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Grade	**100.00** out of 100.00
Feedback	If you have satisfied the completion requirements for this assessment, you may proceed to claim your CME credit via the AAP Transcript tool.

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Question 1

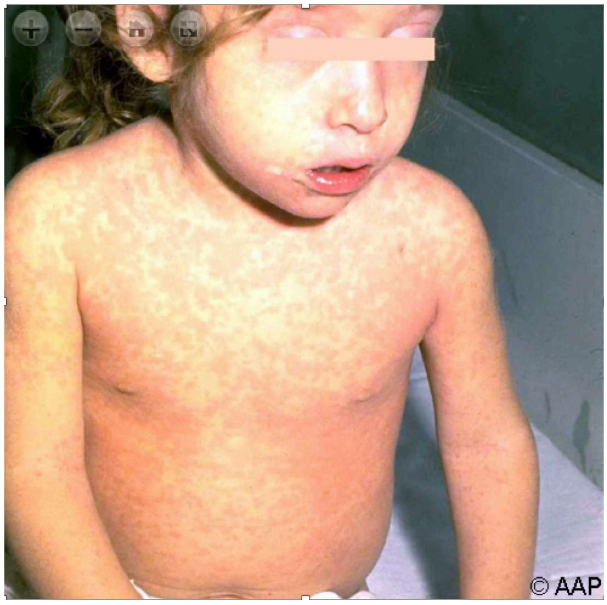
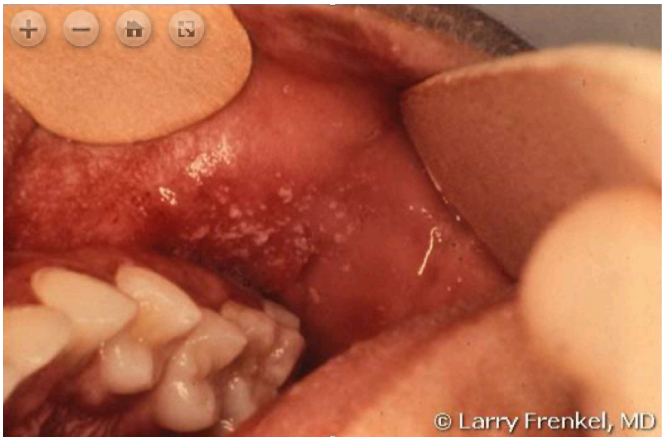
Correct

1.00 points out of 1.00

Comment

A previously healthy unvaccinated 5-year-old is evaluated in the emergency department for a 3-day history of high-spiking fever, cough, runny nose, and eye redness. The father reports that the child has been increasingly fussy and refusing to eat, and that their fever has persisted despite acetaminophen use. A new rash appeared this morning on the child's face.

On examination, the child appears ill. Vital signs reveal a temperature of 40.5 ℃, blood pressure of 95/55 mm Hg, heart rate of 165 beats/min, respiratory rate of 30 breaths/min, and oxygen saturation of 94% in room air. The child's eyes have conjunctival injections bilaterally, and they have a diffuse, blanching, erythematous, maculopapular rash on the face, trunk, and extremities (**Figure 1**). Oropharynx is tacky-dry with some white spots on the inner cheeks and a dry coated tongue (**Figure 2**). Lung auscultation reveals bilateral diffuse rales. He is admitted to the pediatric intensive care unit for further management.

Figure 1. Koplik spots of measles; small, white spots located on buccal mucosa.	Figure 2. Maculopapular rash associated with measles infection.
	
All images Reproduced with permission from American Academy of Pediatrics. Measles. In: Kimberlin DW, Banerjee R, Barnett ED, Lynfield R, Sawyer MH, eds. *Red Book: 2024-2027 Report of the Committee on Infectious Diseases*. 33nd ed. American Academy of Pediatrics; 2024.	

Of the following, the MOST appropriate isolation practice for this patient is

- A. airborne isolation ✓
- B. contact isolation

C. droplet isolation

D. protective isolation

Your answer is correct.

PREP Pearl(s)

- Airborne isolation is designed to prevent transmission of infectious agents that are very small and remain viable and suspended in the air for long distances.
- Airborne isolation includes placement in an airborne infection isolation room. In addition to negative pressure, airborne infection isolation rooms have a high air exchange rate.
- Personal protective equipment worn by practitioners observing airborne precautions should include respiratory protection in the form of an N-95 mask (or equivalent), eye protection, fluid resistant gown, and gloves.

Critique

The child in the vignette has an acute febrile illness with key findings that include fever, cough, coryza (runny nose and rhinorrhea), and conjunctivitis. These findings, along with a diffuse maculopapular rash involving the entire body (**Figure 1**), are highly suggestive of measles infection. In addition, patients may also have Koplik spots (small, white spots on buccal mucosa) (**Figure 2**). Measles is one of the most contagious infectious diseases and is spread by contact with infected secretions, including through small aerosolized respiratory droplets. The virus remains active and contagious in the air or on infected surfaces for up to 2 hours. As such, the preferred isolation for this patient is airborne isolation. The spread of the measles virus is complicated by the fact that it can be transmitted by an infected person from 4 days before the onset of the rash to 4 days after the rash erupts, so that patients may not realize they were exposed to the virus until symptoms begin.

Measles symptoms usually begin within 2 weeks after initial exposure. The early symptoms are often nonspecific, including fever, rhinorrhea, cough, and conjunctivitis. The presence of Koplik spots is highly suggestive of measles and may appear before the typical maculopapular rash, which usually erupts 7 to 14 days after initial exposure. The rash usually begins on the face and upper neck and then spreads downward in subsequent days to involve the trunk and extremities, including hands and feet. Complications of measles are most common in children younger than 5 years, especially those children who are malnourished or immunocompromised. Patients who are deficient in vitamin A are independently at risk for complications from measles. There is no specific treatment for measles, and experts agree that vaccination against measles is the most effective way to prevent measles. The current recommendation from the Centers for Disease Control and Prevention (CDC) is that all children should be vaccinated against measles.

Because of the high risk of transmission, patients suspected of having measles should immediately be isolated when hospitalized. The recommended isolation for a patient with measles is airborne isolation. Other conditions that require airborne isolation include tuberculosis, varicella, and anthrax. A complete list of infectious agents can be found on the CDC website. The goal of airborne isolation is to prevent transmission of infectious agents that are very small and remain viable suspended in the air for long distances. Best practices suggest that patients should be masked and placed in an airborne infection isolation room, a specific type of negative pressure room. In addition to negative pressure, airborne infection isolation rooms have a higher air exchange rate (6-12 per hour, 12 preferred) to further dilute and remove airborne contaminants and directly exhaust to the outside via a HEPA filter. Personal protective equipment worn by

practitioners who enter the room of a patient requiring airborne precautions should include, at minimum, respiratory protection in the form of an N-95 mask (or equivalent), eye protection, fluid-resistant gown, and gloves.

Contact precautions are used to contain diseases that are spread by direct contact with the patient or indirect contact with the patient environment. Personal protective equipment includes use of gowns and gloves at the room entry point, before contact with a patient or patient's environment. Some common organisms that would require contact precautions include methicillin-resistant *Staphylococcus aureus*, *Clostridium difficile*, and norovirus. Droplet isolation is designed to prevent transmission of infectious diseases spread by large respiratory droplets through coughing, sneezing, or even talking. A standard or surgical face mask is required, and standard precautions should be followed when handling items that may be contaminated with respiratory secretions. Examples of conditions requiring droplet precautions include seasonal influenza, pertussis, parainfluenza, and streptococcal pharyngitis. Protective isolation, or reverse isolation, is reserved for immunocompromised patients at increased risk of incidental exposure to infectious pathogens. The specific personal protective equipment required may vary depending on the patient's condition and the health care setting, but generally includes mask, gown, and gloves worn by the caregiver.

Suggested Reading(s)

- American Academy of Pediatrics. Measles. In: Kimberlin DW, Banerjee R, Barnett ED, Lynfield R, Sawyer MH, eds. *Red Book: 2024-2027 Report of the Committee on Infectious Diseases.* 33rd ed. American Academy of Pediatrics; 2024. Accessed December 1, 2025. Red Book Online
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Content Domain

- Infectious Disease, infection prevention and control

Learning Objectives

- Plan for the isolation of a patient with highly communicable disease

The correct answer is: airborne isolation

View Peer Results

Question 2

Correct

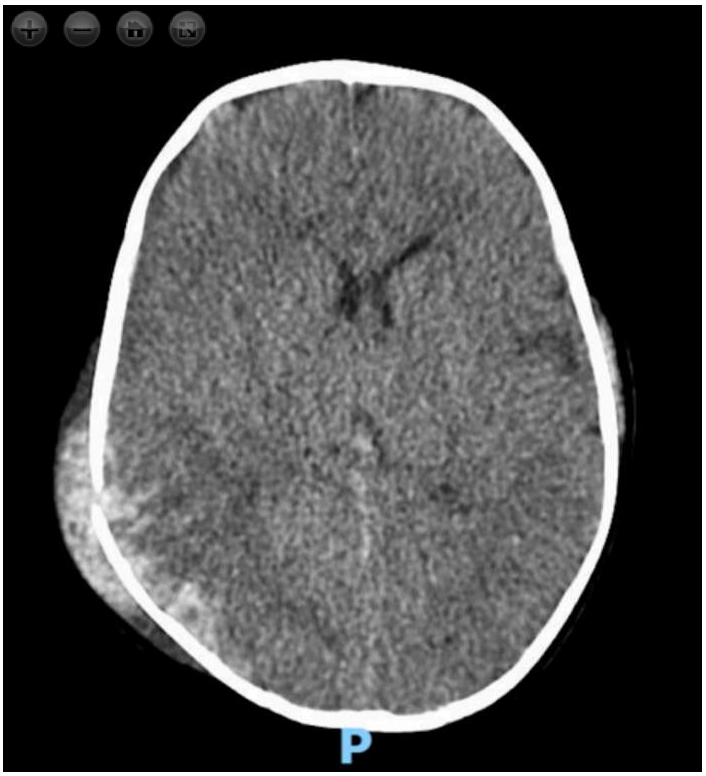
1.00 points out of 1.00

Comment

A 2-month-old infant's mother returns home to find him sleeping in the bassinet. She notices that he is making unusual breathing sounds and appears pale. She picks him up, but he is limp and unarousable.

Emergency medical services arrive and place him on a 100% nonrebreather mask. He does not open his eyes or cry on insertion of a peripheral intravenous catheter. His blood glucose level is 120 mg/dL (6.66 mmol/L). On arrival at the emergency department, his vital signs reveal a temperature of 37.4 °C, blood pressure of 156/84 mm Hg, heart rate of 138 beats/min, respiratory rate of 8 breaths/min, and oxygen saturation of 95%. The infant is intubated, and head computed tomography is performed (**Figure 1**).

Figure 1. Head computed tomogram of the patient in the vignette.



Courtesy of A. Au

Of the following, the MOST likely disorder associated with this patient's diagnosis is

A. bleeding disorder

B. inborn error of metabolism

C. retinal hemorrhage ✓

D. vitamin D deficiency

Your answer is correct.

PREP Pearl(s)

- Children with abusive head trauma have increased mortality and morbidity compared with those with unintentional traumatic brain injury.
- Children with abusive head trauma may present with vomiting, irritability, and/or increased head circumference.
- Apnea and seizures are frequently seen in patients presenting with abusive head trauma.

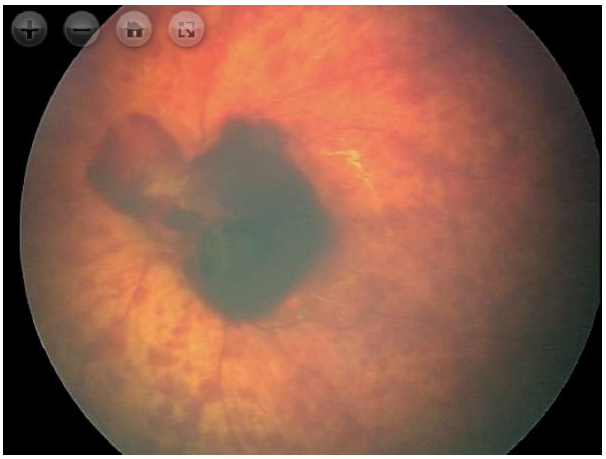
Critique

The infant in the vignette is suspected of having an abusive head trauma. Previously referred to as "shaken baby syndrome," this term was replaced with "abusive head trauma" by the American Academy of Pediatrics in 2009 to better encompass the varied mechanisms, including shaking and/or blunt injury, that cause head and spinal injuries.

Abusive head trauma is a subset of intentional trauma (child abuse and neglect) with high morbidity, which is seen generally in children younger than 4 years. Children with abusive head trauma have increased mortality and morbidity compared with those with unintentional traumatic brain injury. Children with abusive head trauma are often subject to delayed presentation and repeated injury. Apnea is associated with abusive head trauma, and seizures are seen in 28% to 50% of patients on presentation. Polytrauma can result in anemia, hypotension, and shock. Thus, patients with abusive head trauma are at significant risk for secondary brain injury due to hypoxia, hypotension, and seizures.

Abusive head trauma is more commonly seen in families with low socioeconomic status, young parental age, and domestic violence and in children with low birth weight, chronic illness, and congenital abnormalities. Children may present with vomiting, irritability, and/or increased head circumference. Clinical features of abusive head trauma may include the presence of retinal hemorrhage (**Figure 2**) and subdural hemorrhages. Retinal hemorrhages are seen in 85% or more of patients, occur bilaterally, are diffuse and tend to extend to the ora serrata, and involve all layers of the retina. Subdural hemorrhages are seen in more than 70% of patients and may be acute or chronic in nature.

Figure 2. Diffuse hemorrhagic retinopathy involving all retinal layers with hemorrhages extending to the ora serrata.



Courtesy of T. Nakagawa

Clinicians should suspect child abuse when the history does not match the injuries or the injury is not appropriate for the child's developmental age. Signs of minor abuse may be apparent before more severe injuries. These signs may include bruising, intraoral injuries, and fractures (acute or healing). Fractures with a strong association for child abuse include posteriomedial rib fractures and metaphyseal fractures of long bones. Several clinical prediction rules for abusive head trauma (eg, Predicting Abusive Head Trauma [PredAHT], Pittsburgh Infant Brain Injury Score [PIBIS], and Pediatric Brain Injury Network [PedBIRN-4]) have been developed to aid in the recognition of abusive head trauma. These prediction rules include variables such as presence of bruising, large head circumference, and anemia to determine sensitivities and specificities for intracranial trauma. Clinicians must report suspected or known child abuse.

In this vignette, the child has apparently incurred abusive head trauma, which is associated with apnea, seizure, and retinal hemorrhages. A bleeding disorder could be associated with abusive head trauma, but bleeding disorders will have continued abnormal coagulation studies vs coagulation from release of tissue thromboplastin. Vitamin D deficiency can lead to rickets with deficient mineralization of the bone matrix, which results in bowing of the long bones, frontal bossing, and enlargement of the costochondral junction (rachitic rosary). Inborn errors of metabolism, such as glutaric acidemia type 1, can be mistaken for child abuse. Glutaric acidemia type 1 typically presents in children with hyperammonemia, metabolic acidosis, hypoglycemia, and encephalopathy but can also present with acute or chronic subdural effusions, which are believed to occur from stretching of bridging veins from cerebral atrophy.

Suggested Reading(s)

- DiScala C, Sege R, Reece RM. Child abuse and unintentional injuries: a 10-year retrospective. *Arch Pediatr Adolesc Med.* 2000;154(1):16-22. doi:10-1001/pubs.PediatrAdolescMed.-ISSN-1072
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Content Domain

- Emergency medicine, injuries

Learning Objectives

- Review the clinical features of abusive head trauma

The correct answer is: retinal hemorrhage

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Question 3

Correct

1.00 points out of 1.00

Comment

A 9-month-old child with biliary atresia who had a previous Kasai procedure undergoes a living donor liver transplantation. On postoperative day 6, the child develops a fever. The child is hemodynamically stable, extubated, and awake and interactive.

Laboratory data are shown:

Test	Preoperative	Postoperative day 1	Postoperative day 3	Postoperative day 7
Aspartate aminotransferase	400 U/L	350 U/L	150 U/L	500 U/L
Alanine aminotransferase	450 U/L	400 U/L	120 U/L	650 U/L
Bilirubin	24 mg/dL (410.50 µmol/L)	16 mg/dL (273.66 µmol/L)	8 mg/dL (136.83 µmol/L)	16 mg/dL (273.66 µmol/L)
International normalized ratio	2.0	1.8	1.5	2.0
White blood cells	8,000/µL (8×10^9/L)	10,000/µL (10×10^9/L)	8,000/µL (8×10^9/L)	11,000/µL (11×10^9/L)
Platelets	107×10^3/µL (107×10^9/L)	70×10^3/µL (70×10^9/L)	101×10^3/µL (101×10^9/L)	80×10^3/µL (80×10^9/L)

Doppler ultrasonography of the liver shows a decreased hepatic artery resistive index, with normal portal vein and hepatic vein resistive indices.

Of the following, the BEST next step in management is

- A. percutaneous liver biopsy
- B. percutaneous transhepatic cholangiography with external drainage
- C. relist for transplantation
- D. revascularization of the hepatic artery ✓

Your answer is correct.

PREP Pearl(s)

- Early complications after liver transplantation include vascular, biliary, and infectious complications, primary graft nonfunction, and rejection.
- Vascular complications include stenosis or thrombosis of the hepatic artery portal vein or hepatic vein. Routine postoperative bedside Doppler ultrasonography should be performed frequently for early detection of vascular complications.
- Vascular thrombosis is the leading cause of graft loss requiring retransplantation; hepatic artery thrombosis accounts for most vascular thromboses.
- Hepatic artery thrombosis may be asymptomatic or present with acute necrosis and primary graft failure or with biliary complications, such as bile leak, biliary stricture, or infection secondary to ischemic cholangiopathy.
- Urgent revascularization or surgical or radiologic intervention is indicated when hepatic artery thrombosis occurs in the first 10 days after transplantation.

Critique

Liver transplantation is a standard option for advanced liver failure and certain inherited metabolic defects. Advances in surgical techniques, graft perfusion, perioperative care, and immunosuppression have resulted in excellent graft function and short- and long-term patient survival. Early complications include primary graft nonfunction, vascular complications, biliary complications, rejection, and infections.

Primary graft nonfunction results from ischemia-reperfusion injury of the transplanted liver. It manifests as acute liver failure with coagulopathy, hemodynamic instability, encephalopathy, increase in liver enzyme levels, and multiorgan failure within 7 days of transplantation. Risk factors include prolonged ischemia time, older donor, and steatosis in the graft. Patients who develop primary graft nonfunction should be listed for retransplantation.

Vascular complications are more common in children than in adults and include thrombosis, stenosis, or aneurysm of the hepatic artery, portal vein, and hepatic vein. Vascular thrombosis is the leading cause of graft loss requiring retransplantation; hepatic artery thrombosis accounts for most vascular thromboses. Most centers use protocols that include twice-daily or daily Doppler ultrasonography in the first week after transplantation for early detection of vascular complications. Doppler ultrasonography also provides information on biliary complications, hematomas, and other fluid collections. Hepatic artery thrombosis can be asymptomatic or result in graft ischemia and failure that increases the risk of ischemic cholangiopathy, leading to bile leaks, strictures, or infection. Hepatic artery inflow compromise should be suspected when Doppler ultrasonography shows low resistive indices. Early hepatic thrombosis, within the first 10 days after transplantation, requires urgent revascularization, either surgical (thrombectomy and reanastomosis) or endovascular (intra-arterial thrombolysis, percutaneous transarterial angioplasty, and stent placement). Urgent retransplantation may be needed for graft failure. Hepatic artery thrombosis or stenosis that develops later may not require intervention due to development of collateral circulation that maintains arterial inflow. Some centers routinely start anticoagulation or antiplatelet agents postoperatively to prevent hepatic artery thrombosis. Portal vein thrombosis is less common. Early portal vein thrombosis may present with mild to severe graft dysfunction, persistent ascites, enteric congestion, and bleeding. Doppler ultrasonography usually confirms the diagnosis. Surgical thrombectomy or percutaneous intervention is indicated. Hepatic vein outflow obstruction has an insidious presentation, making the diagnosis challenging. The classic presentation of Budd-Chiari syndrome is rarely seen. Treatment is usually balloon angioplasty and rarely surgery.

Bile leaks or strictures present as jaundice or cholestatic liver injury rather than liver failure. In the early postoperative period, bile leaks are evident by the appearance of bile in the abdominal drains placed during surgery. They are more common in living donor liver transplantations. Ultrasonography or computed tomography may show ductal dilation or bile collection. The leak may resolve spontaneously or require percutaneous biliary intervention, including percutaneous transhepatic cholangiography with external drainage or surgical repair.

Acute cellular rejection rarely presents within days of a liver transplantation. Symptoms are nonspecific and include fever, fatigue, abdominal pain, and increase in levels of transaminases. Antibody-mediated rejection is also rare and presents with fever, acute liver dysfunction, and thrombocytopenia, usually in the first 2 posttransplantation weeks. Diagnosis is confirmed by liver biopsy.

High levels of immunosuppression, ascites, and presence of invasive devices predisposes patients to infectious complications in the early period after liver transplantation, primarily due to bacteria and less frequently *Candida* species. Viral infections are more common after the first month.

Frequent clinical assessment, monitoring of liver function, and Doppler ultrasonography are recommended for early detection of complications. Liver function, monitored by international normalized ratio and factor V or VII and ammonia, improves within a few days of transplantation. Levels of transaminases are generally elevated immediately after transplantation and decrease within a few days but may take a few weeks to return to normal. An increase or plateau in liver function and enzymes suggests vascular complications, primary graft nonfunction, or rejection. Other causes include infection, including sepsis, cardiac dysfunction, or drug toxicity. An increase or plateau in bilirubin and γ-glutamyltransferase levels, suggesting cholestasis, is concerning for biliary leak, vascular complications, infection, rejection, or drug toxicity. Elevation of transaminase levels, international normalized ratio, bilirubin levels, and lactate levels as well as acidosis and clinical signs of hemodynamic instability and encephalopathy suggest primary graft nonfunction. Fever, reduction in platelet count, increase in transaminases, biliary leak or infection, and liver dysfunction should lead to a suspicion of hepatic artery thrombosis. Persistent ascites should lead to exclusion of post-hepatic venous outflow obstruction and portal vein thrombosis.

In this vignette, the child has fever, elevated levels of transaminases, an elevated international normalized ratio, elevated bilirubin levels, increased white blood cell count, and decreased platelet count, which is suggestive of, though not specific to, hepatic artery thrombosis. Doppler ultrasonography shows a decrease in the hepatic artery resistive index, which further supports this diagnosis. Definitive management of early hepatic artery thrombosis is revascularization.

Suggested Reading(s)

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Content Domain

- Critical Care, Liver Failure

Learning Objectives

- Recognize and treat complications of liver transplantation

The correct answer is: revascularization of the hepatic artery

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Question 4

Correct

1.00 points out of 1.00

Comment

An 8-year-old child with a history of well-controlled focal seizures on low-dose monotherapy with levetiracetam experiences an atypical seizure episode. During a family gathering, the child suddenly ceases activity and stares blankly, exhibiting subtle right-hand automatisms that progress to bilateral, forceful, clonic movements of the limbs. The child is brought into the emergency department with ongoing generalized tonic-clonic movements, and a first line agent is administered that successfully terminates seizure activity.

Of the following, the mechanism by which this agent exerts its effect is

- A. γ-aminobutyric acid neurotransmission enhancement ✓
- B. N-methyl-D-aspartate receptor inhibition
- C. synaptic neurotransmitter release modulation
- D. voltage-gated sodium channel blockade

Your answer is correct.

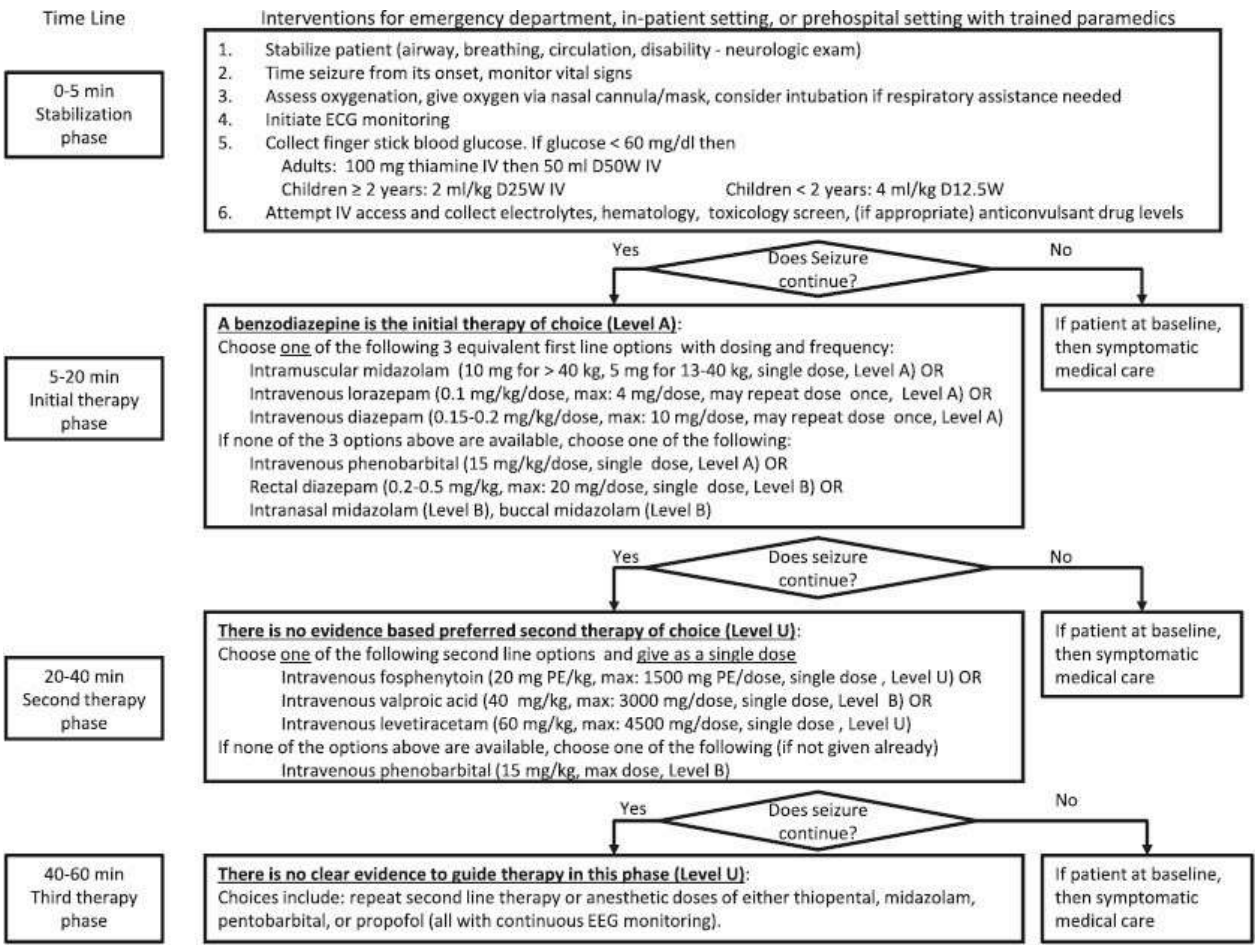
PREP Pearl(s)

- Prompt administration of benzodiazepines is critical in the management of first-time seizures that progress to generalized tonic-clonic activity to halt the seizure and prevent further neurological complications.
- Benzodiazepines are a first-line treatment in the emergency management of seizures due to their mechanism of enhancing GABAnergic inhibition, which increases chloride conductance and hyperpolarizes the neuron, thereby lowering the action potential.

Critique

Early identification and treatment are crucial in pediatric status epilepticus to prevent seizure progression and potential neurological sequelae. While status epilepticus in children has fewer sequelae than in adults, it has a mortality rate of up to 3% to 5%, with 25% of affected children developing subsequent epilepsy. The American Epilepsy Society (AES) now provides an evidence-based treatment algorithm for managing convulsive status epilepticus in both children and adults (**Figure**). The AES analyzed the efficacy, tolerability, and safety of anticonvulsant treatments based on a structured literature review. Key findings note the use of intravenous lorazepam and diazepam are established as efficacious first-line agents, with rectal diazepam and intramuscular, intranasal, or buccal midazolam also being effective as first-line agents.

Figure. Proposed treatment algorithm for status epilepticus.



Disclaimer: This clinical algorithm/guideline is designed to assist clinicians by providing an analytical framework for evaluating and treating patients with status epilepticus. It is not intended to establish a community standard of care, replace a clinician's medical judgment, or establish a protocol for all patients. The clinical conditions contemplated by this algorithm/guideline will not fit or work with all patients. Approaches not covered in this algorithm/guideline may be appropriate.

Reprinted with permission from Glauser T, Shinnar S, Gloss D, et al. Evidence-based guideline: treatment of convulsive status epilepticus in children and adults: report of the guideline committee of the American Epilepsy Society. *Epilepsy Curr*. 2016;16(1):58.

In this vignette, given the acute setting of a prolonged seizure that has transitioned from focal to generalized tonic-clonic activity, the immediate administration of lorazepam, a benzodiazepine, is the most appropriate intervention. Lorazepam and other benzodiazepines act as potent positive allosteric modulators of the γ-aminobutyric acid (GABA)-a receptor, enhancing the inhibitory effect of GABA and leading to increased chloride ion influx.

Gamma-aminobutyric acid is an amino acid that serves as the primary inhibitory neurotransmitter in the brain and a major inhibitory neurotransmitter in the spinal cord. In the synapse, it binds to postsynaptic GABA receptors, enhancing chloride ion influx and inhibiting neuronal activity by hyperpolarizing cells, ultimately suppressing action potential transmission. Benzodiazepines function as potent positive allosteric modulators of the GABA-a receptor. These agents bind to a specific site on the receptor, distinct from the site where GABA binds, known as the allosteric site. By acting as positive allosteric modulators, benzodiazepines increase the affinity of the GABA-a receptor for GABA, leading to enhanced chloride ion influx on GABA

binding. When binding to the GABA-a receptor, neuronal chloride channels open, thereby increasing intracellular chloride concentrations. This influx of chloride ions hyperpolarizes the neuron, further lowering the action potential, resulting in reducing neuronal excitability. This produces an inhibitory effect on neuronal activity manifesting clinically as sedation, anxiolysis, muscle relaxation, and antiepileptic effect.

In the acute setting, the primary management goal in status epilepticus is twofold: to promptly terminate ongoing seizure activity and to prevent its recurrence. Thus, the timely administration of a benzodiazepine, notably intravenous lorazepam or midazolam, represents the essential first initial step, as delayed intervention may exacerbate neuronal excitotoxicity and precipitate further neurologic compromise.

In cases of seizures refractory to first-line therapy, escalation to second-line agents becomes imperative. The selection of such agents is predicated on their efficacy in halting seizure activity while minimizing the risk of adverse effects. Intravenous antiepileptic drugs, such as fosphenytoin, valproic acid, or levetiracetam may be considered. Importantly, the decision to escalate therapy should be guided by clinical judgment, with careful consideration of the patient's underlying medical comorbidities and potential drug interactions.

Blocking of voltage-gated sodium channels is incorrect, because blocking voltage-gated sodium channels to reduce neuronal excitability is the mechanism of action of agents such as phenytoin, fosphenytoin, or carbamazepine, which are often used as second-line agents in status epilepticus, and for longer-term seizure management, but are not the first-line treatment in acute status epilepticus. Sodium channel blockers reduce repetitive neuronal firing but are typically second-line options after benzodiazepines. Enhancement of GABAnergic neurotransmission reflects the mechanism of action of levetiracetam; it is thought that levetiracetam works through binding at synaptic vesicle protein 2A (SV2A), down-regulating neurotransmitter release from these vesicles. This agent's unique mechanism of action, in addition to its favorable site-effect profile, make it a popular option for long-term seizure control. Inhibiting N-methyl-D-aspartate (NDMA) receptors is reflective of the mechanism of ketamine. Blocking NMDA receptors can help reduce excitatory activity in the brain, but this mechanism is not typically targeted in initial treatment of status epilepticus; ketamine may be used, however, in refractory status epilepticus.

Suggested Reading(s)

- Glauser T, Shinnar S, Gloss D, et al. Evidence-based guideline: treatment of convulsive status epilepticus in children and adults: report of the guideline committee of the American Epilepsy Society. *Epilepsy Curr*. 2016;16(1):48-61. doi:10.5698/1535-7597-16.1.48
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Content Domain

- Pharmacology, Anti-seizure Drugs

Learning Objectives

- Understand the mechanism of action of benzodiazepines
- Recognize that benzodiazepines are first-line anti-epileptic drugs (AED)

The correct answer is: γ-aminobutyric acid neurotransmission enhancement

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Question 5

Correct

1.00 points out of 1.00

Comment

An 18-month-old infant was submerged in a backyard pool. After being pulseless and apneic when she was pulled out of the water, she is provided bystander cardiopulmonary resuscitation (CPR). She is intubated by emergency medical services, and CPR is continued en route. Return of spontaneous circulation is achieved at 18 minutes after 3 doses of epinephrine and 2 doses of atropine for pulseless electrical activity. She is transferred to the pediatric intensive care unit for ongoing supportive care. A central line is placed, and she is given fentanyl, 1 µg/kg, for possible pain with the procedure. The ventilator settings are: tidal volume, 6 mL/kg; positive end expiratory pressure, 7 mm Hg; respiratory rate, 24 breaths/min; and fraction of inspired oxygen, 50%.

Arterial blood gas test results are shown:

Laboratory Test	Result
pH	7.28
Pco_2	45 mm Hg
Po_2	95 mm Hg
Bicarbonate	20 mEq/L (20 mmol/L)

Four hours after arrival at the pediatric intensive care unit, she does not react to painful stimuli, and she is not breathing over the ventilator. The nurse states that the infant's pupils are 5 mm, and he does not see any change when he shines a flashlight in her eyes.

Of the following, the BEST next step in determining possible pupillary response in this infant is

A. give naloxone to reverse the effect of fentanyl

B. obtain quantitative pupillometry ✓

C. provide 100% fraction of inspired oxygen via the ventilator

D. wait 8 hours after administration of systemic atropine

Your answer is correct.

PREP Pearl(s)

- Multiple medications cause mydriasis or meiosis of the pupils, but none completely abolish the pupillary light reflex in normal doses administered to pediatric intensive care patients.
- Bedside testing of the pupillary light reflex has poor interrater reliability.

- Using quantitative pupillometry improves reliability in assessing the pupillary light reflex and may have a role in neurologic prognostication.

Critique

The infant in the vignette has likely incurred a severe hypoxic ischemic brain injury and received medications that might confound a pupillary examination. Pupil size is the result of the balance in tone between the dilator pupillae and sphincter pupillae (ie, constrictor) muscles of the iris of the eye. The dilator pupillae is under sympathetic nerve fiber control, whereas the sphincter pupillae constricts due to parasympathetic stimulation. Pupil size is most affected by light stimuli (ie, presence or absence of light). However, the pupil size is also affected by emotional state or anxiety, medications, and intraocular pressure. The pupillary light reflex (PLR) describes the response when light hits the retina and sends a signal (via the optic nerve or cranial nerve II) to the Edinger-Westphal nucleus in the posterior midbrain, which, via cranial nerve III (or the oculomotor nerve), results in pupillary constriction. There are left and right Edinger-Westphal nuclei in the midbrain; when activated, each is responsible for the ipsilateral pupillary constriction. In addition to the direct response, the consensual pupillary response occurs in the contralateral eye. In dim light or darkness, the dilator pupillae muscles contract and cause the pupil size to widen as a result of postganglionic sympathetic fiber innervation by the long ciliary nerve.

Multiple medications can affect pupil size. Systemic atropine, because of its anticholinergic effects, induces mydriasis by inhibiting the contraction of the pupillary sphincter muscle. This process results in the contraction of the dilator pupillae muscle and pupil dilation. However, studies have shown that in doses given for pre-intubation, as well as for bradycardia or resuscitation, pupils dilate but remain reactive to light. Therefore, in this vignette, waiting 8 hours after administration of systemic atropine would not be the best next step for determining possible pupillary response.

The PLR can be assessed despite 2 doses of systemic atropine; however, topical atropine ophthalmic drops can last longer than systemic atropine. Likewise, epinephrine given for resuscitation would not cause pupillary dilation at this point due to its short half-life and inability to abolish the PLR. Opioid medications cause miosis (pupillary constriction). However, 1 dose of fentanyl 4 hours before examination is unlikely to affect current pupil size. In addition, opioids do not abolish the PLR at normally prescribed doses. If naloxone is given, it is unlikely to change pupil size; thus, giving naloxone to reverse the effect of fentanyl would not be the best next step. Patients with severe opioid overdose may have pupillary dilation in the setting of significant hypercarbia and hypoxia. In this case, the usual pupillary constriction from opioids may be overcome via sympathetic activation (stress response). However, this patient does not have opioid overdose, making the administration of 100% fraction of inspired oxygen unnecessary.

Obtaining quantitative pupillometry is correct in this case. Although it remains a useful bedside test, checking the pupil reactivity with a flashlight or penlight is often unreliable and subjective. Multiple studies have demonstrated poor reliability of using a simple light source to check pupil size and reactivity. Quantitative pupillometry was first introduced in 1956, and the technique was modernized with the invention of handheld infrared scanners. Current pupillometers deliver a flash of light and capture multiple images of the pupil in a short period, making multiple measurements to assess pupil size, symmetry, and reactivity. In the last decade, quantitative handheld pupillometry has become standard of care in many intensive care units worldwide. Although the machines are expensive, large randomized controlled trials have demonstrated its superiority over traditional testing. In addition, a recent multicenter, prospective, observational cohort study suggests that there may be a role in quantitative pupillometry in neurologic prognostication in patients with acute brain injury (Oddo 2023).

Clinicians may need to be aware that the manufacturer states quantitative pupillometry may be less accurate in children < 6 months of age because of their smaller pupil size.

Suggested Reading(s)

- Achamallah N, Fried J, Love R, Matusov Y, Sharma R. Pupillary light reflex is not abolished by epinephrine and atropine given during advanced cardiac life support in patients who achieve return of spontaneous circulation. *J Intensive Care Med.* 2021;36(4):459-465. doi:10.1177/0885066620906802
- Couret D, Boumaza D, Grisotto C, et al. Reliability of standard pupillometry practice in neurocritical care: an observational, double-blinded study. *Crit Care*. 2016;20:99. doi:10.1186/s13054-016-1239-z
- Oddo M, Taccone FS, Petrosino M, et al; ORANGE study investigators. The Neurological Pupil Index for Outcome Prognostication in People With Acute Brain Injury (ORANGE): a prospective, observational, multicentre cohort study. *Lancet Neurol*. 2023;22(10):925-933. doi:10.1016/S1474-4422(23)00271-5

Content Domain

- Neurology, neurologic complications of serious disease

Learning Objectives

- Describe ways of determining the pupillary light reflex
- Understand the physiologic mechanism of the pupillary light reflex

The correct answer is: obtain quantitative pupillometry

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Question 6

Correct

1.00 points out of 1.00

Comment

A 13-year-old adolescent is admitted to the intensive care unit for treatment of hypertension. He is receiving a nicardipine infusion currently running at 1 µg/kg/min. He is currently awake and alert with no neurologic deficits. He states that initially he had a headache, which is now improving. Vital signs reveal a blood pressure of 180/95 mm Hg and a heart rate of 165 beats/min. He reports frequent episodes of intermittent headaches accompanied by sweating, nausea, flushing, and feeling "like his heart is going to jump out of his chest." His parents report that he has been doing well in school but has had difficulty sitting still. His teacher recently suggested getting an evaluation for attention-deficit/hyperactivity disorder.

Laboratory data are shown:

Laboratory Test	Result
Sodium	140 mEq/L (140 mmol/L)
Potassium	4.4 mEq/L (4.4 mmol/L)
Chloride	105 mEq/L (105 mmol/L)
Carbon dioxide	24 mEq/L (24 mmol/L)
Urea nitrogen	30 mg/dL (10.71 mmol/L)
Creatinine	0.72 mg/dL (63.65 µmol/L)
Glucose	100 mg/dL (5.55 mmol/L)
Calcium	8.6 mg/dL (2.13 mmol/L)
Phosphorous	3.8 mg/dL (1.23 mmol/L)
Magnesium	2.6 mg/dL (1.07 mmol/L)

Of the following, the MOST useful diagnostic test for determination of the cause of this patient's hypertension is

- A. computed tomography of the brain
- B. renal ultrasonography
- C. thyroid-stimulating hormone measurement
- D. urine collection for fractionated metanephrine ✓

Your answer is correct.

PREP Pearl(s)

- Paroxysmal hypertension, tachycardia, and diaphoresis can be suggestive of a pheochromocytoma.
- Children with hypertension and attention-deficit/hyperactivity disorder should be evaluated for a possible pheochromocytoma.
- Treatment of pheochromocytoma starts with α-adrenergic blockade prior to initiation of β-blockade.

Critique

The young adolescent in this vignette has signs and symptoms consistent with a catecholamine secreting tumor described as a pheochromocytoma or paraganglioma. Pheochromocytomas arise from the chromaffin cells of the adrenal medulla. Paragangliomas are tumors that have an extra-adrenal origin and come from the paraganglia of the autonomic nervous system. Approximately 80% of these catecholamine-secreting tumors are pheochromocytomas, and 20% are the extra-adrenal paragangliomas. These tumors are rare in both children and adults, with an incidence rate estimated at 0.3 cases per million per year, with approximately 20% of cases diagnosed in children. They account for approximately 1.7% of pediatric cases of hypertension.

The clinical signs and symptoms are related to the hypersecretion of norepinephrine, epinephrine, and dopamine by the tumor. The most common presenting symptoms are paroxysmal or sustained hypertension, episodic sweating, and tachycardia or palpitations. Headache is common as well. The classic described triad of episodic headache, sweating, and tachycardia occurring at the same time is rare and not typically seen in children. Other symptoms that occur include panic attacks, orthostatic hypotension, and symptoms associated with an intra-abdominal tumor, such as constipation. Attention-deficit/hyperactivity disorder (ADHD) is more common in children with pheochromocytoma than in the general population, and children with known hypertension and ADHD symptoms should have an evaluation for catecholamine-secreting tumors before taking stimulant medications.

Compared with adults, catecholamine-secreting tumors in children are more likely to have a familial origin and can be malignant. Approximately 80% of the pediatric cases have a familial origin and can be associated with multiple endocrine neoplasia type 2, von Hippel–Lindau disease, or neurofibromatosis type 1. Genetic testing and evaluation are therefore appropriate for any child diagnosed with these types of tumors. Approximately 50% of these tumors diagnosed in children are malignant, with metastatic disease present at the time of the initial diagnosis or becoming apparent years later. Therefore, children diagnosed with catecholamine-secreting tumors require surveillance for metastatic disease throughout their lifetime.

The diagnosis of these tumors is generally made through clinical history and presenting symptoms or as part of a routine workup in patients with a known family history. The diagnosis is confirmed by biochemical testing using a 24-hour urine collection measuring fractionated metanephrines and catecholamines. The diagnosis can also be made by measuring plasma fractionated metanephrines; however, this test has a high false-positive rate and is reserved for patients who are unable to perform the more accurate 24-hour urine collection. Furthermore, measuring the fractionated catecholamines, such as epinephrine and norepinephrine, directly from the plasma is generally not useful, specifically in children, because there is also a significant high false-positive rate. Once the diagnosis is confirmed, further workup to localize the tumor is indicated using computed tomography or magnetic resonance imaging. If the tumor is not localized with these modalities, further imaging with positron emission tomography would be appropriate.

Surgical excision of the tumor is the appropriate treatment for these patients. Preoperative normalization of the blood pressure and resolution of symptoms decrease complications from surgical excision. It is therefore important that these patients be medically optimized before the surgery. A common approach to treatment in these patients is the use of α-adrenergic blockade started approximately 1 to 2 weeks before surgery to slowly lower the blood pressure to the normal range before the surgery. β-Adrenergic blockade is then added a few days preoperatively to help control tachycardia. The β-adrenergic blockade should not be started before the α-adrenergic blockade because the blockade of the peripheral vasodilatory β-adrenergic receptors with an unopposed α-adrenergic receptor stimulation from the increased endogenous catecholamines secreted by the tumor can lead to worsening hypertension.

Although renal ultrasonography may be useful in the workup and evaluation of a patient with hypertension, it would not demonstrate the cause of the hypertension in this vignette. Measurement of serum thyroid-stimulating hormone is unlikely to be helpful, given there are no other described symptoms suggestive of hyperthyroidism, such as exophthalmos or weight loss. Given that this patient does not have signs of elevated intracranial pressure or symptoms suggestive of an intracranial tumor, head computed tomography will not be helpful.

Suggested Reading(s)

- Bholah R, Bunchman TE. Review of pediatric pheochromocytoma and paraganglioma. *Front Pediatr.* 2017;5:155. doi:10.3389/fped.2017.00155
- Kuo MJM, Nazari MA, Jha A, Pacak K. Pediatric metastatic pheochromocytoma and paraganglioma: clinical presentation and diagnosis, genetic, and therapeutic approaches. *Front Endocrinol.* 2022;13:936178. doi:10.3389/fendo.2022.936178
- Nolting S, Bechmann N, Taieb D, et al. Personalized management of pheochromocytoma and paraganglioma. *Endocr Rev*. 2022;43(2):199-239. doi:10.1210/endrev/bnab019

Content Domain

- Cardiology, Hypertension

Learning Objectives

- Recognize the signs and symptoms of a pheochromocytoma

The correct answer is: urine collection for fractionated metanephrine

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