

Case-Based Learning Module: PAIN

INTRODUCTION

After enduring a spinal cord injury (SCI), an individual may experience different types of pain. Pain is common, often chronic, can be present in up to 96% of individuals with a SCI, and may significantly impact quality of life, functioning, and the development of depression.¹⁻⁷ This module will focus on pain associated with SCI with special attention given to neuropathic pain, and will help clinicians to:

- Identify differences between nociceptive and neuropathic pain
- Understand screening of neuropathic pain in SCI
- Treat pain in individuals with SCI in the primary care setting

CASE

Mike, age 29

Mike is a 29 year old male patient in your practice for the last 8 years. He sustained a complete injury to T5 after being hit by a car while riding his bike 3 years ago. Mike presents to your office telling you he is having two different types of pain. The first, he says is a dull, aching type of pain in his left shoulder that hurts when he moves it and is tender whenever someone touches it. He tells you that he has been feeling this pain for approximately 6 months. Mike says the other pain is in both of his legs from his thighs to his toes and feels like a hot/burning and pins and needles type of pain. He says the pain is always there in some form at a level of about 2/10, but he has periods where he feels it is “11/10”. This pain has been present since shortly after his injury, has not changed much since it started. He is looking for you to help him with his pain.

What type(s) of pain is Mike experiencing? Are they the same? Different?

- *Mike is experiencing two different types of pain*
- *Nociceptive: musculoskeletal in his shoulder possibly due to strain from wheelchair use*
- *and neuropathic: below-level pain from his spinal cord injury*

How would you examine Mike?

- *A detailed history with attention paid to the onset, description, daily course and variation, associated symptoms, and factors that worsen or alleviate pain*
- *Ask about home supports and any symptoms of depression*
- *Bedside examination should include testing of pinprick and light touch sensation that can be supplemented with cold and warm sensation*
- *Compare painful area to other sites on the proximal-distal axis*
- *When sensory abnormalities are evoked, map the abnormalities*

How would you begin to treat Mike's pain?

- *Be sure to include Mike in the clinical management and understand his knowledge and pain experience*
- *To treat Mike's MSK pain*
 - *Recommend physical therapy, strengthening and stretching exercises, examining the ergonomics of upper extremity weight bearing (i.e. transfers) and how he is using his wheelchair for potential changes*
 - *Recommend acetaminophen 650 mg q4-6 hours PRN*
- *To treat Mike's below-level neuropathic pain*
 - *Prescribe Pregabalin 150mg/d in divided doses (75 mg BID)*
- *Tell Mike to return to your office if pain persists*

INFORMATION SECTION

Introduction:

Individuals with SCI may suffer from different types of pain, with classifications including nociceptive, and neuropathic pain. Nociceptive pain has been found to be the most common in both the acute, and chronic phase.⁹ Pain has been found to negatively affect sleep, quality of life, physical functioning, and mood.^{3-5,10-12} It should be noted that there is no one pain therapy that is consistently effective,¹³ so close follow up with an individual will be required to ensure pain is adequately being treated.

Clinical Pearl: Pain has been described as the worst problem, and more disabling than the loss of motor or sensory function, by patients with SCI.⁸

Pathophysiology:

Below is a chart outlining the types of pain commonly experienced by individuals with SCI.

Types of Pain Associated with SCI^{13,14,19-22}

Type of Pain	Description/Manifestations	Examples
<u>Nociceptive</u>		
Musculoskeletal (MSK)	May be dull or aching Tenderness on palpation Pain related to movement Imaging consistent with presentation of pain	Mechanical pain Spinal fracture Muscle injury Shoulder overuse syndrome Muscle spasms ¹⁵⁻¹⁸
Visceral	May be dull, tender or cramping & have a relationship to visceral dysfunction or pathology Present in the thorax, abdomen or pelvis <i>If visceral pathology is not found or there is no response to treatment of visceral pathology, this may be indicative of neuropathic pain¹⁴</i>	Urinary tract infection (UTI) Ureteric calculus Bowel impaction ^{15-18,23}
Other	Nociceptive pains that do not fall into MSK or visceral categories ¹⁶ May be directly related or unrelated to the injury to the spinal cord	Skin/pressure ulcer Dysreflexic headache <ul style="list-style-type: none"> • Directly related to SCI Migraine <ul style="list-style-type: none"> • Unrelated to SCI¹⁴

Neuropathic <ul style="list-style-type: none"> • “Pain caused by a lesion or disease of the somatosensory nervous system”³⁰ • “The onset of neuropathic pain is usually within 1 year of SCI, has no primary relation to movement, inflammation, or other local tissue damage, has at least one of the pain descriptors listed below, and is associated with allodynia or hyperalgesia within the distribution of pain”²² 		
At-Level	Presents in segmental pattern within 3 dermatomal levels of the SCI Hot-burning, tingling, pricking, pins & needles, squeezing, cold, electric ^{16,18,23} May have an early onset (days or weeks) ³²	
Below-level	Present more than 3 dermatomal levels below the SCI and usually has a regional distribution Hot-burning, tingling, pricking, pins & needles, squeezing, cold, electric ^{16,18,23} May have a later onset (months or years) ³²	
Other	Pain present above, at or below the level of injury but not directly related to the SCI	Postherpetic neuralgia Diabetic neuropathy Central post stroke pain Compressive neuropathies ^{16,18}

Table 1: Types of pain and description
(adapted from Widerström-Noga et al., 2014)¹⁴

Clinical Pearl: In a 1992 study of upper extremity pain in individuals with a SCI, 55% of individuals with quadriplegia identified pain in the upper extremity, most commonly at the shoulder (46%). In individuals with paraplegia, 64% reported upper extremity pain with 2/3 reporting symptoms of carpal tunnel syndrome and 13% reporting MSK-related shoulder pain.⁶⁵

Clinical Pearl: There may be sensory changes such as allodynia, hypoalgesia or hyperalgesia within the pain distribution at the level of injury to the spinal cord.¹⁴

Not only does pain negatively affect sleep, quality of life, physical functioning, and mood,^{3-5,10-12} it has also been found to have an association with fatigue and depressive symptoms.²⁴⁻²⁹ Individuals with neuropathic pain are more likely to have depression and anxiety.³¹ Both pain and fatigue independently contribute to the development of depression and should, therefore, be carefully evaluated and treated to minimize their effect.²⁴

Clinical Pearl: Syringomyelia- formation of an intramedullary cyst within the spinal cord after traumatic SCI. Although rare (2%), it can cause worsening neurological function. Signs and symptoms may include: reduction in sensation, worsening spasticity, gait ataxia, autonomic dysreflexia and pain.⁶⁴

Screening

Screening for pain in individuals with SCI is important due to the significant impact on quality of life, early identification could lead to earlier diagnosis and management and potentially alleviate morbidity associated with pain.⁶⁶ The recent CanPain SCI Working Group recommended that screening of pain occur regularly using a simple yes/no question (see algorithm).⁶⁶

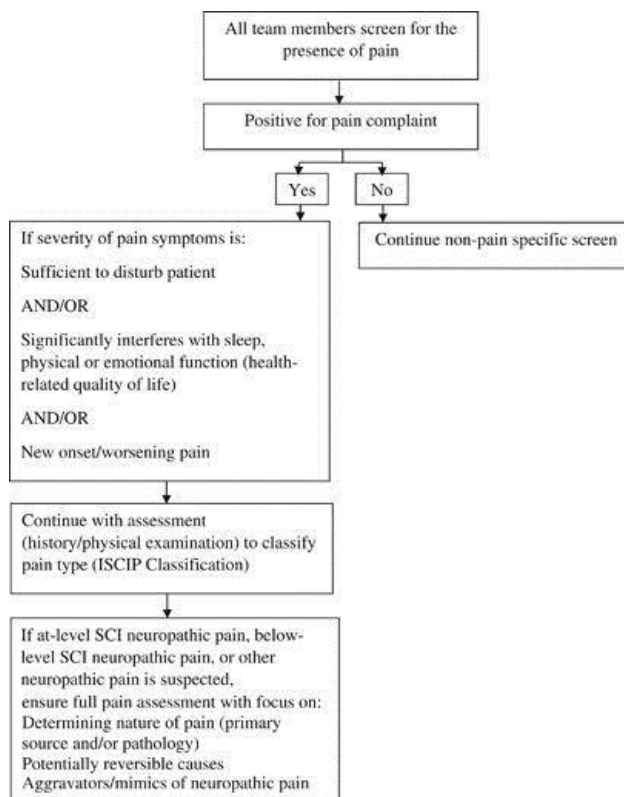


Figure 1: SCI pain screening

Diagnosis

If pain is present, then an assessment to properly diagnose type, characteristics, affect on function and reversible conditions are important.

A detailed history is required with attention to:

- Onset (special attention to new onset or worsening chronic pain)
- Description
- Daily course and variation
- Associated symptoms
- Factors that worsen or alleviate pain²²
- How it affects function (sleep, mood, physical)

It is important to note changes in an individual's pain and associated issues such as spasticity, and AD (see AD and Spasticity CBLMs), as well as determining other causes for pain (i.e. syringomyelia, fractures, etc.). There is no one symptom that will be diagnostic of neuropathic

pain, but certain combinations of symptoms, patient descriptions of pain and bedside examination findings increase the likelihood that the pain is neuropathic.^{33,34} Physical examination should include neurological, musculoskeletal and skin examinations assessing strength, spasticity and sensation⁶⁶ and any other systems as guided by the history. It is important to remember that signs and symptoms in SCI may not be reliable due to altered sensation and serious medical issues may present abnormally (eg. myocardial infarction without chest pain; DVT without calf pain; kidney stone without flank pain) and therefore a high index of suspicion and broad differential necessary (see appendix for red flags).

Investigations should be based on history and physical findings, Xray may be required if suspect fracture or MRI of spine if suspect neurological change.

It is important to include the patient in their clinical management and understand their goals, knowledge and pain experience as it can change with the progression of their symptoms.³⁷ In order to guide diagnosis, the Douleur Neuropathique 4 Questions (DN4), Visual Analog Scale (VAS), or International Spinal Cord Injury Pain Basic Data Set v2.0 (ISCI-PBDS) Classification system (see appendix) may be utilized but are not always practical in the primary care setting.^{14,38-41} See appendix for screening and diagnosis recommendation guidelines.

<p>Clinical Pearl: One study showed that 30% of patients with SCI rated pain relief as more important than regaining the ability to walk.⁴⁹</p>

Treatment

Treatment of pain in individuals with SCI will depend on the type of pain experienced.

Non-Pharmacological Treatments

Physical therapy and Occupational therapy can be important in maintaining/improving range of motion and strength, assessing transfers, seating/positioning, locomotion, education and energy conservation.

Psychologists, peer supports and self-management techniques can be important in managing chronic pain.

²¹ Other treatments that patients have found to be beneficial are hot baths, avoiding stress, distracting activities, physical activity and striking balance between activity and rest.⁶³

Pharmacological Treatments

Pharmacological options for MSK pain will be familiar to primary care practitioners and include simple analgesics, including acetaminophen as a first line therapy, and weak opioids or non-

steroidal anti-inflammatories (NSAIDs) as second line therapy. ^{21,68}

Treatment of neuropathic pain will most often require medication and are recommended as follows:

Medication	Dosage	Comments
First Line Treatment of Neuropathic Pain^{4, 68}		
Gabapentin ^{40,46,51,53, 69}	<ul style="list-style-type: none"> • 100-300 mg/d • May be increased by 100-300 mg/d every week • 1200 – 3600mg/d (divided into 3 doses)⁵² 	Max dose: 3600 mg/d ⁵² Side effects: dizziness, drowsiness, weakness, fatigue, nausea, diarrhea, constipation, blurred vision, headache, breast swelling, dry mouth, loss of balance or coordination
Pregabalin ^{20,40,43-48,50, 69}	<ul style="list-style-type: none"> • 25-150 mg/d • May be increased to 300mg BID within 1 week based on tolerability • May be increased to 600mg BID after 2-3 weeks 	Max dose: 600mg/d Side effects: somnolence, dizziness peripheral edema, dry mouth, fatigue, blurred vision, edema
Tri-cyclic antidepressants ^{40,54,5,69} Amitriptyline Desipramine Nortriptyline	<ul style="list-style-type: none"> • Initial: 10-25 mg/d at bedtime • May increase as tolerated up to 150 mg/d⁵⁵⁻⁵⁸ 	Max dose: 150 mg/d Side effects: confusion, paresthesia, headache, constipation, diarrhea, blurred vision, skin rash, angioedema, nausea
Venlafaxine ⁶⁹	<ul style="list-style-type: none"> • 37.5 mg/d • May increase by 37.5 mg/d in 1 week 	Max dose: 225 mg/d Side effects: dizziness, nausea, drowsiness, hyperhidrosis, hypertension
Second Line Treatment^{40, 68}		
Tramadol ^{40,59}	<ul style="list-style-type: none"> • 50 to 100 mg q4 -6 hours • Tolerability may be improved by starting therapy at 25 mg OD in the morning and titrating dose by 25 mg q3 days until 25 mg QID • Dose may then be increased by 50 mg q3 days as tolerated to reach 50 mg 4 QID • After titration, 50 -100 mg may be given q4 -6 hours as needed 	Max dose: 400 mg/d Side effects: headache, dizziness, drowsiness, fatigue, constipation, diarrhea, nausea, vomiting, stomach pain, anxiety, pruritis, sweating, flushing

Opioid analgesics ⁶⁸ Morphine Oxycodone Fentanyl Hydromorphone	15mg q 12h 10mg q 12h 12-25 µg/h patch 3mg q12h	Risks ⁷¹ - Opioids are related to increase risk of addiction (5.5%), even at low doses - 0.2% risk of non-fatal overdose and 0.1% risk of fatal overdose - Higher doses are linked to increased risk of overdose Side effects: urinary retention, constipation, nausea, vomiting, sedation
Lamotrigine ⁴⁰	<ul style="list-style-type: none"> • Weeks 1 and 2: 25 mg OD • Weeks 3 and 4: 50 mg OD • Week 5 and beyond: Increase by 50 mg daily q1 to 2 weeks 	Side effects: tremors, dizziness, fatigue, blurred vision, diplopia, loss of coordination, dry mouth, mild nausea, stomach pain, insomnia Be aware of rashes and Stevens-Johnson syndrome
Third line agents ⁶⁸		
Nabilone⁷⁰	2 to 6mg daily	- Start slow and go slow when dosing
Nabiximols⁷⁰ (THC and CBD combination - mucosal spray)	4 to 12 sprays daily	- Avoid smoked, oils and edibles due to limited evidence in the literature - As with all psychoactive medications, cannabis can cause mood altering, euphoria, speech changes, dizziness and sedative effects even at low doses. Start low and go slow

Table 2: Medications for treatment of pain

When To Refer:

Referral to a practitioner experienced in managing individuals with SCI (usually physiatry) is indicated when:⁴⁰

- Ongoing pain that is difficult to manage
- Dissatisfaction with current management protocol
- Significant functional impairments and/or significant psychological comorbidity factors from pain

Potential Surgical Interventions:

Potential surgical interventions to treat intractable pain in SCI include, but are not limited to dorsal rhizotomy, dorsal longitudinal T-myelotomy, and spinal cord stimulation.

Some Important Conditions

Upper Extremity Overuse Injuries

The dependency on the upper extremities for mobility, transfers and activities of daily living puts them at risk for injury and disability.⁶⁷

Shoulder

Most commonly injured joint, the rotator cuff is the most commonly injured structure. (tendonitis, tendonosis, partial and full thickness tears)

Elbow

Common conditions include medial and lateral epicondylitis, olecranon bursitis and ulnar nerve entrapment.

Wrist/Hand

Carpal tunnel syndrome is common (21-66% of SCI population), tendonitis and arthritis also common

Heterotopic Ossification (HO)

Formation of ectopic bone in soft tissues around peripheral joints. More common early after traumatic SCI. In SCI occurs in joints below level of lesion (hips most commonly but also can occur in knees, shoulders, elbows). Signs and symptoms may include fever, swelling, decreased range of motion and pain. Bone scan is more sensitive than Xrays early in the process.⁶⁷(See Bone Health CBLM).

Fractures

Bone loss in long bones and pelvis occurs quickly following SCI, resulting in sublesional osteoporosis. Most common fractures include distal femur and proximal tibia. Often difficult to diagnose due to altered sensation. (SCIRE)

Syringomyelia

Syringomyelia is the formation of an intramedullary cyst within spinal cord after spinal cord injury, although rare (2% of individuals with SCI) it can cause a deterioration in functioning. It should be considered if there is a change in neurological status, increased spasticity, increased autonomic dysreflexia or neuropathic pain. Diagnosis is made by MRI. Referral to a specialist would be required for assessment and management (SCIRE)

Resources

<u>For Physicians</u>	<u>For Patients and Caregivers</u>
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International Association for the Study of Pain (IASP) (https://www.iasp-pain.org/)	Canadian Pain Coalition (http://www.canadianpaincoalition.ca/)
IASP Special Interest Group on Neuropathic Pain (https://www.iasp-pain.org/SIG/NeuropathicPain)	Ontario Pain Foundation (http://ontariopainfoundation.ca/)
British Pain Society (https://www.britishpainsociety.org/people-with-pain/)	British Pain Society (https://www.britishpainsociety.org/people-with-pain/)
Oxford Pain Internet Site – Bandolier – for evidence based practice (http://www.bandolier.org.uk/booth/painpag/)	American Chronic Pain Association (https://theacpa.org/)

Table 3: Resources available for physicians, and patients and caregivers (adapted from Haanpää et al., 2009)³⁵

CASE CONTINUED

Part 2

Mike returns to your office 4 months later and tells you that the pain in his shoulder has subsided since he saw you last; however, he now has a cramping pain in his abdomen, the pain in his legs is the same and he is having more periods of “11/10” pain during the day than previously. He says the pain in his legs still feels like it is hot/burning and pins and needles, but now also has periods where he feels like the pain is shooting and someone is squeezing his legs.

Make a list of differentials for Mike’s abdominal pain.

- *Constipation*
- *Neurogenic bowel*
- *Urinary tract infection*
- *Bowel impaction*
- *GERD*

What would you do next and what red flags would you look out for?

- *A detailed history with attention paid to the onset, description, daily course and variation, associated symptoms, and factors that worsen or alleviate pain*
- *Inquire about bowel movements, urine passage, and symptoms related to GERD*
- *Ask about any reduction in sensation, worsening spasticity, and autonomic dysreflexia that may*
 - *If Syringomyelia is possible, order spinal MRI*

How would you treat this pain?

- *Increase Pregabalin to 300 mg/d (150 mg BID) within 1 week based on tolerability*
 - *If pain persists, increase to 600mg/d (300 mg BID) after 2-3 weeks*
- *May change Pregabalin to Gabapentin, or to Amitriptyline (or other TCA)*
- *Refer on to psychiatry if pain persists*

SUMMARY

- Individuals with SCI may suffer from different types of pain, including nociceptive, and neuropathic pain, but nociceptive pain has been found to be the most common
- Screening for pain in individuals with SCI is important
- If pain is present, then an assessment to properly diagnose type, characteristics, affect on function and reversible conditions are important
- Treatment of pain in individuals with SCI will depend on the type of pain experienced
- Referral to a practitioner experienced in managing individuals with SCI (usually physiatry) is indicated when:⁴⁰
 - Ongoing pain that is difficult to manage
 - Dissatisfaction with current management protocol
 - Significant functional impairments and/or significant psychological comorbidity factors from pain

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APPENDIX

INTERNATIONAL SCI PAIN BASIC DATA SET Version 2.0 -

INTERNATIONAL SPINAL CORD INJURY PAIN BASIC DATA SET DATA COLLECTION FORM – Version 2.0

Date of data collection: YYYY/MM/DD

Have you had any pain during the last seven days including today:

No Yes

yes:

Please note that the time period during the last week applies to all pain interference questions. In general, how much has pain interfered with your day-to-day activities in the last week?

No interference 0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10 Extreme interference

In general, how much has pain interfered with your overall mood in the last week?

No interference 0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10 Extreme interference

In general, how much has pain interfered with your ability to get a good night's sleep?

No interference 0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10 Extreme interference

How many different pain problems do you have?

1; 2; 3; 4; >5

Please describe your three worst pain problems:

Worst pain problem:

Pain locations /sites (can be more than one, check all that apply): right (R), midline (M), or left (L)	R	M	L	Type of pain Intensity and duration of pain Treatment of pain
Head				Type of pain (check one):
Neck/shoulders throat neck shoulder				Nociceptive Musculoskeletal Visceral Other
Arms/hands upper arm elbow forearm wrist hand/fingers				Neuropathic At-level SCI Below-level SCI Other
Frontal torso/genitals chest abdomen pelvis/genitalia				Other Unknown
Back upper back lower back				Intensity and duration of pain: Average pain intensity in the last week: 0 = no pain; 10 = pain as bad as you can imagine 0; 1; 2; 3; 4; 5; 6; 7; 8; 9; 10
Buttocks/hips buttocks hip anus				Date of onset: YYYY/MM/DD
Upper leg/thigh				Are you using or receiving any treatment for your pain problem? No Yes
Lower legs/feet knee shin calf ankle foot/toes				

Second worst pain problem:

Pain locations /sites (can be more than one, check all that apply): right (1), midline (1), or left (L)	R	M	L	Type of pain Intensity and duration of pain Treatment of pain
Head				Type of pain (check one):
Neck/shoulders throat neck shoulder				Nociceptive Musculoskeletal Visceral Other
Arms/hands upper arm elbow forearm wrist hand/fingers				Neuropathic At-level SCI Below-level SCI Other
Frontal torso/genitals chest abdomen pelvis/genitalia				Other Unknown
Back upper back lower back				Intensity and duration of pain: Average pain intensity in the last week: 0 = no pain; 10 = pain as bad as you can imagine 0; 1; 2; 3; 4; 5; 6; 7; 8; 9; 10
Buttocks/hips buttocks hip anus				Date of onset: YYYY/MM/DD
Upper leg/thigh				Are you using or receiving any treatment for your pain problem? No Yes
Lower legs/feet knee shin calf ankle foot/toes				

Third worst pain problem:

Pain locations /sites (can be more than one, check all that apply): right (1), midline (1), or left (L)	R	M	L	Type of pain Intensity and duration of pain Treatment of pain
Head				Type of pain (check one):
Neck/shoulders throat neck shoulder				Nociceptive Musculoskeletal Visceral Other
Arms/hands upper arm elbow forearm wrist hand/fingers				Neuropathic At-level SCI Below-level SCI Other
Frontal torso/genitals chest abdomen pelvis/genitalia				Other Unknown
Back upper back lower back				Intensity and duration of pain: Average pain intensity in the last week: 0 = no pain; 10 = pain as bad as you can imagine 0; 1; 2; 3; 4; 5; 6; 7; 8; 9; 10
Buttocks/hips buttocks hip anus				Date of onset: YYYY/MM/DD
Upper leg/thigh				Are you using or receiving any treatment for your pain problem? No Yes
Lower legs/feet knee shin calf ankle foot/toes				

Douleur Neuropathique 4 Questions (DN4) Questionnaire³⁸

Please complete this questionnaire by ticking one answer for each item in the 4 questions below:

INTERVIEW OF THE PATIENT

Question 1: Does the pain have one or more of the following characteristics?

- 1 – Burning
- 2 – Painful cold
- 3 – Electric shocks

Yes	No
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>

Question 2: Is the pain associated with one or more of the following symptoms in the same area?

- 4 – Tingling
- 5 – Pins and needles
- 6 – Numbness
- 7 – Itching

Yes	No
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>

EXAMINATION OF THE PATIENT

Question 3: Is the pain located in an area where the physical examination may reveal one or more of the following characteristics?

- 8 – Hypoesthesia to touch
- 9 – Hypoesthesia to prick

Yes	No
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>

Question 4: In the painful area, can the pain be caused or increased by:

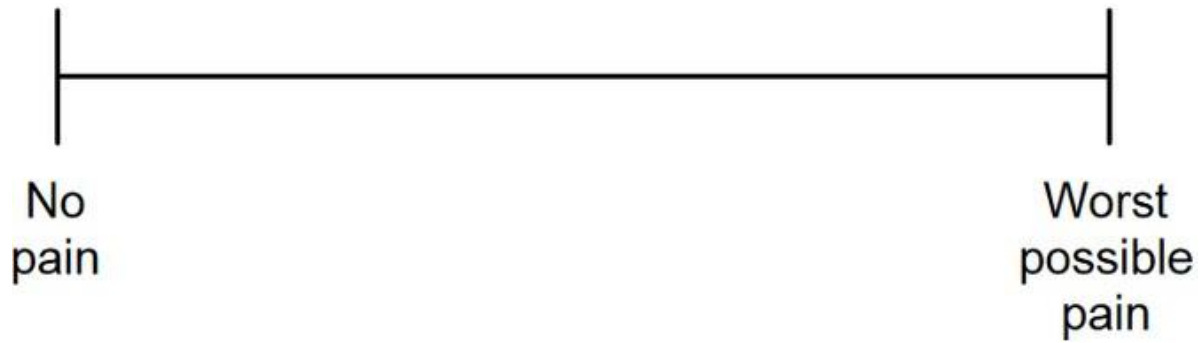
- 10 – Brushing

Yes	No
<input type="checkbox"/>	<input type="checkbox"/>

The total score is calculated as the sum of the 10 items and the cut-off value for the diagnosis of neuropathic pain is a total score of 4/10.

Total
<input type="text"/>

Visual Analog Scale⁴²



Screening and Diagnosis Recommendations from CanPainSCI Working Group⁴⁰

1. All patients with SCI must be screened for pain using a simple yes/no question
2. Any member of the health-care team can, and should, screen for the presence of pain
3. Screening for pain should occur on admission to rehabilitation, regularly during inpatient/rehabilitation and after discharge at each follow up
4. If pain is present at screening, an assessment to determine the type of pain, its intensity and interference should be carried out
5. Diagnosis of neuropathic pain, including its causes, should be informed by (1) a complete patient history, (2) a physical examination, (3) the International Spinal Cord Injury Pain (ISCIIP) Classification system and (4) investigations
6. Assess for serious underlying conditions (red flags) that may cause, aggravate, or mimic neuropathic pain and that require further investigation and prompt medical review
7. Assess and manage psychosocial factors (yellow flags) that may contribute to pain-related stress and disability
8. The ISCIIP Basic Data Set v2.0 should be used as a standardized tool for assessing and documenting pain in patients with spinal cord injury
9. Address patient concerns, expectations and needs as part of the neuropathic pain assessment
10. Standardized evaluation of treatment response should be carried out by the health-care team at regular intervals
11. The evaluation of treatment response should include assessment of changes in pain intensity, mood and function using the ISCIIP Basic Data Set v2.0. Evaluation also includes assessment of adverse events, aberrant behavior and compliance
12. All patients with new-onset or worsening pain need to be reassessed

Red Flags in Patients with Spinal Cord Injury⁶⁶

System	Red Flag Indicators	Red Flag Conditions
Musculoskeletal	History of recent trauma, visible deformity, changes in range of motion, new-onset localized swelling & warmth	Fracture or dislocation, heterotopic ossification, regional pathology that may be contributing to NP presentation & contracture
Dermatologic	Redness, ulceration	Pressure ulcer, ingrown toenail
Cardiovascular	Chest pain, shortness of breath, fevers, chills or sweats, autonomic symptoms, and differences in calf measurements between L & R sides	Abdominal aortic aneurysm, aortic dissection, myocardial infarction, infection & deep vein thrombosis
Respiratory	As for cardiovascular	Pulmonary embolism, deep vein thrombosis, infection or pneumonia
Urinary	Changes in urine appearance or smell, pain over kidneys, new incontinence, leakage between catheterizations, a history of renal or bladder calculi & scrotal or testicular swelling	UTI or pyelonephritis, renal or bladder calculi, urinary retention, testicular torsion & epididymitis
Pelvic*	Relation of pain to menstruation	Ovarian cysts, endometriosis & other genitourinary conditions
Gastrointestinal*	Changes in bowel habit, examination findings of acute abdomen	Stool impaction, constipation, acute abdomen, appendicitis & cholecystitis
Neurologic	Changes in neurologic examination, such as increase or decrease in tone, decline in motor or sensory neurologic level change in reflexes	Peripheral neuropathy, syringomyelia
Other	Fever, chills sweats & weight loss	Malignancy

*Note: examination findings & symptom description may not be present or reliable below the neurologic level of injury: hence, it is important to maintain an index of suspicion