**Introduction**

Pediatric fever is a common presenting complaint in children, though the prevalence of serious bacterial illness has decreased in recent years due to advances in vaccination. Assessing and managing pediatric fever appropriately is critical for pharmacists, as inaccurate diagnosis can lead to unnecessary testing, antibiotic exposure, and patient harm. Key aspects in evaluating fever include identifying infants at highest risk based on age, recognizing signs and symptoms concerning for serious bacterial illness through history and physical exam, utilizing diagnostic testing judiciously, and initiating pharmacotherapy when indicated. Recent controversies center on overtesting and overtreatment of viral illnesses. This section covers the clinical presentation, pathophysiology, diagnostic approach, and management of pediatric fever with a focus on pharmacotherapy.

**Clinical Presentation**

Pediatric fever most commonly occurs in infants and children under 3 years old, with higher risk seen in the first 3 months of life and peak risk under 1 month of age.

* Typical signs and symptoms:
* Fever (elevated temperature, most reliably measured rectally)
* Fussiness, decreased activity or appetite
* Vomiting, diarrhea
* Respiratory symptoms like cough, congestion, or increased work of breathing
* Rash
* Lethargy, irritability, or inconsolability

* Risk factors:
* Age less than 3 months old
* Prematurity
* Immunocompromised state
* Underlying conditions like sickle cell disease, congenital heart disease
* Indwelling devices like ventricular shunts or central venous catheters
* Recent antibiotic exposure
* Lack of vaccinations against H. influenzae, S. pneumonia

Some important pitfalls or potential misdiagnoses associated with the clinical presentation of pediatric fever include attributing serious bacterial illness like meningitis to a benign viral illness, assuming fever alone reliably rules out bacterial infection, oversensitivity of the white blood cell count leading to unnecessary testing or antibiotic exposure, and difficulty differentiating bacterial versus viral meningitis based on cerebrospinal fluid parameters alone. Careful assessment of risk factors and High clinical suspicion is warranted in young febrile infants.

**Pathophysiology**

Fever is defined as a temperature greater than 100.4°F (38°C) when measured rectally. It occurs due to the release of endogenous pyrogens such as interleukin-1, interleukin-6, tumor necrosis factor-alpha, and interferons in response to infection.

The majority of pediatric fevers are caused by viral infections, including upper respiratory infections, viral meningitis, bronchiolitis, and gastroenteritis from pathogens like respiratory syncytial virus, influenza, adenovirus, enterovirus, and rotavirus.

* Serious bacterial illnesses result from infection at normally sterile sites:
* Bacteremia
* Meningitis
* Pneumonia
* Urinary tract infection
* Gastroenteritis
* Osteomyelitis
* Cellulitis
* Septic arthritis

* Key bacterial pathogens by age:
* 0-28 days: Group B streptococcus, Listeria, E. coli, HSV
* 1-3 months: S. pneumoniae, N. meningitidis, H. influenzae
* 3 months: S. pneumoniae, N. meningitidis, S. aureus, Salmonella

Infants have immature immune systems, lack maternal antibodies, and have poor T-cell function, which predisposes them to more disseminated infections. Febrile infants 0-3 months of age have a 6-10% risk of serious bacterial illness. After 3 months, immune function improves with routine vaccinations against S. pneumoniae and H. influenzae, lowering but not eliminating the risk of occult bacteremia. Viral infections like RSV and influenza reduce but don’t exclude bacterial co-infections, especially in neonates under 28 days old.

**Diagnostic Approach**

The diagnostic approach for a pediatric patient presenting with fever begins with a focused history inquiring about the duration of fever, any associated symptoms, sick contacts, and the child's immunization status.

A thorough physical exam includes a full set of vital signs, a cardiac exam for murmurs, inspection for rash, assessment of peripheral perfusion, and an evaluation for meningeal signs, such as nuchal rigidity. Tachypnea, hypoxemia, or signs of shock on initial presentation require immediate stabilization with supplemental oxygen, fluid resuscitation, and vasopressor support if needed.

Once the patient is stabilized, appropriate specimens should be obtained for culture, including blood, urine, stool, and cerebrospinal fluid depending on clinical suspicion, before any antibiotic administration. Empirical antibiotic therapy can then be directed at the most likely pathogens based on age, risk factors, and presentation. A lumbar puncture may be deferred in critically ill patients until stabilization occurs.

* Diagnostic tests:
* Complete blood count (CBC) with differential: elevated WBC predicts serious bacterial illness
* Blood culture: ideally straight stick, not from IV catheter due to contamination risk
* Urinalysis and urine culture: catheterization or suprapubic aspirate specimens to avoid false positives
* Lumbar puncture: nucleic acid amplification or PCR to identify difficult organisms like HSV
* Stool testing: WBCs suggest bacterial gastroenteritis
* Chest x-ray: for respiratory symptoms or high WBC
* Inflammatory markers (CRP, procalcitonin): may help differentiate bacterial from viral illness
* Rapid viral testing (RSV, influenza): positive result may allow reduced testing in infants >28 days old

High risk infants under 28 days old should have a full septic workup including blood cultures, urine cultures, and lumbar puncture with empiric antibiotic therapy. Slightly older infants 29-90 days old can be risk stratified based on clinical criteria to determine appropriate diagnostic testing and need for empiric treatment. Beyond 3 months of age, the evaluation is guided by the clinical presentation and suspicion for serious bacterial illness.

**Management - Overview**

The initial focus when managing a febrile pediatric patient is stabilizing those who appear ill or in shock with interventions like supplemental oxygen, fluid resuscitation, and vasopressor support.

Once stabilized, antibiotic therapy is indicated in cases where serious bacterial illness is likely based on the clinical presentation, exam findings, risk factors, and results of the diagnostic workup. The choice of antibiotic agent, route of administration, and duration of treatment depends on the patient's age and the suspected bacterial pathogen.

In infants 29-90 days old, risk stratification algorithms help identify patients at low risk of serious bacterial illness who may be suitable for outpatient management without antibiotics. Important adjunctive therapies include IVIG for Kawasaki disease and antiviral medications for suspected herpes simplex virus infections. Prevention is also key, through routine childhood immunizations against S. pneumoniae, H. influenzae, and HPV in adolescents. However, the majority of pediatric fevers are due to self-limited viral illnesses that can resolve without any specific antimicrobial therapy.

**Pharmacotherapy**

Initial Management

* Address airway, breathing, circulation first
* Fluid resuscitation 20 mL/kg isotonic fluid boluses for hypotension
* Vasopressor support if fluid refractory (dopamine, norepinephrine)
* Empiric antibiotics should not be delayed for critically ill patients

Antibiotic Selection by Age

Neonates 0-28 days old

* Ampicillin 100 mg/kg/day IV divided q6h
* Covers group B strep, Listeria
* Plus cefotaxime 150 mg/kg/day IV divided q8h
* Third-generation cephalosporin with central nervous system (CNS) penetration
* Or gentamicin 5 mg/kg/day IV divided q8-12h
* Aminoglycoside with broad gram negative coverage
* Consider acyclovir if risk factors for neonatal HSV

Infants 29-90 days old

* Ampicillin 50-100 mg/kg/day IV divided q6h
* Covers group B strep, Listeria
* Plus cefotaxime 50 mg/kg/day IV divided q8h

Beyond 3 months old

* Ceftriaxone 100 mg/kg IV or IM daily
* Third-generation cephalosporin with long half-life, once daily dosing
* Vancomycin 40 mg/kg/day IV divided q6-8h
* For penicillin-resistant S. pneumoniae
* Trimethoprim-sulfamethoxazole
* Oral step-down option for UTIs
* Antivirals like oseltamivir for suspected influenza

Adjunctive Therapies

* IVIG 2 g/kg IV for Kawasaki disease
* Acyclovir 60 mg/kg/day IV divided q8h for suspected HSV

Prevention

* Routine childhood immunizations against S. pneumoniae, H. influenzae, HPV in adolescents
* Penicillin prophylaxis for sickle cell patients until age 5 years old

**Clinical Scenarios**

Clinical Scenario 1:

A 2-week old infant presents with fever of 101°F and fussiness for 1 day. Mother endorses mild congestion but no coughing. On exam, the child has an otherwise normal exam. Per your department's clinical practice guideline, you recommend a full septic workup including CBC, blood culture, urine culture, stool studies, LP, and empiric antibiotics. CSF, urine, and blood cultures have no growth at 36 hours.

Clinical Scenario 2:

A 6-week old has had 5 days of fever, congestion, and cough. Rapid flu test is positive. On exam, the infant has rhinorrhea but is otherwise well-appearing and meeting milestones. As influenza increases the risk of bacterial co-infection in this age group, you recommend a CBC, blood culture, urine culture, and antibiotic treatment until cultures result. All cultures are negative, but the patient receives 2 days of IV antibiotics.

Clinical Scenario 1 Answer Key:

This case highlights that even well-appearing neonates are at high risk of serious bacterial infections. Due to their immature immune systems, minimal or non-specific symptoms cannot be relied upon to rule out bacterial illness. Following clinical practice guidelines to evaluate and empirically treat febrile neonates reduces morbidity and mortality.’

Clinical Scenario 2 Answer Key:

This case reveals a pitfall in management of febrile young infants with confirmed viral illness. Beyond 28 days old, documented influenza significantly reduces the risk of concomitant bacterial infection. A urine culture is still warranted given the risk of UTI, but full sepsis evaluation and empiric antibiotics could have been avoided.

**Tips for Board Exam Questions**

* Febrile neonates (0-28 days old) should always receive a full septic workup with empiric antibiotics, regardless of clinical appearance
* Documented influenza infection reduces but does not eliminate the risk of bacterial co-infection in infants >28 days old
* Criteria exist (Rochester, Philadelphia, Boston) to identify febrile infants 29-90 days old at low risk for serious bacterial illness who may not require a full sepsis evaluation
* First-line treatment of bacterial meningitis is a third-generation cephalosporin like cefotaxime or ceftriaxone
* Hib and pneumococcal vaccination dramatically reduced the prevalence of occult bacteremia in febrile infants and children

**Summary**

Pediatric fever requires a structured approach to identifying patients at high risk for serious bacterial illness based on age, clinical appearance, and diagnostic findings. Neonates 0-28 days old warrant empiric antibiotics and full sepsis workup given high risk. Beyond 28 days old, use of clinical decision rules and documented viral infection can risk stratify patients and guide need for testing/treatment. Bacterial meningitis is of particular concern and requires an LP plus empiric treatment with cefotaxime or ceftriaxone. Advances like Hib and pneumococcal vaccination have reduced but not eliminated the risk of occult bacteremia. Following clinical guidelines reduces variation and improves outcomes when managing febrile children.

**References**

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