Pediatric Emergency Medicine Reports

The Practical Journal of Pediatric Emergency Medicine

Volume 16, Number 5 / May 2011 www.ahcmedia.com

Authors:

Melissa R. Jefferson, MD, Assistant Professor of Pediatrics, Brody School of Medicine, East Carolina University, Greenville, NC.

Beng Fuh, MD, PhD, Assistant Professor of Pediatrics, Brody School of Medicine, East Carolina University, Greenville, NC.

Ronald M. Perkin, MD, MA, Professor and Chairman, Department of Pediatrics, Brody School of Medicine, East Carolina University, Greenville, NC.

Peer Reviewer:

Dennis A. Hernandez, MD, FAAP, FACEP, Medical Director, Pediatric Emergency Services, Florida Hospital for Children, Walt Disney Pavilion, Orlando, FL.

Statement of Financial Disclosure

To reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Dr. Dietrich (editor), Dr. Skrainka (CME question reviewer), Dr. Jefferson (author), Dr. Fuh (author), Dr. Perkin (author), Dr. Hernandez (peer reviewer), Ms. Mark (executive editor), and Ms. Hamlin (managing editor) report no relationships with companies related to the field of study covered by this CME activity.

AHC Media

Pediatric Oncologic Emergencies

Although the diagnosis of cancer in childhood is relatively rare, with an annual incidence of 165 cases per million,[1] it remains the leading cause of death by disease in children, accounting for approximately 10% of all childhood fatalities.[2] Since 1970, childhood cancer survival rates have increased from 45% to more than 80%.[3] This dramatic increase in survival has been accomplished due to the availability of new therapies and therapeutic strategies, as well as to prompt diagnosis and enhanced supportive care, including that provided in the emergency department setting.

The pediatric oncology patient may present with a variety of life-threatening situations, including those resulting from structural or functional compromise of the cardiopulmonary or neurologic systems, hematologic abnormalities, or a compromised immune system. Emergencies in these patients may occur as a result of the disease itself or as a consequence of treatment. The emergency department is often the first point of contact for newly diagnosed pediatric oncology patients, and they may be quite ill on initial presentation. Children with known malignancies often are immunocompromised secondary to their treatment and, as a result, pose unique diagnostic and therapeutic challenges.

This article will highlight six of the most commonly encountered oncologic emergencies.

— Ann Dietrich, MD, FAAP, FACEP, Editor

Emergencies Related to Structural Compromise

Malignancies of the Central Nervous System (CNS). *Brain Tumors.* Brain tumors are the most common solid tumors in childhood and the second most common type of childhood cancer overall.[4] Patients with CNS lesions are at risk for rapid deterioration as a result of increased intracranial pressure (ICP). Consequently, rapid diagnosis may be life-saving in this population. However, children and adolescents with brain tumors often present with non-specific complaints and, as a result, pediatric patients with CNS masses often make several visits to their primary care physician or emergency department prior to obtaining a diagnosis. Careful attention to the history and physical exam can assist the practitioner in determining which patients warrant imaging studies to evaluate for an intracranial mass.

Headache is perhaps the most common presenting complaint for a CNS mass. In a study of 3,291 subjects in the Childhood Brain Tumor Consortium Databank, 62% of children with brain tumors experienced chronic or frequent headaches prior to their first hospitalization.[5] Headache is a common complaint in the pediatric population, and accounts for a significant number of visits to emergency departments and pediatrician offices. Most patients presenting with such a complaint do not require further radiologic investigation. However, specific features of the headache and associated signs and symptoms should increase the practitioner's suspicion that this may be the result of a more serious condition. The practitioner should evaluate for signs of increased ICP or

Executive Summary

- More than 97% of patients with a brain tumor, presenting with a headache, will have a documentable neurologic abnormality found on physical exam.
- Localized or radicular back pain occurs in 80% of children with spinal cord compression.
- Orthopnea, upper body edema, and dyspnea at rest are all associated with increased anesthesia risk in a child with superior mediastinal syndrome.
- Tumor lysis syndrome is characterized by the triad of hyperkalemia, hyperuricemia, and hyperphosphatemia and is often complicated by secondary renal failure and symptomatic hypocalcemia.

localizing signs or symptoms. Table 1 lists symptoms that should raise suspicion that the headache may be secondary to a brain tumor.

A thorough physical examination, including a complete neurological and fundoscopic exam, is essential in making the diagnosis of a brain tumor and evaluating for increased ICP. More than 97% of patients with a brain tumor, presenting with a headache, will have a documentable neurologic abnormality found on physical exam.[5,6] Macrocephaly and splitting of sutures may be present in infants. Limitation in eye movement, visual field defects, seizures, and gait disturbance are suggestive of significant CNS pathology.

A computed tomography (CT) scan should be obtained for gross brain structural evaluation and signs of increased ICP if magnetic resonance imaging (MRI) cannot be performed. CT imaging must be reviewed with caution because it is not very accurate for evaluating brain tumors, especially posterior fossa tumors. MRI is the preferred test to evaluate brain structure, but may not be feasible in the emergency setting. Lumbar puncture should be approached with caution, and preferably deferred if increased ICP is suspected, as this can lead to herniation.

Emergent treatment of increased ICP consists of elevation of the head of the bed, intravenous dexamethasone at a loading dose of 0.5-2 mg/kg, followed by 0.25-0.5 mg/kg IV every 6 hours. Mannitol 20% solution and hypertonic saline solution should also be considered. Intravenous fluids of normal saline at a rate of 75% maintenance may be started. Endotracheal intubation should be considered in severe cases to control airway and partial pressure of carbon dioxide. Immediate pediatric neurosurgical consultation should be obtained. Oncology and radiation oncology consultations should be obtained.

Spinal Cord Compression (SCC). SCC occurs in approximately 3-5% of all pediatric oncology patients.[7] If not detected and treated in a timely manner, SCC may lead to irreversible neurologic damage, including permanent paralysis. SCC is the most common cause of lower limb paralysis in children.[8] Early recognition and treatment of cord compression is essential to decrease long-term morbidity. Appropriate, definitive management is best determined through multidisciplinary consultation with pediatric oncology, neurosurgery, and radiation oncology. SCC may result from virtually any malignancy and can present either at the time of diagnosis or as the disease progresses.

SCC may occur as a result of an infiltrative paraspinous process, tumors originating from the vertebral process, intrinsic spinal cord tumors, or infiltrative lesions. In the pediatric patient, cord compression most frequently results from a paravertebral tumor extending through the intervertebral foramina (e.g., soft-tissue sarcomas, tumors of neurogenic origin).[8] Tumors growing through the intervertebral foramina initially cause mechanical nerve root compression. If growth continues, transverse myelitis (inflammation of gray and white matter of the spinal cord) ultimately may occur. Also, the venous plexus may be compressed at the intravertebral level, resulting in ischemic injury to the cord.[10] Intradural spinal metastasis from an intracranial process (e.g., medulloblastoma) also may lead to cord compromise. These lesions tend to occur in the lumbosacral region. Primary spinal cord tumors, such as an intramedullary astrocytoma, also may be the cause of pain and neurologic symptoms in children. More rarely, leukemic chloromas may be a cause of SCC. Chloromas are more commonly due to acute myelogenous leukemia (AML) as opposed to acute lymphoblastic leukemia (ALL).[11] Leukemic infiltration of the spinal cord has a predilection for the cauda equina or conus medullaris,[12] and patients should be screened for symptoms of cord involvement.[13]

SCC should be suspected in any pediatric oncology patient presenting with back pain or suggestive neurologic findings. Localized or radicular back pain occurs in 80% of children with SCC.[7] Back pain in any child with a malignancy is highly suspicious for SCC and deserves further investigation. Patients with SCC also may present with complaints

Table 1. Symptoms Suggestive of a Brain Tumor as the Etiology of Headache

- **Occipital location of headache**
- **Worsening symptoms**
- **Awakens patient at night**
- **Associated with focal symptoms**
- **Emesis**

of motor or sensory abnormalities. Depending on the rate of tumor growth, the pain and/or deficits may be long-standing (present for weeks to months) and slowly progressive, or more acute in nature. History should elicit the time course and include questioning about changes in gait and bowel or bladder habits. Tenderness to palpation tends to localize to the site of the lesion. A thorough neurologic examination should be performed, with attention to motor strength, reflexes, gait abnormalities, sensation, and sphincter tone. The diagnosis of SCC is particularly challenging in the infant or young child who cannot verbalize back pain; regression in motor milestones or refusal to ambulate may be initial symptoms.

Imaging studies should be obtained as soon as possible. Plain radiographs are insufficiently sensitive. The optimal study in a patient with potential SCC is an MRI. In the rare case where an MRI cannot be performed in a timely manner, CT myelography is an acceptable alternative.

If SCC is suspected, dexamethasone should be initiated without delay. Corticosteroid therapy may decrease cord edema and preserve neurologic function while plans for more definitive therapy are underway. Optimal dosing of dexamethasone is not known; a loading dose of 1-2 mg/kg IV, followed by 0.25-0.5 mg/kg every 6 hours, has been suggested. If lymphoma or a leukemic infiltrate is the cause of the SCC, dexamethasone has the potential to be cytolytic and may lead to tumor lysis syndrome.

Definitive therapeutic options include surgical resection, radiation therapy, and/or chemotherapy. The optimal choice of treatment is best determined by a multidisciplinary team. Treatment choice will be influenced by whether a tissue diagnosis has been made, radio- and chemosensitivity of the tumor, extent of disease, and the degree of neurologic compromise present. Studies have suggested that the degree of neurologic deficit at the time of presentation and the duration of symptoms prior to initiating therapy both correlate with the ultimate functional outcome, regardless of the treatment method employed. When planning definitive therapy, both acute relief of SCC as well as long-term sequelae of the treatment modality used should be considered. Radiation therapy and surgical resection, while offering more immediate benefit in terms of local tumor control, may lead to long-term sequelae in terms of growth problems and scoliosis. For this reason, chemotherapy is generally the treatment of choice in a child with a chemosensitive process such as lymphoma, leukemia, or disseminated neuroblastoma and who has minimal symptoms of SCC.[14] If SCC occurs in the setting of progressive refractory disease, palliative therapy for SCC should not be withheld, as it may have a substantial positive impact on the quality of life.

Mediastinal Mass, Superior Mediastinal/Superior Vena Caval Syndrome. Masses within the mediastinum are fairly common in children, and the differential diagnosis is quite different than one would consider for an adult patient.[15] In the young infant, congenital anomalies should be considered. Children may present with a mass in the posterior mediastinum, often representing a neurogenic tumor such as neuroblastoma. The differential diagnosis of a mediastinal mass in a pediatric patient depends on the age of the child, the rapidity with which symptoms develop, and the mediastinal compartment that contains the mass. The majority of children or adolescents presenting with a mediastinal mass who are experiencing respiratory compromise ultimately will be diagnosed with a malignancy, most often lymphoma. Table 2 shows the differential diagnosis of a mediastinal mass by location within the mediastinum.

Children presenting with an anterior mediastinal mass often have symptoms suggestive of a respiratory infection, such as cough, fever, and wheezing. It is not uncommon for a child with a mediastinal mass to present to a medical facility and receive a diagnosis of a respiratory tract infection or asthma exacerbation on more than one occasion prior to receiving imaging studies and detection of the mass. Therefore, it is critical that the practitioner keep broad differential diagnoses in mind and perform a thorough physical exam and detailed history, especially in the child with wheezing or dyspnea with no previous history of asthma.

Masses in the anterior mediastinum have the potential to create life-threatening compromise of the airway or cardiovascular system. Superior mediastinal syndrome (SMS) refers to compression of the trachea or mainstem bronchi by a mediastinal mass. SMS is closely related to superior vena caval syndrome (SVCS), which refers to compression or obstruction of the vena cava. These two entities often coexist. In children, the trachea and mainstem bronchi are very compliant and vulnerable to collapse

Table 2. Differential Diagnosis of a Mediastinal Mass by Location Within the Mediastinum

Anterior
• Lymphoma
• Leukemia
• Malignant germ-cell tumor
• Benign teratoma
• Thymic lesion (thymic hyperplasia, thymoma, thymic cyst)
• Substernal thyroid
Middle
• Lymphoma
• Tuberculosis
• Histiocytosis
• Sarcoidosis
• Anomalies of the great vessels
Posterior
• Neuroblastoma
• Ganglioneuroblastoma
• Sarcoma

Table 3. Signs and Symptoms of SVCS

- Facial swelling
- Upper body edema
- Cyanosis of the face or upper body
- Plethora
- Conjunctival edema or suffusion
- Headache
- Tachycardia
- Elevated venous pressure
- Vocal cord paralysis, hoarseness
- Dyspnea
- Cough
- Decreased mentation
- Horner's syndrome

from external compression. The superior vena cava is a thin-walled vessel with low intraluminal pressure. Compression by a mediastinal mass or obstruction by a tumor or thrombosis leads to venous stasis and diminished blood return to the heart. (*See Table 3.*) It should be noted that a child with an indwelling central venous catheter may develop SVCS secondary to thrombosis of the catheter. SMS and SVCS generally result from compression from a mass in the anterior compartment of the mediastinum, with lymphoma being the most common cause. Children with leukemia also may present with a mediastinal mass; therefore, it is important that all newly diagnosed leukemia patients have a chest X-ray performed as part of their initial evaluation.

A thorough history and physical exam should be performed on any child or adolescent with a suspected mediastinal mass, with particular attention to signs and symptoms of SMS/SVCS.

Children with SMS and/or SVCS may be asymptomatic at the time of presentation, or they may come to medical attention just prior to cardiopulmonary collapse. In some cases, the airway may be so tenuous that total airway loss may be precipitated by simply placing the child in a supine or flexed position. Once there is suspicion of a mediastinal process, care must be taken to protect the airway. When performing the physical exam or while obtaining imaging studies, it is important that the child not be forced to lie in a position that may precipitate airway collapse. Diagnosis and initiation of therapy should occur in the most expeditious and least invasive manner possible.

Children with evidence of SMS/SVCS must be managed with care to avoid complete loss of the airway or cardiovascular collapse. In particular, the use of procedural sedation or general anesthesia should be avoided until a thorough evaluation of the child's anesthesia risk has been completed. Several clinical factors have been associated with an increased risk for life-threatening anesthesia-related complications in the context of SMS. Orthopnea, upper body edema, and dyspnea at rest have all been associated with increased anesthesia risk.[16] Orthopnea most closely correlates with the level of risk assumed, and questioning for this symptom should occur directly, as parents may not give such information unless it is specifically asked. Although these elements of the physical exam and history should be taken into consideration, it should be noted that the degree of symptoms does not always correlate with the degree of airway compromise,[17] since anesthesia-related deaths have been reported in asymptomatic children with anterior mediastinal masses.[18-20] Therefore, in a child with a known mediastinal mass, a CT scan and pulmonary function testing should be performed prior to subjecting the child to anesthetics. A CT scan can assess the tracheal cross-sectional area (TCA), which can then be compared to well-established norms for age and gender.[21] Pulmonary function testing to determine the peak expiratory flow rate (PEFR) may be done fairly easily at the child's bedside with a handheld device, and readings should be done in both the sitting and supine position. Studies have shown that children with a TCA and PEFR of > 50% for age can be safely given general anesthesia or procedural sedation if needed.[22] Table 4 shows findings for relative contraindications for anesthesia in a child with a mediastinal mass.

In severe cases of SMS, empiric therapy may need to be employed prior to making a tissue diagnosis. In most cases, empiric corticosteroid therapy will provide sufficient tumor reduction.[23] However, administration of steroids may result in tumor lysis syndrome and may impair the ability to make a diagnosis. Steroids, therefore, should be given only in an immediately life-threatening situation after consultation with a pediatric oncologist. Even more rarely, the mass may not be sensitive to corticosteroids, and emergent radiation therapy may be considered.[24] However, in most cases, a tissue diagnosis can be made prior to instituting therapy. If general anesthesia or sedation must be avoided, the use of local anesthesia with the child in a seated position should be considered.

Hematologic Emergencies

Hyperleukocytosis. Leukemia is the most common type of childhood malignancy. Approximately 3500 children are diagnosed with acute leukemia in the United States each year, accounting for approximately one-third of childhood cancers.[25] The presentation of leukemia varies widely, from children presenting with only mild symptoms, such as fatigue, to those presenting in extremis. Likewise, the degree of hematologic derangement in a newly diagnosed pediatric patient ranges from a normal peripheral blood count to life-threatening hyperleukocytosis, defined as a white blood cell (WBC) count of greater than 100,000 per μL.

Hyperleukocytosis is present at the time of diagnosis in approximately 10% of cases of ALL.[26] Among ALL patients, those with infant leukemia, hypodiploid chromosome blasts, and those with T-cell ALL are at

Table 4. Critical Airway: Relative Contraindications to Anesthesia in a Child with a Mediastinal Mass

- Orthopnea
- Upper body edema
- Dyspnea
- Clinical findings of impending respiratory failure
- Tracheal cross-sectional area < 50% normal for age and sex
- Severe compression of one or both mainstem bronchi
- Peak expiratory flow rate of < 50% predicted (performed in sitting and supine position)

particular risk for hyperleukocytosis.[26] The clinician should be certain to obtain a chest X-ray early in the initial management of the ALL patient with hyperleukocytosis, as the presence of a mediastinal mass in these patients is not uncommon.[26] Five percent to 20% of pediatric AML cases will present with hyperleukocytosis, and virtually all patients with chronic myelogenous leukemia (CML) will have hyperleukocytosis at diagnosis.[27,28]

Hyperleukocytosis results in hyperviscosity and leukostasis. Aggregation of leukemic blasts occurs in the microvasculature, which may result in multisystem organ dysfunction. End-organ damage results from interaction between aggregates of leukemic blasts and injured epithelium. This interaction leads to tissue hypoxia, with resultant release of inflammatory cytokines.[29] Myeloblasts are more apt to cause damage due to their larger size and increased adhesiveness.[30] Leukostasis may cause devastating dysfunction in any organ system. In the central nervous system, cerebrovascular accidents, both thrombotic and hemorrhagic, may occur spontaneously. This is most common in the setting of AML.[27] From a cardiovascular standpoint, fatal pericardial hemorrhages secondary to hyperleukocytosis have been reported. Pulmonary complications also may occur, including hypoxia, pulmonary hemorrhage, and respiratory failure. Intra-abdominal complications, including gastrointestinal bleeds, are also possible.[27] Splenic rupture is most commonly a risk in the patient with extreme hyperleukocytosis and CML. In addition to the damage caused by leukostasis, children with hyperleukocytosis from acute leukemia are at risk for the metabolic complications from tumor lysis syndrome, including renal failure, hypocalcemia, hyperphosphatemia, and hyperuricemia. Life-threatening metabolic abnormalities occur more commonly in the setting of hyperleukocytosis in ALL.[27] This topic is covered more thoroughly in the tumor lysis section. Disseminated intravascular coagulation (DIC) is most common in high white-blood-cell count AML patients. All patients with hyperleukocytosis should be screened for a coagulopathy, as correction of these abnormalities may decrease the incidence of bleeding complications.[27]

Patients with hyperleukocytosis should be closely monitored for signs and symptoms of end-organ damage. Neurologic symptoms may include headache, seizures, and altered mental status. On examination, papilledema or retinal vascular distention may be detected. Pulse oximetry should be employed to detect hypoxia, and the patient should be screened for other signs and symptoms of respiratory compromise. Priapism, clitoral enlargement, and dactylitis, all secondary to leukostasis, may be present on physical examination.

Children with hyperleukocytosis are at increased risk of death early in their course of treatment. The threshold at which hyperleukocytosis becomes clinically significant varies by leukemia type. This is most likely due to differences in adhesiveness of the leukemic blasts in different types of leukemia. The risk of fatal complications is highest in patients with AML with hyperleukocytosis. In patients with hyperleukocytosis, early death occurs in approximately 20% of patients with AML and 5% of patients with ALL.[27] Studies have suggested that life-threatening viscosity becomes increasingly prevalent at WBC greater than 200,000/µL in AML and greater than 300,000/µL in ALL and CML.[23]

Aggressive supportive care and prompt consultation with a pediatric oncologist for initiation of cytoreductive chemotherapy reduces the risk of early death in these patients. Supportive care is directed at correction and prevention of metabolic abnormalities and coagulopathies. Table 5 outlines the suggested initial studies and management of the patient with hyperleukocytosis. Hydration should be instituted. Supplemental potassium should not be given, even in the setting of hypokalemia, as hyperkalemia may result from tumor lysis even prior to the initiation of therapy. The patient should be monitored very closely for the development of metabolic abnormalities. Efforts should be made to correct coagulopathies, including the transfusion of platelets if the platelet count is < 25,000 per µL. For the anemic patient, red blood cell transfusion should be avoided if the patient is hemodynamically stable, as this will further increase the blood viscosity. Emergent cranial radiation, which has been used in the past in an effort to prevent intracranial bleeds, is of no proven benefit and is no longer routinely employed or recommended.[27] Leukapheresis and exchange transfusion may be considered as temporizing measures or to reduce the leukemic burden prior to initiation of cytoreductive therapy; however, this remains controversial.[26,31,32] It should be noted that the blast count will rise again quickly after these procedures are completed. Prompt initiation of effective cytoreductive therapy remains critical.

Tumor Lysis Syndrome. Tumor

Table 5. Initial Supportive Therapy in the Setting of Hyperleukocytosis

- Hydration: D5 1/2 NS at 3000 mL/m^2/day. No supplemental potassium should be given. Consider alkalinized fluids if allopurinol is being used and patient is not hyperphosphatemic.
- Treatment of hyperuricemia
  - Allopurinol 300 mg/m^2 divided TID
  - Consider administration of rasburicase if patient is hyperuricemic and not G6PD deficient.
- Transfuse platelets if platelet count is < 25,000/μL.
- Correct other significant coagulopathies.
- Avoid transfusion of packed red blood cells if hemodynamically stable.

NOTE: Management of hyperuricemia and tumor lysis covered more thoroughly in tumor lysis section.

Table 6. Laboratory Studies and Clinical Monitoring

- CBC, calcium, phosphate, magnesium, uric acid, urea nitrogen, creatinine, lactate dehydrogenase at presentation and then every 6-12 hours depending on risk
- Sequential vital signs
- Strict assessment of intake and output
- Body weight once to twice daily
- Cardiorespiratory monitor with multi-lead ECG as needed for hyperkalemia (e.g., if K > 6 mEq/L, look for wide QRS and peaked T waves)
- Close clinical evaluation for signs of hypocalcemia or renal failure

lysis syndrome (TLS) is an oncologic emergency characterized by a triad of hyperkalemia, hyperuricemia, and hyperphosphatemia, and it is often complicated by secondary renal failure and symptomatic hypocalcemia. TLS may occur prior to the initiation of cytoreductive therapy and up to one week after initiation of therapy. When tumor cells lyse, large amounts of intracellular chemicals are released into the circulation and may cause metabolic derangements, which may lead to renal dysfunction and cardiac dysrhythmia.

TLS may occur with any malignancy with rapid cell turnover and high tumor burden. It most commonly occurs in the setting of leukemia or high-grade lymphoma. Children with hyperuricemia or renal insufficiency at presentation are at particularly high risk. Evidence of tumor lysis may be present prior to the initiation of the chemotherapy or after the child receives corticosteroids.

Conditions at highest risk for TLS include:

- ALL or AML (WBC >100,000/μL)
- Leukemia with massive lymphadenopathy and/or organomegaly
- T-cell ALL
- Infant leukemia
- Burkitt's lymphoma
- Large cell lymphoma.

Laboratory monitoring should include CBC and blood chemistries, with specific attention paid to serum potassium, calcium, magnesium, phosphate, uric acid, creatinine, urea nitrogen, and lactate dehydrogenase. Initially, these studies should be done every 6 hours, and then spread out as the tumor lysis improves. Fluid input and output should be monitored closely, and body weight documented twice daily. Sequential vital signs should be performed and a cardiopulmonary monitor with multi-lead ECG should be used to monitor for effects of hyperkalemia. (*See Table 6.*)

Interventions should be initiated to prevent TLS in tumors with a risk of TLS, and aggressive treatments should be started if there is evidence of TLS. These include hydration and alkalinization. Urine alkalinization helps with excretion of uric acid but should be performed with care because a urine pH > 7.5 may lead to precipitation of CaPO4 and xanthine crystals. Hyperkalemia should be treated with hydration, sodium polystyrene sulfonate, calcium gluconate, or insulin and dextrose as needed. Dialysis may be needed. Hyperphosphatemia can be treated with aluminium hydroxide, and dialysis may be necessary.

Hyperuricemia is treated with allopurinol and, when possible, should be started prior to initiation of cytolytic therapy. For severe hyperuricemia, rasburicase may be used. Table 7 outlines suggested intervention for the management of TLS.

Infections in the Immunocompromised Child

Febrile Neutropenia. The advances made in the overall survival rates for children over the past few decades have been due, in part, to an increased intensity of chemotherapy given to pediatric patients. Cancer-directed therapy for this population is often quite cytotoxic to rapidly growing cells, often resulting in hematologic and immunologic suppression and breakdown of normal mucosal barriers. Selected patients may also be receiving radiation therapy, which may result in further tissue injury and impairment of the body's innate immunologic

Table 7. Prevention and Treatment of TLS

Delay and/or titrate cytolytic therapy (if possible) until prophylactic measures can be implemented (see "hydration therapy," "urinary alkalinization," "hyperuricemia management" below). AVOID intravenous radiologic contrast agents that might precipitate renal failure.	
Hydration therapy	• Administer IV fluid: D5 0.2% NaCl + $NaHCO_3$ 40 mEq/L at 3000 mL/m^2/day • Urine output goal: ≥ 100 mL/m^2/hour OR 3 mL/kg/hour (if body weight is < 10 kg) • Urine specific gravity goal ≤ 1.010 • Diuretics may be required (furosemide or mannitol)
Urinary alkalinization (see IV fluid above)	• Urine pH goal 6.5-7.5 to aid in excretion of uric acid Note urine pH > 7.5 may increase precipitation of CaPO4 and xanthine crystals • Adjust amount of $NaHCO_3$ in IV fluid to achieve urine pH and serum [sodium] goals
Hyperkalemia	• Moderate and asymptomatic (≥ 6.0 mEql/L): sodium polystyrene sulfonate orally • Severe and/or symptomatic (> 7.0 mEq/L): –Calcium gluconate 100-200 mg/kg IV –D25 (2 mL/kg) IV + regular insulin 0.1 units/kg IV –Dialysis may be necessary
Hyperphosphatemia	• Aluminum hydroxide 50-150 mg/kg/day divided in 4–6 doses (or 30–40 mL 6 to 8 hours) • Dialysis or continuous renal replacement therapy may be necessary
Hyperuricemia (uric acid crystals form in renal tubules and distal collecting system and cause oliguria)	• Allopurinol 300 mg/m^2 PO divided TID: Decreases production of uric acid by inhibiting xanthine oxidase If possible, start 12-24 hours before induction of cytolytic therapy **OR** • Urate oxidase (rasburicase): Metabolizes uric acid Should be considered in high-risk situations; contraindicated in G6PD deficiency, pregnancy, and lactation

barriers. Additionally, most pediatric cancer patients have indwelling central venous access, representing a further breakdown in the body's natural defenses against infection. As a result, children receiving therapy for cancer are at high risk for life-threatening infections, which are known to occur, especially in the setting of neutropenia. Although fever in the general pediatric patient is a fairly common, often benign presenting complaint, fever in the potentially neutropenic pediatric cancer patient is a medical emergency and needs to be recognized quickly as such, with prompt initiation of treatment.

The generally accepted definition of fever in the neutropenic patient is a single temperature of greater than 38.3°C (101° F) or two consecutive temperatures greater than 38.0°C (100.4°F) taken orally in a 12-hour period and lasting at least 1 hour.[33] It should be noted that axillary temperature is, on average, about 0.6°C lower than oral temperature. Rectal temperature should never be performed in children with neutropenia. Note that the absence of fever in a neutropenic patient with localizing signs or symptoms does not exclude infection. This is particularly true of the child receiving steroid therapy as a part of treatment. Such patients may present with non-specific complaints as the only sign of bacteremia. Clinically significant neutropenia is defined as an absolute neutrophil count (ANC) < 500/μL or < 1,000/μL and expected to decline due to recent chemotherapy administration.

Certain risk factors place the febrile neutropenic patient at particularly high risk. Patients with severe neutropenia, prolonged neutropenia, and those who developed neutropenia over a short period of time are at highest risk for the development of septicemia.[34] Individuals with an ANC of less than 200 are particularly vulnerable, as are those patients who have been neutropenic for more than 10 days.

A thorough history and physical examination should be performed, with particular attention to potential sites of infection (oral lesions, perirectal tenderness, and central venous access sites). Rectal temperatures should be avoided due to the risk of bacteremia from colorectal organisms. Neutropenic patients do not have the ability to mount the same degree of inflammatory response as an immunocompetent host. As a result, the localizing signs and symptoms may be subtle (e.g., pneumonia

Table 8. Frequently Chosen Antibiotics for Febrile Neutropenia

Coverage	Antibiotic
Broad spectrum	Ceftazidime; cefepime; piperacillin-tazobactam; meropenem
Additional Gram-negative coverage	Amikacin; gentamicin; tobramycin
Additional Gram-positive coverage	Vancomycin
Additional anaerobic coverage	Clindamycin; metronidazole
Atypical bacterial coverage	Azithromycin; clarithromycin

may present with mild respiratory symptoms and may not have characteristic findings on examination or CXR). Any reported areas of discomfort should be pursued as potential sites of infection.

The initial laboratory work-up of a febrile neutropenic pediatric oncology patient should include, at a minimum, a CBC, electrolytes, BUN/creatinine, and blood cultures for bacteria and fungi from all lumens of the central venous access device. Peripheral blood cultures are not routinely needed. Urinalysis and urine culture should be obtained. A chest X-ray should be considered and certainly obtained if hypoxia, tachypnea, physical exam findings suggestive of a respiratory infection, or respiratory complaints are present.[35] Stool studies and wound cultures should be considered if the history warrants. Meningitis is fairly rare in the febrile neutropenic patient; however, a lumbar puncture should be considered if there is alteration of mental status or neck stiffness.

Neutropenic patients are at risk for both common and opportunistic infections; therefore, the differential diagnosis of the febrile neutropenic patient is broad. Bacterial infections are the most common type of infection in this patient population and they present the most immediate risk to life. Broad-spectrum antimicrobials should be instituted within 30 minutes of presentation to a medical facility. Administration of broad-spectrum antimicrobials should not be delayed while awaiting laboratory results or imaging studies. The optimal choice of empiric antibiotic therapy is guided by institutional susceptibility and resistance patterns and history and exam findings unique to the individual patient. At a minimum, treatment should include a broad-spectrum beta-lactam antibiotic with antipseudomonal coverage. Potential agents for monotherapy include piperacillin/tazobactam, third- and fourth-generation cephalosporins (ceftazidime, cefepime), or carbapenems (imipenem, meropenem).[36-40]

In certain circumstances, monotherapy may be inadequate as empiric coverage. In the case of clinical sepsis, triple therapy with vancomycin and an aminoglycoside should be considered. Recent data suggest a shift in the overall trend of positive cultures toward increased infection with Gram-positive organisms in the febrile neutropenic patient.[41] There are several circumstances under which Gram-positive coverage should be broadened, including severe mucositis, potential line infections, and concern for cellulitis. In addition, recent treatment with high-dose cytarabine raises the risk for Gram-positive infection, particularly *Streptococcus viridans.*[42] If any of these risk factors are present, there should be a low threshold for adding vancomycin. Abdominal pain may be a particularly ominous symptom in the neutropenic patient, as it may indicate the onset of neutropenic enterocolitis (typhlitis). In such a setting, or in the case of a perirectal infection, coverage should include a broad-spectrum beta-lactam antibiotic with antipseudomonal coverage, vancomycin, and additional anaerobic coverage such as metronidazole. If respiratory symptoms are present, coverage for atypical organisms, and perhaps vancomycin, should be considered. Table 8 shows the suggested initial antibiotic management of the febrile neutropenic patient, and Table 9 shows additional antibiotic coverage for specific indications.

In addition to bacterial infections, oncology patients with prolonged severe neutropenia are at risk for opportunistic infections. Pediatric oncology patients routinely receive prophylaxis against *Pneumocystis jirovecii* (*carinii*), but there are instances of noncompliance, and breakthrough infections may occur even in the patient receiving prophylaxis. Significant hypoxia and diffuse infiltrates on chest X-ray should raise concern for *Pneumocystis jirovecii* pneumonia (formerly PCP). Fungal infections are possible causes of fever in the neutropenic patient. Antifungal coverage should be considered after consultation with the patient's oncologist. Viral infections such as HSV, varicella, RSV, and influenza may be life-threatening in the neutropenic pediatric patient and should be considered in the differential diagnosis. When symptoms and community infection patterns are suggestive, rapid RSV or influenza testing should be employed, and practitioners should have a low threshold for administering antiviral agents to such patients when the situation warrants.

Other Common Oncologic Emergencies

Pleural and Pericardial Effusions. Pleural or pericardial effusions may result from the primary malignancy, from complications of treatment such as radiation therapy, or from infectious complications. Dyspnea and cough are common presenting symptoms. Evaluation should include a chest

Table 9. Indications for Specific Antimicrobial Therapy in Addition to Broad-spectrum Antibiotic

Indication	Antimicrobial Therapy
Clinical sepsis	Broad-spectrum antibiotic + vancomycin + aminoglycoside
High-dose cytarabine chemotherapy or mucositis or cellulitis or concern for CVC infection	Broad-spectrum antibiotic + vancomycin
Pulmonary infiltrates	Broad-spectrum antibiotic + vancomycin + atypical antibacterial agent; if infiltrates are diffuse and hypoxia is present, consider treatment for PJP (PCP)
Abdominal symptoms	Broad-spectrum antibiotic + vancomycin + aminoglycoside + metronidazole or clindamycin
Perirectal lesions	Broad-spectrum antibiotic + vancomycin + metronidazole or clindamycin

radiograph, ECG, echocardiography, and monitoring of central venous pressure. Echocardiography is the most useful test in the confirmation of pericardial effusions. If there is significant respiratory distress or circulatory compromise, thoracentesis and pericardiocentesis for pleural effusion and pericardial effusions, respectively, should be considered in addition to routine resuscitative measures. Steroids should be considered for steroid-responsive tumors.

Bowel Obstruction or Perforation. This may result from the tumor process, such as Burkitt's lymphoma, or as a complication of treatment, such as steroids. Vincristine often leads to constipation and, if not treated, may cause obstipation. Whenever an acute abdomen is suspected in an oncologic patient, the patient should be placed on NPO status and surgical consultation should be obtained.

Syndrome of Inappropriate Antidiuretic Hormone (SIADH). Several agents may cause SIADH with resultant hyponatremia, which may result in mental status changes and seizures. Fluid restriction is usually sufficient in mild cases. Administration of hypertonic solution should be considered in severe cases. Furosemide to promote free water excretion may be helpful. Electrolytes, especially sodium, should be monitored closely.

Pancreatitis. This frequently occurs as a complication of chemotherapy and may present with abdominal pain, nausea and vomiting, anorexia, and fever. Evaluation should include complete blood count, complete metabolic panel, and lipase and amylase enzyme levels. Treatment should include pain management, NPO status, intravenous fluids, and hospital admission. A nasogastric tube should be placed in patients with ongoing emesis, and antibiotics should be administered to febrile or septic patients.

Coagulopathy. This can result either in bleeding or deep venous thrombosis. A complete physical exam, including a careful neurologic exam, should be performed. Laboratory studies should include a complete blood count, PT, APTT, D-dimer, and fibrinogen. Imaging of suspected deep vein thrombosis (DVT) sites should be performed. Treatment with fresh frozen plasma and cryoprecipitate should be considered.[44] Careful anticoagulation should be initiated in patients with DVT with no evidence of bleeding.

Summary

Cancer is the leading medical cause of death in children. Morbidity and mortality are either directly secondary to the cancer or to complications of treatment. The significant improvements in childhood cancer survival that have been witnessed in the past 25 years are due to improvements in chemotherapy, radiation therapy, surgical techniques, supportive care, and the recognition and treatment of oncologic emergencies. Prompt recognition and appropriate management of oncologic emergencies can decrease patient agony, decrease mortality, and minimize long-term sequelae. A multidisciplinary approach involving the emergency department physician, the oncologist, and radiation oncologist is essential in achieving optimal outcomes.

Brain tumors and other cancers that spread to the CNS can cause increased intracranial pressure, the symptoms of which can range from subtle to obvious. Management ranges from observation to administration of corticosteroids, mannitol, cytoreductive chemotherapy, to emergent radiation therapy. Spinal cord compression can result from intradural or extradural malignancies. If not treated promptly, it can result in paralysis and other sequelae. Management includes observation, cytoreductive chemotherapy, corticosteroids, intrathecal chemotherapy, radiation therapy, and surgical decompression.

Mediastinal tumors can result in airway compromise or vascular compromise. If airway compromise is suspected, care should be taken to avoid placing the patient in positions that may worsen airway compromise. Sedation and anesthesia should be

considered with care. Emergent cytoreductive therapy with steroids and/or radiation therapy may be necessary.

Rapid proliferating and high tumor-burden cancers can lead to tumor lysis syndrome. Tumor lysis may occur even prior to the initiation of cytoreductive chemotherapy. Hydration, alkalinization, and allopurinol may be necessary. Rasburicase should be considered in severe hyperuricemia, provided the patient is not G6PD deficient. Severe tumor lysis syndrome may necessitate dialysis.

Fever in the neutropenic patient is an emergency, and prompt evaluation and administration of broad-spectrum antibiotics are needed. Blood culture from indwelling catheters should be collected, preferably prior to initiation of antibiotics. However, the administration of antibiotics should not be delayed for diagnostic studies.

The awareness and vigilance of emergency care providers and other physicians for possible oncologic emergencies are critical in maintaining and further improving good outcomes for children with malignancies.

References

1. Li J, Thompson TD, Miller JW, et al. Cancer incidence among children and adolescents in the United States, 2001-2003. *Pediatrics* 2008; 121:e1470-e1477.
2. Linet MS, Ries LA, Smith MA, et al. Cancer surveillance series: Recent trends in childhood cancer incidence and mortality in the United States. *J Natl Cancer Inst* 1999;91:1051-1058.
3. Ries LAG, Melbert D, Krapcho M, et al, editors. SEER cancer statistics review 1975–2005. Bethesda, MD: National Cancer Institute; 2006.
4. Gurney JG, Smith MA, Bunin GR. CNS and miscellaneous intracranial and intraspinal neoplasms. SEER Pediatric Monograph. In: Ries LAG, Smith MA, Gurney JG, et al, editors. *Cancer Incidence and Survival Among Children and Adolescents: United States SEER Program 1975-1995.* Bethesda (MD): National Cancer Institute; 1999. SEER Program. NIH Pub.No.99-4649:52-63
5. The epidemiology of headache among children with brain tumor. Headache in children with brain tumors. The childhood brain tumor consortium. *J Neurooncol* 1991;10:31-46.
6. Wilne S, Collier J, Kennedy C, et al. Presentation of childhood CNS tumors: A systematic review and meta-analysis. *Lancet Oncology* 2007;8:685-695
7. Lewis DW, Packer RJ, Raney B, et al. Incidence, presentation and outcome of spinal cord disease in children with systemic cancer. *Pediatrics* 1986;78:438.
8. Prasad D, Schiff D. Malignant spinal-cord compression. *Lancet Oncol* 2005;6:15-24.
9. Pollono D, Drut R, Ibanez O, et al. Spinal cord compression: A review of 70 pediatric patients. *Pediatric Hematology Oncology* 2003:20:457-466.
10. Arguello F, Baggs RB, Duerst RE, et al. Pathogenesis of vertebral metastasis and epidural spinal cord compression. *Cancer* 1990;65:98-106.
11. Petursson SR, Boggs DR. Spinal cord involvement in leukemia: A review of the literature and a case of Ph1+ acute myeloid leukemia presenting with conus medullaris syndrome. *Cancer* 1981;47:346-350.
12. Bojsen-Moller M, Nielsen JL. CNS involvement of leukemia. *Acta Path Microbiol Immunol Scan Sect A* 1983;91:209-216.
13. Olcay L, Aribas BK, Gokce M. A Patient with acute myeloblastic leukemia who presented with conus medullaris syndrome and review of the literature. *J Pediatr Hematol Oncol* 2009;31:440-447.
14. Gunes D, Uysal KM, Cetinkaya H, et al. Paravertebral malignant tumors of childhood: Analysis of 28 pediatric patients. *Childs Nerv Sys* 2009;25:63-69.
15. Azarow KS, Pearl RH, Zurcher R, et al. Primary mediastinal masses: A comparison of adult and pediatric populations. *J Thorac Cardiovasc Surg* 1993;106:67-72.
16. Azizkhan RG, Dudgeon DL, Buck JR, et al. Life-threatening airway obstruction as a complication to the management of mediastinal masses in children. *J Pediatric Surgery* 1999;8:61-68.
17. Shamberger RC, Holzman RS, Griscomn NT, et al. CT quantitation of tracheal cross sectional area as a guide to the surgical and anesthetic management of children with anterior mediastinal masses. *J Pediatr Surg* 1991;26:138-142.
18. Yamashita M, Chin I, Horigome H, et al. Sudden fatal cardiac arrest in a child with an unrecognized anterior mediastinal mass. *Resuscitation* 1990;19:175-177.
19. Viswanathan S, Campbell CE, Cork RC. Asymptomatic undetected mediastinal mass: A death during ambulatory anesthesia. *J Clin Anesth* 1995;7:151-155.
20. Bray RJ, Fernandes FJ. Mediastinal tumor causing airway obstruction in anesthetized children. *Anesthesia* 1982;37:571-575.
21. Griscom NT, Wohl ME. Dimensions of the growing trachea related to age and gender. *Am J Roentgenol* 1986;146:233-237.
22. Shamberger RC, Holzman RS, Griscom NT, et al. Prospective evaluation by computed tomography and pulmonary function tests of children with mediatinal masses. *Surgery* 1995;118:468-471.
23. Rheingold SR, Lange BJ. Oncologic emergencies. In: Pizzo PA, Poplack DG, editors. *Principles and Practice of Pediatric Oncology*, 5th edition. Philadelphia: Lippincott Williams & Wilkins; 2006:1202-1230.
24. Loeffler JS, Leopold KA, Recht A, et al. Emergency prebiopsy radiation for mediastinal mass: Impact on subsequent pathologic diagnosis and outcome. *J Clin Oncol* 1986;4:716-721.
25. Smith MA, Gloeckler-Ries LA, Gurney JG. Leukemia. In: Reis LAG, Smith MA, Gurney JG, editors. *Cancer Incidence and Survival Among Children and Adolescents: United States SEER Program 1975-1995.* Bethesda (MD): NCI, SEER Program NIH Pub; 1999. P. 17-34.
26. Eguiguren JM, Schell MJ, Crist WM, et al. Complications and outcome in childhood acute lymphoblastic leukemia with hyperleukocytosis. *Blood* 1992:79:871-875.
27. Bunin NJ, Pui CH. Differing Complications of hyperleukocytosis in children with acute lymphoblastic or acute nonlymphoblastic leukemia. *J Clin Oncol* 1985:3:1590-1595.
28. Rowe JM, Lichtman MA. Hyperleukocytosis and leukostasis: Common features of childhood chronic myelogenous leukemia. *Blood* 1984:63:1230.
29. Stucki A, Rivier AS, Gikic M, et al. Endothelial cell activation by myoblasts: Molecular mechanisms of leukostasis and leukemic cell dissemination. *Blood* 2001;97:2121-2129.
30. Lichtman MA, Rowe JM. Hyperleukocytic leukemias: Rheological, clinical, and therapeutic considerations. *Blood* 1982:60:279-228.
31. Maurer HS, Steinherz PG, Gaynon PS, et al. The effect of initial management of hyperleukocytosis on early complications and outcome of children with acute lymphoblastic leukemia. *J Clini Oncol* 1988:6:125.
32. Inaba H, Fan Y, Pounds S, et al. Clinical and biologic features and treatment outcome of children with newly diagnosed acute myeloid leukemia and hyperleukocytosis. *Cancer* 2008;113:522-529.
33. Hughes WT, Bodey GP, Bow EJ, et al. Guidelines for the use of antimicrobial agents in neutropenic patients with cancer. *Clin Infect Dis* 2002;34:730-751.
34. Bodey GP, Buckley M, Sathe YS, et al. Quantitative relationships between circulating leukocytes and infection in patients with acute leukemia. *Ann Intern Med* 1966;64:328-340.
35. Korones DN, Hussong MR, Gullace MA. Routine chest radiography of children hospitalized for fever and neutropenia: Is it really necessary? *Cancer* 1991;68: 940-943.
36. Uygun V, Karasu GT, Ogunc D, et al. Piperacillin/tazobactam versus cefepime

for the empirical treatment of pediatric cancer patients with neutropenia and fever: A randomized and open-label study. *Pediatr Blood and Cancer* 2009;53: 610-614.

37. Pizzo PA, Hathorn JW, Hiemenz JW, et al. A randomized trial comparing ceftazidime alone with combination antibiotic therapy in patients with fever and neutropenia. *N Engl J Med* 1986;315:552.
38. Chuang YY, Hung IJ, Yang CP, et al. Cefepime versus ceftazidime as empiric monotherapy for fever and neutropenia in children with cancer. *Pediatr Infect Dis J* 2002;21:203-209.
39. Freifield A, Walsh Walsh T, Marshall D, et al. Monotherapy for fever and neutropenia in cancer patients: A randomized comparison of ceftazidime versus imipenem. *J Clin Oncol* 1995;13:165.
40. Lindblad R, Rodjer S, Adriasnsson M, et al. Empiric monotherapy for febrile neutropenia — a randomized study comparing meropenem and ceftazidime. *Scand J Infect Dis* 1998;30:237-243.
41. Hakim H, Flynn P, Knapp K, et al. Etiology and clinical course of febrile neutropenia in children with cancer. *J Pediatr Hematol Oncol* 2009;31:623-629.
42. Lehrbecher T, Varwig D, Kaiser J, et al. Infectious complications in pediatric acute myeloid leukemia: Analysis of the prospective multi-institutional clinical trial AML-BFM 93. *Leukemia* 2004;18:72-77.
43. Arya L, Narain S, Thavarai V, et al. Leukemic pericardial effusions causing cardiac tamponade. *Med Pediatr Oncol* 2002;38:282-284.
44. Fuh B, Perkin R. Clinical presentation, evaluation and management of bleeding disorders in children. *Pediatr Emerg Med Rep* 2009;14:29-40.

Physician CME Questions

43. Cancer is the leading nontraumatic cause of death in children.
    A. true
    B. false

44. Which of the following is an oncologic emergency?
    A. spinal cord compression
    B. tumor lysis syndrome
    C. neutropenic fever
    D. superior mediastinal syndrome
    E. all of the above

45. Which of the following is a sign of increased intracranial pressure?
    A. headache
    B. papilledema
    C. emesis
    D. splitting of sutures
    E. all of the above

46. Steroids are contraindicated in spinal cord compression.
    A. true
    B. false

47. Which of the following cancers is *not* likely to present with a mediastinal mass?
    A. T-cell ALL
    B. Hodgkin lymphoma
    C. neuroblastoma
    D. Wilms' tumor

48. When a child with signs of respiratory distress secondary to a mediastinal mass presents, the following measure should be taken immediately:
    A. intubation
    B. emergent radiation therapy
    C. place in supine position
    D. allow the child to choose preferred posture

49. Which of the following findings is *not* suggestive of tumor lysis syndrome?
    A. hyperkalemia
    B. hyperuricemia
    C. hypercalcemia
    D. hyperphosphatemia

50. Which of the following is *not* part of the management of tumor lysis syndrome?
    A. hydration
    B. alkalinization
    C. fluid restriction
    D. allopurinol
    E. rasburicase

51. Which of the following is a possible complication of hyperleukocytosis?
    A. mental status changes
    B. respiratory distress
    C. thromboembolism
    D. tumor lysis syndrome
    E. all of the above

52. It is important to cover for Pseudomonas in a child presenting with neutropenic fever.
    A. true
    B. false

Answers: 43. A; 44. E; 45. E; 46. B; 47. D; 48. D; 49. C; 50. C; 51. E; 52. A

Pediatric Emergency Medicine Reports

CME Objectives

Upon completion of this educational activity, participants should be able to:

- recognize specific conditions in pediatric patients presenting to the emergency department;
- describe the epidemiology, etiology, pathophysiology, historical and examination findings associated with conditions in pediatric patients presenting to the emergency department;
- formulate a differential diagnosis and perform necessary diagnostic tests;
- apply up-to-date therapeutic techniques to address conditions discussed in the publication;
- discuss any discharge or follow-up instructions with patients.

CME Instructions

Physicians participate in this continuing medical education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge.

To clarify confusion surrounding any questions answered incorrectly, please consult the source material. After completing this activity, you must complete the evaluation form that will be provided at the end of the semester and return it in the reply envelope provided to receive a credit letter. When your evaluation is received, a credit letter will be mailed to you.

Pediatric Emergency Medicine Reports™ (ISSN 1082-3344) is published monthly by AHC Media, a division of Thompson Media Group LLC, 3525 Piedmont Road, N.E., Six Piedmont Center, Suite 400, Atlanta, GA 30305. Telephone: (800) 688-2421 or (404) 262-7436.

Vice President/Group Publisher: Donald R. Johnston
Executive Editor: Shelly Morrow Mark
Managing Editor: Leslie Hamlin

GST Registration No.: R128870672
Periodicals Postage Paid at Atlanta, GA 30304 and at additional mailing offices.

POSTMASTER: Send address changes to ***Pediatric Emergency Medicine Reports***, P.O. Box 105109, Atlanta, GA 30348.

Back issues: $65. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Subscriber Information

Customer Service: 1-800-688-2421

Customer Service E-Mail Address: customerservice@ahcmedia.com
Editorial E-Mail Address: shelly.mark@ahcmedia.com
World-Wide Web page: http://www.ahcmedia.com

Subscription Prices

1 year with 30 ACEP, AMA, or AAP Category 1 credits: $439;
1 year without credit: $389;
Add $17.95 for shipping & handling

Multiple copies:
Discounts are available for group subscriptions, multiple copies, site-licenses or electronic distribution. For pricing information, call Tria Kreutzer at 404-262-5482.
One to nine additional copies: **$350 each;**
10 or more additional copies: **$311 each.**
Resident's Rate: **$194.50**
All prices U.S. only. U.S. possessions and Canada, add $30 postage plus applicable GST.

Accreditation

AHC Media is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

AHC Media designates this educational activity for a maximum of 30 *AMA PRA Category 1 Credit(s)™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Approved by the American College of Emergency Physicians for 30 hours of ACEP Category 1 credit.

This continuing medical education activity has been reviewed by the American Academy of Pediatrics and is acceptable for up to 30 (2.5 per issue) AAP credits. These credits can be applied toward the AAP CME/CPD Award available to Fellows and Candidate Fellows of the American Academy of Pediatrics.
This CME activity is intended for emergency and pediatric physicians.

It is in effect for 36 months from the date of the publication.

This is an educational publication designed to present scientific information and opinion to health professionals, to stimulate thought, and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for use by the layman. Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. Clinical, legal, tax, and other comments are offered for general guidance only; professional counsel should be sought for specific situations.

AHC Media

Pediatric Emergency Medicine Reports

2011 Reader Survey

In an effort to learn more about the professionals who read *Pediatric Emergency Medicine Reports* (PEMR), we are conducting this reader survey. The results will be used to enhance the content and format of *PEMR*.

Instructions: Fill in the appropriate answers. Please write in answers to the open-ended questions in the space provided. Return the questionnaire in the enclosed postage-paid envelope by **July 1, 2011.**

1. Are the articles in *Pediatric Emergency Medicine Reports* written about issues of importance and concern to you?

- O A. Always
- O B. Most of the time
- O C. Some of the time
- O D. Rarely
- O E. Never

2. How would you describe your satisfaction with your subscription to *PEMR*?

- O A. Very satisfied
- O B. Somewhat satisfied
- O C. Somewhat dissatisfied
- O D. Very dissatisfied

Questions 3-14 ask about articles appearing in *Pediatric Emergency Medicine Reports*. Please mark your answers in the following manner:

A. very useful B. fairly useful C. not very useful D. not useful at all

3. Trauma Evaluation (June 2010)	O A	O B	O C	O D
4. Orthopedic Injuries Pt. 1 (July 2010)	O A	O B	O C	O D
5. Orthopedic Injuries Pt. 2 (Aug. 2010)	O A	O B	O C	O D
6. Traumatic Brain Injury (Sept. 2010)	O A	O B	O C	O D
7. Critical Child (Oct. 2010)	O A	O B	O C	O D
8. Streptococcal Syndromes (Nov. 2010)	O A	O B	O C	O D
9. Burn Management (Dec. 2010)	O A	O B	O C	O D
10. Fever in Infants < 3 Mos. (Jan. 2011)	O A	O B	O C	O D
11. Minor Head Trauma (Feb. 2011)	O A	O B	O C	O D
12. Whooping Cough (March 2011)	O A	O B	O C	O D
13. Neonatal Emergencies (April 2011)	O A	O B	O C	O D
14. Oncologic Emergencies (May 2011)	O A	O B	O C	O D

15. Do you plan to renew your subscription to *PEMR*? O A. yes O B. no

If no, why? _____

16. What is your title?

- O A. Practicing emergency medicine physician
- O B. Physician assistant
- O C. Professor/academician
- O D. Emergency medicine manager/director
- O E. Other _____

17. On average, how much time do you spend reading each issue of *PEMR*?

- O A. 21-30 minutes
- O B. 31-59 minutes
- O C. 1-2 hours
- O D. 2-3 hours
- O E. More than 3 hours

18. On average, how many people read your copy of *PEMR*?

- O A. 1
- O B. 2-3
- O C. 4-6
- O D. 7-9
- O E. 10 or more

19. How large is your hospital?

- O A. fewer than 100 beds
- O B. 100-200 beds
- O C. 201-300 beds
- O D. 301-500 beds
- O E. more than 500 beds

20. How would you rate the overall coverage of topics in *PEMR*?

- O A. very useful
- O B. fairly useful
- O C. not very useful
- O D. not useful at all

21. Would you be interested in earning continuing education credits with this publication?

- O A. Yes
- O B. No

Please rate your level of satisfaction with the following items.
A. excellent B. good C. fair D. poor

22. Quality of newsletter	○ A	○ B	○ C	○ D
23. Article selections	○ A	○ B	○ C	○ D
24. Timeliness	○ A	○ B	○ C	○ D
25. Quality of *Trauma Reports*	○ A	○ B	○ C	○ D
26. Length of newsletter	○ A	○ B	○ C	○ D
27. Overall value	○ A	○ B	○ C	○ D
28. Customer service	○ A	○ B	○ C	○ D

29. To which other publications or information sources about pediatric emergency medicine do you subscribe?

_____

_____

_____

30. Which publication or information source do you find most useful, and why? _____

_____

31. Please list the top three challenges you face in your job today.

_____

_____

_____

32. What do you like *most* about *Pediatric Emergency Medicine Reports*?

_____

_____

_____

33. What do you like *least* about *Pediatric Emergency Medicine Reports*?

_____

_____

_____

34. What specific topics would you like to see addressed in *Pediatric Emergency Medicine Reports*?

_____

_____

_____

35. Has reading *Pediatric Emergency Medicine Reports* changed your clinical practice? If yes, how? _____

_____

Contact information (optional): _____

_____

Exclusive to our subscribers

Rapid Access Management Guidelines

Pediatric Emergency Medicine Reports

The Practical Journal of Pediatric Emergency Medicine

Pediatric Oncologic Emergencies

Initial Supportive Therapy in the Setting of Hyperleukocytosis

- Hydration: D5 1/2 NS at 3000 mL/m^2/day. No supplemental potassium should be given. Consider alkalinized fluids if allopurinol is being used and patient is not hyperphosphatemic.
- Treatment of hyperuricemia
  - Allopurinol 300 mg/m^2 divided TID
  - Consider administration of rasburicase if patient is hyperuricemic and not G6PD deficient.
- Transfuse platelets if platelet count is < 25,000/μL.
- Correct other significant coagulopathies.
- Avoid transfusion of packed red blood cells if hemodynamically stable.

NOTE: Management of hyperuricemia and tumor lysis covered more thoroughly in tumor lysis section.

Critical Airway: Relative Contraindications to Anesthesia in a Child with a Mediastinal Mass

- Orthopnea
- Upper body edema
- Dyspnea
- Clinical findings of impending respiratory failure
- Tracheal cross-sectional area < 50% normal for age and sex
- Severe compression of one or both mainstem bronchi
- Peak expiratory flow rate of < 50% predicted (performed in sitting and supine position)

Laboratory Studies and Clinical Monitoring

- CBC, calcium, phosphate, magnesium, uric acid, urea nitrogen, creatinine, lactate dehydrogenase at presentation and then every 6-12 hours depending on risk
- Sequential vital signs
- Strict assessment of intake and output
- Body weight once to twice daily
- Cardiorespiratory monitor with multi-lead ECG as needed for hyperkalemia (e.g., if K > 6 mEq/L, look for wide QRS and peaked T waves)
- Close clinical evaluation for signs of hypocalcemia or renal failure

Differential Diagnosis of a Mediastinal Mass by Location Within the Mediastinum

Anterior

- Lymphoma
- Leukemia
- Malignant germ-cell tumor
- Benign teratoma
- Thymic lesion (thymic hyperplasia, thymoma, thymic cyst)
- Substernal thyroid

Middle

- Lymphoma
- Tuberculosis
- Histiocytosis
- Sarcoidosis
- Anomalies of the great vessels

Posterior

- Neuroblastoma
- Ganglioneuroblastoma
- Sarcoma

Signs and Symptoms of SVCS

- Facial swelling
- Upper body edema
- Cyanosis of the face or upper body
- Plethora
- Conjunctival edema or suffusion
- Headache
- Tachycardia
- Elevated venous pressure
- Vocal cord paralysis, hoarseness
- Dyspnea
- Cough
- Decreased mentation
- Horner's syndrome

Symptoms Suggestive of a Brain Tumor as the Etiology of Headache

- Occipital location of headache
- Worsening symptoms
- Awakens patient at night
- Associated with focal symptoms
- Emesis

Indications for Specific Antimicrobial Therapy in Addition to Broad-spectrum Antibiotic

Indication	Antimicrobial Therapy
Clinical sepsis	Broad-spectrum antibiotic + vancomycin + aminoglycoside
High-dose cytarabine chemotherapy or mucositis or cellulitis or concern for CVC infection	Broad-spectrum antibiotic + vancomycin
Pulmonary infiltrates	Broad-spectrum antibiotic + vancomycin + atypical antibacterial agent; if infiltrates are diffuse and hypoxia is present, consider treatment for PJP (PCP)
Abdominal symptoms	Broad-spectrum antibiotic + vancomycin + aminoglycoside + metronidazole or clindamycin
Perirectal lesions	Broad-spectrum antibiotic + vancomycin + metronidazole or clindamycin

Prevention and Treatment of TLS

Delay and/or titrate cytolytic therapy (if possible) until prophylactic measures can be implemented (see "hydration therapy," "urinary alkalinization," "hyperuricemia management" below). AVOID intravenous radiologic contrast agents that might precipitate renal failure.	
Hydration therapy	• Administer IV fluid: D5 0.2% NaCl + $NaHCO_3$ 40 mEq/L at 3000 mL/m^2/day • Urine output goal: ≥ 100 mL/m^2/hour OR 3 mL/kg/hour (if body weight is < 10 kg) • Urine specific gravity goal ≤ 1.010 • Diuretics may be required (furosemide or mannitol)
Urinary alkalinization (see IV fluid above)	• Urine pH goal 6.5-7.5 to aid in excretion of uric acid Note urine pH > 7.5 may increase precipitation of CaPO4 and xanthine crystals • Adjust amount of $NaHCO_3$ in IV fluid to achieve urine pH and serum [sodium] goals
Hyperkalemia	• Moderate and asymptomatic (≥ 6.0 mEql/L): sodium polystyrene sulfonate orally • Severe and/or symptomatic (> 7.0 mEq/L): –Calcium gluconate 100-200 mg/kg IV –D25 (2 mL/kg) IV + regular insulin 0.1 units/kg IV –Dialysis may be necessary
Hyperphosphatemia	• Aluminum hydroxide 50-150 mg/kg/day divided in 4–6 doses (or 30–40 mL 6 to 8 hours) • Dialysis or continuous renal replacement therapy may be necessary
Hyperuricemia (uric acid crystals form in renal tubules and distal collecting system and cause oliguria)	• Allopurinol 300 mg/m^2 PO divided TID: Decreases production of uric acid by inhibiting xanthine oxidase If possible, start 12-24 hours before induction of cytolytic therapy **OR** • Urate oxidase (rasburicase): Metabolizes uric acid Should be considered in high-risk situations; contraindicated in G6PD deficiency, pregnancy, and lactation

Frequently Chosen Antibiotics for Febrile Neutropenia

Coverage	Antibiotic
Broad spectrum	Ceftazidime; cefepime; piperacillin-tazobactam; meropenem
Additional Gram-negative coverage	Amikacin; gentamicin; tobramycin
Additional Gram-positive coverage	Vancomycin
Additional anaerobic coverage	Clindamycin; metronidazole
Atypical bacterial coverage	Azithromycin; clarithromycin

Supplement to *Pediatric Emergency Medicine Reports*, May 2011: "Pediatric Oncologic Emergencies."
Authors: Melissa R. Jefferson, MD, Assistant Professor of Pediatrics, Brody School of Medicine, East Carolina University, Greenville, NC; Beng Fuh, MD, PhD, Assistant Professor of Pediatrics, Brody School of Medicine, East Carolina University, Greenville, NC; and Ronald M. Perkin, MD, MA, Professor and Chairman, Department of Pediatrics, Brody School of Medicine, East Carolina University, Greenville, NC.