

THERAPUTICS

Therapeutics, Case #1

Written by Rebecca Chasnovitz, M.D.

A three-year-old has acute otitis media. She is not allergic to any medications. Which if any antibiotics would you prescribe and why?

Definitions for Specific Terms:

Acute otitis media (AOM)- Must meet all 3 of the following criteria:

- Acute onset
- Presence of a middle ear effusion (see physical exam findings)
- Signs or symptoms of middle ear inflammation (see physical exam findings)

Review of Important Concepts:

Historical Points

- The time course of symptoms must be acute to meet the definition of acute otitis media.
- The patient's age, severity of symptoms, and reliability for follow-up help determine whether or not to prescribe an antibiotic (see clinical reasoning).
- The patient's past history of ear infections, any underlying medical issues such as cleft lip/palate, and recent antibiotic use may influence the choice of antibiotic.

Physical Exam Findings

The best way to diagnose a middle ear effusion is with pneumatic otoscopy demonstrating limited mobility of the tympanic membrane. However, other signs of a middle ear effusion on routine ear exam are bulging of the tympanic membrane, an air fluid level, and otorrhea. Signs of middle ear inflammation include otalgia and tympanic membrane erythema, cloudiness, or opacification.

Clinical Reasoning

1. What medications should be used to treat pain in AOM?
 - a. Ibuprofen should be used in all patients to treat symptoms of pain, regardless of one's decision to treat or not to treat with antibiotics.
 - b. Topical benzocaine may also provide pain relief, though evidence is not as strong as that for ibuprofen.

2. What are the complications of AOM?

The more common consequences of AOM are pain and discomfort experienced by the child and loss of parental time at work. However, about 90% of children with AOM will have symptomatic relief of otalgia and fever within 2-3 days regardless of antibiotic use. This improvement may be because many of pathogens in AOM are viruses (20-50%), or because even in cases of confirmed bacterial AOM, the majority of infections resolve without antibiotics. Thus, "watch and wait" is becoming a

more accepted management option for patients initially presenting with AOM if they have reliable follow-up.

3. According to the AAP Clinical Guidelines, when should antibiotics be prescribed in AOM in healthy children?

The AAP recommends antibiotics for:

- a. Children less than 6 months old with suspected AOM,
- b. Children between 6 months and 2 years of age if the physical diagnosis is certain OR, in cases of uncertain diagnosis, if the symptoms are severe, defined as moderate to severe otalgia or fever greater than 39 degrees Celsius,
- c. Children 2 years or older only if the diagnosis is certain AND symptoms are severe,
- d. Children being observed off of antibiotics with no improvement in symptoms after 48-72 hours from start of illness.

4. What is the first-line choice of antibiotic in AOM?

The most common bacterial pathogens in AOM are *Streptococcus pneumoniae* (25-50%), nontypeable *Haemophilus influenzae* (15-30%), and *Moraxella catarrhalis* (3-20%), so the recommended first-choice antibiotic is Amoxicillin 80-90 mg/kg/day. The AAP recommends the standard 10 day course for children less than 6 years old. Studies on shorter courses are limited, but a 5- to 7-day course may be appropriate for older children with less severe symptoms. Symptoms of ear pain and fever usually improve 48-72 hours after initiating treatment. Persistence of a middle ear effusion on ear exam after resolution of acute symptoms is very common and is NOT an indication for a longer treatment course or change in antibiotic therapy.

5. What are the side effects of amoxicillin?

Common side effects of amoxicillin include nausea, vomiting, diarrhea, and rashes. Antibiotics alter normal flora and can increase the risk of yeast infections and resistant organisms. Rare adverse effects of amoxicillin include anaphylaxis, hepatitis, and Stevens-Johnson syndrome.

Diagnosis:

Acute otitis media

Suggestions for Learning Activities:

- What is the differential diagnosis for ear pain?
- Why might a patient's symptoms not improve after starting an antibiotic?
- Identify the local resistance patterns for AOM in your region.

Other Resources:

- AAP Clinical Practice Guidelines: Diagnosis and Management of Acute Otitis Media. *Pediatrics* 2004;113(5):1451-1465.
- Gould JM, Matz PS. Otitis Media. *Pediatrics in Review* 2010;31(3):102-116.

Therapeutics, Case #3

Written by Rebecca Chasnovitz, M.D.

A four-year-old girl has urinary urgency and dysuria. A clean catch urine shows 50-100 white blood cells. How would you manage this child?

Definitions for Specific Terms:

Pyuria- >10 WBC/HPF on unspun urine or >5 WBC/HPF on spun urine

Urinary tract infection (UTI)- The diagnosis is confirmed by a positive urine culture from urine collected before the initiation of antibiotics. A significant culture finding is at least 100,000 colonies/ml of a single organism on a clean catch specimen or at least 50,000 colonies/ml on a catheterized specimen (although >10,000 colonies/ml of a single organism on a catheterized specimen in a patient with high pre-test probability may also represent a UTI). There are several ways to classify UTIs, though clinically differentiating between the types can be difficult:

Lower UTI (cystitis)- Infection of the bladder and/or urethra

Upper UTI (pyelonephritis)- Infection of the kidneys, renal pelvis, and/or ureters

Complicated UTI- UTI (upper or lower) in the presence of an underlying condition that increases the chance of therapeutic failure, such as a functional or anatomic abnormality of the urinary tract, an indwelling urinary catheter, recent urinary tract infection, instrumentation, recent antibiotic use, or immunocompromised.

Review of Important Concepts:

Historical Points

- Classic symptoms of acute cystitis include dysuria, urinary frequency, and urinary urgency. However, children are not always able to give you this history and may present with more generalized complaints such as fatigue, irritability, abdominal pain, vomiting, and enuresis (especially new onset). The classic symptoms of pyelonephritis include fever, chills, and flank pain, but again, the only sign in young children may be fever.
- Risk factors for UTI include recent antibiotic use, history of a previous UTI, urine withholding (common in children learning daytime bladder control), chronic constipation (dilated rectum can obstruct outflow) and other causes of incomplete bladder emptying such as a neurogenic bladder or anatomic abnormality, immunocompromise, catheterization, and family history of recurrent UTIs. Uncircumcised male infants have an increased risk of UTI in the first year of life, and in adolescents, sexual activity is also a risk factor. Also ask about chemical irritants such as bath products and spermicides and drug exposures, which can cause non-infectious pyuria.

Physical Exam Findings

1. Vitals should include a temperature, blood pressure, and review of growth charts (recurrent UTIs can lead to poor weight gain).
2. Abdominal exam should evaluate for suprapubic and costovertebral tenderness.

3. External genital exam should always be performed to look for anatomic abnormalities such as phimosis or labial adhesions, vaginal foreign body, vulvovaginitis, and vaginal or penile discharge.
4. Also inspect the sacrum for dimples, pits, and tufts of hair, which may suggest a neurogenic bladder.

Clinical Reasoning

1. How do you interpret urine dipstick and microscopy results?
The presence of nitrite (more specific but less sensitive than LE), leukocyte esterase, pyuria, bacteruria, and/or white blood cell casts are all suggestive of UTI, though a urine culture is necessary to establish the diagnosis. Always ask how the specimen was obtained. Catheterized specimens are the gold standard. In children who are capable, mid-stream clean catch urine can also be used, but the clinician should evaluate for signs of a “dirty” or improperly collected urine, including squamous cells and a mixture of organisms. Bagged specimens are generally not recommended, especially in ill-appearing patients, due to low specificity and poor positive predictive value, although a negative bagged urine culture might be used to exclude UTI in a well-appearing child.
2. What is the differential diagnosis for pyuria?
WBC in the urine represent inflammation, not necessarily infection. Thus, the differential includes urinary tract infection, chemical cystitis, contaminated urine specimen, vaginal foreign body, vulvovaginitis, drug side effect, appendicitis (secondary to inflammation of to the adjacent ureter to the appendix), Kawasaki disease, SLE, and Behcet’s disease.
3. What are the risks and benefits of antibiotic treatment in UTI?
In the pre-antibiotic era, mortality from UTI was as high as 20%, likely due to urosepsis and secondary bacteremia, and is now very rare. However, the current evidence is unclear on whether antibiotics affect the long-term complications of UTI – recurrent UTIs, renal scarring, hypertension, and renal failure. Prophylactic antibiotics are also now controversial, as they do not clearly prevent recurrent infections and increase the risk of resistant organisms.
4. What is the first-line antibiotic treatment for an uncomplicated UTI?
 - a. Selection of an initial antibiotic should depend on the most prevalent local organisms and resistance patterns, and should be changed as necessary depending on the organism isolated by urine culture and its susceptibility. However in general, the most common pathogen in UTIs is E Coli (~90%). Other pathogens include other gram negative organisms (Klebsiella, Proteus, Enterobacter, Pseudomonas, and Serratia), Enterococcus, Staphylococcus saprophyticus, Chlamydia and Neisseria gonorrhoea (in sexually active adolescents), GBS (in infants), Candida (in immunocompromised patients), and adenovirus. Second or third generation cephalosporins have good activity against E Coli and other gram negative organisms, although they are NOT effective against Enterococcus species and Staphylococcus saprophyticus.
 - b. Traditional antibiotic choices for UTI – amoxicillin, amoxicillin-clavulanate (augmentin), nitrofurantoin, first-generation cephalosporins, and TMP-SMZ – show increasing rates of resistance to E Coli but should be used if the isolated organism shows susceptibility.
 - c. Patients should show improvement in symptoms within 24-48 hours of starting antibiotics.
5. When might you hospitalize a patient with UTI?
Consider hospitalization in patients who are infants (less than 2 months old), ill-appearing, dehydrated, unable to take fluids by mouth, and/or unable to take oral antibiotics.

6. Is UTI an indication for imaging?

The latest report from the AAP no longer recommends imaging as a necessary part of follow-up for UTI in children. This recent change was based on a meta-analysis of data from recent, randomized-control trials that do not support antimicrobial prophylaxis to prevent future febrile UTIs, and thus, reflux identified on VCUG would not change management. Consider ultrasound in a child who fails to improve with appropriate antibiotic treatment to evaluate for perirenal abscess and pyonephrosis.

Diagnosis:

Culture grew >100,000 colonies/ml of E Coli.

Suggestions for Learning Activities:

- Identify a bacteriogram for UTI and resistance patterns of E Coli in your region.
- If the patient were a 1-month-old male infant, how would that change your management?
- If the patient were a 16-year-old female, how would that change your management?
- How might patients with a neurogenic bladder and UTI present differently?

Other Resources:

- Zork, Kiddoo, & Shaw. Diagnosis and management of pediatric urinary tract infections. *Clin Microbiol Rev.* 2005 April; 18(2): 417–422.
- Raszka & Khan. Pyelonephritis. *Pediatr Rev*, Oct 2005; 26: 364 – 370.
- Finnell, Carroll, & Downs. Diagnosis and management of an initial UTI in febrile infants and young children. *Pediatrics*, Sept 2011; 128(3): e749-e770.

Therapeutics, Case #8

Written by Rebecca Chasnovitz, M.D.

A two-year-old presents with a persistent pruritic rash on his arms and legs. He has patches of erythema with obvious excoriations on the extensor surfaces of his arms and legs and also in the antecubital fossae. How would you treat this condition?

Definitions for Specific Terms:

Macule- Flat, less than 0.5 cm area of skin with a different color than the surrounding skin

Patch- Flat, greater than 0.5 cm area of skin with a different color than the surrounding skin

Papule- Raised, less than 0.5 cm area of skin

Plaque- Raised, greater than 0.5 cm area of skin

Excoriation- Punctate or linear break in the skin produced by mechanical means, usually scratching

Lichenification- Thickened skin with prominent skin markings usually due to chronic scratching

Scale- Flakes or layers of excess stratum corneum, usually white or grey in color

Crust- Flakes or layers of dried serum, blood, or purulent exudates, color varies but often red or yellow

Ointment- The thickest moisturizer, with the highest oil content

Cream- Medium thickness moisturizer, with more water than oil

Lotion- The thinnest moisturizer, with more water content than a cream

Review of Important Concepts:

Historical Points

- Aggravating factors- Triggers for atopic dermatitis (commonly known as eczema) can include fragrant soaps, shampoos, and detergents, abrasive fabrics, nickel, synthetics, dyes, rubber, temperature changes from hot to cold, sweating, dust, animal dander, pollen, and food allergies. However, many of these may also trigger contact dermatitis.
- Exposures- Family members or classmates with similar recent onset skin findings could indicate an infectious condition, such as scabies. Elicit a medication history as well, as drug reactions can cause a wide variety of rashes.
- Past medical history- A chronic, relapsing history of pruritic rash is more supportive of atopic dermatitis. Children with a history of asthma, allergies, or atopic dermatitis are three times as likely to develop a second component of the atopic triad; so patients presenting with one component should always be screened for symptoms of the other disorders. A history of

recurrent skin or sinopulmonary infections suggests a possible associated immune deficiency such as Wiscott-Aldrich or Job syndrome.

- Family history- Children with a first-degree family member (parents, siblings) with a history of asthma, allergies, or atopic dermatitis are more likely to develop atopic dermatitis.

Physical Exam Findings

The patient's presentation with pruritic, erythematous patches and overlying excoriations is most consistent with atopic dermatitis. Flexor more often than extensor surfaces of the extremities and the atecubital fossae are classic locations for eczema in this age group. However in practice, flares can occur on any part of the body and can present with patches, papules, plaques, scale, dry skin, and lichenification. Oozing, weeping, and crust may indicate a secondary bacterial infection. Central clearing with peripheral papules suggests possible tinea infection.

Clinical Reasoning

1. What is the differential diagnosis for a pruritic skin rash?
 - a. The differential diagnosis includes atopic dermatitis (ie eczema), contact dermatitis, seborrheic dermatitis, scabies, tinea, psoriasis, impetigo, drug eruptions, immune deficiency syndromes (Wiscott-Aldrich, Job syndrome), ichthyosis vulgaris, and zinc deficiency.
 - b. Frequent follow-up to monitor response to therapy is important, given the similar presentations of many of these skin disorders.
2. What is the treatment for atopic dermatitis?
 - a. Moisturize and hydrate dry skin- Patients should apply a thick, dye-free, fragrance-free moisturizer such as an ointment or cream at least twice daily. One brand is not recommended more than another. Inexpensive options include petroleum jelly and shea butter. Moisturizers should be applied after application of topical medications and after bathing. Patients should pat skin dry (rubbing can irritate the skin) after bathing in luke warm water to hydrate the skin and then immediately apply the moisturizer. Frequent moisturizing should become a daily routine, even between flares.
 - b. Avoid irritants- In general, switching to fragrant-free bath products and detergents may help prevent flares, as well as avoiding dryer sheets and bubble baths. Patients should be attentive to their personal triggers, such as certain metals, fabrics, or dust, and limit their exposures to a reasonable extent. Finally, patients should be encouraged to scratch as little as possible, as scratching leads to worse itching, which promotes more scratching – a difficult cycle to break.
 - c. Decrease inflammation-
 - Topical steroids- Classic pharmacologic treatment for eczema flares involves a limited course of a topical steroid. Topical steroids are divided into Classes I-VII based on strength. Class I topical steroids (ex. Clobetasone) are about 1800 times more potent than Class VII preparations (ex. Hydrocortisone). Selection of a steroid should be based on the severity of the flare, generally using the lowest strength steroid that achieves remission. There is no evidence-based consensus on length of treatment. Generally, topical steroids should be used until the patient achieves reasonable control of symptoms and then either discontinued between flares or switched to a low-potency long-term treatment. Treatment decisions should involve a discussion of risks and benefits with parents and should include frequent follow-ups to evaluate for improvement. Education on the chronic, relapsing nature of

eczema and specific indications for when to use steroids is important for compliance with and effectiveness of management.

- Topical calcineurin inhibitors- TCIs work by blocking the production and release of proinflammatory cytokines after activation of T cells and mast cells. Tacrolimus and pimecrolimus are FDA approved as second-line agents for short-term therapy of moderate to severe atopic dermatitis in patients 2 years and older. Studies on the long-term safety of these agents are ongoing, but current data do not support an increased association with systemic immunosuppression or skin cancer. TCIs are an appropriate alternative for patients who do not show improvement with topical steroids.
- d. Treat secondary infections- Patients with atopic dermatitis have an increased risk of secondary infection. Pathogens include common skin bacteria (MSSA, MRSA) as well as viral (HSV) and fungal (tinea) infections. Consider bacterial, viral, and fungal culture of the skin in patients who do not respond to typical antibiotics for cellulitis.
3. What are the side effects of topical steroids?
 - a. Local adverse effects of topical steroids include skin atrophy, striae, telangiectasias, hypopigmentation, rosacea, perioral dermatitis, acne, cataracts, and glaucoma.
 - b. Lower potency preparations, shorter courses of therapy, and avoiding application to areas of thin skin (face, neck, groin) decrease the risk of adverse effects.
 - c. Many parents are concerned about the systemic side effects of steroids, including hypothalamic-pituitary-adrenal axis suppression, stunted growth, and decreased bone density. However, systemic complications with topical steroids are rare when used properly.
 4. What can you do about the itching, doctor?

Constant itching can impair sleep and affect school performance, as well as decrease quality of life for the patient and caregiver. Unfortunately, there are no good medications to treat the pruritis associated with atopic dermatitis. First-generation antihistamines are often used at night for their sedating side effects to help with sleep disturbance, but no rigorous trials have evaluated their effectiveness.

Diagnosis:

Atopic dermatitis

Suggestions for Learning Activities:

- Identify a reliable patient education resource on atopic dermatitis for children and caregivers.
- List at least one topical steroid in each class.
- List possible causes of treatment failure after 2 weeks of therapy.

Other Resources:

- Krakowski, Eichenfield, & Dohil. Management of atopic dermatitis in the pediatric population. *Pediatrics* 2008;122(4):812 -824.
- Epps, RE. Atopic dermatitis and ichthyosis. *Pediatr Rev* 2010;31:278-28.