Exercise Prescription in the Rehabilitation of the Cancer Patient: Current Guidelines

PDH Academy Course #PT-18XX
3 CE Hours

Course Abstract
There is a widespread understanding of the importance of physical exercise for patients with cancer; however, limited resources exist to assist physical therapists in the development of treatment plans. This course begins with an overview of the current evidence, followed by an examination of common cancer diagnoses and the adverse effects of the cancer treatment for each relevant to physical activity. It next discusses the aspects of the rehabilitation evaluation that help determine appropriate and evidence-based exercises to fit each patient's limitations and needs. It concludes with guidelines for exercise prescription in regards to aerobic capacity, strength, and flexibility, as well as the addition of special exercises and recreational activities. Case studies are provided.

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Approvals
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Target Audience & Prerequisites
PT, PTA – no prerequisites

Learning Objectives
By the end of this course, learners will:
- Recognize evidence pertaining to previous and current theories about the relationships between cancer and exercise
- Identify surgical and nonsurgical interventions for common cancers
- Recall considerations pertinent to the development of an exercise-based treatment plan, with attention to the evidence supporting each
- Recall contraindications to the development of an exercise-based treatment plan
- Distinguish between prescription guidelines for aerobic, resistance, and flexibility exercises, as well as special exercises

Timed Topic Outline
I. Former and Current Theories on Cancer and Exercise (35 minutes)
   - General Fitness and Cancer, Exercise as an Intervention in Treating Cancer
II. Common Therapeutic Interventions to Cancer and their Relevance to Physical Activity (20 minutes)
   - Cancer Surgery, Chemotherapy, Radiation, Targeted Therapy, Stem Cell Transplant Therapy
III. Considerations in the Evaluation and Development of an Exercise-Based Treatment Plan (35 minutes)
    Increasing Strength, Improving General Flexibility, Reducing Fatigue, Improving Cardiorespiratory Function, Psychosocial Outcomes
IV. Cancer-Specific Contraindications and Reasons to Stop an Exercise Program (15 minutes)
    Breast Cancer, Colon Cancer, Gynecologic Cancer, Prostate Cancer, Hematologic Malignancies in Adults
V. Aerobic Exercise Prescription Guidelines (10 minutes)
VI. Resistance Exercise Prescription Guidelines (10 minutes)
VII. Flexibility Exercise Prescription Guidelines (10 minutes)
VIII. Special Exercise Prescription Guidelines (10 minutes)
IX. Case Studies (20 minutes)
X. Conclusion, References, and Exam (15 minutes)

Delivery Method
Correspondence/internet self-study, with a provider-graded multiple choice final exam. To earn continuing education credit for this course, you must achieve a passing score of 80% on the final exam.

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Course Author Bio and Disclosure
Jeffrey P. Larson, PT, ATC, is the director of physical therapy at the Tioga Medical Center in Tioga, ND. He is a graduate of North Dakota State University and the University of Utah. He holds degrees in both athletic training and physical therapy. He is also a medical writer and founder of Northern Medical Informatics, a medical communications business that he operates with focus on continuing education for the allied healthcare professions as well as consumer health education. He is a member of the American Physical Therapy Association and the American Medical Writers Association.

DISCLOSURE: Financial – Jeffrey Larson receives a consulting fee as an author of continuing medical education for Northern Medical Informatics, and received a stipend as the author of this course. Nonfinancial – No relevant nonfinancial relationship exists.
Introduction

As the world population is growing and aging, cancer has become a leading and rising cause of death worldwide, with the overall number of cases also on the rise (NCI, 2017). According to the National Cancer Institute, 38.5% of people will be diagnosed with some form of cancer in their lifetime.

In the past, it was difficult to find exercise programs designed to address the specific symptoms and struggles of cancer patients and survivors: patients being treated for cancer were often advised by their physicians to rest and reduce their physical activity. Then, in the late 1980s, two pioneer oncology nurses from Ohio State University – Mary L. Winningham, PhD and Mary MacVicar, PhD – provided research which advanced the knowledge about the role and efficacy of exercise therapy following a cancer diagnosis (Jones & Alfano, 2013). Their early research demonstrated that interval aerobic exercise training was not only practicable, safe, and acceptable, but that it also caused significant improvements in aerobic capacity, body composition, and patient-reported nausea. However, testing the efficacy of exercise training in this setting was a radical change from the norm at this time, and their conclusions were in direct contrast to the standard recommendation for patients undergoing cytotoxic therapy, which generally was to rest and avoid exercise, especially high-intensity aerobic training. Thus interest in the area of exercise-oncology remained limited in the years immediately following Winningham and MacVicar’s initial landmark study.

In 2001, additional published research included a large randomized controlled trial investigating the effects of supervised or home-based aerobic training on physical functioning and quality of life in 121 operable breast cancer patients. During and following cancer treatment, aerobic exercise training was found to reduce the decline in physical functioning in patients receiving chemotherapy, and improved physical functioning in those following the completion of cancer therapy (Segal, 2001). This was the first study to be published in the Journal of Clinical Oncology, the official journal of the American Society of Clinical Oncology (ASCO). This publication immediately elevated the credibility of exercise prescription as a supportive care intervention in the oncology setting from this point on. Today, excluding symptoms of severe painful movement, rapid heart rate, or shortness of breath, research shows exercise is safe during and after cancer treatment.

As we know, prescribed exercises and lifestyle advice provided by physical therapists can help people reduce their risk of getting cancer and improve their overall physical functioning and quality of life. Post-cancer diagnosis, physical therapists can also make a unique contribution to helping this patient population achieve health and a good quality of life. In fact, as a result of the increased involvement and interest by the profession, the American Physical Therapy Association (APTA) House of Delegates approved board certification in the area of oncology in 2016. The mission of the Oncology Section is to advance physical therapist practice for persons affected by cancer and chronic illness by maximizing movement and wellness across the lifespan. It is anticipated that the first oncology specialist certification examination will be administered in spring 2019. (Resources for applying to become a board certified specialist in this specialty area can be obtained from the American Physical Therapy Association.)
However, despite the widespread understanding of the importance of physical exercise for patients with cancer, there are still limited resources readily available on specific guidelines to assist in the development of the treatment plan. This course addresses these limitations by emphasizing appropriate exercise options in accordance with medical associations such as the American College of Sports Medicine and the National Cancer Institute, along with reference to several recent evidence-based research studies. Its goal is to increase and improve upon the capability of rehabilitation professionals to serve the unique needs of cancer patients and survivors, assisting the physical therapist to determine specific exercises appropriate to the treatment plan for each cancer patient and/or cancer survivor.

We will begin with an overview of the current evidence, followed by an examination of common cancer diagnoses, including breast, prostate, colon, hematologic, and gynecologic cancers, and the adverse effects of the cancer treatment for each relevant to physical activity. Next we will discuss the aspects of the rehabilitation evaluation that help determine appropriate and evidence-based exercises to fit each patient’s limitations and needs. The course concludes with guidelines for exercise prescription in regards to aerobic capacity, strength, and flexibility, as well as the addition of special exercises and recreational activities.

### Section 1: Former and Current Theories on Cancer and Exercise

In the past, a cancer diagnosis was in essence a death sentence. However, advances in prevention, detection, and treatment have led to better outcomes: the 5-year survival rate of all cancers diagnosed between 2003 and 2009 was 68%, which was almost a 20% increase from 1975-1977.

In 2014 the American Cancer Society estimated that approximately 13.7 million Americans have a history of cancer. Given an aging population contributing to a high incidence of cancer, and medical advances improving survival rates, the population of cancer survivors (a term used to describe any living person who has ever received a cancer diagnosis, regardless of his or her current disease status) is quickly expanding. Recent estimates suggest there are currently almost 12 million cancer survivors living in the United States (Morgan Lee, 2013).

As the incidence and prevalence of cancer increases, so, too, does the number of patients living with cancer as a chronic condition. Patients with advanced cancer (i.e. locally advanced or metastatic incurable cancer) are also living longer than in previous decades (NCI, 2017). Since advanced cancer is rarely compatible with employment, and since the condition may consume considerable healthcare resources, this population in particular faces a major public health concern.

The numbers indicate that the need for rehabilitation among cancer survivors, as well as patients with advanced cancer will continue to increase. Timely rehabilitation at appropriate volumes will not only improve quality of life but also reduce healthcare costs (Minna, 2015).

For the physical therapist, cancer rehabilitation is an evolving area. Given the increasing rates of cancer survivorship in the United States, physical therapists in outpatient settings should expect...
to encounter and treat patients who are surviving cancer and have physical problems secondary to cancer treatments. Physical therapists who practice in general settings and in tertiary care settings, similarly, should be cognizant of important aspects of their patients’ cancer-specific medical histories.

Despite improvements in medical treatments for cancer, including surgical resection, radiation therapy, and chemotherapy, survivors of cancer often experience significant physical impairments and functional limitations during and after cancer treatments. These concerns include cancer-related fatigue (CRF), deconditioning, pain, muscle shortening and contractures, peripheral neuropathy, lymphedema, and genitourinary dysfunction. In addition, clinicians have discovered that certain physical limitations are consistently observed in patients with specific cancers. For example, urinary and sexual dysfunctions are common in men treated for prostate cancer, whereas upper extremity dysfunction and lymphedema are common in women with breast cancer; likewise, people with head and neck cancers may have difficulty with eating and speaking.

As the field of cancer rehabilitation develops and the number of therapists who treat patients with cancer or a history of cancer grows, understanding distinctions in the medical history of patients with cancer may improve patient care and contribute to our existing knowledge of medical issues as they relate to movement or functional impairments in patients with cancer. One particular study described clinical characteristics of patients with cancer referred for outpatient physical therapy, and explored patterns in frequency of impairments between type of cancer and mode of cancer treatment. Specifically, the authors sought to examine the frequency of cancer types, modes of cancer treatment, comorbidities, and impairments in patients with a variety of cancers. A retrospective medical record review was used to identify all patients referred for outpatient physical therapy over a 2-year period (from August 2008 to August 2010) at the University of Florida Davis Cancer Center. The patients referred to this clinic are primarily patients with cancer or with a history of cancer who are currently undergoing or previously underwent cancer treatment. A representative 3-month volume for this clinic was 122 new patients with cancer or a history of cancer and 7 patients who did not have cancer. Thus, on average, more than 90% of the new patients evaluated at this clinic fit these characteristics.

In a study published in April 2015 in *Physical Therapy Journal*, investigators sought the characteristics of patients with cancer that were referred for outpatient physical therapy. Over the course of two years, data from 418 patients were examined. Genitourinary and breast cancers were the most common types of cancer in their sample, and strength loss and soft tissue dysfunction were listed as the most common impairments. Lymphedema was the most common issue for people with breast cancer, and incontinence was the most common complaint for people that had genitourinary cancers such as prostate cancer. Pain and high fatigue levels were found to be prevalent in individuals that had undergone radiation therapy. This study demonstrated that therapy services are indeed being utilized for individuals that have survived cancer, particularly breast and genitourinary cancer. Yet, this study also suggested that a large portion of cancer survivors are not seeking out rehabilitation services, even though they would likely find it highly beneficial (Alappattu, 2015).

### Demographic and Clinical Information

<table>
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<tr>
<th>Data</th>
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<tbody>
<tr>
<td>Age (y), $\bar{X} \pm SD$</td>
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<td>57.9 ± 14.3</td>
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<td>Sex, female, n (%)</td>
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<td>Race, n (%)</td>
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<tr>
<td>Caucasian</td>
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<td>African American</td>
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<td>Hispanic</td>
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<td>Asian</td>
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<tr>
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<td>No. of physical therapy sessions, $\bar{X} \pm SD$</td>
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<tr>
<td>Metastatic, yes, n (%)</td>
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<tr>
<td>Recurrent condition, yes, n (%)</td>
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<tr>
<td><strong>Cancer type, n (%)</strong></td>
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<tr>
<td>Blood</td>
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<tr>
<td>Bone or joint</td>
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<td>Breast</td>
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<td>Head or neck</td>
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<td>Genitourinary</td>
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<td>Respiratory</td>
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<td>Skin</td>
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<tr>
<td>Soft tissue</td>
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<tr>
<td><strong>Referral source, n (%)</strong></td>
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<tr>
<td>Adult hematology-oncology</td>
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<tr>
<td>General medicine</td>
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<tr>
<td>Gynecologic oncology or obstetrics and gynecology</td>
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<tr>
<td>Neurosurgery or neurology</td>
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<tr>
<td>Orthopedic oncology or orthopedic surgery</td>
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<td>Otolaryngology</td>
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Pediatrics or pediatric hematology-oncology 13 (3.1)
Plastic surgery 1 (0.2)
Radiation oncology 228 (54.5)
Surgical oncology or general surgery 14 (3.3)
Urology 119 (28.5)
Unavailable 2 (0.5)

Comorbidities, n (%)  
Angina 3 (0.7)  
Anxiety or panic disorders 13 (3.1)  
Arthritis 64 (15.3)  
Asthma 25 (6.0)  
COPD or other pulmonary disease 21 (5.0)  
Degenerative disk disease 3 (0.7)  
Depression 26 (6.2)  
Diabetes 71 (17.0)  
Hearing impairment 5 (1.2)  
Heart attack 6 (1.4)  
Heart disease 58 (13.9)  
Hypertension 185 (44.3)  
Neurological disease 19 (4.5)  
Osteoporosis 5 (1.2)  
Peripheral vascular disease 8 (1.9)  
Stroke 15 (3.6)  
Upper gastrointestinal disease 43 (10.3)  
Visual impairment 15 (3.6)  

General Fitness and Cancer  
Physical activity is an economical, noninvasive approach for disease prevention advocated by public health agencies internationally. One-third of cancer deaths in the United States each year can be attributed to diet and physical activity habits, including being overweight and/or obese. Likewise, the number of deaths from cancer is lower in both men and women who are physically
fit compared to those who are more sedentary. This strongly suggests that physical activity affects cancer risk by helping individuals maintain a healthy body weight. This is accomplished by balancing caloric intake with energy expenditure, which has various beneficial effects on the immune system such as boosting the ability to fight diseases, contributing to higher energy levels. Adopting a physically active lifestyle involves making deliberate decisions and changing lifestyle patterns to engage in active rather than sedentary behaviors. The health benefits of physical activity in preventing cancer accumulate over the course of a lifetime – and although encouraging healthy activity patterns in childhood and early in life is important, increasing the level of physical activity at any age can reduce the risk of some cancers (Kushi, 2012).

Almost all of the evidence linking physical activity to cancer risk comes from observational studies where individuals report on their physical activity and are followed for years for diagnoses of cancer. Data from such observational studies can give researchers signs about the relationship between physical activity and cancer risk. However, such studies cannot definitively establish that being physically inactive causes cancer, or that being physically active protects against cancer, because physically inactive people may differ from their counterparts in ways other than their level of physical activity. Genetics and environmental and behavioral factors, rather than the variances in physical activity, could be other possible explanations (NCI, 2017).

That said, exercise has a number of biological effects on the body which may reduce the risk of specific cancers. Exercise can lower the levels of hormones, such as insulin and estrogen, and of certain growth factors that have been associated with cancer development and progression in the breast and colon. Exercise can modify the metabolism of bile acids, resulting in decreased exposure of the gastrointestinal tract to these suspected carcinogens as seen in colon cancers. Increased activity can reduce the amount of time it takes for food to travel through the digestive system, which decreases gastrointestinal tract exposure to possible carcinogens also related to colon cancers.

In fact, colon cancer is one of the most extensively-studied cancers in relation to physical activity. A meta-analysis of 52 epidemiologic studies examining the association between physical activity and colon cancer risk found that the most physically active individuals had a 24% lower risk of colon cancer than those who were the least physically active (NCI, 2017).

Likewise, numerous studies suggest physically active women, both premenopausal and postmenopausal, have a lower risk of breast cancer than inactive women. In a 2013 meta-analysis of 31 prospective studies, the average breast cancer risk reduction associated with physical activity was 12% (NCI, 2017). Another study showed a probable association between physical activity and postmenopausal breast cancer risk. It was supported by more than 100 epidemiologic studies, with strong biologic rationale supporting fat loss as an important mediator of this association. The researchers found that a dose-response effect of exercise on total fat mass and several other adiposity measures including abdominal fat, especially in obese women, provide a basis for encouraging postmenopausal women to exercise at least 300 minutes per week to potentially lower risk of postmenopausal breast cancer (Friedenreich, 2015).
Many studies have examined the relationship between physical activity and the risk of endometrial cancer. In a meta-analysis of 33 studies, the average endometrial cancer risk reduction associated with high versus low physical activity was 20%. Some evidence exists that the association between physical activity and endometrial cancer risk may reflect the effect of physical activity on obesity, which is a known risk factor for endometrial cancer (NCI, 2017).

Gastric cancer is the fourth most common cancer worldwide, and the second leading cause of cancer-related mortality, causing more than 700,000 deaths annually. There have been several studies reporting an inverse association between physical activity and risk of gastric cancer. In one particular study a systematic review was performed with meta-analysis of observational studies that investigated the association between physical activity and risk of gastric cancer. The authors identified 16 studies reporting 11,111 cases of gastric cancer among 1,606,760 patients. Meta-analysis demonstrated that the risk of gastric cancer was 21% lower among the most physically active people as compared with the least physically active people with moderate dissimilarities among studies. The study concluded that the meta-analysis of published observational studies indicated that physical activity is associated with reduced risk of gastric cancer and that in addition to a numerous of other health benefits, lifestyle interventions focusing on increasing physical activity may decrease the global burden of gastric cancer (Cancer Prev Re 2014).

Less is known about whether physical activity reduces risk of other cancers, which, together, constitute 75% of cancer incidents in the United States and 61% of cancers worldwide. In another study, authors examined leisure-time physical activity in relation to the risk of 26 different cancer types in a pooled analysis of 12 prospective cohort studies and 1.44 million participants. Various levels of leisure-time physical activity were associated with lower risks of 13 cancers:

- Esophageal
- Adenocarcinoma,
- Liver
- Lung
- Kidney
- Gastric cardia (a form of stomach cancer that occurs in the top portion of the stomach near the junction of the esophagus)
- Endometrial
- Myeloid
- Myeloma
- Colon
- Head and neck
- Rectal and bladder
- Breast

The conclusion reached by the researchers was that leisure-time physical activity was associated with lower risks of many cancer types. Health care professionals, including physical therapists,
counseling inactive adults should emphasize that most of these associations were evident regardless of body size or smoking history, supporting broad generalizability of findings (JAMA Intern Med., 2016).

Exercise as an Intervention in Treating Cancer

Exercise guidelines have long existed for the general population. However, with the increased awareness of exercise’s effects on cancer, experts in both fields have come together in an effort to produce exercise information for those professionals working with this special population. Numerous societies and organizations are active, via research and synthesis, in developing exercise guidelines for the treatment and prevention of cancer. For example, the American Cancer Society (ACS) publishes Nutrition and Physical Activity Guidelines, which serve as a foundation for the communication, policy, and community strategies that optimally affect dietary and physical activity patterns among Americans. These Guidelines, updated every 5 years, are developed by a national panel of experts in cancer research, prevention, epidemiology, public health, and policy. They were last revised in 2017, based on synthesis of the most recent scientific evidence on diet and physical activity in relation to cancer risk (ACS, 2017). In conjunction with the information and recommendations provided by the ACS, as well as the American Heart Association (AHA), the American College of Sports Medicine (ACSM) compiles guidelines for the rehabilitation professional; the most recent version was assembled in 2010 (Schmitz et al, 2010). Staying current on these literature updates allows the physical therapist to review and apply the most recent evidence regarding the effectiveness of exercise in cancer treatment, as well as the role exercise has in the prevention of cancer.

As we’ve discussed, while colon and breast cancers have the most compelling body of evidence connecting exercise to cancer prevention, current literature suggests that exercise programs can reduce the risk of several types of endometrial cancer, as well as advanced prostate and possibly pancreatic cancer. Researchers also suspect exercise may also play a role in lowering the risks of lung, non Hodgkin’s lymphoma, ovarian, testicular, and uterine cancers (Watson, 2004). The effect of exercise on preventing several forms of cancer helps to demonstrate the importance of the rehabilitation professional’s involvement in the treatment of patients with cancer. In addition, due to recent research, the use of exercise as a promising adjunct therapy for cancer treatment-related symptoms continues to gain attention and support in oncology rehabilitation.

For example, because of its effectiveness in preventing or reducing fatigue, literature supports the use of an exercise program as an adjunct therapy for cancer-related fatigue (CRF), weight loss, weight gain, general weakness, and to enhance overall quality of life (QOL) (Watson, 2004). In fact, while still significantly underutilized, an exercise program formulated by a rehabilitation professional is one of the few interventions proposed to diminish CRF, along with various psychosocial symptoms. In one meta-analysis of 113 unique studies it was found that exercise interventions, psychological interventions, and the combination of both reduced cancer-related fatigue during and after cancer treatment. Reduction was not due to time, attention, or education. In contrast, pharmaceutical interventions did not improve cancer-related fatigue to the same magnitude. The researchers concluded that clinicians should prescribe exercise or psychological interventions as first-line treatments for CRF (Mustian, 2017). As we’ll discuss
again later in the course, exercise has also been found to be an effective intervention for reducing CRF in patients with Hodgkin’s disease, prostate cancer, and breast cancer. Further, resistance exercise has been shown to reduce fatigue and improve quality of life and muscular fitness in men with prostate cancer receiving androgen deprivation therapy (Segal, 2003; Jones & Alfano, 2013).

Compelling evidence from recent studies suggests that regular physical activity in the months following treatment for colorectal cancer may decrease the risk of recurrence and death. In an Australian study patients showed that the probability of surviving for 10 years post-diagnosis was 73% for the patients who exercised regularly prior to the cancer diagnosis, compared to 54% among those who did not exercise (Goldman, 2011). Similar studies have shown that patients with early- to later-stage colorectal cancer without distant metastases who engaged in regular activity after diagnosis decreased the likelihood of cancer recurrence and mortality by 40-50% or more compared with patients who engaged in little to no activity (National Cancer Institute, 2006). In another study of 2,293 colorectal cancer survivors, adherence to the recommendation of 150 minutes or more of moderate-intensity physical activity per week was associated with lower risk of all-cause and cardiovascular disease mortality. This study is the first to show an association between more leisure time spent sitting and a higher risk of mortality among colorectal cancer survivors (Campbell, 2013).

Section 2: Common Therapeutic Interventions to Cancer and their Relevance to Physical Activity

To provide optimal rehabilitative guidance to cancer survivors in terms of activity and exercise, clinicians need to have an understanding of the common therapeutic approaches to cancer. Through an understanding of these treatments it is possible to appreciate the body systems adversely affected and the positive or negative implications for exercise tolerance.

Remain mindful that, for persistent adverse side effects of cancer treatment, there may also be predisposing host factors including age, gender, and other co-morbid health conditions which combine to influence the incidence and severity of the disease. Generally speaking, the adverse effects of cancer treatments may be immediate, occurring during a period of days or weeks, or even after months or years. Persistence of cancer and cancer treatment effects can be described as both “long-term” and “late.” Long-term effects are side effects or complications that begin during or shortly after treatment and continue afterward for which the cancer survivor must compensate. Late effects are distinct from long-term in that they appear months or years after treatment completion (American Cancer Society, 2018).

Cancer Surgery

Cancer surgery can be more or less invasive depending on the location of the surgery and amount of involvement to nearby organs. Preventive surgery is performed to remove body tissue that is likely to become cancerous, even though there are no signs of malignancy present at the time of medical intervention, such as the surgical removal of pre-cancerous polyps from the colon. The
procedure may also have a curative goal, whereby the tumor(s) and diseased tissue are removed while preserving as much non-diseased tissue as possible. Surgery for cancer can be the sole form of intervention, but it is often combined with other forms of treatment such as chemotherapy and radiation. For example, approximately one-half of cancer patients who are surgical candidates also undergo radiation which may be performed before or after the surgery (American Cancer Society, 2018).

A third type of surgery, debulking surgery, involves removing part but not all of the cancer. This type of surgery is used to treat problems caused by a more advanced cancer. It is performed in situations where removing the entire cancerous tumor would cause too much damage to an involved organ or nearby tissues, such as often is the case with ovarian cancer. The surgeon may remove as much of the tumor as possible and attempt to treat the remaining malignant tissue with radiation or chemotherapy (American Cancer Society, 2018).

Many side effects of cancer surgery are similar to those of other surgical procedures, and generally depend on the location and extent of the surgery. For example, breast surgery, one of the most common surgical cancer interventions, can result in pain and tenderness to the region of the surgical site. Depending on the extent of the surgery, (i.e. partial versus radical mastectomy), the removal of a significant amount of breast tissue can result in a woman's weight shifting, creating a sense of being off-balance, which can cause additional strain and discomfort in the neck and back (Meretoja, 2014). In the presence of scar tissue, skin around any cancer excision site is likely to become less supple and flexible. To return to breast surgery, after mastectomy, the skin in the area may become tight, which can also result in less mobility in the muscles of the anterior chest, shoulder, and arm with associated negative changes in range of motion and strength. Surgical treatment of cancer can also cause changes in sensation, resulting in numbness or tingling, over the surgical region.

Cancer surgery can potentially cause changes to the body that lead to cancer-related fatigue (CRF). While in the body, some cancers release proteins called cytokines, understood to cause fatigue. Following the cancer’s effect and its removal, the body's need for energy can increase, which in conjunction with weakened muscles may further contribute to fatigue. Pain prior to and following cancer surgery can cause an individual to be less active, eat less, sleep less, and become depressed, all of which may add to CRF: unrelenting postoperative pain occurs in as many as 50% of surgical patients (American Cancer Society, 2018).

Lymphedema, the build-up of lymph fluid in the fatty tissues directly under the skin, can be a result of cancer, cancer treatments, tumors, diseases, or anything that changes or damages the normal, healthy lymph system. The excess of lymph causes swelling, or edema, most often in the arms or legs but potentially also the face, neck, abdomen, and genitals. In the event that lymphedema is a side effect of cancer surgery, it is referred to as secondary lymphedema (Kuerer, 2009).

Diarrhea and/or loose stools are a common side effect from cancer surgery involving the intestinal region. In particular, they are often experienced after colon cancer surgery, which removes a part of the colon during the excision of the cancer, shortening its length and
decreasing the amount of time stool sits in the colon. Thus the colon absorbs less water from the stool, resulting in the passage of loose or watery stools. Depending on the extent of the surgery, nerve damage is also of concern as a side effect of colon cancer surgery (States News Service, 2017). In some cases, colon cancer patients undergo a colostomy: a surgery that re-routes the movement of digested food and moves the colon out through the abdominal wall.

**Surgical Cancer Biopsy**

Surgery is not only a form of treatment for cancer; it also plays a key role in diagnosing and staging the disease. In some cases the tumor may need to be partially or totally removed to facilitate this process. If not contraindicated, biopsies, or minor operative procedures to take tissue samples, usually involve less risk than a more complex surgery. The physician may recommend a biopsy when any initial cancer screening or testing suggests an area of tissue abnormality. Examples include a mole on the skin which has changed shape recently, indicating the possibility of melanoma or a mammogram displaying a lump or mass, indicating the possibility of breast cancer. The tissue samples are used for diagnosis, and may also help determine whether the cancer originated: at the site of the biopsy sample, or somewhere else in the body. Sites that are commonly biopsied include the breast, skin, bone marrow, GI tract, lung, liver, bladder, colon, and lymph nodes.

Some biopsies are performed endoscopically; others under image guidance, such as ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI) in the radiology suite. The method of biopsy is based on several factors, such as the size, shape, location, and characteristics of the abnormality. Pain at the biopsy site is the most common post-operative complaint, along with the possibility of infection at the site and reactions to the drugs used as a local anesthesia (Cancer Treatment Centers of America, 2018).

**Chemotherapy**

Chemotherapy, defined as the use of drugs to treat cancer, interacts closely with the cell cycle. It works only on cells that are in the actively reproducing phase of the cycle, rather than those in the resting phase. However, when chemotherapy drugs attack reproducing cells, they do not differentiate between cancer cells and those of normal tissues. Thus, each chemotherapy session involves determining the balance between destroying the cancer cells and sparing the normal cells. Damage to normal cells, which causes pain, weakness, and fatigue, is a primary cause of side effects.

Certain chemotherapy drugs can damage bone marrow, affecting the production of red blood cells. A low red blood cell count, or anemia, produces symptoms of fatigue and shortness of breath, and can lead to serious complications such as reduced oxygen in the blood, requiring higher demands on the heart to pump sufficient oxygen to the organs. Cardiac-related symptoms include arrhythmia, shortness of breath, and chest pain, all which may delay the schedule of chemotherapy treatments. Anemia can be relieved with a blood transfusion or with medication. Also caused by chemotherapy or other medications, a low white blood cell count – indicated by a low level of neutrophils (neutropenia) – can increase the risks of infection for the chemotherapy patient.
Low numbers of platelets in the blood, or thrombocytopenia, can cause bleeding, varying in severity from mouth/gum blood loss to more severe and threatening internal hemorrhaging (Niederhuber JE, et al., 2014). The most common cause of thrombocytopenia in people with cancer is bone marrow suppression related to chemotherapy: it destroys rapidly dividing cells, such as those in the bone marrow which become platelets. Thrombocytopenia related to chemotherapy is often a short term problem.

CRF is reported to affect 70-100% of patients receiving chemotherapy. Although the exact pathology of CRF is uncertain in chemotherapy, the course and progression of malignancy itself may have some part in this symptom, as well as the results of treatment-related anemia. Patients commonly report joint mild pain following chemotherapy which usually diminishes within a few weeks: this is a particular problem with various chemotherapy agents including the taxanes (taxol and taxotere). An additional side effect is diminished appetite and change in taste perception of familiar foods, which can result in weight loss. Nausea and diarrhea, which both can cause marked weakness and fatigue, are related concerns (National Cancer Institute, 2017).

**IMAGE 1**

**Radiation**

Approximately one-half of all cancer patients receive some type of radiation therapy during the course of their treatment. Radiation therapy uses high-energy radiation to kill cancer cells by damaging their DNA, stopping their division or causing cell death. Like chemotherapy, radiation therapy can damage normal cells as well as cancer cells, and treatment is carefully planned to minimize side effects. The radiation used for cancer treatment may come from a machine outside the body, called external-beam radiation therapy, or may originate from radioactive material placed in the body near tumor cells or injected into the bloodstream, termed internal radiation therapy or Brachio therapy (National Cancer Institute, 2017). Radiation therapy can be delivered before, during, or after surgery, depending on the type of cancer being treated; patients may receive radiation therapy only, or in combination with chemotherapy. It may be used with the intent of curing a cancer by eliminating a tumor, or preventing cancer recurrence, or both. It can also be delivered with palliative intent, to relieve symptoms and reduce the suffering caused by cancer (American Cancer Society, 2018).

Early side effects of radiation may be seen a few days or weeks after treatments have initiated and may continue for several weeks after treatments have concluded; other effects may not present until months, or even years, later. As with previously-discussed interventions, CRF is a common early effect of radiation. Although the specific cause is unknown, tumors can cause the immune system to make substances that lead to fatigue; it may also be caused by anemia, poor nutrition, pain, drugs such as steroids or chemotherapy as an adjunct therapy, depression, and stress. Later effects of radiation may include thinning of the skin in the area treated, which is of concern as it impacts wound healing. As in the previous example, since radiation is a local treatment, many side effects depend on the area of the body being treated. For example, mucositis, an inflammation inside the mouth, is a potential short-term side effect when radiation
is given to the head and neck region; symptoms usually improve within weeks after treatments are completed (American Cancer Society, Treatments and Side Effects, 2018).

**IMAGE 2**

**Targeted Therapy**

Research in genetics, and gene changes in cells impacted by cancer, has led to the development of newer drugs that specifically target these gene changes. Targeted therapy drugs work differently from standard chemotherapy drugs: they are often able to attack the cancer cells’ genetic programming while doing little damage to normal cells. These drugs commonly have different (and usually less severe) side effects than traditional chemotherapy drugs. Cancers that may be treated with targeted therapy include types of lung, pancreatic, head and neck, liver, colorectal, breast, and kidney cancers. Future focus and advances against cancer will likely come from this area of cancer intervention (National Cancer Institute, 2014).

Most targeted therapies treat cancer by interfering with specific proteins that help tumors grow and spread throughout the body. This form of therapy aids and boosts the immune system in finding and destroying cancer cells. Some targeted therapies interfere with the division of cancer cells, while others are designed to interfere with the blood supply to a cancerous tumor, controlling its growth and size. In general, targeted therapies are either small-molecule drugs or monoclonal antibodies. Small-molecule drugs, as their name suggests, are small enough to enter cells with little difficulty, and therefore are used for targets inside cancer cells. Monoclonal antibodies are larger drugs that are not able to enter cells easily, and instead attach to specific targets on the outer surface of cancer cells. Some monoclonal antibodies are combined with toxins, chemotherapy drugs, and radiation prior to attaching to a target: the cancer cells take up the cell-killing substances, causing them to die, while untargeted cells are unharmed.

Dependent on the type of treatment received, targeted therapy can cause side effects, the most common of which include diarrhea and liver problems. Other side effects – treatable by medicines – are complications with blood clotting, wound healing, high blood pressure, fatigue, and skin problems. Most side effects of targeted therapy go away after completion of the treatment (National Cancer Institute, 2014).

**Stem Cell Transplant Therapy**

Stem cell transplant therapy is another procedure, used to restore blood-forming stem cells in patients who have had theirs destroyed by very high doses of chemotherapy and/or radiation therapy. Although not working against cancer directly, these procedures restore white and red blood-forming stem cells and platelet stem cells, helping the cancer patient recover their ability to produce stem cells after treatment. The stem cells used in transplants can originate from the bone marrow, bloodstream, or umbilical cord; the donor may be a blood relative, but can also be a person who is not related. Transplants can be autologous, meaning the stem cells come from the patient; allogeneic, meaning the cells come from another individual; or syngeneic, meaning the cells come from an identical twin if available. During a stem cell transplant, the individual receives healthy blood-forming stem cells through a needle intravenously. Once in the
bloodstream, the stem cells travel to the bone marrow, where they replace the cells destroyed by treatment. In some cases, stem cell transplants can directly impact cancer, due to an effect called graft-versus-tumor that can occur after allogeneic transplants. Graft-versus-tumor occurs when white blood cells from the donor attack any cancer cells that remain in the host’s body after high-dose treatments, thereby improving the success of the treatments. These treatments are most often used with patients with leukemia, lymphoma, neuroblastoma, and multiple myeloma. Ongoing clinical trials for other types of stem cell cancer treatments are being studied.

Prior to stem cell transplant, side effects from the high doses of cancer treatment include fatigue, bleeding, and an increased risk of infection. Post-allogenic transplant, there is a possibility of developing a complication called graft-versus-host disease. Graft-versus-host disease generally occurs a few weeks after the transplant, when white blood cells from the donor recognize normal cells in the host’s body as foreign and attack them. This can cause damage to skin, liver, intestines, and many other organs. It is treated with steroids or other drugs that suppress the immune system. The more closely the donor’s blood-forming stem cells match the patient’s, the less likely they are to develop graft-versus-host disease (National Cancer Institute, 2015).

Section 3: Considerations in the Evaluation and Development of an Exercise-Based Treatment Plan

Cancer treatment causes significant debilitation, which leads to reduced physical function and impairs quality of life. Negative effects have been observed across the spectrum of treatment types, from surgery, to radiation, to hormonal treatment and targeted therapies. For example, aerobic capacity, an important indicator of physical fitness and function, has been shown to decrease by 10-33% over a 12-week period of chemotherapy for breast and other cancers. Almost one-third of breast cancer survivors have aerobic capacity below the minimum physiologic threshold required for functional independence.

The declines in physical capacities and physiologic function that are commonly observed in cancer patients can be minimized or prevented with a well-thought out progressive program of restorative exercise. A substantial body of evidence demonstrates that exercise improves a variety of objectively measured and self-reported outcomes. To focus on just a few, exercise during and following treatment has been associated with reductions in cancer recurrence and disease-specific mortality rates of 30-60% in breast and colorectal cancers. Exercise also has been found to prevent or improve many treatment-related negative effects such as fatigue, muscle weakness, declines in cardiovascular function and overall functional ability, neuropathy, altered body composition, and reduced quality of life.

Despite a growing body of evidence for the benefits of exercise for cancer survivors, 80% of oncology care providers, including nurses and physicians, have reported being unaware of the availability of exercise guidelines in this setting, and lack knowledge about when to implement them and where to refer survivors for exercise programs. As a result, few cancer survivors receive formal information about exercise, a referral to physical therapy, or even direction to an appropriate community-based exercise program. To provide optimal care during and following...
treatment, healthcare providers should refer cancer survivors to programs of restorative exercise to reduce their fatigue, weakness, pain, and (in some patients) risk for lymphedema, and to improve their overall functional ability (Schwartz, 2017).

One of the main focuses of an exercise prescription is to regain and improve overall function and quality of life. To do so, as with any plan of care, the clinician must have clear and concise objectives, which lead to realistic, specific goals for the cancer patient. Common objectives, such as those next discussed, rely on the clinician’s ability to focus on bodily systems (i.e. musculoskeletal, hematologic, etc.), taking into account how each is affected by the cancer and subsequent treatment.

**Increasing Strength**

Similarly to any rehabilitative patient afflicted with weakness, strength training helps maintain and build muscle, an extremely important objective and goal for cancer patients. Both the disease process and the treatment of the cancer can result in a reduction of overall strength and loss of lean body tissue, which negatively affects health-related quality of life. Side effects of cancer treatment often include muscle wasting or atrophy. Likewise, a decrease in physical activity levels – commonly associated with other side effects, such as loss of appetite – can intensify muscular wasting and consequently loss of overall body strength, leading patients to experience a negative spiraling effect that further exacerbates the sense of fatigue. All of these effects are of significant concern to the physical therapist treating the cancer patient.

In addressing the cancer patient’s overall strength, the physical therapist can help to counter side effects by reducing fatigue, improving mood, building muscle mass, and reducing body fat. Many of these patients are unfamiliar with strength training exercises, and are often surprised by the fact that a strengthening program can use minimal equipment, consisting solely of isometric exercises, resistance bands, and light weights. As mentioned above, the muscle weakness and atrophy resulting from chemotherapy and/or prolonged bed rest often result in a loss of muscle mass. For example, this is typically seen in gastrointestinal and head and neck cancers to the extent that transfers from sit to stand become a major effort. In these cases, strengthening exercises promote and build lean muscle. In contrast, patients undergoing systemic treatments for breast cancer often show significant weight gain. In those patients, strengthening exercises become important for controlling body weight and losing fat, and generally getting back a healthy body mass index.

The literature supports the efficacy of strength training in cancer patients. Strasser et al. produced an analysis of the research suggesting that cancer survivors who lift weights and do other resistance exercises improve both arm and leg muscles. The analysis looked only at randomized controlled trials, and included studies on resistance training among cancer patients and survivors. The researchers identified 11 relevant studies that included almost 1,200 people. Each study, consisting of mostly breast and prostate cancer patients and survivors, compared a resistance training group to a control. The duration of resistance training exercises varied from 3 months up to a year, with most participating in two training sessions a week. Collectively, it was found that members of the resistance training groups had gained significant gains of muscle
strength in both their arms and legs, lifting an additional 32 pounds in their legs and 15 pounds in their arms as compared to the non-resistance training groups. The strongest gains in arm muscles were found when the participants lifted weights at low intensity, suggesting that lifting a lower-weight dumbbell for more repetitions may be more effective than a heavier dumbbell for shorter reps (Strasser et al. 2013).

In a study by Segal et al., researchers looked at the effects of resistance exercises on a group of 155 men with prostate cancer treated with androgen deprivation therapy (ADT), which can cause side effects of fatigue, functional decline, increase in body fat, and a loss of lean body tissue. The group was scheduled to receive cancer treatment for at least three months. 82 of the men were randomly assigned to an intervention group that participated in a resistance exercise program three times per week for twelve weeks, while the other 73 men were assigned to a waiting list control group that did not involve any form of exercise. After the twelve weeks, the primary outcomes measured by the researchers were fatigue and disease-specific quality of life (via a self-reported questionnaire); secondary outcomes were defined as muscular fitness and body composition measured by changes in body weight, body mass index, waist circumference, or subcutaneous skinfolds. The results showed that men assigned to the intervention group had less interference from fatigue on activities of daily living and a higher quality of life than men in the control group. Men in the intervention group also demonstrated higher levels of upper body and lower body muscular fitness than men in the control group. Researchers concluded that resistance exercise reduces fatigue and improves quality of life and muscular fitness in men with prostate cancer receiving androgen deprivation therapy, and that this method of exercise can be an important component of supportive care for these patients (Segal et al., 2003).

In a similar study, a group of men aged 59-82 years and undergoing ADT participated in progressive resistance training for 20 weeks in a university exercise rehabilitation clinic. The results showed the men had increased their strength, physical function, and balance. Moreover, the study demonstrated that resistance training preserves body composition and bone mass to reduce treatment side effects (Schwartz, 2017). Research further suggests that resistance training should be provided during the first 12 months of ADT, to counteract the side effects of both the treatment, which are most severe during this time span, and the disease itself.

In another study, Hardee et al. examined the independent associations of leisure-time aerobic physical activity and resistance exercise on all-cause mortality in cancer survivors. The study consisted of 2,863 male and female cancer survivors, aged 18 to 81 years, who received a preventive medical examination while enrolled in an aerobics center in Texas. Physical activity and resistance exercise were assessed by self-report at the baseline medical examination. The researchers stated that increased levels of physical activity were found to improve health outcomes after cancer diagnosis. However, their study looked more specifically into which type of physical activity was to be considered more beneficial for long-term cancer survival. In the study, cancer survivors who reported performing resistance exercise at least once per day of the week had a 33% reduction in all-cause mortality compared with individuals who did not report participation in resistive exercise (Hardee et al., 2014).

**Improving General Flexibility**
Necessary for balance and activities of daily living, flexibility allows greater freedom of movement and enhances body awareness and proprioception. Improving flexibility is important for cancer patients, especially after surgery or long periods of inactivity, and provides a range of benefits during treatment, recovery and remission. Importantly, flexibility exercises can usually be implemented despite extreme fatigue, weakness, and potential breathing difficulties.

Flexibility exercises help manage the side effects of treatment, such as muscle spasm and tightness, along with assisting in the management of potential post-exercise muscle soreness & tension resulting from an exercise program. Additional benefits include enhancing the patient’s muscle performance by maintaining and increasing joint range of motion: weight-bearing and non-weight bearing joints alike will articulate more effectively and efficiently when the related muscles and tendons have adequate flexibility. Flexibility exercises also assist in reducing the risk of injury and incidence of low back pain, and have been reported to improve posture and muscle coordination, relieve psychological stress and tension, and promote physical and mental relaxation (Kushi, 2012; Schmitz, 2010).

The efficacy of flexibility exercises can easily be seen when considering the case of breast cancer patients and survivors. Although advances in the medicinal treatments available to women diagnosed with breast cancer have resulted in improved survival rates, they are often associated with adverse effects on physical function. Treatments can continue for up to a year, consisting of various modalities such as surgery, chemotherapy, radiation therapy, and reconstruction, all of which may contribute to soft tissue inflexibility leading to diminished arm function. Because of both the protracted time frame and the unique nature of cancer treatment, some adverse effects such as delayed soft tissue healing and/or painful mobility contribute to early arm and shoulder impairments. Others complications leading to impairments, such as adhesive capsulitis of the shoulder (i.e. frozen shoulder), can occur months, or even years, after treatment is withdrawn. Loss of range of motion and pain due to axillary web syndrome (also known as cording) sometimes develops as a side effect of lymph node biopsy or axillary lymph node dissection. This can lead to difficulty with activities of daily living by impacting overhead reaching and lifting, carrying objects, caring for family, and returning to work. As a result of these impairments, women often reduce their activities after treatment, leading to poor activity tolerance and diminished quality of life.

Researchers McNeely et al. conducted a systematic review investigating the effectiveness of exercise, including addressing inflexibly, to reduce shoulder and upper extremity morbidity throughout breast cancer treatment. The review included randomized controlled trials based upon the following outcomes: upper extremity range of motion (ROM), muscular strength, lymphedema, and pain. Types of therapeutic exercises included active ROM or active-assisted ROM, passive ROM/manual stretching, stretching exercises, and strengthening or resistance exercises. 24 studies involving 2,132 participants were included in the review. Ten of these studies examined the effect of early (1–3 days) versus delayed implementation of postoperative exercise: early exercise was more effective than delayed exercise in the short-term recovery of shoulder flexion ROM. The other fourteen studies examined the effect of structured exercise when compared with usual care (for instance, an informational pamphlet) or comparison
interventions (for example, independent exercise). Of these, six were postoperative, three during adjuvant treatment, and five following cancer treatment. Structured exercise programs in the postoperative period significantly improved shoulder flexion ROM in the short term. Physical therapy treatment yielded additional benefit for shoulder function immediately after surgery and at the 6-month follow-up. Also of clinical importance, there was no evidence of increased risk of lymphedema from exercise at any point in time (Galantino, 2013).

Reducing Fatigue

As we’re repeatedly stressed, cancer-related fatigue (CRF) is a common challenging symptom for the patient and rehabilitation professional alike. It has been reported in 40-100% of patients undergoing cancer treatment. In one study, 82% of patients experienced fatigue after their first treatment cycle and 77% reported fatigue after their second cycle. Other reports state as many as 70% of cancer patients reported that fatigue “significantly” or at the minimum “somewhat” affected their daily routine (National Comprehensive Cancer Network, 2018).

The underlying etiology of cancer-related fatigue is not well understood, but it is believed to be a multidimensional symptom associated with physical, mental, and emotional factors. CRF may be primarily due to the disease process, or caused by the cancer treatment and associated sequelae such as treatment-related anemia, a complication commonly experienced in the rehabilitative process. The cause of this anemia is also multifactorial, and can include bone marrow involvement, blood loss, and nutritional deficiencies as well as the side effects of radiotherapy and chemotherapy. Anemia can also be secondary to co-morbidities the patient may be experiencing, such as gastrointestinal bleeding, advancement of the malignancy, or a result of bone marrow toxicity secondary to chemotherapy. Individuals are classified as anemic when their hemoglobin levels are lower than 12 g/dL (National Comprehensive Cancer Network, 2018). To illustrate the extent of treatment-related anemia’s occurrence: a report by Glaspy et al. documented that more than one third of the nearly 4,300 patients in their study became anemic after three cycles of chemotherapy (Watson, 2004). Interestingly, it is also proposed that cognitive-behavioral factors, including cognitive or emotional responses to fatigue and coping strategies used by the individual, may maintain CRF during survivorship (Corbett, 2017).

IMAGE 3

In the past, rehabilitative clinicians have treated fatigue with rest. In contrast, current research shows this may actually worsen the problem over a long period of time. A comprehensive literature review by Cornea and colleagues examined the role of exercise in the management of fatigue following a cancer diagnosis. The included seven studies focused on the relationship between fatigue and aerobic exercise or fatigue and general fitness. Exercise interventions combined with control groups were initiated during treatment in five studies and post treatment in two studies. Throughout the treatment range (2 weeks-6 months), four of the studies were supervised in a clinical setting whereas 3 were home-based programs. Fatigue was measured by various self-report scales or clinical observation; hemoglobin levels were also assessed in one of the studies. Overall, the results demonstrated that increased physical exercise is associated with less fatigue during and after cancer treatment. Increased fatigue from pre- to post-intervention
was noted in the non-exercise control group, and higher hemoglobin levels and lower fatigue was found in the exercise group compared to the control group at post-intervention. The study also revealed less fatigue experienced by those who adhered to the exercise intervention compared with those who did not (National Cancer Institute, 2018).

Improving Cardiorespiratory Function

Exercise prescription focused on improving general cardiorespiratory function has been found to be beneficial to individuals undergoing cancer treatment. Generally, the literature suggests that aerobic exercise, following cancer diagnosis and in conjunction with cancer treatment, can have a positive effect on physical functioning and quality of life. For persons undergoing chemotherapy or radiation treatments, which exhaust physical and emotional reserves, moderate-intensity aerobic exercise training should be performed to maintain endurance, strength, and function (National Center on Physical Activity and Disability 2009). Moderate-intensity aerobic exercise training may also offer profound psychological benefits for persons in cancer therapy, particularly with regard to depression (National Center on Health, Physical Activity and Disability, 2018).

In one particular study, six weeks of aerobic exercise performed at 80% of maximal heart rate for 30-35 minutes, five days per week, reduced fatigue in women being treated for cancer. Improving cardiovascular function also elevates mood, offering drug-free relief for the feelings of depression that may accompany a cancer diagnosis. In another study, 10 weeks of aerobic exercise at 60% of maximum heart rate for 30-40 minutes, four days per week, reduced depression and anxiety in female cancer patients. Addressing cardiovascular fitness can also help control weight, a critical factor, as studies have shown that gaining weight during and after treatment raises the risk of a cancer recurrence, particularly for breast, colon and prostate cancers (Schmid, et al, 2014).

One review of the literature consisted of several randomized clinical trials, the vast majority of which used an aerobic exercise intervention in the form of walking or cycling. Within the eighteen studies reviewed, twelve studies focused exclusively on women with early stage breast cancer, and six studies used subjects with hematological malignancies. The exercise outcome measures were levels of physical functioning including a 6 and 12-minute walk test, cycle test (including supervised cycle ergometer), and treadmill tests. Recorded symptoms that were nausea, depression, anxiety, sleep disturbances, fatigue, and emotional distress. After completing the exercise program consisting of 3 times weekly for 10-12 weeks, women with breast cancer reported less nausea, increased functional capacity, and higher maximal oxygen uptake during exertion. Compared with the control groups it was also noted that the exercise group had a reduction in fat mass, and increased lean body mass. The studies suggested that survivors of breast cancer who engage in regular aerobic related exercise will maintain a higher quality of life as compared to those who do not exercise (Visovsky 2005).

Interestingly, all of the types of physical activity we’re previously discussed can also have a positive effect on the cancer survivor’s cardiovascular system. One particular study by Rahnama et al. investigated the effects of exercise training on maximum aerobic capacity, resting heart rate
(RHR), blood pressure, and anthropometric variables (measurable characteristics of the body that can be defined, standardized, and referred to a unit of measurement) in postmenopausal women with breast cancer. Twenty-nine women with breast cancer who received surgery, chemotherapy, and radiotherapy with current hormone therapy were divided into two groups; intervention and control. Subjects in the intervention group performed 15 weeks of combination exercise training including walking for 25-45 minutes (2 sessions per week) and resistance training for 60 minutes (2 sessions per week on days distinct from walking days). In pre and post tests, VO2max, RHR, blood pressure, body weight, body mass index (BMI) and waist to hip ratio (WHR) were measured in both groups. The study found substantial differences for VO2max, RHR, body weight, BMI and WHR between intervention and control groups after 15 weeks. Exercise training had positive effects on the VO2max, RHR, body weight, BMI and WHR in postmenopausal women with breast cancer. No significant different was found for blood pressure between two groups. It was concluded that exercise training may improve maximum aerobic capacity, RHR and anthropometric variables in postmenopausal women with breast cancer (Rahnama et.al. 2010).

In a related study, a randomized controlled trial tested the effects of a specially designed strength and endurance training on the independence and quality of life in lung cancer patients during palliative chemotherapy. 46 patients were randomized into two groups receiving either conventional physical therapy or special physical therapy training. Methods used were a questionnaire, the 6-Minute Walk Test, stair walking, the Modified Borg Scale, and assessing muscle strength. 29 patients completed the trial, and followed up by answering the Barthel Index of Activities of Daily Living questionnaire. The results of this questionnaire showed the training program had a positive impact on the patient’s independence in carrying out activities of daily living. In addition, the physical training had a positive effect on the patients’ endurance and strength capacity. This study demonstrated that even lung cancer patients receiving a palliative chemotherapy treatment can benefit from endurance training as a physical activity intervention (Henke et al 2014).

**Psychosocial Outcomes**

Cancer treatments (i.e. surgery, chemotherapy, radiotherapy) can extend from months to years and potentially reduce quality of life which includes one’s psychosocial well-being. Common psychological and emotional patterns seen in cancer and the treatment of the disease include depression, anxiety, stress, body-image concerns, decreased self-esteem, and loss of a sense of control. Although the afore-mentioned side effects tend to peak during treatment, psychological and emotional therapy-related symptoms may persist months or years following treatment.

Another major goal of a prescribed exercise program for cancer is to improve body image and thereby improve quality of life. Cancer patients may often undergo extensive surgery or receive treatments that can alter physical appearance and change the patients’ feelings about how other people view them. Some cancers are usually associated with loss of weight and muscle mass, and evidence from cancer literature shows physical activity can help this group of patients by improving body composition from performing exercises to build lean muscle and improve endurance. Physical exercise, such as walking and/or swimming, can help social and emotional
wellbeing by relieving the tension in muscles, relaxing the mind, providing distraction from negative thoughts and worries (Cancer Institute, 2018).

Women undergoing surgery for breast cancer experience side effects such as fatigue, reduced quality of life (QOL), and depression. Physical activity (PA) is associated with improved psychological adjustment during treatment and survivorship. One study examined the relationship between the QOL, including depression and physical activity, in women who recently underwent surgery for breast cancer. At two to ten weeks post-surgery, 240 women with non-metastatic breast cancer reported on intensity and duration of moderate and vigorous PA, fatigue (intensity and interference), depressed mood, clinician-rated depression, and functional QOL. Women that reported greater amounts of weekly moderately vigorous physical activity reported less fatigue interference, greater functional QOL, less depressed mood, and lower clinician-rated depression. The study concluded that women who are more physically active in the months after breast cancer surgery show greater psychological adaptation in the initial phases of their treatment (Knobf, 2014).

A specific area in need of more research is the role of physical activity in depression, which is frequently reported in women undergoing treatment for breast cancer and may be characterized by symptoms such as sadness, hopelessness, and loss of interest in pleasurable activities. While depressed breast cancer patients have worse health outcomes overall, physically active breast cancer survivors report significantly less depression and mood disturbance (Stagl, J. 2014).

In one related study it was noted that moderate-intensity aerobic exercise training may offer profound psychological benefits for persons in cancer therapy, particularly with regard to depression (National Center on Health, Physical Activity and Disability, 2018).

**Section 4: Cancer-Specific Contraindications and Reasons to Stop an Exercise Program**

The 2010 ACSM exercise and cancer survivorship guidelines provide the most recent recommendations regarding assessments to be conducted prior to cancer exercise programs. Before initiating any cancer survivorship exercise program, it is best to have the attending oncologist provide a medical clearance and share with the clinician any detailed instructions related to the specific type of patient’s cancer and treatment.

Following that, it is important for the treating clinician to evaluate for peripheral neuropathies and musculoskeletal morbidities resulting from recent or past cancer treatment. Evaluation of fracture risks is also extremely critical, especially in those patients with identified metastasis to the bone: patients with bone metastasis may need to alter their program with regard to intensity, duration, and mode given their increased risk for skeletal fractures. In addition, this population faces an increased risk of fracture related to hormonal therapy and/or a diagnosis of osteoporosis.

In developing the program, the clinician needs to adhere to guidelines for exercise prescription from evidence-based sources (such as the above-mentioned ACSM) regarding cardiovascular and pulmonary contraindications. Given the toxicity of radiotherapy and chemotherapy as well
as long term late effects of cancer surgery, the potential for adverse cardiopulmonary events are higher among cancer survivors than aged matched comparisons. Exercises may require modifications, and individuals may have a need for increased supervision.

In the event a surgical procedure was required, the program may need to be modified or delayed to allow adequate time for the patient to heal and recuperate following surgery; this may take up to eight weeks.

Infection risks are generally higher for patients undergoing chemotherapy or radiation, as they likely have a compromised immune system. The clinician should use good judgment to aid in reducing infection risks in physical therapy clinics and related exercise facilities frequented by cancer patients and survivors.

The exercise tolerance of each patient needs to be continuously monitored, both while in treatment and immediately after each session is completed.

Regardless of the type of oncological treatment intervention, an exercise program is to be avoided for individuals experiencing extreme fatigue, anemia, or ataxia.

Following are more cancer-specific guidelines and contraindications.

**Breast Cancer**

If the patient has had radiation therapy after breast cancer surgery, the proper prescribed exercises become increasingly important in helping to maintain upper extremity flexibility. Because radiation can affect the upper extremity long after treatment is completed, it is particularly crucial to educate the patient and develop good compliance with the exercises.

As with all cancer sites, the clinician will need to allow adequate time for soft tissue healing after breast cancer surgery; surgical recovery may take as long as eight weeks.

While exercises can be often initiated soon after surgery, the therapist needs to communicate with the treating oncologist as to specifically when this should occur, especially in cases when surgical drains and sutures (stitches) have been used and removed. Patients experiencing upper extremity complications immediately following breast cancer treatments (i.e. infection, abnormal swelling and/or edema) need to resolve these issues prior to engaging in an exercise program (American Cancer Society, 2017).

Breast cancer-specific risks of injury include lymphedema; individuals experiencing this condition should be educated and encouraged to wear well-fitting compression garments during exercise. Reasons to stop an exercise program include changes in upper extremity symptoms, such as an increase in swelling (ACSM, 2010).

**Colon Cancer**

In the event of any surgical involvement for the intervention of colon cancer, the clinician will need to allow adequate time for healing after surgery; the number of weeks required will be patient-specific and determined by the oncologist.
Patients with an osteotomy require physician permission prior to beginning exercises involving lifting and/or weight training, as there are hernia risks secondary to weak abdominal muscles. Also, these patients need to be educated about the dangers of activities such as contact sports, and the related risks of a blow to the abdominal region. The exercise program for the colon cancer patient needs to be stopped in the event of hernia or osteotomy related infection (ACSM, 2010).

**Gynecologic Cancer**

Similar to other cancer sites, adequate time is needed in the healing process after gynecologic cancer surgery, with the number of weeks specific to the patient and determined by the oncologist. Women with swelling and/or inflammation of the abdomen, groin, or lower extremities need to seek medical care to resolve these issues before training the lower extremities.

Contraindications for the program include changes in swelling or inflammation of the abdomen, groin or lower extremities. Any such occurrence should result in the reduction or avoidance of lower extremity and lower body exercise until after appropriate medical assessment and intervention resolves the issues.

Risks of injury for the gynecologic cancer patient include exercising the lower body: although it is necessary for the therapist to focus on this area, being proactive to prevent injury is definitely encouraged, given the potential for lower extremity swelling or inflammation in this population. In addition, women with lymphedema should wear a well-fitting compression garment during exercise. Any changes in swelling or inflammation of the abdomen, groin, or lower extremities should result in the reduction or avoidance of lower extremity and lower body exercise until after appropriate medical assessment and intervention resolves the issues (ACSM, 2010, American Cancer Society, 2010).

**Prostate Cancer**

In the event of any surgical involvement for the intervention of prostate cancer, the clinician will need to allow adequate time for healing after surgery, as determined by the oncologist.

Prostate cancer carries no specific risk of further injury, contraindications, or reasons to stop exercise at this time (ACSM, 2010).

**Hematologic Malignancies in Adults**

Hematologic malignancies include a very large number of genetically diverse diseases such as lymphomas and myelomas. Various treatments are available for people with hematological malignancies, from a watch-and-wait approach to single- or multi-agent (combination of drugs) chemotherapy, radiotherapy, immunotherapy, and stem cell transplantation. Individuals with hematological malignancies often endure long phases of therapy and immobility, which reduce their physical performance level. In addition, many patients suffer from a reduced number of red cells and platelets, which can cause an inability to perform activities of daily living and diminish
their quality of life; this factor may also influence medical therapy. Finally, multiple myeloma patients should be treated as if they are osteoporotic.

Similar to previously-mentioned cancers, there needs to be adequate time for healing after any surgical intervention before an exercise program can be initiated. Hematologic cancer carries no specific risk of further injury, contraindications, or reasons to stop exercise at this time (Olsen, 2013).

**Section 5: Aerobic Exercise Prescription Guidelines**

Before implementing and modifying the aerobic component of an exercise program for the cancer patient, the clinician needs to have a good understanding of the exercise parameters for the general population.

Moderate-intensity physical activity is defined as physical activity done on a scale relative to an individual's personal capacity, usually 11-14 on a scale of 1 to 20, with the participant still able to carry on a conversation. Vigorous-intensity physical activity is usually 17-19 on a scale of 1 to 20 (American Heart Association, 2018).

Program guidelines for individuals under age 65 without the need for changes are moderately intense cardio 30 minutes a day, five days a week or vigorously intense cardio 20 minutes a day, three days a week. The moderate/30-minute recommendation is for the average healthy adult to maintain health and reduce the risk for chronic disease; to lose weight or maintain weight loss, 60 to 90 minutes may be necessary (Kushi, 2012, ACSM, 2010).

Guidelines for individuals over age 65 without the need for program modifications are also moderately intense cardio 30 minutes a day, five days a week or vigorous intense cardio 20 minutes a day, three days a week. However, older adults or adults with chronic conditions should develop an activity plan with a clinician, in order to manage risks and take therapeutic needs into account (such as adding a balance exercise to reduce the risk of falls) (Kushi, 2012, ACSM, 2010).

Using an objective method to obtain an exercise range for the patient can be helpful for modifying an aerobic exercise program as well as providing documentation of a baseline and progression within the plan of care. To obtain an exercise range the clinician finds the low and high end of the range as follows:

\[
\text{low end of exercise range} = (\text{HR max} - \text{HR rest}) \times 0.5 + \text{HR rest}
\]

\[
\text{high end of exercise range} = (\text{HR max} - \text{HR rest}) \times 0.65 + \text{HR rest}
\]
The Karvonen Formula is a mathematical formula that helps determine the target heart rate for an individual’s exercise range. It uses both maximum and resting heart rates (the maximum heart rate can be estimated using 220 minus the age of the individual).

For example, a 53 year old man who has finished cancer treatment has a maximum heart rate of 220-53= 167.

His resting heart rate is 57.

His exercise ranges are found as follows:

<table>
<thead>
<tr>
<th>Low End: (HR max – HR rest) x .5 + HR rest = low end of exercise range</th>
</tr>
</thead>
<tbody>
<tr>
<td>(167-57) x .5 +57 = 112</td>
</tr>
<tr>
<td>High End: (HR max – HR rest) x .65 + HR rest = high end of training zone</td>
</tr>
<tr>
<td>(167-57) x .65 + 57 = 129</td>
</tr>
</tbody>
</table>

This individual’s exercise range would be 112-129 BPM.

Another method used at the beginning of an exercise program and for those who have received exercise restrictions utilizes a percentage scale of the target heart rate determined using the Karvonen Formula. Those who are beginning the program may start with a lower heart rate range of 55-65% of target heart rate. If the patient is familiar with exercise on an intermediate basis the range may increase to 60-80%. Very fit individuals may tolerate and benefit from exertion up to 85%.

Several common modes of aerobic exercise include using a stationary exercise bike, stationary and recumbent exercise bike, elliptical trainer, and/or treadmill; simply walking without any device is also an option. When appropriate, swimming is also an excellent form of aerobic exercise.

Clinicians need to consider the physical and cognitive requirements of the aerobic activity prescribed, and also consider each patient's pre-treatment activity level.

Equipment modifications and/or adaptations may be required to fit the needs of each cancer patient. For example, restricted range of motion can cause problems within the aerobic program. The clinician needs to ensure that the patient has adequate range of motion for the activity prescribed such as the stationary bike or treadmill. Stretching the upper and lower extremities prior to the program can be very helpful. Similarly, if a patient lacks appropriate trunk strength to safely maintain an upright position on an exercise bike, the clinician can change the exercise mode to a recumbent bike or similar device to support the trunk while exercising in a seated position.
Cognitive impairments may require the clinician to not only remain close for supervision but also provide verbal cueing in order to keep the patient on task while obtaining the heart rate needed for the program.

Alterations of the aerobic component will also likely be necessary. Along with consulting the treating clinician(s) such as the oncologist, physiatrist, or primary care physician, it is recommended to begin the program with ACSM and AHA guidelines in mind, and then revise it according to symptoms, risks, ability, and safety on an individual basis. Anemia is one symptom that may require alteration of intensity and duration of the program as it will present as shortness of breath. Cardiopulmonary symptoms such as chest pain with or without exertion, once cleared of any specific pathology, will also require program modifications.

One study looked at databases of medical literature in terms of physical exercise interventions intending to improve the oxygen system. The search included nine randomized controlled trials covering 818 people, the majority of whom studied suffered from acute leukemia, multiple myeloma, or lymphoma. The study compared an oxygen-focused physical exercise intervention plus standard care to standard care alone. In five trials participants received their own stem cells or stem cell transplantation from a donor. The aerobic exercise interventions consisted of various walking programs of different durations and intensity. The aerobic exercise interventions added to standard care were found to improve quality of life, especially physical functioning, depression, and fatigue (Bergenthal, 2014).

Section 6: Resistance Exercise Prescription Guidelines

As noted earlier, resistance exercise has been shown to reduce fatigue, improve quality of life, and increase muscular fitness in men with prostate cancer. This form of exercise can also be an important component of an exercise program for many other forms of cancer and cancer prevention. For example, Courneya and colleagues found that women with breast cancer participating in a resistance training program during chemotherapy had dose reductions and fewer delays in their chemotherapy treatments.

The 2010 ACSM roundtable guidelines for resistance training exercise for cancer survivors are also consistent with the 2008 U.S. DHHS “Physical Activity Guidelines for Americans.” Cancer survivors are encouraged to participate in two or three weekly sessions, using a variety of exercises and equipment, and including exercises for the major muscle groups. The guidelines suggest that two to four sets of each exercise will help adults improve strength and power. For each exercise, 8-12 repetitions improve strength and power, 10-15 repetitions improve strength in middle-age and older persons starting exercise, and 15-20 repetitions improve muscular endurance.

Precautions for resistance exercise include close supervision for patients with known metastasis or osteoporosis. Similarly, in treating lymphedema, resistance exercise must be done methodically: the individual should start a program without any additional resistance and slowly
progress to adding resistance with weights. Any weight lifting should be limited to weights the patient can manage using correct form throughout full range of motion.

Following are three studies investigating strength training within the cancer exercise program, with reproducible parameters for clinical purposes (Courneya, 2012).

In a study by Sander, the safety and effectiveness of an upper extremity resistance exercise for breast cancer survivors was examined by using a protocol that is applicable and clinically reproducible. An 8-week exercise program included examples of intensity, repetitions, frequency, and determination of starting weight. The 8-week intervention phase consisted of 6 upper extremity free weight exercises performed twice weekly in one group and 3 times weekly by a second group.

The study used a program that begins with a 5-minute warm-up such as walking at a comfortable pace. This is followed by a pre-exercise upper extremity stretching program which then progresses to the 6 strengthening exercises, using safe lifting techniques, proper form, timing, and breathing.

Subjects were instructed to perform 2 sets of 12 repetitions of the following exercises:

- Front shoulder raise
- Biceps curl
- Triceps kickback
- Wrist extension
- Single arm bent over row with scapular retraction
- Overhead shoulder press

The following exercise guidelines were used:

- Perform exercises proximal to distal to proximal which assists in moving interstitial fluid toward central circulation.
- Perform each repetition in a slow, controlled motion, using a 2-second count concentric contraction and a 2-second count eccentric contraction
- Perform exercises on the unaffected side first followed by the affected side
- Use a 30 to 60 second rest period between sets
- Progress exercises as a percentage of the calculated 1 repetition maximum (1 RM), advancing from 60% to 80% throughout the intervention.
- Use a calculated 1 RM to determine the amount of weight lifted. For each exercise the patient lifts a weight that challenges them enough so that they can perform no more than 10 repetitions.

The 1 RM is used to determine the starting weights and calculated according to the following formula:

\[
1 \text{ RM} = [(0.033 \times \text{number of repetitions performed}) \times \text{repetition weight}] + \text{repetition weight}
\]
All subjects improved in the amount of weight lifted; none experienced an increase in arm volume indicating no significant increase in lymph. In fact, there was a small decrease in arm volume from baseline to follow-up, which suggests exercise can improve lymph flow, providing another benefit for the breast cancer patient (Sander, 2008).

As previously discussed, in a related study by Segal et al., the effects of resistance exercise were examined on fatigue and health-related quality of life in men with prostate cancer receiving androgen deprivation therapy. This is considered the first study to demonstrate that resistance exercise, rather than aerobic exercise, has a benefit of reducing the symptoms of fatigue related to cancer and its treatment.

Resistance exercises consisted of a 12-week program of nine strength-training exercises performed three times per week, at 60% to 70% of one repetition maximum (1 RM). In this study, 1 RM is defined as the maximum amount of weight that can be lifted once. Two sets of eight to 12 repetitions of the following nine exercises were performed:

- Leg extension
- Calf raises
- Leg curl
- Chest press
- Latissimus pulldown
- Overhead press
- Triceps extension
- Biceps curls
- Modified curl-ups

The authors’ exercise guidelines were:

1. Start resistance at 60% of the patient’s 1 RM
2. Increase the resistance by 5 lb when able to complete more than 12 repetitions

After the 12 week period, the study clearly demonstrated that resistance exercise improved symptoms of fatigue and health-related quality of life in men with prostate cancer receiving androgen deprivation therapy (Segal, 2003).

In another study, a home-based aerobic and progressive resistance exercise program was designed by a certified exercise scientist from the American College of Sports Medicine (ACSM) which adhered to the ACSM guidelines for exercise testing and prescription. The exercise intervention was designed to be delivered easily and quickly to implement concurrently by patients during the course of receiving radiation therapy.

The strengthening component of the exercise program, an individually tailored therapeutic resistance band exercise prescription, was designed to provide low to moderately intense progressive resistance exercise (3-5 exercise rating of perceived exertion on the ACSM revised
rating scale) 7 days a week for the entire 4-week period to maintain muscle strength in the upper body. An additional walking component focused on the lower body.

Patients were given a set of three color-coded therapeutic resistance bands, representing low and moderate levels of resistance. They were instructed to begin with an individually determined number of sets (1 set = 8-15 repetitions) for each of the 8 exercises:

- Bicep curl
- Triceps extension
- Overhead press
- Rows
- Chest press
- Internal and external rotation
- Lateral and front raises
- Horizontal adduction, and abduction

The relevant ACSM exercise guidelines were:

- Begin at a low to moderately challenging level up to 7 days a week.
- If the goal is maintaining strength instruct patients to perform resistance band exercises as many as 7 days a week.
- Instruct patients to increase the intensity by changing the band color or shortening the initial length of the band for increased resistance.
- Instruct patients to progressively increase from their individual baseline sets and repetitions to a maximum of 4 sets of 15 repetitions for each exercise daily over the course of the 4-week intervention at an optimally challenging rate.

The study showed significantly more strength and endurance post intervention and at the 3-month follow-up compared with the control participants. Participants in the exercise group exhibited significantly higher quality of life and significantly lower cancer-related fatigue post intervention and at 3-month follow-up than the controls. Daily minutes of resistance exercise and number of resistance exercise days were assessed to evaluate intervention adherence. Participants in the exercise intervention showed good adherence to and compliance with the intervention, with significantly more number of resistance exercise days post intervention and at the 3-month follow-up compared with the control participants (Mustian, 2009).

Section 7: Flexibility Exercise Prescription Guidelines

By helping manage associated side effects, flexibility exercises provide a range of benefits during treatment, recovery, and remission of cancer.

Radiation and chemotherapy may cause scar formation in the joint, which may result in limitation in range of motion. This limitation can be prevented, and normal range of motion can be gained, via flexibility exercises.
Upper and lower extremity and trunk muscle groups benefiting from flexibility exercises include:

- Biceps/triceps
- Pectorals major/latissimus dorsi
- Anterior deltoids/posterior deltoids
- Trapezius/deltoids
- Abdominals/spinal erectors
- Left and right external obliques
- Quadriceps/hamstrings
- Anterior tibialis/gastrocnemius

Static stretching is the method most recommended as a component of the home program, but it is also beneficial in the clinic setting. Static stretches involve an individual (with or without assistance) stretching to the point of tension (slight discomfort) at the end of the joint range of motion, and sustaining a holding position for a determined period of time.

The ACSM’s static stretching guidelines include:

- Stretch patient to a point of mild discomfort (not pain), hold the stretch steady without any form of a bounce movement
- Instruct patient to inhale and slowly exhale as you stretch to the point of tension
- Hold stretch 15 to 30 seconds
- Perform 2 to 4 repetitions per stretch, 5 to 7 days a week

Proprioceptive neuromuscular facilitation (PNF) stretching is another method used in which the stretched muscles are contracted isometrically and then relaxed. One specific form of PNF is referred to as the “contract relax” method, which takes advantage of this brief period of time immediately following the isometric contraction. Isometric contractions provide a preparation to the stretch receptors, allowing accommodation to increase passive stretch of the muscle.

In this technique, the patient’s affected body part is passively moved until resistance is felt. After assuming an initial passive stretch, the patient is then told to contract the muscle isometrically. This contraction is held for five to ten seconds or until fatigue is felt by the clinician. The patient is instructed to relax or let go for up to 5 seconds. The clinician then moves the limb to a new stretch position. This final passive stretch is held for 10-15 seconds. These exercises are repeated two or three times. The muscle is then relaxed for 20 seconds before performing another PNF technique. Verbal cueing that can be very helpful to both the patient and the clinician are “Hold – don’t let me move you” and “Now let go and relax” (Sullivan, 1982).

In a related study, authors wanted to identify whether painless dynamic PNF techniques can reduce lymphedema, and subsequently provide basic reference data for use in the treatment of lymphedema patients. Subjects were upper extremity lymphedema patients who were receiving rehabilitation treatment. A total of 40 women participated and received PNF techniques before the application of lymph compression bandages. Group 1 of 20 subjects were administered PNF techniques three times a week for 30 minutes each time. Group 2 of 20 subjects received only
edema reducing massage for 30 minutes. The interaction between treatment method and treatment time was significant, which indicated that the change in edema at different measurement times was different according to treatment methods. In this study, Group 1 had a steeper rate of decline in edema than Group 2. The authors concluded both massage and PNF techniques helped to lower edema rates. Four weeks after the beginning of treatment, a larger degree of decline in edema was exhibited in the PNF group than in the massage group (Hwang, 2013).

Precautions for flexibility/stretching exercises include:

- During static stretching, the patient should not experience pain or bounce to achieve a greater stretch
- PNF stretching is not recommended for children and people whose bones are still growing
- PNF stretching is not recommended for people who are experiencing bone metastasis or are at risk of fractures
- PNF stretching is very strenuous and should be performed for a given muscle group no more than once per day, but can be used in conjunction with static stretching (Sullivan, 1982)

Section 8: Special Exercise Prescription Guidelines

Just as there are complementary and alternative nutritional practices for the cancer patient and survivor, various less traditional physical activities are also practiced.

One example is Pilates, a gentle form of exercise that engages the mind, body, and spirit. The exercises help develop muscular flexibility and strength while increasing metabolism and promoting lymphatic, respiratory, and circulatory function. Pilates has been described as improving balance and coordination, and helping relaxation. Pilates can be done throughout one’s life, wherever and in any position – even while seated. For these reasons it can be an excellent approach to healing for breast cancer survivors.

Rehabilitation professionals should initially encourage interested patients to seek out trained Pilates exercise instructors with knowledge of breast cancer and related precautions. Women with breast cancer could begin with individual Pilates exercise sessions to ensure safe performance of exercises, and later proceed to community-based group classes.

Research is now documenting the benefits of the Pilates method for breast cancer recovery. One study suggests that Pilates exercise programs, with their low intensity and focus on neuromuscular control, may be beneficial for women living with breast cancer by promoting flexibility of the shoulder joint. Participants were 4 volunteers who had undergone AD (axillary dissection is performed for breast cancer staging and application of radiation therapy to the breast or axilla, which can contribute to reduced shoulder mobility) and completed radiation therapy for stage I to IV breast cancer at least 6 months prior, and who had restricted shoulder ROM secondary to breast cancer treatments. Visual analyses of the data suggested a modest
effect of the Pilates exercise program in improving shoulder abduction and external rotation ROM. Statistically significant improvement in shoulder internal and external rotation in the affected UE was shown for the one participant with pre-existing metastatic disease. The study noted it is unlikely that many women could afford to attend individualized Pilates exercise sessions 3 times a week for 3 months, therefore community based group classes would be a reasonable option. The study concluded that Pilates exercise can be a starting point from which women could gradually return to their normal activities after cancer treatments (Keays, 2008).

Another study published in 2012 found that, after 12 weeks of Pilates, 13 participants who were breast cancer survivors improved their shoulder and neck flexibility. Improvements were also noted in mood, body image, and quality of life. Although volume increased on the affected arm (a sign of lymphedema), it’s worthy of note that this program did not modify the exercises for the class, and that the sessions increased in frequency over the 12-week period (Aaronson, 2014).

Yoga, another option, can help the cancer patient react to stress in beneficial ways by counteracting the body’s natural responses to it. Yoga exercises can stimulate the parasympathetic nervous system to convey relaxation to the body by stabilizing blood pressure, lowering heart rate, and reducing the body's demand for oxygen. Yoga exercise has been documented to increase lung capacity, improve digestion, and provide improvements in the immune system. It may also be of significant value in addressing cancer-related pain and discomfort.

Although individuals might choose to begin with individual yoga exercise sessions to ensure the safe performance of exercises, it is less of an issue than other forms of exercise, and it is reasonable to begin with community-based group classes. Yoga practices include yoga postures and stretches, breathing practices, imagery, meditation, and progressive relaxation. While each technique has its own specific purpose, all techniques have the common aim of helping to develop a focused awareness of what is happening in the body and mind – emotionally, physically and spiritually. In general, yoga exercises for cancer patients should focus on extending awareness of physical, emotional, sensory, and thinking processes. The program should encompass slow, deliberate movements adapted to specific needs and physical limitations (DiStasio, 2008).

An M.D. Anderson Cancer Center study reported on the results of a yoga study. The study followed 61 women receiving 6 weeks of radiation treatment for breast cancer. Half the women took a yoga class twice a week; the other half did not. Compared with the women who did not take yoga, the women in the yoga group reported having more energy and less daytime sleepiness, better physical functioning, and better overall quality of life (breastcancer.org, 2015).

Tai chi is another form of exercise that incorporates gentle movements and deep breathing and may help relieve stress. Tai chi can be led by an instructor, or can be self-taught following books or videos. The slow movements of tai chi don’t require physical strength, and the exercises can be easily adapted to individual abilities.

In a Wilmot Cancer Center study, 21 women who had been treated for breast cancer were randomly assigned either to practice tai chi or to participate in a psychosocial support group,
both for 1 hour, 3 times a week for 12 weeks. In this study, researchers studied women’s heart and lung function, muscular strength, and flexibility. While the women in the psychosocial support group showed improved flexibility, the women in the tai chi group showed improvements in all 3 categories, as well as a slight reduction in percentage of body fat (breastcancer.org, 2013).

**Case Study #1**

Seen in physical therapy for evaluation is Mrs. Jones, a 62 year old female who is a breast cancer survivor diagnosed 2 years ago. She has no comorbidities, and is generally healthy despite being overweight and sedentary.

She received both chemotherapy and cancer surgery for her cancer treatment. Her chemotherapy resulted in persistent neuropathy of both upper and lower extremities. She also has lymphedema in her right arm as a result of having five lymph nodes removed from the axillary region. She is right hand dominant. She reported no other lingering adverse effects of treatment. She takes Herceptin as an adjuvant breast cancer treatment, meaning it is applied after initial treatment for cancer, especially to suppress secondary tumor formation.

Patient’s Goal: Her goal is to return to bowling but she has not bowled for 5 yrs. and has not regularly exercised.

Her assessment revealed as follows:

**U/E Manual Muscle Test:**

Shoulder abduction: L 3+/5 to -4/5, R 2+/5 to 3-/5

Shoulder adduction: L 3+/5 to -4/5, R 3/5 to 3+/5

Shoulder adduction flexion, and extension: L 3+/5 to -4/5, R 2+/5 to 3-/5

Shoulder internal and external rotation: L 3+/5 to -4/5, R 2+/5

Elbow, wrist and hand: L 3+-4-/5 in all planes throughout, R 3/5 to 3+/5 in all planes throughout

**L/E Manual Muscle Test:**

Hip flexion: L 4-/5 to 4/5, R 3+/5 to -4/5

Hip extension, abduction, adduction and internal and external rotation: 4-/5 bilaterally

Knee and ankle: 4-/5 bilaterally and in all planes of motion throughout

Her overall assessment reveals that she has low muscular strength especially to the R U/E, and functionally showed limited ability to raise her left arm higher than her shoulder.

**Cardiorespiratory endurance:**

Poor to Fair
Gait, balance, agility and coordination:
Ambulates without an assistive device and appears within age-matched normative values.

Safety concerns:
Client is currently sedentary. Major limitations and concerns for exercise prescription for this person will be the right upper extremity lymphedema, and the bilateral peripheral neuropathy of her U/E and L/E’s, all of which may alter the ability to hold weights and her bowling ball. Balance and the likelihood of falls can be an issue of concern secondary to the peripheral neuropathy as well. Her cardiorespiratory response to aerobic exercises will need to be monitored.

Exercise Prescription
Bowling will require stamina, agility, flexibility, balance and strength. Therefore the fitness program should include activities to enhance all of these components. The intensity of bowling is estimated at 3 MET but could be higher depending upon specifics.

Cardiorespiratory exercise
Three times weekly for 20 minutes starting at a comfortable pace. Modes for aerobic activity can vary from weight supported aerobic activities to swimming or biking. Increase intensity and duration in alternating weeks, and by no more than 10% per week until she reaches the United States Department of Health and Human Services (US DHHS) guidelines for moderate-intensity exercise (https://health.gov/paguidelines/guidelines/).

Strength training
Twice weekly, one set for each major muscle group. 8 to 10 exercises. 48 hours between sessions. It is important the program be supervised for the first several months by the clinician and that the patient’s lymphedema be stable during any upper body strength training programming. It is recommended the client should wear a well fitted compression garment during the sessions. She should select variable resistance machines rather than dumbbells because of the peripheral neuropathy. Grip strengthening exercises will be critical for each hand but especially her right hand as needed to hold a bowling ball.

Lower body exercises will proceed as with any patient unless peripheral neuropathy interferes. In this event, the program should be altered the same manner for the upper and lower extremities. For the upper body and extremities, the patient should start with the lightest weights and progress by the smallest possible increments but only after she has had two to four sessions at the same weight that resulted in no change of lymphedema symptoms. The limited range of motion in the right shoulder needs to be considered when choosing any strength training, along with a consult by a certified lymphedema therapist. The lymphedema therapist needs to clear the patient for upper body strength training before resuming after any hiatus from the program.

Upper body exercise training should be started also in a supervised setting to ensure that the patient learns the proper biomechanics for each exercise. The goal is to avoid increases in
inflammation and injury as a result of improper form because these are likely to exacerbate lymphedema. Consequently the increments of resistance progression should be small and attention should be given to avoiding the overuse of smaller muscles to do exercises intended for larger muscles. For example she should not finish a second row by curling her wrists because this will require more work from the small muscles of the wrist than they are able to do and may result in an injury or inflammatory response that would exacerbate her lymphedema.

Regular performance of weight training 2-3 times per week is necessary for ensuring that this mode of exercise is effective and safe. If the patient cannot attend regularly because of other commitments, progressive strength training should not be included in her exercise program. For example, if she comes twice weekly for a month, but then has to go away for several weeks to care for a family member, then returns for three weeks, twice weekly, then has a business trip for one week, then comes twice weekly for two weeks followed by a vacation for two weeks, she should not increase the weights; rather, she should continue to use the lightest resistance weight possible. It is recommended that only patients who are able to attend sessions on a regular basis over a course of more than a month should progress with resistance. The patient with lymphedema should back off on the resistance when she has a gap in exercise performance of a week or more to avoid the inflammatory responses that can exacerbate lymphedema.

Flexibility

Passive stretching of all major muscle groups is recommended at end of each exercise session, but benefits can be experienced by also stretching at the beginning of the session, in this particular case especially the R upper extremity. In either scenario, it is important that additional attention will need to be upon the right shoulder, elbow, wrist, and hand.

Case Study #2

Seen in physical therapy for evaluation is Mr. Horton, a 62 year old Caucasian male diagnosed as having Hodgkin's lymphoma with metastasis to lumbar spine area (L5-S1). Prior to his diagnosis Mr. Horton reported a four month history of pain in his low back and the pain moved into his left hip. He stated this pain was different from his previous episode of low back pain as it was lower into his hip. His chief complaint was that when he came home from work as a computer programmer for a large company, he was very tired and unable to do anything recreational such as his hobby: fishing. He had noticed some weight loss at the time and reported pain wakening him up at night and difficulty getting comfortable during sitting for long periods of time. He had started doing several of the stretches and light exercises that were given to him by his previous therapist for treating low back pain. They helped a minimal amount at the onset but in general did not seem to make a difference.

Mr. Horton returned to his primary care provider, and after further medical screening and testing, was diagnosed having Hodgkin's lymphoma with metastasis to lumbar spine. He began chemotherapy and radiation treatment after having surgery to remove pelvic malignant lymph nodes. He is 1 year post-operative cancer surgery and has just completed his last session of
chemotherapy and radiation one month ago. He is to begin physical therapy per primary care provider to increase cardiovascular/pulmonary health, improve strength and flexibility, improve lymphedema and reduce fatigue and symptoms produced from the cancer and treatments.

Clinical Impressions: Hodgkin's lymphoma is a form of cancer with unknown etiology. Important clinical features include origination and spread of cancer within lymph nodes. The most frequently listed symptoms include painless, swollen lymph nodes, and constitutional symptoms. In Mr. Horton’s case, a non-specific symptom – not commonly mentioned in research but commonly experienced by patients – is low back pain. Lymphoma-related LBP can occur due to swollen lymph nodes in the abdominal region putting pressure on the muscles, nerves, and other tissues complimenting to LBP, and the incidence of metastases is high, such as in this case.

Patient's Past Medical History: Patient reports HTN and high cholesterol, both managed medically. He reports his mother passing away from breast cancer 10 years ago. Patient reports no other significant past medical history (liver, lungs, DM, kidneys), and he does not smoke and rarely drinks alcohol socially because he notices that drinking makes his pain worse.

Patient’s Goal: His primary goal is to decrease his pain and increase his stamina so that he can return to his work and fishing.

His assessment revealed as follows:

U/E ROM:
Shoulder: within functional limits (WFL) Bilaterally
Elbow: WFL Bilaterally
Wrist and Hand: WFL Bilaterally

L/E ROM:
L Hip: Flexion 70 degrees (with some discomfort on end range). All other planes of motion WFL
R Hip: WFL
Knee: WFL Bilaterally
Ankle: WFL Bilaterally

Lumbar ROM:
75% of normal during flexion, side bending and rotation. No increase in pain with movement

U/E Manual Muscle Test:
Shoulder: 4/5 Bilaterally in all planes.
Elbow, wrist and hand: 4/5 Bilaterally in all planes.

L/E Manual Muscle Test:
Hip 4/5 Bilaterally in all planes.
Knee and ankle: 4-/5 bilaterally and in all planes of motion.
Reflexes: +2 for L3/4, L5, and S1
Sensation: Normal
Cardiorespiratory endurance:
Poor to Fair: After walking for 2 minutes, Mr. Horton became tired and fatigued and required a rest break.
Gait, balance, agility and coordination:
Ambulates without an assistive device. Slight decreased hip and knee flexion noted throughout swing through phase of gait, especially at end of walking 2 minutes.

**Exercise Prescription**

Primary goal for Mr. Horton’s program is to decrease fatigue, decrease risk of any future falls, and promote endurance. Intervention includes patient education of fatigue management, falls risk assessment, general aerobic exercise, and lymphedema treatment including educating patient on lymphedema management at home.

**Cardiorespiratory exercise**

Begin at 10 minutes per day and transition to three times weekly for 20 minutes starting at a comfortable pace. Begin with low impact aerobic training (cycle ergometer, bicycle) progressing to ambulation over ground. Modes for other aerobic activity can vary such as swimming. Progress to 30 minutes a day, 3-4 times/week. Increase intensity and duration in alternating weeks, and by no more than 10% per week until he reaches the United States Department of Health and Human Services (US DHHS) guidelines for moderate-intensity exercise (https://health.gov/paguidelines/guidelines/).

**Strength training**

L/E strengthening will be important for Mr. Horton along with improving his overall muscular endurance. Functional closed chain exercises such as mini-squats, lunge matrix, stair training with additional focus on hip flexors and abductors, quadriceps, and ankle dorsiflexors muscles will be beneficial. Strength training beginning at twice weekly is advised by the US DHHS with one set for each major muscle group with 8 to 10 exercises, 8-12 reps of each exercise, 2-3 sets, to point of fatigue but not beyond that point. 20-30 minutes, and progress as tolerated with 48 hours between sessions. It is important the program be supervised for the first several months by the clinician. Lower body exercises will proceed as with any patient unless and low back pain or any peripheral neuropathy interferes. In this event, the program should be altered the same manner for the upper and lower extremities.

For the upper body and extremities, the patient should start with the lightest weights and progress by the smallest possible increments but only after he has had two to four sessions at the same
weight that resulted in no change of any symptoms. Upper body exercise training should be started also in a supervised setting to ensure that the patient learns the proper biomechanics for each exercise. The increments of resistance progression should be small and attention should be given to avoiding the overuse of smaller muscles to do exercises intended for larger muscles.

Regular performance of weight training 2-3 times per week is necessary for ensuring that this mode of exercise is effective and safe. If the patient cannot attend regularly because of other commitments, progressive strength training should not be included in her exercise program. For example, if he comes twice weekly for a month, but then has to go away for several weeks, then returns for three weeks, twice weekly, then is gone for one week, then comes twice weekly for two weeks followed by a vacation for two weeks, he should not increase the weights; rather, he should continue to use the lightest resistance weight possible. It is recommended that only patients who are able to attend sessions on a regular basis over a course of more than a month should progress with resistance. Any patient with lymphedema should back off on the resistance when they have a gap in exercise performance of a week or more to avoid the inflammatory responses that can exacerbate lymphedema.

**Flexibility**

Passive stretching of all major muscle groups is recommended at end of each exercise session, but benefits can be experienced by also stretching at the beginning of the session, in this particular case especially the L hip. In either scenario, it is important that additional attention will need to be upon the hips and gentle stretching to the low back.

**Rationale for Progression**

Similar to other cancer survivor exercise programs the clinician will progress this patient to maintain/improve his level of fitness after treatment and promote overall better quality of life. Progress patient as he can tolerate, being aware of effects of medical treatment and always coordinate with the primary care provider and oncologist.

**Conclusion**

A cancer diagnosis no longer carries the dark stigma of hopelessness as it did just several decades ago. Because of major advances in prevention, detection, and treatment, better outcomes have resulted in an expanding population of cancer survivors. Still, as the incidence and prevalence of cancer increases, so too does the number of patients living with cancer as a chronic condition.

Cancer rehabilitation – the area of physical medicine responsible for addressing the musculoskeletal, cardiopulmonary, and functional impairments associated with cancer treatment, survivorship, and advanced disease – is an evolving area for the physical therapist. Despite improvements in medical treatments for cancer, patients potentially face significant physical impairments and functional limitations during and after cancer treatments, including cancer-
related fatigue (CRF), deconditioning, pain, muscle and tendon inflexibility, contractures, peripheral neuropathy, lymphedema, and genitourinary dysfunction.

Increasingly, physical therapists need to be prepared to encounter and treat patients who are not only surviving cancer, but also have physical problems secondary to cancer treatments. An ability to create evidence-based, medically-supported treatment plans that provide timely and appropriate exercise-based rehabilitation at proper volumes can improve quality of life and potentially reduce healthcare costs.
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1. A meta-analysis of 52 epidemiologic studies examining the association between physical activity and colon cancer risk found that the most physically active individuals had a ________ risk of colon cancer than those who were the least physically active.
   a. 24% lower
   b. 13% lower
   c. 5% lower
   d. 13% higher

2. In one meta-analysis of 113 unique studies it was found that ________ reduced cancer-related fatigue during and after cancer treatment.
   a. Exercise interventions, pharmaceutical interventions, and the combination of both
   b. Exercise interventions, psychological interventions, and the combination of both
   c. Only exercise interventions, psychological interventions, and the combination of both
   d. Only pharmaceutical interventions

3. Studies have shown that patients with early- to later-stage colorectal cancer without distant metastases who engaged in regular activity after diagnosis decreased the likelihood of cancer recurrence and mortality by ________ compared with patients who engaged in little to no activity.
   a. 15-20%
   b. 25-30% or more
   c. 30-45%
   d. 40-50% or more

4. ________: A surgery that involves removing part but not all of the cancer, performed in situations where removing the entire cancerous tumor would cause too much damage to an involved organ or nearby tissues.
   a. Biopsy
   b. Curative surgery
   c. Debulking surgery
   d. Preventive surgery

5. Research in genetics, and gene changes in cells impacted by cancer, has led to the development of ________: often able to attack the cancer cells’ genetic programming while doing little damage to normal cells.
   a. Brachio therapy
   b. Chemotherapy drugs
   c. External-beam radiation therapy
   d. Targeted therapy drugs
6. Stem cell transplant therapy is most often used with patients with ________.
   a. Breast cancer
   b. Head and neck cancers
   c. Leukemia, lymphoma, neuroblastoma, and multiple myeloma
   d. Ovarian, testicular, and uterine cancers

7. In a study by Hardee et al., cancer survivors who reported performing ________ at least once per day of the week had a 33% reduction in all-cause mortality compared with individuals who did not report participation.
   a. Aerobic exercise
   b. Flexibility training
   c. Resistance exercise
   d. None of the above

8. In a study (Schwartz, 2017), a group of men aged 59-82 years and undergoing androgen deprivation therapy (ADT) participated in progressive resistance training for 20 weeks in a university exercise rehabilitation clinic. The results showed: ________
   a. The men had increased their strength, physical function, and balance
   b. Resistance training preserves body composition and bone mass to reduce treatment side effects
   c. Both of the above
   d. Neither of the above

9. ________ exercises help manage the side effects of treatment, such as muscle spasm and tightness, along with assisting in the management of potential post-exercise muscle soreness & tension resulting from an exercise program. Additional benefits include enhancing the patient’s muscle performance by maintaining and increasing joint range of motion; reducing the risk of injury and incidence of low back pain; improving posture and muscle coordination; relieving psychological stress and tension; and promoting physical and mental relaxation.
   a. Aerobic
   b. Flexibility
   c. Proprioception
   d. Strength

10. Researchers McNeely et al. conducted a systematic review investigating the effectiveness of exercise, including addressing inflexibly, to reduce shoulder and upper extremity morbidity throughout breast cancer treatment. Outcomes included: ________
    a. Physical therapy treatment yielded benefit for shoulder function immediately after surgery and at the 6-month follow-up
    b. Structured exercise programs in the postoperative period did not improve shoulder flexion ROM in the short term, but long term benefits were found
    c. There was evidence of increased risk of lymphedema from exercise in the postoperative period
    d. All of the above
11. Various studies have found that ________ reduced fatigue in women being treated for cancer; reduced depression and anxiety in female cancer patients, and can also help control weight, a critical factor, as studies have shown that gaining weight during and after treatment raises the risk of a cancer recurrence, particularly for breast, colon and prostate cancers.
   a. Aerobic exercise
   b. Balance training
   c. Flexibility training
   d. Resistance exercise

12. Which of the following is NOT a consideration a physical therapist should be aware of when creating an exercise program?
   a. Given the toxicity of radiotherapy and chemotherapy as well as long term late effects of cancer surgery, the potential for adverse cardiopulmonary events are higher among cancer survivors than aged matched comparisons.
   b. Infection risks are generally higher for patients undergoing chemotherapy or radiation, as they likely have a compromised immune system.
   c. Patients with bone metastasis may need to alter their program with regard to intensity, duration, and mode given their increased risk for skeletal fractures.
   d. Regardless of the type of oncological treatment intervention, an exercise program is to be Accelerated for individuals experiencing extreme fatigue, anemia, or ataxia.

13. Risks of injury for the ________ patient include exercising the lower body: although it is necessary for the therapist to focus on this area, being proactive to prevent injury is definitely encouraged, given the potential for lower extremity swelling or inflammation in this population.
   a. Breast cancer
   b. Gynecologic cancer
   c. Hematologic malignancy
   d. Prostate cancer

14. With the exception of allowing time for healing after surgery, ________ carries no specific risk of further injury, contraindications, or reasons to stop exercise at this time.
   a. Breast cancer
   b. Colon cancer
   c. Gynecologic cancer
   d. Prostate cancer

15. Considering aerobic exercise prescription, program guidelines for individuals ________ are moderately intense cardio 30 minutes a day, five days a week or vigorously intense cardio 20 minutes a day, three days a week.
   a. Under age 65 who wish to lose weight or maintain weight loss
   b. Under age 65 with chronic conditions
   c. Under age 65 without the need for changes
   d. None of the above

16. When using the Karvonen Formula, an individual's maximum heart rate can be estimated using 220 minus ________.
a. 50% of the individual's weight
b. The age of the individual
c. The individual's body mass index
d. The individual's resting heart rate

17. ________ is considered the first study to demonstrate that resistance exercise, rather than aerobic exercise, has a benefit of reducing the symptoms of fatigue related to cancer and its treatment.
   a. Bergenthal: looked at databases of medical literature in terms of physical exercise interventions intending to improve the oxygen system
   b. Mustian: a home-based aerobic and progressive resistance exercise program was designed by a certified exercise scientist from the American College of Sports Medicine (ACSM)
   c. Sander: the safety and effectiveness of an upper extremity resistance exercise for breast cancer survivors was examined by using a protocol that is applicable and clinically reproducible
   d. Segal et al.: the effects of resistance exercise were examined on fatigue and health-related quality of life in men with prostate cancer receiving androgen deprivation therapy

18. Considering flexibility exercise prescription, ________ is the method most recommended as a component of the home program, but it is also beneficial in the clinic setting.
   a. Contract/relax stretching
   b. Proprioceptive neuromuscular facilitation (PNF) stretching
   c. Resistance/release stretching
   d. Static stretching

19. Which of the following is NOT one of the precautions for flexibility/stretching exercises?
   a. During static stretching, the patient should bounce to achieve a greater stretch
   b. PNF stretching is not recommended for children and people whose bones are still growing
   c. PNF stretching is not recommended for people who are experiencing bone metastasis or are at risk of fractures
   d. PNF stretching is very strenuous and should be performed for a given muscle group no more than once per day, but can be used in conjunction with static stretching

20. In general, yoga exercises for cancer patients ________.
   a. Need no adaptations
   b. Should encompass swift, dynamic movements
   c. Should focus on extending awareness of physical, emotional, sensory, and thinking processes
   d. All of the above