What is chemotherapy induced peripheral neuropathy (CIPN)?
Chemotherapy induced peripheral neuropathy (CIPN): The presence of tingling, burning, itching and unpleasant sensations due to nerve damage by chemotherapy. Peripheral nerves are nerves outside the brain and spinal column. The pain is limited to the nerves of fingers and hands, and feet and toes.

What are the symptoms of CIPN?
The symptoms appear first in the body parts farthest from the trunk-the toes and soles of the feet, and then the fingers and hands. The symptoms occur in both right and left sides of the body equally and progress in a “glove and stocking” pattern-that is the symptoms ascend up the legs and arms. The symptoms depend on the types of nerves that are damaged.

Sensory nerves are the ones usually affected and may cause the following:
- Pain
- Numbness
- Burning
- Tingling
- Sharp, shooting, electrical pain
- Exaggerated pain response to something that would not normally cause pain such as stroking

Motor nerves may cause the following:
- Weakness
- Difficulty with walking or balance
- Difficulty with fine motor skills: writing, buttoning buttons, tying shoe laces
- Muscle cramps

Autonomic nerves may cause the following:
- Constipation/Diarrhea
- Urinary retention/incontinence
- Sexual dysfunction
- Blood pressure alterations (either high blood pressure or low)

How do I manage with CIPN?
If you have sensory loss you need to depend more on using visual clues. Try the following suggestions;
- Make sure areas are well lit. Turn on lights before entering a room
- Ensure that stairwells are well lit.
- Keep pathways and stairwells clear of clutter
- Remove extension cords that may pose a problem
- Remove small area rugs, or ensure that they are well secured by tacking or taping them down
- Keep a night light in your room and along the path you walk during the night and the route to your bathroom.
- Keep a flashlight within reach, use a key chain with a flashlight to see key holes
- Check your feet and hands every day for signs of injury, cuts, and bruises. Apply a triple anti-biotic ointment to any open area and cover with a band-aid. Keep covered for at least 3 days.
- Inspect shoes to make sure they contain no hidden objects, little pebbles, stones that might cause problems
- Wear shoes with closed toes, and a snug fit. You can slip out of shoes or slippers if they do not come over your instep and do not have a back.
- Always wear shoes or slippers to protect your feet from injury
- Do not use hot water bottles or heating pads, consider a non-breakable thermometer to check for bath water temperature.
- Consider installing grab bars in your shower or tub.
- Wear rubber gloves when washing dishes, especially cutlery.
- In the kitchen use heavy duty pot holders and mitts when using the oven
- Wear gloves and socks in cold weather

If you have motor loss the following items may be purchased to assist you

- Button hook to help with buttons
- Zipper pulls
- Sock aids
- Elastic shoe laces
- Shoes with Velcro closures
- Special pens and pencils and utensils to hold objects more easily

If you have autonomic nervous system loss

- Dangle your legs and take deep breaths prior to arising and standing up
- Consume a high-fiber diet and adequate fluid intake for constipation

What interventions are used to prevent or reduce the effects of CIPN?

**PHARMACOLOGICAL INTERVENTIONS**

**Alpha-Lipoic Acid** - No studies have been done using alpha-lipoic acid in the oncology population, but there is evidence of the benefits of alpha lipoic acid in patients with diabetic neuropathy. In a group of 1254 patients with diabetic neuropathy treated for three weeks with alpha lipoic acid there was significant clinical improvement. (Ziegler et al., 2004) Alpha-lipoic acid is a powerful antioxidant which occurs naturally, in small amounts, in such foods as spinach, broccoli, beef, yeast, kidney, and heart. It is also available as a supplement, but those who want to purchase alpha-lipoic acid supplements have to make sure that what they get is Stabilized R Alpha Lipoic Acid

**Glutamine** – Results of two non-randomized, non-placebo- controlled studies indicate that CIPN may be reduced by the administration of glutamine with Taxanes. (Taxol and Taxotere) (Vadhat et al., 2001; Stubblefield et al., 2005)

**Vitamin E** - Vitamin E is an anti-oxidant that protects against cellular oxidative damage and reduces numbness, tingling, burning and pain. There are three studies that examined the protective effect of Vitamin E on the development of CIPN following chemotherapy. One study used 300 mg per day and another study 600 mg per day during chemotherapy and
for 3 months following the completion of therapy. Both studies reported the incidence of CIPN to be lower than in a control group that did not receive Vitamin E. (Argyriou et al., 2005; Pace et al., 2003) A third study examined the blood levels of Vitamin E in two groups of patients and found that the group of patients with lower blood levels of Vitamin E developed CIPN (Bove, 2001)

**Neurontin gabapentin** and **Lyrica**: A range of drugs that act on the central nervous system such as drugs originally intended as antidepressants and antiepileptic drugs have been found to be useful in managing neuropathic pain. Commonly used treatments include using a tricyclic antidepressants such as amitriptyline. One study showed relief with amitriptyline in patients with taxane induced neuropathic pain (Seidman et al., 1998). Antiepileptic therapies such as gabapentin (**Neurontin**) or sodium valproate also are promising in reducing CIPN pain (Gilron et al., 2005). These have the advantage that besides being effective in many cases they are relatively low cost. Gabapentin is available as a generic drug. Pregabalin is marketed by Pfizer under the trade name **Lyrica**.

**NON-PHARMACOLOGIC INTERVENTION**

**Acupuncture** - There are 5 studies examining acupuncture with peripheral neuropathy- but only one with CIPN. In the CIPN study once weekly acupuncture for six weeks followed by four weeks of rest and then another six week course of acupuncture the patients reported an increase in sensation, gait and balance. There was a report of decreased pain, numbness and tingling that occurred with the first treatment. (Wong & Sagar, 2006) In a study of 90 diabetic patients there was improved peripheral nerve function in the acupuncture group compared with the Western medicine group (Jiang et al., 2006).

**Capsaicin ointment** - There are no studies of capsaicin ointment in the treatment of CIPN. However, there is a study in patients with symmetrical diabetic neuropathy. In a double blind study one foot was treated with a placebo and one foot with capsaicin ointment. A significant decrease in numbness and tingling was found in the capsaicin treated feet. (Forst 2002).

**PHYSICAL THERAPY**

**Exercise** - An analysis of studies evaluating exercise for peripheral neuropathy (none in patients with CIPN) demonstrated that exercise improved functional ability. Progressive resistive exercises, aerobic exercise and stretching exercise in the treatment of diabetic neuropathy found significant improvement in stance, functional reach, and ankle motor nerve conduction. Exercise programs are effective in reversing muscle loss related to peripheral neuropathy. Your TurningPoint therapist can help you establish a personalized exercise program. (Richardson, 2001; Balducci, 2006; White, 2004)

**Anodyne Therapy/ Pulsed infrared therapy**. Pulsed infrared has not been studied in the CIPN population. Pulsed infrared light is delivered to the foot in an effort to improve foot circulation by stimulating nitric acid production. Three studies have been done on patients with diabetic neuropathy. Significant improvement in sensation and decreased pain were found. (Arnall et al., 2006)

**Transcutaneous Nerve Stimulation/TENS** – These therapies have not been investigated in the oncology population, but studies in the diabetic population with peripheral neuropathy demonstrate benefit. One study (Forst ,2004) demonstrated improvement in numbness, sharp shooting pains, and tingling, but no change in vibration.

**High Frequency electrical stimulation** – One study found that high frequency electrical stimulation was more effective than TENS in improving pain and peripheral neuropathy symptoms. (Reichstein, 2005).
**GLOSSARY:**

**After Sensation:** Abnormal persistence of sensory perception provoked by a stimulus even though the stimulus has ceased.

**Allodynia:** The condition in which ordinarily painless stimulus, once perceived is experienced as painful. *Mechanical allodynia* refers to abnormal perception of pain from usually non-painful mechanical stimulation. Pain may be caused by clothing, bedding. *Static allodynia* is pain upon application of light pressure, *dynamic allodynia* occurs by moving the stimulus. *Thermal allodynia* refers to the abnormal sensation of pain from usually non-painful thermal stimulation such as cold or warmth. Pain worsens when the painful region is exposed to a warm or cold external environment.

**Anesthesia:** The complete loss of sensation

**Dysesthesia:** An abnormal and unpleasant sensation such as a sense of burning, stabbing, numbness, prickling, stinging, tingling brought on by touching.

**Hyperalgesia:** Exaggerated pain response from a usually painful stimulus. Can be mechanical or thermal. Summation and after sensation are usually present.

**Hyper/hypohidrosis:** Sweating greater than or less than would be expected considering the temperature and environment.

**Lhermitte’s sign:** Pain resembling a sudden electric shock throughout the body produced by flexing the neck

**Paresthesia:** Abnormal, but not necessarily unpleasant sensation resulting from injury to one or more nerves described as numbness, prickling, stinging, burning.

**Romberg’s sign:** Inability to maintain body balance when eyes are closed and feet are together. Sign is positive if patient sways and loses balance.

**Summation:** Abnormally increasing painful sensation to a repeated stimulus although the actual stimulus remains constant. The patient describes the pain as growing and growing.