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Neuropathology in Canada: The First One Hundred Years

Marc R. Del Bigio 1

N. Barry Rewcastle 2

1. Department of Pathology, University of Manitoba, Winnipeg, Canada

2. Retired; formerly of Department of Pathology & Laboratory Medicine, University of Calgary, Calgary, Canada

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Correspondence to:

Marc R. Del Bigio, MD PhD FRCPC

Department of Pathology, University of Manitoba

401 Brodie Centre, 715 McDermot Avenue

Winnipeg MB R3E 3P5 Canada

Phone (204) 789-3378

Fax (204) 789-3931

Email [marc.delbigio@umanitoba.ca](mailto:marc.delbigio@umanitoba.ca)

## **Abstract**

We describe the evolution of neuropathology in Canada, beginning with William Osler who began working in Montréal in 1874 and finishing with the major period of expansion in the 1970s. Organized services began in the 1930s, in Montréal with the neurosurgeons Wilder Penfield and William Cone, and in Toronto with Eric Linell and Mary Tom, who both began their careers as neuroanatomists. Jerzy Olszewski and Gordon Mathieson, who trained in Montréal and Toronto, drove the creation of the Canadian Association of Neuropathologists in 1960. Training guided by the Royal College of Physicians and Surgeons of Canada was formalized in 1965, with the first certifying examination in 1968 and the subsequent creation of formal structured training programs. The number of neuropathologists in Canada increased rapidly through the 1960s and 1970s, with individuals coming from both clinical neuroscience and anatomic pathology backgrounds, a pattern that persists to the present day.

*"Neuropathology is the study of anything that interests a Neuropathologist"*

Jerzy Olszewski, 1963 (attributed by John Kaufmann)

## **Introduction**

In recognition of the fiftieth anniversary of the Canadian Association of Neuropathologists (CANP) in 2010, we offer a concise history of the profession in Canada. Herein we highlight the personalities involved in the development of neuropathology, summarize the contributions of the early practitioners, emphasize influences of the other clinical and basic neurosciences, and describe the formalization of the training of neuropathologists in Canada. In so doing, we document the evolution of this specialty to its present place in Canadian medicine. Our intent is to cover the first 100 years of neuropathology in Canada, beginning with Sir William Osler's interests in autopsy pathology during the 1870's and ending with individuals who began their careers before the mid-1970s, most of whom are now either retired or deceased. Table 1 summarizes the provision of neuropathology services across Canada beginning with Osler to the present day. General histories of neuropathology and its relationships to psychiatry, neurology, the basic neurosciences, and the other branches of laboratory medicine have previously been published (1-3), as have histories of the clinical neurosciences in Canada (4).

## **The Earliest Practitioners of Neuropathology in Canada**

The first neuropathologists in Canada obtained their pathology and neuroscience training in Europe. The earliest documented neuropathology activities in Canada were sporadic and transient. The individuals gained considerable fame for aspects of medicine other than neuropathology, perhaps because physicians were more broadly trained in past times.

**William B. Osler** (1849–1919) (later Sir William) was born at Bond Head, Ontario, a tiny community of a few hundred people on the south side of Lake Simcoe, north of Toronto. Osler was considered by some to be "Canada's foremost pathologist of the nineteenth century" (5). He pursued preclinical studies in Toronto, a city that had at the time three independent and very antagonistic medical schools (6). Thus, he was encouraged to move to Montréal for clinical studies. Harvey Cushing considered Montréal at that time to rival only Philadelphia for excellence in clinical teaching in North America (7). Osler received his MD degree from McGill University in 1872. The following year was spent in Berlin under the instruction of the famous pathologist Rudolf Virchow. He returned to the Montreal General Hospital in 1874. During the following 10 years he performed almost 1000 autopsies

(7-9) (Figure 1). His increasing interest in localization of brain functions and psychopathology prompted him to secure the brains of criminals. He went to extreme lengths to obtain some specimens, on occasion sending assistants to attend executions and perform brain removals on the spot including one “in an out-of-the-way place and in the dead of a Canadian winter with the temperature 10° [Fahrenheit] below zero” (7, 10). Osler’s activities in neuropathology continued after his move to Philadelphia in 1884. Almost 200 of his approximately 1400 published works concerned neurological disorders, the details often derived from autopsies he had performed. Many techniques Osler used for studying histology were learned during visits to the laboratories of prominent European neuropathologists (9, 11, 12). Osler’s attitudes had a profound effect on the development of the profession of neurosurgery through his friendships with Victor Horsley and Harvey Cushing. Wilder Penfield (see below), while on a Rhodes scholarship, met Osler in Oxford in 1915 and the first autopsy that Penfield performed was under Osler’s direction (9). Both Cushing and Penfield declared their intellectual and inspirational debt to Osler (12). Osler was appointed Professor of Medicine at Johns Hopkins University in 1888 and Regis Professor at Oxford University in 1904. He achieved worldwide fame for his contributions to medical education. Osler died in 1919 in Oxford England. He had requested that his brain go to the Wistar Institute in Philadelphia, but only the gross appearance of his brain was documented. In 1959 Penfield had Osler’s brain repatriated to Montréal, where a complete examination was performed by Gordon Mathieson; nothing extraordinary was found (13).

**Ernest Jones** (1879-1958) was born in Gowerton, Wales. He obtained MB and BS degrees from the University of London in 1901. He gained his first experience in pathology as a house physician under John Rose Bradford. Following his decision to become a neurologist, Jones subsequently received training under Victor Horsley and William Gowers at the National Hospital for Nervous Diseases in London (euphemistically known as Queen Square, and now called the National Hospital for Neurology and Neurosurgery) where he also conducted neuropathology research on rabies-infected brains. Among several postings, he served as pathologist at the West End Hospital for Nervous Diseases and lecturer in practical neurology at the London School of Clinical Medicine. In 1907 Jones went to Munich for post-graduate study in neurology, studying cortical histology under Alois Alzheimer. He also studied psychiatry and became acquainted with the writings of Sigmund Freud (14, 15). Some writers indicate that Jones’ arrogance and poor judgment made it difficult for him to secure a neurology posting in England (16). He therefore moved to Toronto in 1908 where, with recommendation from William Osler, he secured several appointments including Demonstrator in Pathology and Medicine at the University of

Toronto, pathologist at the Toronto Hospital for the Insane, and director of the outpatient clinic at the Toronto Asylum, which was under the direction of the psychiatrist Charles K. Clarke (17-20). In his biography, Jones wrote, “He [Clarke] possessed little scientific knowledge, but his heart was set right” and “I became the Lord High Everything Else. It was my duty to conduct the pathological examinations in a little laboratory we started, to carry out psychological research ...” (15). While in Toronto, Jones authored more than 70 papers, including 10 neuropathology articles, most concerning the pathology and cerebrospinal cytology related to syphilis (21). However, influenced strongly by Freud, Jones’ efforts became increasingly directed toward psychoanalysis. He helped found the American Psychoanalytical Association in 1911. In 1913 Jones returned to England, about which he wrote, “I was fully aware of the hopelessness of pursuing any further academic career there”, and practiced neuropathology no more. He nevertheless gained high international standing and many honours in the psychoanalytical community (14, 17, 22).

**William Boyd** (1885-1979) was born in Portsoy Scotland. He received his MB ChB degrees from the University of Edinburgh in 1908. From 1909-11 he worked as physician at the Kingsway Hospital, an asylum institute, in Derby England. During this time he conducted autopsies and performed the work on which he based his MD thesis, the subject of which was cerebrospinal fluid changes in neurologic diseases. In 1912 he received diplomas in Psychiatry and Psychological Medicine, following which he became a pathologist at the Winwick Hospital, a mental institute. The next year he moved to the Wolverhampton Royal Infirmary in England. Boyd was lured to Winnipeg in 1915 by his close friend Alexander Gibson, who had been appointed professor of Anatomy two years earlier (23, 24). Boyd’s first book “Physiology and Pathology of the Cerebrospinal Fluid”, published in 1920 (25), was the world’s first work dedicated to CSF cytology; it predated that of J. Godwin Greenfield’s by 5 years (26). While in Winnipeg (Figure 2), Boyd wrote an excellent and detailed account of the neuropathology of encephalitis lethargica, which occurred during the influenza pandemic of 1918 (27) as well as a lesser paper concerning brain tumours (28). He remained as professor of pathology at the University of Manitoba until 1937, during which time he wrote the early editions of three separate textbooks on pathology. These books emphasized relationships between morbid anatomy, disturbed function, and clinical symptoms. The success of the books attracted numerous job offers. Eventually Boyd moved to the University of Toronto, where he replaced Oskar Klotz, who prior to his untimely death had voiced a lack of respect for Boyd (23). Despite his early work in Winnipeg, “Boyd had little enthusiasm for neuropathology, and when [the neuropathologist Eric] Linell was away he would have a great throw-out

of specimens to the dismay of the returning Linell” (23). During his tenure in Toronto, Boyd took responsibility for teaching, creation of a pathological museum, autopsies, clinico-pathological conferences, and he continued to update his textbooks. Even after retirement he still attended many of the monthly pathology conferences held in the conference room of the Banting when each teaching hospital took turns in providing the evening’s agenda. Pathology trainees were expected to present a case or topic, which they did with trepidation knowing full well that Boyd would always critique the quality of their presentation (Barry Rewcastle, personal recollection).

### **Development of Neuropathology in Montréal, 1930s-1950s**

The formal impetus for the development of diagnostic neuropathology in Canada came with the evolving needs of neurosurgery. During the second quarter of the 20<sup>th</sup> century, these activities proceeded in parallel in Toronto and Montréal; however, the two centres took very different routes toward this development.

**Wilder G. Penfield** (1891-1976) was born in Spokane, Washington (Figure 3). After obtaining his bachelor degree from Princeton University in 1913, he studied on a Rhodes scholarship in Oxford, England during 1915-6. There he met Osler and Charles Sherrington, who respectively stimulated his interest in pathology and neurophysiology. Penfield subsequently received his MD from Johns Hopkins in 1918, and then trained in surgery and neurosurgery in Boston for one year with Harvey Cushing. He returned to Oxford in 1919 to work again in Sherrington’s neurophysiology laboratory for two years (29). He also spent time with J. Godwin Greenfield, the preeminent English neuropathologist, whom Penfield regarded as a “clinical pathologist, rather than a cytologist aloof from bedside problems” (30). At that time Penfield became interested in the possibility that glial cells might contribute to the healing process in the brain and the subsequent development of epilepsy (31). He began working as a neurosurgeon at Presbyterian Hospital in New York in 1921. In 1923 Penfield spent time in Boston to observe Cushing’s approach to brain tumours and to work with the pathologist Frank Mallory to learn staining methods for scars and tumours. The same year he performed an autopsy on a hydrocephalic child in the parents’ apartment, reflecting the lessons he had learned from Osler on the value of post-mortem examination. The grateful parents made a donation to form a Fund for Hydrocephalus Research (31). Frustrated by his incomplete understanding of glial cells, Penfield decided to go to Madrid, Spain in 1924, where he worked with Pío del Río Hortega, who was a disciple of Santiago Ramón y Cajal. There he developed a reliable method for staining oligodendroglia (29). Upon his return to New York,

he was offered the opportunity to resume neurosurgery and do the neuropathology examinations on surgical and autopsy specimens (31).

**William V. Cone** (1897-1959) was born in Conesville, Iowa and received his MD from the University of Iowa in 1922 (Figure 4). He studied brain pathology at the psychiatric clinic of Samuel Orton. In 1924 he moved to New York to study neurology, but soon relocated to the Presbyterian Hospital in New York where, under Allen Whipple, he obtained training in surgery and was allowed to pursue his interests in neurocytology and neurosurgery (32). Upon Penfield's return from Spain, Cone became his apprentice. From 1924 to 1928 Penfield acted as neurosurgeon, neuropathologist, and investigator at the Presbyterian Hospital. Cone became an expert in both neuropathology and neurosurgery. Together they established the Laboratory of Neurocytology in 1925 (31). During this period, they published some extremely important and insightful papers concerning the pathology of oligodendroglial and microglial cells (33-35).

Penfield's opportunity to move to McGill University in Montréal to develop neurosurgery at the Royal Victoria Hospital came in 1928 (12). Prior to the move, Penfield returned to Europe to study surgical resection of epileptogenic brain scars with Otfried Foerster in Breslau, Germany, and to study neuropathology and neuroanatomy with Cecile and Oskar Vogt in Berlin for 6 months. He also met Dorothy Russell, the English pathologist who was to gain renown for her work on brain tumours (29, 31). At that time he solidified his concept for a textbook on neuropathology. Penfield invited Cone to join him in Montréal. Although Cone was offered free reign and his own neuropathology laboratory if he stayed in New York, he decided to leave (32). Penfield and Cone moved to Montréal in 1928, but their roles were to change with Penfield taking charge of the neurosurgery, devoting more time to neurophysiology experimentation, and planning long-term growth. Cone served as neurosurgeon and took charge of the Laboratory of Neuropathology "during his spare time" (36).

In Montréal, Penfield met **Pierre Masson** (1880-1959). Masson was born in Dijon, France. He had completed medical studies in Paris in 1907. His 1909 doctoral thesis concerned ganglioneuromas of the sympathetic nervous system. After working at several centres in France and making extensive studies of neuroendocrine neoplasms, Masson moved to the Université de Montréal in 1927. There he became Chairman of the Faculty, as well as Director of the Anatomical Pathology laboratories in three teaching hospitals (37). He wrote a classic article concerning the pathology of schwannomas (38). Masson was revered as a superb educator and histopathologist (39).

In 1932 Penfield finished editing and then published the world's first multiauthor textbook on neuropathology, a three volume masterpiece entitled "Cytology and Cellular Pathology of the Nervous

System” (40). Penfield contributed the chapters on the neuroglia, tumours of the meninges, and hydrocephalus. Cone wrote the chapter concerning optic nerve pathology, Masson wrote about neural tumours of the intestine, and William Boyd wrote about CSF cytology. Also in 1932, Penfield secured funding for the founding of the Montreal Neurological Institute (MNI), which opened in 1934 (41, 42). The success of the MNI was assured by Penfield’s broad vision. Cone’s compulsive work habits, affirmed by several writers (31, 43), assured that he remained an expert neurosurgeon and neuropathologist. One writer noted “If he [Cone] took holidays, it was in the neuropathology laboratory” (44). Cone corresponded with Greenfield in the mid-1930s while the latter was writing book chapters concerning neurological staining techniques (45, 46). Penfield and Cone contributed to the training of many individuals who were to gain world renown as neuropathologists. Among these were Dorothy S. Russell who was at the MNI in 1929. Later, with Lucien J. Rubinstein, she wrote the seminal textbook “Pathology of Tumours of the Nervous System” in 1959 (47). Russell and Penfield continued to correspond until 1972 (45). Webb E. Haymaker received his M.Sc. degree under Penfield’s guidance in 1934-5 and went on to serve as Chief of Neuropathology at the Armed Forces Institute of Pathology (AFIP) from ~1942 to 1962 (48). Kenneth M. Earle went to Montréal in 1949 intending to become a neurosurgeon, but was forced by circumstance to spend time first in neuropathology and neuroanatomy with Jerzy Olszewski. This experience caused him to train in neuropathology instead and he eventually went on to head neuropathology at the AFIP beginning 1962 (49). Of note, Earle was concerned about the validity of training in Montréal and his ability to sit the American board certification examinations in neuropathology, which had begun in 1948. The board responded that Penfield and Cone “were ‘recognized’ in the field of neuropathology” and allowed him to sit the examination (49). Igor Klatzo was at the MNI from 1948-54; he was subsequently appointed as Head of the Neuropathology Laboratory at the National Institutes of Health (NIH) in Bethesda MD in 1956, where he remained until retirement in 1994 (2, 50). The Canadian industrialist George H. Duggan made numerous donations to McGill University; in the 1940s-50s trainees (among these Kenneth Earle, Mark Rayport, and John Hunter) were funded by the Duggan Fellowship during their neuropathology rotation. It is worthwhile noting that the MNI neuropathology service was an excellent training ground in part because of the large workload; Cone’s records indicate that 600 surgical specimens and 62 autopsy brains were examined in 1946, 396 and 59 respective specimens in 1954, and 545 and 74 respective specimens in 1958 (51). The Montréal story continues below.

### **Development of Neuropathology in Toronto, 1930s-1950s**



**Eric A. Linell** (1891-1983) was born in Reston, England and received his MB from the University of Manchester in 1914 (52) (Figure 5). His subsequent MD thesis, awarded in 1920, concerned the anatomy of the peripheral nervous system (53). He showed some early interest in pathology, publishing an autopsy report of carcinoma of the larynx (54), but had no formal training in pathology. In 1923 he was recruited to the University of Toronto to teach neuroanatomy (55). **Mary I. Tom** (c1898-1971) was born in Goderich, Ontario (Figure 6). She earned her MB at the University of Toronto in 1922 and was appointed to the Department of Anatomy, working in Professor Playfair McMurrich's laboratory. There she applied the recently described gold and silver impregnation techniques perfected in Madrid to the study of embryology and histology (56, 57). In 1923, following training with Cushing in Boston, Kenneth G. McKenzie, a 1914 University of Toronto graduate, returned to the Toronto General Hospital (TGH) to become Canada's first full-time neurosurgeon. He was determined to establish a neurosurgical service complemented by a neuropathology laboratory with dedicated pathologists (58) as Cushing had done in Boston. In Linell's words (Barry Rewcastle, personal recollection) McKenzie 'discovered' Mary Tom and himself in the anatomy department. There, they started receiving neurosurgical material for study, creating the beginnings of what was to become a cross indexed archive of blocks, slides and reports of all neurosurgical and neuroautopsy cases, which grew over the ensuing decades. Under this influence and using techniques described by Penfield and Cone, Linell also used experimental models to study brain scars (59).

These were years of significant urban population increases in Canada, and hospital expansion followed. The TGH pathology building rapidly became inadequate so the university agreed to provide a new building to accommodate pathology staff offices, a tissue laboratory, an autopsy suite with gallery seating, specimen archival storage, library, lecture theatre, museum, photography unit, microbiology laboratory, pathological chemistry, offices for university clinical department heads, as well as animal research laboratories. It was named in honour of Frederick G. Banting (but it is not the building where insulin was discovered, as many visitors have discovered to their disappointment). McKenzie encountered reluctance to the creation of a dedicated neuropathology unit (60), but found support through Sir Robert Falconer, President of the University of Toronto (Eric Linell, personal communication to Barry Rewcastle). Thus neuropathology was created as an official division of the University of Toronto and it was to the Banting Institute that Linell and Tom transferred in 1932 to form a semiautonomous neuropathology unit (56, 61, 62) adjacent to the relocated Department of Pathology, headed by Professor Oskar Klotz (1878-1936) (63). Linell was promoted to full professor with

budgetary and administrative control; this was possibly the first full-time professorial appointment in neuropathology in North America (52).

Linell and Tom shared the reporting of specimens from McKenzie's surgical service and the hospital autopsy service. McKenzie signed the earliest reports on surgical specimens; later they were co-signed by the evolving neuropathologists and, in the 1940's, only by the neuropathologists (Barry Rewcastle, personal observation). Referrals from the Ontario mental hospital service in Toronto and the Ontario Hospital School in Orillia gradually increased. McKenzie and Linell developed a strong working relationship (55), publishing a few clinical and research papers together (64, 65). Linell and Tom also worked in close collaboration with the neurologist Herbert H. Hyland, who arrived in 1930 and had himself spent time training under the British neuropathologist Greenfield (66). Murray L. Barr had his initial training in neurohistological techniques during the summer of 1936 in Linell's laboratory (67). Barr discovered sex chromatin (the "Barr body") in the cat hypoglossal nucleus and went on to become a founder of specialty of cytogenetics; he impressed both Linell and Tom by his ability to determine the gender of patients using cresyl violet stained sections (Mary Tom, personal communication to Barry Rewcastle).

**Jason A. Hannah's** (1899-1977) career in neuropathology represents an interesting and little known footnote in this history. Born in Stittsville, Ontario, he graduated in medicine from Queen's University in Kingston in 1928. He was persuaded to do postgraduate work in pathology and the following year did a fellowship at the University of Edinburgh with the neuropathologist F. Esmond Reynolds where he learned the silver and gold impregnation techniques of Ramon y Cajal. The Province of Ontario planned to create a division of neuropathology linked to the Ontario psychiatric hospitals and devoted to research of neurological and psychiatric diseases. In 1930 Hannah was appointed Provincial Neuropathologist at the Ontario Department of Health. Unfortunately Oskar Klotz, the Professor of Pathology at the University of Toronto, was not supportive of the government position. Klotz was determined to keep neuropathology firmly affiliated with the university pathology department, rather than let it be controlled by neurosurgeons, as it was in Montréal, or by the provincial government (68). Nevertheless, he offered Hannah limited research space at the Banting Institute in 1932, the same year Drs. Linell and Tom moved there. Hannah hired a technician and began work with the encouragement of Linell. He conducted autopsies on patients from the psychiatric hospitals and published a few neuropathology reports concerning Alzheimer's disease and subdural hematomas (69, 70). However, he was never offered an academic appointment and eventually resigned his government position in 1937. He went on to establish Associated Medical Services, the first physician-sponsored, non-profit

prepayment plan in Canada for meeting the costs of medical and hospital care. When the government entered the health insurance business, Hannah persuaded the company board to use the financial reserves to create the Hannah Institute for the History of Medicine in 1972 (71, 72), which exists today as a charitable organization supporting history of medicine and health services (73).

Over the years, Dr. Tom took over the majority of the surgical reporting and Dr. Linell covered autopsy neuropathology, worked in clinicopathological research, and lectured to the medical undergraduates (52). Linell was described as an Edwardian style gentleman, wearing crisp shirt and tie, neat suit, and bowler hat to and from work. One historian wrote that Linell “smoked a pipe continuously and his hands were wizened from the constant exposure to formalin” (23). Linell’s brain cutting technique continued unvarying for decades; he made one horizontal cut through the cerebrum and then a midsagittal cut through the lower cerebrum, brain stem and cerebellum, thus yielding three rather large pieces. At a later time, small blocks for microscopy were taken and all sections were routinely stained with hematoxylin and eosin (H&E), phosphotungstic acid hematoxylin (PTAH), Masson’s trichrome, and cresyl violet. In occasional cases Cone and Penfield’s silver method was used for senile plaques and neurofibrillary tangles. Tom and Linell faithfully attended neurosurgical rounds, but seldom the anatomical pathology rounds (Gordon Mathieson, personal communication). Biweekly teaching conferences were instituted for staff and residents. Together with their trainees, they produced a steady stream of publications related to clinical neuropathology (62). Trainees who spent time with them included the New Zealand pathologist W. Stewart Alexander in 1949, who later described what is now known as Alexander’s disease (74) then worked briefly in Regina before returning to New Zealand. He was followed by the English pathologist Lionel Wolman from ~1950-2, Clarisse L. (Aszkanazy) Dolman from ~1952-4, and Gordon Mathieson in 1954-5 (see below). Linell was one of the founding participants of the Canadian Neurological Association in 1949 (52). He retired from neuropathology service in 1955, after which he was elected president of the Toronto Academy of Medicine and was secretary to the Medical Historical Club of Toronto (6); during his tenure several formal tributes to Osler were established (75). Following Linell’s retirement, Mary Tom did not wish the headship and so became acting head of the division (61). The search for a successor to Linell was surrounded by some speculation. Apparently Dr. Alexander was asked but declined (Gordon Mathieson, personal communication). Similarly, despite having spent several months in Toronto in 1954-5, Igor Klatzo declined the position and went to the NIH. The position remained unfilled until Jerzy Olszewski accepted the professorship in 1959 (see below). It was during this interregnum that the budgetary and

administrative functions fell under the purview of the Department of Pathology, sometimes to neuropathology's advantage with the acquisition of new microscopes.

Here it is worth highlighting the cultural and academic differences between the Montréal and Toronto neuropathology services. The former was run by neurosurgeons who had been trained in well-established neuropathology and experimental laboratories in Europe and the United States and who controlled a service very separate from the Pathology Department at McGill. Only scant official correspondence exists between Penfield and Horst Oertel, George Lyman Duff, and Gardner McMillan, the successive heads of Pathology at McGill from the 1930s to the 1950s (45). This is contrasted with the organization in Toronto. There, neuroanatomists, at the behest of the neurosurgeons, became self-taught with respect to neuropathology and worked closely within the Department of Pathology. Aside from Linell's brief correspondence with Cone in 1932 to request advice on staining techniques (51), there was no formal interaction between the developing Toronto and Montréal neuropathology laboratories. Montréal had a highly visible institute and leadership well connected with the international scene. In Toronto, the clinical neurosciences were very much grounded in their parent departments and were much less visible. Prior to 1960, it is likely that Dr. Tom had not attended an international neuropathology meeting (Barry Rewcastle, personal recollection).

### **National organization of Canadian Neuropathology in the 1950s – 1960s**

Coincident with progress in Montréal and Toronto, neuropathology was being established as a worldwide specialty distinct from the other clinical neurosciences and from the other aspects of laboratory medicine (2, 76-84). This was formalized in the creation of professional societies including the American Association of Neuropathologists founded in 1930 (preceded by the Neuropathology Club, which started in 1925) (1, 85), the German Society of Neuropathology founded in 1950 (86, 87), the International Committee of Neuropathology founded in 1950 (and reorganized in 1967 as the International Society of Neuropathology), the British Neuropathological Society founded in 1962 (preceded by the Neuropathological Club, which started in 1950) (88), the Japanese Society of Neuropathology founded in 1960 (89), and the Scandinavian Society of Neuropathology founded in 1965. In regions where neuropathology failed to establish a distinct identity, some have argued that it was a less vibrant specialty (90), while others hold the opposite to be true (91). Specific journals for publishing works in neuropathology were established including *Journal of Neuropathology & Experimental Neurology* in 1942 (1) and *Acta Neuropathologica* in 1961 (92, 93), as well as several others in following decades. From the historical vantage of the early 1960s, the contributions of Osler,

Boyd, Masson, and Penfield to the field of neuropathology were clearly respected (94). However, it took the vision and work of several eager individuals to create a national specialty society of neuropathology in Canada. Among these, two who had the opportunity to work in both the Toronto and Montréal environments were the major driving forces.

**Jerzy (aka George) Olszewski** (1913-1964) was born in Wilno, Poland (now Vilnius, Lithuania) (Figure 7). He graduated from the local medical school in 1937 and then became a research assistant of Maximilian Rose, the renowned Polish neuroanatomist, at the University of Wilno (95). Olszewski worked as a research associate for Cecile and Oskar Vogt at the Institute for Brain Research and General Biology in Neustadt im Schwarzwald near Freiburg, Germany from 1944-1948 (95). In 1947 he received the degree of Doctor of Medicine from Freiburg University; his thesis concerned cytological interrelationships of neurons in different species (96). Wilder Penfield's correspondence explains how Olszewski came to Canada (45). Oskar Vogt wrote Penfield in 1947, recommending Olszewski. Penfield replied that he "had no plans for cytoarchitectural work". Olszewski responded that he was asking for any kind of work, including physical (as he had done during the war) and that he really "wanted to become a citizen of a free and democratic country". Finally, Penfield assented in January 1948 saying that Olszewski's request was "too much for anyone to resist" and offered him the position of Fellow at the MNI (49). Olszewski, along with his colleague and friend Igor Klatzo (1916-2007), moved to the MNI in 1948. He arrived in Canada already immersed in neurological science and with a profound, probably unparalleled, knowledge of brain anatomy. His publications at this time were purely anatomical and his position was that of neuroanatomist. Olszewski occupied a comfortable office on the 6th floor of the MNI. As Assistant Professor of Neuroanatomy, Olszewski devoted himself largely to neuroanatomical studies and the creation of unrivalled cytoarchitectural atlases of the animal and human brainstem and thalamus. "Cytoarchitecture of the Human Brainstem", co-authored with Donald W. Baxter, was published in 1954; the foreword was written by Greenfield, the leading British neuropathologist (97-99). Olszewski received his PhD degree for work on the stereotactic atlas of the primate thalamus (100). He was colour-blind and most comfortable working with the 'blue' stains that nicely demonstrated internal neuronal structure (Gordon Mathieson, personal communication). While his research interests now included vascular permeability in the brain, he began to realize how his cytological skills could be applied to neuropathology. This change in the main focus of his work was the result of spontaneous requests for help, at first anatomical and then increasingly neuropathological. In the Annual Report of the MNI for the academic year 1954-55, Olszewski is listed as neuroanatomist and neuropathologist, albeit in a section titled "Neuroanatomy and Medical Neuropathology" to distinguish

his work from Cone's. Klatzo's expertise shifted in parallel; in 1954 he moved to Bethesda, Maryland where he became chief of the Laboratory of Neuropathology and Neuroanatomical Sciences at the National Institutes of Health (NIH) (50). This transition period was marked by an increasing number of autopsy cases studied in Olszewski's melded neuroanatomy and neuropathology laboratory and by the interests of his graduate students, including Michel Vulpe, Bohdan Rozdilsky, and Ramon Molinar. Cases were accessioned in two large registration books, one for the MNI and one for referred in cases. These roughly kept pace with each other, indicating that even at this early stage a widening circle of pathologists sought Olszewski's opinion. In contrast to Cone who was almost constantly immersed in neurosurgical duties, Olszewski was an available source of help for the neurosurgical residents and fellows in the "surgical neuropathology" section. A major undertaking of an exclusively pathology-related project, was the translation from German, and publication in collaboration with Alan B. Rothballer (a neurosurgeon), of Klaus-Joachim Zülch's monograph "Brain Tumors, their Biology and Pathology" (101).

In 1956, Olszewski made known his intention to take up a position at the University of Saskatchewan. Cone generously offered to relinquish his position in neurosurgical pathology together with his staff and laboratories if this would help persuade Olszewski to stay in Montréal. Dr. T. Rasmussen (later director of the MNI) wrote to the Principal of McGill about Olszewski, "He is a scientist of international reputation and is one of a rapidly vanishing breed of highly trained microscopic neuroanatomists. As such he is a mainstay in the scientific work of the Institute. He is also becoming a first rate neuropathologist and in our long range plans we are counting on him." However, Ken Earle wrote "Olszewski was never his own boss and I suspect that is why he left for Saskatchewan" (49). Olszewski, along with his student Bohdan Rozdilsky, moved to Saskatoon in 1956, where his appointments at the Medical College were in experimental neuropathology and in teaching. Friends speculated that this move, from the worldly environment of the MNI to a new medical school on the prairies, was needed to fully establish his new identity as neuropathologist rather than neuroanatomist. There, Olszewski developed an active diagnostic and experimental neuropathology unit in the new medical school. Peter J. Dyck, now a world authority on peripheral nerve disorders, was a resident in neurology at the time. He wrote, "Olszewski, my mentor who was well known to many pioneer neuroscientists in the USA and Europe, introduced me to the integration of clinical and neuropathological findings and rich accounts of history and science" (102, 103). In Saskatoon Olszewski lived with his mother and spent the "happiest years of his life in Canada" (104). Following his death in 1964,

Olszewski's will directed a donation to the University of Saskatchewan for a bursary in the name of his mother, the "Mrs. J. Olszewska Neuropathology Fund".

In 1959, after three short but very productive years in Saskatoon, Olszewski moved to the University of Toronto, to assume the vacant chair of neuropathology. This was viewed as the opportunity to "test the merits and the scope of his carefully fostered concepts of the teaching and practice of neuropathology" (104). However, in practice, virtually all the diagnostic neuropathology and training of residents fell upon the shoulders of Mary Tom, leaving Olszewski to pursue his research (57). Along with his international reputation, Olszewski brought to the laboratory a keen diagnostic acumen, contemporary standards in experimental neuropathology, and the genesis of an academic training program. Several very able students came to Toronto during this period. Henry M. Wisniewski left Poland to spend 1 year in Olszewski's laboratory, where he studied blood-brain barrier permeability; he subsequently went on to become one of the world's most respected investigators in demyelinating and neurodegenerative disorders (105). Peter W. Lampert, who was at the time training in pathology in Toronto, was inspired by Olszewski to study neuropathology; he went on to serve as chief of experimental neuropathology at the AFIP and was in 1969 appointed head of neuropathology at the new University of California School of Medicine at San Diego (106). Charles Tator, a neurosurgical trainee, did his PhD under Olszewski's direction, and went on to be one of the leaders in Canadian neurosurgery. Among the Canadian neuropathologists trained or inspired by Olszewski were N. Barry Rewcastle, John B. Richardson, John H.N. Deck, Kenneth Berry, and Melvyn J. Ball. In 1963, along with J. Clifford Richardson and John C. Steele, Olszewski described the pathological features of progressive supranuclear palsy, also known as Steele-Richardson-Olszewski syndrome (107, 108). Unfortunately, Olszewski died unexpectedly following a myocardial infarct in 1964 and Mary Tom retired in 1965, leaving the regeneration of the Toronto neuropathology program to Barry Rewcastle (see below). Many accolades highlight Olszewski's personal, professional and scientific attributes (96). While he was noted to be "devoted in a monastic way to his work" (95), he was by no means a recluse. Donald Baxter said at a memorial address, "George Olszewski had more friends than any other human being I have known" (104). One of Olszewski's particular talents, and perhaps the main reason for his legacy, was to encourage an environment in which ideas were freely exchanged. He did this through generous contribution of his time to teaching in many settings including at his home, to educating trainees at all levels, to the creation of journal and scientific clubs (109), and to organization of CANP (see below).

**Gordon Mathieson** (1927- ) completed his medical education in Aberdeen, Scotland, the city of his birth, in 1949 (Figure 8). Following 1 year as a house physician and 2 years service in the British

Army, he enrolled in a Fellowship in Pathology at University of Aberdeen. Before completion, in response to an advertised position, Mathieson wrote Linell, and then moved to Toronto where he worked as a Fellow in Neuropathology under Linell and Tom from 1954-55. With respect to autopsy neuropathology, the Fellow's job was to review the hospital chart and make an abstract, which was dictated and then typed onto a filing card. Unfortunately microscopic examinations were often greatly delayed, leading to an erosion of interest on the part of clinicians and residents. Tom's handling of surgical specimens was more prompt, but lack of a dual head microscope impeded thorough consultation and teaching (Gordon Mathieson, personal communication). In 1955 Mathieson moved to the intellectually stimulating environment of the Montreal Neurological Institute, where he obtained his M.Sc. in neurophysiology. There he found neuropathology to be largely neurosurgical pathology under the direction of the neurosurgeon Dr. Cone. Olszewski, with his profound depth of neuroanatomical knowledge, was just beginning to help with neurological autopsy cases. The key person in the day-to-day conduct of surgical neuropathology was the "senior resident in neuropathology" who invariably was a neurosurgical trainee, not a career pathologist or a neuropathologist in training. The individual would collect excised tissue specimens as they became available. Images of smear preparations, and less often frozen sections, were immediately produced using a Polaroid instant photography camera, and then shown to the surgeon. Sometimes after surgery Cone would drop in and look at the slides. Although there was not a regular sign-out session, occasional meetings were held in the conference room where there were many microscopes. The slides were passed around before being discussed by Cone and Penfield. Mathieson spent 1 year at MNI, then returned to Aberdeen to complete his pathology fellowship. He became lecturer in pathology in 1956, the same year Olszewski left for Saskatoon. Mathieson was invited to return to the MNI in 1957 as Assistant Professor (and later Associate Professor) and neuropathologist. His interactions with Cone were episodic and usually brief, with only rare more substantive discussions of some diagnostic problem. Cone gave the impression that laboratory work of any sort was peripheral to his main interests, which concerned the surgical care of patients (Gordon Mathieson, personal communication). No doubt Cone's psychological troubles during that period (32) precluded development of a worthwhile collaboration. In 1959, while at work, Cone committed suicide with cyanide (32, 110). Initially the neurosurgical pathology responsibilities were transferred to Gilles Bertrand, another neurosurgeon, however soon Mathieson was put in charge of neuropathology service and education at the MNI. He was able to capitalize on the substantial neurosurgical activity at MNI, making significant contributions to the understanding of the pathology in epilepsy (111). Fellows continued to arrive from abroad including Miroslaw J. Mossakowski, who went



on to be one of the leaders of neuropathology in Poland (112). Mathieson also trained future leaders in Canadian neuropathology including Stirling Carpenter, Vital Montpetit, Juan Bilbao, Kathleen Meagher-Villemure, and Yves Robitaille. Mathieson remained in Montréal until 1979 when he moved to Memorial University of Newfoundland as Professor of Pathology.

The same year that Mathieson took charge at MNI, neuropathology services became formalized at the French speaking institutions in Montréal. **Françoise J. Robert** (1930-1998) was born in France and graduated from medical school in 1953 at the Université de Montréal (Figure 9). She trained in neuropathology at the Massachusetts General Hospital under E.P. Richardson in the mid-1950s and did additional clinical training in neurology at National Hospital for Nervous Diseases in London. She took the position of clinical neuropathologist at the Hôpital Notre Dame in Montréal in 1959. For many years she collaborated with the neurosurgeon Jules Hardy, who pioneered the trans-sphenoidal resection of pituitary tumours, and established herself as an expert in pituitary pathology (113). Locally Dr. Robert excelled as a teacher, eventually establishing a residency-training program that persists at the time of writing. She always demanded detailed perfection, and imparted the necessity of accuracy and clarity to a generation of neuroscientists and pathologists (Yves Robitaille, personal communication) (114).

The neuropathologists active in the early 1960s were critical to the formation of the Canadian Association of Neuropathologists (CANP). The American Association of Neuropathologists (AANP) always held its annual meeting in Atlantic City, New Jersey in early summer, and a few Canadian neuropathologists attended the meeting regularly. In June 1959, during the midmorning coffee break, Olszewski and Mathieson were walking along the boardwalk, when Mathieson commented that it was rather odd that when Canadian neuropathologists met it was always in Atlantic City. Olszewski replied, “We could of course form our own Canadian group”. They immediately agreed and went on to explore ways and means of establishing such a group. Letters were written across the country, not just to the few other known neuropathologists, but also to heads of pathology, neurology, and neurosurgery, seeking interested parties. Practicing neuropathology became the essential qualification for eligibility (Gordon Mathieson, personal communication). A founding meeting was held in Montréal on 9 June 1960 to discuss the creation of an association (115). The CANP held its first annual scientific meeting 14 June 1961 in Montréal. Olszewski, who was elected president, chaired the meeting. Mathieson and Robert were elected Secretary-Treasurer and Member of Committees of Management respectively. Other established and future neuropathologists including Drs. Tom, Rozdilsky, Rewcastle, Gagnon, and Carpenter, as well as ten others, attended the meeting. Although the numbers were small, enthusiasm was high and the participants felt it to be a worthwhile venture, which has been repeated on an annual

basis to the time of writing. Dr. Tom served briefly as president of the CANP in 1963-4. Following Olszewski's death in 1964, Mathieson took on the presidency, a position served until 1967 followed by Dr. Robert (1968-70), David Robertson (1971-3), Jacques Lamarche (1974-6), Barry Rewcastle (1977-9), Morrison Finlayson (1980-2), Clarisse Dolman (1983-5), and others. During this early period, Drs. Mathieson, Robertson, Dolman, Carpenter, Rewcastle, Rozdilsky, Robert, and Berry, as well as others faithfully attended the CANP meeting. The organization has grown uninterrupted since then, acting as a vibrant and independent professional society for neuropathologists in Canada. Importantly, Olszewski and Mathieson realized early on that the tiny organization would constantly be in danger of being absorbed by larger organizations, such as the Canadian Association of Pathologists (CAP) or the Canadian Neurological Association. Although Linell was a founding member of the Canadian Association of Pathologists (CAP) in 1950 and David Robertson chaired some CAP committees in 1971 (116), the CANP was and remains only loosely aligned with the CAP. Solicitations to join the CAP were rebuffed in 1969 (Gordon Mathieson, personal communication) and again in 1981 (117). In 1993, the CANP resolved to "pursue active liaison with the Canadian Association of Pathologists and other divisions of Laboratory Medicine"; subsequently the CANP sponsored neuropathology workshops at the CAP meeting, but no conjoint meetings have been held (117). Similarly the relationship with the Canadian Neurological Society (reorganized in 1965 as the Canadian Neurological Sciences Federation), with a decision not to join in 1966, and reaffirmed in 1972. In the 1990s increased cooperation but not integration with the CNSF was recommended (117).

### **Expansion of Neuropathology across Canada 1960s-1970s**

The 1960s and 1970s saw a wave of rapid change with the introduction of the Canada's publicly funded universal health insurance system ("medicare") in 1966, increasing population, hospital expansion, technological advances, and expanded residency training. Soon all major centres across Canada had specialized clinical neuroscience units. This created the needs for neuropathological expertise for examination of tissue specimens from the nervous system, collaboration in the performance of autopsies (hospital and forensic), participation in educational activities, and research.

### **East of Montréal**

In Atlantic Canada, **Anthony J. Lewis** worked at Halifax's Dalhousie University from 1965-69 (having moved from Winnipeg, see below), at a time when neurosurgery was already well established. **Virgilio E. Sangalang**, who did pathology training in Kansas followed by a 3-year neuropathology fellowship with E.P. Richardson in Boston at the Massachusetts General Hospital, arrived in Halifax in 1967. Until Gordon Mathieson moved to St. John's Newfoundland in 1978, Sangalang was the sole consulting neuropathologist in the Maritime Provinces after Lewis's departure. **Francois Gagné** worked as an anatomical pathologist at Laval University and Hôpital Enfant-Jesus in Québec City beginning in the mid-1950s. Essentially self-taught with respect to neuropathology, he was a member of the CANP from 1961-1967, and provided diagnostic services until 1992 (Peter Gould, personal communication). Also in Québec City, **Jacques H. Thibault** provided neuropathology services beginning 1972, having trained at Yale University under Elias E. Manuelidis. **Jacques B. Lamarche** graduated in Medicine from Laval then went to Yale from 1961-67 where he trained in Anatomical Pathology and Neuropathology under Manuelidis. He worked at the Boston University School of Medicine then spent one year at Oxford University in neurology and immunology. From 1970-1997 he served as neuropathologist, and for the last 5 years also as department chair, at the Université de Sherbrooke.

## **Montréal**

A few years after Dr. Mathieson had established himself in Montréal, academic neuropathology at McGill affiliated hospitals (the Montreal Neurological Institute and the Montreal General) expanded rapidly. **Stirling Carpenter** was training in neurology at the University of Vermont. As an elective he spent 1 year in 1960 at the MNI with Mathieson. He then completed his neurology residency, decided to become a neuropathologist, spent 2 years of army service in neuropathology at the AFIP, and went to UCLA for a final year of general pathology. Carpenter was offered a job as Assistant Neuropathologist at the MNI in 1965. Meanwhile, Hungary-born **George Karpati** (1934-2009), who had obtained his medical degree from Dalhousie University in 1960, completed his neurology residency at the MNI and went on to do fellowship training in muscle disease with King Engel at the National Institutes of Health in Bethesda. He returned to Montréal in 1967 and proceeded to set up a laboratory to study muscle disease. Although Carpenter expressed initial reluctance about electron microscopic examinations of muscle biopsies, stimulated by a case of adult glycogenosis and some fortuitous observations in appendix and skin biopsies of children with storage diseases, he became an avid proponent of this technique for a wide range of diseases (Stirling Carpenter, personal communication). A long-lasting and

substantial collaboration grew between the two (Figure 10), with Carpenter doing the histology and ultrastructure of muscle biopsies and Karpati focusing on the histochemical and molecular aspects. The result was a large number of publications and the textbook “Pathology of Skeletal Muscle” (118). The first edition in 1984 was met with innumerable highly praising reviews, leading to publisher’s comments in the revised edition that “This book has been described as the 'bible' of muscle disease...” Both had illustrious careers. Following Mathieson’s departure from MNI, Carpenter served as Chief of Neuropathology from 1979-94. Karpati became “the organizing mind, and the scientific nucleus, for the attraction of a strong group with diverse interests in muscle and nerve where the common language is that of cell/molecular biology and genetics” (119). Among many other achievements, he contributed to the identification of the function of dystrophin (120) and was considered “one of the world's foremost investigators of neuromuscular disease” (121).

A short distance from the MNI, on the other side of the McGill campus at the Montreal General Hospital, the clinical neurosciences were also expanding rapidly. The need of a neuropathologist was very apparent, which led to negotiations with **Morrison H. Finlayson** (1929-1982). Born in Vilna, Alberta, he obtained his MB ChB from University of Edinburgh in Scotland in 1958. After postgraduate pathology and neurology training in Alberta, from 1961-62 he worked as a neuropathology research assistant at the National Hospital for Nervous Diseases in London. He then completed his neurology and pathology training at McGill, obtaining certification in both specialties (122). His recruitment to the Montreal General in 1966 was complicated by the fact that the Québec College of Physicians and Surgeons did not recognize neuropathology as a specialty and Finlayson had not spent the required months in general pathology for full certification. However, eventually the College agreed that his activities would be strictly limited to neuropathology and neurology (123). Finlayson directed the residency training in pathology for several years and served as the Canadian delegate to the International Society of Neuropathology from 1978-1982 (122). Although linked through McGill affiliations, the Montreal General and MNI neuropathology services were distinct. Nevertheless, Finlayson and Mathieson shared difficult cases and interacted regularly at a variety of rounds and the Montreal Neurological Society (Gordon Mathieson, personal communication).

Others contributed to the Montréal neuropathology scene in the 1960s. **Luis A. Oliva** (1931-2007) graduated from medical school in the Dominican Republic in 1955, and then trained in neurosurgery in Philadelphia, Paris, and Montréal. He did neuropathology and general pathology training at the Université de Montréal under Dr. Robert, finishing in 1969. He taught neuropathology through McGill, served as consultant neuropathologist and acted as chief of laboratories at two Montréal

area hospitals until retirement in 2006. During this period, Dr. Robert provided services at Hôpital Notre Dame and the Montreal Jewish General, and taught through the Université de Montréal until her death in 1998. In the context of this dynamic environment, Kathleen Meagher-Villemure and Yves Robitaille joined the MNI in the late 1970s.

## **Toronto**

As noted above, Olszewski's death was entirely unexpected, and another transfer of responsibility was forced. **N. Barry Rewcastle** (1931-) (Figure 11) was a 1955 graduate of the University of St. Andrews, Scotland. After interning at the Vancouver General Hospital, he undertook general pathology training first at the Shaughnessy Hospital in Vancouver, and then in Toronto until 1960. Often asked 'why neuropathology' there were perhaps two seminal events that triggered his career interest in neuropathology. First, early in his training, a neurologist asked why pathologists did not examine carotid and vertebral arteries of patients dying with cerebral infarctions. Second, while chief pathology resident at St. Michaels Hospital, he was sent up to the 'big house' (as the Toronto General Hospital-Banting complex was known to trainees) to consult Dr. Mary Tom on how to examine a brain from a hypoglycaemic coma patient. Following residency training in neuropathology, he became a graduate student and Medical Research Council (MRC) research fellow for 4 years supervised by Olszewski. During that period he developed electron microscopy with the intent of studying blood brain barrier permeability; 1963 was spent in the electron microscopy unit at the Deutsche Forschungsanstalt für Psychiatrie in Munich, Germany. On return to Toronto in 1964, Rewcastle was to join Olszewski and Tom, both of whom had university funded positions, as the first hospital-funded neuropathologist in Toronto. With Olszewski's untimely death and Tom's retirement, Rewcastle found himself professionally alone at a time when significant changes were occurring in Toronto, particularly in the areas of neuroscience faculty recruitment and expansion of residency training programs. He was appointed as Acting Head of the division in 1965 and Professor and Head of the Division of Neuropathology and Senior Pathologist at the Toronto General Hospital in 1970 (61).

The large downtown Toronto hospitals were independent institutions and as they expanded so did their neuroscience units and the need for neuropathologists. **Marjorie E. Platts** (1930-2008), a 1956 Toronto medical graduate, completed general pathology training in Toronto in 1962. She then spent a year with Lucien Rubinstein at Stanford University. Platts was recruited to the Princess Margaret Hospital and Ontario Cancer Centre in 1966 where she practiced both neuropathology and anatomic

pathology until 1997. **John H.N. Deck**, who had been one of Platts' medical classmates, worked in general practice for a few years, and then took General Pathology residency training, which he finished in 1965. Having done his rotation in neuropathology near the time of Olszewski's death, he was inspired to train further in neuropathology, eventually becoming certified in both specialties. Like Platts, he trained under Rubinstein from 1966-8 before returning to Toronto where he practiced neuropathology at the Toronto Western Hospital. In addition, Deck performed autopsies for the Office of the Chief Coroner, becoming an expert in forensic aspects of neuropathology. McGill-trained **Juan M. Bilbao** began working at St. Michael's Hospital in 1972 where he became a world authority on muscle and peripheral nerve pathology (124). As the Sunnybrook Hospital developed, Rewcastle provided consultation and teaching services there until the arrival of Anthony J. Lewis in 1978, the same year that **Anders A. Sima** joined Rewcastle at the Banting Institute/TGH site. Sima received his MD degree from the University of Goteborg in 1973 and PhD in neuropathology in 1974. After a year at Queens, he joined the faculty of the University of Toronto and proved to be an extremely productive researcher, focusing on diabetes. Developments at the Hospital for Sick Children are discussed in a later section.

At the Banting Institute there were four funded residency-training positions in neuropathology and, for many years, grant-supported research fellows and summer students. Among the residents would be a neurosurgical trainee, at least two neurology trainees, and a variable fourth position often occupied by a pathology trainee. Specific areas of clinical collaboration developed. The neuromuscular service developed with **John. G. Humphrey** after his return in 1960 from a fellowship with Dr. Milton Shy at the then National Institute for Neurological Diseases and Blindness in Bethesda. Humphrey was considered the 'Dean' of neuromuscular neurologists in Canada (125). In addition to his electrophysiological laboratory, he established a diagnostic muscle histochemistry laboratory initially within the hospital, later to be incorporated into the Neuropathology laboratory. This expanded to include fibre quantitation, nerve teasing, and study by electron microscopy. Another more unusual collaboration with the neurosurgeon Ronald Tasker related to surgical stereotactic lesion localization. Rewcastle found himself in many peculiar Toronto locations retrieving brains from Tasker's deceased patients. This allowed pathological confirmation and accurate anatomical tract localization, from which developed a method for sectioning basal brain structures based on stereotactic atlas coordinates. Numerous publications resulted from these clinical interactions.

With the initiation of a neuropathology-training program in 1968, rotations at other hospitals including St. Michael's, the Toronto Western, the Wellesley/Princess Margaret Hospital, and the Hospital for Sick Children (HSC) had to be called upon. By the early 1970's there were as many as nine

trainees at any time. Rewcastle introduced a monthly slide session hosted at the HSC pathology conference facility, which was furnished with individual microscopes. This served as a continuing education program for staff and residents by sharing interesting material from the downtown teaching hospitals and discussing difficult diagnostic problems. A visiting speaker program complemented these monthly meetings. John Groves of McMaster University in Hamilton regularly participated. Dr. Peter Little of the Ontario Veterinary College (University of Guelph) enlivened the sessions. On many occasions he demonstrated interesting cases of hereditary animal diseases that mimicked human conditions; he reported that affected animals, rather than be used as a model of human disease for research, were often destroyed to prevent loss of breeders' reputations (Margaret Norman, personal communication). He also demonstrated lesions that to the neuropathologist appeared inflammatory but to the veterinary pathologist indicated toxicity (Barry Rewcastle, personal recollection). As director of the Toronto Neuropathology Residency Program, Rewcastle always encouraged career neuropathology trainees to seek specialized training beyond that which was provided locally because he considered that certified neuropathologists would always be recruited to and practice in academic settings. He inspired a significant number of future leaders in neuropathology including John H. N. Deck, Melvyn J. Ball, Laurence E. Becker, Dawna L. (Duncan) Armstrong, Allan J. Yates, Catherine Bergeron, Bernadette Curry, William C. Halliday, and David R. Hinton. In 1981, Rewcastle left to take up a position as Head of the Department of Pathology at the University of Calgary. Deck then took leadership of neuropathology services at the Toronto General and Toronto Western hospitals, while the University Division Head was Laurence E. Becker from 1982 to 1991.

### **Elsewhere in Ontario**

**David M. Robertson**, a native of Melville, Saskatchewan was a medical graduate of Queen's University in 1955 (Figure 12). He trained in General Pathology at Queen's and received Royal College certification in 1960. Dr Robert More, the department head, recognized the need to develop neuropathology and encouraged Robertson to become a neuropathologist. He went on to train in Neurology at the Toronto General Hospital with Henry Barnett, and then trained in neuropathology at the National Hospital for Nervous Diseases in London, England with William Blackwood, and at Duke University Medical School in Durham, North Carolina with Stephen Vogel. In 1962, Robertson came back to Kingston General Hospital and started his career in diagnostic neuropathology. He had an enormous impact on neuropathology at Queen's as well as in Canada and abroad. At one point in time

fully a quarter of all neuropathologists in Canada had some or all of their training at Queen's (126). At a neuropathology meeting in 1983, attendees agreed that a North American multiauthor neuropathology textbook would be a worthwhile contribution. Over "a few oysters and beers" Robertson and Richard L. Davis (University of California at San Francisco) decided to take on the task (David Robertson, personal communication). They became good friends and edited the very successful "Textbook of Neuropathology" (127), which went to three editions. When the need for a second neuropathologist arose in 1970, **Herbert J. Manz** another native of Saskatchewan who had trained in general pathology at McGill and then in neuropathology at Queen's was recruited; he stayed only until 1974. In 1975 **Samuel K. Ludwin**, a South African who trained in both anatomical pathology and neuropathology (under Lucien Rubinstein) at Stanford University, arrived at Queen's. Ludwin became an authority on multiple sclerosis, and was president of the International Society of Neuropathology in 2000. Completing a trio that drove a thriving educational program, **Sukriti Nag**, who had trained in pathology at University of Lucknow (India) and in neuropathology at Queen's, was recruited in 1978. A year later Robertson became head of the Department of Pathology at Queen's. In 1993 Nag moved to Toronto to lead the neuropathology program there.

At the University of Western Ontario in London, the Department of Clinical Neurological Sciences, the first such multidisciplinary department in Canada, was established in 1969. It was under the direction of the neurosurgeon Charles Drake (128) and the neurologist Henry Barnett (129), both of whom had trained and worked in Toronto. They lured the neuropathologist **Melvyn J. Ball** to join them that year. While a medical student at the University of Toronto, he secured a 1961 summer job in Olszewski's lab by responding affirmatively to the question "Are you good with your hands?" (Melvyn Ball, personal communication). There he learned histology, attended brain cutting sessions with Drs. Olszewski, Tom, and Rewcastle, and was "smitten with this enormous academic fun" that inspired him to train in pathology and neuropathology following medical graduation in 1963. As the department in London, Ontario expanded, more neuropathologists were recruited in 1972, allowing Ball to do additional training at the National Hospital for Nervous Diseases in London, England. The two new recruits were **John C.E. Kaufmann** and **Joseph J. Gilbert**. Gilbert graduated from McGill in 1965 then trained in neurology for 3 years with Morris Victor followed by 2 years neuropathology with Betty Banker at Case Western Reserve University in Cleveland; he became certified in both specialties. Kaufmann had graduated in medicine from University of Cape Town in 1947, then trained in anatomical pathology. His training and early work in neuropathology, from 1956 to 1972, was effectively an apprenticeship at the South African Institute for Medical Research in Johannesburg under Neville



Proctor, who had studied under J. Godwin Greenfield and Webb Haymaker (John Kaufmann, personal communication). Ball, who became an authority on neurodegenerative diseases, moved to Oregon in 1989. Gilbert contributed significantly to the understanding of neuroinflammatory disorders before taking on administrative positions in 1991. Kaufmann published many papers concerning vascular diseases before retiring in 1990. Together the three started one of the most successful Canadian neuropathology training programs.

In Ottawa, **Vital J. A. Montpetit** graduated from medicine in 1961 and trained in General Pathology. He completed training in neuropathology at McGill in 1969, and became certified in both specialties. He then assumed a neuropathology position at the University of Ottawa, where he remained until retirement until 2001. Anthony Lewis joined him in 1970 and stayed until 1978.

### **Western Canada**

**Clarisse L. (Aszkanazy) Dolman** (1921-1988) was born in Vienna, Austria and graduated from medicine at the University of Toronto in 1947 (Figure 13). Following qualification in pathology she studied neuropathology under Drs. Linell and Tom from 1952-4 then went to Vancouver to join the faculty of the University of British Columbia (UBC) in 1954. She served initially as a general pathologist, including head of the autopsy service, then shifted almost exclusively to neuropathology in the 1960s (130). Dolman served as president of the CANP from 1982-1985. She published extensively on a wide range of neuropathology subjects, but her legacy lies in the book, “Ultrastructure of Brain Tumors and Biopsies: a Diagnostic Atlas”, published in 1984; it was the first specialty coverage of this important facet of neuropathology (131). **Kenneth Berry** (1932-2006) joined Dolman in 1965. Berry had graduated from medicine at UBC in 1956, and then went to Toronto to train in neurology followed by neuropathology with Olszewski early 1960s. Upon his return to Vancouver he served as Head of the Division of Neurology at St. Paul’s Hospital from 1965-72, the Head of Neuropathology Service at Vancouver General Hospital from 1987-1994, and was the Director of the training program in neuropathology from 1987-1994. He introduced muscle enzyme histochemistry as a diagnostic tool. Dolman and Berry started the neuropathology training program at UBC in 1973.

In Edmonton, the clinical neurosciences were expanding and the need for a trained neuropathologist became pressing. **Bruce W. Mielke**, who had trained in general pathology at the University of Alberta, becoming certified in 1965, was awarded a one-year fellowship to train in neuropathology under Dr. Richard Lindenberg at the State of Maryland Medical Examiner's Office in

Baltimore, MD. Upon his return from Baltimore, Mielke established the neuropathology laboratory and gained a reputation for his diagnostic neuropathology skills and as an expert in forensic neuropathology. For the most part, however, Mielke's expertise in neuropathology was self-taught. For the duration of his career he undertook service duties in neuropathology, anatomical pathology, and ophthalmic pathology. Another anatomical pathologist, Dr. T.K. Shnitka, assumed the nerve and muscle pathology responsibilities until the arrival in 1971 of J. Gilles Blain, who had certifications in neurology and neuropathology. From 1971 to 1974 Blain worked in Edmonton, where he established the muscle histochemistry laboratory (Edward Johnson, personal communication). He then worked in Sherbrooke, Québec (1975-9) and briefly at the Montreal Neurological Institute (1980-1), and after 1982 restricted his practice to neurology. Edmonton did not have a fully trained, full-time neuropathologist until the arrival of Edward S. Johnson in 1980. Up to his retirement in 1997, Mielke contributed significantly to teaching, diagnostics, administration, and neurosurgical research.

In southern Alberta, the University of Calgary did not have a formalized neuropathology service until after 1980, at which time the Department of Clinical Neurosciences was being established. Bernadette Curry, a graduate of the University of Glasgow and already an established pathologist at the Foothills Hospital, was approached and agreed to pursue further training and qualification in neuropathology, which she accomplished in Toronto. Following Curry's return in 1980 and Rewcastle's arrival in 1981 as Head of the University Department of Pathology, neuropathology grew rapidly in the next 3 years with recruitment of Roland N. Auer, Arthur W. Clark, Irma M. Parhad (1948-1994), and Harvey B. Sarnat; approval of a neuropathology training program followed in 1990.

Neuropathology in Saskatchewan sprung from events in Montréal. **Bohdan Rozdilsky** (1916-2004) received his medical and anatomical pathology training in Lviv, Ukraine. He came to Montréal in 1955 as a PhD student under Olszewski. When Olszewski moved to Saskatoon in 1956, Rozdilsky went with him to continue his studies on the permeability of blood vessels in the brain and the toxic effects of bilirubin (132). During his research training, he was exposed to clinical aspects of neuropathology. When Olszewski moved to Toronto in 1959, the neurologist Donald Baxter initially assumed responsibility for the neuropathology service (133), however shortly thereafter Rozdilsky took over. He had a long and academically productive career as the sole neuropathologist in Saskatoon until his retirement in 1986.

In early decades Winnipeg had only inconsistent coverage by individuals trained in neuropathology. **Anthony J. Lewis** (1927-2000) served at the Children's Hospital from 1960-1965 (see below). **Dikran Houropian** came from Egypt to Winnipeg where he trained in pathology. From 1970-

72 he obtained research and clinical training in neuropathology at Albert Einstein College of Medicine in New York, then he returned to Winnipeg and served on staff from 1973-4 at the General Hospital. However, he then departed to become one of the leaders in American neuropathology (134). Prior to the arrival of Anders A.F. Sima in 1982, two anatomical pathologists, John Taylor and Larry Lu who were self taught with respect to neuropathology, provided services.

### **Pediatric Hospitals**

Recognizing that children suffered neurologic disorders distinct from those in adults, some children's hospitals began to recruit pathologists whose focus would be on pediatric neurological disorders. **William L. Donohue** graduated from University of Toronto in 1932 then studied pathology at Columbia University and neuropathology at the National Hospital for Nervous Diseases in London, England. In 1938 he was appointed Assistant Pathologist at the Hospital for Sick Children in Toronto and from 1947 to 1972 was Chief of Pathology (135). Approximately one third of Donahue's ~50 publications concerned pediatric neuropathology topics, particularly viral diseases of the brain. From the mid 1960's to the mid 1970's, Patrick E. Conen took on overlapping duties related to electron microscopy and muscle pathology. The Hospital for Sick Children recruited John T. Groves (1925-2005) in 1962 to focus on neuropathology. Groves had trained in pathology in London, England and received training in Neuropathology at the AFIP. However, in 1965 he moved to Hamilton General Hospital where he worked until retirement in 1992.

Bruce Hendricks, then chief neurosurgeon at Hospital for Sick Children, suggested to **Margaret G. Norman**, a 1958 medical graduate and 1965 General Pathology trainee at the University of Toronto, that she should consider the position. She learned pediatric pathology in New York at the Babies Hospital followed by 18 months neuropathology training with E. P. Richardson at the Massachusetts General Hospital in Boston (Margaret Norman, personal communication). Norman returned to Toronto in 1970 to formally establish a neuropathology service at the Hospital for Sick Children (136). The busy service included training of residents (including her successor, Laurence Becker). In 1974 Norman moved to become the first director of laboratories at the new Children's Hospital of Eastern Ontario located in Ottawa. In 1980, she again moved, this time to Vancouver, as neuropathologist at the Children's Hospital of British Columbia. She became well known for her many contributions to teaching, clinical research projects, diagnostic studies in pediatric and developmental neuropathology, and handling of medicolegal cases involving child neglect and abuse (136). Most of her resident

teaching in Vancouver concerned pediatric pathology, but some trainees (including Harry Vinters) specifically focused on pediatric neuropathology. Norman's 1995 book "Congenital Malformations of the Brain: Pathological, Embryological, Clinical, Radiological and Genetic Aspects" (137), co-authored by specialists from related fields, was considered "by far the best book ever written on human brain malformations" (138). She retired in 1996.

When Norman left the Hospital for Sick Children, **Laurence (Larry) E. Becker** (1943-2002) and Dawna L. (Duncan) Armstrong were recruited in 1974. Armstrong, a 1961 graduate of the University of Manitoba medical school and of the University of Toronto neuropathology residency program, stayed until 1977 before moving to the Texas Children's Hospital in Houston. Becker had graduated from the University of Alberta medical school in 1967 and interned at the Montreal General Hospital. His neuropathology residency was done at the University of Toronto, mentored by Rewcastle, Norman and Platts, and was followed by two-year research fellowship at John Hopkins Medical School with Richard T. Johnson. Becker returned to Toronto in 1974, initially to a staff position at the Toronto General Hospital, intending to establish a laboratory at the Banting Institute. However, upon Norman's departure he moved to the neighbouring hospital. His association with HSC would span 28 years and during this time he would contribute enormously to research, teaching and administration. His interests included developmental neuropathology (especially Down syndrome), neuro-oncology, and the study of Sudden Infant Death Syndrome (SIDS) (139, 140). One of the most long lasting and important international collaborations forged was with Sachio Takashima from Tokyo, Japan. The two had a mutual interest in Down syndrome and developmental neuropathology. Despite Takashima's initially weak English and Becker's lack of Japanese, the two forged a friendship that persisted until Becker's premature death. Takashima sent many fellows to train in Toronto, while Becker travelled to Japan at every opportunity to do science and to learn about the culture (Edna Becker, personal communication) (141). Becker contributed to numerous hospital, university, and international academic committees and was Pathologist-in-Chief at Sick Kids beginning in 1994. With over 300 peer-reviewed publications, Becker was one of the world's most respected pediatric neuropathologists.

The Children's Hospital of Winnipeg hired University of London-educated Anthony J. Lewis (1927-2000) to provide pediatric pathology and pediatric neuropathology services 1960. In 1965 he moved to Halifax, then to Ottawa, and finally settled in 1978 at the Sunnybrook Hospital in Toronto where he focused on adult neuropathology until retirement in 1992. In the 1980s, somewhat dependent on the political organization and the geographical arrangements, individuals with neuropathology

expertise were recruited to other pediatric hospitals in Halifax (Atilano G. Lacson), Montréal (Kathleen Meagher-Villemure), and Calgary (Harvey B. Sarnat)

### **Formalizing Neuropathology training in Canada**

Provincial bodies were tasked with licensure of physicians to practice, but little attention was paid to those claiming to be specialists. In 1929 Stanley Ryerson of the Toronto Faculty of Medicine found that about one third of practitioners claimed to be specialists, but he deplored the great lack of training in many (142). The Royal College of Physicians and Surgeons of Canada (RCPSC) was founded in 1929, by an Act of the Canadian Parliament (143). It was established primarily to oversee postgraduate medical education, initially general medicine and surgery with more specialties included in later decades (144, 145). Eventually the Canadian Medical Association (CMA) encouraged the RCPSC to assume specialist certification by examination and this was introduced in 1946 via approved training programs, including certification in General Pathology. Thus for many years individuals with an interest in the morphological aspects of clinical neuroscience were encouraged to acquire neuropathology expertise through a relatively informal apprenticeship under someone already involved in neuropathology. In the absence of a formal certification process, not all chose to acquire comprehensive training. A most important advance was the 1965 introduction of eligibility for certification in neuropathology following 5 years training (145). Those already certified in pathology or neurology could become a certified neuropathologist following an additional 2-3 years training. Initially there was a mandatory rotation in clinical neurosciences, however, this was perceived as an anomaly by some and was eventually subsumed into the general internship year or offered as an optional rotation. Under the proctorship of Lucien J. Rubinstein, the RCPSC offered the first examination in neuropathology in 1968. Clarisse Dolman, Gordon Mathieson, Barry Rewcastle, and David Robertson were the first four to receive certification (146). In 1969, Rewcastle became chair of the neuropathology examining committee. Training programs were officially recognized by the RCPSC at Université de Montréal (in 1970, withdrawn in 1980, and reapproved in 1996), University of Toronto (in 1972), Queen's University (in 1972, withdrawn in 2006), University of British Columbia (in 1973), University of Western Ontario (in 1974), McGill University (in 1974, withdrawn in 2006), and University of Calgary (in 1990).

Of interest is a review of the number of individuals practicing neuropathology in Canada, either in general diagnostic neuropathology or in a focus area (i.e. neuromuscular disease or pediatric neuropathology), in each decade from 1930 to the present based on available information (see Table 1).

In the first two decades the numbers were small. These practitioners, practicing in Montréal and Toronto, had either received supplemental training outside Canada or were self-taught. Among those starting work in the 1930-59 era, 4 preceded neuropathology training with training in pathology and 6 with training in clinical or basic neurosciences. During the 1960-79 era, the respective numbers were 23 and 13. Among those currently in practice, there is a fairly even balance between direct entry to neuropathology from medical school, entry from another clinical neuroscience, and entry subsequent to training in anatomical pathology (147). Following introduction of the RCPSC neuropathology certification examination, the number of formally trained and certified neuropathologists progressively increased across the country. By the 1980s Canada had approximately 50 formally trained neuropathologists (~75% with certification), a level that persists to the time of writing (147). Of note is the transition of neuropathology from an eccentric niche area prior to the 1960s to a widely recognized laboratory medicine specialty (Gordon Mathieson, personal comment).

## **Conclusion**

The profession of neuropathology in Canada evolved in parallel with changes elsewhere in the world, initially driven by personal interests in diseases of the nervous system and, beginning in the 1930s, by the needs of neurosurgical services. The earliest practitioners came from or were trained in Europe, the United Kingdom, and the United States. Since the time of the earliest practitioner in Canada, William Osler, to the present time, individuals who have chosen to practice neuropathology in Canada have come from varied professional backgrounds including clinical neurosciences, basic neurosciences, and anatomical pathology. The majority of those who assumed leadership roles had varied training including strong backgrounds in neuroscience research. The Canadian Association of Neuropathologists, formed in 1960, played a critical role in strengthening communication between neuropathologists across the country and in the creation of a unique Canadian training system, under the auspices of the Royal College of Physicians and Surgeons of Canada. The system has continued to evolve and adapt to changing medical needs. By the mid-1970s neuropathologists were practicing in all major Canadian centres as invaluable team colleagues.

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Dr. Del Bigio holds the Canada Research Chair in Developmental Neuropathology. He is the current chair of the Specialty Committee in Neuropathology for the RCPSC, a position first occupied by Dr. Rewcastle.

## Figure Legends

Figure 1. William Osler carefully dissecting a brain removed at autopsy, c1886. Note the absence of gloves. (Cropped and retouched image; original courtesy of The William Osler Photo Collection. Osler Library of the History of Medicine, Montréal, Québec, Canada)

Figure 2. William Boyd creating photomicrographs in Winnipeg, c1925. (Cropped and retouched image; original courtesy of the University of Manitoba Faculty of Medicine Archives, William Boyd Biographical Records)

Figure 3. Wilder Penfield at the Montreal Neurological Institute, c1963. (Reproduced courtesy of the Montreal Neurological Institute, McGill University)

Figure 4. William Cone at the Montreal Neurological Institute, c1959. (Reproduced courtesy of the Montreal Neurological Institute, McGill University)

Figure 5. Eric Linell posing with fixed brain, c1955. (Reproduced courtesy of the University Health Network Archives, Toronto)

Figure 6. Mary Tom as she appeared in the 1939 group photograph at the Banting Institute in Toronto. (Cropped and retouched image; original courtesy of the University Health Network Archives, Toronto)

Figure 7. Jerzy (George) Olszewski in Toronto, c1963. (Photograph courtesy of Dr. Barry Rewcastle)

Figure 8. Gordon Mathieson in British military attire in 1951, prior to his move to Toronto to begin training in neuropathology. (Photograph courtesy of Dr. Gordon Mathieson)

Figure 9. Françoise Robert at the first Pituitary Club meeting in Montréal, 1981. (Photograph courtesy of Dr. France Berthelet)



Figure 10. George Karpati (left) presenting a certificate to Stirling Carpenter (right) at the Montreal Neurological Institute, 2006 (Reproduced courtesy of the Montreal Neurological Institute; photographer Owen Egan)

Figure 11. Barry Rewcastle at brain cutting session in Calgary, c1985. (Photograph courtesy of Dr. Barry Rewcastle)

Figure 12. David Robertson as Vice President (Medical) at the Kingston General Hospital shortly before retiring from diagnostic neuropathology, c1993. (Reproduced courtesy of KGH Archive)

Figure 13. Clarissa Dolman at the Vancouver General Hospital, c1963 (Photograph courtesy of Dr. Katerina Dorovini-Zis)

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