## Development Committee

<table>
<thead>
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<th>City/Location</th>
</tr>
</thead>
<tbody>
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<td>Ankara, Turkey</td>
</tr>
</tbody>
</table>

*This program was sponsored by Pfizer Inc.*
Learning Objectives

• After completing this module, participants will be able to:
  – Explain the pathophysiology of neuropathic pain
  – Discuss the prevalence of neuropathic pain
  – Apply a simple diagnostic technique for the diagnosis of neuropathic pain
  – Understand the impact of neuropathic pain and its comorbidities on patient functioning and quality of life
  – Select appropriate pharmacological and non-pharmacological strategies for the management of neuropathic pain
  – Know when to refer patients to specialists
Table of Contents

• What is neuropathic pain?
• How common is neuropathic pain?
• How can neuropathic pain be differentiated from nociceptive pain?
• What is the impact of neuropathic pain?
• How should neuropathic pain be treated based on its pathophysiology?
Pathophysiological Classification of Pain

Multiple pain mechanisms may coexist (mixed pain)

Central sensitization/dysfunctional pain

Nociceptive pain
- Somatic
- Visceral

Neuropathic pain
- Peripheral
- Central

- Somatic
- Visceral
- Peripheral
- Central

- Nociceptive pain
- Neuropathic pain
- Central sensitization/dysfunctional pain

What is neuropathic pain?

**Neuropathic Pain**
Pain caused by a lesion or disease of the somatosensory nervous system

**Peripheral Neuropathic Pain**
Pain caused by a lesion or disease of the peripheral somatosensory nervous system

**Central Neuropathic Pain**
Pain caused by a lesion or disease of the central somatosensory nervous system

## Nociceptive vs. Neuropathic Pain

<table>
<thead>
<tr>
<th>Nociceptive</th>
<th>Neuropathic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Usually aching or throbbing and well-localized</td>
<td>• Pain often described as tingling, shock-like, and burning – commonly associated with numbness</td>
</tr>
<tr>
<td>• Usually time-limited (resolves when damaged tissue heals), but can be chronic</td>
<td>• Almost always a chronic condition</td>
</tr>
<tr>
<td>• Generally responds to conventional analgesics</td>
<td>• Responds poorly to conventional analgesics</td>
</tr>
</tbody>
</table>

Neuropathic Pain Is Characterized by Changes in Pain Response to Painful Stimuli

- Pain intensity
- Stimulus intensity

Hyperalgesia
(increased response to a stimulus that is normally painful)

Allodynia
(pain due to stimulus that does not normally provoke pain)

Normal pain response

Response after injury

Hyperexcitability

Pathophysiology of Neuropathic Pain

Peripheral mechanisms

- Membrane hyperexcitability
- Ectopic discharges
- Transcriptional changes

Central mechanisms

- Hyperexcitability
- Loss of inhibitory controls
- Reorganization

Sensitization
- Peripheral
- Central

Neuropathic pain

Neuropathic Pain is Prevalent Across a Range of Different Conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>% affected by peripheral neuropathic pain</th>
<th>% affected by central neuropathic pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>11–26%(^1)</td>
<td>8%(^9)</td>
</tr>
<tr>
<td>Cancer</td>
<td>~33%(^2)</td>
<td>75%(^10)</td>
</tr>
<tr>
<td>HIV</td>
<td>35–53%(^3–5)</td>
<td>~55%(^11)</td>
</tr>
<tr>
<td>Post-surgical</td>
<td>20–43% of mastectomy patients(^6,7)</td>
<td></td>
</tr>
<tr>
<td>Chronic low back pain</td>
<td>Up to 37%(^8)</td>
<td></td>
</tr>
<tr>
<td>Postherpetic neuralgia</td>
<td>7–27% of patients with herpes zoster(^1)</td>
<td></td>
</tr>
</tbody>
</table>

HIV = human immunodeficiency virus

Discussion Question

WHAT PROPORTION OF YOUR PATIENTS SUFFER FROM NEUROPATHIC PAIN?
5–20% of the General Population May Suffer from Neuropathic Pain

Summary of Selected Prevalence Studies

Discussion Question

WHAT ARE SOME OF YOUR BIGGEST CHALLENGES IN DIAGNOSING PATIENTS WITH NEUROPATHIC PAIN?

HOW DO YOU OVERCOME THESE CHALLENGES?
Diagnosing Neuropathic Pain Is Challenging

- Diverse symptoms
- Difficulties in communicating and understanding symptoms
- Multiple, complex mechanisms
- Recognition of comorbidities

The 3L Approach to Diagnosis

Listen\textsuperscript{1,2}

- Patient verbal descriptors of pain, questions and answers

Locate\textsuperscript{1,3}

- Somatosensory Nervous system lesion or disease

Look\textsuperscript{1,4}

- Sensory abnormalities in the painful area

**Listen** to the Patient Description of Pain

- **Question** patients about their pain
- **Be alert** and ask for *common verbal descriptors* of neuropathic pain
- Use analogue or numerical scales to quantify the pain
- Use screening and assessment tools to distinguish neuropathic pain from non-neuropathic pain

2. Gilron I et al. *CMAJ* 2006; 175(3):265-75;  
Listen: Pain History in Neuropathic Pain

Identify the Following:

• Duration
• Frequency
• Quality
• Intensity
• Distribution and location of pain
• Extent of interference with daily activity

Areas of Further Exploration

• Previous medical history
• Exposure to toxins or other drug treatment (e.g., cancer chemotherapy, radiation)
• Use of pain medications
• Associated psychological and mood disturbance
Listen: Neuropathic Signs and Symptoms Can Vary Widely

In One Individual

• Wide spectrum of signs and symptoms often **co-exist** at the same time
• Signs and symptoms **may vary within an individual over time**

Between Individuals

• Signs and symptoms **vary among individuals** with the same underlying etiology
• Signs and symptoms are shared across neuropathic pain states

Listen:
Recognizing Neuropathic Pain

Be alert for common verbal descriptors of neuropathic pain:

- Burning
- Tingling
- Shooting
- Electric shock-like
- Numbness

**Listen:** Sensory Symptoms of Neuropathic Pain

Lesion or disease of the somatosensory nervous system

**Positive symptoms**
(due to excessive neural activity)

- Spontaneous pain
- Allodynia
- Hyperalgesia
- Dysesthesia
- Paresthesia

**Negative symptoms**
(due to deficit of function)

- Hypoesthesia
- Anesthesia
- Hypoalgesia
- Analgesia

Sensory abnormalities and pain paradoxically *co-exist*

Each patient may have a combination of symptoms that may change over time (even within a single etiology)

**Listen:** Positive Sensory Symptoms of Neuropathic Pain

<table>
<thead>
<tr>
<th>Positive symptom</th>
<th>Definition</th>
<th>Typical verbal descriptors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous pain</td>
<td>Painful sensations felt with no evident stimulus</td>
<td>Electric shock-like, burning</td>
</tr>
<tr>
<td>Allodynia</td>
<td>Pain due to a stimulus that does not normally provoke pain (e.g., touching, movement, cold, heat)</td>
<td>Vary with stimulus</td>
</tr>
<tr>
<td>Hyperalgesia</td>
<td>An increased response to a stimulus that is normally painful (e.g., cold, heat, pinprick)</td>
<td>Vary with stimulus</td>
</tr>
<tr>
<td>Dysesthesia</td>
<td>An unpleasant abnormal sensation, whether spontaneous or evoked</td>
<td>Shooting, piercing, burning</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>An abnormal sensation, whether spontaneous or evoked</td>
<td>Tingling, buzzing, vibrating</td>
</tr>
</tbody>
</table>

### Listen: Negative Sensory Symptoms of Neuropathic Pain

<table>
<thead>
<tr>
<th>Negative symptom</th>
<th>Definition</th>
<th>Typical verbal descriptor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoesthesia</td>
<td>Diminished sensitivity to stimulation</td>
<td>Numbness</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>Total loss of sensation (especially tactile sensitivity)</td>
<td>Numbness</td>
</tr>
<tr>
<td>Hypoalgesia</td>
<td>Diminished pain in response to a normally painful stimulus</td>
<td>Numbness</td>
</tr>
<tr>
<td>Analgesia</td>
<td>Absence of pain in response to stimulation that would normally be painful</td>
<td>Numbness</td>
</tr>
</tbody>
</table>

Locate the Region of Pain

Correlate the region of pain to the lesion in the somatosensory nervous system*

Body maps are useful for the precise location of pain symptoms and sensory signs.

Body maps allow identification of the nerve damage.

*Note that in cases of referred neuropathic pain, as can occur for example in some cases of spinal cord injury, the location of the pain and of the lesion/dysfunction may not be correlated
Look for Sensory and/or Physical Abnormalities

- Inspect the painful body area and compare it with the corresponding healthy area\textsuperscript{1,2}

- Conduct simple bedside tests to confirm sensory abnormalities\textsuperscript{1-4}

WHAT BEDSIDE TESTS DO YOU TYPICALLY USE IN YOUR PRACTICE? WHY?
**Look**: Simple Bedside Tests

Stroke skin with brush, cotton or apply acetone

Light manual pinprick with safety pin or sharp stick

- **Sharp, burning superficial pain** → **ALLODYINIA**
- **Very sharp, superficial pain** → **HYPERALGESIA**

DO YOU USE A SCREENING TOOL FOR NEUROPATHIC PAIN IN YOUR PRACTICE?
IF SO, WHICH TOOL AND WHY?
# Neuropathic Pain Screening Tools

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>LANSS</th>
<th>DN4</th>
<th>NPQ</th>
<th>painDETECT</th>
<th>ID Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pricking, tingling, pins and needles</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Electric shocks of shooting</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hot or burning</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Numbness</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Pain evoked by light touching</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Clinical examination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brush allodynia</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raised soft touch threshold</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Altered pin prick threshold</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Neuropathic pain screening tools rely largely on common verbal descriptors of pain.

Select tool(s) based on *ease of use and validation in the local language*.

Some screening tools also include bedside neurological examination.

---

DN4 = Douleur Neuropathique en 4 Questions (DN4) questionnaire; LANSS = Leeds Assessment of Neuropathic Symptoms and Signs; NPQ = Neuropathic Pain Questionnaire

Sensitivity and Specificity of Neuropathic Pain Screening Tools

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Sensitivity*</th>
<th>Specificity*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Interview-based</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPQ</td>
<td>10 sensory-related items + 2 affect items</td>
<td>66%</td>
<td>74%</td>
</tr>
<tr>
<td>ID-Pain</td>
<td>5 sensory items + 1 pain location</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>painDETECT</td>
<td>7 sensory items + 2 spatial characteristics items</td>
<td>85%</td>
<td>80%</td>
</tr>
<tr>
<td><strong>Interview + physical tests</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LANSS</td>
<td>5 symptom items + 2 clinical exam items</td>
<td>82–91%</td>
<td>80–94%</td>
</tr>
<tr>
<td>DN4</td>
<td>7 symptom items + 3 clinical exam items</td>
<td>83%</td>
<td>90%</td>
</tr>
</tbody>
</table>

Tests incorporating both interview questions and physical tests have higher sensitivity and specificity than tools that rely only on interview questions

*Compared with clinical diagnosis
DN4 = Douleur neuropathic en 4 questions; LANSS = Leeds Assessment of Neuropathic Symptoms and Signs;
NPQ = Neuropathic Pain Questionnaire; NR = not reported
LANSS Scale

- Completed by physician in office
- Differentiates neuropathic from nociceptive pain
- 5 pain questions and 2 skin sensitivity tests
- Identifies contribution of neuropathic mechanisms to pain
- Validated

LANSS = Leeds Assessment of Neuropathic Symptoms and Signs
**DN4**

Completed by physician in office

Differentiates neuropathic from nociceptive pain

- 2 pain questions (7 items)
- 2 skin sensitivity tests (3 items)
- Score $\geq 4$ is an indicator for neuropathic pain
- Validated

**DN4 = Douleur neuropathique en 4 questions**

Clinical Approach to Suspected Neuropathic Pain


Are verbal descriptors and history suggestive of neuropathic pain?1

Yes

Can you detect sensory abnormalities using simple bedside tests?1,2

Yes

Probable nociceptive pain

No

Can you identify the responsible somatosensory nervous system lesion/disease2

Yes

Neuropathic pain is likely: initiate treatment3

No

Consider specialist referral and if neuropathic pain is still suspected, consider treatment in the interim period3

No

Whenever possible, treat the underlying cause/disease
Discussion Question

HOW HAS NEUROPATHIC PAIN AFFECTED SOME OF YOUR PATIENTS?
Patient-Reported Burden of Neuropathic Pain Is Significant

<table>
<thead>
<tr>
<th>Activities of daily living</th>
<th>Psychological burden</th>
<th>Physical burden</th>
<th>Neuropathic pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Reduced quality of life</td>
<td>• Depression</td>
<td>• Physical disability</td>
<td></td>
</tr>
<tr>
<td>• Sleep disturbances</td>
<td>• Psychological distress</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Drowsiness when awake</td>
<td>• Difficulty in concentration</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Both the **intensity** of the pain and the **duration** of the condition exacerbate the patient’s burden.

Chronic Neuropathic Pain Has a Significant Impact on Daily Functioning

BPI = Brief Pain Inventory, which scores extent pain interferes with activities in last 24 hours from 0 (does not interfere) to 10 (completely interferes)

Patients with Peripheral Neuropathic Pain Experience Significant Comorbid Symptoms

- Difficulty sleeping
- Lack of energy
- Drowsiness
- Concentration difficulties
- Depression
- Anxiety
- Poor appetite

% patients with moderate to very severe discomfort

n = 126

Neuropathic Pain Is Associated with Sleep Disturbance, Anxiety and Depression

Pain

Functional impairment

Anxiety and depression

Sleep disturbances

Management of Neuropathic Pain

The earlier a diagnosis is made, the more opportunities there are to improve patient outcomes.

- Improved physical functioning
- Improved psychological state
- Improved sleep quality
- Improved overall quality of life
- Reduced pain

Diagnosis
- Treatment of underlying conditions
- Pharmacological and non-pharmacological treatment of neuropathic pain
- Treatment of comorbidities

Goals in the Treatment of Neuropathic Pain

1st goal: >50% pain relief*
... but be realistic!

2nd goals:
Restoration or improvement in:
- Sleep
- Mood
- Function
- Quality of life

*Note: pain reduction of 30–50% can be expected with maximal doses in most patients
Multimodal Treatment of Neuropathic Pain

- Lifestyle management
- Stress management
- Pharmacotherapy
- Interventional procedures
- Education
- Biofeedback
- Complementary therapies
- Physical or occupational therapy
- Sleep hygiene

Various Non-pharmacological Treatments Are Available for Neuropathic Pain$^{1-6}$

Physiotherapy$^1$

Alternative therapies and spiritual healing$^{1-4}$

Psychotherapy/CBT$^{6,7}$

Patient education$^1$

Multimodal pain management programs$^{5,6}$

Various non-pharmacological treatment modalities are mentioned in guidelines, but no modality is universally recommended$^{1-5}$

CBT = cognitive behavioral therapy

WHAT NON-PHARMACOLOGICAL APPROACHES TO NEUROPATHIC PAIN MANAGEMENT HAVE YOU FOUND HELPFUL FOR YOUR PATIENTS?
Evidence for Non-pharmacological Therapies in Neuropathic Pain

• Studied therapies include:
  – Acupuncture
  – Electrostimulation
  – Herbal medicine
  – Magnets
  – Dietary supplements
  – Imagery
  – Spiritual healing

• Limited evidence for most modalities

The effectiveness of B vitamins in reducing chronic neuropathic pain has not been established

– Magnets
– Dietary supplements
– Imagery
– Spiritual healing

– Cannabis extract
– Carnitine
– Electrostimulation
– Magnets

IASP NeuPSIG Recommendations: Interventional Management of Neuropathic Pain

**Weakly Recommended**
- Epidural or paravertebral nerve block(s) for herpes zoster
- Epidural steroid injection(s) for radiculopathy
- Spinal cord stimulation for failed back surgery syndrome with radiculopathy and complex regional pain syndrome 1

**Not recommended**
- Sympathetic nerve blocks for postherpetic neuralgia
- Radiofrequency lesioning for lumbar radiculopathy

IASP = International Association for the Study of Pain; NeuPSIG = Neuropathic Pain Special Interest Group

Mechanism-Based Pharmacological Treatment of Neuropathic Pain

Medications affecting peripheral sensitization:
- Capsaicin
- Local anesthetics
- TCAs

Medications affecting descending modulation:
- SNRIs
- TCAs
- Tramadol, opioids

Medications affecting central sensitization:
- $\alpha_2\delta$ ligands
- TCAs
- Tramadol, opioids

SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Role of $\alpha_2\delta$-Linked Calcium Channels in Neuropathic Pain

Binding of $\alpha_2\delta$ ligands to $\alpha_2\delta$ inhibits calcium channel transport

- Increased numbers of calcium channels
- Increased calcium influx
- Increased neuronal excitability

INCREASED PAIN SENSITIVITY

Calcium channels transported to nerve terminals in dorsal horn

Injury stimulates production of calcium channel

Nerve injury

Note: gabapentin and pregabalin are $\alpha_2\delta$ ligands
Adverse Effects of $\alpha_2\delta$ Ligands

<table>
<thead>
<tr>
<th>System</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digestive system</td>
<td>Dry mouth</td>
</tr>
<tr>
<td>CNS</td>
<td>Dizziness, somnolence</td>
</tr>
<tr>
<td>Other</td>
<td>Asthenia, headache, peripheral edema, weight gain</td>
</tr>
</tbody>
</table>

$\alpha_2\delta$ ligands include gabapentin and pregabalin

CNS = central nervous system

Inhibiting reuptake of serotonin and norepinephrine enhances descending modulation.
### Adverse Effects of Antidepressants

<table>
<thead>
<tr>
<th>System</th>
<th>TCAs</th>
<th>SNRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digestive system</td>
<td>Constipation, dry mouth, urinary retention</td>
<td>Constipation, diarrhea, dry mouth, nausea, reduced appetite</td>
</tr>
<tr>
<td>CNS</td>
<td>Cognitive disorders, dizziness, drowsiness, sedation</td>
<td>Dizziness, somnolence</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Orthostatic hypotension, palpitations</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Other</td>
<td>Blurred vision, falls, gait disturbance, sweating</td>
<td>Elevated liver enzymes, elevated plasma glucose, sweating</td>
</tr>
</tbody>
</table>

CNS = central nervous system; TCA = tricyclic antidepressant; SNRI = serotonin-norepinephrine reuptake inhibitor

Pharmacological Management of Neuropathic Pain

**STEP 1**
Initiate treatment with one or more **first-line** treatments:
- $\alpha_2\delta$ ligands (gabapentin, pregabalin)
- SNRIs (duloxetine, venlafaxine)
- TCAs* (nortriptyline, desipramine)
- Topical lidocaine (for localized peripheral pain)

**STEP 2**
- If there is partial pain relief, add another first-line medication
- If there is no or inadequate pain relief, switch to another first-line medication

**STEP 3**
If first-line medications alone and in combination fail, consider **second-line** medications (opioids, tramadol) or **third-line** medications (bupropion, citalopram, paroxetine, carbamazepine, lamotrigine, oxcarbazepine, topiramate, valproic acid, topical capsaicin, dextromethorphan, memantine, mexiletine) or referral to pain specialist

*Use tertiary amine TCAs such as amitriptyline only if secondary amine TCAs are unavailable
Note: there is insufficient support for the use of nsNSAIDs in neuropathic pain
nsNSAID = non-specific non-steroidal anti-inflammatory drug; SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant
# Prescribing Recommendations for First-Line Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Starting dose</th>
<th>Titration</th>
<th>Max. dosage</th>
<th>Trial duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>α₂δ ligands</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gabapentin</td>
<td>100–300 mg at bedtime or tid</td>
<td>↑ by 100–300 mg tid every 1–7 days</td>
<td>3600 mg/day</td>
<td>3–8 weeks + 2 weeks at max. dose</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>50 mg tid or 75 mg bid</td>
<td>↑ to 300 mg/day after 3–7 days, then by 150 mg/day every 3–7 days</td>
<td>600 mg/day</td>
<td>4 weeks</td>
</tr>
<tr>
<td><strong>SNRIs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duloxetine</td>
<td>30 mg qd</td>
<td>↑ to 60 mg qd after 1 week</td>
<td>60 mg bid</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>37.5 mg qd</td>
<td>↑ by 75 mg each week</td>
<td>225 mg/day</td>
<td>4–6 weeks</td>
</tr>
<tr>
<td><strong>TCAs</strong> (desipramine, nortriptyline)</td>
<td>25 mg at bedtime</td>
<td>↑ by 25 mg/day every 3–7 days</td>
<td>150 mg/day</td>
<td>6–8 weeks, with ≥2 weeks at max. tolerated dosage</td>
</tr>
<tr>
<td><strong>Topical lidocaine</strong></td>
<td>Max. 3 5% patches/day for 12 h max.</td>
<td>None needed</td>
<td>Max. 3 patches/day for 12–18 h max.</td>
<td>3 weeks</td>
</tr>
</tbody>
</table>

SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

But... Patients with Chronic Pain of Just One Type of Pain Pathophysiology May be Rare

- Patients may have different pathophysiologic mechanisms contributing to their pain
  - e.g., complex regional pain syndrome has multiple potential mechanisms, including nerve injury and inflammation – “mixed pain state”

- Therapies that will work better for a particular patient are likely to depend on the mechanisms contributing to the patient’s pain

- Patients with mixed pain may benefit from combination therapy

Discussion Question

WHAT TREATMENT APPROACH WOULD YOU TAKE WITH A PATIENT SUFFERING FROM MIXED PAIN DUE TO COMPLEX REGIONAL PAIN SYNDROME?
Complex Regional Pain Syndrome

• **What is it?**
  – Exaggerated response to trauma, characterized by intense prolonged pain, delayed recovery of function, vasomotor disturbances and trophic changes
  – Causes are unclear, but may include exaggerated local inflammatory response, nerve injury and involvement of the central and peripheral nervous systems

• **How common is it?**
  – Thought to occur in 1 in 2000 cases of limb trauma

• **How should it be treated?**
  – Physiotherapy is the mainstay of treatment
  – Combination of pharmacological agents may be necessary

Key Messages

• Neuropathic pain is pain caused by a lesion or disease of the somatosensory nervous system
• Up to 10% of the population may suffer from neuropathic pain, which is associated with significant patient-reported burden
• Neuropathic pain can be distinguished from nociceptive pain through common verbal descriptors and simple bedside tests
  — Several easy screening tests are also available
• Non-pharmacological therapies, including patient education, are important components of neuropathic pain management
• When it comes to pharmacotheraphy, most treatment guidelines consider antidepressants and α2δ ligands as first-line therapy for most types of neuropathic pain