## Symptom Management Guidelines: CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY

### Definition(s)

- **Chemotherapy-Induced Peripheral Neuropathy (CIPN):** injury, or degeneration of the peripheral nerve fibers (motor, sensory, autonomic) caused by certain neurotoxic chemotherapy 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.
- **Hypesthesia:** decreased sensitivity to sensory stimuli.

### Contributing Factors

#### Chemotherapy Agents
- High dose, high cumulative doses, or concurrent neurotoxic chemotherapy increases risk.
- Platinum drugs, Vinca Alkaloids, Taxanes, Cytarabine, Interferon, Thalidomide, Bortezomib. 

#### Other
- Peripheral neuropathy from pre-existing co-morbidity may develop into a more severe or persistent CIPN (e.g. alcoholism, Vitamin B deficiency, diabetes, HIV, congenital neuropathy, hypothyroidism, connective tissue diseases, toxic neuropathy, post-herpetic neuralgia).
- Tumor infiltration & compression of spinal nerves.
- Paraneoplastic syndromes (cytokines excreted from tumor cells).
- Radiation therapy involving the spine.
- Surgical trauma.

### Consequences

- **Sensory symptoms:** Dys/paresthesia, hyper/hypoesthesia, hypo/areflexia, pain, diminished vibratory or cutaneous sensations.
- **Motor symptoms:** Weakness, gait and/or balance disturbance, difficulty with fine motor skills, wrist or foot drop.
- **Autonomic symptoms:** Constipation, urinary dysfunction, sexual dysfunction, orthostatic hypotension.
- **Quality of life:** exacerbation of other symptoms (e.g. pain, fatigue).
- **Interference with activities of daily living (ADLs), compromised role function at home & work (may need gradual return to work-)**
- Chemotherapy dose delays, reductions, discontinuation of treatment.
- **Patient safety – risk for falls, tripping, burns, frostbite.**
### Focused Health Assessment

<table>
<thead>
<tr>
<th><strong>GENERAL ASSESSMENT</strong></th>
<th><strong>SYMPTOM ASSESSMENT</strong></th>
<th><strong>PHYSICAL ASSESSMENT</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Contact &amp; General Information</strong></td>
<td><strong>Normal</strong></td>
<td><strong>Vital Signs</strong></td>
</tr>
<tr>
<td>• Physician name – oncologist, family physician</td>
<td>• Do you have any pre-existing peripheral neuropathy?</td>
<td>• Frequency – as clinically indicated</td>
</tr>
<tr>
<td>• Pharmacy</td>
<td><strong>Onset</strong></td>
<td>• Assess patient for orthostatic hypotension and heart rate</td>
</tr>
<tr>
<td>• Home health care</td>
<td><strong>Provoking / Palliating</strong></td>
<td><strong>Observe Patient General Appearance:</strong></td>
</tr>
<tr>
<td>• Other health care providers</td>
<td>• When did the symptoms begin?</td>
<td>• Observe gait as patient walks - note any hesitation, stumbling, unsteadiness, holding onto walls</td>
</tr>
<tr>
<td>• Allergies</td>
<td><strong>Quality (in last 24 hours)</strong></td>
<td>• Observe for any involuntary movements, tremors, spasms, wrist or foot drop</td>
</tr>
<tr>
<td><strong>Consider Contributing Factors</strong></td>
<td>• Can you describe symptoms?</td>
<td>• Observe any difficulty with closing buttons, shaky handwriting, holding objects, keyboard use</td>
</tr>
<tr>
<td>• Cancer diagnosis and treatment(s) – note type and date of last treatment</td>
<td>- <strong>Sensory</strong>: numbness, tingling, pain, or burning</td>
<td></td>
</tr>
<tr>
<td>• Medical history (e.g. diabetes, vitamin B deficiency, alcohol use)</td>
<td>- <strong>Motor</strong>: falls, tripping, muscle weakness, abnormal gait, or paralysis</td>
<td></td>
</tr>
<tr>
<td>• Medication profile</td>
<td>- <strong>Autonomic</strong>: constipation, urinary dysfunction, sexual dysfunction, orthostatic hypotension</td>
<td></td>
</tr>
<tr>
<td>• Recent lab or diagnostic reports</td>
<td>• Are symptom(s) intermittent or constant?</td>
<td></td>
</tr>
<tr>
<td><strong>Quality</strong></td>
<td><strong>Region / Radiation</strong></td>
<td><strong>Observe Patient General Appearance:</strong></td>
</tr>
<tr>
<td>(in last 24 hours)</td>
<td>• Where are you experiencing your symptoms? (e.g. toes, fingers, symmetrical)</td>
<td><strong>Observe Patient General Appearance:</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Severity / Other Symptoms</strong></td>
<td>• Observe gait as patient walks - note any hesitation, stumbling, unsteadiness, holding onto walls</td>
</tr>
<tr>
<td></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>
<td>• Observe for any involuntary movements, tremors, spasms, wrist or foot drop</td>
</tr>
<tr>
<td></td>
<td>• Are there any accompanying symptoms? (e.g. pain)</td>
<td>• Observe any difficulty with closing buttons, shaky handwriting, holding objects, keyboard use</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td><strong>Understanding / Impact on You</strong></td>
<td></td>
</tr>
<tr>
<td>• What medications or other strategies are you using right now? How effective? Side effects?</td>
<td><strong>Value</strong></td>
<td></td>
</tr>
<tr>
<td>• What medications or strategies have been effective in the past?</td>
<td>• 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)?</td>
<td></td>
</tr>
<tr>
<td><strong>Understanding / Impact on You</strong></td>
<td><strong>Value</strong></td>
<td>• What do you believe is causing this problem? What is your comfort goal or acceptable level for this symptom (0 – 10 scale)?</td>
</tr>
<tr>
<td>• 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)?</td>
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</tr>
</tbody>
</table>
**PERIPHERAL NEUROPATHY GRADING SCALE(S)**
Adapted NCI CTCAE (Version 4.03)

<table>
<thead>
<tr>
<th>NORMAL</th>
<th>GRADE 1</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>Normal</td>
<td>Asymptomatic; clinical or diagnostic observations only; intervention not indicated</td>
<td>Moderate symptoms; limiting instrumental ADLs (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>
</tr>
<tr>
<td>Sensory Grade</td>
<td>Normal</td>
<td>Asymptomatic; loss of deep tendon reflexes or paresthesia</td>
<td>Moderate symptoms; limiting instrumental ADLs (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)</td>
</tr>
</tbody>
</table>

**PAIN GRADING SCALE**

| No pain | Mild pain | Moderate pain; limiting instrumental ADL (e.g. preparing meals, shopping, managing money) | Severe pain, limiting self care ADL (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 & follow-up care as required

- **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

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### 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

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthostatic hypotension</td>
<td>• Dangle legs prior to getting up, hold onto secure surfaces when getting up and change positions slowly</td>
</tr>
<tr>
<td>Constipation</td>
<td>• Adequate daily fluid intake &amp; high fibre diet</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>• Adequate daily fluid intake, bladder re-training exercises, empty bladder at same time every day</td>
</tr>
<tr>
<td>Sexual dysfunction</td>
<td>• Consider pharmacological intervention e.g. Viagra</td>
</tr>
</tbody>
</table>

### Non-Pharmacological Management
- Complementary Alternative Medicine (CAM) therapy may be helpful for some individuals
- Relaxation techniques, deep-breathing, meditation, yoga, visual or guided imagery
- Massage, Acupuncture, Transcutaneous electrical nerve stimulation (TENS)

### Pharmacological Management
In collaboration with physician and pharmacist the following may be prescribed:
- Mild to moderate neuropathic pain
  - Acetaminophen, or NSAIDs
  - Anticonvulsants (e.g. gabapentin or pregabalin), or tricyclic antidepressants (e.g. amitriptyline, nortriptyline, imipramine)
  - Topical analgesic agents (e.g. capsaicin, lidocaine cream)

### Patient Education and Follow-Up
- All patients should receive information about:
  - Specific neurotoxic effects that can be expected from their chemotherapy regimen
  - Platinum 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
- Physician follow-up – up in ambulatory care setting may be indicated

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**GRADE 2 – GRADE 3**

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

### Patient Assessment and Care
- Collaborate with physician:
  - 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, 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 or tricyclic antidepressant
  - Opioid (short or long acting)
  - Corticosteroid
  - Methadone
  - Ketamine or Lidocaine/Mexiteline infusion
  - Cannabinoids

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

EMERGENT:
Requires IMMEDIATE medical attention

Patient Care and Assessment
- 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
- Notify physician if on active chemotherapy treatment, will require treatment delays until symptoms resolve or discontinuation. Refer to specific chemotherapy protocols for direction: http://www.bccancer.bc.ca/health-professionals/professional-resources/chemotherapy-protocols
- Monitor vital signs and assess for other complications – Spinal cord compression alert guidelines

RESOURCES & REFERRALS

Possible Referrals
- Patient Support Centre or 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

Related Online Resources
- E.g. Fair Pharmacare; BC Palliative Benefits. Can be found in “Other Sources of Drug Funding Section” http://www.bccancer.bc.ca/health-professionals/professional-resources/pharmacy/financial-support-benefit-lists

Bibliography List
- http://www.bccancer.bc.ca/health-professionals/professional-resources/nursing/symptom-management
# Appendix A: Chemotherapy Induced Neurotoxicity

(Table adapted from Up-to-date 2013 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>
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<td></td>
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<tr>
<td>Cisplatin</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></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 dyesthesias 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><strong>Acute neurotoxicity</strong></td>
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<tr>
<td><strong>Vinca Alkaloids</strong></td>
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<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>
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<tr>
<td>Vinblastine</td>
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<tr>
<td>Vinorelbine</td>
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<tr>
<td><strong>Taxanes</strong></td>
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<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><strong>Other</strong></td>
<td></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 paresthesias</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thalidomide</td>
<td>Mild-mod distal symmetric sensory loss</td>
<td>Weakness, tremor, muscle cramps</td>
<td>Constipation</td>
<td>Can persist for more than 1 yr</td>
</tr>
</tbody>
</table>

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