

## Fever - Questions

1. After completing a full rule-out sepsis work-up on a 1-week-old girl with bronchiolitis and fever to 38.5, your next step in management is to:
  - A. Observe and provide supportive care with frequent suctioning and supplemental oxygen
  - B. Initiate treatment with ceftriaxone 50 mg/kg/dose IV q24 hrs
  - C. Initiate treatment with ceftriaxone 50 mg/kg/dose IV q12 hrs
  - D. Initiate treatment with ampicillin 100 mg/kg/dose IV q6 hrs and cefotaxime 50 mg/kg/dose IV q6 hrs
  - E. Initiate treatment with acyclovir 20 mg/kg/dose IV q8 hrs
  
2. You are called by the Emergency Department to admit an ill-appearing 1 year-old boy with fevers, anemia, thrombocytopenia, and hypofibrinogenemia. Vital signs are stable at this time. The most appropriate next step in the evaluation and management of this patient is:
  - A. Administer normal saline bolus
  - B. Obtain cultures and start empiric broad-spectrum antibiotics
  - C. Transfuse packed red blood cells and platelets
  - D. Transfuse cryoprecipitate
  - E. Obtain bone marrow aspirate and biopsy
  
3. Upon further history and exam, the patient was noted to have splenomegaly, ferritin >10,000, and exposure to Epstein Barr Virus (EBV). What additional laboratory test would be most helpful in the patient's evaluation?
  - A. EBV titers
  - B. EBV PCR
  - C. HIV titer
  - D. HIV PCR
  - E. Soluble IL-2 receptor
  
4. You are paged by the nurse to evaluate a 8-year-old boy with history of relapsed ALL, now Day +70 s/p matched related donor HSCT (hematopoietic stem cell transplant) who is persistently febrile to 38.5 despite empiric therapy with ceftazidime and vancomycin for 2 days. He has now developed headaches and sinus tenderness. The fever is most likely related to:
  - A. Upper respiratory infection
  - B. Bacterial infection
  - C. Re-activation of viral infection (including CMV, EBV, HSV)
  - D. Fungal infection (including *Aspergillus*)
  - E. Graft-vs-host disease (GVHD)

5. You are paged by the nurse to evaluate a 15-year-old girl with high-risk pre-B cell ALL in induction. She was admitted for febrile neutropenia and has now developed abdominal pain, vomiting, and distension. This is concerning for development of:

- A. Acute gastroenteritis
- B. Typhlitis
- C. Constipation
- D. Urinary tract infection
- E. Pancreatitis

## Fever - Answers

1. After completing a full rule-out sepsis work-up on a 1-week-old girl with bronchiolitis and fever to 38.5, your next step in management is to:

- A. Observe and provide supportive care with frequent suctioning and supplemental oxygen
- B. Initiate treatment with ceftriaxone 50 mg/kg/dose IV q24 hrs
- C. Initiate treatment with ceftriaxone 50 mg/kg/dose IV q12 hrs
- D. Initiate treatment with ampicillin 100 mg/kg/dose IV q6 hrs and cefotaxime 50 mg/kg/dose IV q6 hrs
- E. Initiate treatment with acyclovir 20 mg/kg/dose IV q8 hrs

In children less than 2 months of age, the rate of a serious bacterial illness is between 5-9%. Common bacterial organisms in this age group include *E. Coli*, *Klebsiella*, Group B *Streptococcus*, *Enterococcus*, *Enterobacter*, and *Listeria*. Although a viral illness decreases the chance of a bacterial infection, it does not eliminate the risk. Since the risk of bacteremia in febrile infants with cold symptoms is the same as those without cold symptoms, the workup should be done regardless. Because of the infant's age is less than 2 months, she is at risk of a serious bacterial infection (including bacteremia, UTI, or meningitis). Once cultures are obtained, empiric therapy should be started with ampicillin (to cover *Listeria* and Group B *Streptococcus*) and cefotaxime (to cover gram negatives). Until the CSF results are known and meningitis is ruled-out, meningitic doses should be started empirically. Because of her young age and potential hyperbilirubinemia caused by displacement of bilirubin from albumin by ceftriaxone, ampicillin and cefotaxime were chosen as first-line antibiotics.

2. You are called by the Emergency Department to admit an ill-appearing 1 year-old boy with fevers, anemia, thrombocytopenia, and hypofibrinogenemia. Vital signs are stable at this time. The most appropriate next step in the evaluation and management of this patient is:

- A. Administer normal saline bolus
- B. Obtain cultures and start empiric broad-spectrum antibiotics
- C. Transfuse packed red blood cells and platelets
- D. Transfuse cryoprecipitate
- E. Obtain bone marrow aspirate and biopsy

The differential diagnosis is broad and includes sepsis with disseminated intravascular coagulation (DIC), leukemia/lymphoma with DIC, and hemophagocytic lymphohistiocytosis. The most appropriate next step is to obtain cultures and start broad-spectrum antibiotics. Since the patient's vital signs are stable the normal saline bolus is not indicated at this time, however patient should be closely monitored for clinical decompensation after administration of antibiotics. Since the patient does not have active bleeding, transfusions would not be the first step in the patient's management but can be initiated after patient receives antibiotics. Bone marrow aspirate and biopsy may be necessary for the patient's evaluation however it would not be the appropriate next step.

3. Upon further history and exam, the patient was noted to have splenomegaly, elevated ferritin >10,000 mcg/L, and exposure to Epstein Barr Virus (EBV). What additional laboratory test would be most helpful in the patient's evaluation?

- A. EBV titers
- B. EBV PCR
- C. HIV titer
- D. HIV PCR
- E. Soluble IL-2 receptor

With this additional information, the most likely diagnosis includes EBV infection with secondary hemophagocytic lymphohistiocytosis (HLH). Although ferritin may be elevated in infections, levels >10,000 mcg/L are 90% sensitive and 96% specific for HLH. (Allen CE, et al. Highly elevated ferritin levels and the diagnosis of hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer* 2008;50: 1227-1235) HLH is characterized by fevers, splenomegaly, cytopenia (at least 2 cell lines), elevated ferritin, elevated triglycerides, low fibrinogen, elevated soluble IL-2 receptor, low/absent NK cell function, and hemophagocytosis.

4. You are paged by the nurse to evaluate a 8-year-old boy with history of relapsed ALL, now Day +70 s/p matched related donor HSCT (hematopoietic stem cell transplant) who is persistently febrile to 38.5 despite empiric therapy with ceftazidime and vancomycin for 2 days. He has now developed headaches and sinus tenderness. The fever is most likely related to:

- A. Upper respiratory infection
- B. Bacterial infection
- C. Re-activation of viral infection (including CMV, EBV, HSV)
- D. Fungal infection (including *Aspergillus*)
- E. Graft-vs-host disease (GVHD)

Bone marrow transplant patients day <30 have significant neutropenia and are at-risk for bacterial infection (including gram-negative rods, *S. epidermidis/aureus*, *Streptococcus*). Patients day +30-100 have decreased cellular immunity and are at-risk for viral reactivation (including EBV, CMV, HSV, VZV) and fungal infections (including *Aspergillus*, *Pneumocystis*) and parasitic infections (including *Toxoplasma gondii*).

5. You are paged by the nurse to evaluate a 15-year-old girl with high-risk pre-B cell ALL in induction. She was admitted for febrile neutropenia and has now developed abdominal pain, vomiting, and distension. This is concerning for development of:

- A. Acute gastroenteritis
- B. Typhlitis
- C. Constipation
- D. Urinary tract infection
- E. Pancreatitis

Patients with febrile neutropenia may develop typhlitis, a necrotizing colitis that usually involves the cecum. Typhlitis may be secondary to mucosal injury related to

chemotherapy and profound neutropenia which place the patient at-risk for translocation of gut bacterial flora that result in necrosis of the bowel wall. Symptoms include abdominal distension, nausea, vomiting, diarrhea (may be bloody), peritoneal signs, or septic shock. Imaging modalities include KUB, ultrasound, or CT scan. These can demonstrate intramural bowel air, free air, or cecal thickening. Management includes broad spectrum antibiotics with coverage of gram-negative rods including *Pseudomonas* (strongly consider double-coverage for resistant GNR such as amikacin) and anaerobes, IV hydration, bowel rest, and supportive care. Acute gastroenteritis, constipation, urinary tract infection, and pancreatitis (especially related to asparaginase) can also cause symptoms, however, because typhlitis can lead to significant complications (including perforation), it must be evaluated.