The Hematology and Oncology Pediatric Patient: A Review of Fever and Neutropenia, Blood Transfusions, and Other Complex Problems

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A home health nurse arrives at the home of a 3 year old boy with pre-B cell acute lymphocytic leukemia (ALL) who is receiving induction chemotherapy. On arrival, his mother states he has not been feeling well with decreased oral intake...
since receiving his chemotherapy 2 days ago. He has not urinated today and has been vomiting despite treatment with anti-emetics. The home health nurse notes that the child is lethargic and feels warm to touch. He has rigors and his capillary refill is delayed. The home health nurse calls 911.

FEVER AND NEUTROPENIA

Neutropenia is a condition in which a patient has an abnormally low number of neutrophils. These cells play an important role in the body's immune response. Neutropenia is a common side effect of chemotherapy because chemotherapeutic agents target rapidly dividing cells such as neutrophils. Patients who are neutropenic are at risk for serious bacterial infections (SBIs), such as bacteremia, pneumonia, and meningitis. Oncology patients receiving chemotherapy are at even higher risk for SBI if they have a central venous line. Because fever may be the first and only sign of an SBI in an oncology patient, families are discouraged from giving antipyretics to the patient for any indication as not to mask a fever.

Neutropenia is defined by calculation of an absolute neutrophil count (ANC). The ANC is calculated by taking the total number of white blood cells and multiplying it by the percentage of neutrophils plus the number of band forms seen on a complete blood count with differential. For example, a patient with a white blood cell count of 3000 with 2% bands and 8% neutrophils has an ANC of 300. For the oncology patient receiving chemotherapy, neutropenia is defined as an ANC less than 500.¹

VIGNETTE, CONTINUED

Emergency Medical Services (EMS) arrives several minutes later and finds the child listless on the couch in the living room. He is pale, febrile and tachycardic with thready pulses. He is weak but opens his eyes spontaneously and follows simple commands. He is loaded on the stretcher for transport to the local hospital. In the ambulance, you place him on a monitor and obtain a set of vital signs that show a heart rate of 197 with sinus tachycardia on the monitor, blood pressure of 70/palp, respiratory rate of 30 and oxygen saturation of 96% on room air. He is tachypneic with clear breath sounds bilaterally and normal work of breathing. He has weak pulses and mottled skin with a capillary refill of greater than 5 seconds.

EMERGENCY MEDICAL SERVICES ASSESSMENT

An oncology patient receiving chemotherapy is at risk for sepsis or other SBIs. Regardless of the presenting complaint, it is important to evaluate and stabilize the patient’s "airway, breathing, and circulation" (ABCs) systematically.

Primary assessment: ABC

- Airway: Make sure that the patient has an intact protected airway.
- Breathing: Check for irregular breathing patterns or apnea, place on pulse oximetry, and apply oxygen as indicated by oximetry, increased respiratory rate or effort, diminished circulation, or altered mental status.
- Circulation: Place the patient on a monitor for transport and document if the child is tachycardic, has a widened pulse pressure (diastolic less than half the systolic pressure), and/or is hypotensive; do not hesitate to attempt to obtain peripheral access via either intravenous or intraosseous routes to give fluids (many oncology patients will have a central line or port-a-catheter; however, you should only access these if you are trained to do so).

It cannot be stressed enough that early recognition and treatment of shock are necessary to improve this patient’s outcome. Furthermore, never administer rectal medications or check rectal temperatures in a child at risk for neutropenia because this may result in disruption of mucosa and introduction of bacteria into the blood stream.² It is always good to review reference ranges of vital signs in children to quickly recognize any vital sign abnormalities.

Applying the ABCs to the patient in the vignette, the child is maintaining his airway and is tachypneic with an otherwise acceptable respiratory examination. It would be okay to provide some oxygen for comfort. His most pressing issue is his cardiovascular status. He is tachycardic and hypotensive. Unless you are trained to properly access his port-a-catheter, peripheral access should be obtained (place an IV; consider an IO if IV access cannot be obtained quickly) followed by immediate infusion of normal saline (or lactated Ringers if saline is not available). He should be transported on a monitor with frequent assessments of heart rate and blood pressure. You should immediately notify the receiving hospital emergency department (ED) staff that you are transporting this critically ill patient.
VIGNETTE, CONTINUED

The charge nurse at the community hospital is notified that EMS is en route with a 3 year old boy with ALL. The child was reportedly sluggish, warm to touch, hypotensive and tachycardic. EMS was able to obtain one site of peripheral IV access and is administering normal saline. What items should the nursing staff have ready for when this patient arrives? Is it appropriate to triage this patient in the waiting room?

On arrival of the child to the ED, the nurse immediately places him in a room under neutropenic precautions. He is placed on a monitor and a complete set of vital signs are obtained: temperature 39.0°C, heart rate 147, respiratory rate 20, blood pressure 90/60. He weighs 15 kilograms.

EMS reports that they have given a total of 500 mL of normal saline en route with some improvement in perfusion. Now that the child is in the ED, what things should the nursing staff be prepared to do quickly to provide the best care for the patient?

NURSING ASSESSMENT

Treating a pediatric oncology patient in the ED may be an overwhelming task for a nurse who is not accustomed to caring for such a complex patient. This section outlines key nursing points to keep in mind, and Table 1 summarizes the top 10 clinical considerations for emergency nurses when caring for the pediatric oncology patient. To ease this stress and prevent further exposure to other sick patients in the waiting room, it is important to immediately place the patient into a treatment, resuscitation, or isolation room. These patients should be assigned a high-acuity triage level.

In the ED, one should assume that all patients receiving chemotherapy are neutropenic until proven otherwise. Neutropenic precautions (gown, gloves, and mask) should be implemented to prevent the spread of infection to the patient. Good hand washing, preferably where the family can observe care providers doing so, is highly recommended; this may be the single, most effective intervention toward the reduction of nosocomial infections. Whenever possible, the patient should have their own stethoscope and thermometer, one that will not be used to examine other patients. Finally, never administer rectal medications or check rectal temperatures in a child at risk for neutropenia because this may result in disruption of the mucosa and introduction of bacteria into the bloodstream.

Upon immediate arrival to the treatment or resuscitation room, all patients should be placed on a monitor and have vital signs, including a blood pressure with an appropriately sized pediatric cuff, monitored closely. A manual blood pressure measurement is preferred to automated because a manual will provide the most accurate reading. A physician should be notified immediately if the child demonstrates any alterations in mental status, tachypnea, tachycardia, altered perfusion, or hypotension. Furthermore, in addition to hypotension, watch for a widened pulse pressure (diasystolic pressure that is less than half of the systolic) or a lower mean arterial pressure. Finally, observe for any trending in vital signs away from normal because this may indicate that there is not much time before the child decompensates clinically. As stated above, recognition and treatment of shock are necessary to maximize the patient’s outcome.

Pediatric oncology patients will usually present with some type of intravenous access readily available. Central lumen catheters are common, along with implanted ports for both blood draws and fluid and medication administration. Many families are usually very reliable in applying a topical anesthetic before leaving home, thus making initial access in the ED somewhat less traumatic for the patient.

<table>
<thead>
<tr>
<th>TABLE 1. Top 10 clinical priorities for oncology patient nursing care.</th>
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<tbody>
<tr>
<td>1. Assign a high-acuity triage category and isolate or place in a treatment room as soon as possible.</td>
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<td>2. Initiate protective isolation (neutropenic precautions).</td>
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<td>3. Wash hands thoroughly. Stock supplies that can remain in the room to prevent contamination (eg, stethoscope or thermometer).</td>
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<td>4. Place on full cardiopulmonary monitoring. Place on oxygen if needed for comfort. Check vital signs often. Remember, a hypotensive patient may be septic.</td>
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<td>5. Avoid invasive procedures. This includes avoiding rectal thermometers/medications, urine catheterization, intramuscular injection, and tampons for adolescent females.</td>
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<td>6. Access the child’s central line, or obtain peripheral vascular access immediately.</td>
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<td>7. Central line management: use only 10-mL syringes to flush central lines.</td>
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<td>8. If febrile or concern for sepsis, draw laboratory studies in this order: blood culture, BMP, CBC, type and screen, and PT/PTT.</td>
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<td>9. If febrile, initiate antibiotics within 60 minutes of room arrival. Always ask about allergies to any medications because these patients may have reactions that are different.</td>
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<td>10. If febrile (temperature of &gt;38.0°C or &gt;100.5°F), administer acetaminophen; dosing is 15 mg/kg every 6 h. Never give ibuprofen because of risk for platelet dysfunction.</td>
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| CBC, complete blood cell count; BMP, basic metabolic profile; PT, prothrombin time; PTT, partial thromboplastin time. |
patient. Although topical anesthetics do an adequate job at numbing the access site for pain control, the analgesia may not be fully appreciated until 30 to 60 minutes after application, depending on the type of anesthetic used. For example, EMLA (eutectic mixture of local anesthetics) typically takes about 40 to 60 minutes to achieve satisfactory anesthesia, whereas ELA-MAX (4% liposomal lidocaine) is effective in 30 minutes. Therefore, if a topical analgesic has not been applied before arrival, do not waste time with application in the ED if it will delay treatment. An alternative to consider is ethyl chloride spray, which will provide some instantaneous numbing effects. Eliminating pain with needle sticks is a preferred approach for stable patients; life-saving treatment should not be delayed in a truly emergent patient. Finally, if available staff do not possess a level of comfort in accessing central lines or mediports, peripheral intravenous access should be pursued as an alternative. For a patient with a concern for sepsis or shock, optimal vascular access should be large bore (in children, this equates to the largest gauge IV that can be reasonably placed).

Laboratory evaluation and administration of prophylactic antibiotics should not be delayed. A good target for blood sample collection and initiation of empiric antibiotics is within 60 minutes of patient arrival to the ED. It is important that you draw a blood culture from each lumen of a central line if present. Obtain the culture from the first blood drawn (your waste) and place it into separate blood culture bottles if there are 2 or more lumens. This will help to distinguish which lumen might be the source of the infection; therefore, accurate labeling is crucial. If no central line is present, then a blood culture may be collected via peripheral puncture. Another important laboratory test result to obtain is a complete blood count with differential to assess for neutropenia. Other studies that may be considered once vascular access is established include metabolic panel, coagulation studies, and type and screen. The treating physician may also request viral and/or fungal cultures, urine analysis and culture, or radiographic studies. Keep in mind that, in addition to avoiding rectal medications, other invasive procedures such as urine catheterization and administration of intramuscular injection should be avoided when collecting laboratory test results and administering medications.

Family Considerations for Nurses and Health Care Providers

Taking the family into consideration as well as the patient is a vital component of the care of the pediatric oncology patient in the ED. Many of these patients and their families feel as if they have lost control in their lives. The ED may be a very stressful and unfamiliar place for them and remind them of their initial diagnosis. Often, oncology families show their uneasiness with the ED environment by frequently questioning care decisions and methods that are used. This is often simply because methods used, and not necessarily the care itself, sometimes differ from what they are accustomed to from the oncology team. This situation can often be de-escalated or avoided altogether by including family in the plan of care. Understanding what the family expects and what they are used to and communicating what will actually occur and why will help ease the stress associated with a variation in the way care is delivered in the ED. Parents and patients are usually very well educated about the child’s disease. Be respectful of their knowledge of the disease, treatment, and the parent's knowledge of their child. Ask them how they usually have things done or what makes the patient more comfortable. They may offer useful information regarding optimal approaches (eg, best peripheral access site) or care issues unique to the patient (eg, reactions to medications). Be upfront and update them on their child’s care. Talk to the family openly about what you are doing and why the interventions are being performed.

VIGNETTE, CONTINUED

The ED physician is notified by the charge nurse that EMS has just brought a 3 year old boy with ALL, who is ill-appearing. On arrival to the room, the physician washes her hands and dons her neutropenic precautions attire prior to entering the room. She reviews the vital signs and learns that the child has received just over 20 mL/kg of normal saline from EMS. She makes note that the child is tachycardic and febrile. The nurse is preparing to access the child’s central line, while the physician performs a complete physical exam. The exam is remarkable only for a child with alopecia and pallor. He is alert and in no distress. The central line site does not have any erythema or exudates. His capillary refill is 2-3 seconds. In addition to another fluid bolus, what other interventions or medications should the physician order? What other information does the physician need to complete the work-up? What is the disposition of this patient?

PHYSICIAN ASSESSMENT

If not already done, the nursing staff should be instructed to place the patient on a cardiorespiratory monitor. It is important to obtain and scrutinize
a complete set of vital signs. The physician must assess the following questions quickly: (1) Is the patient stable? (2) Is the child truly febrile? (3) How is the respiratory status? and (4) Is there evidence of hypovolemic or septic shock?

• An easy, quick way to calculate systolic hypotension in a child is to compare the measured pressure with \[\frac{\text{age in years} \times 2}{70}\]. A blood pressure less than this likely represents hypotension and should be addressed immediately.4

Any abnormal values should be addressed systematically. Fluid resuscitation (20 mL/kg) should begin immediately and rapidly (IV push or under pressure) to treat hypotension and shock. Rapid administration of isotonic fluid is associated with improved patient outcomes in septic shock. Patients with blood pressure changes may require multiple boluses to achieve a satisfactory response. If the child's blood pressure does not improve after 2 or 3 fluid boluses, administration of inotropic infusions should be considered, and consultation with a pediatric tertiary care center, if not already achieved, should be pursued.

After assessing the vital signs and addressing any abnormal values, perform a complete physical examination, looking for a focus of infection. It is especially important to make note of the child's mental status. Pay close attention to the central line, examining for any signs of inflammation or infection. It is important to keep in mind, however, that neutropenic patients may not have an adequate immune system to exhibit outward signs of inflammation such as erythema, warmth, and purulent drainage.1,5 Look in the patient's throat and ears and assess for upper respiratory infection symptoms. Remember, common things being common, oncology patients are at risk for upper respiratory infections, otitis media, and pharyngitis just as any other child. Finally, evaluate for any evidence of mucositis secondary to chemotherapy, bearing in mind that mucositis may be present in genital and perirectal regions and not just the oral mucosa.2

Laboratory evaluation should include a complete blood count with differential and a blood culture with sampling from all lumens of the central line, if present. Additional tests may be obtained at the discretion of the physician based on physical examination findings and in consultation with the child's specialty care provider.1 In addition, a venous blood gas and a serum lactate may be useful in evaluating the patient's metabolic state and severity of septic shock. Remember that shock is a clinical diagnosis, one that requires urgent intervention. No laboratory test should be relied upon to make the diagnosis and drive the initiation of therapy. It is important to bear in mind that chest radiographs may be falsely reassuring if the child is unable to mount an adequate immune response to show infiltrates.1 In this instance, the physician must rely on clinical suspicion based on physical examination findings to make the clinical diagnosis of pneumonia.

Antibiotics should be started without delay (Table 2). It cannot be stressed enough that antibiotics should not be withheld while awaiting laboratory results when septicemia is suspected! Ideally, antibiotics should be given within 1 hour or less of patient arrival to the ED. Early initiation of broad-spectrum antibiotics significantly reduces infection-related mortality in patients with chemotherapy-induced fever and neutropenia.2 Common organisms implicated in septicemia in patients receiving chemotherapy include gram-negative organisms such as Escherichia coli, Klebsiella pneumonia, and Pseudomonas aeruginosa and gram-positive organisms such as Staphylococcus aureus and streptococci.2,6 Patients with central lines are at especially high risk for infections with S aureus, coagulase-negative staphylococci, and viridians streptococci.7 Monotherapy with cefepime (50 mg/kg every 8 hours) or meropenem (20 mg/kg every 8 hours in children >3 months old) has proven to be good coverage for children with chemotherapy-induced neutropenia and fever. If these choices are not readily available, a β-lactam drug plus an aminoglycoside or a cephalosporin plus an aminoglycoside is a good alternative starting point.7 To avoid drug resistance, studies have shown that vancomycin (15 mg/kg) should not be administered empirically unless there are signs of hypotension, sepsis, or shock on evaluation, the

**TABLE 2. Empiric antibiotic recommendations for fever and neutropenia in children.**

<table>
<thead>
<tr>
<th>First-line agents</th>
<th>Cefepime 50 mg/kg every 8 h, or Meropenem 20 mg/kg every 8 h (if &gt;3 mo old)</th>
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<tbody>
<tr>
<td>Alternative choices</td>
<td>β-Lactum plus aminoglycoside, or Cephalosporin plus aminoglycoside</td>
</tr>
<tr>
<td>Indications for vancomycin</td>
<td>Hypotension, sepsis, or shock</td>
</tr>
<tr>
<td></td>
<td>Inflamed central venous access entry site</td>
</tr>
<tr>
<td></td>
<td>Recent administration of high-dose AraC</td>
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Ara-C, cytarabine.
central line is inflamed, or the child has received high-dose arabinoslycytosine (AraC). It is acceptable and encouraged to discuss antibiotic choices with the child’s oncologist because regional variations in drug resistances and subtleties in patient history may influence the type of antimicrobial(s) chosen.

After the child’s vital signs have been stabilized and antibiotics have been administered, the child’s oncologist should be notified. The oncologist can often provide recommendations on continuing care and disposition, including admission to the local hospital or transfer to the tertiary care center for further evaluation. In the case of the child in the vignette, safe transfer to the tertiary care center is likely indicated.

**VIGNETTE, CONTINUED**

The child is given a total of 50 mL/kg of normal saline boluses with improvement in mental status, perfusion and vital signs. Laboratory evaluation is significant for an ANC of 310. He is given a dose of cefepime after a blood culture is obtained. The physician speaks with the oncologist on call at the tertiary care center who accepts the patient for transfer. The physician determines that the patient may be transported safely by a ground EMS team and updates the family.

**OTHER ONCOLOGY EMERGENCY CARE CONSIDERATIONS**

In addition to fever and neutropenia and associated risk of sepsis, other complications of chemotherapy that may be seen include severe anemia, bleeding, tumor lysis syndrome, disseminated intravascular coagulopathy, tumor compression, and other cardiopulmonary emergencies. Chemotherapy targets rapidly dividing cells, and therefore, depletes all blood cell lines, causing anemia and thrombocytopenia. Chemotherapy patients may require short-term transfusion of blood products. Peripheral neuropathy also is common in these children. Affected children may lack sensation, range of motion, and strength as a result. Chemotherapy-induced nausea and vomiting are perhaps one of the most common side effects of chemotherapy and arguably one of the most uncomfortable for the patient. Table 3 provides a quick reference of common side effects of specific chemotherapeutic agents.9

It is also important to identify the signs and symptoms of tumor lysis syndrome because this can save a child’s life. Tumor lysis syndrome usually occurs in patients with bulky, rapidly proliferating, and treatment-responsive tumors. Tumor lysis syndrome occurs when large numbers of neoplastic cells are killed with the initiation of chemotherapy, leading to release of intracellular ions and metabolic byproducts into the systemic circulation. Clinically, the syndrome is characterized by rapid development of hyperkalemia, hyperuricemia, hypercalcemia, hyperphosphatemia, and acute renal failure. The main principles of tumor lysis syndrome management are: (1) identification of high-risk patients with initiation of preventive therapy (new solid tumor diagnosis), and (2) early recognition of metabolic and renal complications with prompt supportive care. Aggressive intravenous hydration not only helps correct electrolyte disturbances by diluting extracellular fluid but also increases intravascular volume. Increased intravascular volume enhances renal blood flow, glomerular filtration rate, and urine volume, which aids the elimination of these cellular toxins.

Finally, in addition to fever with neutropenia and complications of chemotherapy, the oncology patient may present to the ED with the complaint of abdominal pain. The oncology patient with abdominal pain may be receiving induction or maintenance
chemotherapy. They may also be in remission. The ED provider should begin the patient's assessment as they might for any child with a complaint of abdominal pain. This would include a complete history, thorough physical examination, and laboratory and/or radiographic studies (such as ultrasound or computed tomographic scan of the abdomen), as appropriate. In addition to evaluation for routine considerations, such as gastroenteritis, appendicitis, and trauma, the practitioner should also consider problems unique to this population such as an abdominal mass or leukemic infiltrate in the bowel. In other words, it is important not to minimize the complaint of abdominal pain in the oncology patient because it could indicate spread or recurrence of their disease.

A Few Words About Transfusions and Administration of Blood Products

In addition to oncology patients receiving chemotherapy, children with hematological disorders such as sickle cell disease, aplastic anemia, bleeding disorders, and platelet dysfunction may have depleted cell lines and require transfusion of red blood cells or platelets. Indications for transfusion of red blood cells include an acute blood loss of greater than or equal to 10% to 25% of the patient's blood volume, symptomatic anemia, oxygen requirement, asymptomatic anemia with bone marrow failure, and a hematocrit less than or equal to 18% to 20%. If time allows and the situation is not emergent, ensure that a type and cross-match is sent via proper protocol to reduce the risk of transfusion reaction. In addition to a simple type and cross-match, some patients require additional blood product preparation before it can be transfused. For example, oncology patients or those who are immunocompromised require leukofiltered and irradiated blood, whereas patients with sickle cell anemia require matching of other specific blood antigens (such as Kell, C, and E). If packed red blood cells are needed emergently, as in a trauma patient or severe gastrointestinal bleed, it is best to give type-specific or O-negative blood, preferably after a type and cross-match is collected from the patient. When in doubt, it is a good idea to consult with the patient's hematologist or the blood bank before transfusing blood products.

As with adult care, pediatric blood product administration has several “golden rules” that physicians and nurses must follow. The first and foremost is education of a patient and family and informed consent. Families who have a child who has required blood products in the past are usually quite familiar with their child's disease and often have done research to understand the disease and therapeutic interventions. This being said, you can expect them to request laboratory results including blood counts and plan of care. Involving them upfront with all results will help them feel like a partner in their child's care. Parents may also offer insight on prior transfusions, any associated reactions, and need for pretreatment. Newly diagnosed patients and families will need a more thorough explanation of reasoning behind blood product administration before consent is signed.

When ordering packed red blood cells in pediatric patients, order the appropriate dose based on the patient's size. A standard unit of blood contains 250 to 300 mL. In general, a pediatric patient should be transfused 10 to 15 mL/kg of packed red blood cells. Platelets should be given to any patient who has a low platelet count and is actively bleeding or requires an invasive procedure. When transfusing platelets, 1 random donor pack raises the platelet count by 40 000 per 10 kg of weight. Platelets are also available in leukoreduced and irradiated options for immunocompromised patients; inquire in advance regarding the availability of these products in your institution. In general, blood product can remain unrefrigerated for no more than 4 hours and are typically ordered to be administered over 2 hours in children. This rate may be further reduced if necessary if there is a history of minor reactions to blood products or if a reaction is noted (see below). An exception to this is the actively bleeding patient (ie, trauma patient) who may require rapid infusion of blood products. Platelets, plasma, and cryoprecipitate typically infuse over 30 minutes. Blood products should be connected directly to the venous access catheter and never be “piggybacked.”

Monitoring blood product administration is most important over the first 15 minutes because this is when most reactions will occur. Obtain vital signs including temperature, heart rate, and blood pressure before the start of the infusion to establish the patient's baseline and watch for trends suggestive of a reaction. Reactions to blood products vary but generally begin with an alteration in temperature and are best initially detected in these patients by visual cues. Flushing, pruritus, dyspnea, chills, or rash may alert ED staff to stop the infusion and investigate further. Vitals signs may reflect fever, tachycardia, hypertension, or hypotension. Pain in the chest or back may also be present. When such a
reaction occurs, the infusion should be stopped immediately, and the blood tubing should be replaced with normal saline to keep the vein open. The ED physician must be notified immediately, and staff should follow hospital policy for infusion reactions. If a minor reaction occurs, a good rule of thumb is to slow the infusion to a quarter rate at first then back to full rate at 15 minutes if no additional reaction is noted. Flush the line with saline once the infusion is complete.

Immunoglobulin therapy initiation in patients with idiopathic thrombocytopenic purpura (ITP) can also be considered a blood product but is treated differently, as intravenous immunoglobulin (IVIG) is generally a more time-consuming therapy, one that usually involves inpatient admission. Factors 8 and 9 infusions are also in a different category because these factor replacements are achieved with quick push infusions and are often done at home by trained parents. Often, these patients will either go home immediately post infusion in the ED or not need to come to the hospital setting at all. Once again, it cannot be stressed enough the importance of speaking to a hematologist or other pertinent pediatric specialist before administration of these blood products to a pediatric patient.

**SUMMARY**

In conclusion, there are many special considerations in the care and treatment of the pediatric oncology and hematology patient. However, if a systematic approach is taken, the ED care provider should feel confident in his or her ability to choose the best course of treatment for this very special type of patient. Always regard the families of these patients as partners in emergency care and as vital sources of patient- and disease-specific information. Finally, timely consultation with the child's specialty care provider will guide medical decision making in the ED and decisions regarding disposition.

**REFERENCES**


**Additional Reading**