# Quinolones: A Comprehensive Review

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**With the recent introduction of agents such as gatifloxacin and moxifloxacin, the traditional gram-negative coverage of fluoroquinolones has been expanded to include specific gram-positive organisms. Clinical applications beyond genitourinary tract infections include upper and lower respiratory infections, gastrointestinal infections, gynecologic infections, sexually transmitted diseases, and some skin and soft tissue infections. Most quinolones have excellent oral bioavailability, with serum drug concentrations equivalent to intravenous administration. Quinolones have few adverse effects, most notably nausea, headache, dizziness, and confusion. Less common but more serious adverse events include prolongation of the corrected QT interval, phototoxicity, liver enzyme abnormalities, arthropathy, and cartilage and tendon abnormalities. The new fluoroquinolones are rarely first-line agents and should be employed judiciously. Inappropriate use of agents from this important class of antibiotics will likely worsen current problems with antibiotic resistance. Applications of fluoroquinolones in biologic warfare are also discussed. (Am Fam Physician 2002;65:455-64. Copyright© 2002 American Academy of Family Physicians.)**

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The first quinolone, nalidixic acid (NegGram), was introduced in 1962. Since then, structural modifications have resulted in second-, third-, and fourth-generation fluoroquinolones, which have improved coverage of gram-positive organisms.

## Mechanism of Action

Quinolones rapidly inhibit DNA synthesis by promoting cleavage of bacterial DNA in the DNA-enzyme complexes of DNA gyrase and type IV topoisomerase, resulting in rapid bacterial death.[1-3] As a general rule, gram-negative bacterial activity correlates with inhibition of DNA gyrase, and gram-positive bacterial activity corresponds with inhibition of DNA type IV topoisomerase.[1]

## Pharmacokinetics

Like aminoglycosides, the quinolones exhibit concentration-dependent bacterial killing. Bactericidal activity becomes more pronounced as the serum drug concentration increases to approximately 30 times the minimum inhibitory concentration (MIC).[1,4] Higher drug concentrations paradoxically inhibit RNA and protein synthesis, thereby reducing bactericidal activity.[1] Quinolones have a postantibiotic effect of about one to two hours.[1]

When used in combination with agents from other antibiotic classes, such as beta-lactams and aminoglycosides, the quinolones are not predictably synergistic.[1] Although the effects of most combinations are indifferent or additive, ciprofloxacin (Cipro) and rifampin (Rifadin) appear to be antagonistic against *Staphylococcus aureus*.[5]

Quinolones are well absorbed following oral administration, with moderate to excellent bioavailability.[1,4] Serum drug levels achieved after oral administration are comparable to those with intravenous dosing, which allows an early transition from intravenous to oral therapy and a potential reduction of treatment costs.[6]

Food does not impair the absorption of most quinolones. However, quinolones chelate with cations such as aluminum, magnesium, calcium, iron, and zinc. This interaction significantly reduces absorption and bioavailability, resulting in lower serum drug concentrations and less target-tissue penetration.[1,4]

Elimination half-lives for the quinolones vary from 1.5 to 16 hours. Therefore, most of these drugs are administered every 12 to 24 hours. The quinolones are eliminated by renal and nonrenal routes. To avoid toxicity, dosages often need to be adjusted in patients with renal or hepatic impairment.[1,4] The

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majority of quinolones are excreted renally; however, sparfloxacin (Zagam), moxifloxacin (Avelox), and trovafloxacin (Trovan) are excreted hepatically.

Quinolones are widely distributed throughout the body. Tissue penetration is higher than the concentration achieved in plasma, stool, bile, prostatic tissue, and lung tissue. Intracellular concentration is exceptional in neutrophils and macrophages. Quinolones also penetrate well in urine and kidneys when renal clearance is the route of drug elimination. Penetration into prostatic fluid, saliva, bone, and cerebrospinal fluid does not exceed serum drug levels. Because cerebrospinal fluid levels of quinolones are predictably poor, these agents are inadequate for first-line treatment of meningitis.[1,4,7]

## Antimicrobial Activity

The quinolones can be classified into four generations based on antimicrobial activity *(Table 1)*.[8] First-generation agents, which are used less often today, have moderate gram-negative activity and minimal systemic distribution. Second-generation quinolones have expanded gram-negative activity and atypical pathogen coverage, but limited gram-positive activity. These agents are most active against aerobic gram-negative bacilli. Ciprofloxacin remains the quinolone most active against *Pseudomonas aeruginosa*.[1,9,10] Third-generation quinolones retain expanded gram-negative and atypical intracellular activity but have improved gram-positive coverage. Finally, fourth-generation agents improve gram-positive coverage, maintain gram-negative coverage, and gain anaerobic coverage.[10]

Marginal susceptibility and acquired resistance limit the usefulness of second-generation quinolones in the treatment of staphylococcal, streptococcal, and enterococcal infections.[9] The presently available fluoroquinolones with in vitro activity against *Streptococcus pneumoniae* (including current penicillin-resistant strains) are levofloxacin (Levaquin), sparfloxacin, gatifloxacin (Tequin), moxifloxacin, and trovafloxacin. Levofloxacin and sparfloxacin exhibit inferior in vitro streptococcal activity compared with gatifloxacin, moxifloxacin, and trovafloxacin. Gatifloxacin is two to four times more active than levofloxacin against *S. pneumoniae* in vitro, and moxifloxacin is four to eight times more active.[11] Compared with ciprofloxacin and levofloxacin, the fluoroquinolones gatifloxacin, moxifloxacin, and trovafloxacin have greater in vitro activity against *S. aureus* and some Enterococcus strains.[11,12]

Although gatifloxacin and moxifloxacin have in vitro anaerobic activity, only trovafloxacin is labeled for the treatment of anaerobic infections. Clinafloxacin, an investigational fluoroquinolone, has the most potent in vitro anaerobic activity.[13]

Ciprofloxacin, ofloxacin (Floxin), and the newer fluoroquinolones have exceptional intracellular concentrations. Moxifloxacin, gatifloxacin, levofloxacin, and the investigational drug gemifloxacin have exceptional activity against Legionella, Chlamydia, Mycoplasma, and Ureaplasma species.[9] Intracellular respiratory pathogens such as *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, and *Legionella pneumophila* are predictably susceptible to fluoroquinolones.[1,9] These antibiotics are regarded as second-line antituberculous agents and should be reserved for the treatment of resistant tuberculosis.

## Resistance to Quinolones

Quinolone resistance has multiple mechanisms and significant clinical impact. Mutations may occur rapidly during fluoroquinolone therapy and may be the most significant factor limiting the use of these antimicrobials.

TABLE 1
**Comparison of Quinolone Generations**

| *Quinolone generations* | *Microbiologic activity* | *Administration and characteristics* | *Indications* |
|---|---|---|---|
| First generation | | | |
| Nalidixic acid (NegGram)<br>Cinoxacin (Cinobac) | Enterobacteriaceae | Oral administration<br>Low serum and tissue drug concentrations<br>Narrow gram-negative coverage | Uncomplicated urinary tract infections<br>Not for use in systemic infections |
| Second generation | | | |
| Class I | Enterobacteriaceae | Oral administration<br>Low serum and tissue drug concentrations<br>Improved gram-negative coverage compared with first-generation quinolones<br>Limited gram-positive coverage | Uncomplicated urinary tract infections<br>Not for use in systemic infections |
| Lomefloxacin (Maxaquin)<br>Norfloxacin (Noroxin)<br>Enoxacin (Penetrex) | | | |
| Class II | | | |
| Ofloxacin (Floxin)<br>Ciprofloxacin (Cipro) | Enterobacteriaceae, atypical pathogens; *Pseudomonas aeruginosa* (ciprofloxacin only) | Oral and intravenous administration<br>Higher serum, tissue, and intracellular drug concentrations compared with class I agents<br>Coverage of atypical pathogens | Complicated urinary tract and catheter-related infections<br>Gastroenteritis with severe diarrhea<br>Prostatitis<br>Nosocomial infections<br>Sexually transmitted diseases<br>Not for use in community-acquired pneumonia because of associations with pneumococcal bacteremia and meningeal seeding due to poor pneumococcal susceptibility) |
| Third generation | | | |
| Levofloxacin (Levaquin)<br>Sparfloxacin (Zagam)*<br>Gatifloxacin (Tequin)<br>Moxifloxacin (Avelox) | Enterobacteriaceae, atypical pathogens, streptococci | Oral and intravenous administration<br>Similar to class II second-generation quinolones but with modest streptococcal coverage<br>Increased hepatic metabolism (sparfloxacin and moxifloxacin) | Similar indications as for second-generation quinolones<br>Community-acquired pneumonia in hospitalized patients or if atypical pathogens are strongly suspected<br>Community-acquired pneumonia in nonhospitalized patients with risk factors for resistant pneumococcal infection† |
| Fourth generation | | | |
| Trovafloxacin (Trovan)* | Enterobacteriaceae, *P. aeruginosa* (reduced or absent), atypical pathogens, methicillin-susceptible *Staphylococcus aureus*, streptococci, anaerobes | Oral and intravenous administration<br>Similar to third-generation quinolones but with improved gram-positive coverage and added anaerobic coverage | Consider for treatment of intra-abdominal infections. |

**—Sparfloxacin and trovafloxacin have significant nonrenal elimination pathways; these agents should not be used to treat urinary tract infections.*

*†—Risk factors for penicillin-resistant pneumococcal infection include age younger than five years or older than 65 years, recent course of antibiotics, comorbid disease or alcohol abuse, immunodeficiency state or human immunodeficiency virus infection, day-care attendance, recent hospitalization, and institutionalization (e.g., long-term care facility, prison).*

*Adapted with permission from Owens RC Jr, Ambrose PG. Clinical use of the fluoroquinolones. Med Clin North Am 2000;84:1447-69.*

In vitro susceptibility to methicillin-resistant *S. aureus*, methicillin-resistant *Staphylococcus epidermidis*, and vancomycin-resistant Enterococcus species is variable and unpredictable. Although the newer fluoroquinolones have shown promising in vitro activity against gram-positive bacteria based on MIC data, physicians should be cautious when using quinolone antibiotics to treat life-threatening gram-positive infections. Continued overuse of these antimicrobials in clinical medicine and agricultural feed will promote gram-positive and gram-negative resistance and is likely to limit the effectiveness of the quinolones in the near future. Overuse of a single agent will ultimately result in resistance to the entire class.[1]

## Therapeutic Uses of Quinolones

### GENITOURINARY INFECTIONS

Because of their extensive gram-negative coverage, quinolone antibiotics were initially used to treat urinary tract infections. The higher genitourinary drug concentrations that occur with renally cleared quinolones promote their effectiveness in the treatment of genitourinary infections. Given in three- to 10-day courses, most quinolones are as effective as trimethoprim-sulfamethoxazole (Bactrim, Septra) in treating uncomplicated urinary tract infections caused by susceptible *Escherichia coli*.[14,15]

Complicated urinary tract infections include those in patients with stones or obstructive uropathies and in patients with catheter-related infections. These infections are often associated with nosocomial, antibiotic-resistant gram-negative pathogens and gram-positive bacteria, and with Candida species. Because ciprofloxacin, ofloxacin, lomefloxacin (Maxaquin), enoxacin (Penetrex), levofloxacin, and gatifloxacin have higher renal clearance and greater renal concentration, they are optimal choices for the treatment of complicated urinary tract infections.[1]

Ciprofloxacin has been shown to be more effective than trimethoprim-sulfamethoxazole and aminoglycosides in seven- to 10-day courses for the treatment of complicated urinary tract infections. However, few patients maintain sterile urine six weeks after any antibiotic therapy.[1,9] Bacterial resistance and Candida superinfection often limit treatment in complicated urinary tract infections, with an estimated failure rate of at least 2 percent.[15,16] Failure rates as high as 20 percent may be encountered with infections caused by pathogens such as *P. aeruginosa*.[1]

A seven- to 10-day course of orally administered norfloxacin (Noroxin) or ofloxacin has been successful in the treatment of uncomplicated pyelonephritis, with a bacteriologic cure rate equal to that for trimethoprim-sulfamethoxazole.[1] In the treatment of acute uncomplicated pyelonephritis in nonpregnant women, similar efficacy has been shown for levofloxacin, in a dosage of 250 mg per day for seven to 10 days, and ciprofloxacin, in a dosage of 500 mg twice daily for 10 days. However, relapses were more common with levofloxacin.[1,9] Gatifloxacin, in a dosage of 400 mg per day, has compared favorably with ciprofloxacin, in a dosage of 500 mg twice daily, in the treatment of complicated urinary tract infections and pyelonephritis, with cure rates of 93 percent and 91 percent, respectively.[11]


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Fluoroquinolones, especially levofloxacin and ciprofloxacin, are valuable in the treatment of complicated urinary tract infections and pyelonephritis. Yet bacterial resistance, relapse of infections, and recurrent infections remain critical issues. Complex genitourinary tract infections continue to be a niche for this antibiotic class.

#### PROSTATITIS

Quinolones are effective in the treatment of prostatitis because of their excellent penetration into prostatic tissue. When taken for four to six weeks, norfloxacin, ciprofloxacin, levofloxacin, and ofloxacin have eradication rates of 67 to 91 percent.[1,17] Treatment failures have been associated with shorter treatment courses (e.g., two weeks) and less susceptible bacteria, specifically *P. aeruginosa* and Enterococcus species.[1,9,15,18]

Levofloxacin is an excellent first-line agent in the treatment of prostatitis. Ciprofloxacin should be reserved for use in patients with resistant gram-negative, pseudomonal, and enterococcal prostatitis, because of its superior activity against *P. aeruginosa* and enterococci.

#### RESPIRATORY DISEASES

Acute bacterial sinusitis may be the complication of an initial viral illness. The primary bacterial isolates are *S. aureus*, *S. pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*.[9] The U.S. Food and Drug Administration (FDA) has labeled gatifloxacin, moxifloxacin, sparfloxacin, and levofloxacin for use in the treatment of acute bacterial sinusitis. Clinical trials comparing fluoroquinolones with amoxicillin–clavulanate potassium (Augmentin), cefuroxime axetil (Ceftin), and clarithromycin (Biaxin) have demonstrated the efficacy of the quinolone antibiotics.[9] However, we believe that quinolones should not be used as first-line agents in the treatment of acute bacterial sinusitis because of the potential for development of bacterial resistance.

*Quinolones are effective in the treatment of prostatitis because of their excellent penetration into prostatic tissue.*

Acute bronchitis may follow a viral illness, but antimicrobial therapy generally is not warranted unless the patient has underlying pulmonary disease. Fluoroquinolone therapy for acute bacterial bronchitis has been effective against *H. influenzae* and *M. catarrhalis*, the primary pathogens.[1,9] The use of ciprofloxacin for *S. pneumoniae* and *P. aeruginosa* bronchitis has resulted in clinical treatment failures and the development of bacterial resistance.[1] Generally, levofloxacin, sparfloxacin, ofloxacin, gatifloxacin, and moxifloxacin have compared favorably with cefuroxime, cefaclor (Ceclor), amoxicillin-clavulanate potassium, and amoxicillin.[1]

Community-acquired pneumonia is the sixth leading cause of death in the United States. Even with optimal therapy, this illness is associated with mortality rates of approximately 14 percent in hospitalized patients and less than 1 percent in patients not requiring hospitalization.[19,20] *S. pneumoniae, H. influenzae*, and *M. pneumoniae* are the pathogens most commonly identified in community-acquired pneumonia; less commonly isolated pathogens include viruses, *S. aureus, C. pneumoniae*, *M. catarrhalis*, *Klebsiella pneumoniae*, and *L. pneumophila*.[19,20] The pathogens most often responsible for death in patients with community-acquired pneumonia are *S. pneumoniae, S. aureus*, and *L. pneumophila*.

Antibiotic choices for outpatient and inpatient treatment of pneumonia were stratified in a recent consensus statement from the Infectious Diseases Society of America (IDSA)[19] and in guidelines formulated by the Centers for Disease Control and Prevention (CDC).[20] Preference was not given to a specific antibiotic class. Listed antibiotic choices for outpatient treatment included macrolides, doxycycline (Vibramycin), and fluoroquinolones. Antibi-

otic choices for hospitalized patients included fluoroquinolones or extended-spectrum penicillins (piperacillin [Pipracil], piperacillin-tazobactam [Zosyn], or ampicillin-sulbactam [Unasyn]), carbapenems (meropenem [Merrem] and imipenem-cilastatin [Primaxin]) and cephalosporins, plus adjunctive macrolides, aminoglycosides, clindamycin (Cleocin), or metronidazole (Flagyl).[19,20]

For treatment of community-acquired pneumonia in patients hospitalized in a general ward, IDSA[19] recommends a macrolide with an extended-spectrum cephalosporin (cefotaxime [Claforan] or ceftriaxone [Rocephin]), or a beta-lactam/beta lactamase inhibitor combined with a macrolide, or a fluoroquinolone alone (levofloxacin, gatifloxacin, or moxifloxacin [listed in order of improved activity against *S. pneumoniae*]). For the treatment of patients hospitalized in an intensive care unit, the IDSA guidelines recommend a macrolide or a fluoroquinolone (levofloxacin, gatifloxacin, or moxifloxacin) plus an extended-spectrum cephalosporin (cefotaxime or ceftriaxone) or a beta-lactam/beta-lactamase inhibitor.

We are cautious when using quinolones and macrolides in elderly patients because of drug interactions and adverse effects. In addition, fluoroquinolones should not be used as first-line agents for empiric therapy unless a life-threatening or "atypical pneumonia" (e.g., *L. pneumophila* infection) is suspected.

For the treatment of atypical pneumonias, macrolides are likely to be equivalent to fluoroquinolones and are currently more cost-effective. Quinolones provide exceptional coverage against atypical pathogens when infection with these organisms is suspected in patients with community-acquired pneumonia. However, ofloxacin has been associated with treatment failures, and ciprofloxacin has displayed reduced activity against Chlamydia species.[1,9]

Compared with other quinolones, moxifloxacin and gatifloxacin have been shown to have superior in vitro activity against pneumococci. Although this activity may make moxifloxacin or gatifloxacin an attractive choice for pneumococcal infections, these agents should probably be reserved for treatment of infections with atypical pathogens or for life-threatening pneumonias.[1,9,11,21,22]

Of the fluoroquinolones, ciprofloxacin and trovafloxacin have been studied most extensively in the treatment of nosocomial pneumonia. Ciprofloxacin has been found to be comparable in efficacy to imipenem-cilastatin in mechanically ventilated patients, especially those infected with pathogens from the Enterobacteriaceae family, but it has also been associated with poorer responses and higher clinical failure rates in patients with nosocomial pneumonia caused by *S. aureus* or *P. aeruginosa*.[1] The efficacy of the newer quinolones (moxifloxacin and gatifloxacin) in the treatment of nosocomial pneumonia is currently being assessed in clinical trials.

At present, quinolones are best used in combination antimicrobial therapy for nosocomial pneumonia. Fluoroquinolone monotherapy may worsen the increasing problem of antibiotic resistance in the nosocomial setting.

#### SEXUALLY TRANSMITTED DISEASES

Based on 1998 guidelines from the CDC,[23] ceftriaxone is the agent of choice for treatment of uncomplicated *Neisseria gonorrhoeae* urethritis and cervicitis. A single dose of ciprofloxacin or ofloxacin should be considered as alternative treatment in, for example, patients with penicillin allergy.[23] Recently, gatifloxacin was reported to be as effective as ofloxacin against *N. gonorrhoeae*.[11] A seven-day course of ofloxacin or sparfloxacin has been found to be as effective as doxycycline in the treatment of *C. trachomatis* infections. Finally, ciprofloxacin has been reported to be as effective as trimethoprim-sulfamethoxazole for treating chancroid caused by *Haemophilus ducreyi*.[1]

Pelvic inflammatory disease is a polymicrobial infection. Quinolone treatment options include ofloxacin plus metronidazole, ofloxacin plus cefoxitin (Mefoxin), and cipro-

floxacin plus clindamycin.[1,9] Fluoroquinolone monotherapy is incomplete.

#### GASTROENTERITIS

Prophylactic antimicrobial therapy is not recommended for the prevention of diarrhea in travelers.[9] Norfloxacin or ciprofloxacin has been found to be comparable to trimethoprim-sulfamethoxazole in the treatment of traveler's diarrhea caused by Shigella species, enterotoxigenic *E. coli*, or *Campylobacter jejuni*.[1]

Ciprofloxacin and ofloxacin are the agents of choice for treatment of enteric typhoid fever.[1] Norfloxacin has been found to be superior to both trimethoprim-sulfamethoxazole and doxycycline in the treatment of *Vibrio cholerae* infection.[1]

#### SKIN AND SOFT TISSUE INFECTIONS

Because of limited data, the role of fluoroquinolones in the treatment of skin and soft tissue infections remains uncertain. Most fluoroquinolones have limited gram-positive activity; thus, they should not be considered first-line agents for skin and soft tissue infections. Diabetic foot infections, which are polymicrobial, can be treated with quinolones in combination with other antibiotics.[9] We exercise caution when *S. aureus* is isolated.

*Gastrointestinal and central nervous system effects (e.g., headaches, dizziness, drowsiness) are the most frequent adverse events with quinolone therapy.*

TABLE 2
**Adverse Effects of Quinolones***

| |
|---|
| Gastrointestinal: nausea, vomiting, diarrhea, abdominal pain |
| CNS: headache, dizziness, drowsiness, confusion, insomnia, fatigue, malaise, depression, somnolence, seizures, vertigo, lightheadedness, restlessness, tremor |
| Dermatologic: rash, photosensitivity reactions, pruritus |
| Other: QTc prolongation, hepatotoxicity, abnormal or bitter taste, tendon rupture |

*CNS = central nervous system; QTc = corrected QT interval.*

**—Because quinolones have been associated with arthropathy and chondrotoxicity in immature animals, they are not recommended for use in children and adolescents younger than 18 years of age, or in pregnant or breastfeeding women.*

*Information from references 5, 6, 11, and 24 through 35.*

## Adverse Events

Although quinolones are well tolerated and relatively safe, certain adverse effects are common with all agents in this antibiotic class *(Table 2)*.[5,6,11,24-35] Gastrointestinal and central nervous system (CNS) effects are the most frequent adverse events, occurring in 2 to 20 percent of patients treated with quinolones.[3,5,6,33-35]

Prolongation of the corrected QT interval (QTc) may precipitate fatal ventricular arrhythmias such as torsades de pointes. Secondary to its effects in prolonging the QTc, grepafloxacin (Raxar) was withdrawn from the U.S. market in 1999. Because of reported QTc prolongation, sparfloxacin and moxifloxacin should not be used in patients with a known predisposition to arrhythmias (e.g., hypokalemia, bradycardia) or in patients who are receiving antiarrhythmic drugs or other medications that might prolong the QTc.[11,24-27,33,34]

## Drug Interactions

Clinically significant drug interactions are known to occur with all quinolones *(Table 3)*.[6,7,11,24-32] When products containing multivalent cations (calcium, aluminum, magnesium, iron, zinc), including sucralfate (Carafate), antacids, nutritional supplements, and multivitamin and mineral supplements, are taken within two to four hours of an orally administered quinolone, the maximum

serum concentration of the quinolone may be reduced by 25 percent to approximately 90 percent.[1,36]

## Applications of Fluoroquinolones in Biologic Warfare

*Bacillus anthracis* (anthrax) spores have recently been deployed as a biologic weapon in the United States. Fluoroquinolones have a role in postexposure prophylaxis and chemotherapy for specific agents that could be used in biologic warfare *(Table 4)*.[37] Specific fluoroquinolones are indicated for prophylaxis or treatment of anthrax, cholera, plague, brucellosis, and tularemia. Ciprofloxacin is the drug of choice for postexpo-

TABLE 3
**Potential Interactions Between Quinolones and Other Drugs**

| |
|---|
| **Any quinolone*** |
| Decreased absorption of quinolones if didanosine (Videx) or multivalent cations are administered concomitantly or less than two hours before or after a quinolone.† |
| May increase anticoagulant effects of warfarin (Coumadin)‡ |
| May increase caffeine levels§ |
| May increase cyclosporine (Sandimmune) levels§ |
| May increase theophylline levels§ |
| May prolong QTc if used concomitantly with antiarrhythmics (e.g., class IA and III agents) or with cisapride (Propulsid)‖ |
| May increase risk of CNS stimulation and convulsions if used concomitantly with nonsteroidal anti-inflammatory drugs |
| May lead to hypoglycemia and/or hyperglycemia if used concomitantly with antidiabetic agents (oral hypoglycemics or insulin)¶ |
| **Gatifloxacin (Tequin)** |
| Increased serum digoxin (Lanoxin) levels# |
| **Trovafloxacin (Trovan)** |
| Decreased absorption if used concomitantly with sodium citrate and citric acid oral solution (Bicitra) |
| Decreased effect of orally administered trovafloxacin if used concomitantly with intravenously administered morphine |

*QTc = corrected QT interval; CNS = central nervous system.*

**—Listed as interactions with quinolones as a class; interactions may be more likely with some quinolones than others.*

†—*Products that contain multivalent cations (calcium, aluminum, magnesium, iron, and zinc) include antacids, nutritional supplements, and multivitamin and mineral supplements. Newer fluoroquinolones, such as gatifloxacin (Tequin), moxifloxacin (Avelox), and trovafloxacin (Trovan), may not interact significantly with calcium-containing products. Avoid concomitant use of fluoroquinolones and sucralfate (Carafate).*

‡—*Because some fluoroquinolones are known to enhance the effects of warfarin, the prothrombin time and International Normalized Ratio should be monitored closely if warfarin or a warfarin derivative is used concomitantly with any quinolone.*

§—*Monitor for toxicity.*

‖—*Although cisapride has been removed from the market, it can still be obtained from the manufacturer.*

¶—*Monitoring of blood glucose levels may be recommended.*

#—*Clinical significance is unknown.*

*Information from references 6, 7, 11, and 24 through 32.*

TABLE 4
**Selected Potential Biologic Pathogens: Postexposure Prophylaxis and Treatment**

| *Pathogen* | *Postexposure prophylaxis* | *Treatment* |
|---|---|---|
| *Bacillus anthracis* (anthrax) | Agent of choice: ciprofloxacin (Cipro)*<br>Alternative: doxycycline (Vibramycin) | Agents of choice: ciprofloxacin, doxycycline<br>Alternative if organisms are penicillin sensitive: penicillin G |
| *Vibrio cholerae* (cholera) | Not available | Agents of choice: oral rehydration therapy, tetracycline, doxycycline, ciprofloxacin, norfloxacin (Noroxin) |
| *Yersinia pestis* (plague) | Agents of choice: doxycycline, ciprofloxacin<br>Alternative: tetracycline | Agents of choice: streptomycin, gentamicin, ciprofloxacin<br>Alternative: doxycycline |
| *Brucella melitensis* (brucellosis) | Agents of choice: doxycycline plus rifampin (Rifadin) | Agents of choice: doxycycline plus rifampin<br>Alternative: ofloxacin (Floxin) plus rifampin |
| *Francisella tularensis* (tularemia) | Agent of choice: doxycycline<br>Alternatives: tetracycline, ciprofloxacin | Agent of choice: streptomycin<br>Alternatives: gentamicin, ciprofloxacin |

**—Levofloxacin (Levaquin) and ofloxacin are alternatives for postexposure prophylaxis in mass casualty settings.*

*Adapted from Kortepeter M, et al., eds. USAMRIID's Medical management of biological casualties handbook. 4th ed. Frederick, Md.: U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, 2001. Retrieved November 2001 from http://www.usamriid.army.mil//education/bluebook.html.*

sure prophylaxis for anthrax until sensitivities are available. Although penicillin resistance has only rarely occurred in the natural setting of anthrax, the former Soviet Union developed a *B. anthracis* strain that was resistant to both penicillin and tetracycline.[37]

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