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.

Hyperesthesia: increased sensitivity to sensory stimuli.

Hypoesthesia: decreased sensitivity to sensory stimuli.

Constituting Factors

Chemotherapy Agents

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

Appendix A: Chemotherapy Induced Neurotoxicity below

Other

- Immunotherapy – checkpoint inhibitors.
- 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.
<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></td>
<td><strong>Vital Signs</strong></td>
</tr>
<tr>
<td>- Physician name – oncologist, family physician</td>
<td>Normal</td>
<td>Frequency – as clinically indicated</td>
</tr>
<tr>
<td>- Pharmacy</td>
<td></td>
<td>- Assess patient for orthostatic hypotension and heart rate</td>
</tr>
<tr>
<td>- Home health care</td>
<td></td>
<td><strong>Observe Patient General Appearance:</strong></td>
</tr>
<tr>
<td>- Other health care providers</td>
<td></td>
<td>- Observe gait as patient walks – note any hesitation, stumbling, unsteadiness, holding onto walls</td>
</tr>
<tr>
<td>- Allergies</td>
<td><strong>Onset</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><strong>Provoking / Palliatiing</strong></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></td>
<td><strong>Quality (in last 24 hours)</strong></td>
</tr>
<tr>
<td>- Medical history (e.g. diabetes, vitamin B deficiency, alcohol use)</td>
<td><strong>Can you describe symptoms?</strong></td>
<td></td>
</tr>
<tr>
<td>- Medication profile</td>
<td>- <strong>Sensory:</strong> numbness, tingling, pain, or burning</td>
<td><strong>Where are you experiencing your symptoms?</strong> (e.g. toes, fingers, symmetrical)</td>
</tr>
<tr>
<td>- Recent lab or diagnostic reports</td>
<td>- <strong>Motor:</strong> falls, tripping, muscle weakness, abnormal gait, or paralysis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- <strong>Autonomic:</strong> constipation, urinary dysfunction, sexual dysfunction, orthostatic hypotension</td>
<td><strong>How bothersome is this symptom to you?</strong> (on a scale of 0 – 10, with 0 not at all and 10 being the worst imaginable)</td>
</tr>
<tr>
<td></td>
<td>- Are symptom(s) intermittent or constant?</td>
<td><strong>Are there any accompanying symptoms?</strong> (e.g. pain)</td>
</tr>
<tr>
<td></td>
<td><strong>Region / Radiation</strong></td>
<td><strong>Treatment</strong></td>
</tr>
<tr>
<td></td>
<td>- Where are you experiencing your symptoms? (e.g. toes, fingers, symmetrical)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Severity / Other Symptoms</strong></td>
<td></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></td>
</tr>
<tr>
<td></td>
<td>- Are there any accompanying symptoms? (e.g. pain)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Treatment</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- What medications or other strategies are you using right now? How effective? Side effects?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- What medications or strategies have been effective in the past?</td>
<td><strong>What is your comfort goal or acceptable level for this symptom (0 – 10 scale)?</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Understanding / Impact on You</strong></td>
<td></td>
</tr>
<tr>
<td></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>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**PERIPHERAL NEUROPATHY GRADING SCALE(S)**
NCI Common Terminology Criteria for Adverse Events (Version 4.03)

<table>
<thead>
<tr>
<th>GRADE 1 (Mild)</th>
<th>GRADE 2 (Moderate)</th>
<th>GRADE 3 (Severe)</th>
<th>GRADE 4 (Life - threatening)</th>
<th>GRADE 5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Motor Grade</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<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>
<td>Life – threatening, consequences; urgent intervention indicated</td>
<td>Death</td>
</tr>
<tr>
<td><strong>Sensory Grade</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<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>
<td>Life – threatening, consequences; urgent intervention indicated</td>
<td>Death</td>
</tr>
</tbody>
</table>

**PAIN GRADING SCALE**

<table>
<thead>
<tr>
<th>GRADE 1 (Mild)</th>
<th>GRADE 2 (Moderate)</th>
<th>GRADE 3 (Severe)</th>
<th>GRADE 4 (Life - threatening)</th>
<th>GRADE 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild pain</td>
<td>Moderate pain; limiting instrumental ADL (e.g. preparing meals, shopping, managing money)</td>
<td>Severe pain, limiting self- care ADL (e.g. bathing, dressing, feeding self, using the toilet, taking medications)</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

*A semi-colon indicates ‘or’ within the description of the grade and a single dash (-) indicates a grade is not available*

**Step-Up Approach to Symptom Management:**
Interventions Should Be Based On Current Grade Level and Include Lower Level Grade Interventions As Appropriate

**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

The information contained in these documents is a statement of consensus of BC Cancer Agency 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 judgment in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is at your own risk and is subject to BC Cancer Agency’s terms of use, available at www.bccancer.bc.ca/legal.htm.
### 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**
- 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
- 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 in ambulatory care setting may be indicated

---

**GRADE 2 – GRADE 3**

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

### Patient Assessment and Care
- 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, folate level
  - If on active chemotherapy treatment, may require treatment delays or reductions until

---

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symptoms resolve. Refer to specific chemotherapy protocols for direction:
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 (Refer to protocol specific algorithm if patient is on Immunotherapy
  - Methadone
  - Ketamine or Lidocaine/Mexiletine infusion
  - Cannabinoids

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
- If patient on Immunotherapy, remind patient to present 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:
  http://www.bccancer.bc.ca/health-professionals/professional-resources/chemotherapy-protocols
- Monitor vital signs and assess for other complications (available to internal BCCA staff)
  Spinal cord compression alert guidelines

RESOURCES & REFERALS

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

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"
  http://www.bccancer.bc.ca/health-professionals/professional-resources/pharmacy/drug-funding

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>Platinum Compounds</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Medication</th>
<th>Description</th>
<th>Severity/Onset</th>
<th>Common Symptoms</th>
<th>Outcome/Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>Distal, symmetric sensory loss; Painful paresthesias or numbness</td>
<td>Normal; Rare</td>
<td>May progress for few months once drug discontinued</td>
<td></td>
</tr>
<tr>
<td>Carboplatin</td>
<td>Similar to Cisplatin but less severe</td>
<td>Normal; Rare</td>
<td>Similar to Cisplatin</td>
<td></td>
</tr>
<tr>
<td>Oxaliplatin</td>
<td>Paresthesias and dysesthesias in hands, feet, and perioral area; often induced or worsened by cold</td>
<td>Cramps, jaw tightness, and spasms in throat muscles; None</td>
<td>Often resolves within 1 week</td>
<td></td>
</tr>
<tr>
<td>Acute neurotoxicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vinca Alkaloids</td>
<td>Vincristine; Vinblastine; Vinorelbine</td>
<td>Distal sensory loss in lower extremities; Less common; distal, symmetric weakness in lower limbs, may progress to foot drop; Constipation common with Vincristine; Orthostatic hypotension less common</td>
<td>Often resolves within 3 months; can persist with Vincristine</td>
<td></td>
</tr>
<tr>
<td>Taxanes</td>
<td>Paclitaxel; Docetaxel</td>
<td>Mild, distal sensory loss (greater in feet than hands); Occasional mild weakness in feet; Rare</td>
<td>Often resolves within 3 months; can persist</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Bortezomib</td>
<td>Mild-mod distal symmetric sensory loss in lower extremities; Occasional mild distal weakness in lower limbs; Occasional, including orthostatic hypotension, diarrhea and constipation</td>
<td>Often resolves within 3 months; can persist</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Thalidomide</td>
<td>Mild-mod distal symmetric sensory loss; Weakness, tremor, muscle cramps; Constipation</td>
<td>Can persist for more than 1 yr</td>
<td></td>
</tr>
</tbody>
</table>

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