**Adolescents and Young Adults, Late Effects, Palliative Care**

1. A 19-year-old man is referred to your clinic after 1 week of fevers and increased fatigue. His CBC reveals a WBC count of 75,000/µL, hemoglobin of 5.5 g/dL, and platelets of 15,000/µL. On peripheral blood smear, 86% of the WBCs are large, immature cells with scant cytoplasm and prominent nucleoli.

Which cytogenetic finding is more likely to occur in this teenage patient compared with an infant or young child with a similar presentation?

A. t(12;21)

B. High hyperploidy (51-65 chromosomes)

C. t(4;11)

D. t(9;22)

E. t(1;19)

**Explanation**

Adolescents and young adults (AYAs) with acute lymphoblastic leukemia have different cytogenetic abnormalities compared with infants and young children, which may be a factor in their decreased survival. Philadelphia chromosome–positive leukemia with t(9;22) is rare in young children (approximately 5% of diagnoses); however, the rate increases with age, with an incidence of 10% to 25% in AYAs. Patients with this translocation are considered to be at very high risk. Current treatment includes tyrosine kinase inhibitors.

More favorable cytogenetic factors, such as t(12;21) and high hyperdiploidy, are more common in young children than AYAs. MLL rearrangements, particularly t(4;11), are the most common cytogenetic abnormality in infants and are associated with poor prognosis. The t(1;19) translocation was originally associated with an unfavorable prognosis; however, treatment with more intensive approaches has improved results, and it is no longer thought to be a prognostic factor. This translocation occurs in most age groups at approximately the same rate.

2. A 20-year-old woman with a history of Wilms tumor treated with nephrectomy, chemotherapy (vincristine, doxorubicin, and actinomycin), and flank radiation presents 18 years after completion of therapy. She has been lost to follow-up but presents with complaints of fatigue and shortness of breath with running.

Which screening test is most likely to determine the cause of her fatigue?

A. Renal function panel

B. Pulmonary function test

C. Echocardiogram

D. Abdominal X ray

E. CBC

**Explanation**

Treatment-related sequelae can develop many years from completion of therapy for childhood cancer. Compared with the general population, survivors are at a 15-fold increased risk of developing heart failure. Cardiovascular disorders are the third leading cause of death for survivors. Exposure to anthracyclines and radiation, including to the heart, places survivors at increased risk of cardiomyopathy, which typically occurs many years after therapy completion. Younger age at treatment, female sex, higher dosages of anthracyclines, and exposure to chest radiation increase the risk of treatment-induced cardiomyopathy. Screening guidelines based on cumulative dosage of anthracyclines and exposure to chest radiation have been developed by the Children’s Oncology Group to aid in early detection of these late effects.

3. A 25-year-old girl with a history of Hodgkin lymphoma presents to the oncology late effects clinic. She was treated with nitrogen mustard, vincristine, procarbazine, and prednisone followed by 25.5 Gy modified mantle radiation at age 15.

What screening is needed for subsequent malignancies?

A. Annual CBC

B. Annual urinalysis

C. Annual mammography and breast MRI

D. Colonoscopy every 5 years

E. Annual thyroid ultrasounds

**Explanation**

Subsequent malignancies are the leading cause of nonrelapse late mortality for childhood cancer survivors. The incidence of subsequent malignancies increases with age, and Hodgkin lymphoma survivors are at particularly high risk. Female patients who have received radiation to the breast are at increased risk for breast cancer. The Children’s Oncology Group Long-Term Follow-Up Guidelines recommend annual mammography and MRI starting at age 25 or 8 years after breast radiation exposure, whichever occurs last. Although procarbazine and nitrogen mustard increase the risk of myelodysplasia/acute myeloid leukemia, the recommendations are to perform an annual targeted history and physical examination. In addition, the patient is at elevated risk of thyroid cancer due to exposure to radiation. Monitoring for thyroid cancer should be performed annually with a physical examination. The risk of thyroid cancer should be discussed with patients, and decisions about screening with ultrasound made through shared decision making. If screening thyroid ultrasounds are performed, they should be repeated every 3 to 5 years. Early screening for colon cancer is recommended for patients who received abdominal radiation. This patient received mantle radiation, which includes the neck, chest, and axilla, not the abdomen.

4. A 14-year-old girl presents to survivor clinic for her first visit after transferring care from another institution. She was treated for acute myeloid leukemia (AML) at 2 years of age. She has been doing well since that time, but her family reports that she is struggling in school, especially with concentration and math.

Which of the following treatments that she received places her at greatest risk for neurocognitive deficits?

A. Etoposide

B. Asparaginase

C. Daunorubicin

D. High-dose cytarabine

E. Mitoxantrone

**Explanation**

Neurocognitive deficits can occur in survivors treated with high-dose cytarabine, high-dose methotrexate, intrathecal methotrexate, and cranial radiation. These deficits are typically functional deficits in executive function, attention, memory, processing speed, visual-motor integration, and fine motor dexterity. Survivors also may have learning deficits, particularly in math and reading comprehension. New deficits may emerge over time. A meta-analysis of childhood acute lymphoblastic leukemia survivors treated with chemotherapy-only treatment regimens showed a significant impairment in IQ and other neurocognitive domains. Survivors with concerns may benefit from a formal neuropsychological evaluation.

5. An 18-year-old man with history of multiply relapsed leukemia is interested in discussing his risk of infertility due to cancer treatment. He underwent two hematopoietic stem cell transplants as part of his treatment.

After reviewing his previous treatment, which of the following agents contributes to his risk of azoospermia?

A. Cytarabine

B. Methotrexate

C. Busulfan

D. Fludarabine

E. Etoposide

**Explanation**

Risk of infertility is one the most common concerns voiced by young adult survivors of childhood cancer. Survivors treated with hematopoietic stem cell transplant have a high risk of gonadal dysfunction due to conditioning regimens and previous treatments. Surgery, radiation, and chemotherapy that affect the hypothalamic-pituitary-gonadal axis and reproductive organs increase the risk of infertility. Treatment factors that affect this axis and may lead to infertility include surgical removal of reproductive organs (oophorectomy/orchiectomy), alkylating agent chemotherapy, hypothalamic-pituitary radiation, and radiation to the reproductive system. Pelvic or spinal surgery may also lead to sexual dysfunction, including retrograde ejaculation in men after retroperitoneal lymph node dissection. Radiation fields that may affect reproductive organs in women include abdominal, pelvic, lumbosacral spine, and total body. In men, these fields include pelvic, testicular, sacral spine, and total body. Alkylating agents used for treatment of childhood cancer include busulfan, carmustine, chlorambucil, cyclophosphamide, ifosfamide, lomustine, mechlorethamine, melphalan, procarbazine, thiotepa, cisplatin, carboplatin, dacarbazine, and temozolomide.

6. A 17-year-old girl was just diagnosed with Hodgkin lymphoma. Her 20-year-old brother was treated for Ewing sarcoma last year and was offered fertility preservation options before treatment. The patient would like to discuss her fertility preservation options.

Which of the following fertility preservation options is considered experimental?

A. Oocyte cryopreservation

B. Sperm cryopreservation

C. Surgical sperm extraction

D. Embryo cryopreservation

E. Ovarian cryopreservation

**Explanation**

The American Society of Clinical Oncology has fertility preservation guidelines for patients with cancer that were used to inform the Children’s Oncology Group Supportive Care Guidelines. For postpubertal male patients, sperm cryopreservation is considered standard of care and can be collected through ejaculation or surgical sperm extraction, if necessary. For postpubertal female patients, embryo and oocyte cryopreservation are no longer considered experimental; however, ovarian stimulation takes approximately 2 to 3 weeks, which will delay initiation of cancer therapy, making these options impractical for many patients with cancer. Other techniques, such as gonadal shielding and oophoropexy, can be attempted for patients receiving radiation, although they may not be successful. Currently, ovarian and testicular tissue cryopreservation, the only fertility preservation options for prepubertal patients, are considered experimental. There is conflicting evidence about the use of gonadotropin-releasing hormone agonists for ovarian suppression. Although these medications may be used to suppress menstruation during chemotherapy, their impact on fertility preservation is controversial.

7. A 23-year-old woman with a history of rhabdomyosarcoma at age 4 years comes to the survivor clinic to discuss late effects. She is worried about her risk of infertility. Which of the following factors is *not* known to affect the risk of infertility for female survivors of childhood cancer?

A. Age at treatment

B. Dosage of alkylating agent chemotherapy

C. Location of radiation

D. Current age

E. Race

**Explanation**

Many factors can affect the risk of infertility. Surgery, radiation, and chemotherapy that affect the hypothalamic-pituitary-gonadal axis and reproductive organs increase the risk of infertility. In general, female patients maintain ovarian function at higher cumulative alkylating agent dosages than testicular function in male patients. However, the risk of infertility increases with increased dosage of alkylating agents and radiation. Female patients are at high risk for premature ovarian insufficiency when they receive ovarian radiation dosages greater than 20 Gy. Compared with postpubertal girls, prepubertal girls are able to tolerate higher dosages of gonadotoxic chemotherapy and radiation before development of premature ovarian insufficiency. All girls are born with a finite number of primordial ovarian follicles that decrease over time until the number approaches 1,000 follicles, and menopause ensues. In female survivors of childhood cancer who have received gonadotoxic therapy, there may be an abrupt drop in the primordial follicle pool, leading to premature ovarian insufficiency or ovarian failure. However, women with a decreased ovarian reserve due to cancer therapy may have a window of time between the end of cancer treatment and the onset of ovarian insufficiency in which they are fertile and could conceive or undergo fertility preservation measures. There are no data supporting a difference in risk for infertility due to cancer treatment based on race.

8. A 13-year-old boy with newly diagnosed osteosarcoma of the right distal femur is admitted for his first course of chemotherapy. He has significant nausea and complains of persistent pain in the area of his tumor that fluctuates from 6 to 10 out of 10 depending on his activity. He seems to respond well to a dose of IV morphine.

What is the best pain regimen for this patient?

A. IV Tylenol scheduled every 6 hours with IV morphine as needed

B. IV morphine scheduled every 4 hours with IV morphine as needed

C. Vicodin scheduled every 4 hours with IV morphine as needed

D. IV morphine as needed with no scheduled medications

E. Morphine patient-controlled analgesia (PCA) with demand dosing without a basal rate

**Explanation**

This patient is complaining of persistent moderate to severe pain. World Health Organization (WHO) guidelines on the pharmacologic treatment of persistent pain in children with medical illness suggest that pain regimens should include dosing at regular intervals (around the clock) while the patient is monitored for side effects. Pain regimens also should be adapted to the individual child and use the appropriate route. The oral/enteral route should be used when possible; however, this patient has significant nausea. In addition, the WHO guidelines use a two-step strategy for pain management. Ibuprofen or acetaminophen is the gold standard for mild pain, and morphine is the gold standard for moderate or severe pain relief. Combined analgesics, such as Vicodin, Lortab, and Percocet, are not recommended for pain control in pediatrics.

9. A 15-year-old girl with metastatic Ewing sarcoma presents for a routine clinic visit. She has been on high dosages of opioids for several weeks as an outpatient, and her pain has been well controlled. Initially, she had multiple side effects from her opioids, but the majority of them have resolved.

Which of the following opioid side effects does not improve with time?

A. Constipation

B. Urinary retention

C. Sedation

D. Pruritus

E. Nausea

**Explanation**

Opioid use is associated with multiple adverse effects, which tend to occur more frequently with daily dosing, higher dosages, long-term therapy, and decreased renal or hepatic function. Common opioid side effects include sedation, constipation, pruritus, nausea, urinary retention, sweating, hyperalgesia, and myoclonus. Although tolerance develops to most side effects, constipation does not improve with time. It is important to ensure patients receiving opioids have a proper laxative regimen. Sennosides-only therapy has been shown to be superior to sennosides plus docusate in a small randomized controlled trial.

10. A 19-year-old man with acute myeloid leukemia (AML) is awaiting count recovery and develops severe mucositis. He has not been able to eat for the past 2 weeks, and his pain is being managed with a morphine patient-controlled analgesia (PCA) pump. He becomes septic and is transferred to the ICU. As his condition worsens, he develops multisystem organ failure, and the ICU attending decides to change him to a fentanyl PCA.

Which of the following is the most likely reason why the ICU attending rotated the patient onto a fentanyl PCA?

A. Cardiac failure

B. Oversedation

C. Pulmonary failure

D. Renal failure

E. Severe ileus

**Explanation**

Morphine and oxycodone should be avoided for patients with renal insufficiency or renal failure. Morphine is metabolized in the liver to morphine-3-glucuronide (M3G), morphine-6-glucuronide (M6G), and normorphine. These metabolites are excreted renally. In patients with renal impairment, increased levels of M6G and M3G can lead to increased opioid side effects, increased nociception, and increased hyperexcitability. Patients with renal failure should be switched to fentanyl or methadone if possible. Other reasons to rotate opioids include increased side effects with poor pain control and opioid-induced hyperalgesia.

11. An 8-year-old boy who was diagnosed with metastatic embryonal rhabdomyosarcoma at 6 years of age presents with increased abdominal and leg pain. He is found to have multifocal relapsed disease. His physician consults the palliative care team to meet with the family.

Which of the following is true of palliative care?

A. Palliative care is another name for hospice.

B. It is best to consult palliative care 3 to 6 months before anticipated death.

C. Palliative care focuses mainly on the spiritual and psychosocial needs of patients and families and not physical needs.

D. Symptom management is one of the key components of palliative care.

E. Patients cannot receive palliative care along with curative therapy.

**Explanation**

Palliative care is specialized medical care for people with a serious illness. It can be provided along with curative therapy as an extra layer of support to improve quality of life for patients and the family. It is appropriate for oncology patients of any age and any stage of disease and is most beneficial when introduced early in the disease course. Palliative care teams are interdisciplinary and comprehensively manage the physical, psychological, social, and spiritual needs of patients and families. The key components of palliative care are communication (establishing goals of care), medical decision making and advanced care planning, care coordination, and symptom management.

12. A 17-year-old boy, who was diagnosed with osteosarcoma at 15 years of age, presents with increased work of breathing and leg pain. He is found to have multifocal relapsed disease. His sister died of rhabdomyosarcoma 2 years earlier, and the family is interested in early admission to hospice.

What is the criterion for admission to hospice?

A. Severe pain with the need for continuous pain medications at home

B. Medical condition necessitating skilled nursing assistance at home

C. Prognosis estimated by the physician to be fewer than 6 months

D. Patient or family’s desire for death at home

E. Need for durable medical equipment for home

**Explanation**

Both palliative and hospice care address physical, psychological, social, and spiritual needs of patients, but there is a key distinction. Whereas palliative care is specialized medical care for patients of any age and any stage of disease, hospice care is a community-based service meant for patients at late stages of their disease. Patients are not eligible for hospice care unless their prognosis is estimated to be fewer than 6 months if the disease follows its usual course. Historically, children were not eligible for hospice care if they were still receiving curative or restorative therapy, were technology dependent, or had block nursing at home. The Patient Protection and Affordable Care Act, passed in 2010, included the Concurrent Care for Children requirement, a provision that requires state Medicaid programs to pay for both curative and hospice care for children younger than 21 years if the child is within the last 6 months of life, based on the expected disease course.

13. A 3-year-old girl with relapsed high-risk neuroblastoma was admitted overnight for end-of-life care. Her parents have noticed she has seemed more comfortable over the past several days.

Which of the following changes are *not* commonly seen in the days before death?

A. Increased somnolence

B. Respiratory changes

C. Warm skin with increased sweating

D. Decreased appetite

E. Increased secretions

**Explanation**

In the days and weeks before death, the body begins to shut down. The dying process is different for each person, and families often do not know what to expect. Changes that occur in the days before death include increased somnolence, less interactivity, decreased appetite, weight loss or gain, respiratory changes, skin changes (pallor, cool, mottled), and increased secretions. Patients may also develop urinary or bowel incontinence or terminal delirium, which can be marked by agitation, confusion, decreased attention, altered cognition, and hallucinations. At the end of life, interventions to consider include discontinuing vital sign assessment, nonessential medications or testing, and other interventions that cause distress (eg, suctioning, turning, and repetitive awakening). Excessive artificial nutrition and hydration should be avoided. Providers should work with families to provide comfort care consistent with their wishes.

14. A 12-year-old boy with refractory Ewing sarcoma is admitted for end-of-life care. He develops worsening dyspnea and appears to be afraid and complains of shortness of breath.

Which of the following is *not* suggested for the treatment of dyspnea at the end of life?

A. Oxygen saturation monitoring

B. Opioids

C. Fan to the face

D. Nasal cannula if hypoxic

E. Decreased intravenous fluids

**Explanation**

At the end of life, dyspnea is a common, subjective finding. Treatment should not be based on objective data, such as oxygen saturation measurements or respiratory rate. Instead, treatment should be based on subjective data, such as patient-reported shortness of breath, a startled expression, or distressed appearance. First-line treatment of dyspnea is opioids. If that patient does not have concurrent pain, a lower dosage (1/3 to 1/2 of the typical pain dosage) can be used. In addition, placing a fan near the face, decreasing intravenous fluids, and increasing the head of the bed or repositioning can provide comfort. If the patient is hypoxic, oxygen via nasal cannula or other noninvasive oxygen delivery mode may improve symptoms. Benzodiazepines may be helpful if there is a component related to anxiety. Vital sign monitoring is not necessary at the end of life, and it should not be assumed that patients with oxygen saturations greater than 90% do not have dyspnea if there are subjective findings.

15. A 24-year-old woman with a history of acute lymphoblastic leukemia presents to the survivor clinic. She was diagnosed at 20 years of age. The practitioner in the clinic recently saw another patient who was also 24 years old and received similar therapy, but she was diagnosed at 8 years of age.

Which of the following side effects or late effects is more common in patients who were treated at a younger age?

A. Vincristine neuropathy

B. Steroid-induced osteonecrosis

C. Treatment-associated premature ovarian insufficiency

D. Asparaginase-associated pancreatitis

E. Anthracycline-induced cardiomyopathy

**Explanation**

Although survival rates for younger children have improved drastically over the past several decades, adolescents and young adults (AYAs) with cancer have seen less of an improvement in survival. In addition, for many diseases, AYAs have a lower survival rate than young children with the same disease. This difference is probably based on multiple factors, including differences in disease biology; increased comorbidities that limit treatment; poor access to health services, including insurance coverage, leading to delayed diagnosis and decreased enrollment in clinical trials; poor compliance; unmet psychosocial needs; and unique pharmacokinetics, leading to different toxicity profiles compared with those treated at an earlier age. For example, asparaginase-related pancreatitis, thromboembolism, and hyperglycemia (steroid- and asparaginase-related) are more common for AYAs than for younger patients. Furthermore, studies have shown that young children have an oral clearance rate of dexamethasone and methotrexate that is twice as rapid as the rate for AYAs, leading to increased osteonecrosis and mucositis in AYAs. In addition, although AYAs tend to receive lower dosages of vincristine because of dose capping, studies have shown that AYAs report increased vincristine neurotoxicity. Among other common late effects of cancer therapy, premature ovarian insufficiency is more common among female patients who were exposed to gonadotoxic therapy after puberty than among those with prepubertal exposure. Anthracycline-associated cardiotoxicity is more common in patients who were treated at a younger age.