnam were seminal in the development of neurology as a distinct medical specialty.

Montreal: 1850–1900

Osler and the Study of the Nervous System

William Osler's contributions at Montreal General Hospital and McGill are legendary. After attending Trinity College in Toronto and graduation from medical school at McGill in 1872, he took several tours to Europe, visiting scientists and clinicians in England, Germany, Austria, and France. Upon return to Montreal, he was appointed Pathologist at Montreal General, with responsibility for the infectious disease unit and recognition as Lecturer in Medicine at McGill. Devoted to anatomical dissection and microscopy, which he had observed in Europe, he examined the autopsies of over 900 patients and catalogued their diseases. His carefully prepared written summaries of each case became the model for descriptive medical teaching and formed the basis for his classic textbook, *Principles and Practice of Medicine*, which became the standard medical description of internal medicine for much of the early 20th century. First published in 1892, Osler's 1,079-page textbook contained 225 pages devoted to diseases of the nervous system and muscle. It is said that in penning these detailed autopsy summaries, he became an accomplished writer of great clarity and succinctness.

Among the many neurological cases Osler described were tuberculous meningitis (1876), pneumonia with meningitis (1876), an article on Giacomini's method of preserving the brain (1880), examples of the study of brains of criminals (1882), and a single case of Jacksonian epilepsy of 14 years standing. In 1884, he autopsied a stroke patient who had paralysis of one leg and described the anatomic "leg centre" (1884). Among his writings were descriptions of neurosyphilis, to which some have attributed the famous quote, "He who knows syphilis knows medicine."

In a "Letter from Leipzig" published in a Canadian medical journal in 1884, Osler wrote, "It is very hard to adjust the two great functions of a University . . . . The work which shall advance the science, which brings renown to the professor and to the University, is the most attractive, and in German laboratories occupies the chief time of the director. This function is especially exercised, and the consequence is that medical literature teems with articles issued from the various laboratories. On the other hand, the teaching function of an Institute is apt to be neglected in the more seductive pursuit of the 'bauble reputation.'"

Osler was a great admirer of Jean-Marie Charcot and visited his hospital clinic at the Salpetriere in Paris. Among the descriptions of diseases of overlapping interest was Osler's publication in 1880 of the first instance of familial amyotrophic lateral sclerosis, occurring in the family of Samuel Farr. This family has since been traced in studies led by Robert Brown of the University of Massachusetts, showing that the mutation was in the SOD1 gene, the first identified genetic locus for mutations that cause familial autosomal dominant inheritance of the disease.

Harvard Connections

In 1876, Osler arranged a visit to Boston. His purpose was to inquire into the curriculum at Harvard Medical School and to compare it with his own efforts at McGill, where he was emerging as a preeminent pedagogue—while still in his 20s. (A longer visit of a week came two years later.) Harvard President Charles Eliot, now six years into his tenure, had begun instituting a number of changes at the medical school. A chemist by training, he was outraged by the lack of scientific training of medical students, both in their preparation for medical school admittance and in the classes they were assigned during the first two years. Three-quarters of admitted students had only a high school diploma, and during two years of preclinical instruction, students had just five months of lectures, delivered by faculty who repeated the same lectures in the first and second years. As late as 1870, a medical student without any particular qualifications required for entry to Harvard could graduate with a medical degree, even if he had failed four of the nine required courses.

Eliot's changes were a work in progress. During his visit, Osler was impressed with the physiology lectures delivered by Henry Pickering Bowditch and by the laboratory facilities. By this time, Harvard Medical School was located immediately adjacent to Massachusetts General Hospital on the banks of the Charles River, where anatomy students allegedly tossed cadaver remnants directly into the river. Osler made special reference to autopsy studies conducted at the hospital and expressed the wish that these excellent facilities were available to him at McGill.

Over the course of Osler's lifetime he became close friends with Bowditch and Harvey Cushing, as well as James Putnam and other senior faculty in the medical school and at Massachusetts

General, visiting both institutions several times. In 1904, President Eliot invited Osler to give the annual "Ingersoll Lecture on the Immortality of Man." He entitled his talk "Science and Immortality," with the lecture attended by his wife, a Bostonian who was the great-granddaughter of Paul Revere, as well as his in-laws. According to a 2011 article in *The Pharos*, "Osler was reluctant to disclose his innermost beliefs, particularly with his in-laws present. Years before, when asked about his own religion, he replied, 'I'm of the religion of all sensible people. And what is that? No sensible man discusses his religion.'" During his talk, he conceded that science and medicine could contribute nothing to the topic of immortality. President Eliot apparently found the lecture, "a brilliant and charming essay" but disappointing. Nevertheless, the next month Osler was granted an honorary doctor of laws at Harvard commencement.

Sir William Osler was also a pediatric neurologist, greatly enjoying children and attending to their complaints and maladies. He left McGill in 1884 for a post at the University of Pennsylvania, and would go on to faculty appointments at Johns Hopkins and Oxford.

Boston: 1866–1912

Pioneering Work at Massachusetts General

James Jackson Putnam was born in Boston in 1846, the son of James Gideon and Elizabeth Cabot (Jackson) Putnam. Elizabeth was the daughter of James Jackson, one of the original founders of Massachusetts General and an acclaimed professor at Harvard Medical School. After graduation from Harvard College in 1866 and Harvard Medical School in 1870, Putnam was appointed as a "house pupil" at Massachusetts General, the equivalent of an internship position. Following this brief period in clinical medicine, he traveled extensively to Europe, visiting London, Leipzig, and Vienna, where he made acquaintance with Theodor Meynert in Germany and Hughlings Jackson in London.

Upon return to Boston in 1872 and following his experience in Europe, Putnam introduced electrotherapy as a treatment modality at Massachusetts General, where as previously mentioned, he was initially given the unusual tile of Electrician. At Harvard Medical School, he was appointed Lecturer on the Application of Electricity in Nervous Diseases. Around this time and finding the hospital facilities wanting, he established a neuropathological laboratory in his own home and at Massachusetts General went on to start one of the first neurology clinics in the U.S.

Putnam was a founder of the Boston Society of Psychiatry and Neurology, established in 1880, and was one of seven charter members of the American Neurological Association, founded in 1875, serving as its president in 1888. By 1893, he had been promoted to Chair of Diseases of the Nervous System at Massachusetts General and to the rank of professor at Harvard, a position he held until he retired to emeritus status in 1912. During a long career, his work included publication of over 100 papers on clinical and pathological studies of diseases of the nervous system and muscle and more than 30 on psychoanalysis and related topics. Among Putnam's many contributions to neurology were his early description of paresthesias in the hands, papers on neuritis related to lead and arsenic toxicity, and influential studies of neuroendocrine disorders.

In the early 20th century, Putnam became enamored of Freudian psychoanalysis and was a party to the only visit Freud made to the United States. The occasion was a 1909 meeting at Clark University in Worcester, where Freud gave five lectures delivered in German that included the first description of his conceptualization of the Oedipus complex. He was then taken by Putnam to an estate in the Adirondacks for a week of vacation, a rustic experience that was not altogether to Freud's liking, as reflected in subsequent comments. Referred to as the Putnam Camp, the property was originally established in 1875 by three prominent Boston families—those of Putnam, Bowditch, and William James. Putnam later visited Freud in Europe in 1911 and retired from his position as head of neurological services on his return to Boston.

Conclusion

William Osler, during his tenure as Pathologist (1874–1884), is considered the early prototype of the Canadian academic neurologist, carrying out extensive clinical and pathological studies as previously noted. These studies were arguably the earliest nervous system research at Montreal General. After he left Montreal, the legacy of clinical-pathological correlations continued with new advances in light microscopy, tissue preparation, and staining techniques and remained the main research activities of neurologists and neurosurgeons at Montreal General throughout the first part of the 20th century. In 1903, the Province of Quebec was the first in Canada to recognize neurology as a specialty separate from internal medicine. David A. Shirres was the hospital's first designated neurologist (1903–1921), and was primarily a clinician who published most of his studies in Montreal medical journals.

Osler passed away in England in 1919 at the age of 70, a year after Putnam, who died in Boston in December of 1918 at age 73.

CHAPTER THREE

1900–1950: Emergence of Neurological Centers of Excellence

Key Events in Early Twentieth Century

As the 20th century unfolded, developments along several fronts would impact the educational, clinical, and research missions of the Montreal General and Massachusetts General Hospitals. These included:

1. Relocation of Harvard's Medical School in 1906
2. Publication in 1910 of Flexner Report on state of medical education in the U.S. and Canada
3. Formation of Rockefeller Foundation in 1913
4. Opening in 1913 of Peter Bent Brigham Hospital, located across Shattuck Street from Harvard Medical School
5. Establishment in 1926 of a Harvard-affiliated neurologic unit for clinical care and research at Boston City Hospital
6. Plans for construction of the Montreal Neurological Institute (1928) in association with the Royal Victoria Hospital (opened in 1893 and named in honor of long-reigning Queen Victoria), establishing a new academic competition with Montreal General at McGill

1. New Harvard Medical School Facility on Longwood Avenue

In September 1906, Harvard Medical School opened a new campus consisting of five Beaux-Arts Vermont marble buildings, four for research and education and a fifth containing a library and space for administrative functions. The opening ceremony was led by Harvard President Charles Eliot, who was nearing the end of his 40-year term as president. The new campus on the former Francis estate on Longwood Avenue was made possible through a land purchase funded by donations from the Rockefeller family and the renowned Henry Higginson (founder and philanthropic supporter of the Boston Symphony Orchestra, which held its inaugural concert in 1881).

2. Flexner Report of 1910

At the beginning of the 20th century, there was growing criticism about the state of medical education in the U.S. and the unregulated diploma mills that charged tuition, with minimal

requirements for admission or for graduation. A different model of rigorous admission procedures and curriculum reform with increased attention to the scientific foundations of medical practice was emerging from a new school in Baltimore. Founded with philanthropic support from a Quaker named Johns Hopkins and encouraging among other things the admission of women, the school would bear his name. Hopkins' contribution of $7 million, of which half was to be used to found a hospital, was the largest philanthropic contribution in the history of the United States up until that time. The hospital opened in 1889.

15 years later, in 1904, the American Medical Association created a Committee on Medical Education and with support from the Carnegie Foundation appointed Abraham Flexner as the leader of the now-famous review it commissioned. Flexner, a child of German immigrants, had studied in Europe and was fully aware of the rigorous standards in Germany and England, both for admission to medical school and the education that usually required four years of medical training. Altogether, the European model required a minimum of six years of education, followed by more advanced clinical training.

Urged on by the educational opportunities afforded by new medical models like that established at Johns Hopkins, Flexner initiated in 1905 a systematic review of the majority of medical schools in both the U.S. and Canada. Many of the schools were proprietary schools with tuition requirements, where teaching often failed to educate the students adequately for the rapid advances in science occurring at the turn of the century. This evaluation found that both Harvard and McGill had deficiencies that ought to be corrected, but appeared to give a nod to McGill for establishing requirements for a four-year college education prior to admission and for more rigorous didactic and laboratory teaching. One analysis of Flexner's report included this summation:

> *"Flexner found a handful of schools worthy of praise for their fine programs, including Harvard, Western Reserve, Michigan, Wake Forest, McGill, and Toronto, but reserved his highest praise for Hopkins, "the model for medical education."*

3. Rockefeller Foundation and Institute

The Standard Oil Company was one of the largest corporations in the U.S. at the turn of the 20th century. A plan to form a new philanthropic foundation had been discussed by the Rockefeller family for over a decade, funded by proceeds from the emerging government-ordered breakup of the oil company and other major assets owned by the family. Failing to get federal support for this plan due to concerns about overreach from a private foundation with limited oversight, John D. Rockefeller, Sr., sought approval from the state of New York, which granted it in 1913. With a contribution of $50 million, he created the largest charitable philanthropic entity in the country. The foundation was to play a significant role in the development of planning for neurological research and clinical work in both Montreal and Boston.

There were several important individuals in the early history of the Rockefeller Foundation. Frederick Gates (the grandfather of a neighbor in Brookline, Massachusetts), disheartened

by the prospect of serving as a Baptist pastor in the Midwest, accepted an invitation from Rockefeller to manage the business and philanthropic work of the foundation. The outcome was the establishment of a wide range of activities in science, agriculture, medicine, and public health in the United States and abroad. In 1913, the Rockefeller Institute and University in New York opened.

Another person who played a key role in the evolution of the Rockefeller Foundation was Alan Gregg, who was born in Colorado and educated at Harvard, where he received his degree from the medical school in 1916. Following a year of internship at Massachusetts General, he joined the U.S. Harvard Medical Unit in France. After his return in 1919, he signed on with the foundation and would spend his entire career there.

Between 1924 and 1926, Gregg personally surveyed and wrote reports about medicine in Italy, Ireland, and Russia, as well as other countries. His engagement during these years had close affinity to the work of Abraham Flexner. Gregg's familiarity with leading European figures in psychiatry, neurology, and brain research encouraged his pursuit of support of the latter. By 1926, Alan Gregg, the chief financial representative for medical research at the Rockefeller Foundation, was eager to explore key opportunities at McGill and Massachusetts General.

4. Construction of Peter Bent Brigham Hospital

Peter Bent Brigham, a direct descendent of one of the original immigrant families that settled in Cambridge, Massachusetts, in 1630, was a self-made millionaire businessman, real estate mogul, and director of a local railroad chain. Following his death in 1877 and as specified in his will, money was set aside to be spent a quarter century later on a hospital. The Peter Bent Brigham Hospital (later Brigham and Women's Hospital) opened in 1913 in the Harvard orbit, located directly across Shattuck Street from Harvard Medical School, establishing a highly competitive, often fractious cross-town relationship in health care, teaching, and research with Massachusetts General Hospital. This rivalry would endure for nearly a century until the two institutions were merged in 1994.

5. Boston City Hospital

In 1848, a cholera epidemic swept through Boston, prompting the planning of a hospital for the working poor of the city. Massachusetts General Hospital was unwilling to accept patients with infectious diseases, chronic disorders, and post-partum illness. It was decided that a new institution, Boston City Hospital, should care "for persons of temperate and industrious habit who by sickness or accident require that attention for which they are unable to pay." The first patients were admitted in 1864. It was located in downtown Boston along European models of healthcare facilities, with a central building and separate pavilions spread out along the periphery. For many years between the first and second world wars, Boston City Hospital's clinical and research activities were the responsibility of Harvard Medical School.

The Rockefeller Foundation offered Harvard University a substantial gift to "establish an academic Department of Neurology." Dependent on the university contributing an equal annual amount, Boston City Hospital constructed a new neurological unit and medical wards.

The model espoused hospital-based research laboratories contiguous floor-by-floor with the patient wards, a design not too different from what would be built at the Montreal Neurological Institute. With the encouragement and support of the Rockefeller Foundation, Boston City Hospital selected Stanley Cobb in 1925 as the head of the unit, with an appointment at Harvard Medical School.

Boston City Hospital emerged as one of the preeminent U.S. training venues for neurology in the years before and after the second world war. It became a leading incubator for many outstanding leaders: Stanley Cobb, Houston Merritt, and Tracy Putnam (who with Merritt discovered the anticonvulsant activities of diphenylhydantoin [Dilantin]), and Derek Denny-Brown. The intermingling of the principal characters in our story and of links between Montreal General and Massachusetts General are quite remarkable.

6. Establishment of the Montreal Neurological Institute

In 1928, McGill leaders recognized the importance of clinical neuroscience, as evidenced by the recruitment of Wilder Penfield to establish a new neurological institute affiliated with the Royal Victoria Hospital. An American originally from Spokane, Washington, Penfield was educated at Princeton, Oxford, and Johns Hopkins. It was during his stay at Merton College, Oxford, that he first met Osler in 1924. On return to New York to a position at the Presbyterian Hospital Neurological Institute, Penfield met with David Rockefeller, who encouraged him to continue his interest in the surgical treatment of epilepsy. When medical politics in New York were not conducive to the idea, Penfield accepted an offer from the dean of McGill School of Medicine and the medical director of the Royal Victoria Hospital to establish a neurological institute in Montreal. At the time, Simon Flexner, the brother of Abraham, was the first director of the Rockefeller Institute for Medical Research and a member of the foundation's board of trustees. Doubtless his acquaintance with the best medical schools described in the Flexner Report played a role in favoring McGill. After Alan Gregg met with Penfield, the foundation appropriated a $1.25 million grant. Penfield, along with his neurosurgical colleague William Cone, led the planning for establishment of the Montreal Neurological Institute, which opened in 1934.

Development of Neurology: Interplay of Activities Between Montreal and Boston

Organization of Hospital Governance and Fiduciary Arrangements at McGill and Harvard

The medical enterprises at Harvard and McGill followed a nearly identical model: multiple not-for-profit hospitals affiliated with but not owned by the respective university. From their beginnings, Montreal General and Massachusetts General were independent in governance structure and operations of medical care and teaching, although as we've seen, the origin of McGill was actually embedded in the opening of the hospital. Later, McGill's medical school moved to the main McGill campus on the eastern edge of Mount Royal between Montreal General and the Royal Victoria. Other affiliated hospitals were added to each medical school/university to provide additional medical care and expand the education and research missions.

In Boston, after the move of the medical school in 1906, as previously noted, an accompanying hospital, the Peter Bent Brigham, opened in 1913. In 1914, the Children's Hospital of Boston (now Boston Children's Hospital) moved from a location near Symphony Hall to Longwood Avenue.

In Montreal, The Children's Memorial Hospital (now Montreal Children's Hospital) opened its doors in 1904. A bilingual institution, it was the first hospital in Montreal with the sole mandate of caring for sick children and the explicit charge to care for both English- and French-speaking children.

Hospitals for the Jewish community also opened in both cities. During an era of religious separatism and anti-Semitism, Boston's Jewish community founded Beth Israel Hospital in 1916 to meet the needs of the growing Jewish immigrant population. The hospital relocated to a new facility in Boston's burgeoning Longwood Medical area in 1928, and during the Depression, Beth Israel was one of only two hospitals in Boston that treated welfare recipients. In Montreal, the Jewish General Hospital opened in 1934, available to all patients regardless of race, religion, language, or ethnic background.

Neurology at McGill and Montreal General

At Montreal General, much of the progress in clinical neurology in the 20th century is due to Fred Mackay, who took charge of the department in 1921 after the retirement of David Shirres. Mackay graduated in medicine at McGill in 1912, receiving the Holmes Gold Medal, named for the first dean of McGill's medical school, Andrew Fernando Holmes and presented to the graduating student with the highest aggregate standing.

Fred Mackay's tenure as chief of neurology spanned nearly 40 years. He entered the armed forces during WWI and would go on to take special interest in the clinical syndrome of "shell shock." His later work focused on peripheral nerve injuries, reporting a study of over 600 cases. On return to Montreal after a year at the London Neurological Hospital at Queen Square, he was encouraged to serve as consultant to the Division of Veteran's Affairs before assuming the post at Montreal General. He later became fascinated with the clinical disorders of hysteria and malingering. A chain smoker with a chronic cough, he died of lung cancer in 1947 and was succeeded by Francis McNaughton, who was then followed by Preston Robb, both of whom eventually crossed town to the Montreal Neurological Institute, leaving the Montreal General bereft of any academic pursuits until the arrival of Donald Baxter in 1963.

When the Montreal Neurological Institute opened in 1934 in a separate building directly across University Avenue from the Royal Victoria Hospital, it was designed as a specialty neurological hospital combined with research laboratories. With the Montreal Neurological Institute, Penfield's dream of creating one of the leading neurological/neurosurgical units in North America—and one of a few select such endeavors worldwide—was realized. By the beginning of the second world war, it had become McGill's primary site for the majority of nervous system disease inquiry and treatment. The office of the Department of Neurology and Neurosurgery was housed there, with Penfield its leader for several decades. Montreal General essentially became a satellite institution, particularly in neurology and neurosurgery, with faculty commonly rotating among the hospitals and the unstated understanding that eventual appointment to the Montreal Neurological Institute would be the prize for the most able.

For 40 years, the Montreal Neurological Institute dominated all aspects of the research and education in the Department of Neurology and Neurosurgery at McGill, with a few other hospitals joining the academic circuit, including the Children's Hospital and in 1934, the Jewish General Hospital. Notably, the education of medical students and of residents in neurology and neurosurgery was a combined effort of the department using all of the hospitals.

Mid-20th Century: Evolution of Neurology in Boston

Stanley Cobb

As stated earlier, during the early 1920s, the Rockefeller Foundation initiated support for research on diseases of the nervous system. As Alan Gregg encouraged the idea of the formation of a neurological institute, New York, Boston, and Montreal were considered, with a resulting early commitment to Penfield and McGill.

In Boston, Gregg began direct negotiations with Stanley Cobb, who had been born in 1887. He had a lifelong serious stutter that likely led him toward the study of diseases of the brain after graduation from Harvard College and Harvard Medical School. After completing residency at Johns Hopkins, he accepted a position in 1919 at Harvard to teach neurology. With an interest in epilepsy (like Penfield), the Rockefeller Foundation supported Cobb for two years of training in Europe. On return from Europe, he was appointed as the Bullard Professor of Neuropathology at Harvard Medical School, with instructions to develop a neurological unit at Boston City Hospital, which had the impact of shifting a portion of the focus of brain research from Massachusetts General to Boston City.

Ten years later, Massachusetts General recruited Cobb to establish a new department of psychiatry, with the title of psychiatrist-in-chief and a commission to focus on understanding mental illness in the context of a general hospital with close links to medicine, neurology, and neurosurgery. This time the Rockefeller Foundation had a role granting money to Cobb and Massachusetts General for the revolutionary concept of integrated psychiatric care. McLean Hospital, affiliated with Massachusetts General Hospital as it had been since opening in 1818, and Harvard Medical School continued to treat chronic forms of mental illness in a pastoral setting. Cobb wanted to address diseases of the nervous system with updated techniques and research studies available in a fully equipped academic setting with access to biochemistry, imaging, and electrophysiological studies. But he never removed himself from a commitment to the relevant areas of established psychiatry.

Cobb and many of the faculty in the department underwent psychoanalysis to give themselves a degree of credibility in the Boston medical community. In 1934, he helped organize the Boston Psychoanalytic Institute. Many of the graduates of the program went on to careers in psychoanalysis, giving wind to the sails of the movement that resulted in Boston becoming one of the main centers in the United States for the Freudian approach. When Carl Jung received an honorary degree from Harvard in 1936 he stayed with Cobb.

Yet Cobb was a monist: He believed in the unity of brain and mind. He valued both neuroanatomy and psychoanalysis. He wrote; "No biological process takes place without change of structure.

Whenever the brain functions, there is organic change. The brain is the organ of the mind. Therefore, all function is organic, and mind and body are one."

In 1940, Cobb published an account in the Lowell Lectures entitled "Borderlands of Psychiatry," a classic that remains an incredible description of the disorders that frame the edges of neurology and psychiatry, with a strong bias—deservedly—toward the notion that the brain is the seat of many poorly understood and often stigmatized disorders. His work led to his often-designated role in "the formation of biological psychiatry."

Under Stanley Cobb's guidance, the Harvard Neurological Unit at Boston City emerged in the 1930s and 1940s as a preeminent location for neurological research in the United States.

Derek Denny-Brown

Soon after the departure of Stanley Cobb, the dean of Harvard Medical School sought to address the leadership void in the neurological unit at Boston City Hospital. With advice from Gregg and following an international search, Derek Denny-Brown, a New Zealander, was appointed—only to be diverted by draft into the British Navy not long after arrival in Boston. He was appointed the James Jackson Putnam Professor of Neurology with the understanding that he would begin after release from military service, which occurred in 1941. He served in this role until retirement in 1972.

The unit was under the jurisdiction of Harvard Medical School until the mid-1970s, and graduates of the program became part of the shuffle around the Boston neurological scene, with impacts on neurological appointments elsewhere.

Among those who were at Boston City, Raymond Adams became chief of Neurology at Massachusetts General in 1951; Joseph M. Foley moved to Cleveland (where I trained) in 1961; H. Richard Tyler became chief at Brigham and Women's Hospital in 1954, and Norman Geschwind moved to Beth Israel Hospital in 1975 as Harvard Medical School's James Jackson Putnam Professor of Neurology, a title he had received while still at Boston City Hospital upon the retirement of Denny-Brown.

After the war, Penfield attempted to recruit Raymond Adams from Boston City Hospital to head neurology at the Montreal Neurological Institute but was unsuccessful. The leaders who led the efforts there were recruited from Montreal General, first Francis McNaughton, then later Preston Robb. After the latter's retirement in 1976, the post went to me, and I remained there for two years before recruitment away to Massachusetts General and Harvard Medical School as Bullard Professor of Neurology.

Charles Miller Fisher

Charles Miller Fisher was born in 1913 in Waterloo, Ontario, then with a population of about 45,000. Fisher's father George and mother Frieda had nine children. His mother died while giving birth to her tenth child when Fisher was 11 years old. According to one account, he and his siblings "were mostly raised by two Mennonite sisters who were housemaids and lived with the family."

Fisher attended public high school in Waterloo and was awarded a scholarship to the University of Toronto. After premed and medical school, he took an internship in Detroit. He married Doris

Stiefelmeyer, a high school acquaintance, in Montreal in 1939. From Detroit, Fisher moved to Montreal to train in internal medicine, and when the war began, enlisted in the Royal Navy. The war was hard on Fisher, with a period of four years of imprisonment under the Nazis, although his later recounting of it showed no lament or self-pity.

After the war, he returned to Canada in 1944 to rejoin his wife Doris and daughter Elizabeth, who was born while he was serving in the Navy. After a debriefing and reentry to Canadian medicine in Halifax, Nova Scotia, he chose Montreal for further postgraduate training and became enamored of the advances in neurology and neurosurgery occurring under Penfield's group at the Montreal Neurological Institute. Discarding earlier interests in diabetes and metabolic disorders, he began neurological training in 1945.

Following the suggestion of Penfield, Fisher chose to undertake postdoctoral work at Boston City Hospital with Denny-Brown. He returned to Montreal and worked at Montreal General for nearly a decade before relocation to Boston to work with Raymond Adams.

Fisher commented that he thought Denny-Brown and Adams were among the very few neurologists who "knew everything."

Conclusion

The events of the first half of the 20th century established the key academic structures at Montreal General and Massachusetts General that would lead to some remarkable advances in the clinical neurosciences over the next 50 years, as described in the next chapter.

CHAPTER FOUR

1950–2000: Emergence of Neurology-Based Neuroscience and Neurogenetics

Introduction

On graduation from medical school in Edmonton in 1962, my interests focused on specialization in neurology. I undertook a careful assessment of opportunities for training in Canada, Great Britain, and the United States. In Canada, the obvious consideration was the Montreal Neurological Institute, but I was told that although preeminent in neurosurgery under Wilder Penfield, neurology was less distinguished academically and served primarily as the handmaiden to the surgeons, with a major focus on epilepsy. The National Hospital for Neurology and Neurosurgery in London was the foremost English-speaking site in Europe, and my neurology mentor in medical school, George Monckton, had trained there. But I sensed it too was falling behind some of the extraordinary work ongoing in the United States. In the U.S., I considered the programs at Minnesota (with Abe Baker), Michigan (with Russel DeYoung), New York Presbyterian (under Houston Merritt), and Boston with two major programs, one at Boston City Hospital (with Derek Denny-Brown) and the other at Massachusetts General (under Raymond Adams). My application to Massachusetts General was unsuccessful. It was during a visit to Cleveland in 1963, aligned with a family vacation with my wife's parents, who lived east of Cleveland, that I met Joseph M. Foley, whose demeanor and enthusiastic introduction to the opportunities in neurology provided the answer I was seeking.

I began training in 1964. My intrigue with Cleveland for neurology training was strengthened as I became acquainted with the excellent group of junior faculty members Foley had recruited, many of them coming along with him from Boston.

Over time as I completed training in Cleveland and graduate school in Rochester, I came to realize (when I accepted a position at McGill in 1970) that there was an incredible linkage in the evolution of neurology during the period of 1950–2000 among the triad of clinical and research enterprises in Boston, Cleveland, and Montreal. This was one of the unique connections in neurology on the continent and formed a sustained connection between the two countries. Biased as my perspective is, it is fascinating to assess the various interactions, recruitments, and interrelationships that were forged among these three places, which will be a focus of my description of the evolution of major advances in neurology during this period.

The Future Takes Shape

At the beginning of the second half of the 20th century, numerous major developments were afoot at both Montreal General and Massachusetts General. A few are highlighted below.

- In Boston, Raymond Adams is appointed in 1951 as Bullard Professor of Neuropathology at Harvard Medical School and chief of the Neurology Service at Massachusetts General. After considering an offer from Wilder Penfield for a similar appointment at the Montreal Neurological Institute, he turns it down in favor of the Boston offer. (Four chiefs of service would serve at Massachusetts General during the 50-year period: Raymond Adams (1951–1978), Joseph Martin (1978–1989), Verne Caviness (1989–1991), and Anne Young (1991–2000).
- In Montreal, plans unfold for building a new, state-of-the-art hospital on Cedar Avenue on the southeastern edge of Mount Royal. It opens in 1955, with the cornerstone from the Dorchester Street hospital placed into the new. The new hospital would incorporate a university clinic of laboratories for medical research.
- In 1955, C. Miller Fisher leaves Montreal General to join the staff at Massachusetts General, where he is part of a growing clinical and research enterprise that includes another Canadian, Maurice Victor.
- A search begins at Montreal General for new chiefs of Neurology and Neurosurgery, with appointment in 1963 of Donald Baxter and Joseph Stratford, respectively, to these positions. The recruitment is led by new Chair of Medicine Douglas Cameron and Chief of Surgery H. Rocke Robertson.
- The first major new research appointment in Neurology at Montreal General is the recruitment in 1964 of Albert Aguayo, who was completing training in the laboratory of Jerzy Olszewski at the University of Toronto. His appointment would herald establishment of a new academic clinical and research enterprise that would be among the best in Canada over the next 40 years. Leaders of the division over this period are Donald Baxter (1963–1979), Albert Aguayo (1979–1990), and Garth Bray (1990–2000).
- The Montreal Neurological Institute embraces a world-renowned effort in a number of clinical and research areas, establishing basic science divisions with units of neurophysiology (Herbert Jasper), systems neuroscience (Peter Gloor), psychology (Brenda Milner), neurochemistry (Leon Wolfe), and neuromuscular disorders (George Karpati).

New Leadership at Montreal General and Massachusetts General

In 1951, when Raymond Adams was appointed neurologist-in-chief at Massachusetts General and Bullard Professor of Neuropathology at Harvard Medical School, the staff he led amounted to a handful of people. During his nearly 30-year tenure, he would expand the department and establish one of the first large programs in pediatric neurology in the U.S. He directed clinical

care and research focused on the development of clinical-pathological correlates of diseases of the central and peripheral nervous systems and transformed the program into one that was internationally recognized and served as a preeminent training ground for leaders in neurology in the second half of the 20th century.

As Adams was taking the helm in Boston, Francis McNaughton, who had been promoted to Neurologist at Montreal General following the death of Fred Mackay in 1947, was wrapping up his limited tenure there. Among other accomplishments, McNaughton convinced the hospital's medical board that there should be a separate Department of Neurology and Neurosurgery (as was the case at the Montreal Neurological Institute.) McNaughton was Neurologist and Harold Elliot Neurosurgeon to the hospital. Neurology was assigned five beds on a small ward shared with Psychiatry (which had become a separate specialty at Montreal General in 1948); neurosurgery patients were cared for on surgical wards of the hospital.

After the departure of McNaughton in 1951, Harold Elliot became head of the Department of Neurology and Neurosurgery, with Preston Robb as Neurologist to the hospital. The other neurologists were Norman Viner, William Tatlow (who had trained at the National Hospital for Neurology and Neurosurgery), David Howell, and C. Miller Fisher. Fisher became interested in patients with stroke and began a diligent pursuit of autopsy findings after stroke, leading to his first major contribution, showing the importance of carotid artery atherosclerosis in the pathogenesis of stroke. He coined the term transient ischemic attacks (TIAs) and described the visual loss as "like a shade coming down over the eyes."

Due to retirements and departures, neurology at Montreal General lacked stability during the 1950s: Norman Viner retired in 1952; in 1954, Preston Robb and Bernard Graham left for positions at the Montreal Neurological Institute and Montreal Neurological Hospital, respectively; C. Miller Fisher accepted a position at Massachusetts General. By the end of the decade, the only neurologists at Montreal General were William Tatlow, appointed in 1952 and in charge of the EEG laboratory, and David Howell, appointed in 1954 as a neurologist and neuropathologist.

When Montreal General moved to its new location on Cedar Avenue in 1955, the Department of Neurology and Neurosurgery was assigned its own ward of 35 beds. Because these beds were not fully utilized, Neurology and Neurosurgery were each assigned 10 beds on separate wards. When Elliott objected to this arrangement, a committee of the medical board recommended the dissolution of the Department of Neurology and Neurosurgery and the creation of Divisions of Neurology and of Neurosurgery in the Departments of Medicine and of Surgery, respectively. This new administrative arrangement came into effect in 1961. William Tatlow was named interim director of the Division of Neurology until 1963, when Donald Baxter was recruited. Harold Elliott remained director of the Division of Neurosurgery until 1962, when he was replaced by Joseph Stratford.

Efforts to introduce neurological research at Montreal General had been made by Preston Robb during his tenure. He was told by a senior administrator that "it was not in the tradition of the hospital," and "research was the responsibility of the university." This attitude changed dramatically with the appointments of Douglas Cameron as chief of Medicine and H. Rocke Robertson as head of Surgery.

Five Decades of Key Contributors

A panoply of individuals had the energy and vision to develop programs in education, clinical work, and research in neurology during the period between 1950 and 2000. This account knits together some of the many relationships that emerged among centers in Boston, Cleveland, and Montreal.

Joseph M. Foley

Joseph Foley grew up in an Irish enclave in the Dorchester area of Boston. His father was a garbage collector and his mother stayed home to raise the family. Although uneducated herself, she insisted her children attend college.

After undergraduate work at the College of the Holy Cross in nearby Worcester, Foley was among the few Irish accepted to Harvard Medical School, graduating in 1941. His internship at Bellevue Hospital in New York was interrupted by draft into service in the Medical Corps of the U.S. Navy. He received a Bronze Star and the French Croix de Guerre for his heroism overseas in the D-Day invasion in 1944.

After his service in the Navy, he returned to Harvard Medical School and to Boston City Hospital, assuming the research and teaching positions he held prior to the war and where he would stay for the next 13 years. He became legendary in the Denny-Brown era, serving as a foil for students and residents against the ofttimes irascible head professor. In 1961, he was named chief of the Division of Neurology in the Department of Medicine at Case Western Reserve. It would be his academic home for the next 25 years, until retirement in 1986. During his tenure, he served as president of both of the prominent neurological associations, the Academy of Neurology (1963–1965) and the American Neurological Association (1974–1975).

At his death in 2012 at age 96, the dean at Case Western noted, “Dr. Foley played a key role in shaping the legacy that is Case Western Reserve University School of Medicine. In his role as emeritus professor of neurology and director of the Division of Neurology in the Department of Medicine at Case Western Reserve and University Hospitals, he taught generations of physicians, cared for countless patients, and graced our community with both his humor and compassion.”

For those who knew him well, as I did, he was a generational epitome of the physician-scientist, a beloved teacher, and mentor. He insisted when I interviewed for the residency in Cleveland that I cross town to the Metropolitan Hospital to meet Maurice Victor.

Maurice Victor

Among those at Massachusetts General in the 1950s was a brilliant Canadian doctor from Winnipeg, Maurice Victor, whose work on neurological complications of alcohol became legendary. Victor, the son of immigrant parents from the region of what is now Belarus and Lithuania, was born in Saskatchewan, grew up in Winnipeg, and received both his undergraduate (1938) and medical degrees (1943) from the University of Manitoba.

He was drafted during WWII, rising to captain in the Canadian army, with decoration for service in Europe. He immigrated to the United States to train in hematology and neurology and was recruited by Raymond Adams to Massachusetts General in 1955. Victor and his spouse and academic colleague, Betty Banker, a neuropathologist who trained with Denny-Brown at Boston City Hospital, would move to Cleveland in 1962 to form a new neurology department at the Metropolitan Hospital, affiliated with Case Western Reserve. He led a residency training program separate from that created by Foley across town, but Foley worked closely with him and insisted that I pursue my interest in neuropathology with Betty Banker, a move that proved incredibly important.

Among the trainees in the program at the Metropolitan Hospital was Garth Bray, who also came from the University of Manitoba. Garth Bray, Donald Lawrence (see below), and I would all spend time in Cleveland, each of us later joining the new activities that Albert Aquayo and Donald Baxter were putting in place at Montreal General in the period between 1969 and 1976.

Adams and Victor later worked together to create the leading textbook, *Principles of Neurology*, now in its tenth edition. Victor retired in 1986 and died of prostatic cancer in 2001, at age 81.

Donald Baxter

Donald Baxter grew up in Ontario and graduated from medical school at Queens University in Kingston, Ontario, in 1951. After a one-year internship at the Kingston General Hospital, Baxter spent the following year as a research fellow at the Montreal Neurological Institute, supervised by George Olszewski. Based on his work with Olszewski, he received an MSc from McGill in 1953. This research work resulted in the publication of *Cytoarchitecture of the Human Brainstem*, which became a standard work in the field of neurology and brain research.

Following a year as an assistant resident in medicine at the Kingston General Hospital, Baxter joined the Denny-Brown group at Boston City Hospital to work with Foley in neuropathology and to complete a neurology residency (1955–1957). There he met and became a lifelong friend of Betty Banker.

Baxter returned to Canada in 1957 to join the Department of Neurology and Neurosurgery at the University of Saskatchewan, until leaving for Temple University in Philadelphia in 1962. The following year, he was recruited to Montreal General as director of the Division of Neurology. Highly respected among his peers, he was elected president of the Canadian Neurological Association (1969–1970).

Baxter's vision for the Montreal General Division of Neurology, composed of "physician-scientists," was encouraged by the chiefs of Medicine and Surgery. He recruited, supported, and encouraged promotion of a series of new investigators over the next 16 years until his move in 1979 to the Montreal Neurological Institute as chair of the McGill Department of Neurology and Neurosurgery and as neurologist-in-chief. Baxter was director of the institute from 1984 to 1992. Recognized for his distinguished work, he was named an officer of the Order of Canada in 1995**.**

Donald Lawrence

Donald Lawrence was born in Kingston, Ontario, Canada, and after graduation from medical school at McGill in 1957 and two years of internship and residency at Montreal General, he arrived in Boston to train in neurology with Simeon Locke at the Deaconess Hospital. It was for him a remarkable experience, with a chance to visit Boston City Hospital for rounds with Derek Denny-Brown, and Massachusetts General for rounds with Maurice Victor, C. Miller Fisher, and Raymond Adams.

In 1962, the acquaintances in Boston who had moved to Cleveland—Joseph Foley, Maurice Victor, and Betty Banker—proved a strong incentive for Lawrence to choose a laboratory at Case Western Reserve for an NIH-funded fellowship in anatomy and physiology with Heinrichs Kuypers. Lawrence later followed Kuypers to the Netherlands in a junior faculty position for four years, returning to Montreal to join the Division of Neurology at Montreal General in 1972. He resumed the practice of neurology and became a renowned neurology professor, for many years working as the lead organizer and tutor of the second-year medical school course in neuroscience and neurology. He later assumed the important role as head of the admissions committee of the Faculty of Medicine.

Albert Aguayo

Albert Aguayo hailed from Argentina, graduating from medical school at the National University of Cordoba in 1959. He immigrated to Canada for a rotating internship at Port Arthur General Hospital in Thunder Bay and continued training in neurology under J.C. Richardson at the University of Toronto, where he would spend time in neuropathology with Jerzy Olszewski. In 1964, he was recruited by Donald Baxter to complete a final year of residency at Montreal General, and following a McLaughlin Fellowship that took him to England to work with John Walton, he returned to McGill as an assistant professor of neurology and neurosurgery in 1967. He became a key figure in the organization and planning of a new era in neurology at Montreal General.

Aguayo went on to succeed Donald Baxter as head of the Division of Neurology after Baxter moved to the Montreal Neurological Institute in 1979. Aguayo became the founding director in 1985 of McGill University's Center for Research in Neuroscience. The recognition given to the commitment by McGill opened up additional funding opportunities from Quebec and the federal government. Later he developed and supervised a Canada-wide Neural Regeneration and Functional Recovery Network (subsequently called the Neuroscience Network of the federal government's Centers of Excellence program).

Aguayo is best known for his revolutionary research that demonstrated that nerve fibers in the central nervous system are capable, when supported by a bridge of tissue from a peripheral nerve, to regenerate with fibers growing across the severed portion of the optic pathway. This observation established a new frontier of research and inquiry into the capacity of regeneration in the central nervous system.

Aguayo's finding completely revolutionized research into regenerative medicine. Although he was also highly skilled in clinical neurology, it was his broad-based knowledge and familiarity with the basic science communities in North America and Europe that gave him leverage

to recruit and lead an innovative group at McGill, which became renowned for leadership in neurological education and research. He served a four-year term as director of the International Brain Research Organization.

Aguayo was subsequently awarded the Canada Gairdner Prize (1988) for the discovery of the regrowth of neural connections in injured mammalian central nervous systems. He was appointed a fellow of the Royal Society of Canada in 1984 and elected as an officer of the Order of Canada in 1993.

A 2011 inductee into the Canadian Medical Hall of Fame, Aguayo's achievements were summarized by the group this way:

> *"As a highly-skilled researcher and visionary thinker, Dr. Aguayo's innovative experiments between 1975 and 1985 revolutionized regenerative neuroscience, questioning the central dogma of the time that neurons could not regenerate. By utilizing some of the most advanced anatomical and physiological techniques then available, his team was the first to show that nerve fibers and function in the central nervous system of adult mammals could be restored after injury. Neural repair today stands in a prominent position due to his exceptional research."*

Garth Bray

The last recruit to the Montreal General Division of Neurology in the 1960s was Garth Bray, a graduate of the University of Manitoba (1961) who had spent four years at the Metropolitan Hospital (affiliated with Case-Western University) in Cleveland with Maurice Victor and Betty Banker. His first two years there were devoted to clinical training in neurology, supervised by Maurice Victor; the third year involved routine neuropathology under Betty Banker's direction. The fourth year was devoted to electron microscopy of dystrophic muscle, the main research interest of Banker.

Bray returned briefly to Winnipeg but was soon enticed by Donald Baxter and Albert Aguayo to come to Montreal. His collaboration with Aguayo became one of extraordinary benefit to both. They initially investigated the cellular basis of hereditary neuropathies in humans and in mice. In subsequent work with Aguayo and research fellows, Bray contributed to electron microscopic studies of synapse formation by regenerated central nervous system neurons.

In 1990, Garth Bray succeeded Albert Aguayo as director of the Montreal General Hospital Division of Neurology. As a clinical educator, Bray worked with the Canadian Neurological Sciences Federation to ensure that advances in the emerging field of molecular biology were introduced into educational activities of the federation.

Michael Rasminsky

Michael Rasminsky joined the Division of Neurology at Montreal General in 1973. It was a critical appointment that brought new experience in electrophysiological approaches in the evaluation of abnormalities in experimental peripheral neuropathy. He had attended medical school at

Harvard and completed neurology training at the Albert Einstein College of Medicine in New York. After completion of graduate work (and a PhD) with Tom Sears at the London National Hospital for Neurology and Neurosurgery, where he developed a technique to record conduction patterns in single nerve fibers in laboratory animals, he chose Montreal General for a faculty appointment and began a collaboration with Albert Aguayo and Garth Bray in experimental studies of demyelination and neural regeneration.

For several years during this period, Rasminsky, Aguayo, and Bray teamed up with Massachusetts General clinician-scientists Robert Young and Bhagwan Shahani to sponsor an annual continuing medical education course on neuromuscular diseases, with alternated venues between Montreal and Boston.

Leo Renaud

Leo Renaud trained in neurology, neuromuscular diseases, and electromyography. After graduating from medical school, he worked at the Montreal Neurologic Institute, receiving a PhD derived from electrophysiological studies of the limbic system with Peter Gloor. When he joined the faculty at Montreal General, he brought incredible new techniques for the analysis of hypothalamic-pituitary regulation and together with Paul Brazeau performed the first iontophoretic experiments demonstrating that neuropeptides have electrophysiological excitation capacity. He later moved to the University of Ottawa to lead a distinguished group of scientists at the Loeb Institute.

Leo's appointment would be critical in my own work, extending physiological studies on growth hormone regulation to an examination of the electrophysiological actions of neuropeptides in regulating excitability of neuronal firing in the central nervous system. I believe the work we carried out with Paul Brazeau, who provided the recently identified hypothalamic regulatory peptides somatostatin and gonadotropin-releasing hormone, would establish the recognition required for consideration and approval of an appointment at Massachusetts General Hospital and Harvard Medical School.

Richard Murphy

Richard Murphy grew up in Massachusetts and earned his PhD at Rutgers in 1974. He established his research career at Massachusetts General, where he undertook a post-doc with Barry Arnason and Michael Young. Murphy would go on to be appointed assistant professor of cell biology and anatomy at Harvard Medical School and then associate professor in 1981 before being recruited to the University of Alberta in 1986 as chair of the Department of Anatomy. In 1992, he crossed Canada to become director of the Montreal Neurological Institute, succeeding Donald Baxter and becoming the first research scientist to hold the post. He strengthened the institute's molecular and cellular neuroscience capacity and hired a score of outstanding young scientists. In 2000, he was recruited away by the Salk Institute in La Jolla, becoming the president and CEO until his retirement and return to the Boston area in 2007.

Jack Antel

Another Canadian, Jack Antel grew up in Winnipeg, graduated from medical school at the University of Manitoba, and arrived at Montreal General in 1969 for internship and a year of medical residency. Following recommendations from Garth Bray, he chose Cleveland over the Mayo Clinic in 1971 for a neurology residency with Maurice Victor. And after seeking advice from neuropathologist Betty Banker, he chose the growing field of neuroimmunology for postdoctoral training, joining Barry Arnason at Massachusetts General in 1974 and following him to the University of Chicago in 1976, before returning to Montreal a decade later as neurologist-in-chief at the Montreal Neurological Institute. His recruitment there was facilitated by Donald Baxter, who was now director of the institute. Antel was chair of the McGill Department of Neurology and Neurosurgery from 1990 to 2000. As chair, he worked closely with Aquayo, Bray, Rasminsky and others at Montreal General in a combined program.

Antel established a major center of neuroimmunology at the Montreal Neurological Institute, developing collaborations with other investigators at Montreal General and McGill and receiving worldwide acclaim for advances in understanding the basis of autoimmune disorders like multiple sclerosis. In the 1990s, Antel worked closely with Montreal Neurological Institute Director Richard Murphy in actively recruiting basic scientists to appointments in the department.

In the ensuing years, Antel's close affinity with Massachusetts General led to research collaborations with Steve Hauser at the University of California, San Francisco and later in the training of Amit Bar-Or, a graduate of the McGill School of Medicine.

Amit Bar-Or

Amit Bar-Or's early years included time spent in Israel, the U.S., and Canada. During medical school at McGill, a neurology rotation with Michael Rasminsky at Montreal General and a lab-based experience with Jack Antel and Wee Yong at the Montreal Neurological Institute hooked him on the field of neuroimmunology. Encouraged by Antel, Rasminsky, and Bray, Bar-Or went to Boston, where he completed a medicine internship and neurology residency training with mentors that included C. Miller Fisher and Raymond Adams at Massachusetts General Hospital. He maintained clinical presence at Massachusetts General while completing a three-year lab-based fellowship in cellular and molecular neuroimmunology with David Hafler and Howard Weiner at the Center for Neurologic Diseases of Brigham and Women's Hospital, in an affiliation with the Massachusetts Institute of Technology.

Bar-Or then moved back to McGill and the Montreal Neurological Institute, where he enjoyed a close collaboration with Jack Antel for nearly two decades. He established a neuroimmunology lab at the institute, rising to become one of the leading international figures in translational neuroimmunology. His work contributed to elucidation of mechanisms underlying immune regulation and immune–central nervous system interactions relevant to injury and repair. In his role as associate director for translation at the Montreal Neurological Institute, Bar-Or worked with Guy Rouleau, the institute's director, until he was recruited away to the University of Pennsylvania and the Children's Hospital of Philadelphia in 2017.

Guy Rouleau

Guy Rouleau received his medical degree from the University of Ottawa in 1980. After a residency in internal medicine and neurology at Montreal General and the Montreal Neurological Hospital, he joined James Gusella (another Canadian) at Massachusetts General as a post-doc and graduate student, receiving his PhD from Harvard in 1989. Aguayo and Bray recruited him back to Montreal General to establish a center for the study of neurogenetics, with a focus on populations unique to the Quebec region.

After a time at the University of Montreal as director of the Sainte-Justine Research Center, Rouleau began his appointment as director of the Montreal Neurological Institute on January 1, 2013. Since then, he has been building a framework for the future of the institute by creating new collaborations and reinforcing the lines of communication between the bench and the bedside. He has also been a leader in the identification of genes linked to amyotrophic lateral sclerosis, epilepsy, schizophrenia, and autism. In 2012, Rouleau published a paper identifying for the first time ever a gene that causes essential tremor, the most common movement disorder.

In 2020, Rouleau received two accolades unique to Canada: the Gairdner Foundation Wightman Award for leadership in Canadian medical advances and selection as an officer of the Order of Canada.

Remarkably, of the seven heads of the Montreal Neurological Institute (Penfield, Ted Rasmussen, William Feindel, Baxter, Murphy, David Colman, and Guy Rouleau) three spent three or more years in Boston, either at Boston City or Massachusetts General Hospitals.

David Hubel

In 1981, the Nobel Prize was awarded to a scientific partnership years in the making between David Hubel and Torsten Wiesel, both at Harvard Medical School: *"For their discoveries concerning information processing in the visual system."* Hubel, a Canadian, and Wiesel, from Sweden, had worked together since their meeting in laboratories at Johns Hopkins. In 1959, they were recruited to Harvard, where Hubel remained on the faculty, moving to emeritus status in early 2000 but remaining active in teaching and research until his death at 87 in 2013.

Hubel was born in Windsor, Ontario, the grandson of parents who immigrated to Canada from Bavaria. He grew up in Montreal, graduating from McGill University, with a major in mathematics and physics and then entering medical school. David Hubel, someone I admired immensely, and I had a number of shared experiences. What follows is an excerpt from the foreword he wrote for my memoir: *Alfalfa to Ivy: Memoir of a Harvard Medical School Dean:*

> *We were both born in Canada of parents who were U.S. citizens; and so we both grew up as dual citizens, with consequent advantages and disadvantages of both citizenships—not the least being subject to military service in both countries. Both of us went to school in Canada—from elementary school through college and medical school. Elementary schools and high schools were small; we walked to our schools, which never closed because of bad weather . . . . After medical school we both did protracted residencies in neurology and in research, at starvation wages or no wages at all. We both did stints at*

the Montreal Neurological Institute (MNI) and at the Montreal General Hospital ("MGH North"), and we both ended up, finally, at Harvard. Today we are both semi-retired members of the Harvard Medical School Department of Neurobiology."

So it was an extraordinary pleasure for me to become acquainted with David when I arrived in Boston in 1978 and to be with him and Torsten when the Nobel Prize announcement was made that Monday morning in October 1981. We formed a close friendship that continued during our appointments in the Department of Neurobiology and until the time of his death from kidney failure. His office/laboratory was immediately beneath mine at Harvard in the Goldenson Building, where I could hear him as he practiced his musical pleasures on piano and violin. We consulted often on the politics and science of medical research and on the vagaries of internecine relationships between Harvard's medical school and its hospitals.

David Caplan

David Caplan was born in Ontario, Canada, and attended MIT for an undergraduate degree, followed by a PhD with Noam Chomsky. Caplan returned to his Canadian roots in Montreal and McGill for a medical degree after his father, a psychoanalyst, insisted he consider medicine and become a doctor—the only proper profession. After graduation from McGill, and an internship at Montreal General, he headed to Boston for a residency with Norman Geschwind at Boston City Hospital. With the credentials of an aphasiologist, Caplan returned to Montreal in 1982, this time to the Montreal Neurological Institute, working closely with neuropsychologists in the Department of Psychology. Although in the same institution as the renowned Brenda Milner, most of his clinical observations and research were quite distinct from hers. Six years later, he was recruited to Massachusetts General to lead the group in cognitive testing and diagnosis and management of patients with language disorders, a position he still holds today.

Boston and Montreal: 1980–2000

The last two decades of the 20th century saw the maturation of developmental and regenerative neuroscience (a focus at Montreal General) and genetic advances that extended to an ability to discern the link between genes and proteins associated with disease (at Massachusetts General).

Montreal General

During this period, research in the Center for Research in Neuroscience evolved into four major themes: Cellular and Developmental Neurobiology, Neuronal and Synaptic Signaling, Neural Regeneration, and Molecular Approaches to Neurologic Diseases. By 1995, there were 10 principal investigators, 40 graduate students, 16 post-doctoral fellows, and total funding of nearly $3 million, with lab space of over 16,000 square feet.

Massachusetts General

In the late 1970s, efforts by Marjorie Guthrie and Nancy Wexler led to government-sponsored research to establish the genetic basis of Huntington's disease. The neurology department at

Massachusetts General was one of two Centers Without Walls funded by the NIH (the other at Johns Hopkins) with a goal of emphasizing collaborative work. With familial linkage studies of families from Venezuela and the U.S., a linkage to chromosome 4 was reported in 1983, and 10 years later the genetic aberration was characterized. During this time, the work at Massachusetts General was led by a scientist, James Gusella. His undergraduate work had been at the University of Ottawa, and after completion of graduate work in David Housman's laboratory at MIT, he was recruited to head the genetic aspects of the work on Huntington's disease at Massachusetts General.

As the gene for Huntington's disease was being studied, additional development of molecular neuroscience of neurological diseases (led by Gusella and colleagues) resulted in the identification of genes for familial Alzheimer's disease (led by Gusella, Peter St. George-Hyslop, and Rudy Tanzi), amyotrophic lateral sclerosis (led by Robert Brown), and brain tumors (led by Guy Rouleau). The group was strengthened by appointment of Marcy MacDonald, another Canadian who had attended the University of Ottawa with Gusella and Rouleau. It was Rouleau's leadership of studies of the genetic basis of disorders in the intermarried and consanguineous families of French-Canadian descent that resulted in his receiving the previously mentioned 2020 Gairdner Foundation Wightman Award, the most distinguished award for Canadian national leadership in health.

Peter St. George-Hyslop, also a Canadian, discovered the genetic identity of two genes, presenilin 1 and 2, which cause early-onset Alzheimer's disease; this work led to new hypotheses about the role of membrane proteins in neurodegeneration and neuroinflammation. After five years as a post-doctoral researcher at Massachusetts General in Boston, he returned to Canada to a distinguished career in Alzheimer's research at the University of Toronto. In recent years, he has also had appointment in the faculty of medical sciences at the University of Cambridge, England.

Hospital Mergers in Montreal and Boston

In an extraordinary manifestation of the impact of healthcare reforms and mergers directed by an effort to promote efficiency and reduce costs, both Montreal General and Massachusetts General entered into formal discussions in the 1990s to piece together an entirely new administrative governance structure. In Montreal, the university led planning with the province of Quebec to establish in 1997 the McGill University Medical Center (MUHC), which was delayed in construction for over 15 years, eventually opening in 2015. The Royal Victoria closed, the Children's Hospital relocated to MUHC, and Montreal General remained as a stroke and trauma center. The Montreal Neurologic Institute maintained a separate campus adjacent to the McGill stadium on the edge of the main university campus, with uncertain plans about the timing for a relocation to the main MUHC site.

In Boston, negotiations between hospital administrators and hospital boards forged an agreement (without any direct participation by Harvard) to form a partnership between Brigham and Women's Hospital and Massachusetts General Hospital in 1994 to create Partners HealthCare (which changed its name to Mass General Brigham in 2020). At Harvard Medical School, the merger created a tempest of other hospital mergers, with Beth Israel Hospital and

the Deaconess Hospital forming Beth Israel Deaconess Medical Center—later to be joined by the Lahey Clinic network to form Beth Israel Lahey Health. Boston Children's Hospital remains independent. The activities made the relationships in teaching, clinical care, and research across the Harvard-affiliated hospitals a major challenge for the dean at Harvard Medical School.

Union of Professional Sports and the Two Hospitals

For sports enthusiasts who follow professional hockey, the century-long rivalry between the Montreal Canadiens and Boston Bruins is legendary. Les Canadiens, established as a hockey franchise in 1909, has been owned and supported by the Molson family from the beginning. Not surprisingly, medical care of the team became a shared responsibility between the owners (who remain attached to many aspects of Montreal General Hospital governance and leadership) and the medical staff, beginning with E. MacKay in 1950. He was followed by Montreal General internist Doug Kinnear and surgeon David Mulder, also affiliated with Montreal General for many years.

In recent decades the same relationship between professional sports teams and Massachusetts General evolved with establishment of sports medicine under orthopedic surgeon Bert Zarins (beginning in 1976) along with Dinesh Patel. In 1976, Zarins became the team physician of the Boston Bruins (followed in 1982 by appointment as team physician of the New England Patriots), an arrangement that continued into the 21st century. An evolving sports clinic network led to care of all of the professional teams, including the Boston Red Sox and the New England Revolution (soccer).

Since 1975 the Boston Bruins franchise has been owned by the Jacobs family, which included Larry Jacobs, a distinguished University of Buffalo neurologist with an interest in multiple sclerosis, who was an early advocate for treatment of the disease with interferons. Recently the family contributed $30 million to rename the medical school at Buffalo as the Jacobs School of Medicine and Biomedical Sciences.

In Montreal and Boston, the link between sports and medicine contributed to the advancement of both.

ACKNOWLEDGEMENTS

I am especially grateful to Patricia Cleary for assistance in the editing of this manuscript. Thanks are also extended to Garth Bray, Tim Johnson, and Fred Lovejoy for reading and commenting on the text.

W. Bull and M. Bull. *Something in the Ether: A Bicentennial History of Massachusetts General Hospital, 1811–2011* (Memoirs Unlimited, 2011).

J. Hanaway and J.H. Burgess, Eds. *The General: A History of the Montreal General Hospital* (McGill-Queens University Press, 2016).