Review of the History of Non-traumatic Spinal Cord Dysfunction

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Background: The incidence of non-traumatic spinal cord dysfunction (SCDys) is reported to be higher than traumatic spinal cord injury (SCI) in many countries. No formal review of the history of SCDys has been published. **Objective:** This article aims to identify key highlights in the history of SCDys. **Method:** An electronic literature search was conducted (January 2017) using MEDLINE (1946–2016) and Embase (1974–2016) databases for publications regarding the history of SCDys. Publications on the history of SCI and a selection of neurology textbooks and books on the history of neurology were reviewed for potentially relevant references. The focus of the literature search was on identifying publications that detail key highlights regarding the history of the diagnosis and management of the most common SCDys conditions, as well as those of historical significance. **Results:** The electronic search of MEDLINE and Embase identified 11 relevant publications. The majority of publications included were identified from the authors' libraries and a selection of books on neurology and the history of neurology. **Conclusions:** This review outlines the history of SCDys, taking a broader historical perspective and covering the increasing awareness of the role of the spinal cord and knowledge of neuroanatomy. Key milestones in the history of the diagnosis and management of the most common SCDys conditions are presented. An appreciation of the history of SCDys increases our understanding of the large number of people who contributed to our current knowledge of these conditions and in some situations helps guide efforts regarding prevention of SCDys. **Key words:** history of medicine, neurology, neurosurgery, spinal cord damage, spinal cord diseases, spinal cord dysfunction, spinal cord injury, review

The incidence of non-traumatic spinal cord damage, subsequently referred to as non-traumatic spinal cord dysfunction (SCDys), is reported to be higher than that of traumatic spinal cord injury (SCI) in many countries, with the best evidence for this from Australia and Canada.^{1,2} However, high-quality studies on the epidemiology of SCDys are lacking.³ SCDys is associated with older age,¹⁻⁴ and the causes are extremely varied and heterogeneous.^{3,5} The most common causes are degenerative conditions of the spinal column, benign or malignant tumor, vascular problems resulting in infarction or hemorrhage, infections, or inflammation.³⁻⁵ As a result of population aging, it is anticipated that the incidence of SCDys will increase dramatically in coming decades.¹

In spite of the increasing incidence of SCDys and these conditions being common in spinal

rehabilitation units, no detailed review of the history of SCDys has been published, as far as we are aware. An understanding of the history of SCDys provides an appreciation of the work of those physicians and surgeons who have contributed to this field and made it scientific and puts current knowledge in a broader context. It is only by reflecting on how knowledge and understanding have evolved and progressed over time that it is possible to truly appreciate how far the fields of neurology, neurosurgery, and spinal cord medicine have advanced. By studying the history of SCDys, we more fully understand the contribution of new advances. Information about the history of SCDys informs us about how we came to know what we know, helps us to appreciate why research is critical, and explains why doing research poses challenges. The aim of this article is to review the achievements through medical history regarding the discoveries

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leading to the diagnoses of the various conditions that cause SCDys and important aspects of their management.

Methods

Literature search: History of SCDys

An electronic literature search was conducted (January 2017) using MEDLINE (1946-2016) and Embase (1974-2016) databases for publications regarding the history of diagnosis or management of SCDys, with a focus on the most common reported causes of these conditions (degenerative, benign or malignant tumor, vascular problems resulting in infarction or hemorrhage, infections, or inflammation). The terms used in the literature search were the same as those used in a previously proposed gold standard comprehensive search strategy for SCDys.⁶ The results of this gold standard comprehensive search were combined with the search term “history”. Only publications in English were included. Publications on the history of SCI units and the field of spinal cord medicine were excluded. A summary of the search strategy and results is shown in **Figure 1**. The reference sections of the included publications were also screened for potentially relevant references.

In addition to the electronic literature search, a number of other sources were examined for potentially relevant publications. These included the following: the authors’ personal libraries, a selection of publications that reported on the history of SCI,⁷⁻¹⁴ a book on spinal cord diseases,¹⁵ and books on neurology¹⁶⁻¹⁹ and the history of neurology.²⁰⁻²⁷ We decided to include older books, because more recent books tended not to include historical background. References in any language that were identified from the above sources were included if they related to key developments in the history of the diagnosis or management of SCDys conditions. We did not plan to obtain and review every relevant reference identified from the above sources. This is because many were written hundreds of years ago and would be very difficult to locate and many were written in languages in which we were not fluent.

It would be impossible to detail here every publication and contributor to scientific discoveries

Figure 1. Flow chart of the search methodology and overview of results regarding history of spinal cord dysfunction (SCDys).

and advances that were involved with the diagnosis and management of conditions that cause SCDys. Progress in medicine is always the result of the combined efforts of many and builds on the work of predecessors and contemporaries. With this in mind, the focus of the literature search was on identifying publications that detail key highlights regarding the history of the diagnosis and management of the most common causes of SCDys, as well as those of historical significance, including congenital, genetic, degenerative, tumor, vascular, infections, and inflammatory conditions. Publications regarding causes of SCDys considered rare were generally not included; in a few instances, we briefly mention some rare conditions where

they form part of a more common etiology subgroup.

Results

Electronic literature search

The electronic search of MEDLINE and Embase identified only 11 publications of relevance.^{10,28-37} The results of this search are summarized in **Figure 1**. The majority of publications included in this review were identified from the supplementary sources that were searched, especially the selection of books on neurology and the history of neurology.

History of SCDys

Overview

There is evidence that spina bifida has existed since the dawn of man.³⁸ The ancient Egyptian Edwin Smith Papyrus, from around 3,000 to 2,500 BCE and believed to have been written by the physician Imhotep, includes the first reports of SCI but does not describe any cases of SCDys.³⁹⁻⁴¹ Hippocrates (460-377 BCE) reported his belief that cold and moisture during winter were associated with paraplegia.⁴² Aulus Cornelius Celsus (1st century BC) reiterated this belief.⁴³ Even up to the 16th century, some clinicians supported the belief that cold caused SCDys.⁴⁴ Hippocrates, however, was the first to describe SCDys resulting from paralysis due to infection of the spinal cord, possibly caused by tuberculosis.⁴²

A clearer understanding of the pathophysiology of conditions that cause SCDys started to emerge as an understanding of neuroanatomy developed. Key milestones in the understanding of spinal cord anatomy and functioning from the period of Galen to the late 19th century have been discussed in detail previously.²² Thomas Willis gave the first accurate descriptions of vascular supply of the spinal cord in 1664.⁴⁵ The first publication devoted entirely to the spinal cord was published in 1666 by the Dutch physician, Gerard Blaes.⁴⁶ During the 18th century, knowledge and understanding of the structure and functions of the spinal cord started to improve as a result of physicians, such as Frank's study of the spinal cord⁴⁷ and Percivall Pott's work

on tuberculosis.^{48,49} It was only in the 19th century that the spinal cord was recognized as an extension of the brain⁵⁰ and a greater understanding of structure and function of the spinal cord was acquired.⁵¹⁻⁵³ An appreciation of the different diseases that can affect the spinal cord started to emerge, but even then there were numerous misconceptions.^{54,55} It was not until 1866 that it was recognized that the spinal cord could be damaged by circulation disturbances as well as inflammation, but debate on this matter persisted for some time.¹⁷ In the later 19th century, advances in the understanding of the blood supply of the spinal cord by Duret,⁵⁶ Adamkiewicz,⁵⁷ and Kadyi⁵⁸ were pivotal in increasing our understanding of the neuroanatomical basis for infarction and vascular malformations. It was not until 1921 that Basso and Hassin clarified the distinction between myelitis and myelomalacia.⁵⁹

Beginning in the 20th century, neurological disorders were classified into the broad categories of trauma, infections, vascular, nutritional, degeneration, inflammatory or demyelinating, and hereditary.²³ These categories, with the exception of trauma, form the basis of the current recommended classification of the etiology of SCDys.⁵

Key highlights in the history of SCDys regarding the diagnosis and management of associated conditions are presented in the following sections. These sections are structured according to the major categories of SCDys, and the focus is on the more common causes of SCDys. Surgery has a role in the management of numerous conditions. Key neurosurgical highlights are given in relevant sections, and additional details can be found elsewhere.^{29,32,38,60-63}

Genetic

Hereditary spastic paraplegia. Hereditary spastic paraplegia was described by Ernst Adolf Gustav Gottfried von Strümpell (1853-1925), a German neurologist, in 1880.⁶⁴ Maurice Lorrain, a French physician, published his description some years later.⁶⁵ It is now known that these are a heterogeneous group of genetic neurodegenerative disorders characterized by progressive weakness of the lower limbs and spasticity and typified

pathologically by retrograde axonal degeneration of the corticospinal tracts and posterior columns. Over recent years, genetic studies have identified the key cellular functions that are essential for maintenance of the axonal homeostasis in hereditary spastic paraplegia.⁶⁶

Friedreich's ataxia. Friedreich's ataxia is named after Nikolaus Friedreich (1825-1882), a German neurologist.⁶⁷ A more detailed description and the eponymous name were subsequently given by Brousse.⁶⁸ With recent advances, the genetics and pathophysiology of this condition are much more understood.⁶⁹

Motor neurone disease (amyotrophic lateral sclerosis). Motor neurone disease was first described in detail by Aran in 1850.⁷⁰ The French physician Jean-Martin Charcot (1825-1893) recognized the occurrence of both upper and lower motor neurone features in 1873.⁷¹ Although motor neuron disease remains inevitably fatal and there are no definitive treatments, there has been progress regarding therapy and management strategies that can improve survival.^{72,73}

Congenital

As noted above, spina bifida has existed as long as humanity. Archeological findings and a large number of anthropological figures from early civilizations provide evidence of children with characteristic features.³⁸ A description of spinal bifida was given by Hippocrates.⁷⁴ The oldest definitive description of spina bifida is by the Dutch clinician Pieter van Foreest (1522-1597) in the late 1500s.⁷⁵ Nicolaas Tulp (whose real name was Claes Piereszoon) coined the term *spina bifida* in 1641.⁷⁶

For hundreds of years, the surgical treatment of spina bifida typically involved ligation or amputation of the dural sac. The outcome of this was almost always fatal because of central spinal fluid leakage and infection or the secondary progressive untreated hydrocephalus.³⁸ By the early 20th century, better surgical concepts of repair started to emerge, with multilayer closures using dura, fascia, muscles, and skin advocated by Charles H. Frazier in 1918.⁷⁷ This approach was further refined and standardized by Ingraham and Hamlin in 1943.⁷⁸ Ingraham and Hamlin, however,

advocated that surgery should be delayed until 18 months of age to allow adequate assessment of the patient's neurological outcome, but this was not universally accepted. A study by Sharrard in 1967 confirmed that better results were obtained by performing the surgery in the perinatal period⁷⁹; this is now routine practice in most countries. More details regarding the history of the surgical management of spina bifida⁸⁰ and other aspects of this condition have been published previously.³⁸

There is an enormous amount of evidence that periconceptional supplementation with folic acid daily prevents spina bifida.⁸¹ This is a low-cost intervention.⁸² To be effective, the folic acid supplementation needs to occur before conception. To address this requirement, many countries have introduced compulsory folic acid supplementation of flour, which has reduced the incidence of neural tube defects substantially.⁸³ Unfortunately, many countries with inadequate resources to implement effective supplementation also lack the resources to address the lifelong consequences of spina bifida. Folic acid supplementation remains the cheapest strategy for the prevention of any cause of SCDys.^{84,85} Important developments during the 20th century regarding the isolation and synthesis of folic acid as well as neural tube defects prevention programs are discussed elsewhere.⁸⁶

Degenerative conditions of the spinal column

Sir Johnathan Hutchinson (1828-1913) is credited with describing the first clinical account of a prolapsed intervertebral disc resulting in paraplegia in 1866, but definitive confirmation was not possible due to the limitations of investigations available at the time.^{87,88} The recognition that extrinsic compression in the region of the intervertebral foramen may initially involve the nerve roots causing a radiculopathy and, with progression, result in partial and then complete cord compression was first noted by Hermann Oppenheim (1858-1919) in 1923.⁸⁹ Cervical spondylotic myelopathy was described in 1928 by Stookey and was reported to be due to compression of the spinal cord by cartilaginous nodules of degenerative disc.⁹⁰ The appreciation that posterior cervical disc prolapse with osteophyte formation can impinge on

either the spinal cord resulting in myopathy or the nerve root at the exit foramen resulting in a radiculopathy, or a combination of both, was first recognized by Brain in 1952.⁹¹ Clarke and Robinson were the first to distinguish cervical spondylitic myelopathy from acute disc prolapse in 1956.⁹² A history of the surgical management of prolapsed intervertebral disc has been previously published.⁶⁰ The first surgical removal of a prolapsed lumbar intervertebral disc was performed by Mixter and Barr in 1934.⁹³ The major developments in prolapsed intervertebral disc surgery progressed from a full laminectomy to hemilaminectomy and then partial hemilaminectomy,⁶⁰ as described by Love in 1939.⁹⁴

Ossification of the posterior longitudinal ligament is a hyperostotic condition of the cervical spine that is associated with SCDys. It was reported by Key in 1838.⁹⁵ It is common in Japan and is relatively rare elsewhere.⁹⁶ A detailed account of the history of ossification of the posterior longitudinal ligament is available.⁹⁷

It is now recognized that the best-practice management of people with degenerative conditions of the spinal column resulting in SCDys includes access to appropriate imaging investigations and surgery for treatment where there is spinal canal compromise causing severe symptomatic cord compression.^{98,99} There is, however, inadequate good quality evidence regarding the other clinical scenarios regarding whether surgery should be performed and, if so, the type of surgery and timing of these procedures.^{62,63}

Tumor

The French surgeon Claude-Nicolas Lecat (1700-1768) performed the first rudimentary attempt at the surgical removal of an intraspinal tumor in 1753.¹⁰⁰ In 1874, von Leyden discussed the possible surgical removal of spinal tumors.¹⁰¹ Macewen reported a “connective tissue tumour” and a “fibrous tumour” when trephining the spine for fracture and scoliosis in 1888.¹⁰² The first successful resection of an intradural tumor, a fibro-myxoma, was performed in 1887 by Sir Victor Horsley (1857-1916), after the diagnosis was made by Sir William Gowers (1845-1915).¹⁰³ The first report of resection of an intramedullary spinal cord

tumor was by Christian Fenger in 1890,¹⁰⁴ and the first successful resection was performed by Anton von Eiselsberg in 1907.¹⁰⁵ In 1911, Charles Elsberg described a 2-stage strategy for the removal of intramedullary tumors.¹⁰⁶ Following these initial reports, however, the complication rate remained very high and many neurosurgeons recommended a conservative approach with biopsy, dural grafting, and radiation therapy regardless of histological diagnosis. A summary of early surgical management of spinal tumors has been published.⁶⁰ During the latter half of the 20th century, major developments, such as bipolar cautery (1940s), the operating microscope (1950s), ultrasonic aspirator (1970s), intraoperative ultrasound imaging (1980s), magnetic resonance imaging (1980s), intraoperative neurophysiological monitoring (1990s), plated bayoneted forceps (1990s), and the surgical laser (2000s), significantly improved outcomes for patients with spinal cord tumors.³²

The benefits of radiotherapy for spinal tumors was documented by Wood in the 1950s.¹⁰⁷ Radiotherapy is now routine for many primary and secondary spinal cord tumors and is often used in conjunction with surgery.¹⁰⁸

Spinal cord damage secondary to radiotherapy treatment for spinal cord tumors, Hodgkin's disease, and mediastinal or head and neck cancers was first reported in the 1940s.¹⁰⁹ It is now recognized that there are 2 patterns of radiation myelopathy, an early (transient) and a progressive (delayed) pattern.¹¹⁰ The early onset pattern typically starts from 6 weeks to 6 months after radiotherapy and improvement usually occurs in most cases within 2 to 9 months, although some people have persisting symptoms. The pathophysiology involves a transient demyelination secondary to a loss of oligodendroglial cells.¹¹¹ Progressive myelopathy typically starts 6 months to 10 years after radiotherapy, and risk factors include older age, previous irradiation in childhood, higher radiation doses, and large portals involving the thoracic or lumbar spinal cord.¹¹⁰

Para-neoplastic myelitis was documented relatively recently. Presenting as a rapidly progressive necrotic myelopathy, it was first described by Mancall and Rosales in 1964¹¹² and is now recognized to occur in a number of tumors. In 1979, a subacute motor neuropathy was described

in association with lymphoma¹¹³ and has since been described in association with small-cell lung carcinoma¹¹⁴ and other malignancies.

It is now accepted best practice that patients with suspected spinal tumor require rapid access to magnetic resonance imaging as secondary malignant tumors may require prompt surgery and/or radiotherapy, especially within the first 48 hours of symptom onset, in order to reduce the progression from bony lesions to symptomatic SCDys and to limit the severity of the neurological impairment.¹¹⁵ The role of surgery, radiotherapy, and chemotherapy in spinal cord tumors is complex and beyond the scope of this article, but reviews on this have been published.¹¹⁶⁻¹¹⁸

Vascular

Infarction. In 1825, Sir Astley Paston Cooper (1768-1841) gave the first account of ligation of the abdominal aorta, with the patient developing loss of sensation in their lower limbs and incontinence of urine and feces,¹¹⁹ but he did not recognize the role of spinal cord infarction in the clinical symptoms.¹⁰ In 1857, Gull described a case of paraplegia due to obstruction of the abdominal aorta.¹²⁰ Brown-Sequard described a number of patterns of paralysis arising from vascular disturbances in 1860.¹²¹⁻¹²³ In 1909, Spiller described clinical details and postmortem findings of thrombosis of the anterior spinal artery.¹²⁴ In 1910, the concept of embolism affecting the spinal cord was proposed by Bastian.¹²⁵ It was only in 1934 that Shennan firmly established the link between aortic aneurysms and spinal cord infarction, with a report of 17 of his own cases and 300 other cases from the preceding century.¹²⁶ The anterior spinal artery syndrome as a distinct entity was described in 1944 by Davison¹²⁷ and Beck in 1952.¹²⁸ It was not until the advent of aortic surgery in the 1950s, however, that spinal cord ischemia emerged as a major clinical entity.¹²⁹ A more detailed history of spinal cord infarction has been published previously.¹⁰

There is now evidence that the early detection of spinal cord ischemia by intraoperative neurophysiologic monitoring and postoperative neurological examination may enable management strategies that can prevent permanent SCDys.¹³⁰ It is believed that improvements in vascular surgery,

such as endoluminal stenting of abdominal aortic aneurysms instead of open repair, may help prevent spinal cord infarction, but the evidence is currently inconclusive.¹³¹

Spinal cord claudication was distinguished as a separate condition from intermittent claudication due to peripheral vascular disease by Dejerine in 1906.¹³² In 1961, another type of neurogenic claudication was documented, by Blau and Logue, due to ischemia or compression of the cauda equina from lumbosacral stenosis.¹³³

Hemorrhage. Subdural spinal cord hemorrhage was first described by the French physician M Gaultier de Claubry in 1808,^{134,135} and subarachnoid spinal cord hemorrhage was described by Charles-Prosper Ollivier d'Angers (1796 -1845) in 1827.¹³⁶ These conditions are uncommon but are mentioned here for completeness. Prompt diagnosis with magnetic resonance imaging and surgery is vital to improving patient outcome.¹³⁷

Arteriovenous malformation. In 1865, Rudolf Ludwig Carl Virchow (1821-1902) was the first to classify arteriovenous malformations, based on autopsy findings, but he described them as neoplasms.¹³⁸ Early descriptions of intraspinal vascular abnormalities were given by Hebold in 1885¹³⁹ and Berenbruch in 1890.¹⁴⁰ Likewise, the lesion was not recognized as a vascular malformation at surgery, but it was confirmed as such at autopsy. Krause was the first to identify a spinal lesion as a vascular abnormality at the time of surgery, but he did not attempt to resect it.¹⁴¹ In 1912, Charles Elsberg was the first to attempt to excise a spinal arteriovenous malformation.¹⁴² The advent of selective arteriography¹⁴³ and neurosurgical advances (outlined in the tumor section of this article) played major roles in improving the surgical and clinical outcomes for patients since the 1960s.^{28,30} Additional historical details, including advances in the understanding of the pathology of arteriovenous malformations and an outline of the evolution of the classification of spinal arteriovenous malformations, are available elsewhere.^{28,30}

Infection

Viral. The English physician Michael Underwood (1736-1820) provided descriptions of what was

quite likely poliomyelitis in 1789.¹⁴⁴ Jakob von Heine (1800-1879) was a German physician who described polio in 1840 and subsequently named the condition.¹⁴⁵ The Swedish pediatrician Oskar Karl Medin (1847-1928) was the first to highlight the epidemic nature of the disease in 1890,¹⁴⁶ and the infectious nature of the polio virus was confirmed by Wickman in 1907.¹⁴⁷ Many epidemics around the world affected tens of thousands of people annually during the 1940s and 1950s. An inactivated poliovirus vaccine was developed by Jonas Edward Salk in 1952 and was licensed for use in 1955.¹⁴⁸ Subsequently, Albert Bruce Sabin developed an oral polio vaccine.¹⁴⁹ The 2 vaccines have eradicated polio from most countries in the world and reduced the global incidence from an estimated 50,000 in 1980 to fewer than 1,000 in 2001.¹⁵⁰ Polio is still endemic in Nigeria, Afghanistan, Pakistan, and Lao People's Democratic Republic (<http://polioeradication.org/polio-today/polio-now/>). It hoped that a global polio vaccination program will eliminate poliomyelitis as a cause of SCDys,¹⁵¹ and this is a major focus of SCDys prevention.⁸⁵ A review of the epidemiology of poliomyelitis and progress toward eradication has been published.¹⁵⁰

Acquired immunodeficiency syndrome emerged in the United States in 1981; in 1983 it was proven to be due to a retrovirus, human immunodeficiency virus.¹⁵² During the subsequent epidemic spread of this virus, it was noted in 1985 that some patients were affected by a form of white matter vacuolar degeneration of the spinal cord.¹⁵³

Bacterial. As mentioned in the overview section above, it is asserted that Hippocrates first described infection of the spinal cord, possibly due to tuberculosis.⁴² There are a number of bacterial infections that can cause SCDys, the most notable of these will be discussed below.

Some assert that syphilis was brought back to Europe by those who travelled with Columbus, but others believe that it existed in Europe beforehand but was unrecognized.^{154,155} The neuro-syphilis complication resulting in paralysis due to tabes dorsalis was first correctly identified by Sir William Withey Gull (1816-1890) in 1856 as due to lesions of the posterior column.¹⁵⁶ Noguchi and Moore discovered that the cause of syphilis was the spirochete

Treponema pallidum in 1913.¹⁵⁷ Early treatments of syphilis, including the use of mercury, arsenic, and malaria infection, have been reviewed elsewhere.¹⁵⁴ It was not until 1943 when penicillin was introduced as a treatment for syphilis by Mahoney and colleagues that a definitive cure was found.¹⁵⁸

A Frenchman, Jacob Dalechampius, in 1610 described progressive paraplegia associated with kyphosis, which was likely to be due to tuberculosis.¹⁵⁹ However, it was Percivall Pott (1714-1788), a British surgeon, who is acknowledged by many to have been the first, in 1782, to describe paraplegia due to spinal cord compression and abscesses from tuberculous spondylitis, known as Potts paraplegia (Potts disease).^{48,49} An overview of the early surgical management of spinal tuberculosis has been previously published.⁶⁰ By the early 20th century, it was realized that the results from surgery were generally so poor that conservative management became accepted as best practice.⁶⁰ Tuberculosis resulting in arachnoiditis and flaccid paralysis was first described in 1947 by Ransome.¹⁶⁰ A history of the medical management of tuberculosis can be found elsewhere.¹⁶¹ It was not until the advent of antibiotics in the 1940s that definitive treatment became possible.¹⁶¹ Screening for tuberculosis and the early and effective treatment of tuberculosis bacillus, especially in the spinal column before cord compression occurs, can prevent SCDys.¹⁶²⁻¹⁶⁴ Unfortunately, however, in many developing countries, especially in Africa and Southeast Asia, tuberculosis remains a common cause of SCDys,¹⁶⁴ and this remains an ongoing focus for the prevention of SCDys.

The first case of spinal epidural abscess was reported by the Italian anatomist Giovanni Battista Morgagni (1682-1771) in 1761.¹⁶⁵ A case series in 1833 by Albers provided clinical descriptions that are very similar to the typical presentations seen today.¹⁶⁶ The first report of surgical intervention was of a laminectomy in 1892 by the French physician Delorme.¹⁶⁷ The survival rate for patients was typically very poor until the introduction of antibiotics in the 1940s.¹⁶⁸ An overview of early surgical management of osteomyelitis⁶⁰ and a detailed review of epidemiology, risk factors, etiology, management, and outcomes of spinal epidural abscess are available elsewhere.¹⁶⁹

It is estimated that half the occurrences of spinal epidural abscess are initially misdiagnosed and that SCDys occurs in 4% to 22% of these patients.¹⁷⁰ Accepting that there are large challenges to the early recognition of bacterial infections causing SCDys,^{171,172} including tuberculosis bacillus, it is possible that some cases of paralysis could be prevented by education programs focusing on health care professionals.⁸⁵

Fungal. Fungal infections are a rare cause of SCDys and are briefly mentioned to complete this section. Fungal infections typically occur in patients who are immunocompromised. The first case of blastomycosis was reported by Versé¹⁷³ in 1914. Actinomycosis affecting the spinal cord was first reported in 1946 by Assis and Mignone.¹⁷⁴

Inflammatory

Multiple sclerosis. It is possible that the first clinical description of multiple sclerosis was of St. Lidwina of Schiedam (1380-1433) who had a relapsing neurological disorder at 18 years of age.¹⁷⁵ Charles-Prosper Ollivier d'Angers is credited with describing the first clinical report of multiple sclerosis in 1824.¹⁷⁶ In 1837, Sir Robert Carswell (1793-1857) reported on the pathology of multiple sclerosis.¹⁷⁷ Jean Cruveilhier (1791-1874) is credited with correlating the gross pathology with clinical case description.¹⁷⁸ Charcot produced an important synthesis of the clinical and pathological features of multiple sclerosis in 1868.¹⁷⁹ The first English description of multiple sclerosis was by Moxon in 1875.¹⁸⁰ Important definitive work on the pathology of multiple sclerosis was made by Müller in 1904¹⁸¹ and Dawson in 1916.¹⁸² Significant developments in multiple sclerosis research were facilitated by the breakthrough of experimental allergic encephalomyelitis in 1935 by Rivers.¹⁸³ Currently, the etiology is recognized to be multifactorial, with viral and genetic components, and treatments that reduce the risk of progression are now available.^{184,185}

Transverse myelitis. For many years myelitis was used as a general term that covered a wide range of conditions, including inflammatory and ischemic, without a full appreciation of the pathophysiological mechanisms.^{186,187} It is only

since the middle of the 20th century that the current differentiation became well established.¹⁶

It is now well recognized that transverse myelitis can be caused by a wide range of autoimmune, inflammatory, and infectious etiologies, with the acute management directed by the suspected etiology and the rapid initiation of appropriate treatment increasing the chance of better outcomes.^{188,189}

Neuromyelitis optica. Jacob Augustus Lockhart Clarke (1817-1880) gave the first report of neuromyelitis optica in 1865,¹⁹⁰ 15 years before Wilhelm Heinrich Erb provided what others consider to be the first thorough description.¹⁹¹ The term *neuromyelitis optica* was coined by Eugene Devic in 1894.^{192,193} Recent developments have shown that neuromyelitis optica is caused by antibodies to aquaporin-4, the most common water channel in the central nervous system, which distinguishes it from multiple sclerosis.¹⁹⁴

Other etiologies of spinal cord dysfunction

Syringomyelia. Abnormal cavitation within the spinal cord was described by Charles Estienne in 1546.¹⁹⁵ It is reported that Johann Conrad Brunner gave the first descriptions of syringomyelia as early as 1688,³⁷ but others have asserted that Portal gave the first description in 1804.¹⁹⁶ The term *syringomyelia* was coined by Ollivier d'Angers,^{35,55} however he did not believe in the existence of a central canal. The clinical syndrome was fully described by Gull in 1862¹⁹⁷ and Clarke in 1867,¹⁹⁸ differentiating hydromyelia from syringomyelia.

The first attempt at surgery for syringomyelia was by Abbe in 1891.¹⁹⁹ Surgical management for syringomyelia had very poor outcomes until 1949 when Kirgis and Echols devised a drain of twisted tantalum.²⁰⁰ A review of early surgical management of syringomyelia is available elsewhere.⁶⁰ It was not until the 1960s that Gardner proposed obstruction to cerebrospinal fluid flow as important in the etiology of syringomyelia.²⁰¹ More detailed reviews of the history of syringomyelia have been published previously.^{202,203}

Deficiency: Pernicious anemia. The association of vitamin B12 deficiency (pernicious anemia)

with degeneration of the spinal cord was made by Leichtenstern in 1884, but he attributed both to tabes dorsalis.²⁰⁴ Lichtheim identified the histological differences between pernicious anemia and tabes dorsalis in 1887.²⁰⁵ The term *subacute combined degeneration of the spinal cord* was devised by Russell in 1900.²⁰⁶ In 1926, Minot and Murphy successfully treated patients with pernicious anemia by feeding them a diet of calf liver,²⁰⁷ for which they subsequently received the Nobel Prize. In 1929, Castle distinguished between gastric (intrinsic) and dietary (extrinsic) causes of pernicious anemia.²⁰⁸ Additional historical details about pernicious anemia have been published.⁸⁶

Toxicity: Lathyrism. Lathyrism, associated with consumption of large amounts of the grass pea *Lathyrus sativus*, is one of the oldest neurotoxic diseases; it was known to the ancient Hindus, being mentioned in the ancient Ayurvedic text Bhav Prakash,²⁰⁹ and Hippocrates.²¹⁰ The first detailed description of the clinical features of lathyrism and the relationship to the consumption of *Lathyrus sativus* was by Francis Buchanan in 1811.²¹¹ The first account of a mass outbreak, in India, was in 1844 by Sir William Henry Sleeman.²¹² The toxic amino acid believed responsible was only identified in 1987.²¹³ *Lathyrus sativus* is a hardy crop that is easy to grow, is resistant to floods,

diseases, and drought, and is nutritious and rich in protein, so it is a staple food for the impoverished, even today. Addressing poverty will help to reduce future outbreaks of lathyrism.

Conclusions

This review has outlined the history of non-traumatic SCDys, taking a broader historical perspective and covering the increasing awareness of the role of the spinal cord and knowledge of neuroanatomy. Key milestones in the history of the diagnosis and management of the most common SCDys conditions due to congenital, genetic, degenerative, tumor, vascular, infectious, inflammatory, and other causes have been presented. An appreciation of the history of SCDys increases our understanding of the large number of people who contributed to our current knowledge of these conditions, including many of the doyens of medicine and surgery. In some situations, this appreciation of the history of SCDys also helps guide efforts regarding prevention of SCDys.

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