A Review of the Epidemiology of Painful Diabetic Peripheral Neuropathy, Postherpetic Neuralgia, and Less Commonly Studied Neuropathic Pain Conditions

Alesia Sadosky, PhD*; Anne M. McDermott, ScD†; Nancy A. Brandenburg, PhD*; Marcie Strauss, MPH†

*Pfizer Global Outcomes Research, New York, New York; †Outcomes Research Consultant, Silver Spring, Maryland, U.S.A.

Abstract: Although the burden of neuropathic pain is well-recognized, the descriptive epidemiology of specific neuropathic pain conditions has not been well-described. While painful diabetic peripheral neuropathy and postherpetic neuralgia have been widely evaluated, many other peripheral and central neuropathic pain syndromes have been less frequently studied. This review summarizes incidence and/or prevalence information about two relatively frequent neuropathic pain conditions—painful diabetic peripheral neuropathy and postherpetic neuralgia—and similarly summarizes the more limited epidemiologic information available for other peripheral and central neuropathic pain conditions. The data suggest that while our knowledge is still incomplete, the high frequency of several of these conditions in specific populations should be considered an important impetus for further studies designed to evaluate their contribution to the overall burden of neuropathic pain.

Key Words: neuropathic pain, peripheral neuropathy, central pain, diabetic peripheral neuropathy, postherpetic neuralgia, trigeminal neuralgia

The International Association for the Study of Pain (IASP) has defined neuropathic pain as “pain initiated or caused by a primary lesion or dysfunction in the nervous system.”¹ Neuropathic pain can be further characterized as being of either peripheral or central origin, depending upon the site of the lesion within the nervous system.

The presence of neuropathic pain, whether of peripheral or central origin, continues to present a significant burden to individuals and society by increasing disability and reducing productivity and quality of life with concomitant increases in healthcare resource utilization and costs.²,³ An initial step in evaluating the extent of this burden is characterizing the epidemiology of neuropathic pain.
Painful diabetic peripheral neuropathy (DPN) and postherpetic neuralgia (PHN) are commonly studied peripheral neuropathic pain syndromes. However, less frequent neuropathic pain conditions also contribute to the overall disease burden, but there is a paucity of epidemiologic data for many of these conditions, and many reviews of neuropathic pain do not distinguish among the various syndromes. Therefore, the purpose of this article is to summarize what is currently known regarding the incidence and/or prevalence not only of DPN and PHN, but also of the less frequently studied neuropathic pain conditions for which fewer descriptive epidemiologic studies are available.

To identify relevant articles with the most recent available epidemiologic data, Medline was searched using the terms “epidemiology,” “incidence,” and “prevalence” in combination with appropriate terms identifying the syndrome or condition. “Epidemiology” was also used as a specific search criterion and abstracts were reviewed to identify population-based studies or large case series in instances where no population-based studies were identified. English-language articles were the primary source, but relevant population-based studies were translated from other languages.

**PERIPHERAL NEUROPATHIES**

**DPN**

Diabetic neuropathy is a late complication of diabetes mellitus resulting from decreased blood flow and high blood-sugar levels. A population-based study from the Mayo Clinic indicated that diabetic neuropathies are common among patients with diabetes, affecting 66% of patients with insulin-dependent diabetes mellitus and 59% of patients with noninsulin-dependent diabetes mellitus. Several types of diabetic neuropathy have been distinguished including focal and multifocal neuropathies such as cranial, truncal, focal limb (due to nerve entrapment), and amyotrophic neuropathy; and the generalized symmetric polyneuropathies that are not necessarily limited to sensorimotor pathways, but may also include autonomic neuropathies of the cardiovascular, gastrointestinal, and/or genitourinary systems. The sensory neuropathies, often referred to as distal symmetric sensorimotor polyneuropathies, may further be characterized by being acute or chronic. While the acute form is considered to be relatively rare, the chronic form is the most common of the diabetic neuropathies, and includes painful DPN, which represents most of the available epidemiologic data.

While an adjusted annual incidence of 54 per 100,000 has been reported for diabetic polyneuropathy in an urban general population in the U.K., prevalence estimates within the diabetes population ranged from 16.3% to 50%. This variability in prevalence is likely due to differences in definition, method of assessment, and patient selection. Based on data from the National Health and Nutrition Examination Survey (NHANES) in the U.S.A., 28.5% of individuals with diabetes were estimated to have peripheral neuropathy defined as at least one insensate area upon monofilament testing of both feet.

Painful DPN is a variant of distal symmetrical sensorimotor polyneuropathy. A recent study in the U.K. using the General Practice Research Database (GPRD) reported an incidence of painful DPN of 15.3/100,000 patient-years (95% CI 14.9 to 15.7), with a significant trend in increasing incidence across the study periods ($P < 0.001$). The prevalence of painful DPN has been reported in several studies. In the Mayo Clinic study, 20% of the patients were reported to be symptomatic, and in the NHANES study, 10.9% of adults with diabetes had symptomatic peripheral neuropathy, where “symptomatic” was defined as numbness, loss of feeling, painful sensations, or tingling in the feet for at least 3 months. In a U.K. study, the prevalence of chronic (at least 1 year) painful peripheral neuropathy was estimated to be 16.2% of diabetic patients in an urban community. Similarly, in a case-control study, Partanen et al. reported a prevalence of painful DPN in 20% of patients with noninsulin-dependent diabetes mellitus after 10 years of follow-up, whereas only 7% of patients had pain at baseline (new diagnosis).

A more recent cross-sectional, community-based, two-phase study of patients with diabetes utilized a postal questionnaire (phase 1) followed by a clinic visit that included a neurologic history and examination (phase 2). Although 63.8% of the responders to the questionnaire reported pain, a total prevalence of 26.4% was determined for painful DPN based on phase 2, with 19% having pure neuropathic pain and 7.4% having mixed pain that included a neuropathic component.

Diabetic cohort studies indicate that prevalence of diabetic polyneuropathy increases with age, duration of diabetes, and worsening of glucose tolerance. These are likely the same risk factors associated with painful DPN. Based on the published studies, the best estimate of overall prevalence of painful DPN in the diabetic population is 15%.
PHN
Postherpetic neuralgia consists of pain persisting or recurring at the site of herpes zoster (HZ) rash (shingles); however, no uniform temporal criteria apply. Three common definitions of PHN include pain one month after rash onset, pain 3 months after rash onset or pain at rash healing. Additionally, PHN has been thought of as a continuum of zoster pain, with a consideration of overall duration rather than distinguishing acute HZ pain from PHN.

The incidence of PHN has been reported in several studies. Data from an older, community-based study in Rochester, Minnesota, reported an annual incidence of approximately 11.6 per 100,000 person-years. A subsequent British general-population study provided good agreement, reporting an adjusted annual incidence of PHN of 11 per 100,000 and a lifetime prevalence of 70 per 100,000. An unadjusted incidence of 40.2/100,000 patient-years was reported in a more recent study that used the U.K. GPRD over a study period January 1992–April 2002. That study showed a trend toward a significant decrease in incidence over the study period (P < 0.001).

The estimated prevalence of PHN in the population of patients with HZ ranges from 7% to 27%, with the lower estimate coming from an Icelandic study, and the higher estimate from a community-based study in the U.K. with PHN in both studies considered at 3 months after HZ.

HIV-Related Neuropathies
The presence of human immunodeficiency virus (HIV) is often associated with several different types of neuropathies including distal symmetrical polyneuropathy (DSP), inflammatory demyelinating polyneuropathy (IDP), progressive polyradiculopathy (PP), mononeuropathy multiplex (MM), autonomic neuropathy, and diffuse infiltrative lymphocytosis syndrome (DILS). These neuropathies may also occur secondary to treatment, as many of the drugs used in the management of HIV patients are known to be neurotoxic, especially the antiretrovirals, although the antibacterials, anticancer drugs, and other agents may also be contributory factors.

Distal symmetrical polyneuropathy is the most common HIV-associated neuropathy, and is frequently observed in individuals with advanced immunosuppression. Most studies that have reported the prevalence of HIV-related neuropathy have suggested that peripheral neuropathy is present in 30% to 38% of HIV-positive patients. However, prevalence rates as high as 63% have also been reported and in one recent study, 62% of patients presented with DSP of which 10% were asymptomatic DSP and 52% were symptomatic. In a study that reported other forms of HIV-related neuropathy, MM was present in 11%, IDP was present in 4%, and PP, autonomic neuropathy, and monoradiculopathy were all present in 1% of the patients.

Although evidence of peripheral neuropathies is present in the earliest stages of HIV infection and they are observed in nearly all patients with end-stage HIV, the presence of symptomatic neuropathies is less frequent. Berger et al. in a study of patients with HIV associated with injection drug abuse, reported that 71% of peripheral neuropathies were asymptomatic. In a study conducted among HIV-positive individuals having low CD4 cell counts and hemoglobin levels as study inclusion criteria, 45% of patients did not have DSP at baseline, 20% had asymptomatic DSP, and 35% had symptomatic DSP with paresthesias or pain.

It has been suggested that painful polyneuropathy occurs in up to 50% of patients with acquired immunodeficiency syndrome (AIDS), with the highest rates of polyneuropathy found among patients in palliative care settings. However, most studies have reported lower rates of symptomatic neuropathy. Similarly, in a study of pain syndromes among ambulatory AIDS patients, only 27.5% of the patients had pain associated with a polyneuropathy, and another study conducted among hospitalized AIDS patients reported pain in 23% of the patients who had signs of peripheral neuropathy at the time of the neurologic exam. A study conducted in Zimbabwe reported that 22% of patients had DSP, which was characterized clinically by painful paresthesias and sensory loss.

Using a sample size weighted average from data in the identified studies, the frequency of HIV-related neuropathy was calculated to be 48%, with an average frequency of painful HIV-related neuropathy of 35%. This is probably the best estimate given the available data.

Trigeminal Neuralgia
Trigeminal neuralgia (TN), also known as “tic dououreux,” is a neuropathic pain condition affecting the facial area. The IASP defines TN as “a sudden, usually unilateral, severe, brief, stabbing, recurrent pain in the distribution of one or more branches of the fifth cranial nerve.” Although etiologically it is most frequently
associated with vascular compression of the trigeminal nerve, other causes are also observed; between 2% and 4% of cases are associated with multiple sclerosis (MS) and tumors as the underlying cause account for approximately 2% of cases. Additionally, associations with arterial hypertension, Charcot-Marie-Tooth disorder, arteriovenous malformation, and bony abnormalities at the base of the skull have been reported, but such cases are rare.

Trigeminal neuralgia displays a paroxysmal pattern and these paroxysms, which may only last for a few minutes or seconds, are frequently triggered by non-noxious stimuli or normal activities such as talking, chewing, and swallowing. The pain spreads rapidly at the beginning of the attack, recedes slowly, and is commonly recurrent. In an epidemiologic study of TN in the population of Rochester, Minnesota, during a 40-year period with an average follow-up of 13.5 years, only 29% of patients had a single episode, but three or more episodes were reported in 52% of patients. TN has been reported to be associated with substantial patient burden, interfering with daily functioning and characterized by reduced health status associated with pain severity.

The epidemiology of TN has been described in three large population studies, one in the U.S.A. performed in Rochester, Minnesota, and two in the U.K. The U.S. study reported an annual age- and gender-adjusted incidence of 4.7/100,000, which was lower than the rate of 8/100,000 reported in a U.K. general practice study of neurological disorders, and both of these were lower than the 26.8/100,000 reported in a study using the GPRD, although the latter represents an unadjusted rate from the perspective of the general practitioner who might have applied a broader definition. However, the data support a higher incidence in females, with female to male ratios of 1.7 to 2.2:1, and an incidence that increases with age, peaking at around 70 years. As TN is an episodic disease with pain-free intervals, an overall incidence rate of 5 to 8/100,000 may provide the best population estimate based on age- and gender-adjusted data.

**Glossopharyngeal Neuralgia**

Glossopharyngeal neuralgia (GPN) refers to a syndrome affecting the ninth cranial nerve that is similar to TN in that it is characterized by paroxysms of excruciating pain lasting seconds to minutes in duration. As with TN, GPN may be idiopathic but is also associated with MS, although probably to a lesser extent than TN. However, in contrast to TN, the pain in GPN is generally localized to the posterior pharynx, tonsillar fossa, and base of the tongue, often with radiation to the external auditory canal or the neck. Its onset is often related to specific trigger factors affecting the throat including swallowing, drinking cold liquids, sneezing, coughing, talking, and clearing the throat.

Glossopharyngeal neuralgia is probably the least characterized neuropathic pain condition with respect to pain quality/severity and patient burden, although Katusic et al. suggested that GPN may not necessarily be a severe condition. Similarly, its epidemiology is poorly characterized. The only available data come from the same epidemiologic study in Rochester, Minnesota, that provided incidence rates for TN. In that study, only 12 patients were identified with GPN and the age- and gender-adjusted incidence was estimated to be 0.8/100,000 population. Despite the small number of patients identified with GPN, the authors reported a peak age of onset between 70 and 79 years, with similar incidence rates for men and women. The left side was predominantly affected (53%), and bilaterality was noted in 25% of cases. Recurrence was noted in four of the 12 patients; the time between episodes ranged from 0.5 to 9 years, and the length of each episode ranged from 6 days to 3 years, with a median episode length of 4 weeks.

**Phantom Limb Pain**

Phantom limb syndrome (PLS) is a broad classification that refers to a variety of sensory phenomena felt after limb amputation and that may vary in frequency, duration, and intensity. These phenomena include phantom limb sensations, which are the perception that the limb is still present; stump pain, which refers to pain perceived at the location of existing body parts in the region of amputation; and phantom limb pain, which is pain perceived in the absent limb. While patient response to these phenomena may vary based on the type, duration, and severity of sensations, it is also important to distinguish among them as their underlying pathophysiologic mechanisms may be different.

Phantom limb pain is uncommon when considering the general population. A recent epidemiologic survey of neuropathic pain conditions using the GPRD database reported an incidence of 1.5/100,000 population (95% CI 1.3 to 1.6). Consequently, characterization of the epidemiology of phantom limb pain has generally been restricted to the population of patients experiencing amputation.
Although the number of amputees is not regularly tracked internationally, The Global Lower Extremity Amputation Study Group conducted a study to estimate incidence rates in 10 centers with populations greater than 200,000 in Japan, Taiwan, Spain, Italy, North America, and England. The incidence rates varied widely, from 2.8/100,000 population per year (Madrid, Spain) to 43.9/100,000 per year among the Navajo in the U.S.A., although in general the incidence increased with age and occurred most frequently in patients >60 years old. While amputation may be performed for a variety of reasons including disease, trauma, congenital or birth defects, and tumors, the study reported that between 25% and 90% of the amputations were related to diabetes. The risk of lower limb amputation among patients with diabetes is especially notable and has been estimated in a U.S. study conducted among Medicare beneficiaries with and without diabetes. The rate of lower-extremity major amputations was 3.83/1000 population per year (95% CI 3.60 to 4.06) for individuals with diabetes, a 10-fold increase compared with individuals not having diabetes (0.38/1000 per year; 95% CI 0.35 to 0.41), although marked geographic variation was observed in both patient groups.

Epidemiologic studies on PLS within amputee populations have almost consistently reported a high prevalence of phantom limb sensations. Although one study reported a prevalence of 66.8% in British veterans, and a Finnish study reported that only 18% of patients had phantom limb sensations 1 year after amputation, most other studies have reported a prevalence in excess of 80%, including a pediatric study that reported phantom limb sensations in 100% of the children and adolescents who underwent amputation.

Of the phantom limb sensations, phantom limb pain may occur during the first year after amputation in 53% to 85% of patients. Although the pain may improve, particularly with respect to frequency and duration, it often remains chronic over the course of months or years, either with no improvement or an increase in pain. In one study, the incidence of phantom pain at 8 days, 6 months, and 2 years after amputation was 72%, 65%, and 59%, respectively, and in another study, pain was experienced by 59% of patients right after amputation and by 53% of patients after 1 year, with the pain being of mild to moderate intensity. In a study that evaluated pain after 5 years post amputation, 72.5% of the patients had pain; 7.5% had constant pain and 20% had frequent pain. Among U.S. veterans with current significant phantom limb pain, 27% had pain for more than 20 days per month, 10% for 11 to 20 days, 14% for 6 to 10 days, and 49% for 5 days or less per month.

Cervical Radiculopathy
Cervical radiculopathy (CR) describes the group of symptoms related to the dysfunction of cervical spinal nerve root(s) that are associated with nerve damage and neuropathic pain. The underlying pathology is not always clear, and although intervertebral disc herniation has been considered the most common cause, spondylotic changes resulting from chronic degeneration of the cervical spine have been suggested to be a more common cause than pure disc herniation. There has also been little consistency with regard to terminology, and definitions are not always presented in a particular study, making it difficult to interpret the literature on the subject. Characteristically, CR has been described as pain in the neck and one or both arms in a radicular pattern, frequently accompanied by varying degrees of other sensory, motor, and/or reflex changes.

Few studies have characterized the epidemiology of CR. A point prevalence of 136/100,000 population was estimated for cervical spondylotic radiculopathy in an Indian study, and an Italian study reported a 6-month prevalence of 350/100,000. However, the best epidemiologic data on CR come from a population-based study in Rochester, Minnesota, which reported a gender- and age-adjusted annual incidence of 83.2/100,000 population, and a peak age-specific incidence rate of 202/100,000 in the 50 to 54 year age group. A confirmed disc protrusion was responsible for CR in only 21.9% of patients. During the median duration of follow-up of 4.9 years, recurrence of the condition occurred in 31.7%. Neck and arm pain was reported in nearly all subjects (97.5%) and 89.7% reported paresthesia, which were nearly all unilateral.

Carpal Tunnel Syndrome
Carpal tunnel syndrome (CTS) is an uncomfortable condition of the wrist and hand that is precipitated by repeated flexion and extension of the wrist, which may cause swelling of the tendon sheaths and increased pressure on the median nerve. Although CTS is commonly considered a condition of repetitive movement that may be related to particular occupations, it is also associated with medical conditions including diabetes and thyroid disorders. CTS symptoms include pain that may radiate up the forearm, numbness, tingling, and reduced
sensation in the hand and wrist. These symptoms often worsen at night or after use of the hand.

The epidemiology of CTS has been characterized in several studies. In general-population studies, annual standardized incidences of 276/100,000 were estimated for an Italian population,\textsuperscript{77} 180/100,000 for a U.K. population,\textsuperscript{78} and age-adjusted rates of 105/100,000 for a U.S. population.\textsuperscript{76} Using a definition of probable or definite CTS, a 2-year incidence of 346/100,000 (crude rate, new cases) has also been reported in the U.S.A.\textsuperscript{79} A recent survey of general practices in the Netherlands reported a small but nonsignificant increase in the crude incidence rate from 130/100,000 in 1987 to 180/100,000 in 2001.\textsuperscript{80}

Studies assessing the prevalence of CTS have suggested that the variation in range, from 1.55\% to 16\%, may result from differences in the assessment methodology and the diagnostic basis, especially in the absence of standardized diagnostic criteria. The lower value of 1.55\% was by self-report in a study by the U.S. Occupational Safety and Health Administration, although the prevalence dropped to 0.53\% based on whether the condition was referred to as CTS by a medical provider.\textsuperscript{73} Similarly, a Swedish study found a prevalence of 3.8\% for clinically certain CTS, which decreased to 2.7\% when CTS was confirmed both clinically and electrophysiologically.\textsuperscript{71} A comparable rate of 3.7\%, representing the lowest possible estimate, was also reported in the U.S. general population using a postal survey.\textsuperscript{81} In a U.K. study, a prevalence range of 7\% to 16\% was reported based on different diagnostic cut-off scores during nerve conduction testing.\textsuperscript{82} In a recent study, Taylor\textsuperscript{83} estimated the prevalence of neuropathic pain conditions in six diverse industrialized countries (U.S.A., Japan, France, Germany, Italy, Spain, and the U.K.), and reported a range of 7\% to 10\% of patients diagnosed with CTS among these countries.\textsuperscript{83}

Based on published studies of clinically confirmed CTS,\textsuperscript{71,81} the best estimate of prevalence in the general population is 3\%.

**CENTRAL NEUROPATHIC PAIN CONDITIONS**

**Central Post-Stroke Pain (CPSP)**

Stroke is not only a leading cause of death, but also significantly contributes to long-term disability in both industrialized and developing countries. CPSP is a sequela of stroke that is characterized by neuropathic pain in areas of the body that have lost part of their sensory innervation by the stroke and has been considered more distressing than other stroke sequelae.\textsuperscript{84} The IASP defines CPSP as pain following an unequivocal stroke episode, where a psychogenic, nociceptive or peripheral neurogenic cause is considered highly unlikely.\textsuperscript{1} Although CPSP was originally termed “thalamic syndrome,” it is now recognized that CPSP may also result from extrathalamic lesions.\textsuperscript{85}

Only one prospective epidemiologic study of CPSP has been reported.\textsuperscript{84} The study population included 207 patients under the age of 81 who survived more than 6 months after stroke and were followed for 1 year in Denmark. Using the IASP definition, the 1-year prevalence of CPSP among stroke survivors was 8\%, and the authors suggested that this number could be even higher as patients with onset of CPSP more than 1 year following stroke would have been missed. Additionally, the occurrence of pain in patients with survivorship of less than 6 months was not described.

Leijon et al.\textsuperscript{85} reported pain onset as late as 2 to 3 years after a stroke, and while some patients reported pain immediately after a stroke, three studies of patients reported a median onset of pain of 1 to 3 months.\textsuperscript{84–86} Although two of these studies were in long-term survivors (>6 months),\textsuperscript{84,85} and the third study did not explicitly state survivorship,\textsuperscript{86} the reported early onset of pain in the included populations suggests that CPSP is a likely occurrence even in patients having short post-stroke survivorship.

No studies have prospectively evaluated the duration of pain or the variability of pain severity or characteristics over time,\textsuperscript{87} but in the epidemiology study by Anderson et al.,\textsuperscript{84} of the 8\% of patients with CPSP, 5\% reported moderate to severe pain and 3\% reported mild pain.

A more recent study by Bowsher\textsuperscript{88} investigated the prevalence of CPSP in a survey of 1071 elderly subjects recruited from family practices in the U.K. Of the 72 subjects who had experienced a stroke, 11\% complained of pain within the body area affected by the stroke at the time of the interview, although the subjects did not have medically confirmed CPSP.

While no age differences were observed for stroke patients with and without pain in the two epidemiologic studies,\textsuperscript{84,88} some studies have reported a tendency for patients with CPSP to be younger than those in the general stroke population.\textsuperscript{86,89}

**MS**

Many country-specific studies on the prevalence of MS have been published over the years. Synthesis of these reports reveals substantial regional variation in
MS prevalence, with higher latitudes generally reporting a higher prevalence.

Pain is commonly reported in patients with MS, and this pain can be of nociceptive or neuropathic origin, and may sometimes have characteristics of both. The prevalence of pain in patients with MS has been reported to range from 50% to 85%, but only a single study, by Osterberg et al., specifically investigated the epidemiology of central neuropathic pain in this patient population. In that study, the prevalence of central pain was determined to be between 27.5% and 31.6%, with the higher number including patients with pain of questionable central origin. These values included TN, which was considered to be central pain, as the authors suggest that a demyelinating lesion in the brainstem is the cause of this condition in patients with MS. When TN was excluded, the prevalence of central pain was 22.6%; prevalence rates specific for TN in patients with MS may range from 1.9% to as high as 4.9%. Osterberg et al. also reported that their observed prevalence of central pain is similar to the 29% to 31% suggested by several previous pain studies of MS patients that included TN and in which patients with dysesthetic pain were considered to have central pain.

Another study reported a prevalence of central pain of 58% in patients with MS. The reason for this higher prevalence than the study by Osterberg et al. may be due to use of the IASP definition of central pain in the former study, whereas in the latter study central pain was diagnosed by exclusion criteria for other types of pain.

Pain and/or sensory complaints were reported by 73.9% of patients with MS in a study by Beiske et al. Although central pain was not specified, the presence of paresthesia in 48.6% of these patients with pain, as well as the presence of burning/neuralgic pain in 31.4%, suggests that a high proportion had central neuropathic pain.

Pain descriptors in patients with MS are generally consistent with other central pain states and include tingling, tiring, burning, and aching, and the majority of MS patients (72%) reported two or more pain qualities. Constant pain has been reported by 62% to 77% of patients, and although episodic pain may occur, 88% of the non-TN patients with central pain in the Osterberg et al. 2005 study reported daily pain, and only 30% of these patients had pain-free periods that lasted minutes or hours.

The presence of central pain may occur as early as 7 years before the clinical onset of MS, and it has been suggested that such pain may be the first symptoms of MS. Alternatively, central pain may occur as many as 25 years after other symptoms emerge, although 57% of patients with central pain report onset within 5 years after MS onset, and 73% report pain onset within 10 years of MS onset.

Spinal Cord Injury

Spinal cord injury (SCI) can be broadly defined as damage to the spinal cord that results from direct injury to the spinal cord itself or indirectly by damage to the bones and soft tissues and vessels surrounding the spinal cord. In an epidemiologic review of SCI, Sekhon and Fehlings reported that the annual incidence of SCI in various countries throughout the world varies from 15 to 40 per million population, with subsequent studies confirming this range of values: the low value has been reported for Australia, and high values from studies in the U.S.A. and Canada.

While SCI can be caused by trauma or disease, in the U.S.A. almost half (47.5%) of reported SCIs were caused by motor vehicle accidents since the year 2000, with falls being the next most common cause (27.9%), followed by acts of violence (13.8%, primarily gunshot wounds) and sports injuries (8.9%).

Chronic pain is commonly a debilitating feature in patients with SCI, often commencing within 6 months after the SCI and continuing throughout life. Prevalence of chronic pain varies depending on the population and the time after injury, and prevalence rates of up to 80% have been reported as long as 5 years after injury. However, the underlying pain mechanisms in SCI may be nociceptive or neuropathic. The site of pain may be either above, at, or below the level of the nerve injury, and while below-level pain is generally considered to be neuropathic, at- or above-level pain can also be neuropathic in origin.

Below-level neuropathic pain has been reported to have a delayed onset (mean 1.8 ± 1.7 years) relative to at-level pain (mean 1.2 ± 1.5 years). Both at-level and below-level pain demonstrated a strong long-term relationship: 60% of patients with at-level pain and 44% of patients with below-level pain at 5 years also reported the same type of pain within 6 months post-injury. Additionally, in patients with below-level pain, severity at 5 years was significantly correlated with severity at 3 months (P < 0.01) as well as 2- (P < 0.01) and 3-year (P < 0.05) time points.

The best data specifically on the prevalence of neuropathic pain in SCI are presented in an evidence report...
developed by the Agency for Healthcare Research and Quality (AHRQ). Although methodological issues including definition, time frame, and sampling bias preclude an estimation of absolute prevalence, evidence suggests that neuropathic pain begins shortly after SCI (likely within the first 8 weeks), with a reported prevalence of acute neuropathic pain of up to 80%. The prevalence of chronic central neuropathic pain ranges from 10% to 82%, although most studies report prevalence estimates between 40% and 70%.

A longitudinal study published subsequent to the AHRQ report investigated the presence of pain during the first 5 years after SCI. Results were fairly consistent with the AHRQ report; 41% of patients reported at-level neuropathic pain and 34% reported below-level neuropathic pain after 5 years. Although there was no difference in central pain prevalence between patients with complete and incomplete SCI, below-level pain was more prevalent among tetraplegics (50%) compared with paraplegics (32%). Pain severity was described as severe or excruciating in 48% of patients with below-level pain.

CONCLUSIONS

Neuropathic pain may be manifested in a variety of different peripheral or central neuropathies that have been inadequately characterized, often because of difficulties in definition and diagnosis. The available studies that present epidemiologic data for some of the less commonly studied neuropathic pain syndromes reviewed here suggest that in many cases there is still incomplete information regarding incidence and/or prevalence in the general population. The lack of epidemiologic information with respect to the general population may in part be a result of the difficulty in obtaining accurate estimates of conditions that are relatively rare or only present in specific populations. A summary of the incidence and prevalence of the different neuropathic pain conditions reviewed here is presented in Table 1.

While there is variation in the frequency of neuropathic pain conditions in the general population, ranging from 0.8 to 8/100,000 for the craniofacial neuralgias and PLS, to 54/100,000 in the case of DPN, there are high-risk populations, such as those suffering stroke, SCI, and amputation, where the prevalence of neuropathic pain may be as high as 80% of patients affected by the condition underlying the neuropathic pain. Even for these conditions, the observed variability in incidence and prevalence rates is often a product of the geographic setting (eg, specific country, rural vs. urban setting), time period evaluated, source of data (eg, patient self-report vs. medical records, general practitioners vs. specialists), and diagnostic or disease definitions. Furthermore, some of the less prevalent syndromes may potentially be associated with greater pain severity and disability than more prevalent neuropathies, and thus may be associated with a greater individual burden.

Although this review summarizes available data on many of the less frequently studied neuropathic pain syndromes, it is not exhaustive, as it did not include several other neuropathies such as the often controver-
sial lumbar radiculopathy, as well as postsurgical neuropathic pain and cancer-related neuropathic pain, of which the latter may result from several different causes including treatment and the cancer itself. Nevertheless, this review can provide a useful resource and an impetus for the recognition and evaluation of these syndromes and their contribution to the overall burden of neuropathic pain.

REFERENCES


