

8. Summary of Key Evidence That Nursing Interventions Influence This Outcome and Gaps in Current Evidence Base

This evidence is based on the integrated reviews and highlights evidence that nursing interventions influence peripheral neuropathy (Section 4). To date, no studies focus on cancer-related peripheral neuropathies in diverse populations.

A. Evidence That Nursing Interventions Influence Peripheral Neuropathy

- Careful physical assessment and monitoring of subjective peripheral neuropathy symptoms is important in the early detection of cancer-treatment related neurotoxicity.
- Passive range of motion and resistance exercises can enhance reinnervation and muscle strength.
- Routine nursing assessment of stance, gait and balance can identify individuals needing assistive devices such as orthotic braces. Some evidence suggests that such devices can improve lower extremity alignment and balance.
- Little evidence exists of the effectiveness of teaching interventions regarding issues of personal safety (ambulation strategies, thermal/ischemic injury risk, management of hypotension).
- Evidence is conflicting regarding the role and efficacy of cytoprotective agents, glutathione, glutamine, vitamin e supplementation, or neurotrophic factors in chemotherapy-induced peripheral neuropathy, and no evidence exists regarding nursing interventions for individuals receiving these emerging therapies.

B. Gaps in the Evidence

Prevalence and Pattern

- In describing peripheral neuropathies, distinguishing between motor, sensory, and autonomic symptoms becomes important. Most peripheral neuropathies demonstrate a mixture of motor and sensory signs.
- Assessment of symptom patterns based on different agents or combination regimens is lacking.
- Evidence surrounding the resolution of cancer therapy-induced peripheral neuropathy is conflicting, with some studies reporting resolution of neuropathy coinciding with the end of treatment and others reporting a more prolonged course.

Assessment and Measurement

- Classification systems of grading chemotherapy-induced peripheral neuropathy vary widely, and guidelines for their use is lacking.
- Most toxicity assessment scales use a combination of objective and subjective items in reporting neurotoxicity.
- Toxicity assessment scales have difficulty in distinguishing subtle differences between toxicity grades, making these differences difficult to delineate.

- The current system for grading chemotherapy-induced peripheral neuropathy lacks a mechanism to adequately follow changes in peripheral nerve function from baseline.
- Toxicity grading scales are lacking in their ability to determine the impact of neurological changes on the individual.
- Some important indicators of grading the neurotoxicity associated with chemotherapeutic agents, such as deep tendon reflexes, sensation, and motor function, are that these measures are, to some degree, dependent on the skill of the examiner. An inherent intra-subject variability in response and intra- or inter-rater variability in the estimation of these responses exist that must be controlled.
- Objective measures of neuropathy fail to capture the impact of peripheral neuropathy on the individual. The impact of peripheral neuropathy on quality of life has not been studied adequately.

Mechanisms/Etiology of Peripheral Neuropathy

- The mechanism of chemotherapy-induced peripheral neuropathy is not fully understood, and the type of injury to the peripheral nerves varies with the chemotherapeutic agent used and total accumulated dose. For example, neurotoxic agents can cause shrinkage and degeneration of the myelin sheath, reducing nerve conduction velocity. Antimitotic agents induce microtubule aggregation in the neurons and have been implicated in axonal atrophy and demyelination. The dorsal root ganglion and the organ of Corti are directly affected by the accumulation of cisplatin and the effects of its metabolites in those tissues, leading to a dose-dependent sensory polyneuropathy and subsequent tinnitus and high-frequency hearing loss. However, the exact mechanisms underlying these processes are not fully understood and warrants further investigation.
- Plant alkaloids, such as vincristine or vinblastine are associated with swelling of unmyelinated axons and of large diameter sensory neurons that can impair anterograde axonal transport, inducing a dose-dependent neuropathy.

Correlates of Neuropathy

- Pain (shooting, burning) can accompany chemotherapy-induced peripheral neuropathy. Some evidence indicates that fatigue and depression also may be common features in peripheral neuropathy.

References:

- Apfel, S.C. (1999). Neurotrophic factors in peripheral neuropathies: Therapeutic implications. *Brain Pathology*, 9, 393-413.
- Armstrong, T., Almadrones, L & Gilbert, M. (2005). Chemotherapy-Induced Peripheral Neuropathy. *Oncology Nursing Forum*, 32(2), 305-311. "ONS Member Access" link to <http://www.ons.org/publications/journals/ONF>
- Ashton-Miller, J.A., Yeh, M., Richardson, J, & Galloway, T. (1996). A cane reduces loss

- of balance in patients with peripheral neuropathy: Results from a challenging unipedal balance test. *Archives of Physical and Medical Rehabilitation*, 77, 446-452.
- Boyd, F.M., Wheeler, H.R. & Shenfield, G.M. (1996). Glutamate ameliorates experimental vincristine neuropathy. *Journal of Pharmacology and Experimental Therapy* 279(1), 410-415.
- Gamelin, L., Boisdron-Celle, M., Delva, R., Guerin-Meyer, V., Ifrah, N., Morel, A., & Gamelin, E. (2004). Prevention of oxaliplatin-related neurotoxicity by calcium and magnesium infusions: A retrospective study of 161 patients receiving oxaliplatin combined with 5 fluorouracil and leucovorin for advanced colorectal cancer. *Clinical Cancer Research*, 10, 4055-4061.
- Hensley, M., Schuchter, L., Lindley, C., Meropol, N., Cohen, G., Broder, G., Gradishar, W., Green, D., Langdon, R., Mitchell, R.B., Negrin, R., Szatrowski, T., Thigpen, J.T., Von Hoff, D., Wasserman, T.H., Winer, E.P. & Pfister, D.G. (1999). American Society of Clinical Oncology Clinical practice guidelines for the use of chemotherapy and radioprotectants. *Journal of Clinical Oncology*, 17(10), 3333-3355.
- Hurvitz, E., Richardson, J. & Werner, R. (2001). Unipedal stance testing in the assessment of peripheral neuropathy. *Archives of Physical and Medical Rehabilitation*, 82, 198-204.
- Kaner, P. (2001). Diagnosis and management of neuropathic pain in patients with cancer. *Cancer Investigation*, 19(3), 324-333.
- McDonald, E.S. & Windebamk, A.J. (2000). Mechanisms of neurotoxic injury and cell death. *Clinical Neurobehavioral Toxicology*, 18(3), 525-537.
- Pace, A., Savarese, A., Picardo, M., Maresca, V., Pacetti, U., Del Monte, G., Biroccio, A., Leonetti, C., Jandolo, B., Cognetti, F. & Bove, L. (2003). Neuroprotective effect of vitamin E supplementation in patients treated with cisplatin chemotherapy. *Journal of Clinical Oncology*, 21(5), 927-931.
- Paulson, L. & Kilmer, D. (2001). Orthotic management in peripheral neuropathy. *Advances in the Diagnosis and Management of Peripheral Nerve Disease*, 12(2) 433-445.
- Postma, T., Heimans, J., Muller, M., Ossenkopple, G., Vermorken, J., & Aronson, N. (1998). Pitfalls in grading severity of chemotherapy induced peripheral neuropathy. *Annals of Oncology*, 9, 739-744.
- Postma, T., & Heimans, J. (2000). Grading of chemotherapy-induced peripheral neuropathy. *Annals of Oncology*, 11, 509-513.
- Rothstein, J. & Kuncl, R. (1995). Neuroprotective strategies in a model of chronic glutamate mediated neuron toxicity. *Journal of Neurochemistry*, 65(2), 643-649.
- Quasthoff, S. & Hartung, H.P. (2002). Chemotherapy-induced peripheral neuropathy. *Journal of Neurology*, 249, 9-17.
- Richardson, J.K., Sandman, D. & Vela, S. (2001). A focused exercise regimen improves clinical measures of balance in patients with peripheral neuropathy. *Archives of Physical and Medical Rehabilitation*, 82, 205-209.
- Vahdat, L. Papadopoulos, K., Lange, D., Leuin, S., Kaufman, E., Donovan, D., Fredrick,



D., Bagiella, E., Tiersten, A., Nichols, G., Garrett, T., Savage, D., Antman, K., Hesdorffer, C.S., Balmaceda, C. (2001). Reduction of paclitaxel-induced peripheral neuropathy with glutamine. *Clinical Cancer Research*, 7, 1192-1197.