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Managing Peripheral Neuropathy



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Chemotherapy-Induced Peripheral Neuropathy defined:

- ❖ "The end result of peripheral, motor, sensory and autonomic neuron damage secondary to neurotoxic chemotherapy agents that inactivate the components required to maintain the metabolic needs of the axon."
- ❖ Sensory
- ❖ Dose-related
- ❖ Cumulative
- ❖ Can be delayed appearing weeks to months after start of therapy

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Drugs commonly associated with PN:

- ✓ Taxanes
- ✓ Platinum-based drugs
- ✓ Vinca Alkaloids
- ✓ Thalidomide
- ✓ Bortezomib

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Symptoms of Chemotherapy-Induced PN

Sensory

- ✓ Paresthesia
- ✓ Hyper- or Hypoesthesia
- ✓ Dysesthesia
- ✓ Pain
- ✓ Numbness and tingling
- ✓ Electrical sensation
- ✓ Hyporeflexia
- ✓ Diminished or absent proprioception
- ✓ Diminished or absent vibratory sensation
- ✓ Diminished or absent cutaneous sensation
- ✓ Diminished or absent sense of sharp / dull

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Symptoms of Chemotherapy-Induced PN

Motor

- ✓ Weakness
- ✓ Gait disturbance
- ✓ Balance disturbance
- ✓ Difficulty with fine motor skills

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Symptoms of Chemotherapy-Induced PN

Autonomic symptoms

- ✓ Constipation
- ✓ Urinary retention
- ✓ Sexual dysfunction
- ✓ Blood pressure alterations

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Symptoms of Chemotherapy-Induced PN

- ❖ Can vary in onset, severity and length
- ❖ Patients describe PN as:
 - ❖ burning
 - ❖ tingling
 - ❖ electric shock sensation
 - ❖ painful numbness
 - ❖ pain during walking

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Risk Factors for Chemotherapy-Induced PN

- ❖ Prior chemotherapy
- ❖ Older age
- ❖ Female gender
- ❖ Comorbid conditions
 - ❖ Diabetes (diabetic neuropathy)
 - ❖ HIV
 - ❖ Alcoholism
 - ❖ Vitamin B deficiency

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Loss of Proprioception

Inability to coordinate the unconscious perception of movement and spatial orientation within the body

- ❖ Patients are at a greater risk for falls
- ❖ May affect ability to drive safely

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Preventative Interventions

- ❖ Amifostine (found to be ineffective)
- ❖ Vitamin E (effective w/ Cisplatin & Paclitaxel)
- ❖ Calcium & Magnesium (effective w/ Oxaliplatin)
- ❖ Carbamazepine (may be effective w/ Oxaliplatin)
- ❖ Glutamine (effective w/ Paclitaxel)
- ❖ Glutathione (may be effective w/ Cisplatin)

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Treatment of Chemotherapy-Induced PN

- ❖ Gabapentin (may lower pain)
- ❖ Nortriptyline (may be effective in decreasing pain, neuropathy)
- ❖ Acetyl L-Carnitine (improvements in sensory & motor neuropathy)
- ❖ Acupuncture (improve sensation and gait)
- ❖ Physical activity / exercise (improvement in stance, functional reach and motor nerve conduction velocity)
- ❖ TENS (helpful in patients with diabetic neuropathy)
- ❖ Capsaicin ointment (used in patients with diabetic neuropathy showing decreases in hypoesthesia)
- ❖ Pregabalin (used in patients with diabetic neuropathy)

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Neurotoxicity Assessment

- ❖ Use of a standardized assessment tool
 - ❖ baseline measurements
 - ❖ ongoing with each treatment
 - ❖ track progress
 - ❖ consider changing drugs within class if appropriate
 - ❖ consider dose reduction if appropriate

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NEUROTOXICITY ASSESSMENT TOOL

Patient Name: _____ Visit Date: _____
 Instructions for Patients?

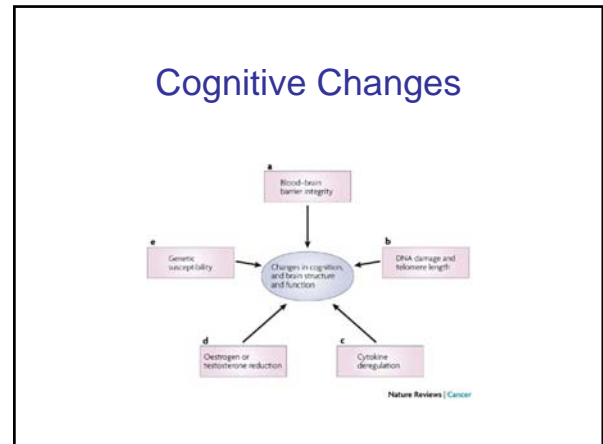
Item	None at all	A little bit	Somewhat	Quite a bit	Very much
1. Have numbness or tingling in my hands	0	1	2	3	4
2. Have numbness or tingling in my feet	0	1	2	3	4
3. Have weakness in my hands	0	1	2	3	4
4. Have weakness in my feet	0	1	2	3	4
5. Have pain in my hands	0	1	2	3	4
6. Have pain in my feet	0	1	2	3	4
7. Have trouble walking	0	1	2	3	4
8. Have trouble climbing stairs	0	1	2	3	4
9. Have trouble holding the weight of small objects which I use in my hand	0	1	2	3	4
10. Have trouble writing	0	1	2	3	4

Instructions for Health Care Professionals
 This assessment tool is designed to help you evaluate patient neurotoxicity, a potential adverse effect of chemotherapy. It is not intended to replace the clinical judgment of the physician. The physician should be consulted for any questions regarding the use of this assessment tool.

NIH Common Toxicity Criteria for Peripheral Neuropathy and Neurotoxicity (Pain)
 Peripheral Neuropathy (NDS/ETS Grade)
 1. None
 2. Loss of deep tendon reflexes or sensation or painless numbness but not interfering with function
 3. Clinical sensory loss or painless numbness interfering with function. Not interfering with function
 4. Sensory loss or painless numbness interfering with ADLs
 5. Painless sensory loss interfering with function

Neurotoxicity (NDS/ETS Grade)
 1. None
 2. Paresthesia or numbness interfering with function
 3. Paresthesia or numbness interfering with function, but not interfering with function
 4. Paresthesia or numbness interfering with function, but not interfering with function

Example from Millennium Pharmaceuticals



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Cognitive Changes

- ❖ "Chemo Brain" patients describe as:
 - ❖ mental fog
 - ❖ mental cloudiness
 - ❖ experience before, during and after treatment
 - ❖ taking longer to finish tasks
 - ❖ trouble remembering common words
 - ❖ trouble multi-tasking
 - ❖ trouble concentrating
 - ❖ forgetful

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Causes of Cognitive Changes

chemotherapy drugs can cause changes

- ❖ Reduction in size of parts of the brain relating to
 - ❖ memory
 - ❖ planning
 - ❖ putting thoughts into action
 - ❖ behavior
 - ❖ inhibition

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Causes

- ❖ Cancer itself
- ❖ Chemotherapy
- ❖ Other drugs
- ❖ Patient age
- ❖ Stress
- ❖ Anemia
- ❖ Sleep problems
- ❖ Infection
- ❖ Depression
- ❖ Fatigue
- ❖ Hormonal changes
- ❖ Anxiety

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How to manage

- ❖ Use a daily planner
- ❖ Exercise your brain
- ❖ Get enough sleep
- ❖ Exercise your body
- ❖ Eat more vegetables
- ❖ Set up and follow routines
- ❖ Minimize multi-tasking (one task at a time)
- ❖ Keep a diary (track memory deficits)

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Altered Brain Function After Chemotherapy

A study by HS Silverman et al. Neurology Reviews, Vol.14 No.11, 2006

- ❖ "Our study demonstrates for the first time that patients suffering from these cognitive symptoms have specific alterations in brain metabolism."
- ❖ Neuropsychologic testing and PET used to examine brain function in 16 women who had adjuvant chemotherapy for breast cancer
- ❖ Patients who had received chemotherapy had a decrease in their resting metabolism in the inferior frontal gyrus.
 - ❖ these patients had to "ramp up" activity more than the control subjects to recall the same information.
- ❖ Study noted that "chemo brain" is well known among cancer survivors but seldom discussed with oncologists in advance of treatment.

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Altered Brain Function After Chemotherapy

A study by HS Silverman et al. Neurology Reviews, Vol.14 No.11, 2006

Recommendations from study:

- ❖ Reassure the patient that memory or cognitive problems are a common side effect
- ❖ Obtain PET scans to determine whether metabolic changes have occurred.
 - ❖ differentiate from those patients that may also have early Alzheimer's or other neurologic problems

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Case Study: Anne

Adjuvant Breast Cancer

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HPI

- ❖ **2005:**
 - ❖ Prophylactic left breast mastectomy for benign breast parachym
 - ❖ Breast conservation surgery May 2005 for a 1.1 cm infiltrating ductal carcinoma grade 3 of 3 with lymphovascular invasion
 - ❖ 0/5 lymph nodes positive
 - ❖ ER+ / PR+ / HER2 3+
 - ❖ Post-op Adjuvant chemotherapy
 - ❖ dose-dense Doxorubicin / Cyclophosphamide (dd AC x 4)
 - ❖ followed by dose-dense Paclitaxel x 4
 - ❖ * Patient deferred Herceptin
 - ❖ Arimidex started post-chemotherapy but discontinued due to intolerance
 - ❖ Femara started then discontinued due to intolerance
 - ❖ Patient refused Tamoxifen

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Review of Treatments / Side effects

Doxorubicin / Cyclophosphamide (dose-dense)

- ❖ persistent nausea by cycle 4/4

Taxol (dose-dense)

- ❖ significant myalgia/arthralgia x 3-4 days after 1st cycle
- ❖ Intermittent left upper quadrant abdominal pain
 - ❖ transitory
 - ❖ may be related to bowel movements

Radiation

- ❖ significant fatigue
- ❖ skin reaction

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Review of Treatments / Side effects

S/P chemotherapy – 2006

Arimidex

- ❖ significant arthralgia leading to D/C
- ❖ switch to Femara (Letrozole) but was intolerant as well
- ❖ Patient refused Tamoxifen

- ❖ Persistent neuropathy secondary to Taxol
 - ❖ anesthesia: persistent decrease to sensation in hands & feet
- ❖ dysesthesia of feet
 - ❖ Neurontin (Gabapentin) started
- ❖ depression / anxiety
 - ❖ Prozac started

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2007

- ❖ Dizziness / "Spaciness"
 - ❖ patient stops Prozac & Neurontin
 - ❖ may be attributable to insomnia
 - ❖ patient averages 3-4 hrs sleep/night

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2009:

- ❖ Right modified radical mastectomy for 1.7 mod diff, IDC without LVI ER+, PR-, HER-2NEU negative
- ❖ Left mastectomy
- ❖ Oncotype DX score = 37 (25% chance of distant recurrence)
- ❖ MUGA: EF = 60%
- ❖ Plan:
 - ❖ TAC x 4 cycles (Taxotere, Adriamycin, Cyclophosphamide)
 - ❖ TC x 2 additional cycles (patient has previous hx of Adria use)

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TAC cycle 1 - October 2009

- ❖ Neulasta given post-chemotherapy to limit neutropenia
- ❖ *FN (despite Neulasta)
- ❖ diarrhea
- ❖ severe bone pain (secondary to Neulasta)
- ❖ continuing painful neuropathy of hands & feet
- ❖ multiple psychosocial issues
- ❖ required hospitalization

PATIENT SAID STOP!

We negotiated:


Weekly Taxotere – November 2009

- significant fatigue continues
- continuing peripheral neuropathy
- mild anemia
- constipation (corrected with Lactulose)

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2009

- ❖ Patient due to complete adjuvant weekly Taxotere mid-February



Holistic Care

- Weekly support group
- Massage
- Got a pet
- Scheduled for training to be a fitter



