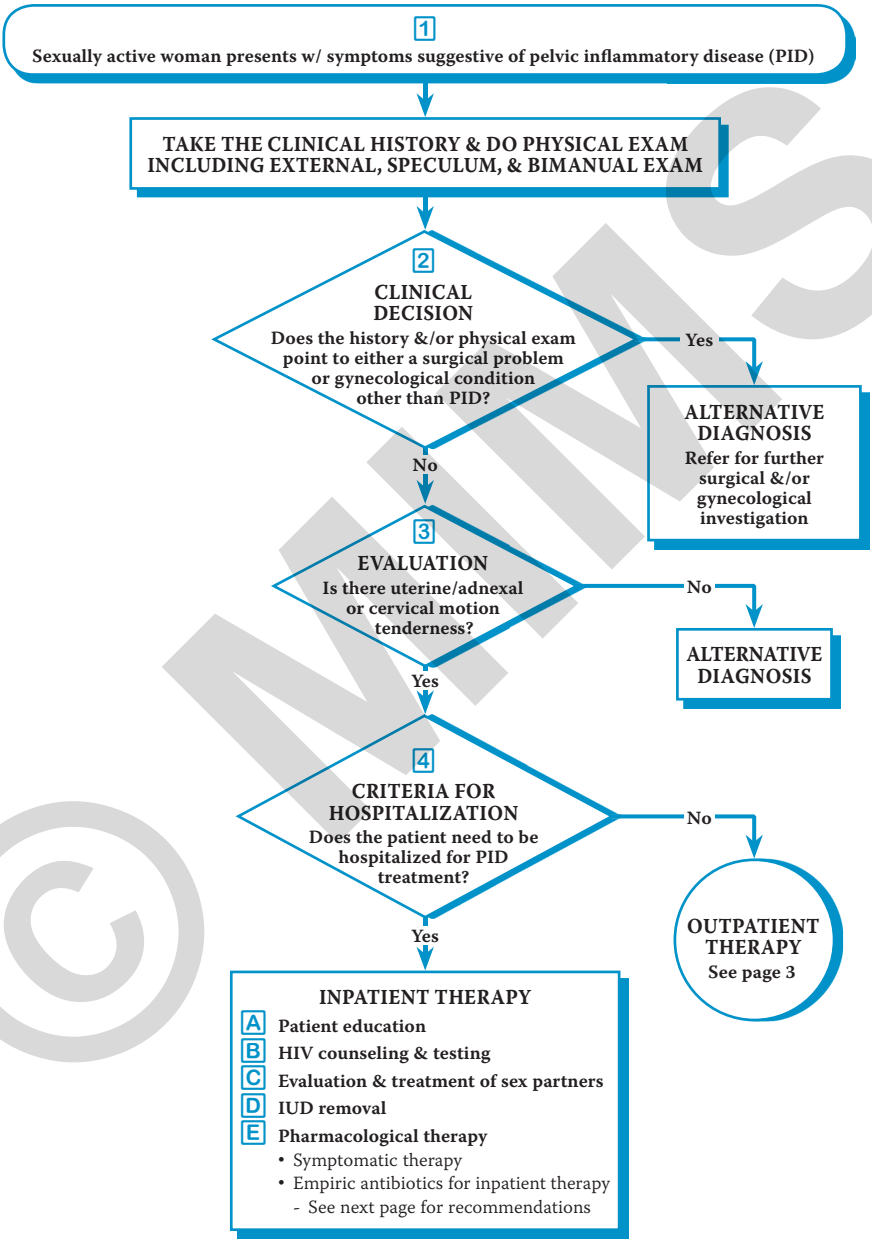
Pelvic Inflammatory Disease (1 of 11)

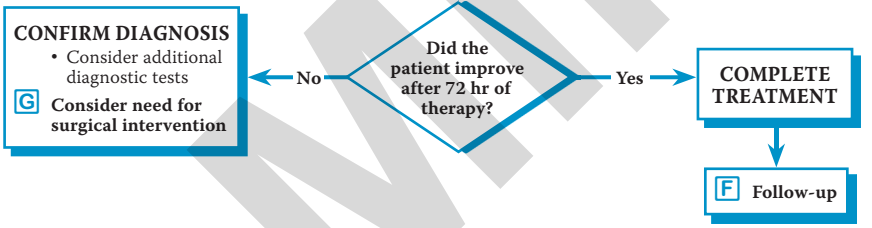


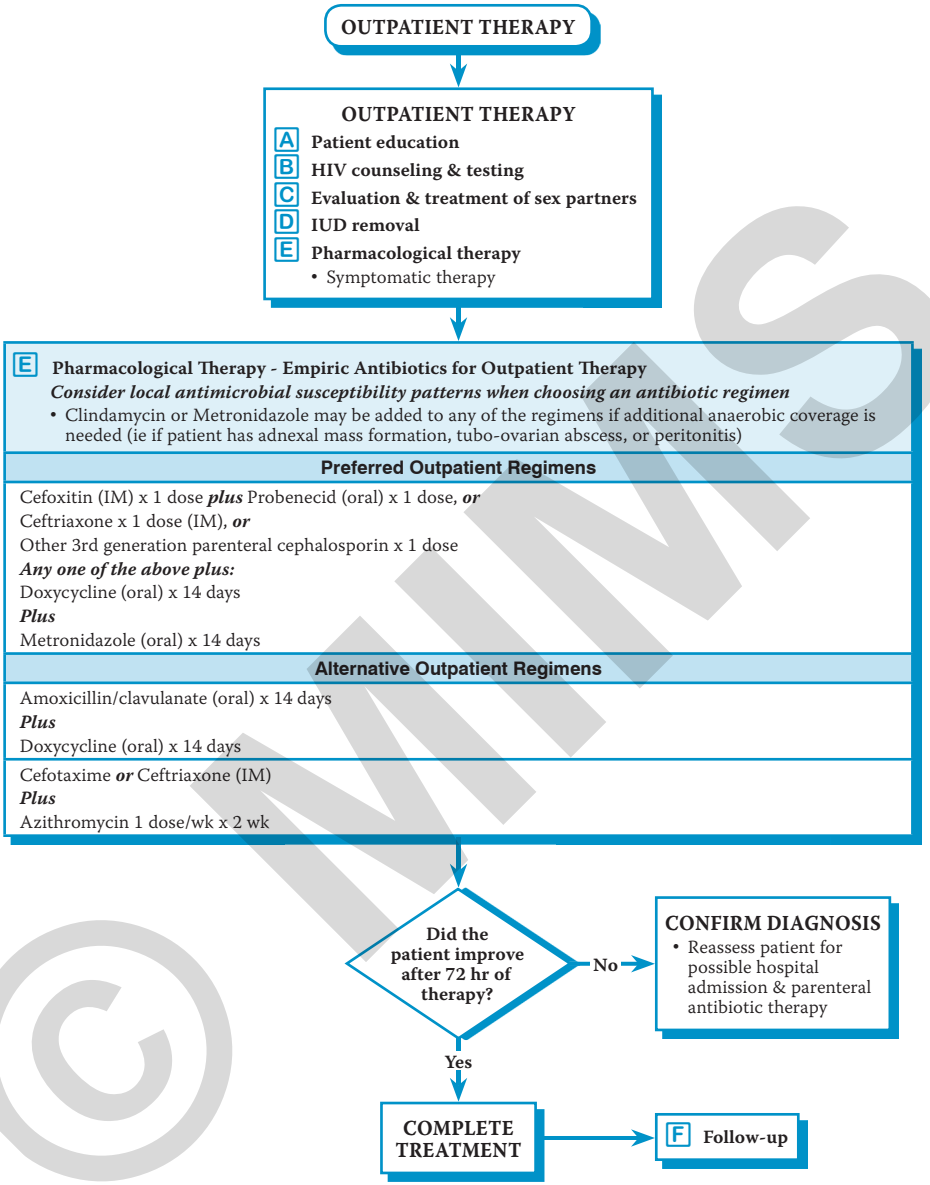
E Pharmacological Therapy - Empiric Antibiotics for Inpatient Therapy

Consider local antimicrobial susceptibility patterns when choosing an antibiotic regimen

- Clindamycin or Metronidazole may be added to any of the regimens if additional anaerobic coverage is needed (ie if patient has adnexal mass formation, tubo-ovarian abscess or peritonitis)

Preferred Initial Inpatient Regimens	Preferred Step-down Regimens
Cefotetan ***or*** Cefoxitin (IV) ***Plus*** Doxycycline (oral/IV)	Doxycycline (oral) ***w/ or w/o*** Clindamycin ***or*** Metronidazole (oral) x 14 days
Cefuroxime ***or*** Ceftriaxone (IM/IV) ***Plus*** Doxycycline (oral/IV)	Doxycycline (oral) ***Plus*** Metronidazole (oral) x 14 days
Clindamycin (IV) ***Plus*** Gentamicin (IV)	Clindamycin ***or*** Doxycycline (oral) x 14 days ***w/ or w/o*** Metronidazole (oral) x 14 days
Alternative Initial Inpatient Regimens	
Aminopenicillin/beta-lactamase inhibitor (IV) ***Plus*** Doxycycline (oral/IV)	
Duration of Treatment • Continue until patient has shown improvement for 24-48 hr then shift to oral step-down regimen	**Duration of Treatment** • Continue for a total of 14 days of treatment





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1 PELVIC INFLAMMATORY DISEASE (PID)

- Ascent of bacteria from the vagina or cervix resulting in infection of the reproductive organs eg uterus, fallopian tubes, ovaries; may be a complication of some STIs

The following are the most common symptoms of PID:

- Lower abdominal pain (crampy or dull)
  - Starts a few days after the onset of the last menstrual period
- Dyspareunia
- Abnormal vaginal or cervical discharge
- Postcoital or irregular vaginal bleeding
- Dysuria
- Fever
- Nausea & vomiting (N/V)
- Some have minimal symptom or silent PID

2 CLINICAL DECISION

The presence of the following points in the history or the presence of these signs & symptoms increases the likelihood of an abdominal surgical problem or a gynecological condition other than PID:

- Patients w/ these conditions should be referred for further surgical &/or gynecological evaluation
- Missed/overdue period
- Recent delivery/abortion/miscarriage
- Bowel signs & symptoms
- Abdominal guarding &/or rebound tenderness
- Abnormal vaginal bleeding
- Abdominal mass

Risk Factors for PID

- Prior episode of PID
- Previous gonorrheal or chlamydial infection
- Bacterial vaginosis
- Multiple sex partners
- Male sex partner w/ gonorrhea or *Chlamydia* infection
- Current douching
- Low socioeconomic status
- Adolescent; younger age at 1st sexual intercourse
- Previous instrumentation of the uterus
  - Insertion of IUD within preceding 3 weeks
  - Hysterosalpingography
  - Termination of pregnancy

Differential Diagnoses

- Ectopic pregnancy
- Endometriosis
- Acute appendicitis
- Adnexal tumors
- Ovarian cyst or torsion
- UTI
- Irritable bowel syndrome
- Functional pain (pain w/ no known physical cause)

3 EVALUATION

- Empiric treatment for PID should be started in sexually active young women & other women at risk for STIs if they are experiencing pelvic or lower abdominal pain, if no cause for the illness other than PID can be identified, & if ≥1 of the following minimum criteria are present on pelvic exam: Cervical motion tenderness, uterine tenderness, or adnexal tenderness
- A low threshold for diagnosis of PID must be maintained because of difficulty in diagnosis & great potential for damage

Additional Criteria Supporting Diagnosis of PID

- Temp >38.3°C
- Abnormal cervical or vaginal mucopurulent discharge
- WBCs on saline microscopy of vaginal secretions
  - Absence of vaginal or endocervical pus cells may rule out PID but their presence is nonspecific
- Elevated ESR, elevated C-reactive protein (CRP), & leukocytosis
  - Nonspecific & can be normal in mild cases
- Lab documentation of cervical infection w/ *Neisseria gonorrhoeae* or *Chlamydia trachomatis*
  - Endocervical or vulvovaginal samples for nucleic acid amplification test or culture
  - Positive result supports the clinical diagnosis of PID & emphasizes the need to treat sex partners; negative result does not exclude PID

Most Specific Criteria for Diagnosing PID

- Endometrial biopsy showing histopathologic evidence of endometritis
  - Not useful in making diagnosis in the acute setting because of the time required to make histopathologic diagnosis
- Transvaginal sonography (TVS) or MRI showing thickened, fluid-filled tubes w/ or without free pelvic fluid or tubo-ovarian complex, or doppler studies suggesting pelvic infection
- Laparoscopic abnormalities consistent w/ PID
  - Considered by some authorities to be the gold standard in diagnosing PID
  - Make an accurate diagnosis possible, yield information on the severity of the condition, & provide access to material that may be sent for bacteriologic culture
  - Typical findings are erythematous & swollen fallopian tubes w/ purulent discharge from the fimbrial end
  - Currently, use is restricted by expense & limited availability

4 CRITERIA FOR HOSPITALIZATION

Patients who fulfill any of the following criteria need to be hospitalized:
- Uncertain diagnosis
- Surgical emergencies eg appendicitis & ectopic pregnancy cannot be excluded
- Suspected pelvic/tubo-ovarian abscess
- Severe illness (N/V or high fever) precluding outpatient management
- Pregnancy
- Inability to follow or tolerate an outpatient regimen
- Concomitant HIV infection
- Unresponsive to an outpatient regimen

A PATIENT EDUCATION

- Patient needs to be informed about the nature of the infection & the importance of taking the full course of medication
- Counsel patients on possible complications of sexually transmitted infection (STI)
- Inform the patient of the possible short-term effects of PID (eg tubo-ovarian abscess) as well as long-term consequence (eg infertility, ectopic pregnancy, chronic pelvic pain)
  - Incidence of long-term adverse effect of PID is directly related to the number of recurrences of PID
- Patients should be advised to avoid unprotected sex until they & their partners have completed therapy & follow-up

Advise patients on how to lower their risk of acquiring STIs:
- Tailor counseling to the patient's specific risk factors
- Abstinence, condom use
- Careful selection of partners

B HIV COUNSELING & TESTING

- STI consultation allows for an opportunity to discuss patient's risk factors for STIs & HIV
- Determine patient's risk for HIV & discuss HIV testing
- Testing for HIV is recommended & should be offered to all persons seeking evaluation & treatment for STIs
  - Pretest & posttest counseling as well as informed consent are part of the testing procedure
  - Concomitant infection w/ HIV may complicate management & control of some STIs
  - HIV-infected patients w/ PID are more common to have tubo-ovarian abscess & usually require surgical intervention

C EVALUATION & TREATMENT OF SEX PARTNERS

- Even if asymptomatic, sexual partners of STI patients are likely to be infected & should be offered treatment to prevent further STI transmission & reinfection
- Examine & treat all partners who had sexual contact w/ the patient during the 60 days preceding the onset of the patient's symptoms
- Treat empirically w/ regimens effective against both *C trachomatis* & *N gonorrhoeae*
  - See Gonorrhea- & Chlamydia-Uncomplicated Anogenital Infection disease management charts for details

D IUD REMOVAL

- No evidence that removal of the IUD provides any additional benefit
  - Effect of continued use of IUD on treatment failure & recurrence of PID is unknown
- May remove if the patient does not want to keep the IUD or if symptoms have not resolved within 72 hours after start of treatment
  - Caution & close clinical follow-up are needed if IUD will not be removed
  - If IUD will be removed, should wait until after therapy has been initiated & at least 2 doses of antibiotics have been given
- Provide contraceptive counseling if IUD is removed
- If patient still requests for an IUD as a contraceptive but is likely to be at risk of future PID, Levonorgestrel-intrauterine system (LNG-IUS) should be recommended

E PHARMACOLOGICAL THERAPY

Symptomatic Therapy
- May give analgesics (eg Paracetamol) for pain

Antibiotic Therapy

General Principles
- Goals of therapy are to control the acute infection & to prevent long-term sequelae

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E PHARMACOLOGICAL THERAPY (CONT'D)

General Principles (Cont'd)
- Initiate antibiotic therapy as soon as presumptive diagnosis has been made because prevention of long-term adverse effect depends on immediate administration of proper antibiotic
  - The risk of tubal infertility or ectopic pregnancy may increase by 3x in female treated >72 hours after symptom onset
  - Treatment w/ antibiotics does not reverse any damage already incurred by the reproductive organs
- All antibiotic regimens must provide adequate coverage for the following possible etiologic organisms for PID:
  - *N gonorrhoeae, C trachomatis,* anaerobes (Bacteroides, Gram-positive cocci), *Mycoplasma hominis*, facultative Gram-negative rods & Gram-positive aerobes
    - Rates of gonorrheal resistance are increasing for quinolones
- The need to eliminate anaerobes in patients w/ PID has not been definitively determined
  - *In vitro* studies show that some anaerobes can cause tubal & epithelial destruction & many women w/ PID also have bacterial vaginitis; recommended regimens should therefore include anaerobic coverage
- Oral vs parenteral therapy
  - Oral & parenteral therapy appear to be similarly effective in patients w/ mild-moderate PID
  - Most trials used parenteral therapy x 48 hr but this time-frame is arbitrary
    - Direct inpatient observation is recommended for at least 24 hr in those who have tubo-ovarian abscesses
  - Time to switch from parenteral to oral therapy should be guided by clinical experience
    - Shift to oral therapy can be started within 24 hours of clinical improvement (ie defervescence, decreased abdominal tenderness, & decreased uterine, adnexal, or cervical cervical motion tenderness)
- Consider drug availability, cost & patient acceptance, together w/ local antimicrobial susceptibility & epidemiology patterns when choosing an antibiotic regimen

Empiric Antibiotic Therapy

Aminopenicillin/Beta-lactamase Inhibitor
- Effective for patients w/ tubo-ovarian abscess when given w/ Doxycycline

Azithromycin
- Data regarding use as monotherapy for PID is limited & should not be used without Ceftriaxone

Cephalosporins
- Recommended agents: Cefotetan, Cefoxitin, Ceftizoxime, Cefotaxime,Ceftriaxone
  - Effective against *N gonorrhoeae,* enteric Gram-negative rods, Streptococci
- Ceftriaxone is less effective than Cefoxitin or Cefotetan against anaerobic bacteria but Ceftriaxone has better coverage for *N gonorrhoeae*
- Limited data on other cephalosporins

Clindamycin
- Good anaerobic coverage
- Usually given when there is associated tubo-ovarian abscess

Doxycycline
- Effective against *C trachomatis*
- Contraindicated in pregnancy
- Should be administered orally when possible due to infusion-associated pain

Gentamicin
- Effective against enteric Gram-negative rods
- Single daily dosing may be used

Metronidazole
- Good anaerobic coverage
- Effective against organisms causing bacterial vaginosis which is often present in PID patients
- Usually given when there is associated tubo-ovarian abscess

F FOLLOW-UP

- Further review 4 weeks after treatment may be useful to ensure the following:
  - Adequate clinical response
  - Compliance w/ oral antibiotics
  - Screening & treatment of sex partners/contacts
  - Recurrence prevention through condom use
- Repeat testing for etiologic organisms may be warranted for patients w/ persistent symptoms, poor compliance w/ antibiotics, or possible reinfection
  - In patients w/ documented infection w/ *C trachomatis & N gonorrhoeae,* some specialists recommend rescreening 4-6 weeks after completion of treatment

G SURGERY

- Considered in severe cases or when pelvic abscess is present

Laparoscopy
- Helps resolve PID early by adhesiolysis & drainage of pelvic abscess

Ultrasound-guided Aspiration
- Less invasive & may be equally effective as w/ laparoscopy

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Dosage Guidelines

AMINOGLYCOSIDE

Drug	Dosage	Remarks
Gentamicin	**Inpatient Therapy:** 2 mg/kg IV loading dose followed by 1.5 mg/kg IV 8 hrly as maintenance dose **or** 5-7 mg/kg IV 24 hrly	**Adverse Reactions** • Ototoxic effects (irreversible ototoxicity resulting in hearing loss, dizziness, vertigo); Renal effects (reversible nephrotoxicity, acute renal failure when other nephrotoxic drugs have been administered); Neuromuscular effects (neuromuscular paralysis, gait instability); Hypersensitivity reactions **Special Instructions** • High plasma levels increase the risk of nephrotoxicity & ototoxicity; therefore, monitoring serum concentrations by measuring peak & trough levels is recommended • Use w/ caution in patients w/ conditions associated w/ muscle weakness (eg myasthenia gravis, Parkinson's), patients w/ preexisting renal dysfunction, vestibular or cochlear impairment, or hypocalcemia

CEPHALOSPORINS

Drug	Dosage	Remarks
Second Generation		
Cefotetan	**Inpatient Therapy:** 2 g IV over 3-5 min 12 hrly	**Adverse Reactions** • Hypersensitivity reactions (urticaria, pruritus, rash, severe reactions eg anaphylaxis can occur); GI effects (diarrhea, N/V, rarely antibiotic-associated diarrhea/colitis); Other effects (candidal infections) • High doses may be associated w/ CNS effects (encephalopathy, convulsions); Rarely hematologic, hepatic & renal effects have occurred • Prolonged prothrombin time (PT), prolonged activated partial thromboplastin time (APTT), &/or hypoprothrombinemia (w/ or w/o bleeding) have been reported & occur most frequently w/ NMTT side chain-containing cephalosporins **Special Instructions** • Use w/ caution in patients allergic to Penicillin, there may be 10% chance of cross sensitivity • Use w/ caution in patients w/ renal impairment
Cefoxitin	**Inpatient Therapy:** 2 g IV over 3-5 min 6-8 hrly **Outpatient Therapy:** 2 g IM as a single dose ***Plus*** Probenecid 1 g PO as a single dose	
Cefuroxime	750 mg IM/IV 8 hrly **Severe Infection:** 1.5 g IV 6-8 hrly	

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Dosage Guidelines

CEPHALOSPORINS (CONT'D)

Drug	Dosage	Remarks
Third Generation		
Cefoperazone	2-4 g/day IV/IM in divided doses 12 hrly	**Adverse Reactions** • Hypersensitivity reactions (urticaria, pruritus, rash, severe reactions eg anaphylaxis can occur); GI effects (diarrhea, N/V, rarely antibiotic-associated diarrhea/colitis); Other effects (candidal infections) • High doses may be associated w/ CNS effects (encephalopathy, convulsions); Rarely hematologic, hepatic & renal effects have occurred • Prolonged prothrombin time (PT), prolonged activated partial thromboplastin time (APTT), &/or hypoprothrombinemia (w/ or w/o bleeding) have been reported & occur most frequently w/ NMTT side chain-containing cephalosporins **Special Instructions** • May be taken w/ food to decrease gastric distress • Use w/ caution in patients allergic to Penicillin, there may be 10% chance of cross sensitivity • Use w/ caution in patients w/ renal impairment • Ceftriaxone should be used w/ caution in patients w/ concurrent hepatic & renal disease & w/ colitis
Cefotaxime	1-2 g IV over 3-5 min/IM 4-12 hrly **Max Dose:** 12 g/day	
Ceftazidime	1 g IV/IM 8 hrly or 2 g IV/IM 12 hrly	
Ceftizoxime	1-2 g IV over 3-5 min/IM 8-12 hrly	
Ceftriaxone	**Inpatient therapy:** 1-2 g IV over 2-4 min/IM 24 hrly **Outpatient therapy:** 250 mg IM as a single dose	
Cephalosporin w/ β-Lactamase Inhibitor		
Cefoperazone/sulbactam	2-4 g/day IV/IM in divided doses 12 hrly	

CHLORAMPHENICOL

Drug	Dosage	Remarks
Chloramphenicol	2-3 g IV over 1 min 6-8 hrly **or** 50 mg/kg/day IV over 1 min divided 6 hrly	**Adverse Reactions** • Hematologic effects (reversible bone marrow depression, rarely severe irreversible aplastic anemia); Hypersensitivity reactions (anaphylactoid reactions); GI effects (N/V, diarrhea, stomatitis, glossitis, bitter taste); Misc effects (optic neuritis, neuropathy, paresthesias) • Gray syndrome can occur in adults & older children given high doses (abdominal distention, vomiting, ashen color, irregular respiration, circulatory collapse, death) **Special Instructions** • Avoid in patients w/ preexisting bone marrow depression or blood dyscrasias • Use w/ caution in patients w/ G6PD • Dosage must be adjusted for patients w/ hepatic or renal insufficiency • Due to narrow therapeutic/toxic ratio, monitor serum levels if possible, particularly in patients w/ hepatic or renal disease

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Dosage Guidelines

MACROLIDE

Drug	Dosage	Remarks
Azithromycin	**Outpatient therapy:** 500 mg-1 g IV once a wk x 2 wk **or** 500 mg IV single dose x 1-2 days then 250 mg PO 24 hrly to complete a 7-day course	**Adverse Reactions** • GI effects (N/V, abdominal discomfort, diarrhea & other GI disturbances, antibiotic-associated diarrhea/colitis); Other effects (candidal infections) • Hypersensitivity reactions are uncommon (urticaria, pruritus, rash, rarely anaphylaxis); Rarely altered cardiac conduction, hepatotoxicity; Dose-related tinnitus/hearing loss have occurred w/ some macrolides **Special Instructions** • Use w/ caution in patients w/ hepatic dysfunction, severe renal impairment, myasthenia gravis • Use w/out the addition of Ceftriaxone is not advised

PENICILLINS

Drug	Dosage	Remarks
Aminopenicillins w/ β-lactamase Inhibitors		**Adverse Reactions** • Hypersensitivity reactions (rash, urticaria, pruritus, severe reactions eg anaphylaxis can occur); GI effects (diarrhea, N/V, rarely antibiotic-associated diarrhea/colitis); Other effects (candidal infections) • Rarely hematologic, renal & hepatic effects have occurred; high doses may be associated w/ CNS effects (convulsions) **Special Instructions** • Avoid in patients w/ penicillin allergy • Use w/ caution in patients w/ renal & hepatic impairment or w/ asthma
Amoxicillin/ clavulanic acid (Co-amoxiclav, Amoxicillin & clavulanic acid, Amoxicillin/ clavulanate)	**Outpatient therapy:** 625 mg PO 8 hrly x 14 days	
Ampicillin/ sulbactam (Sultamicillin: Pro-drug of Ampicillin/ sulbactam; the 2 drugs are linked chemically w/ a double ester)	**Inpatient therapy:** 3 g IV 6 hrly	
Antipseudomonal Penicillin w/ β-lactamase Inhibitor		
Piperacillin/ tazobactam	12 g Piperacillin/1.5 g Tazobactam slow IV in divided doses 6-8 hrly	

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Dosage Guidelines

QUINOLONES		
Drug	**Dosage**	**Remarks**
Ciprofloxacin	400 mg PO 8-12 hrly x 14 days	**Adverse Reactions** • GI effects (N/V, diarrhea, abdominal pain, dyspepsia, diarrhea, rarely antibiotic-associated diarrhea/colitis); CNS effects (headache, dizziness, sleep disorders, restlessness, drowsiness); Dermatologic effects (rash, pruritus, photosensitivity); Hypersensitivity reactions can range from mild (eg rash) to severe/ life-threatening (eg Stevens-Johnson syndrome) • Rarely hematologic effects; hepatic & renal effects • Some quinolones have the potential to prolong the QT interval **Special Instructions** • Administer at least 2 hr before or 3 hr after Al- or Mg-containing antacids, dietary supplements containing Zn or Fe or buffered Didanosine preparations • Avoid exposure to strong sunlight or tanning beds • Use w/ caution in patients w/ epilepsy or history of CNS disorders, in patients w/ impaired renal or hepatic function & in those w/ G6PD deficiency
Moxifloxacin	400 mg PO 24 hrly x 14 days	
Ofloxacin	200-400 mg PO 24 hrly	

TETRACYCLINE		
Drug	**Dosage**	**Remarks**
Doxycycline	**Inpatient therapy:** 100 mg PO/IV 12 hrly **Outpatient therapy or step-down therapy:** 100 mg PO 12 hrly x 14 days	**Adverse Reactions** • GI effects (N/V, diarrhea, antibiotic-associated diarrhea/colitis, dysphagia, esophageal ulceration when taken w/ an insufficient amount of liqd); Dermatologic effect (photosensitivity); Other effects (candidal infections, discoloration of teeth, interference w/ bone growth in young infants/pregnant women); • Rarely renal dysfunction, hepatotoxicity, hematologic effects, pseudotumor cerebri; Hypersensitivity reactions have occurred **Special Instructions** • Use w/ caution in renal or hepatic impairment • Avoid long exposure to sunlight or tanning beds • Doxycycline may be given w/ meals to decrease GI upset - Take w/ plenty of fluids & have the patient sit up for 30 min after taking the medicine • Tetracycline should be taken 1 hr prior or 2 hr after meals; 1-2 hr or 4 hr after antacid • Avoid in children <8 yr & pregnant women • Avoid in patients w/ SLE

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Dosage Guidelines

OTHER ANTIBIOTICS

Drug	Dosage	Remarks
Lincosamide		
Clindamycin	**Inpatient therapy:** 900 mg IV 8 hrly plus an IV antibiotic w/ Gram-negative anaerobic spectrum **Step-down therapy:** 450-600 mg PO 6 hrly to complete 10-14 days of therapy	**Adverse Reactions** • GI effects (diarrhea, severe antibiotic-related pseudomembranous colitis, N/V, abdominal pain, metallic taste); Hypersensitivity reactions (rash, urticaria, rarely anaphylaxis) • Severe dermatologic effects have occurred (erythema multiforme, exfoliative & vesiculobullous dermatitis); Cardiac, Hematologic & hepatic effects have occurred; Other effect (polyarthritis) **Special Instructions** • Use w/ caution in patients w/ GI disease especially w/ history of colitis • Use w/ caution in atopic patients & in patients w/ renal or hepatic impairment • Discontinue if diarrhea occurs
Nitroimidazole Derivative		
Metronidazole	**Inpatient therapy:** 400 mg PO 12 hrly **Outpatient therapy or step-down therapy:** 500 mg PO 8-12 hrly x 14 days	**Adverse Reactions** • GI effects (N/V, metallic taste, diarrhea, constipation, abdominal cramping); CNS effects (weakness, dizziness, headache, mood changes); CV effects (flattening of T-wave, flushing, syncope); Hematologic effects (reversible neutropenia or thrombocytopenia); Dermatologic effects (rash, pruritus) • High dose or prolonged use has caused CNS effects (eg peripheral neuropathy, seizures, aseptic meningitis) or fungal/bacterial infection (eg pseudomembranous colitis, candidal infection) **Special Instructions** • May be taken w/ food to decrease GI upset • Avoid alcohol intake during treatment & until 24 hr after completion of Metronidazole • Use w/ caution in patients w/ severe hepatic impairment, seizure disorder, blood dyscrasia, heart failure, edema, sodium-retaining state • If given >10 days, recommend monitoring CBCs & clinical monitoring for CNS effects

OTHER BETA-LACTAMS

Drug	Dosage	Remarks
Meropenem	500 mg IV 8 hrly	**Adverse Reactions** • GI effects (diarrhea, N/V, antibiotic-associated diarrhea/colitis); Hypersensitivity reactions ranging from mild (eg rash) to severe (eg anaphylaxis) can occur; Other effects (candidal infections, local reactions at inj site) • CNS effects (headache, paresthesias); Rarely severe dermatologic reactions (eg Stevens-Johnson syndrome, etc); Rarely hepatic effects **Special Instructions** • Use w/ caution in patients allergic to penicillins, cephalosporins or other β-lactams & in patients w/ renal impairment

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