Tetracyclines, Chloramphenicol, Macrolides, and Lincosamides

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TETRACYCLINES

Structure and Mechanism of Action

Although all tetracyclines have a similar mechanism of action, they have different chemical structures and are produced by different species of *Streptomyces*. In addition, structural analogues of these compounds have been synthesized to improve pharmacokinetic properties and antimicrobial activity. While several biological processes in the bacterial cells are modified by the tetracyclines, their primary mode of action is inhibition of protein synthesis. Tetracyclines bind to the 30S ribosome and thereby prevent the binding of aminoacyl transfer RNA (tRNA) to the A site (acceptor site) on the 50S ribosomal unit. The tetracyclines affect both eukaryotic and prokaryotic cells but are selectively toxic for bacteria, because they readily penetrate microbial membranes and accumulate in the cytoplasm through an energy-dependent tetracycline transport system that is absent from mammalian cells.

Resistance is related largely to changes in cell permeability and a resultant decreased accumulation of drug due to increased efflux from the cell by an energy-dependent mechanism. Other mechanisms, such as production of a protein that alters the interaction of tetracycline with the ribosome and enzymatic inactivation of the drug, have been reported.

Antibacterial Spectrum

The tetracyclines display broad-spectrum activity and are effective against both gram-positive and gram-negative bacteria, including *Rickettsia*, *Coxiella*, *Mycoplasma*, and *Chlamydia* spp. Tetracycline resistance has increased among pneumococci and gonococci, which limits their use in the treatment of infections caused by these organisms.

Although several congeners of the tetracyclines are available, they all have a similar spectrum of in vitro activity. Minocycline is somewhat more active and oxytetracycline and tetracycline are somewhat less active than other members of this group.
Absorption, Distribution, Metabolism, and Excretion

These antibiotics are partially absorbed from the stomach and upper gastrointestinal tract. Food impairs absorption of all tetracyclines except doxycycline and minocycline. Absorption of doxycycline and minocycline is improved with food. Since the tetracyclines form insoluble chelates with calcium (such as are found in many antacids), magnesium, and other metal ions, their simultaneous administration with milk (calcium), magnesium hydroxide, aluminum hydroxide, or iron will interfere with absorption. Because some of the tetracyclines are not completely absorbed, any drug remaining in the intestine may inhibit sensitive intestinal microorganisms and alter the normal intestinal flora.

The tetracyclines are distributed throughout body tissues and fluids in concentrations that reflect the lipid solubility of each individual agent. Minocycline and doxycycline are the most lipid soluble, while oxytetracycline is the least lipid soluble. The tetracyclines penetrate (but somewhat unpredictably) the uninflamed meninges and cross the placental barrier. Peak serum levels are reached approximately 2 hours after oral administration; cerebrospinal fluid (CSF) levels are only one-fourth those of plasma.

The various congeners differ in their half-lives and their protein binding ability (Table 47.1). Significant differences in serum half-life allow the grouping of the tetracyclines into subclasses: short acting (tetracycline, chlortetracycline, and oxytetracycline), intermediate acting (demeclocycline and methacycline), and long acting (minocycline and doxycycline).

The tetracyclines are metabolized in the liver and are concentrated in the bile. Bile concentrations can be up to five times those of the plasma. Doxycycline, minocycline, and chlortetracycline are excreted primarily in the feces. The other tetracyclines are eliminated primarily in the urine by glomerular filtration. Obviously, these tetracyclines have greater urinary antibacterial activity than those (e.g., doxycycline) that are excreted by nonrenal mechanisms.

Clinical Uses

There is little difference in clinical response among the various tetracyclines. The selection of an agent, therefore, is based on tolerance, ease of administration, and cost. The restriction of their use in pregnancy and in patients under the age of 8 years applies to all preparations.

Two tetracyclines have sufficiently distinctive features to warrant separate mention. Doxycycline, with its longer half-life and lack of nephrotoxicity, is a popular choice for patients with preexisting renal disease or those who are at risk for developing renal insufficiency. The lack of nephrotoxicity is related mainly to biliary excretion, which is the primary route of doxycycline elimination. Doxycycline is the preferred parenteral tetracycline. Doxycycline is a potential first-line agent in the prophylaxis of anthrax after exposure. Doxycycline is the treatment of choice for the primary stage of Lyme disease in adults and children older than 8 years.

Minocycline is an effective alternative to rifampin for eradication of meningococci, including sulfonamide-resistant strains, from the nasopharynx. However, the high incidence of dose-related vestibular side effects renders it less acceptable. Although minocycline has good in vitro activity against Nocardia spp., further studies are necessary to confirm its clinical efficacy.

The tetracyclines are still the drugs of choice for treatment of cholera, diseases caused by Rickettsia and Coxiella, granuloma inguinale, relapsing fever, the chlamydial diseases (trachoma, lymphogranuloma

<table>
<thead>
<tr>
<th>Drug, Trade Name</th>
<th>Preferred Route</th>
<th>Serum half-life (hr)</th>
<th>Serum protein binding (%)</th>
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<tbody>
<tr>
<td>Tetracycline hydrochloride</td>
<td>Oral, IV</td>
<td>8</td>
<td>25–60</td>
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<tr>
<td>Achromycin, Panamycin, Hydrochloride</td>
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<tr>
<td>Chlortetracycline hydrochloride</td>
<td>Oral, IV</td>
<td>6</td>
<td>40–70</td>
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<td>Aureomycin</td>
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<tr>
<td>Oxytetracycline hydrochloride</td>
<td>Oral, IV</td>
<td>9</td>
<td>20–35</td>
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<tr>
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<tr>
<td>Demeclocycline hydrochloride</td>
<td>Oral</td>
<td>12</td>
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<td>Oral</td>
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Some Properties of Tetracycline and Its Congeners
venereum, and psittacosis), and nonspecific urethritis. They are also effective in the treatment of brucellosis, tularemia, and infections caused by *Pasteurella* and *Mycoplasma* spp., although other agents may be equally effective. Tetracyclines are clinically effective in acne because of their antibiotic effect on the degranulated neutrophils in the comedone acidic contents (in which long-term low-dose therapy is popular). Mild to moderate attacks of pelvic inflammatory disease often respond to tetracycline, probably as a result of the drug’s action on anaerobic bacteria and chlamydia.

Tetracyclines no longer can be entirely relied on in the treatment of streptococcal infections; up to 40% of *Streptococcus pyogenes* and 10% of *Streptococcus pneumoniae* are resistant.

### Adverse Effects

Oral administration can cause nausea, vomiting, epigastric burning, stomatitis, and glossitis, and an intravenous injection can cause phlebitis. When given over long periods, use of these agents can result in a negative nitrogen balance, which may lead to elevated blood urea nitrogen. Hepatotoxicity occurs infrequently but is particularly severe during pregnancy, when the combination of uremia and increasing jaundice can be fatal. In addition, these antibiotics are occasionally nephrotoxic and should not be administered with other potentially nephrotoxic drugs. Staining of both the deciduous and permanent teeth and retardation of bone growth can occur if tetracyclines are administered after the fourth month of gestation or if they are given to children less than 8 years of age.

Photosensitvivity, observed as abnormal sunburn reaction, is particularly associated with demeclocycline and doxycycline administration. Superinfection may result in oral, anogenital, and intestinal *Candida albicans* infections, whereas *Staphylococcus aureus* or *Clostridium difficile* overgrowth may cause enterocolitis. Minocycline can produce vertigo.

Minocycline is frequently used in the treatment of chronic facial dermatoses. Increased usage has resulted in local skin pigmentation, particularly at sites of previous tissue trauma that is unrelated to the photosensitization phenomenon characteristic of this class of drug. This effect does not appear to be dose dependent and usually resolves in months to years following drug discontinuation.

Other significant side effects of minocycline may make it unsuitable for some light-skinned patients. In particular, dark bone pigmentation is severe enough to be visible through the mucosae of the alveolar ridges in the mouth and other areas where bone directly adheres to skin (black bone disease). Thyroid staining is visible through the overlying skin of the neck but does not affect the endocrine function of the gland.

Pulmonary eosinophilic syndrome, characterized by extreme hypoxemia, eosinophilia, interstitial pneumonitis, hilar lymphadenopathy, and pleural effusions, can be severe and can occur with as little as 7 to 9 days of therapy with the tetracyclines. In severe cases steroid therapy is required, but the outcome following drug discontinuation is nearly always good.

Pseudotumor cerebri is another potential complication of chronic use of these agents, particularly in individuals treated for severe cystic acne with simultaneous use of isotretinoin. This complication can be induced within several days of initiation of therapy and usually resolves with cessation of treatment.

Chronic use always predisposes to the development of fungal esophagitis, which may be so severe as to require treatment with antifungal therapy. Prompt recognition of dysphagia and cessation of treatment are usually curative.

### Chloramphenicol

#### Mechanism of Action

Chloramphenicol (Chloromycetin) is a nitrobenzene derivative that affects protein synthesis by binding to the 50S ribosomal subunit and preventing peptide bond formation. It prevents the attachment of the amino acid end of aminoacyl-tRNA to the A site, hence the association of peptidyltransferase with the amino acid substrate. Resistance due to changes in the ribosome-binding site results in a decreased affinity for the drug, decreased permeability, and plasmids that code for enzymes that degrade the antibiotic.

The drug-induced inhibition of mitochondrial protein synthesis is probably responsible for the associated toxicity.

#### Antibacterial Spectrum

Chloramphenicol is a broad-spectrum antibiotic that is effective against gram-positive and gram-negative bacteria, including *Rickettsia*, *Mycoplasma*, and *Chlamydia* spp. Chloramphenicol is also effective against most anaerobic bacteria, including *Bacteroides fragilis*.

#### Absorption, Distribution, Metabolism, and Excretion

Chloramphenicol is rapidly and completely absorbed from the gastrointestinal tract and is not affected by food ingestion or metal ions. Parenteral administration is generally reserved for situations in which oral therapy is contraindicated, as in the treatment of meningitis and septicemia or when vomiting prohibits oral administration. The biological half-life of chloramphenicol is 1.5 to
3.5 hours. Although up to 60% of the drug is bound to serum albumin, it penetrates the brain and CSF and crosses the placental barrier.

Chloramphenicol is inactivated in the liver by glucuronosyltransferase and is rapidly excreted (80–90% of dose) in the urine. About 5 to 10% of the administered drug is excreted unchanged. Renal elimination is by tubular secretion and glomerular filtration. Other degradation pathways are known to exist and may account for some of the toxicity seen in neonates and children.

**Clinical Uses**

The potentially fatal nature of chloramphenicol-induced bone marrow suppression restricts its use to a few life-threatening infections in which the benefits outweigh the risks. There is no justification for its use in treating minor infections.

Chloramphenicol is no longer recognized as the treatment of choice for any bacterial infection. In almost all instances, other effective antimicrobial agents are available. Since effective CSF levels are obtained, it used to be a choice for treatment of specific bacterial causes of meningitis: *Haemophilus influenzae*, *Neisseria meningitidis*, and *S. pneumoniae*. Additionally, it was effective against *H. influenzae*–related arthritis, osteomyelitis, and epiglottitis. The development of β-lactamase-producing strains of *H. influenzae* increased the use of chloramphenicol. However, with the advent of third-generation cephalosporins such as ceftriaxone and cefotaxime, chloramphenicol use has significantly decreased. If the patient is hypersensitive to β-lactams, chloramphenicol administration is appropriate therapy for meningitis caused by *N. meningitidis* and *S. pneumoniae*.

Chloramphenicol remains a major treatment of typhoid and paratyphoid fever in developing countries. However, with increasing resistance to ampicillin, trimethoprim-sulfamethoxazole and, to some extent, chloramphenicol, fluoroquinolones and some third-generation cephalosporins (e.g., ceftriaxone) have become the drugs of choice. Salmonella infections, such as osteomyelitis, meningitis and septicemia, have also been indications for chloramphenicol use. Nevertheless, antibiotic resistance patterns can be a problem. As noted previously, nontyphoidal salmonella enteritis is not benefited by treatment with chloramphenicol or other antibiotics.

Chloramphenicol also is widely used for the topical treatment of eye infections. It is a very effective agent because of its extremely broad spectrum of activity and its ability to penetrate ocular tissue. The availability of safer, less irritating instilled ophthalmic antibiotics and the increase in fatal aplastic anemia associated with the use of this dosage form suggest that this agent might best be withdrawn.

Chloramphenicol is an alternative to tetracycline for rickettsial diseases, especially in children younger than 8 years, and alone or in combination with other antibiotics, it has been used to treat vancomycin-resistant enterococci. Another indication for chloramphenicol is in the treatment of serious anaerobic infections caused by penicillin-resistant bacteria, such as *B. fragilis*. Clindamycin and metronidazole are now preferred for treatment of anaerobic infections. Chloramphenicol, in combination with surgical drainage, is useful in treating cerebral abscesses caused by anaerobic bacteria, particularly those that are resistant to penicillin.

**Adverse Effects**

Newborn infants, especially those born prematurely, cannot adequately conjugate chloramphenicol to form the glucuronide; they also have depressed rates of glomerular and tubular secretion. Because of these metabolic deficiencies, high levels of free chloramphenicol may accumulate and cause a potentially fatal toxic reaction, the gray baby syndrome. This syndrome is characterized by abdominal distention, vomiting, progressive cyanosis, irregular respiration, hypothermia, and vasomotor collapse. The mortality rate is high. The syndrome also has been observed in older children and is associated with high serum levels of chloramphenicol.

The presence of multiple metabolites in the serum of neonates treated with chloramphenicol suggests that the biotransformation of chloramphenicol takes place by multiple routes to include oxidation, reduction, and conjugation. The presence of particular metabolites does not appear to correlate with toxicity.

The most publicized adverse affects are those involving the hematopoietic system; they are manifested by toxic bone marrow depression or idiosyncratic aplastic anemia. The bone marrow depression is dose related and is seen most frequently when daily doses exceed 4 g and plasma concentrations exceed 25 μg/mL. The bone marrow depression is characterized by anemia, sometimes with leukopenia or thrombocytopenia, but it is reversible on discontinuation of chloramphenicol.

Aplastic anemia occurs in only about 1 in 24,000 to 40,000 cases of treatment. It is not a dose-related response and can occur either while the patient is taking chloramphenicol for days to months after completion of therapy. The aplastic or hypoplastic response involves all cellular elements of the marrow and is usually fatal. The mechanism is not known, but it occurs most frequently with oral or ocular administration.

**MACROLIDE ANTIBIOTICS**

**Structure**

The *macrolide antibiotics* are those that consist of a large lactone ring to which sugars are attached. Antibiotics in this group include erythromycin (Ilotycin, E-mycin,
Robimycin), clarithromycin (Biaxin), azithromycin (Zithromax), and oleandomycin (Matromycin). Erythromycin and its derivatives (clarithromycin, azithromycin) are the only macrolides in common use, although the acetylated derivative of oleandomycin (troleandomycin, TAO) is available for oral use.

**Mechanism of Action**

Macrolides bind to the 50S ribosomal subunit of bacteria but not to the 80S mammalian ribosome; this accounts for its selective toxicity. Binding to the ribosome occurs at a site near peptidyltransferase, with a resultant inhibition of translocation, peptide bond formation, and release of oligopeptidyl tRNA. However, unlike chloramphenicol, the macrolides do not inhibit protein synthesis by intact mitochondria, and this suggests that the mitochondrial membrane is not permeable to erythromycin.

**Antibacterial Spectrum**

The macrolides are effective against a number of organisms, including Mycoplasma spp., H. influenzae, Strep-tococcus spp. (including S. pyogenes and S. pneumoniae), staphylococci, gonococci, Legionella pneumophila, and other Legionella spp. There has been increasing resistance of S. pneumoniae to macrolides worldwide. This is true especially if the strain is resistant to penicillin. This resistance includes not only erythromycin but also clarithromycin and azithromycin. Approximately 10 to 15% of S. pneumoniae in the United States show complete resistance to macrolides. Staphylococci resistant to erythromycin are resistant to all macrolides. The hemolytic streptococci also exhibit varying degrees of cross-resistance to the macrolides and to lincomycin and clindamycin, although the macrolides are chemically unrelated to the last two agents. There are only minor variations in the antibacterial spectrum of the newer macrolides. Clarithromycin is very active against H. influenzae, Legionella, and Mycobacterium avium-intracellulare, whereas erythromycin is superior against Branhannela, Neisseria, and H. influenzae but less active against mycobacterial species. Clarithromycin and azithromycin have significant activity against Mycobacterium avium complex (MAC), and it is one of the drugs of choice in treating disseminated MAC. Both azithromycin and clarithromycin can be used prophylactically in HIV and AIDS patients to help prevent disseminated MAC.

**Absorption, Distribution, Metabolism, and Excretion**

The macrolides are absorbed from the intestinal tract, although the presence of food interferes with absorption and part of the dose is destroyed because of the relative acid lability of these antimicrobials. To minimize destruction and enhance absorption, erythromycin is administered as a stearate or oleate salt or is enteric coated. Because stearate and estolate erythromycins are not acid labile, the administration of these formulations results in higher blood levels. The O-methyl substitution of erythromycin that results in clarithromycin also confers acid stability and better absorption with food.

The macrolides diffuse readily into tissues and cross placental membranes. CSF levels are about 20% of plasma levels, while biliary concentrations are about 10 times plasma levels. Although the serum levels of clarithromycin and azithromycin are low, these antibiotics concentrate in tissue and reach high levels.

Erythromycin and azithromycin are excreted primarily in active form in bile, with only low levels found in urine. Clarithromycin is metabolized to the biologically active 14-OH metabolite and is eliminated largely by the kidney. The half-life of erythromycin is approximately 1.4 hours, whereas the half-life of clarithromycin is 3 to 7 hours and that of azithromycin approaches 68 hours.

**Clinical Uses**

Although erythromycin is a well-established antibiotic, there are relatively few primary indications for its use. These indications include the treatment of Mycoplasma pneumoniae infections, eradication of Corynebacterium diphtheriae from pharyngeal carriers, the early preparoxysmal stage of pertussis, chlamydial infections, and more recently, the treatment of Legionnaires’ disease, Campylobacter enteritis, and chlamydial conjunctivitis, and the prevention of secondary pneumonia in neonates.

Erythromycin is effective in the treatment and prevention of S. pyogenes and other streptococcal infections, but not those caused by the more resistant fecal streptococci. Staphylococci are generally susceptible to erythromycin, so this antibiotic is a suitable alternative drug for the penicillin-hypersensitive individual. It is a second-line drug for the treatment of gonorrhea and syphilis. Although erythromycin is popular for the treatment of middle ear and sinus infections, including H. influenzae, possible erythromycin-resistant S. pneumoniae is a concern.

The new macrolides have similar indications for use as erythromycin but with some additional areas of potential value. Clarithromycin has activity against Toxoplasma gondii and Mycobacterium avium-intracellulare, and it has expanded coverage against untypable H. influenzae strains that predominate in exacerbations of chronic bronchitis. Azithromycin has less coverage against these organisms, and because of its lower peak serum concentrations and prolonged protein binding, it partitions less well across bronchial membranes. The prolonged half-life and protein binding and the use of an abbreviated one-time dose of azithromycin appear
to be extremely beneficial in the treatment of sexually transmitted diseases.

**Adverse Effects**

The incidence of side effects associated with erythromycin therapy is very low. Mild gastrointestinal upset with nausea, diarrhea, and abdominal pain are reported to occur more commonly when the propionate and estolate salts are used. Rashes are seen infrequently but may be a part of a general hypersensitivity reaction that includes fever and eosinophilia. Thrombophlebitis may follow intravenous administration, as may transient impairment of hearing.

Cholestatic hepatitis may occur when drug therapy lasts longer than 10 days or repeated courses are prescribed. The hepatitis is characterized by fever, enlarged and tender liver, hyperbilirubinemia, dark urine, eosinophilia, elevated serum bilirubin, and elevated transaminase levels. Hepatitis has been associated with the estolate salt of erythromycin but not with other formulations. Although the hepatitis usually occurs 10 to 20 days after the initiation of therapy, it can occur within hours in a patient who has had such a reaction in the past. The hepatitis is believed to be the result of both a hepatotoxic effect and a hypersensitivity reaction; this latter effect is reversible on withdrawal of the drug. Erythromycin and derivatives induce hepatic microsomal enzymes and interfere with the actions of various drugs, including theophylline and carbamazepine.

**LINCOSAMIDES**

**Mechanism of Action**

The lincosamide family of antibiotics includes lincomycin (Lincocin) and clindamycin (Cleocin), both of which inhibit protein synthesis. They bind to the 50S ribosomal subunit at a binding site close to or overlapping the binding sites for chloramphenicol and erythromycin. They block peptide bond formation by interference at either the A or P site on the ribosome. Lincomycin is no longer available for human use in the United States.

**Absorption, Distribution, Metabolism, and Excretion**

Food in the stomach does not interfere with the absorption of either clindamycin or lincomycin. Peak serum levels can be obtained 1 hour after intravenous administration of clindamycin, and approximately 90% of the antibiotic is protein bound.

Lincomycin and clindamycin penetrate most tissues well, including bone. Therefore, bone and joint infections caused by susceptible organisms respond well to treatment with clindamycin. These drugs also concentrate within phagocytic cells, which may offer a therapeutic advantage. Lincomycin and clindamycin do not readily penetrate the normal or inflamed meninges. They do, however, pass readily through the placental barrier. Their half-life is 2 to 2.5 hours.

Both clindamycin and lincomycin are metabolized by the liver, and 90% of the inactivated drug is excreted in the urine. If renal function is impaired, the amount of drug excreted in the feces will be increased.

**Clinical Uses**

Clindamycin is highly active against staphylococci and streptococci other than enterococci. Also, clindamycin has significant antibacterial activity against *S. pyogenes* (group A strep). However, the adverse reaction of pseudomembranous colitis has limited its use to individuals who are unable to tolerate other antibiotics and to the treatment of penicillin-resistant anaerobic bacterial infections. Clindamycin has shown excellent activity topically against *Corynebacterium acnes* in patients with recalcitrant cystic facial acne who cannot tolerate tetracyclines. Precautions should be given to all patients using the topical preparations, since the development of colitis is possible.

Both clindamycin and chloramphenicol have excellent activity against anaerobic bacteria but have potentially life-threatening adverse reactions and should not be used without good justification.

**Adverse Effects**

The major adverse reactions reported are hypersensitivity rashes and diarrhea. The rash is usually itchy, morbilliform, and general. Gastrointestinal intolerance with abdominal pain, nausea, and vomiting occurs infrequently. Hepatotoxicity and bone marrow suppression have been noted.

It is important to differentiate between gastrointestinal irritation and pseudomembranous colitis. In its most extreme form, the colitis results in mucosal ulceration and bleeding and infrequently may necessitate colectomy. On rare occasions it has been fatal.
Study Questions

1. Which of the following best treats the initial stage of Lyme disease in adults?
   (A) Penicillin V
   (B) Erythromycin
   (C) Clarithromycin
   (D) Doxycycline
   (E) Clindamycin

2. Chloramphenicol is the drug of choice for which of the following?
   (A) S. pneumoniae meningitis
   (B) B. fragilis in abdominal abscess infection
   (C) H. influenzae epiglottitis
   (D) Typhoid fever in the United States
   (E) Typhoid fever in some developing countries

3. A 39-year-old man has AIDS and a CD4 count less than 50. Recently he has had chills and fever. Several blood cultures drawn especially for acid-fast bacilli are positive. Which antibiotic should be included in a treatment regimen for this disease?
   (A) Tetracycline
   (B) Amoxicillin
   (C) Cephalexin
   (D) Clarithromycin
   (E) Doxycycline

4. A 37-year-old postal worker has a job at a mail sort facility. An envelope that passed through the facility and was delivered to a governmental office was noted upon opening to have anthrax spores. One of the postal worker’s fellow employees subsequently developed inhalation anthrax. Because of this, medical authorities recommended that other employees working at the same facility be tested and receive prophylactic antimicrobial therapy. The drug of choice is a quinolone. However, this employee has a history of allergy to ciprofloxacin. Which of the following antibiotics is also recognized as being effective prophylactic therapy for potential anthrax exposure?
   (A) Amoxicillin
   (B) Erythromycin
   (C) Clarithromycin
   (D) Doxycycline
   (E) Clindamycin

5. An 18-year-old man sustains a minor laceration of his right forearm. Approximately 2 days later the laceration site becomes red and swollen. He also begins to develop fever and chills. The patient eventually goes to the local hospital’s emergency department. By this point his forearm is swollen and the skin is light brown. Cultures of his wound and two blood cultures 15 minutes apart are obtained. Intravenous cephalosporin is begun. However, over 3 days the discoloration of his forearm begins to ascend to the upper arm and shoulder. Blood cultures are positive in approximately 12 hours for gram-positive cocci in chains. Wound cultures of the laceration also grow similar organisms, and high-dose penicillin G is prescribed. What other antibiotic would be extremely useful in treating this condition?
   (A) Gentamicin
   (B) Clindamycin
   (C) Ciprofloxacin
   (D) Clarithromycin
   (E) Chloramphenicol

Answers

1. D. Doxycycline is the preferred parenteral tetracycline for the primary state of Lyme disease in adults and children older than 8 years of age. Penicillin V (A) would be ineffective. Erythromycin (B) and clarithromycin (C) also are not effective against Borrelia burgdorferi, the gram-negative anaerobe organism responsible for Lyme disease.

2. E. Chloramphenicol is no longer the treatment of choice for any bacterial infection because of the potentially fatal chloramphenicol-induced bone marrow suppression. In the past it has been used against the infections indicated in choices A, B, C, and D. It remains a major treatment for typhoid and paratyphoid fever in some developing countries, since alternative drugs are much more expensive.

3. D. Clarithromycin is one of the recommended antimicrobials for use in combination with other antimicrobials in treating disseminated Mycobacterium avium complex.

4. D. Although ciprofloxacin is the primary agent recommended for prophylaxis against anthrax, doxycycline is an equally effective agent. Amoxicillin (A) is not as effective. The macrolides (B) and (C) also are not as effective. Clindamycin (E) is not indicated for this use.

5. B. This individual most likely has a group A streptococcal infection due to a minor wound. Now it appears he is developing necrotizing fascitis, a serious complication. Sometimes when a large amount of group A streptococcal organisms are present, penicillin is not effective. Clindamycin is usually very active against streptococcal infections because the size of the bacterial inoculum will not affect its efficacy. Actually, the treatment of choice for this condition is immediate and possibly repeated surgical debridement of the involved area. Antibiotics are supportive therapy.
SUPPLEMENTAL READING

CASE STUDY  The Dangers of Vacations

A 28-year-old white man was on vacation for 2 weeks in northern Minnesota in July. He was fishing and hiking in the forest for a number of days. He was healthy, with no known underlying disease or illness. Approximately 3 weeks after returning from his vacation, a red macule–papule developed on his right anterior thigh. Increasing redness developed around the initial site. The central area of this lesion showed some clearing. Several other similar lesions developed on his right leg and trunk. The patient did not note any arthropod bites. Which of the following antimicrobials would be the drug of choice for this patient?

(A) Chloramphenicol
(B) Cephalexin
(C) Doxycycline
(D) Gentamicin
(E) Ampicillin

ANSWER: C. The primary stage of Lyme disease is readily treatable with oral antibiotics. Doxycycline is considered to have the best activity against Lyme disease, so it the drug of choice for treatment in adults unless there is a history of allergy or intolerance to doxycycline.