

UNIT 3

Late Effects of Cancer Treatment

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QUICK OVERVIEW

- Many cancer survivors have a risk of developing late effects or a secondary cancer from cancer treatment received (surgery, systemic cancer therapy, and/or radiation therapy).
- A late effect is defined as a side effect that occurs months to years after a diagnosis of cancer and the completion of treatment, such as chemotherapy, radiation therapy, surgery, or a targeted therapy.
- Although cancer treatments are improving they can still bring late effects. The type of late effect(s) that may develop varies from person to person.
- Long-term side effects or complications differ from late effects of treatment because they begin during treatment and persist beyond the end of treatment.
- Secondary cancers are thought to be a result of previous exposure to chemotherapy and radiation therapy.
- Nursing care involves minimizing risk and facilitating early recognition of the late and long-term effects of cancer and cancer therapy. Treatment of late effects is an important part of cancer care.
- Secondary prevention practices, including lifelong surveillance, risk reduction activities and cancer screening, may reduce the burden of secondary cancers.

INTRODUCTION:

In Canada in 2004, there were an estimated 396,900 male and 456,500 female cancer survivors, for a total of approximately 853,400 Canadians (2.7% overall). This is a 21% increase from the corresponding 679,800 figure reported previously for 1998. The number of people diagnosed with cancer who can expect to survive at least five years is now 60% (National Cancer Institute of Canada, 2004). The growth in the absolute number of cancer survivors presenting with physical complications will continue to increase as a result of improvements in treatment modalities combined with demographic and health trends such as population aging.

Many cancer survivors are at risk for developing some type of late effect from cancer treatment. Late effects, also referred to as delayed effects, can appear months to years after treatment is over. These late consequences of treatment may include secondary cancers, cognitive problems, lymphedema, peripheral neuropathy, and/or cardiovascular conditions. Long-term effects are those side effects or complications of treatment that start during treatment but persist beyond the end of treatment (Eades, Chasen, & Bhargava, 2009). Some cancer survivors may be at risk to have both late effects and long-term effects of the disease and treatments.

Although cancer survivors likely participated in discussions about potential sequelae when treatment decisions were made, they may not recall some or any of that discussion. Nursing care involves minimizing risk and facilitating early recognition of the late and long-term effects of cancer and cancer therapy (Curtiss, Haylock, & Hawkins, 2006). Understanding late effects and educating cancer survivors proactively on effective strategies to manage and minimize the impact of those effects is rapidly becoming a core requirement for nurses and for cancer programs.

By understanding the late effects associated with individual drugs and treatment modalities the nurse can effectively support survivors to implement a survivorship care plan that includes disease-specific follow-up, screening recommendations, and information about possible late effects tailored to each patient.

Meeting the CANO/ACIO Standards and Competencies:

Standards and Competencies relevant to this section:

Reviewing and using this section in practice, the nurse will be addressing in particular the practice standards of Comprehensive Health Assessment and Teaching and coaching.

Practice Standard: Comprehensive Health Assessment

Competencies:

Regularly assesses and monitors for potential acute and chronic physical changes to the individual's response to illness using focused assessment tools.

Practice Standard: Teaching and Coaching

Competencies:

Facilitates the individual/family's understanding of the episodic and chronic nature of cancer. Facilitates the development of self-care in order to manage and anticipate the signs and symptoms of disease, side effects of treatments, and symptom identification.

LITERATURE REVIEW:

There is a broad range of potential late effects and long-term effects that can vary in severity ranging from mildly unpleasant to very severe (Curtiss, Haylock, & Hawkins, 2006; Eades, Chasen, & Bhargava, 2009). The possible physical and psychosocial sequelae of cancer and its treatments differ according to the age of the cancer survivor, the specific type of cancer, and the cancer treatment regimen received (Curtiss et al., 2006; Eades et al., 2009). Newer therapies such as the molecularly targeted therapies may decrease the burden of physical effects in individual cancer survivors. However, research clearly shows that pre-existing risk factors and specific clinical factors combine to increase a person's risk of developing late effects or enhancing long-term side effects such as fatigue (Curtiss et al., 2006; Eades et al., 2009).

Pre-existing Risk Factors	Specific Clinical Factors
<input type="checkbox"/> Age <input type="checkbox"/> Co-morbidities <input type="checkbox"/> Heredity <input type="checkbox"/> Lifestyle factors	<input type="checkbox"/> High-dose therapies <input type="checkbox"/> Combination treatment modalities (radiation and chemotherapy) <input type="checkbox"/> Radiotherapy <input type="checkbox"/> Certain chemotherapy drugs

The acquired physical and functional impairments are often complex for the person with cancer and can be life-threatening, anxiety-provoking, and associated with a negative impact on self-image and self-efficacy (Eades, Chasen, & Bhargava, 2009). Functional difficulties include immobility, incontinence, lymphedema, sleep disturbances, and attention difficulties. The more common long-term side effects or persistent symptoms have been identified as cognitive problems, fatigue, lymphedema, and peripheral neuropathy (Nail, 2001). They vary in terms of the population at risk, presumed causal factors, level of understanding of the natural history of the symptoms, and depth of the research base on preventing or managing the symptoms (Nail, 2001).

Cancer survivors who have experienced organ damage, organ failure, or premature aging due to treatments are likely to live with renal insufficiency, bladder damage, carotid artery disease, cataracts, muscle atrophy, and/or problems with memory and information processing.

Cancer survivors have a 14% higher risk of developing a new cancer, (NCIC, accessed online 2010) also known as a secondary cancer. Secondary cancers are thought to be a result of previous exposure to chemotherapy and radiation therapy. Of the 260,000 10-year cancer survivors in Ontario, second primary malignancies now account for 16% of all cancer incidences in this group (Cancer Care Ontario, accessed online 2010).

Cognitive changes include the inability to concentrate, remember or perform complex cognitive activities, or a combination of these. Such changes are most often related to chemotherapy or whole brain radiation (Curtiss, Haylock, & Hawkins, 2006; Muscari, 2006; ManageCRC.com accessed online 2010; Nail, 2001). Cancer survivors may attribute problems in cognition to fatigue, which raises questions about whether or not strategies to prevent or manage fatigue would also improve cognitive function. Emerging literature about the short- and longer-term cognitive impacts of chemotherapy is generating great interest among oncology health care professionals. This body of evidence is dynamic and changing. Other terms used to describe cognitive changes or impairments are chemo brain, chemo clutter, or brain fog (Muscari, 2006). Cognitive changes have been studied most widely in women undergoing treatment for breast cancer, with 17% to 75% reporting symptoms (ManageCRC.com accessed online 2010).

Fatigue is the most commonly reported symptom of cancer and cancer therapy (Gélinas, Fillion, & Fortier, 2004; Barton-Burke, 2006; Eaton & Tipton, 2009). The National Comprehensive Cancer Network (NCCN) defines fatigue as a common, persistent, subjective sense of tiredness related to cancer, or cancer treatment that interferes with usual functioning (2000). The causes of fatigue are varied and include anemia, hypercalcemia, pain, sluggish thyroid gland, depression, poor nutrition, and lack of physical strength (Gélinas, et al., 2004). The NCCN has clinical practice guidelines for nurses that are evidence based (www.nccn.org).

Lymphedema is one of the most widely recognized persistent symptoms and typically occurs secondary to surgical removal of lymph nodes and or radiation therapy to lymph node bearing areas (Golshan & Smith, 2006). Lymphedema is the abnormal accumulation of lymph fluid in the subcutaneous tissue, which can cause excessive swelling mostly in the limbs (Harris, Hugi, Olivotto & Levine, 2001). Untreated, the increased swelling can cause increased functional impairment and risk for recurrent cellulitis (Eaton & Tipton, 2009; Harris et al., 2001).

Peripheral neuropathy is associated with specific drug regimens and dose levels. In follow-up care it is common to hear cancer survivors report numbness and tingling in the hands and feet many years after completing cancer treatment. When the neuropathy involves a sensory component there are safety issues similar to those addressed in the care of people with diabetic neuropathy. (Armstrong, 2005; Curtiss, 2006) Chemotherapy-induced peripheral neuropathy (CIPN) is a quality of life issue for patients and is becoming seen more commonly because of the influx of chemotherapy agents that cause it (Armstrong, 2005; Curtiss, 2006; Eaton & Tipton, 2009)

Summary

All cancer survivors are at risk of experiencing the psychological impact of late effects, such as anxiety, mood changes, depression, coping ability, living with uncertainty, and relationship changes/problems. There is also the social impact, such as the ability to obtain/retain health insurance, and the ability to reintegrate into the work force (availability of work/ability to perform within the job, etc.). Please refer to the Unit 8: Psychosocial Health and Wellbeing and Unit 9: Return to Work for more information.

FACILITATING A SYSTEMATIC ASSESSMENT:

Major Late Physical Effects by Body System

This section of the unit focuses on the major physical late effects. These effects range from specific sequelae such as radiotherapy-induced cataracts to multisystem consequences of chemotherapy-induced premature menopause, including menopausal symptoms, bone loss, and potential cardiovascular effects.

System Affected	Typical Causes	Typical Cancers	Typical Effects
Endocrine	<ul style="list-style-type: none"> ■ Radiation to the cranium or nasopharynx - can damage the hypothalamic pituitary axis, causing secondary gonadal failure; also the testis is extremely sensitive. ■ Chemotherapy (e.g. alkylating agents, especially high-dose cyclophosphamide, cytosine arabinoside, high-dose cisplatin, etoposide) ■ Hormone therapy ■ Surgery 	Head & Neck Testicular Prostate Gynecological	<ol style="list-style-type: none"> 1. Thyroid changes 2. Low testosterone 3. Reduced libido 4. Impotence 5. Irregular menses 6. Amenorrhea 7. Premature menopause 8. Azoospermia 9. Osteopenia 10. Osteoporosis 11. Infertility 12. Low levels of some hormones depending on area affected.

Subnormal levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and prolactin inhibiting factor have been found in males and females treated for head and neck tumors with 4,000–7,800 cGy of radiation.

Gonadal toxicity may result from surgery, radiotherapy, chemotherapy, and/or hormonal therapy.

Bilateral oophorectomy in premenopausal women leads to abrupt onset of menopause and its associated consequences, including infertility, rapid onset of bone loss, and menopausal symptoms, are typically more severe than with natural menopause.

Pelvic radiotherapy and ovarian ablation with luteinizing hormone releasing hormone agonists have similar consequences to bilateral oophorectomy. Chemotherapy related amenorrhea is prevalent in premenopausal women with breast cancer, and algorithms are available to help predict risk based on age and chemotherapy regimen.

In men, damage to the germinal epithelium of the testis may result from alkylating agents or radiation.

Men treated with androgen-deprivation therapy for prostate cancer experience symptoms of hypogonadism including bone loss, and should be monitored for osteopenia or osteoporosis.

Otto, 2001; Ganz, 2001; Curtiss et al, 2006

System Affected	Typical Causes	Typical Cancers	Typical Effects
Cardiovascular	<ul style="list-style-type: none"> ■ Chemotherapy (e.g. anthracyclines such as doxorubicin, cisplatin, and cyclophosphamide) ■ Targeted Therapies (e.g. ErbB2) ■ Radiotherapy to the field encompassing the heart and mediastinum. ■ People aged 65 or older & those people who received high doses of chemotherapy have a higher risk of heart problems. 	Breast Small-cell lung Ovarian Sarcoma Germ-cell Hodgkin's disease	<ol style="list-style-type: none"> 1. Cardiomyopathy 2. Congestive heart failure 3. Acceleration of coronary artery disease 4. Valvular disease 5. Metabolic syndrome 6. Inflammation of the heart muscle.
Gastrointestinal	<ul style="list-style-type: none"> ■ Radiation (alone or concurrent with chemotherapy) to the pelvis can lead 	Colorectal Gastric Esophageal Gynecological	<ol style="list-style-type: none"> 1. Liver toxicity 2. Hepatic fibrosis 3. Cirrhosis 4. Veno-occlusive disease 5. Fistula formation 6. Chronic diarrhea
Genitourinary	<ul style="list-style-type: none"> ■ Chemotherapy e.g. cyclophosphamide, ifosfamide, and cisplatin ■ Radiotherapy ■ Surgery 	Genitourinary Prostate	<ol style="list-style-type: none"> 1. Hemorrhagic cystitis 2. Nephritis 3. Incontinence 4. Impotence 5. Erectile dysfunction 6. Men who had surgery involving removal of lymph nodes near the kidney, bladder, testicles, or rectum may have a risk of infertility.

<p>Hematological/ Immune</p>	<ul style="list-style-type: none"> ■ Allogeneic bone marrow transplant ■ Peripheral stem cell transplant ■ Chemotherapy ■ Total body irradiation ■ Radiotherapy 	<p>Leukemias Lymphomas Multiple Myeloma</p>	<ol style="list-style-type: none"> 1. Cataracts 2. Hypothyroidism 3. Growth failure 4. Gonadal dysfunction 5. Secondary malignancies 6. Chronic Graft versus Host Disease (GVHD) 7. Avascular necrosis 8. Osteoporosis 9. Risk for serious infection for those with splenectomy.
<p>Lymphatic</p>	<ul style="list-style-type: none"> ■ Surgery (node dissection) ■ Radiotherapy 	<p>Breast Head and neck GU Melanoma Gynecological</p>	<p>Secondary lymphedema</p> <ol style="list-style-type: none"> 1. Peripheral lymphedema 2. Truncal lymphedema 3. Recurrent cellulitis 4. Erysipelas
<p>Musculoskeletal</p>	<ul style="list-style-type: none"> ■ Surgery ■ Radiotherapy ■ Chemotherapy ■ Steroids ■ Hormonal therapy (androgen or estrogen suppressants) 	<p>Breast Sarcoma (bone and soft tissue cancer) Lung Childhood leukemia Prostate</p>	<ol style="list-style-type: none"> 1. Post mastectomy pain syndrome (PMPS) 2. Breast phantom sensations 3. Impingement syndrome (Frozen shoulder) 4. Risk factors are preoperative psychosocial distress & reconstructive surgery. 5. Phantom limb pain due to amputation 6. Post-thoracotomy pain syndrome (occurs in 20- 30% of individuals) 7. Fatigue 8. Osteoporosis

			9. Bone and soft tissue cancer survivors may experience physical and psychological effects of losing all or part of a limb, such as phantom limb pain.
Neurologic	<ul style="list-style-type: none"> ■ Chemotherapy: certain agents &/ or high doses of certain drugs can cause neurotoxicity (interferon alpha, platinum compounds (eg. cisplatin, vinca alkaloids, antimitotics, and taxanes) ■ Cranial radiotherapy for brain tumours 	Primary brain tumour Metastatic disease to the brain Spinal cord	<ol style="list-style-type: none"> 1. Peripheral neuropathy 2. Autonomic neuropathy (postural hypotension) 3. Sensory neuropathy
Pulmonary	<ul style="list-style-type: none"> ■ Chemotherapy (e.g. bleomycin, alkylating agents, methotrexate, nitrosoureas) ■ Radiotherapy to lung fields ■ Concurrent chemotherapy and radiation therapy ■ Recurrent respiratory infections in immunosuppressed patients ■ Bone or Marrow Transplant ■ Steroids such as prednisone & dexamethasone 	Germ cell testicular Breast Lung Genitourinary	Germ cell testicular Breast Lung Genitourinary

References for above tables: Otto, 2001; Ganz, 2001; Curtiss et al, 2006

Late Effects from Surgery:

Late effects from surgery for cancer can vary depending on the surgical site and extent of the procedure. Nurses need to consider adhesions and scarring as well as the impact on body systems related to the site of surgery and what may have been removed in the surgical procedure. Radiation after surgery is common and can impact the long term healing by enhancing scar tissue and causing small visible blood vessels under the skin near the surgical site.

PRIORITY CONTENT FOR PATIENT TEACHING:

Screening for secondary cancer prevention

The prevalence of secondary prevention counseling for cancer survivors is low; this is a missed opportunity to promote healthy behaviours (Sabatino, Coates, Uhler, Pollack, Alley & Zauderer, 2007). With respect to cancer screening in particular, a study of a select group of colorectal cancer patients showed that they were more likely to participate in cancer prevention and cancer screening activities compared to those without a history of cancer (Kunitake, H., Zheng, P., Yothers, G., Land, R.R., Fehrenbacher, L., Giguere, J.K., Wickerham, L., Ganz, P.A., & Ko, C.Y, 2010). Secondary prevention practices, including lifelong surveillance and cancer screening, may reduce the burden of secondary cancers.

Nurses can encourage and educate cancer survivors about the benefits of life-long surveillance. This includes having the person learn how to monitor for new signs or symptoms that may reflect cancer recurrence. Appropriate screening tests are based on type of cancer and cancer treatment:

Cancer Survivors	Screening
Treated for thyroid, head, neck, or throat cancer.	Yearly thyroid exam
Received bleomycin.	Pulmonary Function Testing
Received treatment that could affect the cardiovascular system.	Cardiac testing such as echocardiogram
Received radiation to the chest especially at a young age.	Mammogram
Received treatment that puts them at a higher risk for a second cancer.	Blood testing; CT Scans as appropriate

<p>Received chemotherapy and/or radiation may be at higher risk of dental problems. Chemotherapy may affect tooth enamel. It may also increase the risk of long-term dental problems.</p> <p>High-dose radiation therapy to the head & neck can cause gum disease, change tooth development, & decrease saliva production, resulting in a dry mouth.</p> <p>Treatment history includes the use of bisphosphonates: Risk of osteonecrosis of jaw.</p>	<p>Regular check-ups with the dentist.</p>
<p>Received steroids may be at an increased risk of eye problems, such as cataracts</p>	<p>Regular check-ups with the optometrist or ophthalmologist.</p>

Otto, 2001; Ganz, 2001; Curtiss et al, 2006

Cognitive problems:

- Report any concerns about problems with memory or concentration
- Keep a daytimer to track appointments, medications, and follow-up tests
 (Nail, 2001; Muscari, 2006; Vardy et al, 2008; ManageCRC, accessed online 2010)

Fatigue:

- Identify factors which may increase fatigue and modify as needed
- Treatment-related fatigue is not necessarily an indicator of disease progression
- Strategies to cope with fatigue:
 - Energy conservation
 - Distraction
 - Stress management
 - Exercise
- Diary of fatigue levels to evaluate effectiveness of coping strategies
 (Nail, 2001; Gélinas et al, 2004; Barton-Burke, 2006, Eaton & Tipton, 2009)

Lymphedema:

- Goals to prevent, manage and treat:
 - Avoid injury and infection to the affected limb
 - Gentle exercise and deep breathing to mobilize lymphatic drainage and flow
 - Maintain a healthy body mass index
 - Use compression garments as appropriate (e.g. arm sleeves, leg stockings)
 - Consider combined decongestive therapy: utilization of manual lymph drainage in combination with compression bandaging to redirecting the lymphatic fluid into functioning vessels and lymph nodes
 (Curtiss et al, 2006; Eaton & Tipton, 2009; Harris et. al., 2001; Golshan & Smith, 2006)

Peripheral neuropathy:

- Report persistent symptoms of tingling, numbness or coldness in hands, or feet
- Safety issues: avoid walking barefoot, using care in trimming of fingernails or toenails (Armstrong, 2005; Eaton & Tipton, 2009).

The following teaching content can be provided as appropriate depending on the survivor's past medical history and previous cancer treatment plan.

Cardiovascular risk:

- Encourage dialogue with the health care provider about having a cardiovascular exam regularly
- Explain to your patient the importance of reporting chest pain
- Explain what type of tests might be done: physical exam, EKG, echocardiography.

Gastrointestinal (GI) risk:

- Consult a dietitian if eating remains a concern
- Teach how to manage chronic diarrhea
- Teach what symptoms to report

Genitourinary (GU) and gynecological risk:

- Encourage discussion on sexual health (refer to Unit 7: Sexual Health for more information)
- Explain the importance of reporting symptoms of dysuria, hematuria, erectile dysfunction, vaginal symptoms, or incontinence
- Review teaching about Kegel exercises to strengthen the pelvic muscles that help to control the flow of urine from the bladder

Endocrine risk:

- Explain that hormone levels can be checked with blood tests, and these should be done regularly if the patient is at risk.

Musculoskeletal risk (bone and joint problems):

- Stay active; participate in regular physical activity
- Do not smoke
- Eat foods rich in calcium
- Limit alcohol intake

Neurological risk:

- Follow-up care should include regular physical exams, hearing tests as appropriate, and x-rays.
- Survivors who experience any cognitive problems should talk with their doctor or nurse.
- Teach about cognitive (thought processes) problems and chemobrain.

Pulmonary risk:

- Explain to your patient the importance of reporting a change in their breathing.

Learning Activity: Case Study

D.A. is a 56 year old woman with breast cancer. Two years ago she was diagnosed with ER/ PR +, HER2 neu +, stage II breast cancer. At that time she had a lumpectomy and lymph node dissection followed by radiation, an anthracycline based chemotherapy regimen with herceptin all followed by tamoxifen. She is now being followed every six months by her family physician. She presents with the following concerns:

- SOB with moderate exertion. Prior to her diagnosis she was very active and feels there must be something very wrong with her lungs. She asks you if perhaps her cancer treatment injured her lungs.
- Inability to return to former occupation as nurse as she is just “too tired” to work 12 hour shifts. She also states that she has trouble remembering things and critically thinking through complex patient situations.
- Marital challenges as she states she feels sexually uninterested and has intermittent dyspareunia.
- She had a pelvic fracture after slipping on ice early in the winter and states she does not want to continue taking her tamoxifen. A friend told her that her fall was probably because of “that drug”.
- While in the hospital with her pelvic fracture she had a DVT and continues on low molecular weight heparin (LMWH).

Discussion:

It is critical that you are able to support D.A. in clarifying her concerns and misunderstandings so that together you can effectively work to develop a plan of care to address the challenges she faces.

What late effects need to be identified in the survivorship care plan specific to D.A.’s situation?

Answers:

Her shortness of breath should be carefully assessed to rule out pulmonary embolism or other physical causes such as cancer recurrence and cardiovascular compromise secondary to anthracycline therapy for example.

Her risk of osteoporosis while taking Tamoxifen is actually reduced. If her treatment is switched to an aromatase inhibitor in the future that risk will rise. All women should have a base line bone density test to determine their risk and to use as a comparison to later studies. The nurse may talk to her about the increased risk of thrombo embolism while taking Tamoxifen and how her current anticoagulation therapy will impact (reduce) that risk.

Dyspareunia (or painful sex) and lack of libido can be addressed in a multi-pronged interdisciplinary approach that includes physical assessment, teaching about non hormonal treatments for dyspareunia and couples counseling. Some women may even need to talk to the oncology team about the risks and benefits of hormone therapy after breast cancer when quality of life is severely impacted.

Many patients describe fatigue after the end of treatment and its intensity and trajectory are variable. By exercising and eating a well balanced diet and minimizing stress where possible she can maximize her energy. In addition refraining from smoking and limiting alcohol can be helpful. Journaling may help her identify ways to conserve energy for high priority activities.

For many reasons a referral to supportive care may be needed; not being able to return to work can cause depression and financial hardships, relationship changes are also a concern.

References:

Armstrong, T., Almadrones, L., & Gilbert, M.R.. (2005). Chemotherapy-induced peripheral neuropathy. *Oncology nursing Forum*. 32(2) 305-311.

Barton-Burke, M. (2006). Cancer-Related Fatigue and Sleep Disturbances. *AJN*. 106(3) Supplement. 72-77.

Cancer Care Ontario. Accessed online 2010 www.cancercare.on.ca.

Curtiss, C.P., Haylock, P.J., & Hawkins, R. (2006). Improving the care of cancer survivors. *American Journal of Nursing*. 106(1), 48-52.

Dunne-Daly, C.F. (1995). Programmed Instruction: Potential Long-Term and Late Effects from Radiation Therapy. *Cancer Nursing* 18(1): 67-79.

Eades, M., Chasen, M., & Bhargava, R. (2009). Rehabilitation: Long-term physical and functional changes following treatment. *Seminars in Oncology Nursing*. 25(3), 222-230.

Eaton, L.H. & J.M. Tipton (eds). (2009). Chapter 11: Fatigue in *Putting Evidence into Practice: Improving Patient Outcomes*. p149-171. Oncology Nursing Society: Pittsburgh.

Eaton, L.H. & J.M. Tipton (eds). (2009). Chapter 12: Lymphedema in *Putting Evidence into Practice: Improving Patient Outcomes*. p175-192. Oncology Nursing Society: Pittsburgh.

Eaton, L.H. & J.M. Tipton (eds). (2009). Chapter 15: Peripheral Neuropathy in *Putting Evidence into Practice: Improving Patient Outcomes*. p235-252. Oncology Nursing Society: Pittsburgh.

Ganz, P.A. (2001). Late Effects of cancer and its treatments. *Seminars in Oncology Nursing*. 17(4), 241-248.

- Gélinas, C, Fillion, L, & Fortier, M. (2004). Mieux comprendre la fatigue liée au cancer. *Perspective Infirmière*. Mars/avril. 14-21.
- Golshan, M. & Smith, B., (2006). Prevention and management of arm lymphedema in the patient with breast cancer. *Journal of Supportive Oncology*, 4(8), 381-386.
- Harris, S.R., Hugi, M.R., Olivotto, I.A., & Levine, M.L. (2001). For the steering committee for the clinical practice guidelines for the care and treatment of breast cancer: 11. Lymphedema. *Canadian Medical Association Journal*, 30(2), 8-13.
- Kunitake, H., Zheng, P., Yothers, G., Land, S.R., Fehrenbacher, L., Giguere, J.K., Wickerham, L., Ganz, P.A., Ko, C.Y. (2010). Routine preventive care and cancer surveillance in long-term survivors of colorectal cancer: Results from the national surgical adjuvant breast and bowel project protocols LTS-01. *Journal of Clinical Oncology*, 28(36), 5274-5279.
- Nail, L.M. (2001). Long-term persistence of symptoms. *Seminars in Oncology Nursing*. 17(4), 249-254.
- ManageCRC.com. Accessed online 2010 www.manageCRC.com Cognitive dysfunction secondary to cancer therapy.
- Muscari, E. (2006). Chapter 12: Cognitive impairment in cancer in Carroll-Johnson, R., Gorman, L., & Bush, N. (eds) *Psychosocial Nursing Care: along the cancer continuum* 2nd ed. Oncology Nursing Society: Pittsburgh.
- National Cancer Institute of Canada (NCIC). Accessed online 2010 www.ncic.cancer.ca/research/.
- National Cancer Institute of Canada. Canadian Cancer Statistics 2004, Toronto, Canada, 2004.
- Osoki, R.E. (2003). Chapter 14: Leukemia. In *Cancer Nursing* ed Shirley Otto. 346-379.
- Otto, S. E. (2001) *Oncology Nursing* (4th ed). Mosby: St Louis, Missouri.
- Sabatino, S.A., Coates, R.J., Uhler, R. J., Pollack, L.A., Alley, L.G. & Zauderer, L.J. (2007). Provider Counseling about health behaviors among cancer survivors in the United States. *Journal of Clinical Oncology*, 25 (15), 2100-2106.
- Vardy, J., Wefel, T.A., Tannock, I.F., & Schagen, S.B. (2008). Cancer and cancer-therapy related cognitive dysfunction: an international perspective from the Venice cognitive workshop. *Annals of Oncology*. 19. 623-629.