

Fever

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Core Concepts

In order to master this topic area, students must understand:

Age factors:	Clinical presentation and risk of infection vary by age.
Diagnostic evaluation:	There is a need to prioritize laboratory studies based on the age and clinical situation.
Shock:	Clinical presentation and risk of shock vary by age.
Therapy choice:	Empiric antibiotic therapy is based on most likely organism(s).
Therapy risks:	Benefits of empiric therapy must be weighed against the risks.

Learning Objectives

Students will demonstrate their conceptual mastery by:

- CASE 1:** Analyzing the risks of more than one site of infection in a febrile neonate (*clinical practice*)
- CASE 2:** Developing an appropriate plan for evaluating febrile children of different ages (*clinical practice; communication*)
- CASE 3:** Evaluating the risk/benefit ratio of different antibiotics in clinical situations (*basic science; clinical practice*)
- CASE 4:** Prioritizing steps in the evaluation and management of a febrile child. (*clinical practice*)

Advance Preparation Assignments

- CLIPP Case 10
- CLIPP Case 17
- CLIPP Case 23

Readiness Assurance Questions

1. A four-month-old, previously healthy girl is brought to the physician for 24 hours of fever and fussiness. She has no other reported symptoms, and her mother has not seen any rashes. She is up to date with her immunizations and is scheduled to receive her 4-month-old vaccines in a few days. Her temperature is 39.4 C, respiratory rate is 45 bpm, and heart rate is 150 bpm. She is awake and alert, and interactive. The rest of the physical exam is unremarkable and shows no obvious source of infection. On evaluation, a urinalysis is normal. Her white blood cell count is 15,500 with 80% polymorphonuclear leukocytes, 5% bands, and 15% lymphocytes. As part of her evaluation, a blood culture is obtained. Within 24 hours, the blood culture is reported to be positive, gram stain pending. Which of the following bacteria is most likely to have caused her bacteremia?

- A. *Escherichia coli*
- B. Group B hemolytic streptococcus
- C. *Listeria monocytogenes*
- D. *Neisseria meningitides*
- E. *Streptococcus pneumoniae*

Answer: E

Discussion: This is a case of occult bacteremia, and is a typical presentation for Streptococcus pneumoniae. Even if she had been fully immunized, this would be the most likely organism since the current vaccines do not cover all serotypes. Bacteremia with Group B strep, E. coli, and Listeria are uncommon beyond about 2 months of age. A patient with meningococcus would look much sicker than is described here.

2. A 7-month-old girl is brought to the physician for three days of fever without cough, congestion, or a rash. She has been irritable but consolable, and continues to eat well with no emesis or diarrhea. Temperature is 38.0 C, respiratory rate 35 bpm, heart rate 140 bpm. Physical examination shows an alert and consolable infant who prefers to be held by her mother, and no obvious source for the fever. Which of the following is the most appropriate next step in management?

- A. Admit for observation
- B. Blood culture
- C. Catheterized urine for urinalysis and culture
- D. CT scan of the head
- E. Lumbar puncture

Answer: C

Discussion: While the most common identifiable cause of a fever in this age group is a viral infection, it is important not to miss a urinary tract infection. There may be no symptoms in this age group other than a fever, and a fever can be present with cystitis or pyelonephritis. Therefore, it is important to look for a urinary tract infection.

A 7-month-old with a fever without source usually does not require admission for observation, and the description of this child is reassuring. Prior to the Hib and pneumococcal vaccines, this was a classic age group for occult bacteremia, with a sufficiently high yield on blood culture to justify getting a blood culture. Today, contamination of a blood culture is more common than a true pathogen. An argument could be made for performing a lumbar puncture to make sure meningitis is not present, but the fact that the child, though irritable, is consolable and is eating makes meningitis less likely. Even if a lumbar puncture is performed, a head CT is not needed prior to the procedure. Examination of the fontanel is a better measurement for increased intracranial pressure, and also provides a “pop-off valve,” making herniation unlikely.

3. A 4-year-old girl is brought to the Emergency Department with a one-day history of sudden onset of fever and refusing to walk. She was well the day before the fever. She is complaining of pain in the right knee and wants to keep her leg extended. Temperature is 40 C, heart rate is 157 bpm, and respiratory rate is 30 bpm. She is fussy and complaining of pain. Her right knee is swollen, red, warm to the touch, and an effusion is present. There is decreased range of motion of the knee. All other joints appear normal. White blood cell count is 27,000 with 87% neutrophils and 10% lymphocytes. Which of the following is the best next step in management?

- A. Blood culture
- B. Bone scan
- C. MRI of the knee
- D. Needle aspiration of the knee
- E. Ultrasound of the knee

Answer: D

Discussion: The case points towards a diagnosis of septic arthritis. While a blood culture may reveal the organism, the best source is to tap the joint. Physical examination is usually sufficient to demonstrate an effusion in the knee joint, so neither ultrasound nor MRI is needed. The knee can also be tapped without the use of ultrasound guidance. In contrast, if the hip is infected, ultrasound is very useful in the diagnosis, and is routinely used to help with aspirating fluid from the hip. A bone scan can be useful for osteomyelitis, but has a limited role for septic arthritis.

4. A 6-year-old girl is brought to the physician with fever, sore throat, and decreased oral intake. Her mother pushed her to drink a 24-ounce bottle of a sports drink, but the girl vomited about 5 minutes after finishing it. She has had no other vomiting or diarrhea but the mother notes less frequent urination. On physical examination, she is sleepy but responds appropriately to your questions. Her weight is 20 kg, temperature 38.1 C, respiratory rate 28 bpm, pulse 140 bpm, and blood pressure 110/60 mm Hg. Capillary refill time is 3 seconds. Which of the following is the safest therapy for this child?

- A. Give 400 ml IV normal saline bolus, followed by IV D5 1/2 normal saline at 60 ml per hour
- B. IV D5 1/2 normal saline at 60 ml per hour
- C. IV D5 1/2 normal saline at 120 ml maintenance
- D. No therapy is needed
- E. Oral rehydration solution, 5-10 ml every 5-10 minutes, and advance gradually

Answer: E

Discussion: This is a child with mild to moderate dehydration who would benefit from rehydration therapy (prolonged capillary refill, tachycardia.) The safest form of rehydration is using an oral electrolyte solution, even with moderate to severe dehydration, unless the patient is unable to protect the airway. Though this patient is sleepy, she is able to answer questions. Oral rehydration is effective in a patient who is vomiting by starting with small volumes and slowly increasing the amount given. Answer A would be an appropriate way to treat her dehydration, and then provide her with maintenance fluids. Answer B is only providing fluid at a maintenance rate, so would not make up the deficit. Answer C is twice the maintenance rate, so would eventually make up the deficit, but would then be providing excess fluid.

5. A 4-year-old girl presents to the Emergency Department with fever and vomiting. She has a history of recurrent urinary tract infections and was last treated for a UTI three months ago with trimethoprim/sulfamethoxazole, an antibiotic that has usually been effective for her. She was seen in the clinic 2 days ago with dysuria, frequency, and urinary incontinence. A urinalysis obtained at that time was cloudy with positive leukocyte esterase. On microscopic exam, the urine showed many white cells and many bacteria. She was started on trimethoprim/sulfamethoxazole. Today, she developed a fever that has been as high as 38.3 C, and has started vomiting everything she eats and drinks. She vomited her antibiotic within a minute of taking it. You call the microbiology laboratory and learn that her urine is growing greater than 100,000 colonies per ml. of *Enterococcus faecalis*, and sensitivities are pending. You

decide to admit her for parenteral antibiotics. Which of the following would be the most appropriate choice for her?

- A. Intravenous ampicillin
- B. Intravenous ceftriaxone
- C. Intravenous ciprofloxacin
- D. Intravenous trimethoprim/sulfamethoxazole
- E. Intravenous vancomycin

Answer: A

Discussion: Enterococcus is often seen in children with recurrent urinary tract infections who receive multiple courses of antibiotics, and especially children who receive long-term trimethoprim/sulfamethoxazole. Ceftriaxone and trimethoprim/sulfamethoxazole do not have good coverage for enterococcus so would not be appropriate choices. Vancomycin should be used if there is beta lactam resistance or if the patient is allergic to other choices, but should not be the empiric choice. Ciprofloxacin is more expensive than ampicillin, with more concerns about safety. So ampicillin is the most appropriate choice.

Application Exercises

EXERCISE I

Clinical Scenario

A three-week-old boy is sent to the emergency department by an urgent care clinic because “he might have a urinary tract infection.” He was born at 40 weeks’ gestation following an uncomplicated pregnancy throughout which the mother received routine prenatal care. Following a normal spontaneous vaginal delivery, he was discharged home with his mother on the second day of life. He has done well with no concerns until today when he was fussier than usual, but easily consoled. There has been no change in his breastfeeding or sleep patterns. He has had no vomiting, diarrhea, or respiratory issues. He was taken to an urgent care center where a catheterized urine was obtained. Urinalysis showed many white cells and bacteria, and the dipstick was positive for leukocyte esterase and nitrite. A urine culture is pending. The parents were told to bring the patient directly to the emergency department. On exam, his rectal temperature is 38.5°C, heart rate 145 bpm, respiratory rate 34 bpm. There are no focal findings on physical examination.

Question 1.1 When considering high-value care, which of the following will be least helpful in your evaluation:

- A. 2–3 ml. of blood for a blood culture
- B. Chest x-ray
- C. Complete blood count and differential
- D. Evaluation of cerebrospinal fluid
- E. Nasopharyngeal swab for viruses

Applied concepts:

- *Age factors*
- *Therapy choice*
- *Diagnostic evaluation*



Allow 20 minutes for this question.

- *Team discussion: 10 minutes*
- *Large group discussion: 10 minutes*

See discussion guide on next page.

APPLIED CONCEPTS AND CASE-SPECIFIC TEACHING POINTS			
ANSWER COMMENT	AGE FACTORS	THERAPY BENEFIT	DIAGNOSTIC EVALUATION
A. 2–3 ml. for a blood culture	<p>There are two possible reasons for bacteremia in a young infant with a UTI: bloodstream was seeded from the UTI or the urinary tract was a secondary infection from a bacteremia. In either case, it is important to know if bacteremia is present, indicating a possible need to look for other sites of infection.</p>	<p>Though empiric antibiotics need to be started for this infant, every effort should be made to identify the organism in order to minimize the use of broad-spectrum antibiotics.</p>	<p>This is a good place to discuss why blood cultures require a smaller blood volume from infants than adults. (Bacteria replicate at the same rate in adults or babies, but since babies have a smaller blood volume, there are more bacteria per ml. of blood.) It would also be important to discuss that required blood volume to be collected increases proportionally to the patient's age.</p>
B. Chest x-ray			<p>With no history of respiratory complaints and no findings on exam (including a normal respiratory rate), the yield of a chest x-ray is low, but still worthy of consideration.</p>
C. Complete blood count and differential			<p>Can give a very rough idea of how concerned to be, but it is very important to include the differential.</p>
D. Evaluation of cerebrospinal fluid	<p>Signs and symptoms of meningitis can be very subtle in an infant.</p>	<p>E. coli is a common cause of UTI and meningitis in this age group.</p>	<p>CSF evaluation should include, at a minimum, cell count and differential, glucose, protein, gram stain, bacterial culture, evaluation for Herpes simplex (PCR).</p>
E. Nasopharyngeal swab for viruses (<i>correct answer</i>)		<p>Identification of a virus in this age group does not rule out the possibility of a bacterial infection as well, so empiric antibiotics are still needed.</p>	<p>Opportunity to discuss limitations of these studies, and the need to consider things like time of year and prevalence of the viruses you are looking for. With the advent and more widespread availability of Nucleic Acid Amplification Tests (NAATs) it is important to discuss their cost.</p>

- Question 1.2** After sending appropriate laboratory studies, the decision was made to start antibiotics empirically, being sure to cover the urinary tract infection. Of the following, which is the best choice?
- A. Ampicillin and gentamicin
 - B. Ampicillin and ceftriaxone
 - C. Ciprofloxacin
 - D. Trimethoprim/sulfamethoxazole
 - E. Vancomycin and cefotaxime

Applied concepts:

- *Age factors*
- *Therapy choice*
- *Therapy risk*



Allow 20 minutes for this question.

- *Team discussion: 10 minutes*
- *Large group discussion: 10 minutes*

See discussion guide on next page.

Question 1.2 Discussion Guide

APPLIED CONCEPTS AND CASE-SPECIFIC TEACHING POINTS			
ANSWER COMMENT	AGE FACTORS	THERAPY CHOICE	THERAPY RISK
A. Ampicillin and gentamicin (<i>correct answer</i>)	Excellent coverage for UTI, but also covers disseminated infection in infants	Likely organisms: E. coli, Group B strep, Listeria	
B. Ampicillin and ceftriaxone	Appropriate coverage for UTI, but also covers disseminated infection in infants . However, there are risks to use of ceftriaxone (see “therapy risk”). Would utilize if LP is consistent with meningitis.	Good CNS penetration	Ceftriaxone should not be used under one month of age, especially if the infant has hyperbilirubinemia or may require intravenous calcium. Cefotaxime would be an appropriate alternative. Nurseries that used cephalosporins for empiric purposes saw an increase in organisms resistant to cephalosporins.
C. Ciprofloxacin	Not studied in this population for the common sites of infection.	Not good coverage for Group B strep or Listeria	Theoretical risk of cartilage damage from quinolones
D. Trimethoprim/sulfamethoxazole	Not as good for bacteremia	Not good for meningitis	Contraindicated under 2 months of age as it can cause folate deficiency
E. Vancomycin and cefepime	Opportunity to talk about CNS penetration of vancomycin—usually thought to be fairly low, but it is better in infants	Appropriate empiric coverage for meningitis for older child or adult where concern is more for <i>Streptococcus pneumoniae</i> or <i>Neisseria meningitidis</i> ; <i>Staphylococcus aureus</i> (including MRSA) are low concerns in this scenario	

EXERCISE 2

Clinical Scenario

A three-year-old girl is brought to the emergency department because she has a fever and her “knee hurts” on the right side. She was in her usual state of good health until two days before presentation when she became less active and developed a fever to 101°F. She refused to eat her dinner and went to bed early. Yesterday she wouldn’t eat and just wanted to lie down, saying her knee hurt. She continued to have a fever and it responded to acetaminophen. Today her temperature went up to 102.5°F and she has been very irritable. She refuses to bear weight on her right leg and would not eat or drink anything. There is no history of trauma. She did have an upper respiratory tract infection several days ago. On physical exam, she is irritable and uncooperative. Vital signs: pulse 140 bpm; respiratory rate 32 bpm; temp 102.5°F; blood pressure: patient wouldn’t cooperate; oxygen saturation 98% on room air. Physical examination showed an irritable child who would sit quietly until anyone tried to touch her. HEENT significant for tacky oral mucosa. Cardiac exam showed tachycardia and a capillary refill of 2 seconds. Respiratory exam normal. Unremarkable abdominal exam. Examination of the extremities was remarkable for the right leg only. When she was quiet, she would sit with her knee flexed and her hip flexed and abducted. There was no erythema or swelling evident at any joint. She cried, saying it hurt when you touched her right leg anywhere.

Question 2.1 Which of the following is your top priority for your evaluation/management?

- A. Administer intravenous antibiotics
- B. Administer intravenous fluids
- C. Obtain a blood culture
- D. Ultrasound of hip
- E. X-ray of knee

Applied concepts:

- *Age factors*
- *Therapy choice*
- *Diagnostic evaluation*
- *Shock*



Allow 20 minutes for this question.

- *Team discussion: 10 minutes*
- *Large group discussion: 10 minutes*

See discussion guide on next page.

Question 2.1 Discussion Guide

How will the students employ the exercise’s learning objectives to correctly apply the generalizable concepts and choose the best answer?

APPLIED CONCEPTS AND CASE-SPECIFIC TEACHING POINTS				
ANSWER CHOICES	AGE FACTORS	THERAPY RISKS	DIAGNOSTIC EVALUATION	SHOCK
A. Administer intravenous antibiotics	In this age group, infection is more likely limited to a single location.	Antibiotics should be given as soon as diagnosis is made, but it is important to try to identify an organism.	Giving antibiotics early can prevent identification of the infecting organism, limiting the ability to optimally treat the patient.	If this patient was in shock, it would most likely be due to sepsis.
B. Administer intravenous fluids		The clinical picture is consistent with mild to moderate dehydration. This can be managed with oral rehydration. However, if there is a chance she may need sedation for a joint aspiration, an argument could be made for intravenous fluids.		While parts of the presentation are concerning for shock (tachycardia, borderline capillary refill), other things are reassuring (sitting up quietly at times). She would likely feel better with fluids, but her circulation is okay.
C. Obtain a blood culture		While empiric antibiotics could be used for a full course of treatment (usually 3–6 weeks), identifying an organism allows narrowing of the coverage	It is important to try to identify an organism, and about 40% of children with septic arthritis will have a positive blood culture.	Bacteremia raises concern for sepsis and possible shock.
D. Ultrasound of hip (correct answer)	A child with a septic hip may have pain referred to the knee. Septic arthritis of the hip is a greater risk for serious sequelae (avascular necrosis.)		Physical exam findings usually don’t show the presence of fluid in the hip joint. A septic hip is a medical emergency so rapid diagnosis is important.	
E. X-ray of knee	Usually there are findings on physical exam of the knee when there is septic arthritis.		While plain films of the knee may show changes with septic arthritis, physical exam is usually adequate to show the presence of fluid in the knee.	

Note: This may be a good opportunity to discuss the pathogenesis of AVN—including aspects related to the effect of inflammation on the blood supply—as a “flashback to the basic sciences.”