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Physical Impact of Pediatric Cancer and Its Treatment

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Introduction

Childhood cancer survival rates have greatly improved over the last three decades. However, symptoms experienced during treatment often result in complications that may compromise therapy, negatively influence quality of life, and even more notably threaten chances for long-term survival. Each symptom requires careful assessment and appropriate interventions to reduce the distress and improve daily life for the child with cancer and their family.

This chapter discusses the physical impact of cancer and its treatment on the child. The most common symptoms that should be considered during every clinical assessment are reviewed. Discussion includes an overview of each symptom and unique characteristics experienced by children with cancer. Possible causes, risk factors, and important assessment measures for each symptom are examined with specific recommendations for prevention and management.

Bone Marrow Suppression

Chemotherapy agents and radiation therapy cause myelosuppression, a condition that occurs when bone marrow activity is decreased and produces fewer white blood cells, red blood cells, and platelets. In addition, certain malignancies that metastasize to the bone marrow (e.g., leukemia, lymphoma, neuroblastoma, sarcomas) cause a decrease in the number of normal blood cell precursors. When the myelosuppressive effect is severe enough, the child becomes predisposed to infection, anemia, or bleeding, depending on which blood cell line is affected.

Infection

The risk for serious infection in a child receiving treatment for cancer is related to several factors. Cancer therapy often results in neutropenia which is a decrease in the type of white blood cell (neutrophil) that fights infection. An absolute neutrophil count (ANC) less than 1000 cells/microL is defined as neutropenia. The most common risk factors associated with serious infection include children diagnosed with acute myeloid leukemia (AML) or relapsed leukemia, those receiving highly myelosuppressive chemotherapy for non-hematologic malignancies or undergoing hematopoietic stem cell transplantation, and children with more severe neutropenia (ANC < 500 cells/

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microL) expected to last >7 days (Ahmed and Flynn 2014; Lehrnbecher et al. 2012; Pulsipher 2012). Children with cancer who present with fever are at a lower risk for serious infection when the neutropenia is expected to resolve within a week.

Fever may be the only indication that infection is present; important aspects to consider in the history and physical examination are found in Table 3.1 (Freifeld et al. 2011). The child with fever and neutropenia is at risk for potentially fatal septic shock. Children presenting with an absolute neutrophil count <100/mm^3 and have evidence of focal infection (e.g., mucositis, abdominal pain, cellulitis, upper respiratory infection, perianal tenderness) should be carefully monitored for signs and symptoms of sepsis. Children less than 7 days since receiving intensive chemotherapy with or without dexamethasone, all infants with acute lymphocytic leukemia, patients with leukemia or lymphoma during intensive phases of treatment, patients with Down's syndrome, and those who have experienced a relapse and have fever and neutropenia should be carefully evaluated for sepsis.

Because of the high mortality rate associated with untreated infection, all children with cancer who have severe neutropenia (ANC < 500 cells/microL) and fever are considered at risk for a life-threatening infection until proven otherwise. Families should be taught to contact their healthcare providers at the first signs of infection. Evaluation of a child with fever and neutropenia should be completed as quickly as possible. Immediate medical interventions include: intravenous access to obtain blood specimens and begin hydration, antibiotics that are initiated within 1 hour of assessment of neutropenia and fever, and normal saline bolus for hypotension and blood product support as needed (Lehrnbecher et al. 2012). Medical intervention and antibiotic administration are provided promptly if the child shows any clinical localizing signs of infection regardless of the child's temperature (Koh and Pizzo 2011).

Anemia

Children with cancer may experience anemia that commonly occurs as a consequence of impaired bone marrow production as well as blood loss (Agrawal et al. 2011). Anemia transpires when the body does not have enough red blood cells to carry oxygen to tissues and organs. Anemia can be measured by hemoglobin, the amount of protein in red blood cells, and/or hematocrit, the volume of red blood cells compared to the total blood volume. Normal values of hemoglobin and hematocrit vary according to the child's age and gender. Children are amazingly resilient and tolerate low hemoglobin and hematocrit concentrations well, especially if the decline is gradual.

Signs and symptoms of anemia in the child with cancer are directly related to the severity and onset of anemia as well as the type of cancer.

Table 3.1 History and physical assessment: child with neutropenia

History	Physical assessment
• Date of last treatment and details of therapy (agents, dose, route) • Onset of fever and highest temperature (note: dexamethasone may mask fever) • Other symptoms including nausea, vomiting, diarrhea, pain (e.g., mouth, abdomen, perianal), swelling, redness, drainage • Recent diagnosis of GI or GU tumor • Exposure to infection (e.g., TB, Hx MRSA, recent CVL infection) and seasonal illnesses (i.e., RSV, influenza) • Recent invasive procedure • Recent foreign travel • Renal/hepatic dysfunction	Assess for signs/symptoms of shock: • Entire body for signs, tenderness/pain, induration, redness or discharge from any area; *examine closely the skin, nose, teeth, pharynx, sinuses, joints and extremities, procedure sites, and perineal and perirectal areas* • Central line – if external – note any redness or drainage along tunnel or at exit site • Mental status and changes in the child's awareness of person, place, and surroundings

Symptoms include pallor, headache, dizziness, shortness of breath, fatigue, tachycardia, and heart murmur. Children may complain of tiredness and weakness. Assess the child's level of tolerance for activities of daily living and play, and make adjustments to allow as much self-care as possible without undue exertion.

During times when the child with cancer experiences symptoms related to anemia, advise parents to plan diversional activities that promote rest but prevent boredom and withdrawal. Because short attention span, irritability, and restlessness are common in anemia and increase stress demands on the body, activities such as listening to music, playing games on an electronic devise, reading or listening to stories, working on a favorite hobby, coloring or drawing, playing board and card games, or watching television are appropriate. If the child is in school, it may be necessary for the parents to alert the schoolteacher to the child's physical limitations, particularly in terms of strenuous activity.

Medical interventions for anemia are recommended when the child experiences symptoms that place the child at risk for cardiac decompensation. Packed red blood cell transfusions frequently are required when the hemoglobin falls below 7 g/dL or the hematocrit falls below 21 % (Agrawal et al. 2011). Transfusion of blood products may cause transfusion reactions, manifested by fever, chills, body aches, urticaria, pruritus, and, in severe cases, wheezing, tachycardia, and respiratory compromise. Parents and the child should be educated about the need for blood transfusions and be aware of the possible side effects such as transfusion reactions.

Bleeding

Children with cancer are at risk of bleeding related to thrombocytopenia, described as a drop in the number of platelets that play an important role in blood clotting. Decreased platelet count occurs when treatment given for cancer causes myelosuppression or when platelet production is impaired; the bone marrow produces less platelets and the child is at risk for bleeding. The risk for spontaneous internal hemorrhage does not occur until the platelet count is 20,000 per mm^3 or lower (Agrawal et al. 2011).

Children with low platelets due to cancer or treatment should be carefully assessed for signs and symptoms of bleeding. Healthcare providers should pay close attention for signs of bleeding, inquiring about episodes of bleeding from the nose, mouth, or skin. Presence of blood in the urine and stool is evaluated. If the child has experienced recent vomiting, determine whether there was blood present in the fluid. Healthcare providers should carefully examine the child to determine whether there are signs of active bruising and bleeding on the child's skin; small red or purple spots on the skin are called petechiae and are caused by intradermal hemorrhage. Ecchymoses are larger bruises commonly found on the child's skin when platelets are low.

There are several interventions that minimize bleeding when platelets are low and should be discussed with the family before treatment begins and reinforced during follow-up visits. The family and child should be instructed to avoid ibuprofen, aspirin, and aspirin-containing products. These medications can increase bleeding risks by decreasing the effectiveness of platelets and thereby diminishing their ability to stop bleeding by forming a clot.

Skin punctures are avoided as much as possible because bleeding sites can become easily infected. When finger sticks, venipunctures, intramuscular injections, bone marrow aspirations, or lumbar punctures are performed, aseptic technique must be used along with continued observation for bleeding. The use of razors should be avoided, and a soft toothbrush should be used for dental care. Children should avoid using dental floss and are advised not to eat or chew sharp foods (e.g., tortilla chips, ice) to prevent gingival bleeding. Adolescent female patients may be given oral contraceptives or hormone therapy to suppress menses to decrease the risk of excessive bleeding. Rectal temperatures are avoided to prevent trauma of the gastrointestinal mucosa. When platelets are low, children and parents are advised to avoid activities that might cause injury or bleeding, such as riding bicycles and skateboards, climbing trees and playground equipment, and playing contact sports (Rodgers 2015).

If the child experiences epistaxis (nosebleed), the parents should be instructed to pinch the child's nostrils together with a gauze pad held between the thumb and index finger for at least 10 min. If there is persistent nose bleeding, or if the patient experiences hematuria (blood in the urine) or hematochezia (blood in the stool), the child should be evaluated by their healthcare provider. Platelet transfusions are generally reserved for active bleeding episodes that do not respond to local treatment. These types of transfusions are commonly needed during cancer induction or relapse therapy.

Gastrointestinal Impact

The physiological effects of the cancer diagnosis and/or the related treatment can create a variety of gastrointestinal (GI) issues in pediatric patients. Neurological changes and intestinal obstruction from the disease can create multiple GI symptoms, while destruction of mucosal cells throughout the GI tract from chemotherapy and/or radiation treatment causes multiple side effects. These GI issues are quite common among pediatric oncology patients and are very distressing to the patient and their family. A thorough understanding of these issues, prompt recognition, and comprehensive treatment can assist to minimize the issues and decrease distress.

Mucositis/Esophagitis

Mucositis consists of inflammation or ulceration of the mucous membranes in the oral cavity including the lips, tongue, palate, buccal mucosa, gingiva, or floor of the mouth, while esophagitis involves the mucous membranes of the esophagus (Landers and O'Hanlon-Curry 2008). The prevalence of mucositis and esophagitis among pediatric oncology patients is undetermined because there is no universally recognized definition or assessment tool; however, there is an increased incidence among patients who receive fully ablative chemotherapy, head and neck radiation, or total body irradiation (Hogan 2009). These therapies cause damage or death to the rapidly dividing epithelial mucosal cells and can advance to dysphagia (difficulty swallowing).

Characteristics of mucositis are distinguished according to their etiology. Radiation-induced mucositis typically presents as a whitish discoloration about 2–3 weeks into treatment and develops into deepening erythema with ulcers or inflammation (Hogan 2009). On the other hand, chemotherapy-induced mucositis classically presents 5–8 days after treatment, initially with erythema followed quickly by edema and ulceration (Hogan 2009). Despite the importance of a structured oral assessment, few clinical sites use a formal oral assessment scale (Gibson et al. 2010). Important aspects to consider in assessing the oral cavity include voice, swallow, lips, tongue, saliva, mucous membrane, gingiva, and teeth. A recent systematic review of oral assessment instruments found the Oral Assessment Guide (OAG), as a validated and easy to use scale that was suitable for clinical use (Gibson et al. 2010).

Prevention of mucositis is important because it can cause multiple complications such as pain, infection, malnutrition, dehydration, and decreased quality of life (Hogan 2009). Additionally, severe mucositis may cause a delay and/or reduction of subsequent treatments. Preventative measures include keeping the oral cavity clean with brushing and using nonirritating mouthwashes. Topical and sometimes systemic antifungal, antiviral, and antibiotic medications are used to prevent infections. Research is ongoing to explore methods to decrease saliva production, such as cryotherapy and various medications, to decrease the amount of drug contact with the oral mucous membranes, while additional research is looking at increasing epithelial cell proliferation, such as the use of glutamine, beta-carotene, and prostaglandins (Wohlschlaeger 2004).

Treatment of mucositis and esophagitis primarily focuses on pain control and maintaining nutrition/hydration. Support and close monitoring must be provided for patients with dysphagia, as significant risks are associated with the inability to swallow. In addition to systemic analgesic medication, topical agents such as sucralfate and magnesium hydroxide provide symptomatic relief (Wohlschlaeger 2004). Fluoride rinses and saliva substitutes relieve xerostomia (dry mouth). Fluids and nutrients administered intravenously support the patient's hydration and nutritional requirements during periods of inadequate oral intake. Agents such as vitamin E and granulocyte-macrophage colony-stimulating factor mouthwash are effective in reducing the duration of mucositis among adults but more research is needed with children (Wohlschlaeger 2004).

Anorexia and Cachexia

Anorexia is a loss of appetite and occurs in 6–60 % of all children treated for cancer (Montgomery et al. 2013). Anorexia can be very distressing to the patient and family as eating has cultural, emotional, and religious significance and is often equated as an action of nurturing and caring (Santucci and Mack 2007). Furthermore, anorexia can cause electrolyte disturbances, weight loss, and malnutrition, which can increase morbidities and delays in treatment. Anorexia can be a result of the disease such as brain tumors, poor prognosis or relapsed leukemia, and advanced cancer (Rogers et al. 2008) (see Chap. 14 on palliative care for more information). Taste changes have been reported by children undergoing cancer treatment as one of the primary causes of eating difficulties (Skolin et al. 2006). Other risk factors include mucositis, dysphagia, xerostomia, constipation, pain, and/or a change in environment resulting in the inability of having foods prepared in a culturally familiar manner and eaten in a relaxing environment (Santucci and Mack 2007).

Anorexia can be mild and temporary or can be severe and prolonged. Severe anorexia can lead to cachexia. Cachexia is a multifactorial metabolic syndrome that causes an increase in the catabolic process associated with reduced food intake (Tuca et al. 2013). Cachexia causes a significant loss in weight, muscle mass, and fat that is often not reversible with increased caloric intake (Tuca et al. 2013).

There are multiple methods to assess eating and nutrition in individuals including nutritional history, anthropometric measurements, and laboratory markers. A patient's history is one of the most important methods to obtain data during an assessment and should include an assessment of appetite, 24 hour diet recall or food diary, recent diet changes, food preparation methods, use of vitamins and/or supplements, and gastrointestinal symptoms (Huhmann and August 2008). Anthropometric measurements, such as height and weight, are quick and easy measurements commonly used to evaluate nutritional wellbeing; however, weight can fluctuate in some patients due to fluid shifts and may not accurately represent a patient's nutritional status. Laboratory measurements are another customary method to assess the nutritional status in patients. Serum protein markers, such as albumin and prealbumin, are traditionally used to evaluate the nutritional status and responses to nutritional interventions. However, conditions such as liver or kidney disease, dehydration, and anemia can affect the accuracy of these tests.

Early intervention of anorexia is important to prevent complications and/or cachexia. Discussions on methods to maintain adequate caloric intake should occur early in treatment and strategies to promote eating are provided in Table 3.2. Food should never be forced on the child and patients report being forced to eat caused them to eat less or not eat at all (Rodgers et al. 2010). Patients who are not interested in eating can benefit from high-calorie oral supplementation but children are often reluctant to drink them because of the taste and consistency. Medications such as progestational drugs, corticosteroids, and cannabinoids can be used to stimulate appetites; however, many of these medications are restricted by the disease and age of the child and can cause unwanted side effects (e.g., hallucinations, irritability, fluid retention) (Santucci and Mack 2007). It is important to educate parents and family caregivers about these potential side effects so they can support the child and make decisions that

Table 3.2 Strategies to promote eating

Symptom	Strategy
Mucositis	Select foods that are easy to chew, such as oatmeal Avoid acidic, spicy, or salty foods Serve foods cold or room temperature
Xerostomia	Chew gum, eat hard candy, or brush teeth prior to meals Offer liquid foods (i.e., soup) or add sauces or gravy on the food Provide small sips of water frequently with a straw while eating Moisten lips with a lip balm
Anorexia	Provide small frequent meals Add extra calories to foods (i.e., cheese, butter) Create homemade smoothies or milkshakes with the child's favorite ingredients Allow the child to prepare the meals Avoid forcing the child to eat Provide meals in a comforting, relaxing environment

Information obtained from Rodgers et al. (2010)

take into account their child's psychological and social needs.

Two traditional methods to provide nutritional support include enteral nutrition (EN) and total parenteral nutrition (TPN). EN can be administered through a tube that is passed from the nose to the stomach (nasogastric tube), through a tube inserted directly into the stomach (gastrostomy) by surgery, or through a tube into the small intestine (jejunostomy). TPN is administered through a central venous catheter. EN is beneficial to patients because it preserves the structure and the function of the GI tract; however, it may not be tolerated because the tube placement and feeds can exacerbate symptoms of nausea, vomiting, and diarrhea (Montgomery et al. 2013). TPN may be better tolerated by patients and can provide more caloric, protein, and vitamin supplementation because the nutrition is received intravenously instead of through an already irritated GI tract; however, TPN has been associated with an increased risk of liver complications and infections (Montgomery et al. 2013). Treatment of cachexia includes appetite stimulants and nutritional support but also requires successful treatment of the malignancy to minimize energy expenditure (Santucci and Mack 2007).

Nausea and Vomiting

Nausea and vomiting are commonly occurring symptoms in pediatric oncology with an incidence as high as 90 % among patients receiving chemotherapy (Phillips et al. 2011) and up to 80 % in patients undergoing radiation therapy (Feyer et al. 2011). These symptoms have very distinct characteristics. Nausea consists of a wavelike sensation of GI distress that may lead to retching or vomiting and is often accompanied by sweating, increased salivation, and weakness, while vomiting is a forcible expulsion of the stomach contents through the mouth that may be accompanied by nausea, rapid breathing, and abdominal cramping (Landers and O'Hanlon-Curry 2008). These symptoms can result from:

- Disease such as brain tumors
- Treatment including chemotherapy, radiation, or anesthesia from surgery
- Side effects from medication(s) such as opioids

The specific emetogenic risk for various radiation sites and chemotherapy agents are listed in Table 3.3. Other factors that may increase the risk of nausea and/or vomiting include prior motion sickness, fatigue, emotional stress such as anxiety or fear, sensitivity to strong odors, and previous bad experiences with nausea or vomiting. Nausea and/or vomiting can occur before the start of treatment, referred to as anticipatory; during administration or within 24 hours after treatment, referred to as acute; or more than 24 hours after completion of treatment, referred to as delayed.

Prompt recognition of these symptoms is crucial as they have significant physical and psychological consequences (Table 3.4). Before treatment begins, an assessment of nausea and vomiting should include type of treatment, prior experience with nausea and

Table 3.3 High and moderate emetogenic potential of radiation sites and common chemotherapy agents

Classification	Radiation sites	Chemotherapy agents
High	Total body irradiation	Carboplatin Carmustine >250 mg/m^2 Cisplatin Cyclophosphamide >1 g/m^2 Cytarabine >3 g/m^2/dose Dactinomycin Methotrexate <12 g/m^2 Procarbazine (oral) Thiotepa >300 mg/m^2
Moderate	Upper abdomen Half-body irradiation Upper-body irradiation	Anthracyclines (daunorubicin, doxorubicin, idarubicin) Amifostine >300 mg/m^2 Arsenic trioxide Busulfan Camustine <250 mg/m^2 Clofarabine Cyclophosphamide <1 g/m^2 or oral Cytarabine 200 mg to <3 g/m^2 Etoposide (oral) Ifosfamide Imatinib (oral) Intrathecal chemotherapy Melphalan >50 mg/m^2 Methotrexate >250 mg to <12 g/m^2

Information from Feyer et al. (2011) and Dupuis et al. (2011)

Table 3.4 Consequences of nausea and/or vomiting

Physical	Psychological
Anorexia	Stress
Malnutrition	Anxiety
Electrolyte imbalances	Worry
Dehydration	Nervousness
Weight loss	Reduced quality of life
Fatigue	Frustration
Insomnia	Irritability

vomiting, and effectiveness of previous interventions. Frequent nausea and vomiting assessments should then occur throughout (acute) and after treatment (delayed). Assessments should include current level of nausea and vomiting, effectiveness of pharmacological and non-pharmacological interventions, and level of emotional stress. Anxiety and psychologically conditioned responses may also contribute to anticipatory nausea and vomiting even before chemotherapy infusion and can be addressed with psychological or pharmacologic interventions.

Additional assessments should consist of a thorough evaluation for complications from the nausea or vomiting including anorexia, malnutrition, dehydration, and electrolyte imbalances.

The goal is to prevent nausea or vomiting from occurring. Prevention and treatment strategies consist of various non-pharmacological and pharmacological interventions, which provide individual levels of relief to patients. Therefore, healthcare providers including psychosocial clinicians should encourage a variety of strategies for patients experiencing nausea or vomiting and evaluate the effectiveness of each strategy. Non-pharmacological interventions (Table 3.5) can often be self-initiated by the patient and have little to no side effects. Pharmacological interventions include a variety of antiemetic medications including 5-HT3 receptor antagonists, NK-1 antagonist, dopamine antagonists, benzodiazepines, cannabinoids, and corticosteroids (Phillips et al. 2011). A recent systematic review found 5-hydroxytryptamine-3 (5-HT3) antagonists are more effective than other antiemetic agents even

Table 3.5 Non-pharmacological interventions for nausea and/or vomiting

Category	Strategy
Diet	Eat small frequent meals; avoid getting hungry Maintain adequate hydration Avoid foods with strong odors Eat foods at room temperature Eat bland foods, such as rice, crackers, and gelatin Avoid greasy, fatty, and spicy foods
Cognitive/behavioral	Relaxation Hypnosis Meditation or guided imagery Progressive muscle relaxation Music or art therapy Distraction
Touch therapies	Acupuncture or acupressure Massage
Herbal remedies	Ginger Aromatherapy
Others	Exercise Social support

Information obtained from Rodgers et al. (2010) and Dupuis et al. (2013)

when combined with a corticosteroid (Phillips et al. 2011) and therefore are the drug of choice for prevention and treatment of therapy-related nausea or vomiting. These medications, such as ondansetron, granisetron, and tropisetron, produce little side effects and are generally well-tolerated. The NK-1 antagonist (aprepitant) is also an effective medication but is currently restricted for use only in children 12 years of age and older (Lexicomp 2014). Despite the legalization of marijuana in several states, the medical use of marijuana for nausea and vomiting is controversial due to potential carcinogens and adverse effects on the cardiovascular, respiratory, and central nervous system and the unidentified outcome evidence (Torado 2012). Synthetic oral cannabinoids once commonly prescribed are now recommended for use only in patients with breakthrough nausea and vomiting due to the development of newer antiemetic medications that cause fewer side effects (Torado 2012).

Case Vignette

Abby is a 16-year-old girl who is undergoing chemotherapy for treatment of her osteosarcoma. Abby has experienced significant nausea with her treatment that has caused her to have a poor appetite. Prior to diagnosis, her body mass index (BMI) was at the 75th percentile and she is now at the 50th percentile. Although her BMI is now within normal limits, her recent weight loss is concerning. Abby's mother reports that she is frustrated because she cooks any type of food that Abby appears interested in and makes her eat it right away but she is still losing weight. Abby reports that she is often nauseous when her mom is cooking and feels that she would start vomiting if she was forced to eat. Healthcare providers discuss ways that Abby may become more interested in eating such as allowing Abby to select favorite foods with minimal smells, go to another room during food preparation, and eat small amounts several times a day in a relaxed environment. Healthcare providers educate Abby's mother about cooking with butter, cheese, or whole milk to add extra calories to food and allowing Abby to eat at her own pace because children who are forced to eat often eat less. Abby's nausea is managed through antiemetic medication taken routinely throughout the day and relaxation techniques to decrease anxiety while eating. Weights are monitored closely at each clinic visit and small weight gains are celebrated with the staff.

Diarrhea

Diarrhea is an increase in quantity, frequency, or fluid content of the stool that is different from usual patterns and can be accompanied by abdominal cramping, flatulence, nausea, vomiting, and fever (Landers and O'Hanlon-Curry 2008). Diarrhea is a result of changes in intestinal absorption and motility caused from a variety of

Table 3.6 Interventions for diarrhea and constipation

Symptom	Pharmacological strategies	Non-pharmacological strategies
Diarrhea	After infection has been ruled out, administer anti-motility agents (e.g., loperamide)	Encourage adequate oral hydration Minimize intake of high-fiber foods Avoid fatty or spicy foods, dairy products, and caffeine
Constipation	Administer stool softeners (e.g., docusate), osmotic agents (e.g., lactulose), and/or stimulants (e.g., senna)	Provide daily access to the toilet and encourage privacy during this time Increase fluid and fiber intake Increase physical activity Resolve pain

Information obtained from Santucci and Mack (2007) and Shaw and Taylor (2012)

triggers including chemotherapy, radiation therapy, infection, and bowel resection. The incidence of diarrhea varies greatly due to the variety of potential etiologies. Treatment is likely the cause of diarrhea once infection is ruled out with multiple testing of the stool.

Patients with diarrhea require a thorough assessment of their stool output and associated symptoms. Diarrhea is classified according to duration and severity. Duration can be classified as acute (occurring less than 2 weeks), persistent (lasting 2–4 weeks), or chronic, which can continue longer than 4 weeks (Pessi et al. 2014). Severity is categorized as uncomplicated, comprised of diarrhea without associated symptoms, and complicated, consisting of diarrhea with associated symptoms or complicating factors (Shaw and Taylor 2012). Diarrhea can deplete fluids, electrolytes, and nutrition; therefore, information regarding hydration and nutrition status, such as food and fluid consumption, weight loss, and urine output, must be obtained to identify complications (Shaw and Taylor 2012).

Treatment of diarrhea consists of diet modifications and pharmacological management (Table 3.6). Foods that are fatty or spicy or contain dairy or caffeine should be avoided (Shaw and Taylor 2012). Small frequent meals are best tolerated, and oral intake of water, sports drinks, broth, etc., is imperative in maintaining adequate hydration (Shaw and Taylor 2012). Inability to maintain adequate hydration results in the immediate need for the administration of intravenous fluid and likely hospitalization (Shaw and Taylor 2012). Antidiarrheal medication is indicated once infections are excluded. Loperamide is a standard medication administered orally for treatment of diarrhea and can be administered to children 2 years of age or older (Lexicomp 2014). For patients unable to tolerate oral medication or with persistent or complicated diarrhea, octreotide can be administered to infants or children subcutaneously or intravenously (Lexicomp 2014). Use of probiotics is likely to be effective for diarrhea related to cancer therapy; however, more research is needed to determine the optimal probiotic strain, dosage, and timing (Shaw and Taylor 2012).

Constipation

Constipation involves the infrequent passage of hard, dry stool that can be accompanied with abdominal cramping, abdominal and/or rectal pain, nausea, vomiting, and blood-streaked stools (Landers and O'Hanlon-Curry 2008). Patients may not realize the importance or feel comfortable discussing their bowel movements with others, so healthcare providers should perform a detailed history and provide education. A thorough assessment includes questions of frequency and consistency of stools, associated symptoms, and any personal concerns. Obtaining a past medical history is also important as patients with a previous history of constipation are more prone to developing constipation during their oncology treatment (Pashankar et al. 2011). Constipation is diagnosed when a child with a developmental age of 4 years meets two or more of the following criteria (Pashankar et al. 2011):

- Two or fewer defecations in the toilet weekly
- At least one fecal incontinence per week

- Retentive posturing or stool retention
- Pain or hard bowel movements
- Large stools that may obstruct the toilet

The cause of constipation in pediatric oncology patients is multifactorial and includes effects from the disease, treatment, medication(s), or problems with mobility, diet, hydration, or psychological adjustment (Phillips and Gibson 2008). The primary or metastatic disease can obstruct portions of the bowel or compress the spinal cord resulting in an inability to defecate. Several chemotherapy agents, radiation therapy especially to the pelvic area, and commonly used medications such as opioids, antiemetics, antidepressants, and anticonvulsants cause a decrease in bowel motility and secretions that can progress to constipation (Santucci and Mack 2007). In addition, a decrease in activity, inadequate intake of fluids and fiber, and issues of anxiety, lack of privacy, or limited access to a toilet can result in constipation (Landers and O'Hanlon-Curry, 2008). If left untreated, constipation can cause significant pain, lack of appetite, nausea, vomiting, and anal fissures (small tears in the skin around the anus).

Prevention is key for constipation (Table 3.6). Maintaining regular exercise, adequate hydration, and a high-fiber diet are important strategies to prevent constipation. Often medications are used in the prevention and treatment of constipation. Medications include stool softeners such as docusate, osmotic agents such as lactulose, and stimulants such as senna or bisacodyl (Santucci and Mack 2007). Enemas are rarely used in pediatric oncology patients because of the risk for mucosal trauma and subsequent infection.

Weight Changes

Weight status in children is measured by body mass index (BMI). Children with a BMI ≥ the 95th percentile based on the Centers for Disease Control and Prevention (CDC) growth charts for age and gender are considered obese (CDC 2014a). The term "overweight" is used to describe children with a BMI between the 85th and 94th percentiles and underweight children are those with BMIs less than the 5th percentile (CDC 2014a).

Table 3.7 Disease/treatment factors associated with weight changes

Associations with weight loss	Associations with weight gain
Medulloblastoma	Acute lymphoblastic leukemia
Head and neck cancers	Cranial radiation
Solid tumors with metastasis	Glucocorticoids
Relapsed leukemia or lymphoma	
Brainstem tumors	
Radiation treatment involving the head, neck, or abdomen	

Children often experience weight changes secondary to the disease and the treatments that they receive (Table 3.7). Baseline BMI and nutritional status should be assessed at diagnosis as patients may present with underlying weight or nutritional issues. Weight trends should be monitored throughout therapy. Changes are very patient specific and variable as people may respond differently to chemotherapy and other medications. It is important to monitor weight trends as being underweight, overweight, or obese can decrease survival in many childhood cancers such as acute lymphoblastic leukemia (Orgel et al. 2014), acute myeloid leukemia (Inaba et al. 2012), and osteosarcoma (Altaf et al. 2013). Abnormal weight status can also have a negative impact on survival in children undergoing hematopoietic stem cell transplant (White et al. 2012).

Weight Loss

It is suggested that up to 46 % of pediatric oncology patients experience malnutrition (Bauer et al. 2011). Marked weight loss may be the symptom that first causes families to seek medical attention and prompt the discovery of a cancer diagnosis. Weight loss, greater than 10 % of a child's bodyweight within 6 months prior to diagnosis, is especially important in Hodgkin and non-Hodgkin lymphoma. This weight loss is considered a "B" symptom, which affects staging and treatment.

A decrease in weight *prior* to therapy is usually associated with the disease process. In the case of solid tumors, the growing mass may exert pressure on structures within the abdomen, central nervous system, or other parts of the gastrointestinal tract that interfere with normal digestion or hunger mechanisms. The presence of pain may also cause decreased appetite. Surgery to remove the tumor often helps to alleviate continued weight loss.

Weight loss *during* therapy is mainly due to the side effects of treatment. Chemotherapy can cause taste changes, dry mouth, nausea, vomiting, anorexia, mucositis, or other conditions which impact appetite and food intake (see Table 3.2 for strategies to promote eating). Depression or mood may also influence eating habits. Radiation that involves the head, neck, or abdominal area also increases the risk for weight loss secondary to esophagitis, mucositis, nausea, vomiting, and diarrhea.

Treatment for weight loss consists of identifying the underlying cause. Side effects of treatment interfering with nutritional intake can often be managed symptomatically. Medications can be administered to decrease nausea and vomiting. Pain medications can also be given to alleviate pain, if that is the underlying cause. If warranted, medications can also be administered to increase appetite.

Weight Gain

It is well documented that children treated for childhood acute lymphoblastic leukemia (ALL) often experience weight gain during and after cancer treatment. One study found that obesity rates increased from 14 % at the beginning of therapy to 23 % by the end of therapy in ALL patients (Withycombe et al. 2009). In addition, weight gain appears to continue after therapy with a meta-analysis of 47 studies showing the prevalence of being overweight/obese in ALL survivors ranging from 29–69 % (Zhang et al. 2013). This is significantly higher than the national childhood obesity rate of approximately 17 % (CDC 2014b).

Some brain tumors, in particular craniopharyngiomas, are also associated with an increased risk for obesity. Tumors or treatments (radiation or surgery) that cause hypothalamic-pituitary axis damage are highly problematic. Hypothalamic obesity is a condition that may occur when the normal hypothalamic center functions are disrupted resulting in imbalances in hunger control, satiety, and energy regulation (Lee and Korner 2009). This condition is often described as intractable weight gain and is present in up to 75 % of children with craniopharyngioma (Lustig 2011).

Currently there is no standard treatment to combat excessive weight gain other than recommending that families watch their diet and engage in physical activity. Prevention of obesity is preferred as it is difficult to reverse once it develops. Having a healthy weight is especially critical for childhood cancer survivors as they may already be at risk for cardiovascular issues due to late effects of chemotherapy. Obesity also increases the risk for hypertension, diabetes, metabolic syndrome, depression, decreased quality of life, and secondary cancers (Berenson and Bogalusa Heart Study Group 2012; Kanellopoulos et al. 2013).

When obesity is present, it is important to refer the family for nutritional counseling. Children are often dependent on their parents for food preparation so it is imperative that the whole family be involved in learning healthy eating habits. Likewise, daily family physical activity should be encouraged. In children with hypothalamic obesity, these interventions are often ineffective in significantly reducing weight and may warrant more invasive treatment options such as gastric bypass surgery.

Sensory Impact

Sensory changes occur frequently during cancer therapy and can be either temporary or permanent in nature depending on the underlying etiology. Although most sensory changes are not life threatening, they can be life changing and can negatively impact a child's quality of life.

Neuropathy

Neuropathy occurs when chemotherapeutic drugs damage the peripheral nerves, which are those outside of the central nervous system such as in the hands and feet (Gilchrist 2012). Neuropathy primarily occurs with drugs that are known to be neurotoxic such as cisplatin, carboplatin, vincristine, and vinblastine. Neuropathy can be sensory in nature and lead to symptoms of burning, tingling, or shooting pain in the hands and feet. Neuropathic jaw pain is also frequently reported in children (McCarthy and Skillings 1992). In addition, neuropathy can impact motor function which can lead to foot drop and problems with balance and coordination. Fine motor skills may also be affected leading to difficulty with grasping objects or performing tasks such as buttoning a shirt. Neuropathy has been reported to occur in up to 18.3 % of children treated for acute lymphoblastic leukemia, brain tumors, and Wilms' tumor (Purser et al. 2014).

Neuropathy can be a dose-limiting toxicity which means that the severity of symptoms may mandate that a reduced dosage of chemotherapy be administered until the neuropathy resolves. There is no treatment for neuropathy, once it occurs, other than symptom management. This management may include pain medicines or other medications specifically for nerve pain. Physical therapy services may be ordered to address balance issues and muscle weakness. In general, neuropathy tends to resolve once the causing agent is stopped but can linger for months to years in a small percentage of patients.

Neuropathy can limit mobility and decrease a child's functional status. Participation in sports and other social activities may decline secondary to physical limitations or pain. Neuropathy may increase a child's reliance on parents as they may be unable to complete tasks such as buttoning a shirt or braiding their hair. For adolescents, this may have greater importance as this is the age at which most begin establishing their independence. Emotional consequences may occur secondary to neuropathy and can range from frustration with the inability to complete tasks independently to anger and/or depression. Emotional changes should be anticipated and mental health professionals should be involved in caring for the child.

Case Vignette

Ben is a 6-year-old boy who received vincristine for treatment of his brain tumor. Ben's parents report that he has become more irritable recently and is difficult to console. He is often seen rubbing his stomach and looking at his fingers. The clinic nurse notices that Ben is having difficulty with his fine motor skills. She uses a pain face scale and Ben points to the sad face, representing pain. After spending time playing and talking with Ben, it is determined that Ben has pain in his abdomen and fingers. Ben is diagnosed with central neuropathy (constipation) and peripheral neuropathy (fingertip numbness). A stool softener medication is started for his constipation along with educating Ben's parents to increase his fluid and fiber intake, while gabapentin medication is given for the fingertip numbness. Ben is monitored closely at subsequent clinic visits for his neuropathy.

Vision

Vision changes, such as blurry vision, have been reported in association with multiple chemotherapeutic agents used to treat childhood cancer. These changes are usually short lived and resolve when the chemotherapy is stopped. More severe vision issues, such as decreased vision, have been reported with the use of cisplatin and etoposide (Hilliard et al. 1997). Ocular nerve and optic motor nerve damage have also been reported in those receiving vinblastine and vincristine (Omoti and Omoti 2006). Ophthalmology evaluations are the optimal method for assessing eye and vision changes during treatment.

Alterations in vision can also be secondary to certain cancers and their location. Diseases such as retinoblastoma, optic gliomas, or leukemia that have spread to the central nervous system can physically invade or destroy optic structures. When disease is the cause, vision changes are usually more severe and may include a decrease or total loss of eyesight. In these cases, treatment options to save or spare vision are limited. Depending on the exact location and size of the tumor, surgery or radiation may be considered in the treatment plan. One potential sequelae of surgery is double vision (called diplopia). Treatment for diplopia may consist of occluding the line of vision in one eye, therefore preventing the overlap of visual fields which causes the double vision. This treatment was traditionally done by patching one eye, but more modern methods of treatment include placing an occlusive patch over the inside of one eyeglass lens which directly blocks the line of sight causing the double vision. Children suffering from diplopia may also benefit from completing a vision rehabilitation program. This type of program teaches people to maximize their eye sight through visual training which may include specialized exercises for the eyes.

Hearing

Hearing loss is variable depending on the treatment received and the individual person. Typically, those treated with chemotherapy such as cisplatin or carboplatin tend to be most at risk for auditory changes. Children undergoing brain surgery and/or cranial radiation may also experience hearing loss.

Hearing issues may be reported by patients as “ringing” in the ears or parents/teachers may observe that the child seems to have difficulty hearing or following instructions. Clinicians should be aware that reports of difficulty in school or apparent lack of attention may be indications of hearing loss. Clinicians are also able to predict which children are at risk for hearing loss by using the Children’s Oncology Group Long-Term Follow-Up Guidelines (2013) and screening for the following treatment risk factors: less than 4 years of age during treatment, received a cumulative cisplatin dose of ≥360 mg/m^2, received cisplatin after cranial radiation, received higher dose cisplatin (e.g., cisplatin 5 days per course at 40 mg/m^2 per day), received carboplatin for transplant conditioning, or received any carboplatin given prior to 1 year of age. Pediatric oncology diagnoses most associated with hearing loss include neuroblastoma, osteosarcoma, germ cell tumors, and brain tumors. Recommendations for hearing tests following childhood cancer therapy include a hearing exam at least once after finishing therapy for all children who received cisplatin or carboplatin as part of their chemotherapy regime (Children’s Oncology Group n.d.). In addition, children who received radiation to the brain (cranial), ear, and infratemporal or nasopharyngeal areas should also undergo hearing exams after ending therapy. This is especially important for those who received radiation doses of 30 Gy or higher. Annual follow-up is recommended if problems are detected during the screening.

Hearing tests can be performed by trained audiologists using headphones which emit various frequencies and volumes of sounds. For children too young to be tested using headphones, a brainstem auditory evoked response (BAER) test can be performed while the child is asleep. This type of test uses electrodes placed on the scalp to measure brain wave activity in response to sound. Behavioral exams can assist with screening in younger children (i.e., testing to see if a child turns his/her head toward voices or noises).

Treatment for hearing loss may include having the child wear hearing aids or teachers using amplification systems in the classroom to increase the volume of sound. Cochlear implants are used for severe cases of hearing loss. A cochlear implant involves surgery to place electrodes that can carry sound signals directly to the auditory nerve. Children with hearing loss may also benefit from early speech therapy services.

Taste

Roughly 16.5 % of children undergoing chemotherapy report alterations in taste (Collins et al. 2000). The perception, or reporting, of taste changes may increase with age as 38–77 % of

Table 3.8 Recommendations to manage taste changes

Strategy	Rationale
Experiment with seasonings/spices/sauces	Seasonings can be added to match taste preferences during therapy
Use plastic silverware	May reduce metallic taste in mouth
Allow food to cool off prior to eating	Changing the temperature may change the taste
Try eating eggs, chicken, and beans along with other protein sources	Avoid beef if it does not taste good, or try marinating the beef prior to cooking to change the flavor
Eat smaller, more frequent meals	Finger foods should always be available
Avoid foods that have a strong odor	Foods such as fish or sauerkraut have strong smells and may be bothersome

Adapted from Rehwaldt et al. (2009)

adult cancer patients note a change in taste after receiving chemotherapy (Rehwaldt et al. 2009). Changes in taste may consist of a metallic taste to food or may present as a change in food preferences. Alterations in taste can be distressing and may lead to food aversion and decreased nutritional intake. This side effect can be especially troubling if it limits their ability to receive adequate nutrition.

Some chemotherapeutic agents are known to have a greater risk for taste disturbances, such as cisplatin, carboplatin, and cyclophosphamide. Although there is no action that prevents taste changes, patients and families can be offered suggestions for how to manage the changes. These strategies include avoiding the use of metal silverware and eating colder food for those who experience a metallic taste (Rehwaldt et al. 2009). Other suggestions include eating smaller amounts of food more frequently or trying the addition/deletion of food seasonings such as salt (Table 3.8).

Musculoskeletal Impact

Changes to the musculoskeletal system usually occur in children who have tumors arising from the bone or muscle. Sarcomas represent 20 % of pediatric solid tumors and include diagnoses such as osteosarcoma, Ewing sarcoma, and rhabdomyosarcoma (Burningham et al. 2012). One of the primary treatment options for these types of tumors is surgery. For those tumors that occur in extremities, the surgery can entail either a limb salvage procedure or an amputation. The decision between these two options is based on whether the tumor can be fully surgically resected and which option allows for the greatest amount of physical functioning post-procedure.

As the chemotherapy regimens change and survival rates increase, the quality of long-term physical functioning becomes increasingly important. Those children with lower extremity involvement have a 50 % higher risk for activity limitations as compared to children with upper extremity involvement (Marina et al. 2013). In general, studies show that amputees and patients with limb-sparing surgery have little reported differences in disabilities (Marina et al. 2013).

Both amputees and those with limb-sparing surgery frequently report long-term pain. Phantom pain occurs in up to 76 % of children with limb amputations, but only 10 % of these patients report pain lasting for greater than 12 months (Burgoyne et al. 2013). Persistence of pain following limb-sparing surgery has also been reported and is most likely related to neuropathy or instability/weakness of the joint or fibrosis around the prosthesis (Anghelescu et al. 2011).

A child's self-image can be impacted by the type of surgery that is completed. Limb salvage is usually the desired option by parents and adolescents. There are multiple types of limb salvage procedures some involving implants and prosthesis. Rotationplasty is one type of surgery considered in children with distal femur tumors. This is a surgery which allows for the lower leg to be partially amputated, the foot rotated 180 degrees, and reattached to the upper femur. This type of surgery allows for the ankle to function in place of the knee joint and works well with special prostheses which can allow for greater participation in sports.

As with all medical decisions related to childhood cancer, parents and age-appropriate children should be allowed to participate in decisions related to surgery options. In addition, conversations should occur prior to surgery to prepare children for amputation and may include the use of pictures or dolls with a similar amputation. Adolescents may benefit from talking to another patient who has had an amputation. Parents also need preparation and guidance for how to support their child before and after the surgery. Individual counseling, support groups, and psychosocial assessments are modalities that can assist families with embracing the changes related to limb amputation or limb-sparing procedures.

Integumentary Impact

Alterations to the integumentary (skin) system are common during cancer treatment. Chemotherapy and radiation damage rapidly dividing cells including rapidly dividing healthy cells such as the hair, skin, and nails. This damage is diverse in presentation ranging from a mild skin rash, to photosensitivity, to a severe hypersensitivity reaction. In addition, surgical procedures such as tumor resection, lumbar punctures, bone marrow aspirates, and implantation of venous access devices alter the integrity of the skin. Factors such as malnutrition and immobility can increase the potential for skin breakdown and/or lengthen the healing process (Norville 2008). Assessment of the integumentary system is an important focus.

Alopecia

Radiation and many chemotherapy agents damage the proliferating cells in the hair follicles, causing thinning or complete loss of hair (Alley et al. 2002). Hair loss can occur on the head, eyebrows, eyelashes, and body. Hair loss related to chemotherapy usually occurs throughout the body, whereas hair loss secondary to radiation only affects a specific area. Hair loss usually appears within 1 week of treatment and new growth usually begins several weeks after the final treatment, although in some cases the hair loss may be permanent. It is important to prepare the child and families for hair loss.

Although alopecia causes no significant medical threats, patients have reported high psychological distress and one of the most feared side effects of cancer treatment (Alley et al. 2002). Distress is often correlated with the patient's age with higher distress reported in adolescents. Research has evaluated strategies to prevent hair loss including scalp tourniquets, hypothermic scalping devices, and topical medications; however, no evidence has supported the use of any of these strategies (Alley et al. 2002; Viale 2006). Management of alopecia consists of the use of wigs, hats, and scarves until the hair returns. Most children and adolescents adapt to temporary alopecia; permanent hair loss or thinning due to scalp radiation is much more distressing and is often in the context of other physical or neurocognitive late effects.

Radiation Recall

Radiation recall is an acute inflammatory reaction that occurs on previously irradiated areas of the skin once triggered by precipitating agents (Burris and Hurtig 2010). Diagnosis occurs after an evaluation of the patient's treatment history, symptoms, and physical examination. Signs of radiation recall range from a mild rash, dry desquamation, or pruritis to swelling, edema, vesicles, and maculopapular eruptions, which are usually confined to a specific area of previous irradiation treatment (Burris and Hurtig 2010). The most common precipitating agents are chemotherapy agents such as bleomycin, dactinomycin, daunomycin, etoposide, melphalan, and methotrexate (Norville 2008); however, not all cases of radiation recall are published and additional unknown agents may be causative factors (Burris and Hurtig 2010). Radiation recall is unpredictable. Most cases occur after an initial dose of the precipitating agent but some patients may experience the effect after several exposures to the precipitating agent.

There is no current therapy specific for the prevention or management of radiation recall, although supportive care may be necessary (Burris and Hurtig 2010). Topical or systemic steroids or antihistamines may be indicated to reduce the inflammation when it occurs. As with any type of irritated skin, good hygiene, sun avoidance, and wearing loose clothing are imperative to the healing process. Resolution of the dermatitis is highly individualized. The precipitating agent should be delayed or withdrawn from the patient's treatment regimen as the skin is healing. Re-exposing the patient to the precipitating agent does not always elicit a second reaction, and determination of restarting the medication depends on individual circumstances and the extent, severity, and location of the reaction (Burris and Hurtig 2010). Steroids can be administered prior to the re-exposure, although there is conflicting evidence about the efficacy of the premedication (Burris and Hurtig 2010).

Palmar-Plantar Erythrodysesthesia (Hand-Foot Syndrome)

Palmar-plantar erythrodysesthesia (PPE, also known as hand-foot syndrome) is a common side effect with certain chemotherapy agents. The syndrome was originally described in patients receiving cytarabine but is now noted to be caused by additional chemotherapy agents such as liposomal doxorubicin, 5-fluorouracil, capecitabine, cisplatin, cyclophosphamide, daunorubicin, etoposide, methotrexate, and thiotepa (Webster-Gandy et al. 2007). Incidence of PPE can range from 3–68 % of patients receiving the high-risk chemotherapy agents (Webster-Gandy et al. 2007). Cause of the syndrome is not well understood, although it has been postulated that either the small capillaries in the palms and soles rupture due to an inflammatory reaction or that the chemotherapy agents are excreted in the sweat making the palms and soles more prone to their large number of sweat glands (Viale 2006; Webster-Gandy et al. 2007).

Regardless of the cause, patients suffering from this syndrome have initial symptoms of tingling in their fingers and toes followed with erythema and swelling of their palms and soles that can continue to progress to rash, ulcerations, desquamation, and burning pain (Webster-Gandy et al. 2007). Although PPE is not life threatening, it can cause considerable pain and interfere with activities of daily living. Patients need to be encouraged to promptly report any of these signs and symptoms to their healthcare provider, so that treatment can be initiated.

Preventative measures consist of cooling of hands and feet with ice packs and using specific topical creams and emollients, such as 99 % dimethyl sulfoxide (DMSO) during treatment; however, studies have yet to prove efficacy of these strategies (Webster-Gandy et al. 2007). The most effective treatment for PPE is stopping the aggravating chemotherapy agent and reducing the dose or lengthening the interval for subsequent administrations (Webster-Gandy et al. 2007), although some patients were able to receive further therapy without changes and experienced no further complications (Viale 2006). Treatment also includes supportive therapies such as the use of lotions and creams, avoidance of extreme temperatures, and avoidance of activities that increase pressure to the palms and soles.

Extravasation

Extravasation refers to the unintentional leakage of a chemotherapy medication from the vessel into surrounding tissue that may be responsible for damage to the skin (Gonzalez 2013). This complication occurs in up to 6 % of patients receiving chemotherapy from peripheral devices and up to 4.7 % of patients receiving chemotherapy from central venous access devices (CVAD) (Gonzalez 2013). Symptoms range from irritation and mild swelling, to ulcerations or blisters, to necrosis of the tissue (Gonzalez 2013).

Damage due to extravasation is related to the amount of leakage and type of medication. Classifications of chemotherapy agents known to cause extravasation include alkylating agents, anthracyclines, other anticancer antibiotics, plant alkaloids, and taxanes (Schulmeister 2011). Factors that increase the risk of extravasation from peripheral devices include small fragile veins, multiple previous venipunctures, and sensory deficits that impair the patient's ability to detect a change in sensation (Schulmeister 2011). Factors that increase the risk of extravasation from CVADs include difficulty during insertion of the device, inadvertent slicing or piercing of the catheter before or during insertion, device misplacement or catheter migration, and presence of a fibrin sheath at the catheter tip (Schulmeister 2011).

Prevention is the focus when administering chemotherapy agents that have the potential to cause extravasation. Guidelines have been developed by professional associations and many institutions to outline appropriate intravenous devices and administration steps. Nurses should educate patients on the potential for extravasation and signs/symptoms to report immediately. Needle placement of the peripheral or CVAD should be verified before and throughout medication administration (Gonzalez 2013).

After prevention, prompt recognition and initial management is the next most important action. The infusion must be stopped immediately upon any signs of extravasation and the nurse should attempt to withdraw as much of the medication as possible through the peripheral device or CVAD (Gonzalez 2013). The nurse should then notify the physician and an antidote and/or warm or cold compresses should be administered if applicable. The event should be thoroughly documented and include photographs of the area for later comparison. Allowing patients to verbalize concerns and feelings about the event can alleviate anxiety and worry. Patients should be educated on caring for the site and follow-up care.

General Skin Variations

General changes to the skin include rash, itching, dryness, acne, skin color changes, and photosensitivity and can occur throughout cancer treatment. These changes can be the result of the disease, treatment, or medication side effects. While not life threatening, any change to the skin can be distressing to patients. It is important for healthcare providers to perform frequent assessments of the skin and discuss how skin changes are affecting the patient. Educating the patient on the use of fragrance-free soaps and laundry detergent, frequent application of moisturizers, adequate sun protection, wearing loose comfortable clothing, and avoiding scrubs and loofahs can minimize most skin changes. Maintaining adequate hydration is also important. For patients who have received surgery, incision sites should be monitored during the healing process and scars should be monitored for keloids or tightness that restricts movement.

Nail Dystrophies

Fingernails and toenails are composed of rapidly proliferating cells that keratinize and make up the nail plate and therefore are sensitive to the effect of chemotherapy (Viale 2006). Anthracyclines and taxanes are associated with more risk for nail changes (Norville 2008). Characteristics of nail changes include:

- Mees' lines – transverse white lines
- Beau's lines – transverse grooves
- Pigmentation changes – pale or dark streaks in the nail plate
- Onycholysis – separation or loosening of the nail plate from the nail bed
- Paronychia – infection

Assessment of the nails should be conducted daily and include assessment for discoloration, ridging, pitting, pain in nail beds, separation or loss of the nail, and infection and if nail changes are interfering with activities of daily life (Viale 2006). There is no current treatment for the prevention or management of nail dystrophies, although antibiotics may be indicated for signs of infection around the nail bed and analgesic medication may be indicated for pain. Patients should be instructed to keep their nails trimmed and clean and avoid nail polish and imitation fingernails until the nails have returned to normal.

Pain

Pain is an unpleasant sensory and/or emotional experience associated with real or potential tissue damage (Krane et al. 2011). It is a common symptom among children with cancer due to the disease, treatment, procedures, infections, or a combination of these factors. Pain can be constant or intermittent and can occur suddenly (acute) or persist for months (chronic). Pain is classified as nociceptive (tissue pain) and neuropathic (nerve pain). Nociceptive pain can be further classified as somatic pain occurring in the bones, joints, muscles, skin, or connective tissue or visceral pain occurring in the visceral organs (Jacob 2008). Neuropathic pain results from nerve damage either in the peripheral or central nerves. In addition to these two pain classifications, pain can occur after surgical amputation of an extremity, referred to as phantom limb pain (Krane et al. 2011).

Pain assessments should be performed at an appropriate developmental level for the child. Measurement of pain in infants consists of assessments of behavior such as facial expressions and physiological measurements such as heart rate and respiratory rate (Hockenberry and Kline 2011). Measurement of pain in toddlers relies on assessment of behavior and physiological measurements but the toddler may provide clues about their pain such as guarding a particular area that is causing pain (Jacob 2008). Around 4 years of age, children are able to convey their pain to others either verbally or in the form of identifying their pain with face scales or photos of children in pain (Krane et al. 2011). Children 8 years and older can rate their pain with verbal or visual analog scales (Krane et al. 2011). In addition to a pain rating score, other pain characteristics such as location, intensity, severity, aggravating factors, and alleviating factors should be assessed.

Procedures are a common part of cancer treatment and may cause pain. Although procedural pain is usually brief, it is often accompanied by fear and anxiety if the child does not have a good experience with the initial procedures that can increase significantly with repeated procedures (Hockenberry et al. 2011; Kennedy et al. 2008). Preparation before the procedure should include providing the child with procedural information in an age-appropriate manner (i.e., medical play for toddlers) and providing training in cognitive behavioral interventions (i.e., distraction, relaxation, guided imagery) for use before, during, and after the procedure (Krane et al. 2011; Hockenberry et al. 2011). Ideally preparation should be initiated in advance for school-age children and adolescents, while toddlers and preschoolers have limited understanding of time and need information immediately before the procedure. Techniques such as cognitive behavioral interventions are often used to support the child during procedures but appropriate analgesia should also be provided. If necessary, analgesia medication should continue after the procedure. The decision for procedural sedation is dependent on a child's past experiences with procedures, their developmental level, and their ability to meet necessary expectations during the procedure (e.g., lying still for radiological exams).

Early intervention in the treatment of pain is important regardless of the cause and often requires multimodal strategies (Jacob 2008). Common pharmacological modalities are listed in Table 3.9 and non-pharmacological strategies are listed in Table 3.10. Electronic technologies are now being used to assess pain, deliver treatment, and enhance communication between patients and healthcare providers (see Chap. 20 for more information). Consideration of the patient's previous pain experiences, cultural and spiritual influences, and current pain assessment will guide the practitioner in determining the most efficacious treatment options. Frequent assessments are necessary to determine the effectiveness of current treatment and current pain levels. In addition, effective management of other symptoms, such as nausea, vomiting, constipation, insomnia, and anxiety, can assist to relieve pain. Interdisciplinary pain management teams as well as palliative care teams are often used in pediatric cancer centers to serve as consultants and provide expertise in pain assessment and management (Hockenberry and Kline 2011). Parents' levels of anxiety and distress can affect the child's pain and related distress; therefore, parents should be educated, supported, and

Table 3.9 Pharmacological interventions for pain

Classification	Medications
Non-opioid agents	Acetaminophen; ibuprofen; aspirin; naprosyn; ketorolac
Opioids	Codeine; fentanyl; hydrocodone; hydromorphone; meperidine; methadone; morphone; oxycodone
Anxiolytic agents	Diazepam; lorazepam
Major sedative agents	Midazolam; ketamine; propofol
Topical agents	EMLA or LMX; lidocaine infiltration
Antiepileptic agents	Gabapentin; pregabalin; topiramate
Antidepressants	Amitriptyline; nortriptyline

Information obtained from Krane et al. (2011) and Hockenberry and Kline (2011)

Table 3.10 Non-pharmacological interventions for pain

Classification	Intervention
Cognitive/behavioral	Relaxation Deep breathing Hypnosis Meditation or guided imagery Progressive muscle relaxation Music or art therapy Distraction
Touch therapies	Acupuncture or acupressure Massage Transcutaneous electrical nerve stimulation (TENS) Therapeutic touch
Activity	Exercise Yoga
Other	Sucrose solution for infants Aromatherapy

Information obtained from Krane et al. (2011) and Hockenberry et al. (2011)

encouraged to use positive support for the patient (Hockenberry and Kline 2011). Please see AYA Chap. 12 for specific issues related to opiate use in teenagers.

Headaches

Forty-one percent of children with brain tumors reported headaches at the time of initial diagnosis and 66 % reported headaches at some time during their treatment (Ullrich 2009). Although headaches are a common symptom among children with brain tumors, there are several other causes of headaches among children with cancer. Infection; fevers; side effects of medications such as antiemetics, antihistamines, and steroids; lumbar puncture procedures; and side effects of treatment including surgery, chemotherapy, and radiation can cause headaches in pediatric oncology patients (Ullrich 2009).

Assessment of headaches should include duration, focalization (i.e., unilateral or bilateral), location, pain quality, severity, associated symptoms (e.g., nausea, vomiting, photophobia), and presence of aura (Trottier et al. 2013). A headache diary is a useful method to obtain accurate and detailed information of the headaches. Reports of a headache that awakens the child from sleep, occurs early in the morning, is worse with coughing or Valsalva maneuvers, is associated with vomiting, and is increasing in frequency or severity are classic characteristics of increased intracranial pressure and a brain tumor and require further evaluation (Ullrich 2009). Neuroimaging should only be performed when abnormalities are noted in the history or physical examination (Bonthius and Lee 2013). Neuroimaging studies include computed tomography (CT) or magnetic resonance imaging (MRI). CT scans without contrast are typically performed in acute situations to quickly identify hemorrhage or space-occupying lesions such as tumors (Bonthius and Lee 2013). MRIs provide a high-resolution image of tissues and organs that is more sensitive than a CT scan for small tumors but are usually performed in non-acute situations due to the need for intravenous contrast and possible sedation. Laboratory tests are rarely helpful in diagnosing headaches; however, lumbar punctures can assist with a diagnosis of intracranial infection, malignancy, and/or intracranial hypertension (Bonthius and Lee 2013).

Prevention strategies primarily focus on procedure-related strategies, such as the prevention of lumbar puncture headaches. Use of a small-size and pencil-point spinal needle that is inserted parallel to the long axis is an established effective strategy to prevent lumbar puncture headaches, while extended bed rest, hydration, and the use of caffeine and ibuprofen have no established efficacy (Rusch et al. 2014). Treatment of headaches depends on the underlying etiology. For example, oncological treatment can assist with resolving disease-related headaches while antibiotics are needed for infection related headaches. Headaches resulting from treatment or side effects of medication may require a change in therapy, analgesic medications, and/or non-pharmacological interventions. Nonsteroidal anti-inflammatory drugs (NSAIDS) such as acetaminophen, ibuprofen, and naproxen are often the initial management strategy. Non-pharmacological interventions include guided imagery, acupuncture, hypnosis, meditation, and massage (Bonthius and Lee 2013). If ineffective, opioid or triptan medications can be used for pain relief (Sheridan et al. 2013).

Fatigue

Fatigue is recognized as one of the most frequent and distressing symptoms experienced by children and adolescents with cancer (Chang et al. 2013; Rodgers et al. 2013). Fatigue among children with cancer has been well characterized and is distinct from everyday tiredness (Hockenberry-Eaton et al. 1998, 1999). Changes in activities of daily living, having no energy, feeling socially isolated, having a difficult time concentrating, needing more rest, and finding it difficult to get up in the morning are common experiences for children with cancer. The experience of fatigue differed by developmental level with school-age children emphasizing the physical sensation of fatigue, while adolescents discussed mental tiredness that changes over time and merges with physical sensations of fatigue (Hockenberry-Eaton et al. 1998, 1999; Hockenberry-Eaton and Hinds 2000; Hockenberry et al. 2003). School-age children described “feeling weak” or “tired,” “falling asleep easily,” or being “mad” or “sad” when fatigued. Adolescents described fatigue related to cancer as “physical” or “mental exhaustion.” It is interesting to note that fatigue descriptions first labeled over 15 years ago hold true today (Hockenberry et al. 2014; Kestler and LoBiondo-Wood 2012; Baggott et al. 2010, 2014).

Table 3.11 Causes of fatigue in children with cancer

Influences	Reasons
Treatment	Chemotherapy, radiation therapy, bone marrow transplant, surgery, biologic response modifiers
Environment	Altered schedules or routines, waiting times in the clinic and hospital, hospital noise, sleep/rest interruptions in the hospital
Child characteristics	Cognitive development, emotions, moods, worry, boredom
Family	Expectations of others (e.g., family, relatives, or friends), absence of a schedule

Causes of fatigue in children with cancer are numerous and described in Table 3.11. Fatigue in children with cancer is unrelated to activity and may not be resolved with rest or sleep. While this symptom develops during cancer treatment, it can continue for years after treatment ends (Bower et al. 2014; Meeske et al. 2005). Survivors of childhood cancer who report chronic fatigue have poorer physical, social, emotional, and school functioning than survivors who were not fatigued (Meeske et al. 2007).

To capture the many characteristics of fatigue, multidimensional instruments are needed. In the clinical setting there are important questions to ask the child and parents during each visit. Fatigue-related questions could be framed using a time period such as in the last week or month:

- Are you feeling tired or weak? If yes, on a scale of 1–5, how bad is the feeling?
- Does feeling tired or weak keep you from playing or doing your usual activities?

There are several instruments that provide valid and reliable measures of fatigue frequency and intensity (Table 3.12).

Preventive measures for fatigue during childhood cancer treatment are not effective. Pharmacological interventions are reviewed in Chap. 8 on Psychiatric Issues. The focus for this symptom is on minimizing the debilitating effects

Table 3.12 Fatigue measures

Instrument	Description
Childhood Fatigue Scale (CFS) (Hinds et al. 2010)	Ten items assessing the experience of fatigue-related symptoms during the past week in children 7–12 years. CFS has three subscales that include Lack of Energy, Not Able to Function, and Altered Mood and is available in English and Spanish
Parent Fatigue Scale (PFS) (Hockenberry et al. 2003)	Seventeen items that ask the parent their perceptions of the amount of fatigue experienced by their child in the past week. Four subscales of the PFS include Lack of Energy, Not Able to Function, Altered Sleep, and Altered Mood. Available in English and Spanish
Fatigue Scale–Adolescent (FS-A) (Mandrell et al. 2011)	Thirteen questions designed to evaluate the intensity of fatigue experienced during the past week. Available in English
Multidimensional Fatigue Scale (Varni et al. 2002)	Eighteen-item scale that has child and parent matching versions. Six of the items measure general fatigue, six measure sleep/rest fatigue, and six items measure cognitive fatigue. Available in 22 languages
Peds FACIT-F (Lai et al. 2007)	Eleven-item scale for children with cancer that has stable measurement properties across age, sex, and cancer types. Available in English and Spanish

of fatigue. Patient and family education concerning the impact cancer and treatment can have on energy level and performance should occur at diagnosis. Developing a plan to minimize energy expenditure with consideration of the child's age and stage of development is important. Patients and families often maintain a diary to track energy level and changes in activity during treatment to review during scheduled clinic visits.

While studies are limited, there is information that exercise is beneficial in relieving fatigue. A recent systematic review (Baumann et al. 2013) confirmed that clinical exercise interventions for childhood cancer patients are promising in their effects on the immune system, body composition, sleep, and activity levels. Greater physical activity is associated with improved sleep quantity and efficiency (Orsey et al. 2013). Exercise that involves rhythmic or repetitive movement of large muscle groups (walking, cycling, swimming) should be encouraged. Patients and families should be reminded that the exercise program should be developmentally appropriate, initiated gradually, and occur several times a week.

Stress and worry contribute to fatigue; teaching patient and family stress reduction techniques such as relaxation therapy, guided imagery, or distraction can facilitate rest. Give reminders that nutrition is important to maintain and that regular exercise may improve appetite and increase nutritional intake. Discuss how improved nutrition can promote increased energy and decrease fatigue.

Sleep disruption is a major influence on the child's fatigue level. Encourage the patient and family to develop a specific bedtime and wake time and emphasize the importance of a schedule and routine prior to bedtime. Sleep interruptions are associated with increased fatigue and determining ways to prevent sleep interruptions during nighttime sleep is essential. Rest periods during the day are encouraged but emphasize the importance of keeping naps and rest times short.

Case Vignette

Julia is an 11-year-old girl who was diagnosed with acute lymphocytic leukemia 3 months ago. Before her diagnosis she was very active in dance classes and gymnastics, taking classes three times a week. Her mom describes her daughter as never lacking energy and always engaged in some type of physical activity before her diagnosis. Since her diagnosis Julia complains of being tired all the time and has had to quit her dance and gymnastic classes. Her mother states that Julia is having trouble sleeping and awakens several times each night to go to the bathroom. Julia returned to school a month ago but continues to miss 1–2 school days a week because she is so tired. Julia and her mother meet with her healthcare provider in the cancer clinic and they discuss these feelings as being common in children on chemotherapy for leukemia. They talk about ways that can help minimize the fatigue including frequent rest periods, daily exercise activities, good nutrition strategies, and ways to reduce stress of treatment.

Sleep Disorders

Approximately 30–45 % of oncology patients experience sleep disorders (Linder and Christian 2012). Sleep disorders consist of difficulty initiating or maintaining sleep (insomnia), sleep-wake cycle disorders (circadian rhythm sleep disorders), and excessive somnolence (hypersomnias). Any of these sleep disorders can cause mood, behavioral, and cognitive difficulties such as decreased ability to pay attention and concentrate and increased irritability, depression, and impulsivity (Linder and Christian 2012). Insomnia and circadian rhythm sleep disorders are caused by the disease, psychological stressors, side effects of treatment and medications, and environmental factors and are characterized by difficulty falling asleep and difficulty staying asleep. Somnolence syndrome is caused by cranial radiation that usually appears 4–8 weeks after completion of therapy (Ryan 2000). Somnolence syndrome symptoms range from mild fatigue and daytime drowsiness to excessive sleep and moderate lethargy (Ryan 2000).

Assessment of sleep disorders usually consists of subjective assessments. Essential components of these assessments include sleep latency, sleep duration including number of awakening episodes, sleep quality, daytime alertness and function, current symptoms, medications, and bedtime routines (Vena et al. 2004). This information can be obtained through a verbal history collected by the provider, a formal questionnaire completed by the patient, or a sleep diary kept by the patient for several days then delivered to the provider. Physical assessments of sleep include a polysomnography or an actigraphy. Polysomnography is the gold standard of sleep that occurs in a sleep laboratory and consists of recording the electrical activity of the brain, muscles, and eye movements to evaluate sleep patterns (Vena et al. 2004). Actigraphy is a less invasive procedure that can be used in any location and consists of a battery-operated wristwatch that records periods of activity and nonactivity (Vena et al. 2004).

Treatment of sleep disorders should focus on alleviating the cause and promoting good sleep hygiene practices. Education of basic sleep hygiene should include sleeping and waking at regular times, relaxing before bedtime including no electronic screens at least 30 minutes prior to bedtime, creating a dark, quiet sleep environment, avoiding naps, limiting caffeine, and participating in regular exercise. Non-pharmacological strategies include cognitive restructuring, behavioral strategies, and relaxation. Most sleep disturbances in children are successfully managed with a combination of good sleep hygiene and non-pharmacological strategies (Owens and Mindell 2011). Although there are many pharmacological interventions available to assist with sleep, the majority of these medications are not recommended by the US Food and Drug Administration for the treatment of sleep disturbances in children. The use of sleep medication is primarily based on clinical experience and empirical data from adult studies (Owens and Mindell 2011). If pharmacological intervention is necessary, the provider should consider the cause of the sleep disturbance, the risks and benefits of the medication, potential drug interactions, and the child's medical history (Owens and Mindell 2011). Herbal remedies may be used for sleep disturbances. Melatonin, a dietary supplement, has been effective for sleep disturbances in children with autism spectrum disorders but has not been established in children undergoing cancer treatment. See Chap. 16, Integrative Care, for more information.

Somnolence syndrome is a self-limiting condition with no known long-term consequences, so education and support are the best management for these children (Ryan 2000).

Conclusion

Childhood cancer, its treatment, and related medical procedures cause multiple physical effects. The disease process can affect multiple sites throughout the body and cause a multitude of physical symptoms. Furthermore, the various procedures and treatments aimed at during the cancer may cause further physical consequences. These physical effects can disrupt a child's life, create additional complications, and compromise treatment. Children with cancer report treatment-related symptoms as the worst part of their cancer experience and were remembered long after treatment ended (Woodgate and Degner 2003). Each issue requires careful assessment and appropriate interventions to minimize further complications, improve outcomes, and enhance the quality of life for children with cancer.

Clinical Pearls

Distressing physical symptoms occur frequently in children with cancer and are caused by the disease, aggressive therapy regimens, and medical procedures.

Chemotherapy agents and radiation therapy cause myelosuppression, a condition that occurs when bone marrow activity is decreased and produces fewer white blood cells, red blood cells, and platelets, which can result in susceptibility to infection, fatigue, and increased bleeding.

Nausea and vomiting are two common yet distinct symptoms that are caused from the disease, treatment, and/or side effects of medications. These symptoms can occur before treatment (anticipatory), during treatment (acute), and/or after treatment (delayed).

A change in weight is common during treatment for childhood cancer and dictates that weight status be monitored frequently to assess for significant shifts. Early referrals for nutritional assessment may assist with preventing significant weight loss or weight gain.

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