Definition(s)
- Chemotherapy – Induced Peripheral Neuropathy (CIPN): injury, or degeneration of the peripheral nerve fibers (motor, sensory, autonomic) caused by certain neurotoxic systemic therapy agents. Symptoms usually start in the fingers and toes and spread proximally in a glove and stocking distribution.
- Neuropathic pain: nerve pain initiated by damaged nerves, often described as sharp, tingling, burning, cold, and/or a pins and needles.
- Allodynia: pain caused by a stimulus that does not normally cause pain (e.g. light touch, contact with clothing).
- Areflexia: absence of reflexes.
- Dysesthesia: abnormal spontaneous sensations (burning, stinging, stabbing) from activities that do not normally cause pain.
- Paresthesia: an abnormal skin sensation in the absence of a stimulus (described as burning, prickling, itching, tingling).
- Glove and stocking syndrome: symmetrical manifestation of neuropathy in toes and fingers.
- Hyperesthesia: increased sensitivity to sensory stimuli.
- Hypoesthesia: decreased sensitivity to sensory stimuli.
- Coasting Effect: when symptoms progress for months after treatment cessation.
- Carpal Tunnel Syndrome: median nerve is compressed at the wrist, causing numbness, tingling, burning and pain in the affected hand and fingers.

FOCUSED HEALTH ASSESSMENT

<table>
<thead>
<tr>
<th>PHYSICAL ASSESSMENT</th>
<th>SYMPTOM ASSESSMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vital Signs</td>
<td>*Consider contributing factors</td>
</tr>
<tr>
<td>Frequency as clinically indicated</td>
<td>Normal</td>
</tr>
<tr>
<td>Assess patient for orthostatic hypotension and heart rate</td>
<td>Do you have any pre-existing peripheral neuropathy?</td>
</tr>
<tr>
<td>Observe Patient General Appearance:</td>
<td>Onset</td>
</tr>
<tr>
<td>Observe gait as patient walks - note any hesitation, stumbling, unsteadiness, holding onto walls</td>
<td>When did the symptoms begin?</td>
</tr>
<tr>
<td>Observe for any involuntary movements, tremors, spasms, wrist or foot drop</td>
<td>Provoking / Palliating</td>
</tr>
<tr>
<td>Observe any difficulty with closing buttons, shaky handwriting, holding objects, keyboard use</td>
<td>What brings it on?</td>
</tr>
<tr>
<td></td>
<td>What makes it worse? Better?</td>
</tr>
<tr>
<td></td>
<td>Does it get better in between treatment?</td>
</tr>
<tr>
<td>Quality (in last 24 hours)</td>
<td>Severity / Other Symptoms</td>
</tr>
<tr>
<td>Can you describe symptoms?</td>
<td>How bothersome is this symptom to you? (on a scale of 0 – 10, with 0 not at all and 10 being the worst imaginable)</td>
</tr>
<tr>
<td>Sensory: numbness, tingling, pain, or burning</td>
<td>Are there any accompanying symptoms? (e.g. pain)</td>
</tr>
<tr>
<td>Motor: falls, tripping, muscle weakness, abnormal gait, or paralysis, fine motor changes</td>
<td></td>
</tr>
<tr>
<td>Autonomic: constipation, urinary dysfunction, sexual dysfunction, orthostatic hypotension</td>
<td></td>
</tr>
<tr>
<td>Are symptom(s) intermittent or constant?</td>
<td></td>
</tr>
<tr>
<td>Region / Radiation</td>
<td>Treatment</td>
</tr>
<tr>
<td>Where are you experiencing your symptoms? (e.g. toes, fingers, symmetrical)</td>
<td>What medications or other strategies are you using right now? - How effective? Side effects?</td>
</tr>
<tr>
<td>Severity / Other Symptoms</td>
<td>What medications or strategies have been effective in the past?</td>
</tr>
<tr>
<td>How bothersome is this symptom to you? (on a scale of 0 – 10, with 0 not at all and 10 being the worst imaginable)</td>
<td></td>
</tr>
<tr>
<td>Are there any accompanying symptoms? (e.g. pain)</td>
<td></td>
</tr>
</tbody>
</table>
The information contained in these documents is a statement of consensus of BC Cancer professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient’s care or treatment. Use of these documents is at your own risk.

Understanding / Impact on You
- Do your symptoms affect your role function, mood or ability to do activities of daily living? (e.g. buttoning shirt, writing, pick up small items)?
- Do your symptoms affect your ability to sleep (insomnia)?

Value
- What do you believe is causing this problem?
- What is your comfort goal or acceptable level for this symptom (0 – 10 scale)?

PERIPHERAL NEUROPATHY GRADING SCALE(S)
Adapted NCI CTCAE (Version 4.03)

<table>
<thead>
<tr>
<th>NORMAL</th>
<th>GRADE 1 (Mild)</th>
<th>GRADE 2 (Moderate)</th>
<th>GRADE 3 (Severe)</th>
<th>GRADE 4 (Life-threatening)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor Grade</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>Asymptomatic; clinical or diagnostic observations only; intervention not indicated</td>
<td>Moderate symptoms; limiting instrumental activities of daily living (IADLs) (e.g. preparing meals, shopping, managing money)</td>
<td>Severe symptoms; limiting self-care ADLs (e.g. bathing, dressing, feeding self, using the toilet, taking medications); assistive device indicated</td>
<td>Life – threatening, consequences; urgent intervention indicated</td>
</tr>
</tbody>
</table>

| Sensory Grade |
| Normal | Asymptomatic; loss of deep tendon reflexes or paresthesia | Moderate symptoms; limiting IADLs (e.g. preparing meals, shopping, managing money) | Severe symptoms; limiting self-care ADLs (e.g. bathing, dressing, feeding self, using the toilet, taking medications) | Life – threatening, consequences; urgent intervention indicated |

PAIN GRADING SCALE

| No pain | Mild pain | Moderate pain; limiting IADLs (e.g. preparing meals, shopping, managing money) | Severe pain, limiting self-care, ADLs (e.g. bathing, dressing, feeding self, using the toilet, taking medications) |

*Step-Up Approach to Symptom Management:
Interventions Should be Based on Current Grade Level and Include Lower Level Grade Interventions as Appropriate

PREVENTION – GRADE 1

NON – URGENT:
Prevention, support, teaching, mild symptoms & follow-up care as required

Patient Care and Assessment
- Collaborate with physician:
  - If patient on Immunotherapy
  - To rule out other causes or concomitant causes of peripheral neuropathy or need for further assessment in outpatient setting (r/o spinal cord compression). Facilitate arrangements as necessary.
- Lab tests may be ordered: e.g. vitamin B12 level, thyroid testing, fasting blood sugar or HgA1c, folate level
- If on active chemotherapy treatment, may require treatment delays or reductions until symptoms resolve. Refer to specific chemotherapy protocols for direction: [http://www.bccancer.bc.ca/health-professionals/professional-resources/chemotherapy-protocols](http://www.bccancer.bc.ca/health-professionals/professional-resources/chemotherapy-protocols)

### Prevention of Thermal Injury
- Avoid exposure of fingers and toes to very hot or very cold temperatures
- Avoid ice packs or heating pads. Ensure water temperature in shower or tub is less than 43 °C
- Use gloves when washing dishes or gardening, potholders when cooking
- Reinforce principles of hand and foot care, including daily visual inspection for sores or blisters
- For patients receiving Oxaliplatin:
  - Sensory symptoms exacerbated by cold
  - Wear gloves, socks and scarf to protect against cold temperatures
  - Avoid eating cold food or drinks for few days after treatment

### Fall Prevention
- Clear walkways of clutter, turn on lights when entering a room
- Use skid free shower/bathroom mats
- Remove throw rugs or other objects that could cause falls
- If gait unsteady, use assistive device (e.g. cane, walker)
- Avoid going barefoot or using loose, or tight-fitting shoes

### Exercise/Activity
- Passive range of motion exercises - may enhance reinnervation of denervated muscles
- Resistance exercises – can help strengthen muscles weakened by neuropathy
- Refrain from activities that require precise handwork (e.g. operating power tools or needlework) until symptoms lessen

### Autonomic Symptoms
- Orthostatic hypotension
  - Dangle legs prior to getting up, hold onto secure surfaces when getting up and change positions slowly
- Constipation (See Resources & Referrals)
  - Adequate daily fluid intake & high fibre diet
  - Urinary retention
  - Adequate daily fluid intake, bladder re-training exercises, empty bladder at same time every day
- Sexual dysfunction
  - Consider pharmacological intervention e.g. Viagra

### Non-Pharmacological Management
- Complementary Alternative Medicine (CAM) therapy may be helpful for some individuals
- Relaxation techniques, deep-breathing, meditation-, yoga, visual or guided imagery
- Neurofeedback – cognitive therapy
- Massage, Acupuncture, Transcutaneous electrical nerve stimulation (TENS)
- Cryotherapy for weekly paclitaxel eg, by using frozen socks and gloves before, during, and after drug infusion) may be useful to diminish objective and subjective symptoms of CIPN

### Pharmacological Management
- In collaboration with physician and pharmacist the following may be prescribed: Mild to moderate neuropathic pain and accompanying symptoms
  - Acetaminophen, or NSAIDs
  - Serotonin-norepinephrine reuptake inhibitor (SNRI) (eg. Duloxetine)
  - Anticonvulsants (e.g. gabapentin or pregabalin), or tricyclic antidepressants (e.g. amitriptyline, nortriptlyline, imipramine)
  - Topical analgesic agents (e.g. capsaicin, lidocaine cream)
  - Compounded topical gels (baclofen/amitryptiline/ketamine)
  - A stepped protocol for constipation

### Patient Education and Follow-Up
- All patients should receive information about:
  - Specific neurotoxic effects that can be expected from their chemotherapy regimen
  - Platinum-induced neuropathy can progress for several months after completion of chemotherapy
  - Report signs and symptoms of PN (sensory, motor, autonomic) to health care provider as soon as they are first noticed
  - Strategies around self-care and personal safety

Follow-up:
- Instruct patient/family to call back if symptoms worsen or do not improve
- Arrange for nurse initiated telephone follow-up

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- Physician follow – up in ambulatory care setting may be indicated

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**GRADE 2 - GRADE 3**

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**URGENT:**
Requires medical attention within 24 hours

**Patient Care and Assessment**
- Collaborate with physician:
  - If patient on Immunotherapy
  - To rule out other causes or concomitant causes of peripheral neuropathy or need for further assessment in outpatient setting (r/o spinal cord compression). Facilitate arrangements as necessary.
  - Lab tests may be ordered: e.g. vitamin B12 level, thyroid testing, fasting blood sugar or HGa1c, folate level
If on active chemotherapy treatment, may require treatment delays or reductions until symptoms resolve. Refer to specific chemotherapy protocols for direction: [http://www.bccancer.bc.ca/health-professionals/professional-resources/chemotherapy-protocols](http://www.bccancer.bc.ca/health-professionals/professional-resources/chemotherapy-protocols)

**Pharmacological Management**
- In collaboration with physician and pharmacist the following may be prescribed:
  - Increased titration of dosages of anticonvulsant such as gabapentin, or tricyclic antidepressant such as nortriptyline (equal first-line). SNRIs such as duloxetine are third-line options
  - Opioid (short or long acting)
  - Corticosteroid (Refer to protocol specific algorithm if patient is on Immunotherapy)
  - Methadone
  - Mexiletine, Lidocaine infusion, Ketamine
  - Compounded Topical Gel (baclofen/amitriptyline/ketamine)
  - Medical Cannabinoids

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**GRADE 4**
OR
**Signs of Spinal Cord Compression (e.g. back pain, motor weakness/loss, autonomic dysfunction)**

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**EMERGENT:**
Requires IMMEDIATE medical attention

**Patient Assessment and Care**
- If patient at home, instruct patient or family to call 911 or go to closest EMERGENCY ROOM
- Notify physician of nursing assessment and facilitate arrangements as necessary
- If patient on Immunotherapy, remind patient to present Immunotherapy alert card
  [Immunotherapy alert card](http://www.bccancer.bc.ca/health-professionals/professional-resources/immunotherapy-alert-card)
- Notify physician if on active chemotherapy treatment, will require treatment delays until symptoms resolve or discontinuation. Refer to specific chemotherapy protocols for direction:
RESOURCES & REFFERALS

**Possible Referrals**
- Telephone Care for follow-up
- Physiotherapist
- Occupational Therapist
- Massage therapist
- Acupuncturist
- Patient and Family Counseling
- Pain and Symptom Management/Palliative Care (PSMPC) (if interfering with ADLs and if pt willing to try pharmacological management)
- Home Health Nursing
- Neurologist – referral for nerve conduction studies, electromyography
- Sexual Health Clinic – referral for autonomic symptoms affecting sexual health

**Immunotherapy**
- Immunotherapy Alert Card
- Please refer to protocol specific algorithms to guide management of immune mediated side effects.

**Related Online Resources**
- E.g. Fair Pharmacare; BC Palliative Benefits. Can be found in “Other Sources of Drug Funding Section”

**Bibliography List**
- [http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management](http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management)

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### Appendix A: Chemotherapy Induced Neurotoxicity

(Table adapted from Up-to-date 2018 table: Neurotoxicity Associated with Cytotoxic Chemotherapy Agents)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sensory</th>
<th>Motor</th>
<th>Autonomic</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Platinum Compounds</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin and Oxaliplatin</td>
<td>Distal, symmetric sensory loss</td>
<td>Normal</td>
<td>Rare</td>
<td>May progress for few months once drug discontinued</td>
</tr>
<tr>
<td>(Chronic toxicity)</td>
<td>Painful paresthesias or numbness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboplatin</td>
<td>Similar to Cisplatin but less severe</td>
<td>Normal</td>
<td>Rare</td>
<td>Similar to Cisplatin</td>
</tr>
<tr>
<td>Oxaliplatin</td>
<td>Paresthesias and dysthesias in hands, feet and perioral area; often induced or worsened by cold</td>
<td>Cramps, jaw tightness, and spasms in throat muscles</td>
<td>None</td>
<td>Often resolves within 1 week</td>
</tr>
<tr>
<td>(Acute neurotoxicity)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vinca Alkaloids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vincristine</td>
<td>Distal sensory loss in lower extremities</td>
<td>Less common; distal, symmetric weakness in lower limbs, may progress to foot drop</td>
<td>Constipation common with Vincristine</td>
<td>Often resolves within 3 months; can persist with Vincristine</td>
</tr>
<tr>
<td>Vinblastine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vinorelbine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Taxanes

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sensory Loss</th>
<th>Motor Weakness</th>
<th>Other Symptoms</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel</td>
<td>Mild, distal sensory loss (greater in feet than hands)</td>
<td>Occasional mild weakness in feet</td>
<td>Rare</td>
<td>Often resolves within 3 months; can persist</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>Painful paresthesias</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bortezomib</td>
<td>Mild-mod distal symmetric sensory loss in lower extremities</td>
<td>Occasional mild distal weakness in lower limbs</td>
<td>Occasional, including orthostatic hypotension, diarrhea and constipation</td>
<td>Often resolves within 3 months; can persist</td>
</tr>
<tr>
<td></td>
<td>Painful paresthesia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thalidomide, Pomalidomide, Lenalidomide</td>
<td>Mild-mod distal symmetric sensory loss</td>
<td>Weakness, tremor, muscle cramps, fasciculation's are common</td>
<td>Constipation</td>
<td>Can persist for more than 1 yr</td>
</tr>
<tr>
<td>Brentuximab</td>
<td>Predominantly sensory</td>
<td>Rare</td>
<td>Rare</td>
<td>Often resolves in 3 months after treatment cessation, but may persist</td>
</tr>
<tr>
<td>Anastrozole</td>
<td>Carpal Tunnel Syndrome</td>
<td>Occasional weakness in affected limb</td>
<td>Normal</td>
<td>May persist after treatment cessation</td>
</tr>
</tbody>
</table>

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