

**HISTORICAL REVIEW**

# Osler and Neurology

George C. Ebers

*Can. J. Neurol. Sci.* 1985; 12:236-242

William Osler's bibliography includes over 1400 papers, monographs, and notes touching on almost every subspecialty of medicine (Abbott 1939). He has been claimed by gastroenterologists (Cunha 1948), pediatricians (McGovern et al 1970; Robbins et al 1963), medical librarians, (Bett 1949), veterinarians (Giltner 1926-27) (Murphy 1960) obstetricians (Rucker 1952) and members of other disciplines as one of their own.

Osler published close to 200 papers, reviews, editorials and monographs dealing with neurology, but it is not widely recognized that his contributions to neurology exceed those to many of the other fields. For example, Osler's interest in neuropathology was entirely omitted from the recent excellent monograph "An Oslerian Pathology" (Rodin 1981). The purpose of this paper is to bring into focus his impressive neurological contributions and to document his substantial interest in the neurosciences.

Osler's activities in neurology constituted a microcosm of his overall medical contributions. His interests in the neurosciences began early. In 1884 he wrote on the comparative anatomy of the brain of the seal (Osler 1884a), having given a lecture on "the brain as a thinking organ" in the previous year (Osler 1883a).

**The Mind-Brain Problem**

Osler's early interest in what has been called the mind-brain problem very likely led him to carry out several studies on the brains of criminals, a subject of considerable controversy at that time. In 1879 Benedikt of Vienna (known eponymously by neurologists for Benedikt's syndrome) published a monograph on the abnormalities in the surface anatomy of the brains of criminals (Benedikt 1879). Benedikt had suggested that criminal brains showed the confluence of many primary fissures as well as an extra horizontal frontal gyrus. Osler was unable to confirm these findings. He studied the brains of two criminals and compared them to 34 brains obtained from autopsies at the Montreal General Hospital, noting that confluent fissures were found commonly in "normals" (Osler 1882a). He suggested that the appropriate controls for Benedikt's criminals would have been law-abiding individuals from the same race. Osler emphasized the dangers of attributing criminal behaviour to organic lesions and, in some moralizing uncharacteristic of his scientific papers, he expressed his belief in man's free will and responsibility for his own actions. One of the cases from this study illustrates Osler's tenacity in the pursuit of pathological material. Moreau, a man who had been convicted of axe-

murdering his wife, was to be hanged at Rimouski, Quebec. Osler sent one of his residents to Rimouski in mid-winter to obtain this brain, not an easy task given the time of year and the transportation available (Cushing 1925). Despite his negative findings in criminal brains Osler went to the defense of Benedikt after a Lancet editorial noted the "collapse of Benedikt's attempt to furnish an anatomic basis for crime". In a letter to Lancet, Osler felt that more information was needed before firm conclusions could be reached (Osler 1882b). He kept up his interest in this question and the results of additional studies on criminal brains, which he called Series 2, constitute item 76666 in the Bibliotheca Osleriana.

**Localization**

It was an exciting time in the neurosciences when Osler came on the scene toward the end of the last century. The important studies of Hitzig and Ferrier and others had opened the way for clinical pathological study of focal cerebral lesions and localization of cerebral function was to preoccupy neurologists and neurophysiologists for several ensuing decades. Osler had a vivid interest in these developments and attended the International Medical Congress of 1881, sending back a report of the proceedings which was published. The discussion of localization by Ferrier, Brown-Sequard and others was the highlight (Osler 1881-82a). The level of sophistication in some of Osler's papers on localization is surprisingly high even when viewed in retrospect. He published a paper on sensory aphasia with word blindness in the same year as Dejerine's classical paper on this topic (Osler 1891; Dejerine 1891). He also wrote about the localization of sacral autonomic centres noting the difficulty in distinguishing conus from cauda lesions (Osler 1888a). He also described in the context of these cases a syphiloma of the sacral cord (Osler 1889a). Syphilis was indeed one of his major interests. He published on the inheritance of syphilis (congenital), on tabes dorsalis (Osler 1883b) and provided an excellent discussion of neurosyphilis in his classical text (Osler 1892a). The latter contribution has been emphasized (Harvey et al 1967). In Osler's time the relationship of tabes to syphilis was not certain even though the classical description of tabes by Romberg had occurred around the time of Osler's birth. However, in explaining the fact that some individuals developed tabes without a prior history of syphilis, Osler related a case of neurosyphilis in a physician whom he knew had had syphilis but who had subsequently denied it. Osler left little doubt that his sympathy

From the Department of Clinical Neurological Sciences, University Hospital, London

Received March 21, 1985

Reprint requests to: Dr. George C. Ebers, Associate Professor, Department of Clinical Neurological Sciences, University Hospital, P.O. Box 5339, London, Ontario Canada N6A 5A5

lay with the view that tabes and general paresis of the insane were synonymous with syphilis.

### Subdural Hematoma

Osler wrote an interesting paper on subdural hematoma while he was in Philadelphia (Osler 1888b). He recalled that in the 12 years in which he had been a pathologist at Montreal General Hospital he had not seen such a case. Of significance is the issue he took with the commonly prevailing notion that the disorder was an inflammatory one. Virchow appears to have been responsible for this notion, implicit in the term *pachymeningitis hemorrhagica* which he coined, (a term which is still used in a relatively recent text of neurology (Wilson 1940)); but Osler in his microscopic analysis of subdural hematoma doubted an inflammatory etiology. Osler also made a relevant and accurate observation that many of these patients were found in hostels for the insane and that cerebral atrophy was often associated with this disorder. Although he denies ever seeing a case in Montreal, his original autopsy records include 2 cases which may well have been subdural hematoma, one acute and one chronic, in addition to an acute epidural hematoma. (Osler autopsy records - Osler Library, McGill University, Montreal). Osler was an early member of the American Neurological Association, presented papers at their meetings, and is seen in photographs of this organization taken in 1890's. Osler wrote on encephalopathy and identified the toxic encephalopathy associated with pneumonia and uremia (Osler 1898; Osler 1882c).

### Brain Tumors and Vascular Disease

He wrote several items on tumors of the brain both in the context of localization with clinico-pathological correlation and from the perspective of a working pathologist. He recorded a natural clinical remission in a cholesteatoma in a young physician in which he questioned whether or not the use of leeches had been responsible for the improvement (Osler 1887a). In another patient with Jacksonian epilepsy he invoked "Charcot's rule" with respect to localization (Osler 1884b). Charcot had noted that in cases of focal motor epilepsy, those with associated weakness had lesions involving the motor cortex whereas those without weakness had lesions adjacent to it.

Aneurysm was one of his favourite topics and he wrote numerous papers on aneurysms of the cerebral vessels. Osler thought embolism, endarteritis and atheroma were the chief causes and he supported an embolic mechanism by quoting a description of what may well have been a clot within an aneurysm rather than an embolus (Osler 1887b).

Separate from cerebral aneurysms, Osler had an interest in vascular disease in the nervous system and wrote numerous papers on this topic. In fact, Osler's first appearance in medical print concerned the case of an acute stroke in which Osler, then a young medical student, demonstrated a clot in the middle cerebral artery, perhaps one of the first times this had been documented (Reddy 1871-72) (see Figure 1). Osler attended Walt Whitman during the second of his strokes. He came to know Whitman through his relationship with Morris Bucke, the former superintendent of the London (Ontario) Asylum for the Insane and a close friend of Whitman's (Cushing 1925).

Osler documented the occurrence of transient ischemic attacks (TIA's) in a 62 year old man shortly after Peabody's attribution of this phenomenon to arterial spasm (Peabody 1891). Osler had doubts about this mechanism in view of the sclerotic nature

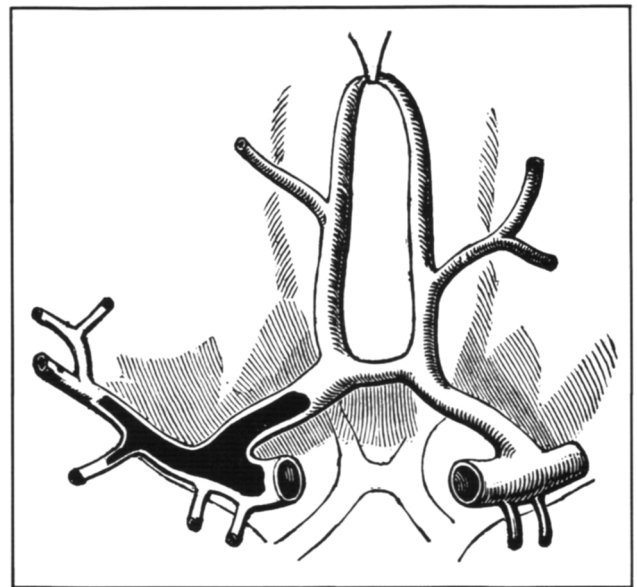


Figure 1 — Diagram from paper by Reddy 1871-72 (autopsy by William Osler) showing clot in internal carotid-middle cerebral arteries.

of the arteries. Osler's literary talents are nowhere more evident than in the description of another man "who had driven his engines at full steam" who also had episodes of transient cerebral ischemia. Referring to the case as "death at the top", he described the sufferer as a man devoted to Venus, Vulcan and Bacchus - a description surely more picturesque than our contemporary recording of cases of beer per week or pack-years of smoking (Osler 1911) (Osler 1911-12). It is interesting to note that Osler has been quoted as espousing spasm as a cause of TIA and also criticized for not embracing this concept by different authors in different generations (Russell 1912; Hachinski 1982). He was still alive to answer Russell's critique but tended not to commit himself completely (Osler 1912) on this issue, although he felt that spasm was the most plausible explanation. Contemporary thinking is that primary spasm is unlikely in the clinical setting he described. Also in the area of vascular disease, Osler reported a case of embolism of the anterior cerebral artery (Osler 1887c), cases of hemiplegia with typhoid fever (Osler 1900a), and a probable post-traumatic carotid cavernous fistula (Osler 1882-83). He wrote on the neurological complications of cases now strongly suggestive of lupus erythematosus (Osler 1895a; Osler 1900b; Osler 1903; Tumulty et al 1949). He also recorded the recurrent laryngeal palsy associated with mitral incompetence and its importance in the differential diagnosis of thoracic aneurysm (Osler 1909). In his autopsied case of this entity he documented the sclerosis of the nerve between the aorta and the left auricle. He also recorded the pupil sign of thoracic aneurysm, an observation which has at times been misquoted. The phenomenon of ipsilateral Horner's syndrome secondary to aneurysm is now well known and often attributed to Osler's description. In fact, going over the original paper, it appears that Osler described pupillary dilatation rather than constriction on the ipsilateral side (Osler 1910a). The reason for this was unclear although irritation of the sympathetic nerve was Osler's explanation. No less an authority than Fielding Garrison, summarizing Osler's contributions in his obituary notice, records that he was the first to relate mycotic aneu-

relate mycotic aneurysms to bacterial endocarditis and to draw attention in his Gulstonian lectures on endocarditis to the cerebral presentations of this disorder including the complication of meningitis (Garrison 1920).

#### Movement Disorders and Psychiatric Disease

Osler maintained his early interest in psychiatric disease and wrote papers on post-febrile insanity (Osler 1890a), the Gilles de la Tourette syndrome which he likened to the Malay disease Latah (probably related to his interest in chorea) (Osler 1890b), and on the form of neurosis known as typhoid spines (Osler 1919a) thought by Pepper to be due to periostitis.

A number of publications addressed movement disorders. He doubted Charcot's view that Huntington's and Sydenham's chorea were similar and wrote an excellent monograph on chorea which is a model of a clinical epidemiologic study (Osler 1894a). The title page of this work is seen in Figure 2. Although Richard Bright had noted the association of heart disease with chorea it was Osler who solidly established it (Osler 1887d; Osler 1887e; Garrison 1920). He classified chorea and clearly separated hereditary chorea from the acquired form. This led to the adoption of rest as treatment for chorea because of the very frequent association with carditis which he helped establish. In his autopsied case of Huntington's chorea he noted the "well-recognized clinical trick" that such patients exhibit of raising their heel suddenly and standing on the balls of their toes. He overlooked the specific caudate nucleus atrophy of this disorder although he did notice that the ventricles were distended (Osler 1894b). He wrote on wry-neck with facial asymmetry contrasting the lack of progression in his two cases with its presence in Romberg's facial hemiatrophy (Osler 1892b).

#### Neuropathology

Osler's medical career was founded on solid pathological observation and his neurological contributions were usually backed up by careful neuropathological study. His interest in neuropathology was not casual - he wrote several papers on neuropathological methods, including an elegant study on the interstitial processes of the central nervous system which included detailed discussion on connective tissues in the nervous system and how they are involved in degenerative, inflammatory and developmental disorders. (Osler 1879; Osler 1892c). His studies on gliomas led him to doubt Klebs' contention that the nerve cells were involved in proliferation (Osler 1885-86). As a working neuropathologist he became aware of and learned many of the new German methods for study of the brain during his visits to Europe. Osler liked to indulge in "quinquennial brain dustings" and his visit to Europe in 1890 with Ramsey Wright of the University of Toronto was typical of this. Of special interest in the present context are the number of neurological figures he visited at that time. These included Strumpel, Weigert, Von Recklinghausen, Naunyn, Goltz, Edinger, Erb, Dejerine and Bouchard among others. He was impressed with Weidersheim's use of different colours of chalk for teaching neuroanatomy and may have adopted this on his return (Osler 1890c). On one of his visits to Charcot's hospitals he was amused by Charcot's attempt to use hypnotism to cure a man with club feet of his inability to walk. He also observed hypnosis at the hands of Luys, a well known neurologist, who hypnotized one of his nurses into giving a lecture on neuropathology, a feat which she performed but with which Osler was very much unimpressed, telling Ramsay Wright that this was "a circus".

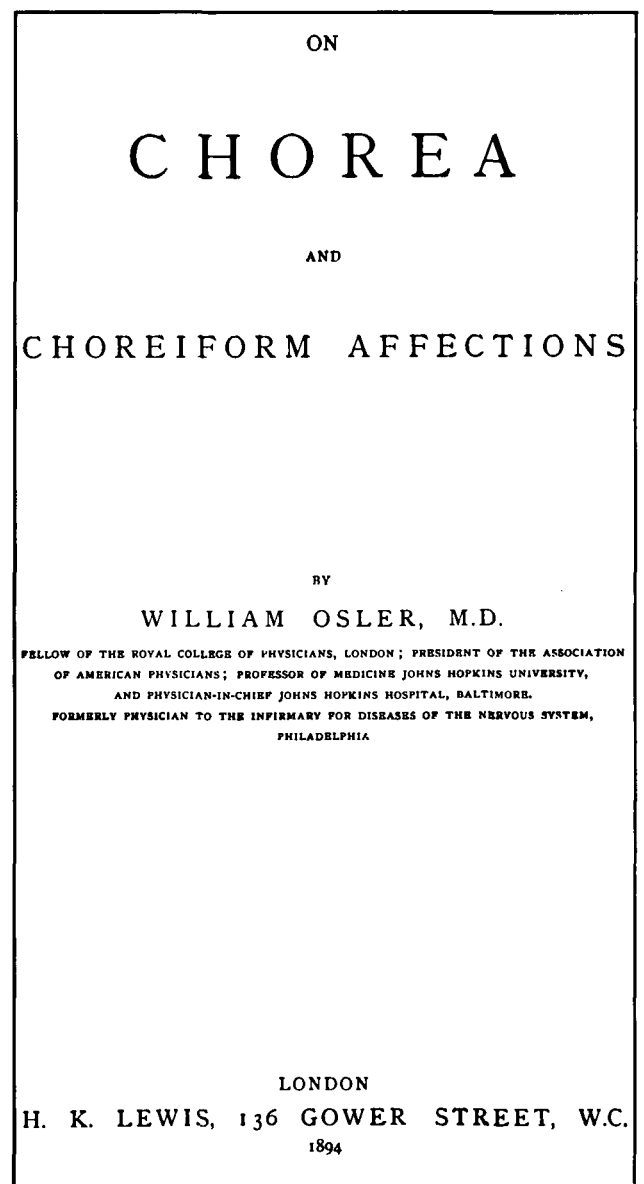


Figure 2 — Title page of Osler's monograph "On Chorea" dedicated to Gowers.

#### Peripheral Nerve

Osler wrote about disorders of the peripheral nervous system including arsenical neuritis and post-typhoid neuropathy which in retrospect may well have been a form of what we now call the Guillain-Barré Syndrome (Osler 1895b). Cushing reports that while on a visit to Toronto Osler's nephew developed an acute paralysis with Osler discussing the differential diagnosis between polyneuritis and poliomyelitis, an issue he had dealt with in print (Osler 1886) noting the sensory changes and better prognosis in the former disorder. Still within the peripheral nervous system, Osler wrote about cervical rib and the neurovascular syndrome it produced. His two papers on the subject demonstrate his characteristic honesty in reporting and give some insight into the man himself. The first case was not correctly diagnosed but the clinical phenomena were clearly identified (Osler 1888c). Some years later when he came to the correct diagnosis he reported the case emphasizing how he had been in

years previously (Osler 1910b). Osler also described the first case of facioscapulohumeral dystrophy in North America (Osler 1889b).

### Meningitis

Osler had a special interest in the subject of meningitis and he wrote several papers and reviews in this area (Osler 1881-82b; Osler 1888d; Osler 1899a). A review of his writings on meningitis is particularly interesting as they document the evolution of general medical understanding of this disorder and the introduction of the lumbar puncture by Quincke which Osler advocated in the investigation of the problem. At the time of his first publications, there was no distinction among the various forms of meningitis. However, gradually specific forms of meningitis were identified - initially epidemic vs non-epidemic and subsequently pneumococcal vs meningococcal (Osler 1914-15; Osler 1919b).

### Cushing's Disease

He made a "remarkable near miss" in the description of Cushing's Disease. He published a case of myxedema with glycosuria but in retrospect, on rereading the case reported, that it is almost certain that this was a case of Cushing's Syndrome (Osler 1899b) as pointed out recently (Altschule 1980). The patient had abdominal striae and other typical features of the disorder. There is no evidence that Cushing (for whom this disease was eventually named) had ever discussed the condition with Osler. In Cushing's text on surgery of the head there is a sketch of a man with a bullet in his head which bears a distinct resemblance to Osler, perhaps the kind of literary joke one might have expected from Osler himself (Cushing 1908).

### Neurological Associations

There is abundant other evidence of Osler's close association with neurologists. The neurologists Gowers and Bastian had written letters of support for Osler's application to the University of Pennsylvania. Osler wrote obituaries for Charcot, Mitchell and Horsley (Osler 1893a; Osler 1914; Osler 1916) and his review of Paget's biography of Horsley was Osler's last published work (Osler 1919c). In this review he described Horsley's removal of a spinal cord tumour as perhaps the most brilliant operation in the whole history of surgery. This latter work permits one to say that Osler began and ended his published medical career in the nervous system. He wrote two monographs of high quality on neurology dedicating the one on chorea to Gowers and that on cerebral palsy of children to Weir Mitchell (Osler 1889c) who had obtained his appointment to the Philadelphia Orthopedic Hospital and Infirmary for Nervous Diseases. The work for both these monographs originated at this institution.

Osler established a neurological journal club while at John Hopkins, the proceedings of which are to be found in the early issues of the *Bulletin of the John Hopkins Medical School*.

Osler made numerous contributions to textbooks and wrote the introduction for Hirt's Textbook (Osler 1889d). The three neurological chapters which he contributed to "Pepper's System of Medicine" comprised one half of the six chapters Osler wrote for this compendium (Osler 1893b; Osler 1893c; Osler 1893d). He wrote the chapter on "Diseases the Direct or Indirect Result of Infection" for "A Textbook of Nervous Diseases by American Authors", edited by Dercum (Osler 1895c).

### Oslerian Reminiscences

Among Oslerian reminiscences was one written by neurologist Pierre Marie (Marie 1926) with whom Osler had visited on numerous occasions. Marie had also written a preface for an early French edition of Osler's textbook of medicine. Osler had numerous biographers and these included many medical and surgical neurologists such as Charles Mills, Dercum, Lewis, Penfield, Courville, Henry Viets, and of course Cushing.

### Osler's Brain

Even after Osler's death his association with the nervous system continued. Probably because of his interest in the mind-brain problem, Osler left his brain to the Wistar Institute in Philadelphia for study, an institution which Osler had helped to open years before. His brain, along with those of two other scholars Granville Hall and Edward Morse were compared in intense detail (Donaldson et al 1928). The findings were also correlated with studies previously done by Myrtel Canavan (who is now eponymously remembered for Canavan's Disease) with the brains of the Southard family in Boston (Canavan 1926). Ernest Southard had been the Bullard professor of neuropathology at Harvard University in whose department Dr. Canavan had worked.

Following Archibald Garrod's seven year term, Osler's successor as Regius Professor of Medicine at Oxford was a neurologist, Sir Farquhar Buzzard, an additional Osler biographer (Buzzard 1928).

### Oslerian Legacies

Osler's legacy to neurology is in part due to his great skills as a teacher. It is worth noting here that the accomplishments of his students are well known but, in particular, that the great English neurologist Sir Charles Symonds, as well as Lord Brain, were both influenced by Osler to pursue neurology. Symonds related that he decided on a career in neurology after seeing Osler diagnose a case of cervical rib (Brain 1960; Symonds 1969). It is certainly possible that Osler had an important influence on the development of 20th century neurosurgery through his relationship with Cushing. Osler was quick to identify, from his clinical pathological studies of the nervous system, the potential for surgical treatment of tumours of the brain localized by clinical findings. Did Osler push Cushing into neurosurgery? After Godlee's celebrated removal of a glioma, Osler wrote an editorial judging such an operation justifiable and possibly lifesaving (Osler 1885a). In a subsequent paper entitled "Conditions of the brain suitable for operative interference", Osler noted that ganglionic hemorrhage was not appropriate. He stated that tuberculomas, gliomas, sarcomas and carcinomas occurred in decreasing order of frequency and that tumours of the dura looked very promising (for surgery) (Osler 1889e). He also mentioned the possibility of treating epilepsy with this new modality. It would seem quite possible that Osler conveyed his enthusiasm for this nascent field to Cushing, a close friend and protégé.

### Osler the Neurological Clinician

Although it has recently been suggested that Osler possibly "did not have the feel for clinical neurology" (Matthews 1982) the observations in the present review give reason to think otherwise. Riese has published a case detailing the autopsy

findings of a patient with symptoms of Parkinson's disease. It was subsequently found that Sir William Osler had made the diagnosis of multiple sclerosis some 50 years previously and this in fact was confirmed at autopsy (Riese 1952). Osler did not recognize Parkinson's disease. Thomas McCrae related the story of a patient with a slowly developing neurological disorder who had had opinions from a remarkable list of American, British, French and German physicians and Osler had been the first to suggest the correct diagnosis - Parkinson's disease (McCrae 1926).

In Osler's writings he relates how he tested for 2 point discrimination and used the rim of the stethoscope to elicit tendon reflexes (Osler 1883b). Osler diagnosed one of the first cases of acromegaly in North America and in his letters to house staff it was clear he was on the lookout for such a case even prior to seeing one because he had read Pierre Marie's classic description in the journal *Brain* or perhaps had discussed it with him (Osler 1890c; Tigertt 1971). Osler wrote on the neurological examination including discussions of brain murmurs in children (Osler 1880) and variations of the normal knee jerk (Osler 1887f).

In reviewing Osler's published writings it is extraordinary how often he was on the correct side of what seemed to have been controversial issues. Examples of these include the subdural hematoma, and tabes dorsalis. Although in retrospect it is possible to find Osler occasionally in error, such as in his early views on the spontaneous generation of blood platelets (influenced by Bastian), it is indeed uncommon. Osler's papers and chapters make entertaining reading today, replete as they are with literary references, aphorisms and medical wisdom, occasional social commentary, and above all, accurate observation. It is fair to state that a few of his papers were not memorable. Oslerian encounters in neurology brought the well known therapeutic nihilist to a discipline spare in practical treatments. Osler's view that nitroglycerin was helpful for epilepsy has not been substantiated (Osler 1888e). Osler's failure in the use of acupuncture analgesia has been recorded (Cushing 1925; Anonymous 1974). He did not find success in treating patients with locomotor ataxia by hanging them upside down for three minutes at a time as suggested by Charcot (Osler 1889f). Nevertheless, Osler's papers usually stand in striking contrast to those adjacent to his in the journals in which he published.

Osler played an important role as a general medical critic for his ability to determine flaws in others' works no doubt added to his general reputation and the esteem in which he was held. In the neurological area we can credit him with "debunking" the gross changes said to be characteristic of the brains of criminals, and the denial of "typhoid spine" as a specific disease entity. He formally reviewed many neurological works for the general medical literature, including Gowers on the spinal cord (Osler 1885b), Bramwell on the same (Osler 1885c) and Mitchell on diseases of women (Osler 1885d).

My interest in Osler was kindled by curiosity as to whether multiple sclerosis is increasing in prevalence. Osler's records and writings have proved to be most interesting in this context. Osler described the first case of multiple sclerosis in Canada at autopsy (Osler 1880-81a) shortly after the description of the first North American case (Seguin et al 1878).

He identified a number of cases premortem and postmortem (Osler 1880-81a; Osler 1880-81b). In some 786 patients autopsied over eight years in the Montreal General Hospital, Osler identified

one definite case and two possible cases of this disorder (G. Ebers 1982; Osler autopsy records, Osler Library McGill University, Montreal). Although these data are obviously severely limited they may represent the best available evidence concerning the prevalence of multiple sclerosis 100 years ago in Osler's time.

In summary it can be stated that Osler's neurological contributions were numerous, and many were first rate. His autopsy records provide a remarkable account of contemporary neurological disease through the eyes of an accurate and careful observer. Both these and his clinical studies of the nervous system have been under-appreciated. Osler belonged as much to Neurology as to any other field of medicine.

#### ACKNOWLEDGEMENTS

I would like to acknowledge the help of Marilyn Franciszyn of the Osler Library, Mrs. Sheila Swanson of the Toronto Academy of Medicine Library and Professor C.G. Roland of McMaster University for helpful discussions and to Drs. William Gibson and C.A. McDowell of the University of British Columbia for reviewing the manuscript. This paper was presented in part at the Osler Society meeting in Atlanta, April 1984 and at the American Academy of Neurology (Ebers 1982).

#### REFERENCES

- Abbott M (1939) *Classified and Annotated Bibliography of Sir William Osler's Publications*. Montreal, The Medical Museum, McGill University.
- Altschule MD (1980) A near miss - Osler's early description of Cushing's syndrome. *N Eng J Med* 302:1153-55.
- Anonymous (1974) Osler, Peter Redpath and acupuncture. *Osler Library Newsletter* 16.
- Benedikt M (1879) *On the Brains of Criminals* (translated by Dr. Fowler). W. Wood and Co. New York.
- Bett WR (1949) Osler the medical historian. *Med Press*, 222:35-37.
- Brain R (1960) Osler and medicine today. *Can Med Assoc J* 83:349-354.
- Buzzard F (1928) The pain, penalty, and prohibitions of old age - can they be prevented. *Bull N Y Acad Med* 4:1068-1077.
- Canavan MM (1926) *Ernest Elmer Southard and his Parents: A Brain Study*. University Press, Cambridge, Massachusetts.
- Cunha F (1948) Osler as a gastroenterologist. *Alameda California Times - Star Press*.
- Cushing H (1908) *Surgery of the head*. In: *Surgery: Its Principles and Practices*. Edited by W.W. Keen, 3:248.
- Cushing H (1925) *The Life of Sir William Osler*. Oxford, Clarendon Press.
- Dejerine J (1891) Sur un cas de celite verbale avec agraphie, Suivi D'Autopsie *Mem Soc Biol* 3:197-2
- Donaldson HH and Canavan MM (1928) A study of the brains of three scholars: Granville Stanley Hall, Sir William Osler, Edward Sylvester Morse. *J Comp Neurol* 46:1-95.
- Ebers GC (1982) Osler and Neurology. *Neurol* 32(2):A229.
- Garrison FH (1920) Sir William Osler, 1849-1919. *Science*, li:55-58.
- Giltner W (1926-7) Osler and veterinary medicine. *J Am Vet Med Assoc* 69:422-432.
- Hachinski V (1982) Transient cerebral ischemia: A historical sketch. In: *Historical Aspects of the Neurosciences*. Edited by F.C. Rose and W.F. Bynum. Raven Press, New York.
- Harvey AM, McKusick VA (1967) *Osler's Textbook Revisited*. New York, Appleton - Century - Crofts.
- Marie P (1926) Osler - educateur. *Int Assoc Med Mus Bull* 9:9.
- Matthews WB (1982) Osler oration. *J Royal Soc Med* 25:307-314.
- McCrae T (1926) The influence of pathology on the clinical medicine of William Osler. *Int Assoc Med Mus Bull* 9:37-41.
- McGovern JP, Davison WC (1970) Osler and pediatrics. *Am J Dis Child* 119:5.

- Murphy DA (1960) Osler now a veterinarian. *Can Med Assoc J* 83: 32-35.
- Osler W (1879) On Giacomoni's method of preserving the brain. *Can Med Surg J* viii:16-17.
- Osler W (1880) On the systolic brain murmur of children. *B Med Surg J* ciii:29-30.
- Osler W (1880-81a) Cases of insular sclerosis. *Can Med Surg J* ix:1-11.
- Osler W (1880-81b) A contribution to the question of spastic spinal paralysis. *Can Med Surg J* ix:100.
- Osler W (1881-82a) The VII international medical congress London. *Can Med Surg J*, Montreal, x:121-125.
- Osler W (1881-82b) Case of tubercular meningitis. *Can Med Surg J* x:603-606.
- Osler W (1882a) The brains of criminals. *Can Med Surg J* x:385-398.
- Osler W (1882b) The brains of criminals. *Lancet* II:38.
- Osler W (1882c) Uremic delirium at a very early stage of interstitial nephritis. *Arch Med*, New York, vii:213-215.
- Osler W (1882-83) Cerebral aneurism and hemorrhage: Erosion of internal carotid into cavernous sinus six weeks after a blow on the head. *Can Med Surg J* xi:335-358.
- Osler W (1883a) On the brain as a thinking organ. *Can Nat* x:109.
- Osler W (1883b) Pre-ataxic tabes dorsalis. *Med News*, Philadelphia, xliii:197-199.
- Osler W (1884a) The brain of the seal. *Can Rec Nat Sci* i:64.
- Osler W (1884b) Fibrogloma of upper end of ascending frontal gyrus. *J Nerv Ment Dis* xlv:82-83.
- Osler W (1885a) Removal of a brain tumor (unsigned editorial). *Med News*, Philadelphia, xlvi:75.
- Osler W (1885b) The Diagnosis of Diseases of the Spinal Cord by W.R. Gowers (initialled book review). *Am J Med Sci*, Philadelphia, lxxix:218-219.
- Osler W (1885c) Diseases of the spinal cord by Byron Bramwell. The Second Edition, Edinburgh: Young J., Pentland, 1884. (Initialled book review). *Am J Med Sci*, Philadelphia, xc:504.
- Osler W (1885d) Lectures on Diseases of the Nervous System, Especially in Women, by S. Weir-Mitchell. Second Edition, Phila. Lea Bros. & Co. (unsigned book review). *Med News*, Philadelphia, xlvi:162.
- Osler W (1885-86) The structure of certain gliomata. *Med Times*, Philadelphia, xvi:394-395.
- Osler W (1886) Multiple neuritis. *Med News*, Philadelphia, xlix:10-11.
- Osler W (1887a) Case of cholesteatoma of the floor of the third ventricle and infundibulum. *J Nerv Ment Dis* xiv:657-73.
- Osler W (1887b) Aneurism of the larger cerebral arteries. *Trans Path Soc Phil* xiii:87-93.
- Osler W (1887c) Embolism of the left anterior cerebral artery - softening of the left frontal lobe. *Trans Path Society Phil*, 202-203.
- Osler W (1887d) Chorea and heart disease. *Med News*, Philadelphia, li:509.
- Osler W (1887e) The cardiac relations of chorea. *Am J Med Sci*, Philadelphia, xciv:371-386.
- Osler W (1887f) The variations of the normal knee jerk (editorial). *Med News*, Philadelphia, li:601.
- Osler W (1888a) On lesions of the conus medullaris and cauda equina and the situation of the ano-vesical centre in man. *Med News*, Philadelphia, lii:669-671.
- Osler W (1888b) Note on pachymeningitis hemorrhagica. *J Nerv Ment Dis*, New York, xiii:608-612.
- Osler W (1888c) Enlargement and congestion of the right arm following exercise of the muscles. *J Nerv Ment Dis*, New York, xiii:246-248.
- Osler W (1888d) Epidemic cerebral spinal meningitis (unsigned editorial). *Med News*, Philadelphia, lii:269.
- Osler W (1888e) Note on nitroglycerin in epilepsy. *J Nerv Ment Dis*, New York, xiii:38-39.
- Osler W (1889a) Case of syphiloma of the cord of the cauda equina - death from diffuse central myelitis. *J Nerv Ment Dis* xiv:499-507.
- Osler W (1889b) On a case of simple idiopathic muscular atrophy involving the face and scapulo-humeral muscles. *Am J Med Sci* xcvi:261-265.
- Osler W (1889c) The Cerebral Palsies of Children. K.R. Lewis, London.
- Osler W (1889d) Introduction in: Hirt, Ludwig. Diseases of the nervous system translated by A. Hoch, Appleton and Co., New York.
- Osler W (1889e) On conditions of the brain suitable for operative interference. *Can Pract* 14:165-167.
- Osler W (1889f) Treatment of locomotor ataxia by suspension. *Med News*, Philadelphia, liv:323.
- Osler W (1890a) Cases of post-febrile insanity. *Johns Hopkins Hospital Reports*, Baltimore, ii:46-50.
- Osler W (1890b) On the form of convulsive tic associated with coprolalia, etc. *Med News*, Philadelphia, lvii:645-647.
- Osler W (1890c) Letters to my house physicians. *N Y Med J* liii:163:191;274;333.
- Osler W (1891) A case of sensory aphasia: word-blindness with hemianopsia. *Am J Sci* ci:219-224.
- Osler W (1892a) The Principles and Practice of Medicine. D. Appleton and Co. New York.
- Osler W (1892b) On the association of congenital wry-neck with marked facial asymmetry. *Arch Ped*, New York, ix:81-85.
- Osler W (1892c) Interstitial processes in the central nervous system. *Trans Cong Am Phys Surg* 1891, New Haven, ii:144-146.
- Osler W (1892-93) Note on arsenical neuritis following the use of Fowler's solution. *Mont Med J* xxi:721-724.
- Osler W (1893a) Jean Martin Charcot, memorial notice. *Johns Hopkins Hospital Bulletin*, Baltimore, ix:87-88.
- Osler W (1893b) Organic Disease of the Brain in: A System of Practical Medicine by American Authors. Edited by W. Pepper. Philadelphia, i:669-725.
- Osler W (1893c) Diseases of the Nerves in: A System of Practical Medicine by American Authors. Edited by W. Pepper, Philadelphia, i:805-849.
- Osler W (1893d) Disease of the Muscles in: A System of Practical Medicine by American Authors. Edited by W. Pepper, Philadelphia, i:850-858.
- Osler W (1894a) On Chorea and Choreiform Affections. P. Blakiston Son & Co., Philadelphia.
- Osler W (1895b) A case of hereditary chorea. *Johns Hopkins Hospital Bulletin*, Baltimore, v:119-120.
- Osler W (1895a) On the visceral complications of Erythema Exudativum Multiforme. *Am J Med Sci* 110:629-646.
- Osler W (1895b) Neuritis during and after typhoid fever. *Johns Hopkins Hospital Reports*, Baltimore, v:397-416.
- Osler W (1895c) Diseases the direct or indirect result of infection: *In: A Textbook of Nervous Diseases* by American Authors, Edited by F.X. Dercum, Philadelphia, 203-226.
- Osler W (1898) Cerebral features of pneumonia. *Maryland Med J*, Baltimore, xxxviii:381-383.
- Osler W (1899a) On the etiology and diagnosis of cerebral spinal fever. *Br Med J* i:1517-1529.
- Osler W (1899b) An acute myxoedematous condition with tachycardia, glycosuria, melaena, mania and death. *J Nerv Ment Dis*, New York, xxvi:65-71.
- Osler W (1900a) Hemiplegia in typhoid fever. *Johns Hopkins Hospital Reports*, Baltimore, viii:363-371.
- Osler W (1900b) The visceral lesions of the erythema group. *Br J Derm* 12:227-245.
- Osler W (1903) On the visceral manifestations of the erythema group of skin diseases. *Trans Assoc Am Phys* 18:599-624.
- Osler W (1909) Paralysis of the left recurrent laryngeal nerve in mitral valve disease. *Mont Med J* xxvii:79-83.
- Osler W (1910a) The pupil symptom in thoracic aneurysm. *Practitioner*, London, lxxiv:417-422.
- Osler W (1910b) Certain vaso-motor sensory and muscular phenomena associated with cervical rib. *Am J Med Sci*, Philadelphia, New York, cxxix:469-472.
- Osler W (1911) Transient attacks of aphasia and paralysis in the states of high blood pressure and arteriosclerosis. *Can Med Assoc J* i:919-926.
- Osler W (1911-12) A case of recurrent aphasia with high blood pressure (discussion). *Proc Royal Soc Med*, London, v, Clinic Section, 113.
- Osler W (1912) Cerebral angiospasm. *Lancet* ii:1463.
- Osler W (1914) Silas Weir Mitchell MD, LL.D. *Br Med J* i:120-121.
- Osler W (1914-15) The epidemiology of cerebral spinal meningitis (remarks and discussion). *Proc Royal Soc Med*, London, ix, Therapeutics and Pharmacology, sect. 1-5.
- Osler W (1916) Sir Victor Horsley (unsigned obituary). *Br Med J* ii:165.
- Osler W (1919a) Typhoid spine. *Can Med Assoc J* ix:490-496.
- Osler W (1919b) Influenza pneumonia: bilateral rigidity, spinal meningitis with hemorrhage into the theca vertebralis and nerve roots. *Lancet*, i:501.
- Osler W (1919c) Book review. *Oxford Magazine* xxxviii:175.

- Peabody G (1891) A contribution to the symptoms and pathology of endarteritis obliterans. Address to The Practitioners Society, New York.
- Reddy J (1871-2) On paralysis with aphasia. *Can Med J* viii:407-408.
- Riese W, Jones GL, East IE, Beamer-Maxwell E, Davis HE (1952) Disseminating demyelinating process of over 50 years duration first seen by Dr. William Osler. *Confinia Neurologia* 12:113-120.
- Robbins BH, Christie A (1963) Sir William Osler the pediatrician. *Am J Dis Child* 106:124-129.
- Rodin AE (1981) Oslerian pathology : an assessment and annotated atlas of museum specimens. Coronado Press, Lawrence, Kansas.
- Rucker MP (1952) Sir William Osler's obstetric interests. *Bull Hist Med* 26:153-160.
- Russell W (1912) Motor and speech paralysis due to cerebral angiospasm. *Lancet* ii:1351.
- Seguin EC, Shaw JC, van Derveer A (1878) A contribution to the pathological anatomy of disseminated cerebrospinal sclerosis. *J Nerv Ment Dis* 5:284.
- Symonds C (1968) Letter to Charles G. Roland, M.D. February 24, 1968. *JAMA*, 210:2239.
- Tigertt WD (1971) Osler on acromegaly. *Can Med Assoc J* 105:1336.
- Tumulty P, Harvey AM (1949) Disseminated lupus erythematosus. *Bulletin of the Johns Hopkins Hosp.* 85:47-73.
- Wilson SAK (1940) *Neurology*. Edited by A N Bruce: E. Arnold Co. London.