

## Chemotherapy-induced Peripheral Neuropathy Fact Sheet

### What is chemotherapy-induced peripheral neuropathy?

Chemotherapy-induced peripheral neuropathy (CIPN) describes the damage to the peripheral nervous system incurred by a patient who has received a chemotherapeutic agent that is known to be neurotoxic. Table 1 describes symptoms caused by drugs in three commonly used classes of neurotoxic chemotherapy agents. While each class of agents has its own mechanism of action, the CIPN that develops is thought to be a length dependent neuropathy that affects distal sites first, and as cumulative doses increase symptoms progress in severity and to more proximal areas. Sensory symptoms and signs typically develop before motor symptoms and a subset of patients will develop painful CIPN<sup>1, 2</sup>. Patients with pre-existing peripheral neuropathy may develop a more severe and persistent CIPN<sup>3</sup>.

Table 1. Commonly used chemotherapy agents associated with peripheral neuropathy

	Incidence of Peripheral Neuropathy	Sensory Symptoms	Motor Symptoms	Other common side-effects
TAXANE CLASS: Paclitaxel (Taxol®) Docetaxel (Taxotere®) Abraxane™	60% <sup>4</sup> 50% <sup>5</sup> 71% <sup>6</sup>	Mild to moderate numbness, tingling, burning/stabbing pain of hands and feet are common which can become severe with increased doses <sup>4-6</sup> Reduced or absent achilles tendon reflex <sup>3</sup>	Weakness of distal muscles has been documented with high cumulative doses of paclitaxel and docetaxel <sup>4, 5</sup>	Neutropenia, anemia, myalgia/arthralgia, nausea, alopecia <sup>4-6</sup>
VINCA ALKALOID CLASS: Vincristine (Onkovin®) Vinorelbine (Navelbine®)	Not listed 25% <sup>7</sup>	Mild to moderate numbness, tingling, burning/stabbing pain of hands and feet are common and can become severe with increased doses <sup>7, 8</sup> Reduced or absent Achilles tendon reflex <sup>3</sup>	Weakness of distal muscles, decreased deep tendon reflexes, and foot drop have been noted with high doses <sup>7, 8</sup>	Granulocytopenia, leukycytopenia, anemia, fatigue, nausea, alopecia <sup>7, 8</sup>
PLATINUM COMPOUNDS: Cisplatin (Platinol®) Carboplatin (Paraplatin®) Oxaliplatin (Eloxatin®)	Not listed 4% <sup>9</sup> 74% <sup>10</sup>	Mild to moderate numbness and tingling of hands and feet can occur after prolonged (4-6 months) of therapy and may develop 3-8 weeks after last dose. <sup>11</sup> Symptoms can become severe with high cumulative doses <sup>11</sup> Reduced or absent Achilles tendon reflex <sup>12</sup>	Weakness is rare but can occur with high doses of Cisplatin and Oxaliplatin <sup>10, 11</sup>	Ototoxicity <sup>10, 11</sup> , vestibular toxicity <sup>11</sup> , anemia, neutropenia, leukocytopenia, thrombocytopenia, nausea <sup>10, 11</sup>

### How should I assess CIPN?

Several measures which quantify the severity of CIPN are described below. In addition, measures of pain, postural control (balance), hand dexterity, and quality of life are useful to document impairments (Body Structure/Function Problems) and changes in functional mobility/disability (Activities/Participation Problems) during treatment.

### MEASURES TO QUANTIFY SEVERITY OF CIPN

#### TOTAL NEUROPATHY SCORE (TNS) (0-32 points)<sup>3</sup>

- A composite score combining subjective sensory symptoms, subjective report of symptoms and amount of difficulty with daily activities, deep tendon reflexes, manual muscle testing of distal muscles, pin sensibility, quantitative vibration thresholds, and nerve conduction studies of sural and peroneal nerves.
- Reliability: Interrater=0.966, Intrarater=0.986<sup>13</sup>; Criterion Validity: Correlates with diabetic neuropathy gold standard measures (r=0.71 to 0.89)<sup>13</sup>
- A modified version of the TNS (mTNS) which excludes nerve conduction testing may be a useful clinical assessment of CIPN<sup>14, 15</sup>

### SEMMES WEINSTEIN MONOFILAMENTS (SWM)

- A method to establish light touch thresholds on the pad of the great toe and the pad of the index finger. More proximal test sites could be beneficial if the neuropathy is more severe. A full set of 20 SWM will provide the tester with a means to test small changes in touch thresholds.
- Reliability: No significant test retest error using t-test analysis<sup>16</sup>; Predictive Validity: Sensitivity=1.0, specificity=0.40<sup>17</sup>

### TUNING FORK

- 128-HZ tuning fork is struck and then held to the skin. The examiner times how long the vibration is perceived.
- Less than 10 seconds is considered impaired

### BIOTHESIOMETER® (Bio-Medical Instrument Company, Newbury, OH)

- A machine that has a hand held device that vibrates at a constant frequency (120Hz) and allows the tester to adjust the amplitude of the vibration. The amplitude of vibration is quantified by the change in the voltage of the machine as the tester turns the dial of the Biothesiometer. Allows the tester to establish a quantitative vibration threshold.
- Normative data for the pad of the great toe, pad of the thumb, and medial malleolus by age group has been established by Bloom et al.<sup>18</sup>
- Reliability: No significant test retest error using t-test analysis<sup>18</sup>; Discriminative validity<sup>19</sup>

### MEASURES TO QUANTIFY PAINFUL CIPN

#### PAIN QUALITY ASSESSMENT SCALE (0-200 points)<sup>20</sup>

- A 20-item questionnaire developed to quantify the quality and intensity of neuropathic pain.
- Reliability: No published information, Discriminative and predictive validity<sup>20</sup>

### MEASURES TO QUANTIFY BALANCE IMPAIRMENTS

#### FULLERTON ADVANCED BALANCE SCALE (0-40 points)<sup>21</sup>

- A battery of 10-tasks which challenge the visual, vestibular, and somatosensory system.
- Reliability: Interrater=0.99, Intrarater=0.99; Criterion validity compared to Berg Balance Score (r=0.75) (Rose, D, personal communication, 2004)

#### NEUROCOM® SENSORY ORGANIZATION TEST (SOT) (0-100 points)

- Patients' ability to maintain upright posture is tested using 6 conditions that alter or remove normal visual, somatosensory, and vestibular information. Particularly useful as the platinum class of chemotherapy agents affect both the peripheral nervous system and the vestibular system.
- Total SOT equilibrium scores are correlated to severity of CIPN (r=-0.638, p=0.002)<sup>15</sup>
- Reliability: ICC=0.66 in healthy adults over 65<sup>22</sup>
- The Clinical Test for Sensory Interaction on Balance (CTSIB) is an alternative to the SOT if you do not have access to a NeuroCom system

#### SINGLE LEG STANCE TIME

- Impaired in patients with diabetic PN and associated with an increased risk for falling
- Quick and simple to perform making it a useful screening measure

### MEASURES TO QUANTIFY HAND DEXTERITY

#### GROOVED PEG BOARD TEST

- A timed test of a patient's ability to place pegs into a slotted board.
- Discriminative validity: impaired in patients with painful CIPN<sup>24</sup>
- High test-retest reliability

### MEASURES TO QUANTIFY QUALITY OF LIFE

#### FUNCTIONAL ASSESSMENT OF CANCER THERAPY-TAXANE (FACT-TAXANE, 0-172 points)<sup>25</sup>

- A 43-item health related quality of life questionnaire that combines the previously validated FACT-general (27-items) with a taxane subscale (16-items). There are 4 constructs addressed in the FACT-general: emotional well-being, functional well-being, physical well-being, and social/family well-being. The taxane subscale combines the previously validated 11-item neurotoxicity subscale with 5-questions that are specific for side-effects associated with taxane chemotherapy. The taxane subscale questions quantify how difficult functional tasks have become and how bothersome symptoms are to the patient.

However, the taxane subscale scale is not designed to determine physical performance status, as mean taxane subscale scores were no different between patients with Karnofsky performance scores of 70-80 and 90-100<sup>25</sup>.

- Reliability: Taxane subscale: Cronbach  $\alpha$ =0.84-0.88; Neurotoxicity subscale: Cronbach  $\alpha$ = 0.82-0.86<sup>25</sup>
- Responsive to change: significant overall linear time effects were found for all scales of the FACT-taxane (scores worsened over time with increased cumulative chemotherapy dose). The largest magnitude of change was observed for the taxane and neurotoxicity subscales.<sup>25</sup>

### **How do I treat patients with CIPN?**

*The following are suggestions for treatment of CIPN. There have been few physical therapy intervention studies that have addressed this specific population; however, there are several case studies, and several studies of patients with diabetic peripheral neuropathy that may help guide the treatment of patients with CIPN.*

### **Addressing Impairments (Body Structure/Function Problems):**

Patients with CIPN need to be educated in strategies to increase their safety with daily activities, as they may have decreased touch thresholds which put them at risk for tissue injury. Interestingly, temperature detection thresholds do not appear to be impaired in patients with taxane-induced PN<sup>24</sup>. Some patients with CIPN will develop neuropathic pain which in severe cases is unrelenting and debilitating<sup>26</sup>. Monochromatic infrared photo energy (MIRE) therapy may decrease neuropathic pain, improve touch thresholds, and improve balance<sup>27-31</sup>. In addition, working with the medical team to manage neuropathic pain may improve function and quality of life<sup>26</sup>.

### **Addressing Functional Mobility/Disability Problems (Activities/Participation Problems):**

Patients who present with CIPN may also present with functional mobility problems such as decreased hand dexterity, decreased postural control (balance), and impaired gait<sup>24, 26</sup>. Unfortunately, there is limited research examining the efficacy of physical therapy treatment for patients with CIPN. Sensory retraining and task specific training may improve hand function. Exercise interventions targeting strength and balance have been shown to be beneficial for patients with diabetic peripheral neuropathy, who have similar symptoms as patients with CIPN<sup>32</sup>. Exercises that challenge the visual, somatosensory, and vestibular systems may also be important components to balance retraining programs<sup>26</sup>.

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**For more information about the Oncology Section, visit [www.oncologypt.org](http://www.oncologypt.org).**

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