National Pharmacy Council

Antibiotic Stewardship Program

Ambulatory Care

February 2018

Disclaimer:

The following guidelines have been developed and adapted from various clinical practice guidelines from reputable professional organizations. These guidelines have been developed using evidence based medicine and are not intended to replace clinical judgment. The treatment medications are not listed in order of preference, and therapeutic decisions should be based on a number of factors including patient history, comorbidities, suspected etiology, antimicrobial susceptibility patterns, and cost. In certain populations (e.g., intravenous drug abusers, immunosuppressed, travelers), the suspected organisms may include a broader range of organisms.

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Dental Infections:

Early diagnosed infections tend to be aerobic gram positive organisms in nature. As the infection progresses, anaerobic bacteria become more prevalent. Beta-lactamase producing bacteria is also a concern, and therapy may need to be adjusted to cover these bacteria if initially unsuccessful.

Odontogenic infections progress in a three-stage manner: inoculation, cellulitis then abscess. Prescribing of antibiotics without directly addressing cause of infection is not recommended. Surgical incision and drainage of any superficial abscess is imperative.

Use the most narrow spectrum antibiotic treatment for the shortest duration required (usually **3 to 7 days**).[1,2,3] Diabetic patients may require longer therapy due to the delayed healing processes. Please consult table below for antibiotic recommendations

Please consult table below for antibiotic recommendations:

Indication	Clinical Features	Antimicrobial Therapy
Dental caries	Toothache, hot/cold sensitivity, low-grade fever, facial swelling	Systemic antibiotics usually **not required**
Simple gingivitis	Gum bleeding, inflammation	Antibiotics typically **not required; however, consider adding** Chlorhexidine 0.12% oral rinse 15 mL swish & spit morning and evening
Acute Necrotizing Ulcerative Gingivitis	Gum bleeding, inflammation, acute pain, necrosis of gingival tissues, fever	Use Chlorhexidine as noted above AND ***If not febrile:*** Antibiotics typically **not required** ***Febrile or refractory to debridement:*** Cover anaerobes • Metronidazole 250-500mg PO q8hours • Amoxicillin/clavulanate 875/125 PO q12hours or 500/125 PO q8hours • Clindamycin 300mg PO q6hours
Odontogenic infections Mild/Early infection	Abscesses, erythema, tenderness of gums, symptoms < 3 days	**1st Line:** Penicillin VK 500 mg PO q 6 hours OR Amoxicillin 500mg PO q 8 hours Penicillin allergy: **Type I reaction**: Clindamycin 300-450 mg PO q6h **Non-type I reaction:** Cephalexin 250-1000 mg PO q6h

Indication	Clinical Features	Antimicrobial Therapy
Odontogenic infections Unresponsive to mild treatment/ Anaerobes or β-lactamase producing bacteria/Late infection	Abscesses, erythema and tenderness of gums, mild treatment ineffective, symptoms > 3 days**	Clindamycin 300-450 mg PO q 6 hours OR Amoxicillin/clavulanate 875/125 PO q12h or 500/125 PO q8h OR Penicillin VK 500 mg PO q 6 hours **PLUS** Metronidazole 500mg PO q 8 hours Immunocompromised (ie uncontrolled DM, HIV, etc): Penicillin VK 500 mg PO q 6 hours **PLUS** Metronidazole 500 mg PO q 8 hours
Severe Odontogenic infections requiring hospitalization	Abscesses, erythema and tenderness of gums, mild treatment ineffective, symptoms > 3 days** plus mandibular pain, trismus, signs sepsis	Hospitalization with broad spectrum antibiotics: • Ampicillin/sulbactam 2 g IV q 4 hours • Penicillin allergy: Clindamycin 600 mg IV q 6 hours

Antibiotic Prophylaxis prior to Procedure:

Infective endocarditis is rare following a dental procedure and proper prophylaxis only prevents a small number of infective endocarditis cases. Prophylaxis is recommended in patients at an increased risk of developing infective endocarditis. Examples of patients at an increased risk of developing infective endocarditis are as follows:

- Artificial heart valves
- A history of infective endocarditis
- Cardiac transplant that develops heart valve problems
- Patients with unrepaired or incompletely repaired congenital heart disease, or completely repaired congenital heart defects with prosthetic material

In 2016 American Dental Association (ADA) & American Academy of Orthopedic Surgeons (AAOS) do not recommend antibiotic prophylaxis prior to dental procedures for most patients.[3]

Antibiotic prophylaxis may be appropriate in a select set of patients with prosthetic joints based on immune status, diabetes control, or history of peri-prosthetic infections and/or time since prosthetic placement. See http://www.orthoguidelines.org/go/auc/default.cfm?auc_id=224995&actionxm=Terms

Antibiotics for Prophylaxis:[3]

- Amoxicillin 500mg 4 capsules by mouth 30 to 60 minutes prior to dental procedure
- Cephalexin 500mg 4 capsules by mouth 30 to 60 minutes prior to dental procedure
- Azithromycin or Clarithromycin 500mg tablet by mouth 30 to 60 minutes prior to dental procedure

*Note the 2016 AAOS and ADA recommendations removed Clindamycin as an option

Reference:

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4. Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association. *Circulation* 2007; 116:1736-54.
5. American Academy of Orthopaedic Surgeons and American Dental Association. Appropriate use criteria for management of patients with orthopaedic implants undergoing dental procedures. https://aaos.webauthor.com/go/auc/terms.cfm?auc (Accessed October 11, 2017)

Clostridium Difficile

Clostridium difficile (C. diff or CDI*)* is an anaerobic infection of the gastrointestinal (GI) tract, which often arise from endogenous sources. Infection with toxin-producing strains of *C. diff* range from symptomless carriage, to mild or moderate diarrhea, to fulminant or fatal pseudomembranous colitis. CDI accounts for 20%-30% of antibiotic-associated diarrhea and is the most commonly recognized cause of infectious diarrhea in healthcare settings. Although mortality is low, attributable costs for severe and recurrent infections is a major burden to the healthcare system, therefore, prevention is key. CDI is difficult to treat and recurs in at least 20% of cases, even when treated appropriately.

Prevention:

Minimize the frequency and duration of antimicrobial therapy to reduce CDI risk. Consider reducing chronic use of proton pump inhibitors (PPIs), as they increase the susceptibility to CDI and can have an additive effect on susceptibility when used with antibiotics. Basic infection control practices are advised to minimize the spread of CDI. This may include hand hygiene, contact isolation and environmental cleaning. Probiotics are **NOT** recommended to prevent primary CDI, as there are limited data to support this approach.

High Risk and Prophylaxis Considerations:	
- Recent hospitalization or known contact in the community - Immunocompromised - Female gender - Age > 65 years	- Prior abx in previous 90 days - Risk of causing *C. difficile*: PPI>H2 Blockers>Antacids - Antineoplastic use in the past 8 weeks - Loss of intestinal function or Ileus/obstruction - Recent procedures: Enema/NG Tube/Surgical Procedure
High Risk Antibiotics: - 3rd/4th generation cephalosporins - Clindamycin - Beta-lactam/Beta-Lactamase Inhibitors	- Fluoroquinolones - Carbapenems
Consider prophylaxis with Vancomycin 125mg PO BID in patients who have had a *C. difficile* infection diagnosis within the last 6 months and placed on high risk antibiotics. Continue vancomycin for duration of concomitant antibiotic therapy PLUS an additional 7 days upon discontinuing the high risk causative antibiotic	

Testing Considerations:

Stool culture is the most sensitive test. Empiric treatment is not recommended unless severe or complicated disease, wait for stool culture results to begin treatment. Test of cure should not be performed.

- Only test patients who have ≥ 3 loose stools in a 24 hour period and not on laxatives.
- Children <2 years old should not be tested for C.difficile when presenting with diarrhea due to high carriage rates and high risk of false positive results

Treatment:

Discontinue antimicrobial agent(s) immediately, as this may influence the risk of CDI. Do **NOT** use antiperistalsis agents such as loperamide, atropine/diphenoxylate, bismuth subsalicylate if a definitive diagnosis of CDI exits.

Clinical definition	Supportive clinical data	Treatment
Initial episode Non-severe	a. Leukocytosis b. WBC <15,000 cells/mm3 c. SCr <1.5x baseline	**Adult**: Vancomycin 125mg PO QID for 10 days **OR** Fidaxomicin 200mg PO BID for 10 days **OR** *Alternative (if above agents are unavailable):* Metronidazole€ 500mg PO TID for 10 days **Peds**: Metronidazole 7.5mg /kg/dose PO TID **OR** Vancomycin 10mg/kg/dose QID
Severe	a. Leukocytosis b. WBC >15,000 cells/mm3 c. SCr >1.5x baseline	**Adult**: Same as non-severe treatment with the exception of Metronidazole **Peds**: Vancomycin 10mg/kg/dose QID for 10 days

Severe, fulminant	Hypotension or shock, ileus, megacolon	Vancomycin 500mg PO QID* (PO or by NG tube) **PLUS** Metronidazole 500mg IV Q8H If ileus **ADD** Vancomycin 500mg in 100mL SWNS rectally QID as retention enema
1st recurrence	If metronidazole was used as initial tx If vancomycin was used as initial tx	Vancomycin 125mg PO QID for 10 days Vancomycin in a tapered and/or pulsed regimen[ǂ] **OR** Fidaxomicin 200mg PO BID for 10 days
2nd or subsequent recurrence	- Pt with >2 recurrences	Vancomycin in a tapered and/or pulsed regimen[ǂ] **OR** Vancomycin 125mg PO QID for 10 days followed by rifaximin 400 mg TID for 20 days (30 days total) **OR** Fidaxomicin 200mg PO BID for 10 days Consider Fecal microbiota transplantation
[€]Metronidazole should not be used beyond the first recurrence or for long-term therapy because of the potential for cumulative neurotoxicity. *[ǂ]Example of tapered/pulsed dose = 125 mg QID for 14 days, BID for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks (6-12 weeks total treatment)*		

References:

1. Abou Chakra CN, Pepin J, Sirard S, et al. Risk factors for recurrence, complications and mortality in Clostridium difficile infection: a systematic review. PLoS One. 2014;9(6):e98400.
2. McDonald LC, Gerding DN, Johnson S, et al. Clinical practice guidelines for Clostridium difficile infection in adults and children: 2017 update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Disease. 2018. Available http://www.idsociety.org/Guidelines/Patient_Care/IDSA_Practice_Guidelines/Infections_By_Organ_System-81567/Gastrointestinal/Clostridium_difficile/
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4. Rao K, Young VB. Fecal microbiota transplantation for the management of Clostridium difficile infection. Infect Dis Clin North Am 2015;29(1):109-22
5. Hota SS, et al. Fecal Transplant vs Vancomycin Taper. CID. 2017:64(3);265-71. Clinical Practice Guidelines for Clostridium difficile Infection in Adults. Infect Control Hosp Epidemiol. 2010;31(5):431-

Helicobacter pylori

Helicobacter pylori (*H. pylori*) is a common infection of the upper gastrointestinal (GI) tract that may lead to gastritis, peptic ulcer disease (PUD), or malignancy. Eradication of *H. pylori* is vital; reviewing current first line treatment options will help to have the highest success rates and the least acquired resistance to therapy. Testing for resistance is costly and/or invasive, so empiric therapy is the best option for Indian Health Service (IHS) patients.

There is a limited amount of quality resistance and sensitivity data for *H. Pylori* in the United States (US). In the US, a recent study showed clarithromycin resistance >30% in a variety of healthcare systems, showing a trend for increasing resistance in different areas around the US. Larger studies looking at US resistance to clarithromycin are missing. Another recent study involving Alaska Natives reports local clarithromycin resistance patterns around 30-36% (compared to 16% in US veterans population), and metronidazole resistance at 42-65% (compared to 20% in US veterans population). For Alaska Natives, consider using amoxicillin-containing regimens over metronidazole-containing regimens, and consider using clarithromycin-containing regimens if resistance patterns are known.
Use local resistance data to determine preferred treatment.

First-line treatment options	Considerations
Triple[ŧ]: 14 days 1. Clarithromycin 500 mg BID, 2. PPI BID, 3. amoxicillin 1g BID *OR* metronidazole 500 mg TID	Use if local resistance patterns support use of clarithromycin Option for PCN allergy
Bismuth Quadruple[ŧ]: 14 days 1. Bismuth 300 mg QID, 2. metronidazole 250 mg QID, 3. tetracycline 500mg QID, 4. PPI BID	Option for PCN allergy Use if previous macrolide exposure for any reason[€] *Possible First-line in Alaska Natives*
First-line treatment options	Considerations
Sequential: 14 days 1. PPI and amoxicillin 1 g BID x 7 days, *then* 2. PPI, tinidazole/metronidazole 500mg, and clarithromycin 500 mg BID x 7 days	Use if local resistance patterns support use of clarithromycin Complex dosing

Alternative First-line options	Considerations
Concomitant*: 14 days 1. PPI BID, 2. clarithromycin 500mg BID, 3. tinidazole/metronidazole 500mg BID, 4. amoxicillin 1 g BID	Use if local resistance patterns support use of clarithromycin Lack of data from North America
Hybrid*: 14 days o PPI and amoxicillin 1 g BID x 7 days, *then* o PPI, amoxicillin 1 g, tinidazole/metronidazole 500mg, and clarithromycin 500 mg BID x 7 days	Use if local resistance patterns support use of clarithromycin Complex dosing Lack of data from North America
Levofloxacin triple*: 14 days 1. PPI BID, 2. amoxicillin 1 g BID, 3. levofloxacin 500mg QD	Use if previous macrolide exposure for any reason Lack of data from North America
Levofloxacin sequential*: 14 days 1. PPI and amoxicillin 1 g BID x 7 days, *then* 2. PPI, amoxicillin 1 g and tinidazole/metronidazole 500mg BID, with levothyroxine 500mg QD x 7 days	Use if previous macrolide exposure for any reason Lack of data from North America
LOAD*: 10 days 1. PPI (double dose) QD, 2. levofloxacin 250mg QD, 3. doxycycline 100mg QD, 4. nitazoxanide 500mg BID	Option for PCN allergy Lack of data from North America
**new to American College of Gastroenterology 2017 guideline update* *[ǂ]PPI-clarithromycin-amoxicillin combinations and Pylera® (bismuth, tetracycline, metronidazole) + plus PPI are the only FDA-approved regimens* *[€]although metronidazole resistance does have an impact on the efficacy of bismuth quadruple therapy, it is not nearly as profound as that of clarithromycin resistance on clarithromycin triple therapy*	

Salvage Therapy for Persistent Infection	Considerations
Bismuth quadruple: Same as above	Use if: received clarithromycin-triple therapy PCN allergy Quinolone exposure
Levofloxacin triple: Same as above	Use if: received bismuth quadruple therapy
Concomitant*: Same as above	Use if: received bismuth quadruple therapy previous quinolone exposure
Rifabutin triple*: 10 days 1. PPI BID, 2. Rifabutin 300mg QD, 3. amoxicillin 1 g BID	Use if: received bismuth quadruple therapy *or* clarithromycin-triple therapy previous quinolone exposure
High-dose dual*: 14 days 1. PPI TID, 2. amoxicillin 1 g TID	Use if: received bismuth quadruple therapy *or* clarithromycin-triple therapy previous quinolone exposure
**new to American College of Gastroenterology 2017 guideline update*	

References *H. pylori*:

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1. 4.. Park JY, Dunbar KB, Mitui M, et al. *Helicobacter pylori* clarithromycin resistance and treatment failure are common in the USA. *Dig Dis Sci*. Published online Feb 29, 2016. Available from: link.springer.com. Accessed Mar 1, 2016.
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5. Luther J, Higgins PDR, Schoenfeld PS, et al. Empiric quadruple vs. triple therapy for primary treatment of *Helicobacter pylori* infection: systematic review and meta-analysis of efficacy and tolerability. *Am J of Gastroenterol*. 2010;105:65-73. Available from: www.researchgate.net. Accessed Mar 1, 2016.
6. Eisig JN, Navarro-Rodriguez T, Sa Teixeira AC, et al. Standard triple therapy versus sequential therapy in *Helicobacter pylori* eradication: a double-blind, randomized, and controlled trial. *Gastroenterology Research and Practice*. 2015;vol 2015:article ID 818043, 5pages. Available from: www.hindawi.com. Accessed Mar 1, 2016.
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8. Seddik H, Ahid S, El Adioui T, et al. Sequential therapy versus standard triple-drug therapy for *Helicobacter pylori* eradication: a prospective randomized study. *Eur J Clin Pharmacol.* 2013;69:1709-1715. Available from: link.springer.com. Accessed Mar 7, 2016.

Lyme Disease

The most common tick-borne disease in the United States caused by the spirochete *Borrelia burgdorferi* and transmitted by the bite of two *Ixodes* ticks found in North America. These species include *Ixodes scapularis* (deer/bear tick) found in the Midwest and Eastern regions of North America and *Ixodes pacificus* (Western black-legged tick) found in the Western coastal region. Prophylactic treatment may be indicated for some patients.

Prophylaxis	
Must meet **ALL** criteria for antibiotic prophylaxis following a tick bite	1. Tick is identified as an adult or nymphal *I. scapularis* tick (deer tick) 2. Tick has been attached for approximately ≥36 hours (by engorgement or time of exposure) 3. Prophylaxis is begun within 72 hours after tick has been removed 4. Local rate of infection with *B. burgdorferi* is ≥ 20% 5. There are no contraindications to doxycycline
Adults Children 8 years and older	**Doxycycline 200 mg PO given once** **Doxycycline 4 mg/kg (max of 200 mg) once**

Preferred Treatment Options		
Medication	Dose for Children	Dose for Children
Oral regimens **Amoxicillin** **Doxycycline** **Cefuroxime**	500mg PO TID 100mg PO BID 500mg PO BID	50mg/kg/day (max 500mg/dose) divided TID *≥8 years old*, 4 mg/kg (max of 200 mg) 30mg/kg/day (max 500mg/dose) divided BID
Parental regimens **Ceftriaxone** **Cefotaxime** **Penicillin G**	2g IV daily 2g IV q8h 18-24 million units IV q4h	50-75 mg/kg (max 2g) IV daily 150-200 mg/kg/day (max 6g/day) IV divided doses q6-8h 200,000-400,000 U/kg/day (max 18-24 million units/day) divided dose q4h
**Please note other alternatives are available but are less effective* **Avoid doxycycline in pregnancy/lactation and children <8 years old* **Switching from IV to oral should be individualized*		

Treatment	
Early Disease	Occurs a few days to one month from a deer/bear tick bite.
erythema migrans	Oral regimen x 14 days (range 14-21 days)
Early Disseminated (neurologic) Disease	Weeks to months after tick bite.
Isolated Facial Nerve Palsy	Oral regimen x 14 days (range 14-21 days)
Meningitis or radiculopathy	Parental regimen x 14 days (range 10-28 days)
Cardiac Disease	Atrioventricular heart block and/or myopericarditis
Asymptomatic	Oral regimen x 14 days (range 14-21 days)
Symptomatic	Parental regimen x 14 days (range 14-21 days)
Late Disease	Monoarticular or oligoarticular form of arthritis that typically involves the knee.
Arthritis without neurologic disease	Oral regimen x 28 days
Arthritis with neurologic disease	Parental regimen x 28 days
Recurrent Arthritis	Oral regimen x 28 days or Parental regimen x 14 days (parental range 14-28 days)

Reference Lyme:

1. Wormser, GP, Dattwyer, RJ, Shapiro, ED, et al. The Clinical Assessment, Treatment, and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis, and Babesiosis: Clinical Practice Guidelines by the Infectious Disease Society of America. Clin Infect Dis m 2006;43:1089.

Sexually Transmitted Diseases

Reference: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Anogenital Warts

Recommended Regimens for External Anogenital Warts (i.e., penis, groin, scrotum, vulva, perineum, external anus, and perianus*)

- Patient applied:
  - Imiquimod 3.75% or 5% cream† ***OR***
  - Podofilox 0.5% solution or gel ***OR***
  - Sinecatechins 15% ointment†

- Provider Administered:
  - Cryotherapy with liquid nitrogen or cryoprobe ***OR***
  - Surgical removal either by tangential scissor excision, tangential shave excision, curettage, laser, or electrosurgery ***OR***
  - Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%–90% solution

Many persons with external anal warts also have intra-anal warts. Thus, persons with external anal warts might benefit from an inspection of the anal canal by digital examination, standard anoscopy, or high-resolution anoscopy.

†Might weaken condoms and vaginal diaphragms

Recommended Regimens for Urethral Meatus Warts

- Cryotherapy with liquid nitrogen ***OR***
- Surgical removal

Recommended Regimens for Vaginal Warts

- Cryotherapy with liquid nitrogen - the use of a cryoprobe in the vagina is not recommended because of the risk for vaginal perforation and fistula formation ***OR***
- Surgical removal ***OR***
- TCA or BCA 80-90% solution

Recommended Regimens for Cervical Warts

- Cryotherapy with liquid nitrogen ***OR***
- Surgical Removal ***OR***
- TCA or BCA 80-90% solution
- Management of cervical warts should include consultation with a specialist.
- For women who have exophytic cervical warts, a biopsy evaluation to exclude high-grade SIL must be performed before treatment is initiated.

Recommended Regimens for Intra-anal Warts

- Cryotherapy with liquid nitrogen ***OR***
- Surgical removal ***OR***
- TCA or BCA 80-90% solution
- Management of intra-anal warts should include consultation with a specialist.

Pregnancy Recommendations

- There is insufficient data on human subjects to determine pregnancy risk with imiquimod therapy. Animal data suggests imiquimod is low risk for pregnant women, but use should be avoided until further data is collected.
- Podofolix (podophyllotoxin), podophillin, and sinecatechins should not be used during pregnancy.
- Removal of anogenital warts can be considered, but resolution may be incomplete or poor until pregnancy is complete.

Management of Sex Partners

- Persons should inform current partner(s) about having genital warts because the types of HPV that cause warts can be passed on to partners.
- Partners should receive counseling messages that partners might already have HPV despite no visible sign of warts, so HPV testing of sex partners of persons with genital warts is not recommended.
- Partner(s) might benefit from a physical examination to detect genital warts and tests for other STDs.

Bacterial Vaginosis

Recommended Regimens

- Metronidazole 500mg orally twice a day for 7 days ***OR***
- Metronidazole gel 0.75%, one full applicator (5 g) intravaginally once a day for 5 days ***OR***
- Clindamycin cream 2%, one full applicator (5g) intravaginally at bedtime for 7 days

Alternative Regimens

- Tinidazole 2 g orally once daily for 2 days ***OR***
- Tinidazole 1 g orally once daily for 5 days ***OR***
- Clindamycin 300 mg orally twice daily for 7 days ***OR***
- Clindamycin ovules 100 mg intravaginally once at bedtime for 3 days*

Clindamycin ovules use an oleaginous base that might weaken latex or rubber products (e.g., condoms and vaginal contraceptive diaphragms). Use of such products within 72 hours following treatment with clindamycin ovules is not recommended.

Pregnancy Recommendations

- Because oral therapy has not been shown to be superior to topical therapy for treating symptomatic BV in effecting cure or preventing adverse outcomes of pregnancy, symptomatic pregnant women can be treated with either of the oral or vaginal regimens recommended for non-pregnant women.
- Treatment is recommended for all symptomatic pregnant women.
- There is insufficient data on human subjects to determine pregnancy risk with tinidazole therapy. Animal data suggests moderate pregnancy risk. Use should be avoided.

Management of Sex Partners

- Routine treatment of sex partners is not recommended.

Cervicitis

Recommended Regimens for Presumptive Treatment*

- Azithromycin 1 g orally in a single dose ***OR***
- Doxycycline 100 mg orally twice a day for 7 days

Consider concurrent treatment for gonococcal infection if patient is at risk for gonorrhea or lives in a community where the prevalence of gonorrhea is high.

Pregnancy Recommendations

- Azithromycin 1 g orally in a single dose

Management of Sex Partners

- Management of sex partners of women treated for cervicitis should be appropriate for the specific STD identified or suspected.
- All sex partners in the past 60 days should be referred for evaluation, testing, and presumptive treatment if chlamydia, gonorrhea, or trichomoniasis was identified or suspected in the women with cervicitis.
- EPT or other effective partner referral strategies are alternative approaches to treating male partners of women who have chlamydia or gonococcal infection.
- To minimize transmission and reinfection, women treated for cervicitis should be instructed to abstain from sexual intercourse until they and their partner(s) have been adequately treated (i.e., for 7 days after single-dose therapy or until completion of 7-day regimen) and symptoms have resolved.

Chancroid

Recommended Regimens

- Azithromycin 1 g orally in a single dose ***OR***
- Ceftriaxone 250 mg IM in a single dose ***OR***

- Ciprofloxacin 500 mg orally twice a day for 3 days ***OR***
- Erythromycin base 500 mg orally three times a day for 7 days

Other Management Considerations

- Men who are uncircumcised and patients with HIV do not respond as well to treatment as males who are circumcised or HIV-negative.
    - Patients with HIV infection might require repeated or longer courses of therapy and treatment failures can occur with any regimen.
- Patients should be tested for HIV infection at the time chancroid is diagnosed.
- If the initial test results were negative, a serologic test for syphilis and HIV infection should be performed 3 months after the diagnosis of chancroid.

Pregnancy Recommendations

- Azithromycin 1 g orally in a single dose ***OR***
- Erythromycin base 500 mg orally three times a day for 7 days

Management of Sex Partners

- Regardless of whether symptoms of the disease are present, sex partners who have had sexual contact with patients who have chancroid during the 10 days preceding the patient's onset of symptoms should be examined and treated.

Chlamydia Infections

Chlamydia treatment in Adults and Adolescents

- Recommended Regimens
    - Azithromycin 1 g orally in a single dose ***OR***
    - Doxycycline 100 mg orally twice a day for 7 days

- Alternative Regimens
    - Erythromycin base 500 mg orally four times a day for 7 days ***OR***
    - Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days ***OR***
    - Levofloxacin 500 mg orally once daily for 7 days ***OR***
    - Ofloxacin 300 mg orally twice a day for 7 days

Pregnancy Recommendations

- Recommended Regimen
    - Azithromycin 1 g orally in a single dose

- Alternative Regimens
    - Amoxicillin 500 mg orally three times a day for 7 days ***OR***
    - Erythromycin base 500 mg orally four times a day for 7 days ***OR***
    - Erythromycin base 250 mg orally four times a day for 14 days ***OR***
    - Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days ***OR***

- Erythromycin ethylsuccinate 400 mg orally four times a day for 14 days

Other Management Considerations

- To maximize adherence with recommended therapies, onsite, directly observed single-dose therapy with azithromycin should always be available for a patient for whom adherence with multiday dosing is a concern.
- In addition, for multidose regimens, the first dose should be dispensed on site and directly observed.

Management of Sex Partners

- Sexual partners should be referred for evaluation, testing, and presumptive treatment if they had sexual contact with the partner during the 60 days preceding the patient's onset of symptoms or chlamydia diagnosis.
- Among heterosexual patients, if health department partner management strategies (e.g., disease intervention specialists) are impractical or not available for persons with chlamydia and a provider is concerned that sex partners are unable to promptly access evaluation and treatment services (EPT), EPT should be considered as permitted by law.
    - EPT although not routinely recommended for management of sex partners with chlamydia because of a high risk for coexisting infections (especially undiagnosed HIV) among their partners, and because data is limited regarding the effectiveness of this approach in reducing persistent or recurrent chlamydia among MSM, it is routinely recommended in the States where it is legal for I.H.S.
- To minimize disease transmission to sex partners, persons treated for chlamydia should be instructed to abstain from sexual intercourse for 7 days after single-dose therapy or until completion of a 7-day regimen and resolution of symptoms if present. Also, to avoid reinfection, patients should be instructed to abstain from sexual intercourse until all of their sex partners are treated.

Ophthalmia Neonatorum and Infant Pneumonia caused by *C. trachomatis*

- Recommended Regimen
    - Erythromycin base or ethylsuccinate 50 mg/kg/day orally divided into 4 doses daily for 14 days*

- Alternative Regimen
    - Azithromycin suspension, 20 mg/kg/day orally, 1 dose daily for 3 days*

An association between oral erythromycin and azithromycin and infantile hypertrophic pyloric stenosis (IHPS) has been reported in infants aged <6 weeks. Infants treated with either of these antimicrobials should be followed for signs and symptoms of IHPS.

Infant Pneumonia Caused by *C. trachomatis*

- Recommended Regimen
    - Erythromycin base or ethylsuccinate 50 mg.kg/day orally divided into 4 doses daily for 14 days

- Alternative Regimen

- Azithromycin 20 mg/kg/day orally, 1 dose daily for 3 days

Chlamydial Infections among Infants and Children

- Recommended Regimen for Infants and Children Who Weigh <45 kg:
  - Erythromycin base or ethylsuccinate 50 mg/kg/day orally divided into 4 doses daily for 14 days

- Recommended Regimen for Children Who Weigh ≥45 kg but Who Are Aged <8 Years:
  - Azithromycin 1 g orally in a single dose

- Recommended Regimens for Children Aged ≥8 years:
  - Azithromycin 1 g orally in a single dose ***OR***
  - Doxycycline 100 mg orally twice a day for 7 days

Epididymitis

For acute epididymitis most likely caused by sexually transmitted chlamydia and gonorrhea

- Ceftriaxone 250 mg IM in a single dose PLUS Doxycycline 100 mg orally twice a day for 10 days

For acute epididymitis most likely caused by sexually transmitted chlamydia and gonorrhea and enteric organisms (men who practice insertive anal sex)

- Ceftriaxone 250 mg IM in a single dose PLUS Levofloxacin 500 mg orally once a day for 10 days ***OR*** Ofloxacin 300 mg orally twice a day for 10 days

For acute epididymitis most likely caused by enteric organisms

- Levofloxacin 500 mg orally once daily for 10 days ***OR***
- Ofloxacin 300 mg orally twice a day for 10 days

Management of Sex Partners

- Men who have acute sexually transmitted epididymitis confirmed or suspected to be caused by *N. gonorrhoeae* or *C. trachomatis* should be instructed to refer for evaluation, testing, and presumptive treatment all sex partners with whom they have had sexual contact within the 60 days preceding onset of symptoms.
- If the last sexual intercourse was > 60 days before onset of symptoms or diagnosis, the most recent sex partner should be treated.
- Arrangements should be made to link female partners to care.
- EPT and enhanced referral are effective strategies for treating female sex partners of men who have chlamydia or gonorrhea for whom linkage to care is anticipated to be delayed.
- Partners should be instructed to abstain from sexual intercourse until they and their sex partners are adequately treated and symptoms have resolved.

Ectoparasitic Infections

Pediculosis Pubic

- Recommended Regimens
  - Permethrin 1% cream rinse applied to affected areas and washed off after 10 minutes ***OR***
  - Pyrethrins with piperonyl butoxide applied to the affected area and washed off after 10 minutes

- Alternative Regimens
  - Malathion 0.5% lotion applied to affected areas and washed off after 8–12 hours ***OR***
  - Ivermectin 250 ug/kg orally, repeated in 2 weeks

- Pregnancy Recommendations
  - Permethrin 1% cream rinse applied to affected areas and washed off after 10 minutes ***OR***
  - Pyrethrins with piperonyl butoxide applied to the affected area and washed off after 10 minutes

- Management of Sex Partners
  - Sex partners within the previous month should be treated.
  - Sexual contact should be avoided until patients and partners have been treated, bedding and clothing decontaminated, and reevaluation performed to rule out persistent infection.

Scabies

- Recommended Regimens
  - Permethrin 5% cream applied to all areas of the body from the neck down and washed off after 8–14 hours* ***OR***
  - Ivermectin 200ug/kg orally, repeated in 2 weeks**

Infants and young children should be treated with permethrin.

- Alternative Regimens
  - Lindane (1%) 1 oz of lotion or 30 g of cream applied in a thin layer to all areas of the body from the neck down and thoroughly washed off after 8 hours†

†Infants and young children aged< 10 years should not be treated with Lindane.

- Pregnancy Recommendations
  - Permethrin 5% cream applied to all areas of the body from the neck down and washed off after 8–14 hours

- Management of Sex Partners and Household Contacts
    - Persons who have had sexual, close personal, or household contact with the patient within the month preceding scabies infestation should be examined.
    - Those found to be infested should be provided treatment.
    - Infants and young children should be treated with permethrin; infants and children <10 years should not be treated with Lindane.

Gonococcal Infections

Uncomplicated Gonococcal Infections of Cervix, Urethra, and Rectum

- Recommended Regimen
    - Ceftriaxone 250 mg IM in a single dose ***PLUS*** Azithromycin 1 g orally in a single dose*

- Alternative regimens, if ceftriaxone not available
    - Cefixime 400 mg orally in a single dose ***PLUS*** Azithromycin 1 g orally in a single dose*

- Regimens to be considered in the presence of cephalosporin allergy:
    - Gemifloxacin 320 mg orally in a single dose ***PLUS*** Azithromycin 2 g orally in a single dose ***OR***
    - Gentamicin 240 mg IM single dose ***PLUS*** Azithromycin 2 g orally in a single dose

In the case of azithromycin allergy, doxycycline (100 mg orally twice a day for 7 days) can be used in place of azithromycin as an alternative second antimicrobial when used in combination with ceftriaxone or cefixime.

Recommended Treatment for Uncomplicated Gonococcal Infections of the Pharynx

- Ceftriaxone 250 mg IM in a single dose ***PLUS*** Azithromycin 1 g orally in a single dose

Recommended Treatment for Gonococcal Conjunctivitis in Adults and Adolescents

- Ceftriaxone 1 g IM single dose ***PLUS*** Azithromycin 1 g orally in a single dose

Treatment of Arthritis and Arthritis-Dermatitis Syndrome*

- Recommended Regimen
    - Ceftriaxone 1 g IM or IV every 24 hours for at least 7 days ***PLUS*** Azithromycin 1 g orally in a single dose

- Alternative Regimens
    - Cefotaxime 1 g IV every 8 hours for at least 7 days ***OR***
    - Ceftizoxime 1 g IV every 8 hours for at least 7 days ***PLUS*** Azithromycin 1 g orally in a single dose

When treating for the arthritis-dermatitis syndrome, the provider can switch to an oral agent guided by antimicrobial susceptibility testing 24-48 hours after substantial clinical improvement, for a total treatment course of at least 7 days.

Recommended Regimen for Gonococcal Meningitis and Endocarditis

- Ceftriaxone 1-2 g IV every 12-24 hours ***PLUS*** Azithromycin 1 g orally in a single dose
- Duration of treatment should be determined in consultation with an Infectious Disease specialist
    - Therapy for meningitis should be continued for 10-14 days
    - Therapy for endocarditis should be administered for at least 4 weeks

Pregnancy Recommendations

- Ceftriaxone 250 mg in a single IM dose + Azithromycin 1 g orally in a single dose
- If a cephalosporin allergy exists and spectinomycin is unavailable, consultation with an infectious disease specialist is recommended.

Management of Sex Partners

- Recent sex partners (i.e., persons having sexual contact with the infected patient within the 60 days preceding onset of symptoms or gonorrhea diagnosis) should be referred for evaluation, testing, and presumptive dual treatment.
- To avoid reinfection, sex partners should be instructed to abstain from unprotected sexual intercourse for 7 days after they and their sexual partner(s) have completed treatment and after resolution of symptoms.
- For heterosexual men and women with gonorrhea for whom health department partner-management strategies are impractical or unavailable and whose providers are concerned about partners' access to prompt clinical evaluation and treatment, EPT with the following treatment regimen can be delivered to the partner by the patient, a disease investigation specialist, or a collaborating pharmacy as permitted by law:
    - Cefixime 400 mg orally in a single dose ***PLUS*** Azithromycin 1 g orally in a single dose
- EPT should not be considered a routine partner management strategy in management of sex partners with gonorrhea because of a high risk for coexisting infections (especially HIV) and because no data exists on efficacy in this population.

***Fluoroquinolones and oral cephalosporins are no longer recommended due to resistance patterns.**

Treatment failure: culture relevant clinical specimens and perform antimicrobial susceptibility test of *N. gonorrhoeae* isolates. The provider should seek treatment advice from an infectious disease specialist and report the case to the CDC through the local or state health department within 24 hours of diagnosis. A test-of-cure should be conducted 1 week after re-treatment, and clinicians should ensure that the patient's sex partners from the preceding 60 days are evaluated promptly with culture and treated as indicated.

EPT:
Due to resistance patterns for oral cephalosporin agents in the treatment of gonorrhea, every effort should be made to ensure that a patient's sex partners from the past 60 days are evaluated and treated with a recommended regimen:

- Ceftriaxone 250mg IM as a single dose* ***PLUS EITHER***
- Azithromycin 1 g PO as a single dose ***OR***
- Doxycycline 100mg PO BID x 7 days

However, because that is not always possible, a provider can still consider EPT with the recommendation that the partner receive a **test-of-cure approximately one week after finishing their medication**. If the patient's partner is not likely to seek evaluation, testing, and treatment, patient delivery of antibiotic therapy to their partners can be considered. The patient must inform their partners of their infection and provide them with written materials about the importance of seeking evaluation for any symptoms suggestive of complications. Patient delivered partner therapy is not routinely recommended for men having sex with men (MSM) due to the high risk for coexisting infections, especially undiagnosed HIV, in their partners.
The oral regimen is:

- Cefixime 400mg PO as a single dose ***PLUS EITHER***
- Azithromycin 1 g PO as a single dose ***OR***
- Doxycycline 100mg PO BID x 7days

Additional Reference:
Guidance on the use of expedited partner therapy in the treatment of gonorrhea. Centers for Disease Control Web site. http://www.cdc.gov/std/ept/GC-Guidance.htm. Accessed 8/19/14.

Gonococcal Infections Among Neonates

Ophthalmia Neonatorum

- Recommended Regimen for Prophylaxis:
  - Erythromycin (0.5%) ophthalmic ointment in each eye in a single application at birth

- Recommended Regimen for Treatment:
  - Ceftriaxone 25-50 mg/kg IV or IM in a single dose, not to exceed 125 mg*

Ceftriaxone should be administered cautiously to hyperbilirubinemic infants, especially those born prematurely.

Recommended Regimen for DGI and Gonococcal Scalp Abscesses in Neonates

- Ceftriaxone 25-50 mg/kg/day IV or IM in a single daily dose for 7 days, with a duration of 10-14 days if meningitis is documented ***OR***
- Cefotaxime 25 mg/kg IV or IM every 12 hours for 7 days, with a duration of 10-14 days if meningitis is documented

Ceftriaxone should be administered cautiously to hyperbilirubinemic infants, especially those born prematurely.

Neonates Born to Mothers Who Have Gonococcal Infection

- Recommended Regimen in the Absence of Signs of Gonococcal Infection
  - Ceftriaxone 25-50 mg/kg IV or IM in a single dose, not to exceed 125 mg

Ceftriaxone should be administered cautiously to hyperbilirubinemic infants, especially those born prematurely.

Recommended Regimen for Infants and Children

- Recommended regimen for infants and children Who Weigh ≤ 45 kg and who have Uncomplicated Gonococcal Vulvovaginitis, Cervicitis, Urethritis, Pharyngitis, or Proctitis
  - Ceftriaxone 25-50 mg/kg IV or IM in a single dose, not to exceed 125 mg IM

- Recommended Regimen for Children Who Weigh > 45 kg and Who Have Uncomplicated Gonococcal Vulvovaginitis, Cervicitis, Urethritis, Pharyngitis, or Proctitis
  - Treat with one of the regimens recommended for adults

- Recommended Regimen for Children Who Weigh ≤ 45 kg and Who Have Bacteremia or Arthritis
  - Ceftriaxone 50 mg/kg (maximum dose: 1 g) IM or IV in a single dose daily for 7 days

- Recommended Regimen for Children Who Weigh ≤ 45 kg and Who Have Bacteremia or Arthritis
  - Ceftriaxone 1 g IM or IV in a single dose daily every 24 hours for 7 days

Herpes Simplex Virus (HSV)

Recommended Regimens for First Clinical Episode of Genital Herpes*

- Acyclovir 400 mg orally three times a day for 7–10 days ***OR***
- Acyclovir 200 mg orally five times a day for 7–10 days ***OR***
- Valacyclovir 1 g orally twice a day for 7–10 days ***OR***
- Famciclovir 250 mg orally three times a day for 7–10 days

Treatment can be extended if healing is incomplete after 10 days of therapy.

Recommended Regimens for Suppressive Therapy in Recurrent Genital Herpes

- Acyclovir 400 mg orally twice a day ***OR***
- Valacyclovir 500 mg orally once a day* ***OR***
- Valacyclovir 1 g orally once a day ***OR***
- Famiciclovir 250 mg orally twice a day

Valacyclovir 500 mg once a day might be less effective than other valacyclovir or acyclovir dosing regimens in persons who have very frequent recurrences (i.e., ≥10 episodes per year).

Recommended Regimens for Episodic Therapy in Recurrent Genital Herpes

- Acyclovir 400 mg orally three times a day for 5 days ***OR***
- Acyclovir 800 mg orally twice a day for 5 days ***OR***
- Acyclovir 800 mg orally three times a day for 2 days ***OR***
- Valacyclovir 500 mg orally twice a day for 3 days ***OR***
- Valacyclovir 1 g orally once a day for 5 days ***OR***
- Famciclovir 125 mg orally twice daily for 5 days ***OR***
- Famciclovir 1 gram orally twice daily for 1 day ***OR***
- Famciclovir 500 mg once, followed by 250 mg twice daily for 2 days

Recommended regimen for suppressive therapy of pregnant women with recurrent genital herpes*

- Acyclovir 400 mg orally three times a day ***OR***
- Valacyclovir 500 mg orally twice a day

Treatment recommended starting at 36 weeks of gestation.

Recommended Regimen for Severe Disease

- IV acyclovir therapy should be provided for patients who have severe HSV disease or complications that necessitate hospitalization (e.g. disseminated infection, pneumonitis, or hepatitis) or CNS complications (e.g. meningoencephalitis).
- Acyclovir 5-10 mg/kg IV Q8 hours for 2-7 days or until clinical improvement is observed, followed by oral antiviral therapy to complete at least 10 days of total therapy.
    - HSV encephalitis requires 21 days of IV therapy.

Management of Sex Partners:

- Symptomatic sex partners should be evaluated and treated in the same manner as patients who have genital herpes.
- Asymptomatic sex partners of patients who have genital herpes should be questioned concerning histories of genital lesions and offered type-specific serologic testing for HSV infection.

Genital Herpes in Patients with HIV infection

Recommended Regimens for Daily Suppressive Therapy in Persons with HIV

- Acyclovir 400–800 mg orally twice to three times a day ***OR***
- Valacyclovir 500 mg orally twice a day ***OR***
- Famciclovir 500 mg orally twice a day

Recommended Regimens for Episodic Infection in Persons with HIV

- Acyclovir 400 mg orally three times a day for 5–10 days ***OR***
- Valacyclovir 1 g orally twice a day for 5–10 days ***OR***
- Famciclovir 500 mg orally twice a day for 5–10 days

Granuloma Inguinale

Recommended Regimen

- Azithromycin 1 g orally once per week or 500 mg daily for at least 3 weeks and until all lesions have completely healed

Alternative Regimens

- Doxycycline 100 mg orally twice a day for at least 3 weeks and until all lesions have completely healed ***OR***
- Ciprofloxacin 750 mg orally twice a day for at least 3 weeks and until all lesions have completely healed ***OR***
- Erythromycin base 500 mg orally four times a day for at least 3 weeks and until all lesions have completely healed ***OR***
- Trimethoprim-sulfamethoxazole one double-strength (800 mg/160 mg) tablet orally twice a day for at least 3 weeks and until all lesions have completely healed

Other Management Considerations

- The addition of another antibiotic to these regimens can be considered if improvement is not evident within the first few days of therapy.
    - Addition of an aminoglycoside to these regimens is an option (gentamicin 1 mg/kg IV Q 8 hours), especially in HIV infected patients, if improvement is not evident within the first few days of therapy.
- Patients should be followed clinically until signs and symptoms have resolved.
- All persons who receive a diagnosis of granuloma inguinale should be tested for HIV.

Pregnancy Recommendations

- Recommended Regimen
    - Azithromycin 1 g orally once per week or 500 mg daily for at least 3 weeks and until all lesions have completely healed
- Alternative Regimen
    - Erythromycin base 500 mg orally four times a day for at least 3 weeks and until all lesions have completely healed

- Addition of gentamicin 1 mg/kg IV every 8 hours can be considered if patient has not improved within the first few days of therapy.

Management of Sex Partners

- Persons who have had sexual contact with a patient with granuloma inguinale within the 60 days before onset of the patient's symptoms should be examined and offered therapy. However, the value of empiric therapy in the absence of clinical signs and symptoms has not been established.

Human Papillomavirus (HPV) Infection

Treatment is directed to the macroscopic (e.g., genital warts) or pathologic precancerous lesions caused by HPV. Subclinical genital HPV infection typically clears spontaneously; therefore, specific antiviral therapy is not recommended to eradicate HPV infection. Precancerous lesions are detected through cervical cancer screening; HPV-related pre-cancer should be managed based on existing guidance.

- Prevention of HPV:
    - Two vaccines currently exist to prevent diseases and cancers caused by HPV: Cervarix and Gardasil
        - Both vaccines protect against most cases of cervical cancer caused by HPV, but Gardasil also protects against most genital warts.
        - HPV vaccines are recommended routinely for boys and girls aged 11-12 years; either vaccine is recommended for girls/women, whereas only one vaccine (Gardasil) is recommended for boys/men.
        - Gardasil is recommended for women up to age of 26 and men who have sex with men up to age 26.
    - Condoms if used consistently and correctly can lower the chances of acquiring and transmitting HPV and developing HPV-related disease. However, because HPV can infect areas not covered by a condom, condoms might not fully protect against HPV.

Lymphogranuloma Vernereum

Recommended Regimen

- Doxycycline 100 mg orally twice a day for 21 days

Alternative Regimen

- Erythromycin base 500 mg orally four times a day for 21 days

Pregnancy Recommendations

- Erythromycin base 500 mg orally four times a day for 21 days

Management of Sex Partners

- Persons who have had sexual contact with a patient who has lymphogranuloma venereum within the 60 days before onset of the patient's symptoms should be examined and tested for urethral, cervical, or rectal chlamydial infection depending on anatomic site of exposure. They should be presumptively treated with a chlamydia regimen:
    - Azithromycin 1 g po single dose ***OR***
    - Doxycycline 100 mg po BID for 7 days.

Nongonococcal Urethritis (NGU)

Recommended Regimens

- Azithromycin 1 g orally in a single dose ***OR***
- Doxycycline 100 mg orally twice a day for 7 days

Alternative Regimens

- Erythromycin base 500 mg orally four times a day for 7 days ***OR***
- Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days ***OR***
- Levofloxacin 500 mg orally once daily for 7 days ***OR***
- Ofloxacin 300 mg orally twice a day for 7 days

Persistent and recurrent NGU

- Men initially treated with doxycycline:
    - Azithromycin 1g orally in a single dose
- Men who fail a regimen of azithromycin:
    - Moxifloxacin 400 mg orally once daily for 7 days
- Heterosexual men who live in areas where T. vaginalis is highly prevalent:
    - Metronidazole 2 g orally in a single dose ***OR***
    - Tinidazole 2 g orally in a single dose

Management of Sex Partners

- All sex partners of men with NGU within the preceding 60 days should be referred for evaluation, testing, and presumptive treatment with a drug regimen effective against chlamydia.
- Expedited partner therapy is an alternative approach to treating female partners for chlamydia in the absence of signs and symptoms of pelvic inflammatory disease.
- If *N. gonorrhea* or *T. vaginalis* is documented, all partners should be evaluated and treated according to the management section for their respective pathogen.
- To avoid reinfection, sex partners should abstain from sexual intercourse until they and their partner(s) are adequately treated.

Pelvic Inflammatory Disease

Parenteral Treatment

Recommended Regimens: All regimens are 14 days in duration

- Cefotetan 2 g IV every 12 hours **PLUS** Doxycycline 100 mg orally or IV every 12 hours ***OR***
- Cefoxitin 2 g IV every 6 hours **PLUS** Doxycycline 100 mg orally or IV every 12 hours ***OR***
- Clindamycin 900 mg IV every 8 hours **PLUS** Gentamicin loading dose IV or IM (2 mg/kg), followed by a maintenance dose (1.5 mg/kg) every 8 hours. Single daily dosing (3–5 mg/kg) can be substituted.
- Additional Info:
    - If using parenteral cefotetan or cefoxitin regimens, oral therapy with doxycycline 100 mg twice daily can be used 24-48 hours after clinical improvement to complete the 14 days of therapy.
    - For the clindamycin/gentamicin regimen, and oral therapy with clindamycin (450 mg orally four times daily) or doxycycline (100 mg twice daily) can be used to complete the 14 days of therapy.
    - When tubo-ovarian abscess is present, clindamycin (450mg PO QID) or metronidazole 500mg po BID)should be used to complete at least 14 days of therapy with doxycycline to provide more effective anaerobic coverage than doxycycline alone.

Alternative Parenteral Regimen

- Ampicillin/Sulbactam 3 g IV every 6 hours **PLUS** Doxycycline 100 mg orally or IV every 12 hours

Recommended Intramuscular or Oral Regimens

These can be considered for patients with mild-moderately severe PID. Women who do not respond to IM/oral therapy within 72 hours should be reevaluated to confirm the diagnosis and should be administered parenteral treatment.

- Ceftriaxone 250 mg IM in a single dose **PLUS** doxycycline 100 mg orally twice a day for 14 days WITH* or WITHOUT Metronidazole 500 mg orally twice a day for 14 days ***OR***
- Cefoxitin 2 g IM in a single dose and Probenecid 1 g orally administered concurrently in a single dose **PLUS** Doxycycline 100 mg orally twice a day for 14 days WITH or WITHOUT Metronidazole 500 mg orally twice a day for 14 days ***OR***
- Other parenteral third-generation cephalosporin (e.g., ceftizoxime or cefotaxime) **PLUS** Doxycycline 100 mg orally twice a day for 14 days WITH* or WITHOUT Metronidazole 500 mg orally twice a day for 14 days

The recommended third-generation cephalosporin are limited in the coverage of anaerobes. Therefore, until it is known that extended anaerobic coverage is not important for treatment of acute PID, the addition of metronidazole to treatment regimens with third-generation cephalosporin should be considered.

Pregnancy Recommendations

- Pregnant women with PID are at high risk for maternal morbidity and preterm delivery. They should be hospitalized and treated parenterally.
- Doxycycline should be avoided in pregnancy.

Management of Sex Partners

- Men who have had sexual contact with a woman with PID during the 60 days preceding her onset of symptoms should be evaluated, tested, and presumptively treated for chlamydia and gonorrhea, regardless of the etiology of PID or pathogens isolated from the woman.
- If a woman's last sexual intercourse was > 60 days before onset of symptoms or diagnosis, the most recent sex partner should be treated.
- Male partners of women who have PID caused by *C. trachomatis* and/or *N. gonorrhea* frequently are asymptomatic.
- Arrangements should be made to link male partners to care. If linkage is delayed or unlikely, EPT and enhanced referral are alternative approaches to treating male partners of women who have chlamydia or gonococcal infections.
- Partners should be instructed to abstain from sexual intercourse until they and their sex partners have been adequately treated (i.e., until therapy is completed and symptoms have resolved, if originally present).

Proctitis

Recommended treatment for acute proctitis

- Ceftriaxone 250 mg IM in a single dose **PLUS** Doxycycline 100 mg orally twice a day for 7 days

Management of Sex Partners

- Partners who have had sexual contact with persons treated for GC, CT, or LGV within the 60 days before the onset of the persons symptoms should be evaluated, tested, and presumptively treated for the respective pathogen.
- Partners of persons with sexually transmitted enteric infections should be evaluated for any disease diagnosed in the person with acute proctitis.
- Sex partners should abstain from sexual intercourse until they and their partner with acute proctitis are adequately treated.

Syphilis

Syphilis Definitions:
Late latent Syphilis is defined as: positive RPR with no symptoms and last negative RPR was > 12 months ago
Early Latent Syphilis is defined as: primary, secondary or RPR turned positive in the last 12 months

Primary and Secondary Syphilis

- Recommended Regimen:
  - Benzathine penicillin G 2.4 million units IM in a single dose

- Recommended Regimen for Infants and Children:
  - Benzathine penicillin G 50,000 units/kg IM, up to the adult dose of 2.4 million units in a single dose

- Alternative Regimens:
  - Doxycycline 100mg orally twice daily for 14 days ***OR***
  - Tetracycline 500mg orally four times daily for 14 days

Latent Syphilis

- Recommended Regimen for Early Latent Syphilis:
  - Adults: Benzathine penicillin G 2.4 million units IM in a single dose
  - Infants and Children: benzathine penicillin G 50,000 units/kg IM, up to the adult dose of 2.4 million units in a single dose

- Recommended Regimen for Late Latent Syphilis or Latent Syphilis with no symptoms, positive RPR and no prior RPR
  - Adults: Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals
  - Infants and Children: benzathine penicillin G 50,000 units/kg IM, up to the adult dose of 2.4 million units, administered as 3 doses at 1-week intervals (total 150,000 units/kg up to the adult total dose of 7.2 million units)

Tertiary Syphilis with Normal CSF Examination

- Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals

Neurosyphilis

- Recommended Regimen for Neurosyphilis and Ocular Syphilis:
  - Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units IV every 4 hours or continuous infusion, for 10–14 days

- Alternative Regimen:
    - If compliance with therapy can be ensured, the following alternative regimen might be considered:
        - Procaine penicillin G 2.4 million units IM once daily PLUS probenecid 500 mg orally four times a day, both for 10–14 days

Primary and Secondary Syphilis among Persons with HIV Infection

- Benzathine penicillin G, 2.4 million units IM in a single dose

Latent Syphilis among Persons with HIV Infection

- Early Latent Syphilis: Benzathine penicillin G, 2.4 million units IM in a single dose
- Late Latent Syphilis: Benzathine penicillin G, at weekly doses of 2.4 million units for 3 weeks

Pregnancy Recommendations

- Pregnant women should be treated with the penicillin regimen appropriate for their stage of infection. Penicillin allergic women: refer to allergist for desensitization.
- Some evidence suggests that additional therapy is beneficial for pregnant women. For women who have primary, secondary, or early latent syphilis, a second dose of benzathine penicillin 2.4 million units IM can be administered 1 week after the initial dose.
- Missed doses are not acceptable for pregnant women receiving therapy for late latent syphilis. Pregnant women who miss any dose of therapy must repeat the full course of therapy.

Management of Sex Partners

- Persons who have had sexual contact with a person who receives a diagnosis of primary, secondary or early latent syphilis within 90 days preceding the diagnosis should be treated presumptively for early syphilis, even if serologic test results are negative.
- Persons who have had sexual contact with a person who receives a diagnosis of primary, secondary, or early latent syphilis > 90 days before the diagnosis should be treated presumptively for early syphilis if serologic test results are not immediately available and the opportunity for follow-up is uncertain.
    - If serologic tests are negative, no treatment is needed.
    - If serologic tests are positive, treatment should be based on clinical and serologic evaluation and stage of syphilis.
- In some areas or populations with high rates of syphilis, health departments recommend notification and presumptive treatment of sex partners of persons with late latent syphilis who have high nontreponemal serologic test titers (i.e., >1:32), because high titers might be indicative of early syphilis. These partners should be managed as if the index case had early syphilis.
- Long-term sex partners of persons who have late latent syphilis should be evaluated clinically and serologically for syphilis and treated on the basis of the evaluation's

findings.

- The following sex partners of persons with syphilis are considered at risk for infection and should be confidentially notified of the exposure and need for evaluation:
    - Partners who have had sexual contact within 1) 3 months plus the duration of symptoms for persons who receive a diagnosis of primary syphilis, 2) 6 months plus duration of symptoms for those with secondary syphilis, and 3) 1 year for persons with early latent syphilis.

Trichomoniasis

- **Recommended Regimen**
    - Metronidazole 2 g orally in a single dose* ***OR***
    - Tinidazole 2 g orally in a single dose

Recommended regimen at any stage of pregnancy

- **Alternative Regimen**
    - Metronidazole 500 mg orally twice a day for 7 days

- **Persistent or Recurrent Trichomoniasis**
    - Metronidazole 500 mg orally twice a day for 7 days
    - If this regimen fails:
        - Metronidazole 2 g orally for 7 days ***OR***
        - Tinidazole 2 g orally for 7 days
        - If this regimen fails, susceptibility testing is recommended

- **Recommended treatment for Women with HIV Infection**
    - Metronidazole 500 mg orally twice daily for 7 days

- **Management of Sex Partners**
    - Concurrent treatment of all sex partners is critical for symptomatic relief, microbiologic cure, and prevention of transmission and reinfections.
    - Current partners should be referred for presumptive therapy to avoid reinfection.
    - Partners should be advised to abstain from sexual intercourse until they and their partners have been adequately treated and any symptoms have resolved.
    - EPT might have a role in partner management for trichomoniasis and can be used in states where permissible by law; however, no one partner management intervention has been shown to be superior in reducing reinfection rates.
    - Though no definitive data exist to guide treatment for partners of persons with persistent or recurrent trichomoniasis in whom nonadherence and reinfection are unlikely, partners benefit from undergoing evaluation and receiving the same regimen as the patient.

Viral Hepatitis

Hepatitis A

Patients with acute hepatitis A usually require only supportive care, with no restrictions in diet or activity. Hospitalization might be necessary for patients who become dehydrated because of nausea and vomiting and is critical for patients with signs or symptoms of acute liver failure. Medications that might cause liver damage or are metabolized by the liver should be used with caution among persons with hepatitis A.

Hepatitis B

No specific therapy is available for persons with acute hepatitis B; treatment is supportive. Persons with chronic HBV infection should be referred for evaluation to a provider experienced in the management of chronic HBV infection. Therapeutic agents cleared by FDA for treatment of chronic hepatitis B can achieve sustained suppression of HBV replication and remission of liver disease.

Vulvovaginal Candiasis (VVC)

Over-the-Counter Intravaginal Regimens

- Clotrimazole 1% cream 5 g intravaginally daily for 7–14 days ***OR***
- Clotrimazole 2% cream 5 g intravaginally daily for 3 days ***OR***
- Miconazole 2% cream 5 g intravaginally daily for 7 days ***OR***
- Miconazole 4% cream 5 g intravaginally daily for 3 days ***OR***
- Miconazole 100 mg vaginal suppository, one suppository daily for 7 days ***OR***
- Miconazole 200 mg vaginal suppository, one suppository for 3 days ***OR***
- Miconazole 1,200 mg vaginal suppository, one suppository for 1 day ***OR***
- Tioconazole 6.5% ointment 5 g intravaginally in a single application

Prescription Intravaginal Agents

- Butoconazole 2% cream (single dose bioadhesive product), 5 g intravaginally in a single application ***OR***
- Terconazole 0.4% cream 5 g intravaginally daily for 7 days ***OR***
- Terconazole 0.8% cream 5 g intravaginally daily for 3 days ***OR***
- Terconazole 80 mg vaginal suppository, one suppository daily for 3 days

Oral Agent

- Fluconazole 150 mg orally in a single dose

Recurrent VVC – defined as 4 or more episodes in a year:

- 7-14 days of topical azole therapy ***OR*** fluconazole 100mg-, 150mg-, or 200mg PO q3days for 3 doses.

Recommended Regimens for Severe VVC (i.e., extensive vulvar erythema, edema, excoriation, and fissure formation)

- Either 7-14 days of topical azole ***OR***
- 150 mg of fluconazole in two sequential oral doses (second dose 72 hours after initial dose)

VVC in Pregnancy

- VVC occurs frequently during pregnancy
- Only topical azole therapies, applied for 7 days are recommended

VVC in HIV Infected Patients

- On the basis of available data, therapy for uncomplicated and complicated VVC in women with HIV infection should not differ from that for seronegative women. However, long-term prophylactic therapy with fluconazole at a dose of 200 mg weekly has been effective in reducing *C. albicans* colonization and symptomatic VVC. This regimen is not recommended for women with HIV infection in the absence of complicated VVC.

Nonalbicans VVC

- The optimal treatment of nonalbicans VVC remains unknown
- Options include:
    - Longer duration of therapy (7-14) days with a nonfluconazole azole regimen (oral or topical) as first line therapy
    - If recurrence occurs, 600 mg of boric acid in a gelatin capsule is recommended, administered vaginally once daily for 2 weeks.

Treatment of Sex Partners

- Uncomplicated VVC is not usually acquired through sexual intercourse; therefore data does not support treatment of sex partners.
- A minority of male sex partners have balanitis, characterized by erythematous areas on the glans of the penis in conjunction with pruritus or irritation. These men benefit from treatment with topical antifungal agents to relieve symptoms.

References

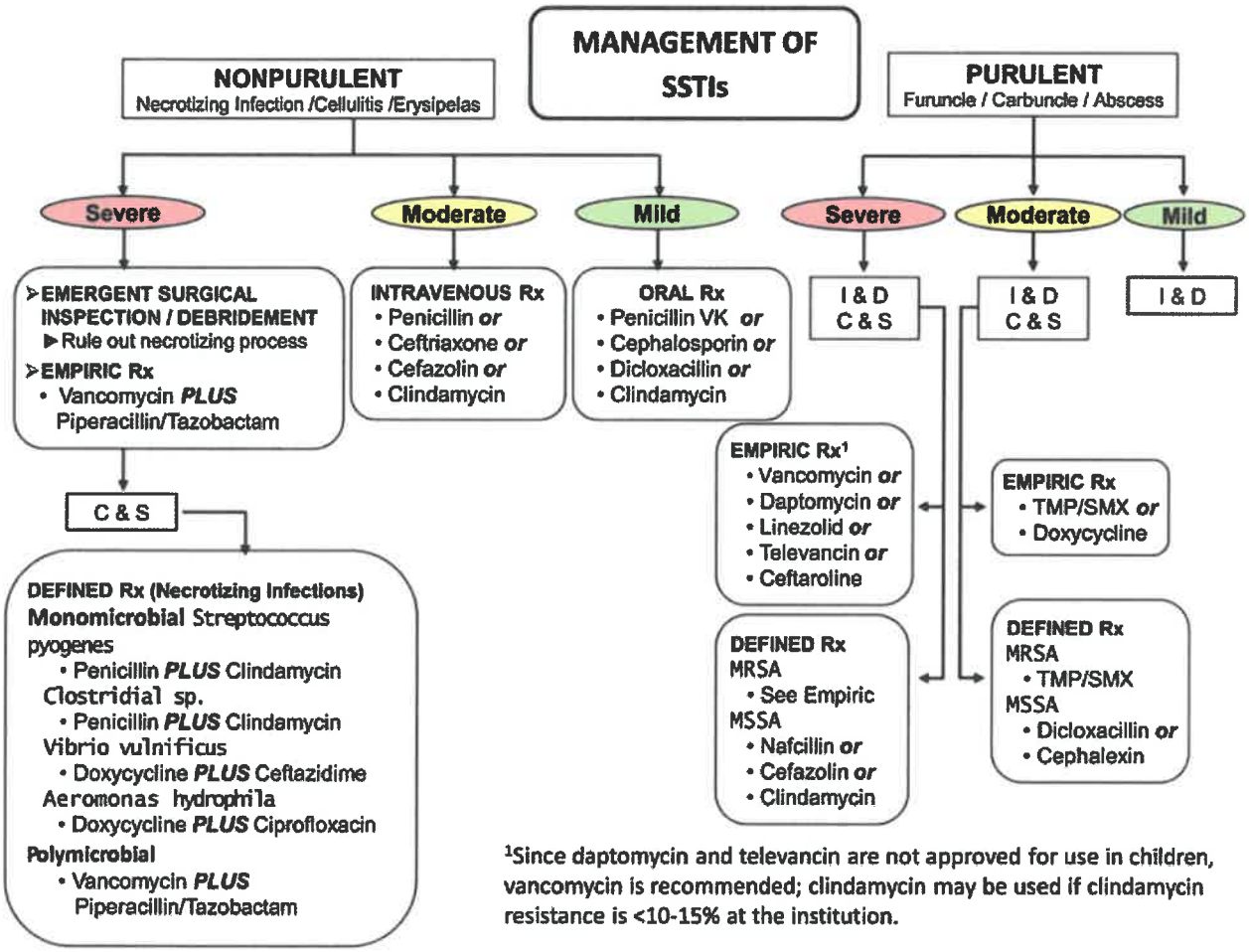
CDC. *Sexually Transmitted Diseases Treatment Guidelines, 2015.*; 2015.

Electronic Reference: https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

Skin Infections:

Skin and soft tissue infections (SSTIs) have extensive overprescribing of antibiotics active for Gram- negative species despite 97% of patients having positive cultures with *Streptococcus* or *S. aureus*. The focus of these recommendations is the diagnosis and appropriate treatment of diverse SSTIs. Emphasis most be placed on the importance of clinical skills in promptly diagnosing SSTIs, identifying the pathogen, and administering effective treatments in a timely fashion.

Our recommendations closely follow the 2014 Infectious Disease Society of America's guidelines for Skin and Soft Tissue Infections, Diabetic Foot Infections and Infections Caused by Methicillin-Resistant Staphylococcus Aureus, all of which can be accessed at: http://www.idsociety.org/.



[1]Since daptomycin and televancin are not approved for use in children, vancomycin is recommended; clindamycin may be used if clindamycin resistance is <10-15% at the institution.

General Culture Information:

1. Cultures should be collected prior to antibiotic initiation when possible
2. **Blood** should be sterile; any organism isolated should be considered pathogenic. However, there are some likely contaminants including:
    a. Coagulase-negative staphylococci
    b. Alpha-hemolytic streptococci
    c. Bacillus spp.
    d. Corynebacterium spp. (except C. jeikeium)
    e. Propionibacterium acnes

    **consider how cultures drawn vs. how many are positive and what the organism is

3. **Tissue and body fluids**: should be sterile; any organism isolated should be considered pathogenic. Judgment should be utilized in evaluation of what could possibly be normal flora present in the source of the specimen.

Normal flora of the eye/ear includes:

a. **Coagulase-negative staphylococci**
b. **Non-hemolytic streptococci**
c. **Alpha-hemolytic streptococci**
d. Diphtheroids

Normal flora of the skin includes:

a. **Coagulase-negative staphylococci**
b. **Propionibacterium acnes**
c. **Alpha-hemolytic-streptococci**
d. **Diphtheroids**
e. Bacillus spp.

Herpes Zoster infection

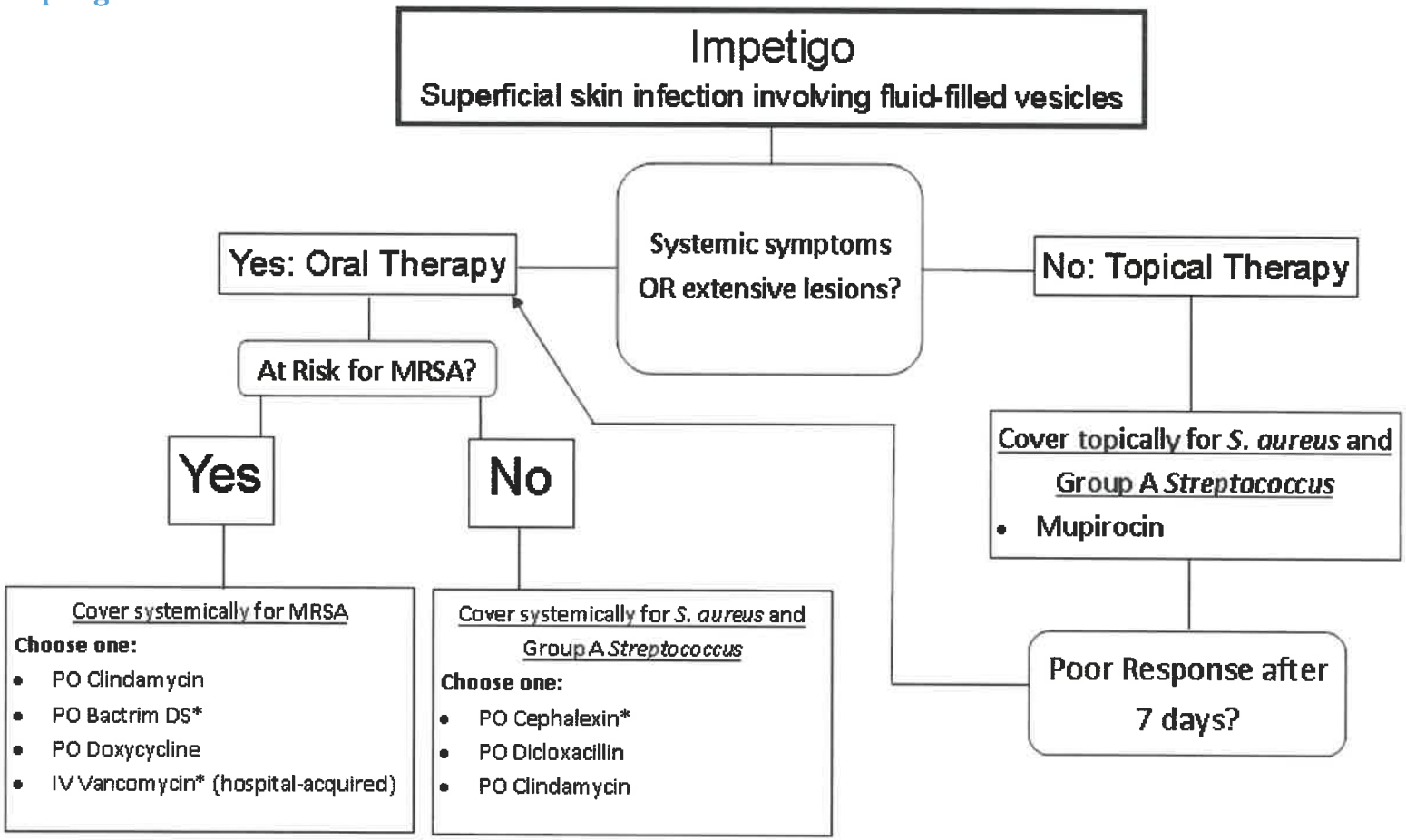
Guidelines adapted from Cohen JI. Herpes Zoster. N Engl J Med 2013;369:255-63

Treatment is recommended even if rash began more than 3 days earlier.

Medication	Dose	Effects Observed in Controlled Trials	Side Effects
Nonimmunocompromised persons			
Acyclovir (e.g., Zovirax)	800 mg orally five times daily for 7–10 days	Reduced time to last new-lesion formation, loss of vesicles, full crusting, cessation of viral shedding, reduced severity of acute pain[10-12]	Malaise
Famciclovir (e.g., Famvir)	500 mg orally three times daily for 7 days	Reduced time to last new-lesion formation, loss of vesicles, full crusting, cessation of viral shedding, cessation of pain[13,14]	Headache, nausea
Valacyclovir (e.g., Valtrex)	1 g orally three times daily for 7 days	Reduced time to last new-lesion formation, loss of vesicles, full crusting, cessation of pain[15,16]	Headache, nausea
Brivudin (e.g., Zostex, Helpin)*	125 mg orally once daily for 7 days	Reduced time to last new-lesion formation, full crusting, cessation of pain[17]	Headache, nausea; contraindicated in persons receiving fluorouracil or other fluoropyrimidines
Immunocompromised persons requiring hospitalization or persons with severe neurologic complications			
Acyclovir (e.g., Zovirax)	10 mg/kg intravenously every 8 hr for 7–10 days	Reduced time to last new-lesion formation, full crusting, cessation of viral shedding, cessation of pain, reduced cutaneous dissemination, reduced visceral herpes zoster[16,19]	Renal insufficiency
Foscarnet (e.g., Foscavir) for acyclovir-resistant VZV†	40 mg/kg intravenously every 8 hr until lesions are healed	Not reported	Renal insufficiency, hypokalemia, hypocalcemia, hypomagnesemia, hypophosphatemia, nausea, diarrhea, vomiting, anemia, granulocytopenia, headache

* Brivudin is not available in the United States and has not been approved by the Food and Drug Administration (FDA).
† Foscarnet is not approved for this use by the FDA.

Impetigo



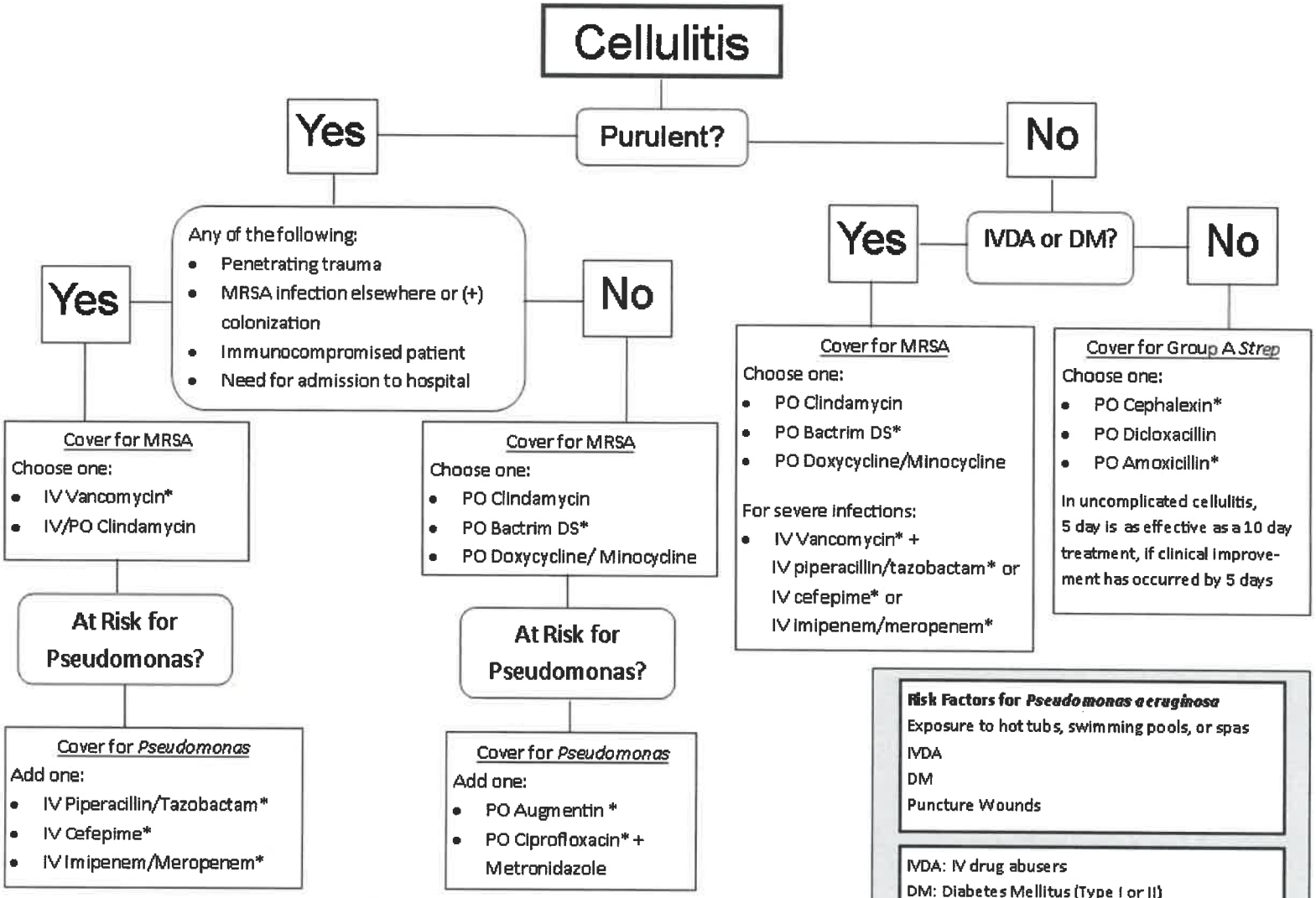
* requires renal dosing

MRSA: Methicillin-resistant *Staphylococcus aureus*

Risk Factors:

IV drug abusers	(+) MRSA nasal swab
Children in daycare	Boil, abscess, or "spider bite"
Homeless	Athletically active adolescents
Jail Patients	Immunocompromised pts.

Antibiotic Dosing		
	Adult	Pediatric
Clindamycin	300–450 mg PO QID	20 mg/kg/d in 3 divided doses PO
Bactrim	1 double strength tablet PO BID	8–12 mg/kg (based on trimethoprim component)in either 4 divided doses IV or 2 divided doses PO
Doxycycline	100 mg PO BID	Not recommended for age <8 yd
Cephalexin	500 mg PO QID	25–50 mg/kg/d 4 divided doses po
Dicloxacillin	250 mg PO QID	N/A



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1. Fish D.N., Perediand S.L., Danziger L.H.,(): 19. Chapter 19 . Skin and Soft-Tissue Infections. In DiPiro J.T., Talbert R.L., Yee G.C., Matzke G.R., Wells B.G., Posey L.(Eds), Pharmacotherapy: A Pathophysiologic Approach, 7e.
2. Stevens D.L., Bisno A.L., Chambers F., et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2 14 Update by the Infectious Diseases Society of America. Clin Infect Dis 14(5()):e9-e52
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4. Lipsky BA , Berendt AR, Cornia PB, et al. 2 12 Infectious Diseases Society of America clinical practice guidelines for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis 1 54:132-73.

Cellulitis treatment for Pediatrics

Pediatric Dosing in MSSA Cellulitis (children age >28 days)
Oral therapy:
Dicloxacillin
25 to 50 mg/kg per day orally divided into four doses

If history of non-type 1 hypersensitivity to penicillin:
Cephalexin
25 to 50 mg/kg per day orally divided into three or four doses

If history of type 1 hypersensitivity to penicillin:
Clindamycin
25 to 30 mg/kg per day orally divided into three doses

Intravenous therapy:
Nafcillin
150 to 200 mg/kg per day intravenously divided into four or six doses

If history of non-type 1 hypersensitivity to penicillin:
Cefazolin
50 mg/kg per day intravenously divided into three doses

If history of type 1 hypersensitivity to penicillin:
Clindamycin
25 to 40 mg/kg per day intravenously divided into three or four doses

Pediatric Dosing in MRSA Cellulitis (children > 28 days)
Oral Therapy:
Clindamycin
30 to 40mg/kg/day divided into 3-4 doses
TMP/SMP
8-12 mg of trimethoprim component/kg/day divided into 2 doses
Doxycycline (children 8 or older)
≤45 kg: 4 mg/kg per day orally divided into two doses
> 45kg: 100 mg twice daily
Linezolid
<5 years: 30 mg/kg/day divided into 3 doses for 10-14 days
5- 11 years: 20 mg/kg/day divided into 2 doses for 10-14 days
≥ 12 years: 600 mg orally twice daily for 10-14 days

Reference:
Stevens DL, et. al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Disease Society of America. *Clin Infect Dis.* June 2014.
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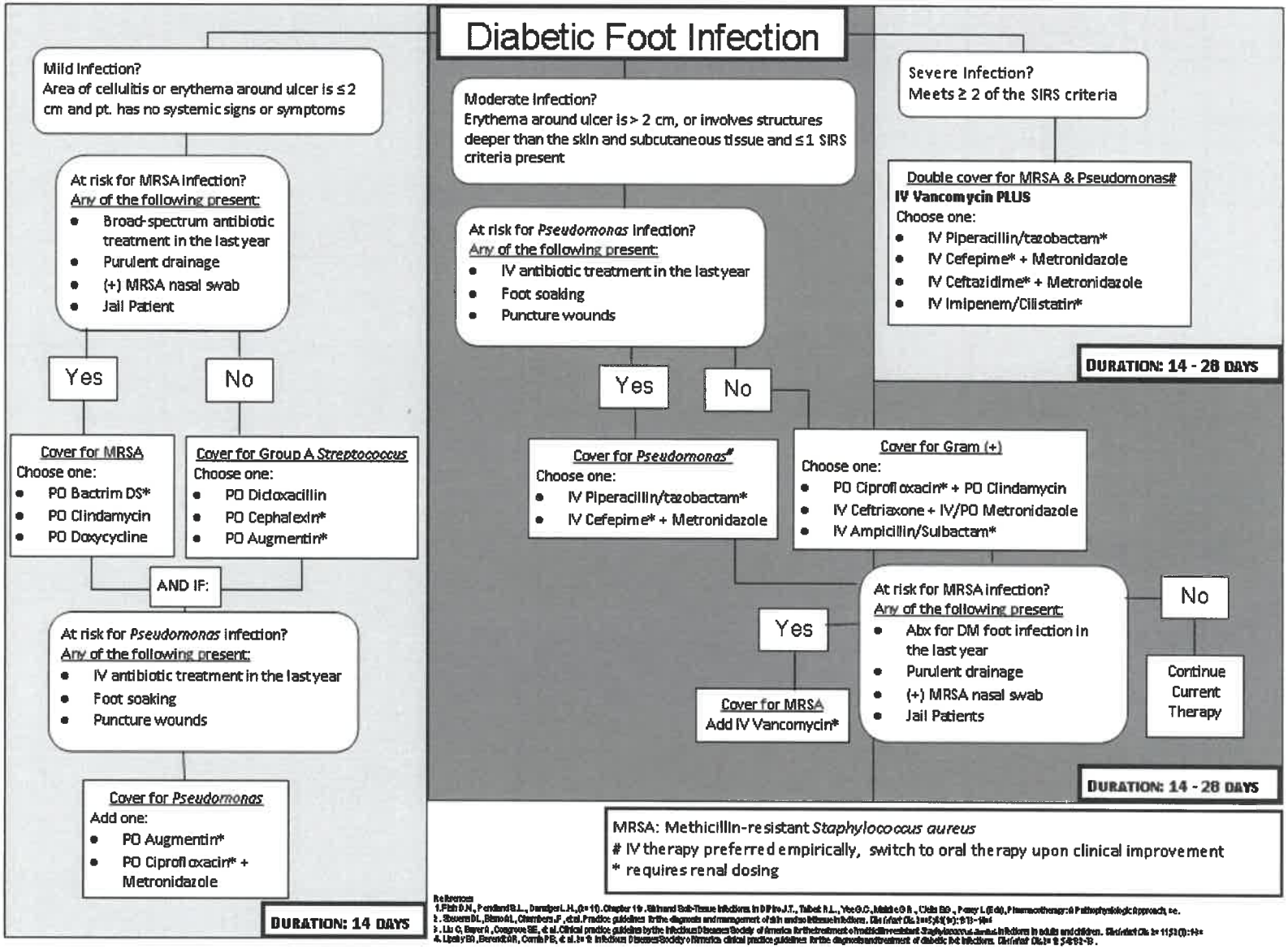
Diabetic Foot Infection



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4. Lipsky BA, Berendt AR, Cornia PB, et al. Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012;54(12):132.

Dog or Cat Bite

- An antimicrobial agents or agents active against both aerobic and anaerobic bacteria should be used.
- Purulent bite wounds and abscess are more likely to be polymicrobial (mixed aerobes and anaerobes), whereas nonpurulent wounds commonly yield staphylococci and streptococci, but may be polymicrobial.
- Tetanus toxoid should be administered to patients without toxoid vaccination within the last 10 years. Tdap is preferred over Td if Tdap has not been previously given.
- Primary wound closure is not recommended for wounds with the exception of those to the face which should undergo copious irrigation, cautious debridement, and preemptive antibiotics. Other wounds should be approximated.
- Postexposure prophylaxis for rabies may be indicated. Consult with local health official to determine if vaccination should be initiated. Also refer to rabies information in this document.

If patient presents with 12 to 24 hours of the bite and meets any of the following criteria:

- immunocompromised
- asplenic
- advanced liver disease
- pre-existing or resultant edema of the affected area
- moderate/severe injury especially to the hand or face or has injuries that may have penetrated
  the periosteum or joint capsule

Then give preemptive antibiotic therapy for 3-5 days. See therapy choices below.

If the patient presents greater than 24 hours from the bite AND the wound from the bite is infected, antimicrobial therapy is warranted.

First line therapy is :

- Amoxicillin/clavulanate 875 mg/125 mg PO BID*

Table 5. Recommended Therapy for Infections Following Animal or Human Bites

Antimicrobial Agent by Type of Bite	Therapy Type		Comments
	Oral	Intravenous	
Animal bite			
Amoxicillin-clavulanate	875/125 mg bid	. . .	Some gram-negative rods are resistant; misses MRSA
Ampicillin-sulbactam	. . .	1.5–3.0 g every 6–8 h	Some gram-negative rods are resistant; misses MRSA
Piperacillin-tazobactam	. . .	3.37 g every 6–8 h	Misses MRSA
Carbapenems		See individual info.	Misses MRSA
Doxycycline	100 mg bid	100 mg every 12 h	Excellent activity against *Pasteurella multocida*; some streptococci are resistant
Penicillin plus dicloxacillin	500 mg qid/500 mg qid	. . .	
SMX-TMP	160–800 mg bid	5–10 mg/kg/day of TMP component	Good activity against aerobes; poor activity against anaerobes
Metronidazole	250–500 mg tid	500 mg every 8 h	Good activity against anaerobes; no activity against aerobes
Clindamycin	300 mg tid	600 mg every 6–8 h	Good activity against staphylococci, streptococci, and anaerobes; misses *P. multocida*
Second-generation cephalosporin			Good activity against *P. multocida;* misses anaerobes
Cefuroxime	500 mg bid	1 g every 12 h	
Cefoxitin	. . .	1 g every 6–8 h	
Third-generation cephalosporin			
Ceftriaxone	. . .	1 g every 12 h	
Cefotaxime	. . .	1–2 g every 6–8 h	
Fluoroquinolones			Good activity against *P. multocida;* misses MRSA and some anaerobes
Ciprofloxacin	500–750 mg bid	400 mg every 12 h	
Levofloxacin	750 mg daily	750 mg daily	
Moxifloxacin	400 mg daily	400 mg daily	Monotherapy; good for anaerobes also
Human bite			
Amoxicillin-clavulanate	875/125 mg bid	. . .	Some gram-negative rods are resistant; misses MRSA
Ampicillin-sulbactam	. . .	1.5–3.0 g every 6 h	Some gram-negative rods are resistant; misses MRSA
Carbapenems			Misses MRSA
Doxycycline	100 mg bid	. . .	Good activity against *Eikenella* species, staphylococci, and anaerobes; some streptococci are resistant

Abbreviations: bid, twice daily; MRSA, methicillin-resistant *Staphylococcus aureus*; qid, 4 times daily; SMX-TMP, sulfamethoxazole-trimethoprim; tid, 3 times daily.

*Preferred regimen in pregnancy.

Rabies

- Rabies is a vaccine-preventable viral disease which occurs in more than 150 countries and territories.
- 40% of people who are bitten by suspect rabid animals are children under 15 years of age.
- Bats are the source of most human rabies death in the Americas, Australia, and western Europe.
  Dogs are the source of infection in all human rabies deaths in Asia and Africa.
- Immediate wound cleansing and immunization within a few hours after contact with a suspect rabid animal can prevent the onset of rabies and death.
- The incubation period for rabies is typically 1-3 months, but can be as short as <1 week to as long as over a year. Initial symptoms of rabies are fever and pain or an unusual or unexplained tingling, pricking or burning sensation (paresthesia) at the wound site. As the virus spreads through the central nervous system, progressive fatal inflammation of the brain and spinal cord develops.

There are 2 forms of the disease:

- Furious rabies exhibits signs of hyperactivity, excited behavior, hydrophobia and sometimes aerophobia with death in a few days from cardio-respiratory arrest.
- Paralytic rabies accounts for 3% of cases and is a less dramatic form of the disease. Muscles gradually become paralyzed, starting at the site of the scratch or bite. A coma develops, followed by death.

Diagnosis

There are no tests available to detect rabies before the onset of disease and clinical diagnosis is difficult unless the signs of hydrophobia or aerophobia are present.

Risk is increased if:

- The biting mammal is a known rabies reservoir or vector species;
- The animal looks sick or has abnormal behavior;
- A wound or mucous membrane was contaminated by the animal's saliva;
- The bite was unprovoked; and
- The animal has not been vaccinated

Our recommendations closely follow the World Health Organization and Centers of Disease Control recommendations. These can be accessed at the following sites:
http://www.who.int/mediacentre/factsheets/fs099/en/ and
http://www.cdc.gov/mmwr/pdf/rr/rr5902.pdf. Accessed 10/23/17

Post-exposure Prophylaxis (see table below):

- Local treatment of the wound as soon as possible. Immediate and thorough flushing and washing of the wound is recommended for a minimum of 15 minutes with soap and water, detergent, povidone iodine or other substances to kill the virus.

- A 4-dose course of a potent rabies vaccine that meets WHO recommendations; and
- Administration of rabies immunoglobulin, if indicated.

Category of Contact with Suspected Rabid Animal	Post-exposure (PEP) measures
Category I – touching or feeding animals, licks on	None
Category II – nibbling of uncovered skin, minor	Immediate vaccination and local treatment of the
Category III – single or multiple transdermal bites or scratches, licks on broken skin; contamination of mucous membrane with	Immediate vaccination and administration of rabies immunoglobulin; local treatment of wound

Doses:
These regimens are for all age groups, including children.

If patient has not previously been vaccinated for rabies:

- Human Rabies Immune Globulin (HRIG) - 20 IU/kg once on day 0* (can be given as late as day 7)

If feasible, the full dose should be infiltrated around and into the wound(s). Any remaining volume should be administered IM at an anatomical site distant from the site of vaccination administration. Do not administer in the same syringe as the vaccine and do not use more than the recommended dose as the HRIG may partially suppress active production of rabies vaccine antibody.

- Vaccine – Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) 1ml, IM in the deltoid area (required site of administration for adults and older children; for younger children, the outer aspect of the thigh may be used. Do NOT use the gluteal area). One dose each should be administered on days 0*, 3, 7, and 14. Immunosuppressed patients will need the full 5-dose regimen given on days 0, 3, 7, 14, and 28.

If patient has been previously vaccinated with an ACIP-recommended rabies vaccine regimen or received another vaccine regimen and has a documented history of response to the prior vaccination:

- HRIG should not be administered

- Vaccine – HDCV or PCECV 1ml IM in the deltoid area (required site of administration for adults and older children; for younger children, the outer aspect of the thigh may be used. Do NOT use the gluteal area). One dose each should be administered on days 0* and 3.

****day 0 is the date when first dose of the vaccine is administered***

Human Bite

The bacteriologic characteristics of these wounds are complex, but include aerobic bacteria, such as streptococci, *S. aureus*, and *Eikenella corrodens*, as well as with multiple anaerobic organisms, including *Fusobacterium*, *Peptostreptococcus*, *Prevotella*, *and Porphyromonas* species. *Eikenella corrodens* is resistant to first-generation cephalosporins, macrolides, clindamycin, and aminoglycosides.

If patient presents with 12 to 24 hours of the bite and meets any of the following criteria:

- immunocompromised
- asplenic
- advanced liver disease
- pre-existing or resultant edema of the affected area
- moderate/severe injury especially to the hand or face or has injuries that may have penetrated the periosteum or joint capsule

Then give preemptive antibiotic therapy for 3-5 days. See therapy choices below.

If the patient presents greater than 24 hours from the bite AND the wound from the bite is infected, antimicrobial therapy is warranted.

First line therapy is :

- Amoxicillin/clavulanate 875mg/125mg
  PO BID* OR
- Ampicillin/sulbactam 1.5 to 3.0 grams
  IV q6h* OR
- Ertapenem 1 gm IV daily*

For patients with Penicillin allergy, alternative regimens include:

- Doxycycline 100mg PO
  BID OR
- Moxifloxacin 400mg PO
  QD OR
- Levofloxacin 750mg PO QD + Clindamycin 300mg PO TID

Preferred regimen in pregnancy.

Tuberculosis

Abbreviations for this section:
LTBI = latent tuberculosis infection
TB = tuberculosis
DOT = direct observed therapy
INH = isoniazid
INH-RPT = isoniazid/rifapentine
HIV = human immunodeficiency virus
AFB = Acid-fast bacilli

The following recommendations closely follow the CDC guidelines from 2000 for latent tuberculosis infection (LTBI); the 2011 update regarding use of isoniazid and rifapentin; the 2013 update regarding the use of bedaquiline fumarate for the treatment of multidrug resistant tuberculosis; and the 2016 guideline update on the treatment of drug-susceptible TB. These references can be found at:
http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf (2000 guideline for LBTI)
http://www.cdc.gov/mmwr/pdf/wk/mm6048.pdf (2011 update on INH-Rifapentin)
http://www.cdc.gov/tb/publications/ltbi/pdf/targetedltbi.pdf (2013 LBTI guide for health care providers based on the 2000 CDC/ATS guideline with the 2011 update in treatment incorporated)
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6209a1.htm?s_cid=rr6209a1_e (for drug-resistant TB, published in 2013)
http://www.cdc.gov/tb/topic/treatment/ltbi.htm (summary update in 2016)
http://cid.oxfordjournals.org/content/early/2016/07/20/cid.ciw376.full.pdf+html (new 2016 guideline for drug-susceptible TB)
Errata: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6245a10.htm

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Thirteen million people in the United States have LTBI. Tuberculosis (TB) develops in 5-10% of persons who get infected with *M. tuberculosis*, typically after a latency of 6-18 months or as long as decades in some patients. Conditions that impair cellular immunity, especially HIV infection, increase the likelihood of disease development at any interval after infection.

Latent Tuberculosis Infection (LTBI)

Isoniazid (INH) is the only FDA-approved medication for TB preventive therapy. However, self-supervised daily regimens have a completion rate of only 60% or less, largely due to the long duration of therapy (6 month to 9 months). Isoniazid-rifapentine (INH-RPT) has been demonstrated to be as effective as daily INH therapy when administered once weekly by direct observed therapy (DOT) for 12 weeks.

Rifampin and pyrazinamide should not be offered to LTBI due to the reports of severe liver injury and deaths.

There are 4 options for LTBI treatment:

http://www.cdc.gov/tb/publications/ltbi/pdf/targetedltbi.pdf page 16-17.

3 month regimen of INH-RPT – once weekly dosing* **(if active TB has been ruled out)**	**First choice for Indian Health Service: DOT should be used** • Otherwise healthy patients 12 years of age or older who have a predictive factor for greater likelihood of TB developing (e.g., recent exposure to contagious TB, conversion from negative to positive on a TB skin test, radiographic findings of healed pulmonary TB) • HIV-infected persons who are otherwise healthy and are not taking antiretroviral medications • Children aged 2-11 years– IF completion of 9 months therapy is unlikely AND the hazard of TB disease is great. **This is NOT recommended for**: • Children 2 years of age or younger (safety not established) • HIV-infected persons receiving antiretroviral treatment (due to drug-drug interactions) • Patients presumed to be infected with INH or RIF-resistant M. tuberculosis • Women who are pregnant or wish to become pregnant (safety unknown)
9 month regimen of INH	Preferred for: • patients with HIV (daily dosing) • children 2-11 years of age (daily dosing) • Pregnant women (with pyridoxine supplements) – (daily or twice weekly* dosing)
6 month regimen of INH	
4 months of RIF - Daily dosing	Can be considered for patients who cannot tolerate INH or who have been exposed to INH-resistant *M. tuberculosis.* It should not be used to treat HIV infected patients who are taking certain combinations of antiretroviral therapy. To check rifamycin drug interactions, please refer to CDC website

Any dosing administered less often than daily dosing is encouraged to be conducted as DOT.

Pregnancy:
In the absence of risk factors, wait until after the woman has delivered to avoid administering unnecessary medication during pregnancy. Supplement with 10-25mg/day of pyridoxine (vit. B6). There is potential for an increased risk of hepatotoxicity during pregnancy and the first 2-3 months of the post-partum period. Consider delaying treatment for LTBI until 2-3 months post-partum unless there is high risk of progression to TB disease (e.g., HIV infected, recent contact).

Breastfeeding is not contraindicated in women taking INH. Supplementation with 10-25mg/day of pyridoxine (vit B6) is recommended for nursing women and for breastfed infants.

Infants and children:
Infants and children under 5 years of age with LTBI have been recently infected and, therefore, are at high risk for progression to disease. DOT should be considered for children of all ages, and is strongly recommended when the 12-dose regimen is used.

Completion of therapy:
Completion of therapy is based on the total number of doses taken and the patient may be given up to one year to complete the minimum number of doses.

Monitoring:
Baseline and routine laboratory monitoring during treatment of LTBI are indicated only in the following situations. When indicated, baseline labs should consist of AST, ALT, and bilirubin.

- Liver disorders
- History of liver disease (e.g., hepatitis B, hepatitis C, alcoholic hepatitis, cirrhosis)
- Regular use of alcohol
- Risk for chronic liver disease
- HIV infection
- Pregnancy or in the immediate post-partum period (within 3 months of delivery)

Laboratory testing is recommended at any time during treatment (whether or not baseline labs where done) for patients with symptoms suggestive of hepatitis (e.g. fatigue, weakness, malaise, anorexia, nausea, vomiting, abdominal pain, pale stools dark urine, chills) or who have jaundice.

It is recommended that the medication be withheld if a patient's transaminase level exceeds 3 times the upper limit of normal if associated with symptoms or 5 times the upper limit of normal if the patient is asymptomatic.

Table 1. Regimens for the LTBI Treatment

http://www.cdc.gov/tb/publications/ltbi/pdf/targetedltbi.pdf Page 18

Drug(s)	Duration	Dose	Frequency	Total Doses
Isoniazid (INH)	9 months	Adult: 5 mg/kg Children: 10-20 mg/kg** Maximum dose: 300 mg	Daily	270
		Adult:15 mg/kg Children: 20-40 mg/kg** Maximum dose: 900 mg	Twice weekly[†]	76
	6 months	Adult: 5 mg/kg Children: Not recommended Maximum dose: 300 mg	Daily	180
		Adult: 15 mg/kg Children: Not recommended Maximum dose: 900 mg	Twice weekly[†]	52
Isoniazid (INH) and Rifapentine (RPT)	3 months	Adults and Children 12 years of age and over: **INH*:** 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum **RPT*:** 10.0–14.0 kg 300 mg 14.1–25.0 kg 450 mg 25.1–32.0 kg 600 mg 32.1–49.9 kg 750 mg *≥50.0 kg* *900 mg maximum*	Once weekly[†]	12
Rifampin (RIF)	4 months	Adult: 10 mg/kg*** Maximum dose: 600 mg	Daily	120

† Intermittent regimens must be provided via directly observed therapy (DOT), i.e., health care worker observes the ingestion of medication.

* Isoniazid (INH) is formulated as 100 mg and 300 mg tablets. Rifapentine (RPT) is formulated as 150 mg tablets in blister packs that should be kept sealed until usage.

** The American Academy of Pediatrics recommends an INH dosage of 10-15 mg/kg for the daily regimen and 20-30 mg/kg for the twice weekly regimen.

*** In the United States, the recommended regimen for treatment of LTBI in children is a 9-month course of INH. For the treatment of LTBI in infants, children, and adolescents when INH could not be tolerated or the child has had contact with a case patient infected with an isoniazid-resistant but rifamycin-susceptible organism the American Academy of Pediatrics recommends 6 months of daily rifampin (RIF) (180 doses) at a dosage of 10-20 mg/kg.

Treatment of TB disease:

A 4-drug regimen of INH, RIF, PZA, and EMB remains the preferred initial treatment of drug-susceptible pulmonary TB. Treatment is initiated even before AFB smear microscopy, molecular tests, and mycobacterial culture results are known in patients with high likelihood of having TB or those seriously ill with a disorder suspicious for TB. Do not delay initiation of treatment due to a negative AFB smear for patients in whom TB is suspected and who have a life-threatening condition.

If therapy is being initiated after drug susceptibility test results are known and the patient's isolate is susceptible to both INH and RIF, EMB is not necessary, and the intensive phase can consist of INH, RIF, and PZA, only. EMB can be discontinued as soon as the results of drug susceptibility studies demonstrate susceptibility to both INH and RIF. Pyridoxine (vit. B6) is given with INH to all persons at risk of neuropathy (e.g., pregnant women; women breastfeeding infants; person infected with HIV; patients with diabetes alcoholism, malnutrition, or chronic renal failure; or those who are of advanced age).

Once daily dosing is always the preferred therapy for both the intensive and continuation phase. DOT should be used in regimens with medication administration less than 7 days per week. DOT is associated with improved treatment success (the sum of patients cured + patients who complete therapy) and with improved sputum smear conversion during treatment, as compared to self-administered therapy.
Use of 3 times weekly therapy in the intensive phase (with or without an initial 2 weeks of daily therapy) may be considered in patients who are not HIV infected and are at low risk of relapse (e.g. pulmonary TB caused by drug susceptible organisms that at the start of therapy is non-cavitary and/or smear negative. *(conditional recommendation; low certainty in the evidence)*
Twice weekly treatment under the same conditions has very low certainty in the evidence.

Based on relapse rates of approximately 20%, patients who have cavitation on initial chest radiograph and who have positive cultures at the completion of 2 months of therapy; expert opinion is to extend the continuation phase with INH and RIF for 3 additional months (i.e., 7 months continuation therapy with 9 months total therapy).

For patients with EITHER cavitation OR positive cultures at completion of 2 months of therapy, factors to consider in extending therapy include:

- >10% below ideal body weight
- Being an active smoker
- Having diabetes
- HIV infection or other immunosuppressing condition
- Having extensive disease on chest radiograph

In individuals with active tuberculosis, utilize the following combinations:

Table 1. Drug Regimens for Microbiologically Confirmed Pulmonary Tuberculosis Caused by Drug-Susceptible Organisms

http://cid.oxfordjournals.org/content/early/2016/07/20/cid.ciw376.full.pdf+html

	Intensive Phase		Continuation Phase				
Regimen	Drug[a]	Interval and Dose[b] (Minimum Duration)	Drugs	Interval and Dose[b,c] (Minimum Duration)	Range of Total Doses	Comments[c,d]	Regimen Effectiveness
1	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	7 d/wk for 126 doses (18 wk), or 5 d/wk for 90 doses (18 wk)	182–130	This is the preferred regimen for patients with newly diagnosed pulmonary tuberculosis.	Greater
2	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	110–94	Preferred alternative regimen in situations in which more frequent DOT during continuation phase is difficult to achieve.	
3	INH RIF PZA EMB	3 times weekly for 24 doses (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	78	Use regimen with caution in patients with HIV and/or cavitary disease. Missed doses can lead to treatment failure, relapse, and acquired drug resistance.	
4	INH RIF PZA EMB	7 d/wk for 14 doses then twice weekly for 12 doses[e]	INH RIF	Twice weekly for 36 doses (18 wk)	62	Do not use twice-weekly regimens in HIV-infected patients or patients with smear-positive and/or cavitary disease. If doses are missed, then therapy is equivalent to once weekly, which is inferior.	Lesser

Abbreviations: DOT, directly observed therapy; EMB, ethambutol; HIV, human immunodeficiency virus; INH, isoniazid; PZA, pyrazinamide; RIF, rifampin.

[a] Other combinations may be appropriate in certain circumstances; additional details are provided in the section "Recommended Treatment Regimens."

[b] When DOT is used, drugs may be given 5 days per week and the necessary number of doses adjusted accordingly. Although there are no studies that compare 5 with 7 daily doses, extensive experience indicates this would be an effective practice. DOT should be used when drugs are administered <7 days per week.

[c] Based on expert opinion, patients with cavitation on initial chest radiograph and positive cultures at completion of 2 months of therapy should receive a 7-month (31-week) continuation phase.

[d] Pyridoxine (vitamin B6), 25–50 mg/day, is given with INH to all persons at risk of neuropathy (eg, pregnant women; breastfeeding infants; persons with HIV; patients with diabetes, alcoholism, malnutrition, or chronic renal failure; or patients with advanced age). For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100 mg/day.

[e] See [426]. Alternatively, some US tuberculosis control programs have administered intensive-phase regimens 5 days per week for 15 doses (3 weeks), then twice weekly for 12 doses.

Table 2. Doses of Anti-TB Drugs For Adults And Children

http://cid.oxfordjournals.org/content/early/2016/07/20/cid.ciw376.full.pdf+html

Drug	Preparation	Population	Daily	Once-Weekly	Twice-Weekly	Thrice-Weekly
First-line drugs						
Isoniazid	Tablets (50 mg, 100 mg, 300 mg); elixir (50 mg/5 mL); aqueous solution (100 mg/mL) for intravenous or intramuscular injection. Note: Pyridoxine (vitamin B6), 25–50 mg/day, is given with INH to all persons at risk of neuropathy (eg, pregnant women; breastfeeding infants; persons with HIV; patients with diabetes, alcoholism, malnutrition, or chronic renal failure; or patients with advanced age). For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100 mg/d.	Adults	5 mg/kg (typically 300 mg)	15 mg/kg (typically 900 mg)	15 mg/kg (typically 900 mg)	15 mg/kg (typically 900 mg)
		Children	10–15 mg/kg	. . .	20–30 mg/kg	. . .[b]
Rifampin	Capsule (150 mg, 300 mg). Powder may be suspended for oral administration. Aqueous solution for intravenous injection.	Adults[c]	10 mg/kg (typically 600 mg)	. . .	10 mg/kg (typically 600 mg)	10 mg/kg (typically 600 mg)
		Children	10–20 mg/kg	. . .	10–20 mg/kg	. . .[b]
Rifabutin	Capsule (150 mg)	Adults[d]	5 mg/kg (typically 300 mg)	. . .	Not recommended	Not recommended
		Children	Appropriate dosing for children is unknown. Estimated at 5 mg/kg.			
Rifapentine	Tablet (150 mg film coated)	Adults		10–20 mg/kg[e]	. . .	. . .
		Children	Active tuberculosis: for children ≥ 12 y of age, same dosing as for adults, administered once weekly. Rifapentine is not FDA-approved for treatment of active tuberculosis in children <12 y of age.			
Pyrazinamide	Tablet (500 mg scored)	Adults	See Table 10	. . .	See Table 10	See Table 10
		Children	35 (30–40) mg/kg	. . .	50 mg/kg	. . .[b]
Ethambutol	Tablet (100 mg, 400 mg)	Adults	See Table 11	. . .	See Table 11	See Table 11
		Children[f]	20 (15–25) mg/kg	. . .	50 mg/kg	. . .[b]
Second-line drugs						
Cycloserine	Capsule (250 mg)	Adults[g]	10–15 mg/kg total (usually 250–500 mg once or twice daily)	There are inadequate data to support intermittent administration.		
		Children	15–20 mg/kg total (divided 1–2 times daily)			
Ethionamide	Tablet (250 mg)	Adults[h]	15–20 mg/kg total (usually 250–500 mg once or twice daily)	There are inadequate data to support intermittent administration.		
		Children	15–20 mg/kg total (divided 1–2 times daily)			
Streptomycin	Aqueous solution (1 g vials) for IM or IV administration.	Adults	15 mg/kg daily. Some clinicians prefer 25 mg/kg 3 times weekly. Patients with decreased renal function may require the 15 mg/kg dose to be given only 3 times weekly to allow for drug clearance.			
		Children	15–20 mg/kg [427]	. . .	25–30 mg/kg[i]	. . .
Amikacin/ kanamycin	Aqueous solution (500 mg and 1 g vials) for IM or IV administration.	Adults	15 mg/kg daily. Some clinicians prefer 25 mg/kg 3 times weekly. Patients with decreased renal function, including older patients, may require the 15 mg/kg dose to be given only 3 times weekly to allow for drug clearance.			
		Children	15–20 mg/kg [427]	. . .	25–30 mg/kg[i]	. . .
Capreomycin	Aqueous solution (1 g vials) for IM or IV administration.	Adults	15 mg/kg daily. Some clinicians prefer 25 mg/kg 3 times weekly. Patients with decreased renal function, including older patients, may require the 15 mg/kg dose to be given only 3 times weekly to allow for drug clearance.			
		Children	15–20 mg/kg [427]	. . .	25–30 mg/kg[i]	. . .
Para-amino salicylic acid	Granules (4 g packets) can be mixed in and ingested with soft food (granules should not be chewed). Tablets (500 mg) are still available in some countries, but not in the United States. A solution for IV administration is available in Europe.	Adults	8–12 g total (usually 4000 mg 2–3 times daily)	There are inadequate data to support intermittent administration.		
		Children	200–300 mg/kg total (usually divided 100 mg/kg given 2 to 3 times daily)			
Levofloxacin	Tablets (250 mg, 500 mg, 750 mg); aqueous solution (500 mg vials) for IV injection.	Adults	500–1000 mg daily	There are inadequate data to support intermittent administration.		
		Children	The optimal dose is not known, but clinical data suggest 15–20 mg/kg [427]			

Table continued on the next page.

Drug	Preparation	Population	Daily	Once-Weekly	Twice-Weekly	Thrice-Weekly
Moxifloxacin	Tablets (400 mg); aqueous solution (400 mg/250 mL) for IV injection	Adults	400 mg daily	There are inadequate data to support intermittent administration.[f]		
		Children	The optimal dose is not known. Some experts use 10 mg/kg daily dosing, though lack of formulations makes such titration challenging. Aiming for serum concentrations of 3–5 µL/mL 2 h postdose is proposed by experts as a reasonable target.			

Abbreviations: FDA, US Food and Drug Administration; HIV, human immunodeficiency virus; IM, intramuscular; INH, isoniazid; IV, intravenous.

[a] Dosing based on actual weight is acceptable in patients who are not obese. For obese patients (>20% above ideal body weight [IBW]), dosing based on IBW may be preferred for initial doses. Some clinicians prefer a modified IBW [IBW + [0.40 × (actual weight − IBW)]] as is done for initial aminoglycoside doses. Because tuberculosis drug dosing for obese patients has not been established, therapeutic drug monitoring may be considered for such patients.

[b] For purposes of this document, adult dosing begins at age 15 years or at a weight of >40 kg in younger children. The optimal doses for thrice-weekly therapy in children and adolescents have not been established. Some experts use in adolescents the same doses as recommended for adults, and for younger children the same doses as recommended for twice-weekly therapy.

[c] Higher doses of rifampin, currently as high as 35 mg/kg, are being studied in clinical trials.

[d] Rifabutin dose may need to be adjusted when there is concomitant use of protease inhibitors or nonnucleoside reverse transcriptase inhibitors.

[e] TBTC Study 22 used rifapentine (RPT) dosage of 10 mg/kg in the continuation phase of treatment for active disease [9]. However, RIFAQUIN and PREVENT TB safely used higher dosages of RPT, administered once weekly [164, 210]. Daily doses of 1200 mg RPT are being studied in clinical trials for active tuberculosis disease.

[f] As an approach to avoiding ethambutol (EMB) ocular toxicity, some clinicians use a 3-drug regimen (INH, rifampin, and pyrazinamide) in the initial 2 months of treatment for children who are HIV-uninfected, have no prior tuberculosis treatment history, are living in an area of low prevalence of drug-resistant tuberculosis, and have no exposure to an individual from an area of high prevalence of drug-resistant tuberculosis. However, because the prevalence of and risk for drug-resistant tuberculosis can be difficult to ascertain, the American Academy of Pediatrics and most experts include EMB as part of the intensive-phase regimen for children with tuberculosis.

[g] Clinicians experienced with using cycloserine suggest starting with 250 mg once daily and gradually increasing as tolerated. Serum concentrations often are useful in determining the appropriate dose for a given patient. Few patients tolerate 500 mg twice daily.

[h] Ethionamide can be given at bedtime or with a main meal in an attempt to reduce nausea. Clinicians experienced with using ethionamide suggest starting with 250 mg once daily and gradually increasing as tolerated. Serum concentrations may be useful in determining the appropriate dose for a given patient. Few patients tolerate 500 mg twice daily.

[i] Modified from adult intermittent dose of 25 mg/kg, and accounting for larger total body water content and faster clearance of injectable drugs in most children. Dosing can be guided by serum concentrations.

[j] RIFAQUIN trial studied a 6-month regimen. Daily isoniazid was replaced by daily moxifloxacin 400 mg for the first 2 months, followed by once-weekly doses of moxifloxacin 400 mg and RPT 1200 mg for the remaining 4 months. Two hundred twelve patients were studied (each dose of RPT was preceded by a meal of 2 hard-boiled eggs and bread). This regimen was shown to be noninferior to a standard daily administered 6-month regimen [164].

Table 3. Suggested Pyrazinamide Doses, Using Whole Tablets, For Adults Weighing 40–90 Kilograms

http://cid.oxfordjournals.org/content/early/2016/07/20/cid.ciw376.full.pdf+html

	Weight, kg[b,c]		
Regimen	40–55	56–75	76–90
Daily (mg/kg)	1000 mg (18.2–25.0)	1500 mg (20.0–26.8)	2000 mg (22.2–26.3)
Thrice weekly (mg/kg)	1500 mg (27.3–37.5)	2500 mg (33.3–44.6)	3000 mg (33.3–39.5)
Twice weekly (mg/kg)	2000 mg (36.4–50.0)	3000 mg (40.0–53.6)	4000 mg (44.4–52.6)

[a] With normal renal function.

[b] Based on estimated lean body weight. Optimal doses for obese patients are not established.

[c] Numbers in parentheses are the calculated mg/kg doses for patients at the highest and lowest body weights in the weight band.

TABLE 4. Suggested ethambutol doses, using whole tablets, for adults weighing 40–90 kilograms

http://cid.oxfordjournals.org/content/early/2016/07/20/cid.ciw376.full.pdf+html

	Weight, kg[b,c]		
Regimen	40–55	56–75	76–90
Daily (mg/kg)	800 mg (14.5–20.0)	1200 mg (16.0–21.4)	1600 mg (17.8–21.1)
Thrice weekly (mg/kg)	1200 mg (21.8–30.0)	2000 mg (26.7–35.7)	2400 mg (26.7–31.6)
Twice weekly (mg/kg)	2000 mg (36.4–50.0)	2800 mg (37.3–50.0)	4000 mg (44.4–52.6)

[a] With normal renal function.

[b] Based on estimated lean body weight. Optimal doses for obese patients are not established.

[c] Numbers in parentheses are the calculated mg/kg doses for patients at the highest and lowest body weights in the weight band.

Table 5. Handling Treatment Interruptions
http://cid.oxfordjournals.org/content/early/2016/07/20/cid.ciw376.full.pdf+html

The earlier the break in therapy and the longer the duration of the break, the more serious the effect on the patient's risk and the greater the need to restart treatment from the beginning. Continuous treatment is more important in the intensive phase of treatment when the bacillary population is the highest and the chance of developing drug resistance is the greatest. The duration of the interruption and the bacteriologic status on the patient prior to and after the interruption are important considerations. DOT is recommended for patients with nonadherence.

Time Point of Interruption	Details of Interruption	Approach
During intensive phase	Lapse is <14 d in duration	Continue treatment to complete planned total number of doses (as long as all doses are completed within 3 mo)
	Lapse is ≥14 d in duration	Restart treatment from the beginning
During continuation phase	Received ≥80% of doses and sputum was AFB smear negative on initial testing	Further therapy may not be necessary
	Received ≥80% of doses and sputum was AFB smear positive on initial testing	Continue therapy until all doses are completed
	Received <80% of doses and accumulative lapse is <3 mo in duration	Continue therapy until all doses are completed (full course), unless consecutive lapse is >2 mo If treatment cannot be completed within recommended time frame for regimen, restart therapy from the beginning (ie, restart intensive phase, to be followed by continuation phase)[b]
	Received <80% of doses and lapse is ≥3 mo in duration	Restart therapy from the beginning, new intensive and continuation phases (ie, restart intensive phase, to be followed by continuation phase)

Abbreviation: AFB, acid-fast bacilli.

[a] According to expert opinion, patients who are lost to follow-up (on treatment) and brought back to therapy, with interim treatment interruption, should have sputum resent for AFB smear, culture, and drug susceptibility testing.

[b] The recommended time frame for regimen, in tuberculosis control programs in the United States and in several European countries, is to administer all of the specified number of doses for the intensive phase within 3 months and those for the 4-month continuation phase within 6 months, so that the 6-month regimen is completed within 9 months.

Completion of therapy:
Completion of therapy is based on the total number of doses taken – not solely on duration of therapy. All of the specified doses of the intensive phase should be administered within 3 months. All of the specified doses of the 4 month continuation phase should be administered within 6 months. Therefore, the 6 month regimen should be completed within 9 months. IF these targets are not met, the patient must be considered to have interrupted therapy and manage as described above in Table 5.

Complicated diagnostic or management situations may require consultation with local and state health departments. This information for regional training and medical consultation centers can be found at: http://www.cdc.gov/tb/education/rtmc.

Detailed recommendations for management of TB in special situations (e.g., HIV infection, extrapulmonary TB, culture negative pulmonary TB, advanced age, children, TB during pregnancy and breastfeeding, renal disease, hepatic disease, etc) are available in the full text of the guideline.
Available at:
http://cid.oxfordjournals.org/content/early/2016/07/20/cid.ciw376.full.pdf+html

Please refer to the full MMWR document for second-line drugs or for multi-drug resistance (Published in 2013).
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6209a1.htm?s_cid=rr6209a1_e 013.
Errata:
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6245a10.htm

Bedaquiline may be used for 24 weeks of treatment in adults with laboratory-confirmed pulmonary multi-drug resistant TB (i.e., resistance to both INH and RIF) when an effective treatment regimen cannot otherwise be provided. The recommended dose is 400mg PO once daily for 2 weeks, followed by 200mg PO three times a week for 22 weeks. It should be taken with food in order to maximize absorption.

Lower Respiratory Tract Infections

Adult Management:
Reference:
Infectious Disease Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. Available at:
http://cid.oxfordjournals.org/content/44/Supplement_2/S27.full.pdf+html
Accessed 4 February 2016. Publication date 2007.

Community-Acquired Pneumonia (CAP) in Adults

Outpatient Treatment

- Previously healthy, no risk for drug resistant Strep Pneumoniae infection:
  - Macrolide: Azithromycin, Clarithromycin, or Erythromycin (level I)
  - Doxycycline (level III)

Outpatient Treatment of CAP	
Previously Healthy No risk for DRSP[1]	Comorbidities Present[2] Risk for DRSP[1]
A. Macrolides a. Azithromycin, Clarithromycin, or Erythromycin (Level I) B. Doxycycline (**Level III**)[3]	A. Beta Lactam PLUS macrolide (Level I) a. **Preferred**: High dose Amoxicillin or Amoxicillin/Clavulanate b. Alternatives: Ceftriaxone, Cefpodoxime, Cefuroxime B. Respiratory Fluoroquinolone a. moxifloxacin, gemifloxacin, or levofloxacin (Level I)[4] b. Macrolide alternative: Doxycycline (**Level II**)[3]

[1]DRSP= Drug Resistant Streptococcus Pneumoniae
[2] Comorbidities= Chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppressing conditions or use of immunosuppressing drugs; use of antimicrobials within the previous 3 months
[3] Please note this is a Level III recommendation and should be used cautiously.
[4] Consider risks (C. difficile, hypoglycemia, neuropathy, tendon rupture and patient risk for tuberculosis). Respiratory quinolones should be used only as second choice for the macrolide/PCN allergic patients.

CAP in Infants and Children Older than 3 months of age

Reference:
The Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society and the Infectious Disease Society of America. Available at: http://cid.oxfordjournals.org/content/44/Supplement_2/S27.full.pdf+html Accessed 4 February 2016. Publication date October 2011

Outpatient Treatment:

- Important to distinguish viral and bacterial pathogens as most preschool-aged children are affected by viruses and do not require antimicrobial therapy (Level: Strong)

Outpatient Treatment of CAP in Children >3 months	
Previously Healthy with Mild to Moderate CAP- *Appropriately immunized*	A. Preferred: Amoxicillin (Level: Strong) B. Alternative: Augmentin
CAP associated with Atypical Pathogens	A. S. pneumo resistant to penicillin (MiC >4.0) a. Preferred: Levofloxacin, if susceptible; Linezolid b. Clindamycin B. Group A Strep a. Preferred: High dose Amoxicillin or Penicillin b. Alternative: Clindamycin c. Macrolide alternative: Doxycycline (Level II) C. Staph. Aureus, methicillin susceptible: a. Preferred: Cephalexin b. Alternative: Clindamycin D. Staph Aureus, methicillin resistant, susceptible to clindamycin: a. Preferred: Clindamycin b. Alternative: Linezolid E. Staph Aureus, methicillin resistant, resistant to clindamycin: a. Preferred: Linezolid b. Alternative: None, parenteral therapy required F. H. influenza: a. Preferred: Amoxicillin or Augmentin (if beta-lactamase producing) b. Alternatives: Cefdinir, cefixime, cefpodoxime, or ceftibuten G. Mycoplasma pneumoniae, Chlamydia Trachomatic, or Chlamydia pneumoniae: a. Preferred: Azithromycin

	b. Alternatives: Clarithromycin, erythromycin; for children >7 doxycycline; for adolescents with skeletal maturity levofloxacin or moxifloxacin
Moderate to Severe CAP with influenza virus- *during widespread local circulation of influenza virus*	A. Preferred: Oseltamivir (Tamiflu); Zanamivir (Relenza) Alternatives: Amantadine (Symmetrel); Rimantadine (Flumadine)

Upper Respiratory Tract Infections

Please find references at the end of this URTI section.

Bronchitis [1,2,5,6]

Adult

- >90% non-bacterial; empiric antibiotics NOT recommended
- Focus of clinical assessment should be to rule out pneumonia
  - Pneumonia is unlikely if all the following findings are absent

Sign	Abnormal Finding
Fever	≥ 38°C
Tachypnea	≥ 24 breaths/min
Tachycardia	≥ 100 beats/min
Evidence of consolidation on chest exam	rales, egophony, fremitus

- Purulent sputum is not predictive of bacterial infection->95% patients with purulent sputum do NOT have pneumonia
- In patients with cough > 3 weeks, vital sign abnormalities or asymmetrical lung sounds consider chest x-ray
- If influenza therapy considered, start within 48 hours of symptom onset
- OTC's have limited efficacy

Pediatric

- Cough illness/bronchitis rarely warrants antibiotic treatment
- Consider Antibiotic treatment for
  - Suspected pneumonia based on fever with focal exam, infiltrates on chest x-ray, tachypnea, or toxic appearance
  - Prolonged cough (>10-14 days) without improvement.
  - If child has underlying chronic pulmonary disease (not including asthma)
- Treat with a macrolides only for children > 5 years of age with suspected mycoplasma or pertussis

Rhinosinusitis [1,3,5,7]

Adults

- Most cases are uncomplicated viral infections
- Reserve diagnosis of bacterial rhinosinusitis to patients with symptoms >7 days of unilateral maxillary facial/tooth pain/tenderness and purulent nasal
- Most bacterial rhinosinusitis improves without antibiotics (absolute benefit 15%).
- Patients with mild symptoms should not receive antibiotics, but symptomatic treatment; most trials for symptom relief have been inconclusive
- Consider antibiotic for patients with moderate or severe symptoms.

- **Empiric Therapy** (S. pneum/H. flu)
  - Amoxicillin/Clavulanate 875/125 po BID x 5-7days

Note: amoxicillin alone may be used based on local antibiogram

  - High dose Amoxicillin/Clavulanate (2 g PO twice daily) is recommended in patients from geographic regions with high rates of penicillin-nonsusceptible (**PNS**) **S. pneumonia** (PNSSP), those with severe infection (e.g., evidence of systemic toxicity with fever of 39C (102F) or higher, and

threat of suppurative complications), age > 65 years, recent hospitalization, antibiotic use within the past month, or who are immunocompromised.

- Beta-lactam allergy:
  - Doxycycline 100mg po BID x 5-7days
  - Clindamycin 300mg PO TID plus Cefpodoxime 200mg BID X 5 days in patients with history of non-type 1 reaction

Note: azithromycin, SMX/TMP, and 2nd/3rd generation cephalosporins are NOT appropriate due to high levels of resistance

Pediatrics

- Most cases are uncomplicated viral infection: Antibiotics not indicated
- Mucopurulent rhinitis (thick, opaque, or discolored nasal discharge) is common with viral rhinosinusitis
- Consider bacterial sinusitis if:
  - Rhinorrhea or day time cough symptoms last more than >10-14days without improvement. or
  - Severe symptoms exist: fever >39^{0}C with purulent nasal discharge; facial swelling or pain
- Initial antibiotic treatment should be a narrow-spectrum agent active against likely pathogens
- Good options are Amoxicillin or amoxicillin/clavulanate

- **Empiric Therapy**
  - Amoxicillin/Clavulanate 45mg/kg/day po BID x 10-14days

Note: amoxicillin alone may be used based on local antibiogram

- High dose amoxicillin/clavulanate 90 mg/kg/day PO BID x 10-14 days is recommended in patients from geographic regions with high rates of penicillin-nonsusceptible (PNS) S. pneumonia (PNSSP), those with severe infection (e.g., evidence of systemic toxicity with fever of 39C (102F) or higher, and threat of suppurative complications), attendance in daycare, age < 2 years, recent hospitalization, antibiotic use within the past month, or who are immunocompromised.
- Non-Type I hypersensitivity to penicillin
  - Clindamycin 30-40mg/kg/day PO TID
- If Haemophilus and Morazella are resistant, may add second drug such as Cefdinir 14mg/kg/day PO divided BID x 10-14 days (other appropriate cephalosporins include: cefpodoxime at 10mg/kg/day PO bid or cefixime 8 mg/kg/day PO bid)
- Type I hypersensitivity to penicillin:
  - Levofloxacin: 6 months to 5 years: Levofloxacin 16-20mg/kg/day PO divided BID x 10-14 days (max dose of 500mg)
  - Levofloxacin: 5 to 16 years of age: 8-10 mg/kg/day PO Q 24 Hours x 10-14

days (max dose of 500mg)

Note: in children with vomiting that precludes oral antibiotics, a single dose of ceftriaxone (50mg/kg/day) may be given IV or IM followed by initiation of oral antibiotics 24hours later.

URI, unspecified [1,4,5,7]

Sore throat, cough and nasal symptoms may be present, without a prominent symptom, may last up to 14 days

- 98% of cases are not bacterial
- Purulent secretions are not predictive of bacterial infections
- Acute cough may be relieved by first-generation antihistamines and decongestant

Pharyngitis [8,9,10,11]

- ADULT Pharyngitis
  - Background
    - Only 5-15% of adult cases are caused by Group A β-hemolytic streptococcal (GAS) pharyngitis
    - Antibiotic therapy of GAS pharyngitis hastens resolution by 1-2 days if initiated within 2-3 days of symptom onset
  - Diagnosis
    - Testing for GAS pharyngitis usually is NOT recommended for adults when s/sx strongly suggest a viral etiology such as cough, rhinorrhea, hoarseness, or oral ulcers
    - Lab testing is not indicated in all patients with pharyngitis
    - Patients with none or only one of the following s/sx should NOT be tested or treated. Rapid Streptococcal antigen test (RAT) is recommended for patients with two or more criteria:
      - History of fever
      - Lack of cough
      - Tonsillar exudates
      - Tender anterior cervical adenopathy
    - Antibiotic therapy restricted to those patient with positive RAT results
    - Cultures are not recommended for routine evaluation or for confirmation of negative results if RAT sensitivity >80%
  - Treatment
    - Benzathine Penicillin G 1.2MU IM x1 Dose
    - Amoxicillin 1000mg QDay x 10 days; ensure compliance prior to selecting
    - Penicillin V 500mg BID x 10 days
    - Amoxicillin 500mg BID x 10 days
    - Penicillin V 250mg QID x 10 days

    If patient has non-type 1 penicillin allergy:
    - Cephalexin 500mg BID x10 days

- Cefadroxil 1Gm Qday x10 days

If patient has type 1 penicillin allergy:
- Clindamycin 300mg TID x10 days
- Azithromycin 500mg Qday x5 days
- Clarithromycin 250mg BID x10 days

Antibiotics NOT recommended:
- Tetracyclines – due to high level of resistance
- Fluoroquinolones – due to unnecessarily broad spectrum
- TMP-SMX – due to resistance and reported clinical failures
- Erythromycin no longer recommended first/second line therapy

- Pediatric Pharyngitis
  - Background
    - GAS is the most common bacterial cause of acute pharyngitis, accounting for 20- 30% of cases in children
  - Diagnosis
    - The signs and symptoms of viral and bacterial pharyngitis overlap so broadly that accurate diagnosis on the basis of clinical grounds alone is usually impossible, however, prominent rhinorrhea, cough, hoarseness, conjunctivitis, and/or diarrhea suggest a VIRAL etiology
    - Rapid Strep Kits or culture should be positive before beginning antibiotic treatment
      - Confirm negative results on antigen tests with culture
  - Treatment
    - Do not treat pending culture results, however, if done so, make sure to stop antibiotics when culture is negative and discourage parents from saving antibiotics
    - Benzathine Penicillin G (< 27kg): 600,000 Units IM x1 Dose
    - Benzathine Penicillin G (>27kg): 1,200,000 Units IM x1 Dose
    - Amoxicillin 50mg/kg (max 1000mg) QDay x10 days; ensure compliance prior to selection
    - Penicillin V 250mg BID x10 days
    - Penicillin V 250mg TID x10 days
    - Amoxicillin 25mg/kg (max 500mg) BID x10 days

    If patient has non-type 1 penicillin allergy:
    - Cephalexin 20mg/kg (max 500mg) BID x 10 days
    - Cefadroxil 30mg/kg (max 1Gm) QDay x 10 days

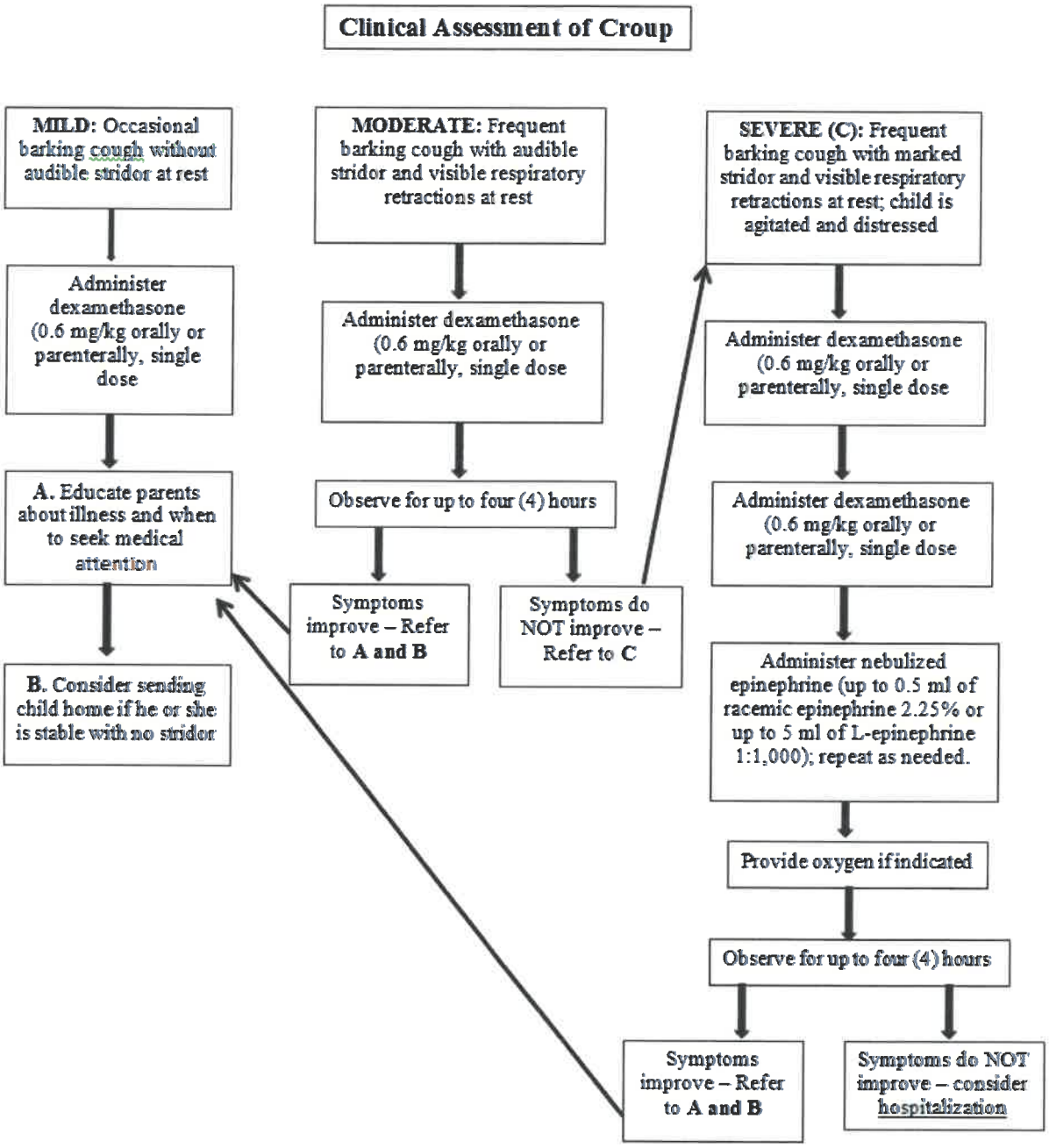
    If patient has type 1 penicillin allergy:

    - Clindamycin 7mg/kg/dose (max 300mg/dose) TID x 10 days
    - Azithromycin 12mg/kg (max 500mg) QDay x 5 days
    - Clarithromycin 7.5mg/kg/dose (max 250mg/dose) BID x 10 days

    Antibiotics NOT recommended:
    - Tetracyclines – due to high level of resistance
    - Fluoroquinolones – due to unnecessarily broad spectrum and risk of cartilage damage in children
    - TMP-SMX – due to resistance and reported clinical failures
    - Erythromycin no longer recommended as first/second line therapy

Croup [12]

- Background
  - Clinical syndrome of upper airway obstruction causing a hoarse voice, barking cough, inspiratory stridor, and variable amounts of respiratory distress – usually of viral origin
  - One of the most frequent causes of acute respiratory distress in children
- Diagnosis
  - Diagnosis is made on clinical grounds and does not typically require any laboratory testing or radiography
  - Lateral neck x-ray may be useful to help detect epiglottitis, bacterial tracheitis, or retropharyngeal abscess
  - Bronchoscopy or direct laryngoscopy may be useful for patients with recurrent croup due to a higher likelihood of a subglottic lesion
  - Endoscopy may be needed to evaluate for GERD
  - Posterior-Anterior chest x-ray and CBC with differential are recommended if lower respiratory tract involvement is suspected
  - Defer all testing if the child is in respiratory distress
- Treatment
  - Stabilization and assessment of airway is paramount
  - Refer to Croup Treatment Algorithm


Clinical Assessment of Croup
MILD: Occasional barking cough without audible stridor at rest
Administer dexamethasone (0.6 mg/kg orally or parenterally, single dose
A. Educate parents about illness and when to seek medical attention
B. Consider sending child home if he or she is stable with no stridor
MODERATE: Frequent barking cough with audible stridor and visible respiratory retractions at rest
Administer dexamethasone (0.6 mg/kg orally or parenterally, single dose
Observe for up to four (4) hours
Symptoms improve – Refer to A and B
Symptoms do NOT improve – Refer to C
SEVERE (C): Frequent barking cough with marked stridor and visible respiratory retractions at rest; child is agitated and distressed
Administer dexamethasone (0.6 mg/kg orally or parenterally, single dose
Administer dexamethasone (0.6 mg/kg orally or parenterally, single dose
Administer nebulized epinephrine (up to 0.5 ml of racemic epinephrine 2.25% or up to 5 ml of L-epinephrine 1:1,000); repeat as needed.
Provide oxygen if indicated
Observe for up to four (4) hours
Symptoms improve – Refer to A and B
Symptoms do NOT improve – consider hospitalization

Otitis Media [13,14,15,16,17]

- Diagnosis
  - Acute Otitis Media (AOM) vs. Otitis Media with Effusion (OME)

AOM	OME
Effusion with ear pain, fever, and bulging yellow/red TM	Effusion only
	No specific signs of infection
	Some non-specific S/S such as Rhinitis, cough, diarrhea, etc.

  - Affects all ages, but mostly infants and young children under the age of 4
  - Second most common organic disease seen by pediatricians, after upper respiratory tract infections

- Treatment
  - Do NOT initially treat otitis media with effusion (OME) with an antibiotic.
  - **AOM**

    -Assess and recommend treatment to reduce pain as necessary
    -<2 years: Treat with antibiotics
    ->2 years: Only treat if severe symptoms such as fever >39°C or moderate to severe pain
    -Nonsevere unilateral in children 6 months to 23 months or nonsevere uni- or bilateral in children 2 years or older: antibiotic therapy should be prescribed or observation offered with close follow-up. When observation is used, a mechanism must be in place to ensure follow-up and initiation of antibiotic therapy if the child worsens or fails to improve within 48 to 72 hours of onset of symptoms.

    - Acute empiric therapy-*Primary regimen*
      - Age < 2 years: 10 days of therapy
      - Age ≥ 2 years: 5-7 days of therapy (5 days may be inadequate for severe infection)
      - Patient has not had antibiotics in the prior month and does not have purulent conjunctivitis:
        - Amoxicillin 80-90mg/kg/day Q12H or Q8H
        - Amox-Clav ES 90/6.4 mg/kg/day BID
      - Patient has had antibiotics in the prior month or fails to respond to Amoxicillin (may take 72h to respond):
        - Amox-Clav ES 90/6.4 mg/kg/day BID
        - Ceftriaxone 50mg/kg IV or IM QDay x3 days

- *Alternative Regimen*
  - Cefdinir 14mg/kg/day Q12H or QDay
  - Cefpodoxime proxetil 10mg/kg/day Q12H
  - Cefprozil 30mg/kg/day Q12H
  - Cefuroxime axetil 30mg/kg/day Q12H
  - Clindamycin 30mg/kg/day Q8H

-Otitis Media, Treatment Failure after 3 Days

- No change in ear pain, fever, bulging TM or otorrhea after 3 days of therapy
- Age < 2 years: 10 days of therapy
- Age ≥ 2 years: 5-7 days of therapy (5 days may be inadequate for severe infection)

- *Primary Regimen* (Patient has not had any antibiotics in the prior month other than in the last 3 days)
  - Amox-Clav 90mg/kg/day of Amoxicillin component BID
  - Cefdinir 7mg/kg Q12H
  - Cefdinir 14mg/kg QDay
  - Cefpodoxime proxetil 10mg/kg/day Q12H
  - Cefprozil 15mg/kg Q12H
  - Cefuroxime axetil 30mg/kg/day Q12H
  - Ceftriaxone 50mg/kg IM x3 days
- Patient **has had** antibiotics in prior month in addition to the last 3 days
  - Ceftriaxone 50mg/kg IM x3 days
  - Clindamycin 20-30mg/kg/day QID + Tympanocentesis

-Newer fluoroquinolones are active against drug-resistant Strep Pneumoniae, but are not approved for use in children
-Vancomycin is active against drug-resistant Strep Pneumoniae
-Ceftriaxone IM x3 days is superior to 1-day treatment against drug-resistant Strep Pneumoniae
-Amox-Clav high dose reported successful for AOM caused by penicillin-resistant Strep Pneumoniae

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Urinary Tract Infections

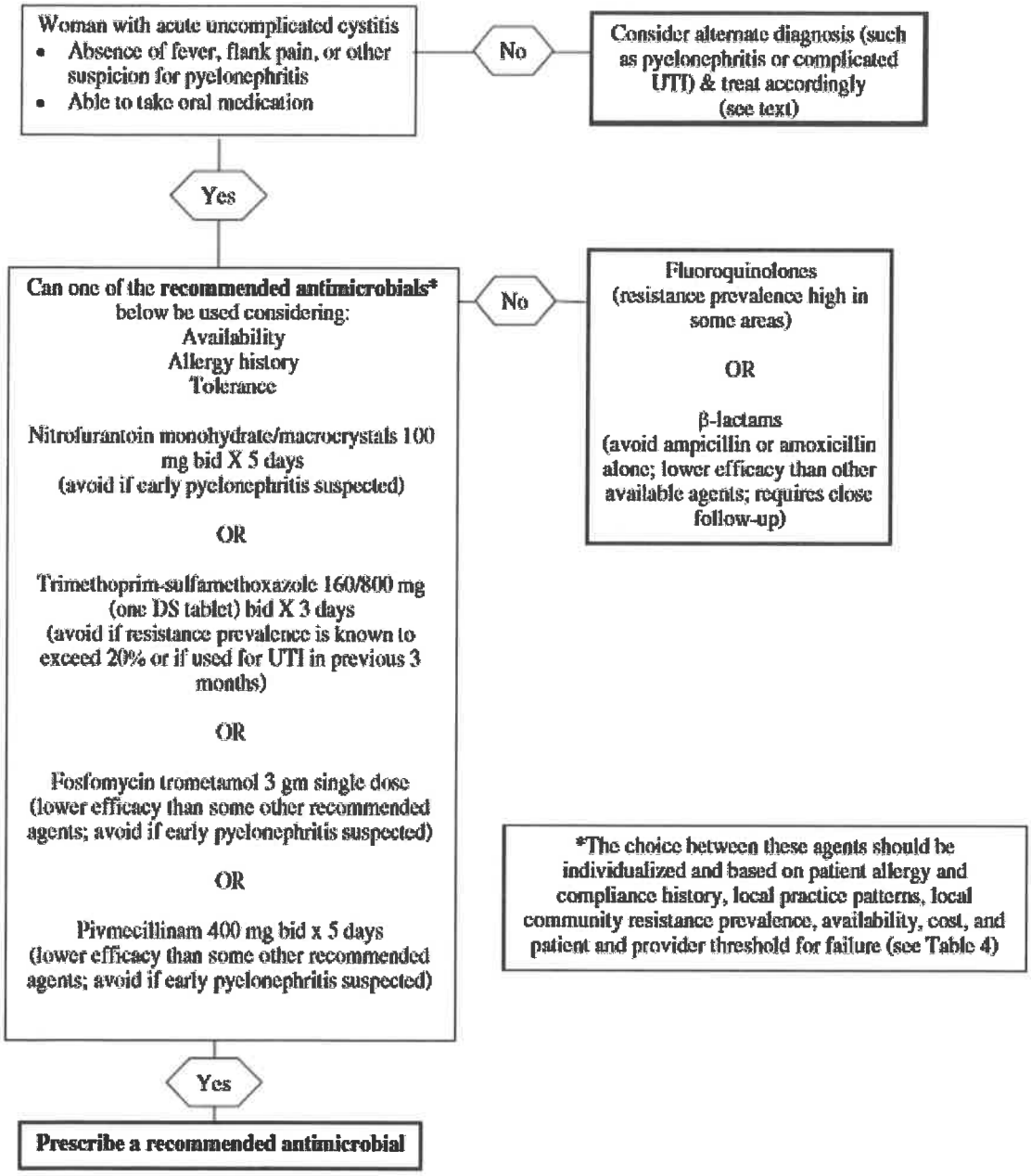
Asymptomatic bacteriuria (ASB)

1. Diagnosis of ASB should be based on culture results:
    - For asymptomatic women, bacteriuria is defined as 2 consecutive voided urine specimens with the same isolated bacterial strain containing counts >105 cfu/ml.
    - A single, clean-catch voided urine specimen with one bacterial species isolated in a quantitative count >105 cfu/mL identifies bacteriuria in men.
    - A single catheterized urine specimen with 1 bacterial species isolated in a quantitative count >102 identifies bacteriuria in women and men.
2. Pyuria accompanying ASB is not an indication for antimicrobial treatment alone.
3. Pregnant women should be screened for bacteriuria by urine culture at least once in early pregnancy (between 12-16 weeks), and they should be treated if the results are positive.
    - The duration of antimicrobial therapy should be 3-7 days.
    - Periodic screening for recurrent bacteriuria should be undertaken following therapy.
    - No recommendation can be made for or against repeated screening of culture-negative women in later pregnancy.
4. Screening for and treatment of ASB before transurethral resection of the prostate is recommended.
    - An assessment for the presence of bacteriuria should be obtained, so that results will be available to direct antimicrobial therapy prior to the procedure.
    - Antimicrobial therapy should be initiated shortly before the procedure.
    - Antimicrobial therapy should not be continued after the procedure, unless and indwelling catheter remains in place.
5. Screening for and treatment of ASB is recommended before other urologic procedures for which mucosal bleeding is anticipated.
6. Screening for or treatment of ASB is not recommended for the following persons:
    - Premenopausal, non-pregnant women
    - Diabetic women
    - Older persons living in the community
    - Elderly, institutionalized subjects
    - Persons with a spinal cord injury
    - Catheterized patients while the catheter remains in situ
7. Antimicrobial treatment of asymptomatic women with catheter-acquired bacteriuria that persists 48 hours after indwelling catheter removal may be considered.
8. No recommendation can be made for screening for or treatment of ASB in renal transplant or other solid organ transplant recipients.

Uncomplicated Cystitis (women)

1. Nitrofurantoin 100 mg PO BID for 5 days

    - Appropriate choice for therapy due to minimal resistance and propensity for collateral damage and efficacy comparable to 3 days of trimethoprim/sulfamethoxazole.
    - Should not be used in patients with CrCl <30 ml/min as insufficient drug is filtered and thus ineffective in the treatment of cystitis. The success of therapy depends on achieving adequate urinary concentrations.
2. Sulfamethoxazole/Trimethoprim 1 DS tablet (800/160 mg) PO BID x3 days
    - Appropriate choice for therapy, however, review of local resistance is imperative.
    - Check local resistance patterns. Should be used with caution and last line for empiric therapy when susceptibility for this is < 80% at your service unit. Also, some studies have shown high levels of resistance when patients have been exposed to sulfamethoxazole/trimethoprim in the last 90-100 days.
3. Cephalexin 500mg po BID for 3-7 days
    - An available option for uncomplicated cystitis to be used cautiously.
    - β-Lactam agents, including amoxicillin-clavulanate, cefdinir, cefaclor, and cefpodoxime-proxetil, in 3–7-day regimens are also appropriate choices
    - Amoxicillin or ampicillin should not be used for empirical treatment given the relatively poor efficacy and the very high prevalence of antimicrobial resistance to these agents worldwide.
    - The β-lactams generally have inferior efficacy and more adverse effects, compared with other UTI antimicrobials.
4. Ciprofloxacin 250 mg po BID for 3 days
    - The fluoroquinolones, ciprofloxacin, ofloxacin, and levofloxacin, are highly efficacious in 3-day regimens, however, have a propensity for collateral damage and should be reserved for important uses other than acute cystitis and thus should be considered alternative antimicrobials for acute cystitis.
5. Fosfomycin trometamol 3 g po as a single dose
    - An appropriate choice for therapy where it is available due to minimal resistance and propensity for collateral damage, however, it appears to have inferior efficacy compared to standard short-course regimens.


Woman with acute uncomplicated cystitis
• Absence of fever, flank pain, or other suspicion for pyelonephritis
• Able to take oral medication
No
Consider alternate diagnosis (such as pyelonephritis or complicated UTI) & treat accordingly (see text)
Yes
Can one of the recommended antimicrobials* below be used considering:
Availability
Allergy history
Tolerance
Nitrofurantoin monohydrate/macrocrystals 100 mg bid X 5 days
(avoid if early pyelonephritis suspected)
OR
Trimethoprim-sulfamethoxazole 160/800 mg (one DS tablet) bid X 3 days
(avoid if resistance prevalence is known to exceed 20% or if used for UTI in previous 3 months)
OR
Fosfomycin trometamol 3 gm single dose
(lower efficacy than some other recommended agents; avoid if early pyelonephritis suspected)
OR
Pivmecillinam 400 mg bid x 5 days
(lower efficacy than some other recommended agents; avoid if early pyelonephritis suspected)
No
Fluoroquinolones
(resistance prevalence high in some areas)
OR
β-lactams
(avoid ampicillin or amoxicillin alone; lower efficacy than other available agents; requires close follow-up)
*The choice between these agents should be individualized and based on patient allergy and compliance history, local practice patterns, local community resistance prevalence, availability, cost, and patient and provider threshold for failure (see Table 4)
Yes
Prescribe a recommended antimicrobial

Complicated Cystitis

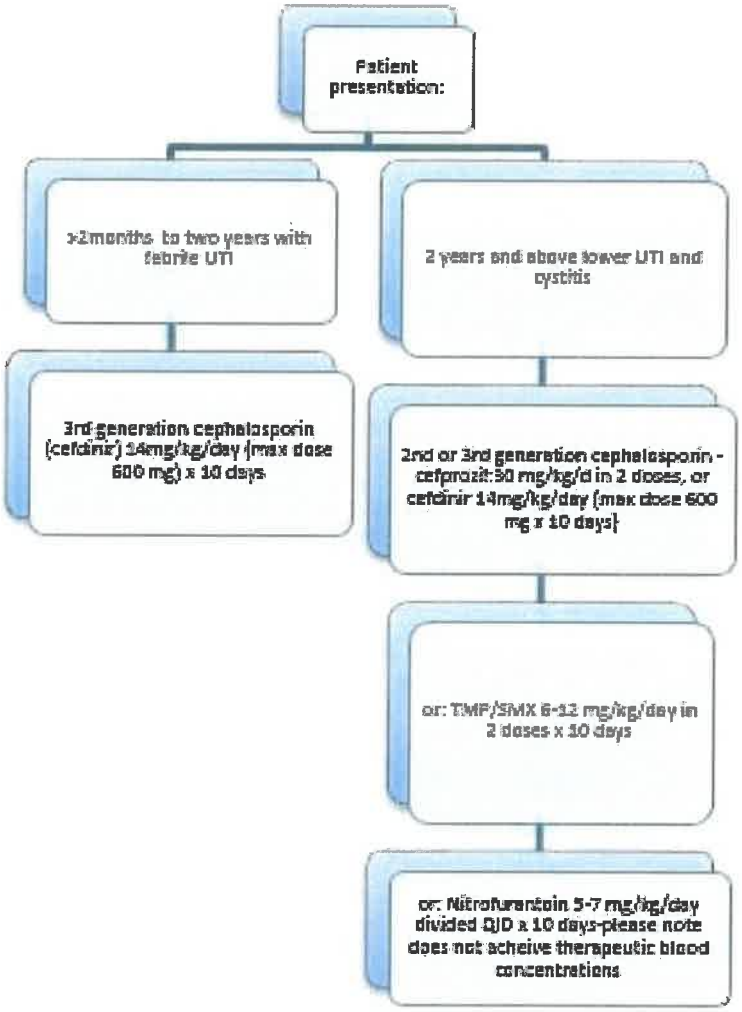
Complicated cystitis is defined as a UTI plus co-morbid condition(s) that increase infection severity such as: diabetes, pregnancy, late diagnosis, foley catheter, obstruction secondary to stone, immunosuppression, and anatomic abnormalities.

1. Nitrofurantoin
    - Not recommended in men for complicated cystitis, UTI with stones, abnormal anatomy nor catheter in place due to the risk that infection has progressed and lack of drug penetration into associated tissues.
    - May be appropriate for patients with diabetes mellitus or pregnancy (contraindicated at full term; 38 weeks or imminent delivery).
2. Sulfamethoxazole/Trimethoprim 1 DS tablet (160/800 mg) po BID for 7-14 days
    - Review of local resistance is imperative
    - Check local resistance patterns. Should be used with caution and last line for empiric therapy when high resistance (>20%) is present at your service unit.
    - Some studies have shown high levels of resistance when patients have been exposed to sulfamethoxazole/trimethoprim in the last 90 days.
3. Ciprofloxacin 500mg PO BID or Levofloxacin 750mg QD for 7-14 days
    - Regimen should be considered last line when first and second line agents are inappropriate (i.e., drug allergy, renal dysfunction, etc.).
    - When local resistance is ≥ 10% the use of fluoroquinolones is cautioned.

Pyelonephritis

1. A urine culture and susceptibility test should always be performed and initial empiric therapy selected and tailored to the uropathogen.
2. Ciprofloxacin 500 mg po BID for 7 days, with or without an initial 400 mg dose of IV ciprofloxacin is an appropriate choice for therapy in patients not requiring hospitalization where the prevalence of resistance of community uropathogens to fluoroquinolones is not known to exceed 10%.
    - If an initial one-time intravenous agent is used, a long acting antimicrobial, such as 1 g of ceftriaxone or a consolidated 24-h dose of an aminoglycoside, could be used in lieu of an intravenous fluoroquinolone. If the prevalence of fluoroquinolone resistance is thought to exceed 10%, an initial 1-time intravenous dose of a long-acting parenteral is recommended.
    - Data are insufficient to make a recommendation about what fluoroquinolone resistance level requires an alternative agent in conjunction with or to replace a fluoroquinolone for treatment of pyelonephritis.
3. A once-daily oral fluoroquinolone such as ciprofloxacin (1000 mg XR for 7 days) or levofloxacin (750 mg for 5 days), is also an appropriate choice with same conditions as above (not requiring hospitalization, local resistance < 10%, and utilizing a long-acting parenteral antimicrobial).
    - If the prevalence of fluoroquinolone resistance is thought to exceed 10%, an initial intravenous dose of a long-acting parenteral antimicrobial, such as 1 g of ceftriaxone or a consolidated 24-h dose of an aminoglycoside, is recommended.
4. Oral Sulfamethoxazole/Trimethoprim 1 DS tablet (160/800 mg) BID for 14 days is an appropriate choice for therapy if the uropathogen is known to be susceptible. If Sulfamethoxazole/Trimethoprim is used when the susceptibility is not known, an initial intravenous dose of a long-acting parenteral antimicrobial, such as 1 g of ceftriaxone or a consolidated 24-h dose of an aminoglycoside, is recommended.
5. Oral β-lactam agents are less effective than other available agents for treatment of pyelonephritis.
    - If an oral β-lactam agent is used, an initial intravenous dose of a long-acting parenteral antimicrobial, such as 1 g of ceftriaxone or a consolidated 24-h dose of an aminoglycoside, is recommended.
    - Data are insufficient to modify the previous guideline recommendation for a duration of therapy of 10–14 days for treatment of pyelonephritis with a b-lactam agent.

Pediatric UTI



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National Pharmacy Council Antimicrobial Stewardship Program (ASP) Recommendations

Guideline Recommendations

1. Inpatient recommended guidelines: separate document
2. AmbuCare recommended guidelines: separate document

Recommendations for ASP implementation at Service Units

1. Identify a local Provider and Pharmacist to champion ASP
   a. Coordinate ASP activities with local Microbiologist and Laboratory Director
2. Education of facility staff (Providers, Pharmacy, Nursing, Lab and Infection Control) on ASP including rationale and referencing CMS transmittal
3. Antimicrobial guidelines for inpatient and ambulatory care infections
   a. Recommend that each Service Unit (SU) develop evidence-based guidelines for their specific most common infections, to include local resistance patterns, local patient specific needs, and local formulary restrictions
   b. Recommend contacting ASP working group for help in developing Evidence Based Medicine (EBM) guidelines utilizing current recommendations as a starting point
4. ASP monitors, surveillance activities
   a. Recommend inpatient prospective audit and feedback activities as a primary focus for hospitalized patients.
   b. Recommend trending antimicrobial utilization with regular feedback to prescribers.
   c. Recommend tracking adverse drug effects – specifically w/ antimicrobials
   d. Develop Service Unit (SU) specific intervention tracking – Access database would be very useful (ex. Anticoagulation Access database)
   e. As programs develop, recommend national monitor for SU to report to
   f. Recommend contacting ASP working group for help in developing SU specific surveillance activities

Antibiogram recommendations

1. Recommended that each Service Unit prepare an Antibiogram
2. Recommend presenting an educational section of the antibiogram
   a. May include important strains that are not included in the antibiogram (*C. difficile*, MTB, KPC, etc)
   b. May include trend data (MRSA, VISA, hVISA, CRE, etc)
3. Recommend use of an Antibiogram toolkit
   a. See AZ Antibiogram Toolkit
4. Recommend contacting ASP working group for help in developing antibiograms
5. ASP rapid diagnostic capabilities
   a. Recommend planning for rapid laboratory diagnostic platforms based on SU data and ASP work group guidelines

Governance:

Determine where local antibiotic stewardship resides: P&T, ICC or both, Med Staff, other?

Clearly define how the information is moved to the Medical Staff and eventually to the

Governing Body.

EHR recommendations

1. Develop EHR pediatric weight based antibiotic quick orders or at minimum attach a drug text to the orderable item with recommended weight based dosing
2. Develop EHR disease state menus with recommended first line, second line medications
3. Develop EHR-instrument interfaces for electronic transfer of identification, susceptibility, and other data to ensure accuracy of results and to facilitate ASP data capture and antibiogram preparation

Ongoing ASP workgroup support

1. Create and continually update an ASP Max Gov site providing links to newest guidelines from nationally recognized organizations for consideration, antibiogram data, educational documents and/or links, and other useful information
2. Provide direct interaction and recommendations with Service Units during the initial implementation phase
3. Provide antibiogram analysis
4. Provide direct interaction and recommendations with Service Units as requested
5. ASP workgroup report quarterly to National Pharmacy and Therapeutics Committee providing updates on national guidelines and formulary recommendations

Sharing information with local and regional health care systems:

1. Recommend all IHS Service Unit (SU) reporting antibiogram data to ASP workgroup
2. Recommend sharing resistance data with health systems that the SU commonly shares patients
3. Recommend sharing antimicrobial formulary with the local health systems
4. Recommend opening a dialog with these local health systems and with the state health departments that the SU covers (this may be multiple states for some SUs)
5. Recommend contacting ASP workgroup when initially developing regional ASP relationships

Local, regional and State health care considerations:

1. Establish Points of Contact (POC)/champions
2. Set an agenda
   a. Initially modest
   b. Discuss long range goal
3. Sharing of data
   a. Facility approval
4. Communication in event of resistant microbe(s). Resistance trends reported.
5. Monthly meetings to initially establish the group with quarterly meetings thereafter and an option for as needed meetings

Educational materials

Educational materials, guidelines, and tracking tools are available on the Max Gov website:
https://login.max.gov/cas/login?service=https%3A%2F%2Fcommunity.max.gov%2Flogin.action%3Fos_destin

ation%3D%252Fpages%252Fviewpage.action%253FspaceKey%253DHHSExternal%2526title%253DAntibiotic%252BStewardship%252BWorkgroup