CHAPTER 6

Chemotherapeutic Agents

Questions

DIRECTIONS (Questions 462 through 563): Each of the numbered items or incomplete statements in this section is followed by answers or by completions of the statement. Select the ONE lettered that is BEST in each case.

462. Which of the following beta-lactam antibiotics is most resistant to staphylococcal beta-lactamases?
   (A) amoxicillin
   (B) ampicillin
   (C) oxacillin
   (D) penicillin G
   (E) ticarcillin

463. Which of the following features best represents an advantage of ampicillin over penicillin G?
   (A) improved activity against gram-negative cocci
   (B) improved activity against gram-negative rods
   (C) improved activity against gram-positive organisms
   (D) improved activity against non-beta-lactamase-producing anaerobes
   (E) improved resistance against beta-lactamases

464. Beta-lactam antibiotics are bactericidal due to their interference with which of the following processes?
   (A) N-acetylation of glucosamine
   (B) N-acetylation of muramic acid
   (C) polymerization of monosaccharides
   (D) ribosomal protein biosynthesis
   (E) transpeptidation reaction

465. Which of the following mechanisms is LEAST likely to contribute to bacterial resistance to penicillins and other beta-lactams?
   (A) impaired penetration of the antibiotic through the outer membrane
   (B) inactivation of the antibiotic by beta-lactamase
   (C) induction of transpeptidase
   (D) modification of target penicillin-binding proteins
   (E) the presence of an efflux pump

466. Which of the following penicillins is the most nephrotoxic?
   (A) amoxicillin
(B) ampicillin
(C) cloxacillin
(D) dicloxacillin
(E) methicillin

467. Which of the following penicillins is cleared primarily by the kidneys and therefore must be administered in a lower dose in patients with compromised renal function?
(A) amoxicillin
(B) cloxacillin
(C) dicloxacillin
(D) nafcillin
(E) oxacillin

468. Clavulanic acid belongs to which of the following groups of drugs?
(A) beta-lactam antibiotics
(B) beta-lactamase inhibitors
(C) cytochrome P450 inducers
(D) cytochrome P450 inhibitors
(E) inhibitors of renal tubular secretion of weak acids

469. Which of the following statements about penicillins is (are) true?
(A) All penicillins are cross-reacting and cross-sensitizing.
(B) Most of the serious adverse reactions to penicillins are caused by hypersensitivity.
(C) The antigenic determinates that are most responsible for hypersensitivity reactions to penicillins are degradation products.
(D) all of the above
(E) none of the above

470. Of the patients who have previously been given penicillin without incident, what percentage will have an allergic reaction when given penicillin?
(A) fewer than 1%
(B) 1 to 5%
(C) 5 to 10%
(D) 10 to 15%
(E) 15 to 20%

471. Which of the following antibiotics is most susceptible to hydrolysis by beta-lactamases?
(A) axetil
(B) cefaclor
(C) cefprozil
(D) cefuroxime
(E) loracarbef
472. Which of the following third-generation cephalosporins achieves concentrations in the cerebrospinal fluid (CSF) sufficient to inhibit most pathogens except, perhaps, *Pseudomonas*?
(A) cefixime
(B) cefoperazone
(C) cefpodoxime proxetil
(D) ceffibuten
(E) ceftriaxone

473. Which of the following antibiotics is excreted mainly through the biliary tract and therefore does not need any dosage adjustment for renal insufficiency?
(A) cefazolin
(B) cefotaxime
(C) cefoxitin
(D) ceftazidime
(E) ceftriaxone

474. Beta-lactamaSe inhibitors are most effective against beta-lactamaSeS produced by which of the following bacteria?
(A) *Citrobacter*
(B) *Enterobacter*
(C) *Pseudomonas*
(D) *Serratia*
(E) *Staphylococcus*

475. The antibiotic action of erythromycifl is due to its interference with which of the following processes?
(A) gene transcription
(B) N-acetylation of glucosamine
(C) N-acetylation of muramic acid
(D) polymerization of monosaccharides
(E) ribosomal protein biosynthesis

476. What is the reason tetracyclines do not inhibit protein biosynthesis in mammalian cells?
(A) An active efflux mechanism in mammalian cells prevents intracellular accumulation of the drug.
(B) Mammalian genes code for proteins that are different from bacterial proteins.
(C) TetracyclineS do not bind to mammalian ribosomes.
(D) Tetracyclines do not block binding of amino acid-charged transfer RNA (tRNA) to the acceptor site of the ribosome-messenger RNA (mRNA) complex in mammalian cells.
(E) Tetracyclines do not penetrate across mammalian cell membranes.
477. Which of the following mechanisms has (have) been described for causing bacterial resistance to tetracyclines?
(A) enzymatic inactivation of the drug
(B) impaired influx of the drug or increased efflux by an active transport system
(C) interference with binding of the drug to the bacterial ribosome
(D) all of the above
(E) none of the above

478. Which of the following factors is (are) known to interfere with absorption of tetracyclines from the intestine?
(A) alkaline pH
(B) antacids
(C) dairy products
(D) divalent cations
(E) all of the above

479. What is the most likely effect of carbamazepine, phenytoin, barbiturates, and chronic alcohol ingestion on the pharmacokinetics of doxycycline?
(A) They increase free levels in the plasma by displacement of doxycycline from plasma proteins.
(B) They prolong the half-life by inhibition of hepatic enzymes.
(C) They prolong the half-life by interference with the excretion of doxycycline by the kidney.
(D) They reduce plasma levels by interference with absorption from the intestine.
(E) They shorten the half-life by induction of hepatic enzymes.

480. Which of the following tetracyclines is most suitable for administration to patients with renal insufficiency?
(A) chlortetracycline
(B) tetracycline
(C) doxycycline
(D) methacycline
(E) oxytetracycline

481. Which of the following tetracyclines has the longest duration of action?
(A) chlortetracycline
(B) demeclocycline
(C) minocycline
(D) oxytetracycline
(E) tetracycline
482. When a tetracycline is given during pregnancy, which tissue will most likely be affected adversely in the fetus?
(A) bone
(B) heart
(C) kidney
(D) liver
(E) skeletal muscle

483. Which of the following statements best describes the interaction of erythromycin or its metabolites with warfarin?
(A) Erythromycin metabolites directly inhibit the biosynthesis of vitamin K-dependent clotting factors, leading to an enhancement of the anticoagulant effects of warfarin.
(B) Erythromycin metabolites lower plasma levels of warfarin by inducing hepatic enzymes that metabolize the anticoagulant.
(C) Erythromycin metabolites raise plasma levels of warfarin by inhibiting hepatic enzymes that metabolize the anticoagulant.
(D) Erythromycin raises plasma levels of unbound warfarin by displacing the anticoagulant from plasma proteins.
(E) Erythromycin raises plasma levels of warfarin by increasing the bioavailability of the anticoagulant.

484. How is the pharmacology of clarithromycin different from erythromycin?
(A) Clarithromycin has better acid stability and oral absorption.
(B) Clarithromycin has fewer drug interactions.
(C) Erythromycin-resistant staphylococci are susceptible to clarithromycin.
(D) Erythromycin-resistant streptococci are susceptible to clarithromycin.
(E) all of the above

485. Cross-resistance is complete between linezolid and which of the following antibiotics?
(A) clindamycin
(B) erythromycin
(C) quinupristin-dalfopristin
(D) all of the above
(E) none of the above

486. The antibiotic activity of type B streptogramins is due to blockade of which of the following processes?
(A) gene transcription
(B) N-acetylation of glucosamine
(C) N-acetylation of muramic acid
(D) polymerization of monosaccharides
(E) ribosomal protein biosynthesis
487. Which of the following antibiotics has the greatest liability for producing toxic effects on the bone marrow?
(A) chloramphenicol
(B) clindamycin
(C) erythromycin
(D) streptogramins
(E) tetracyclines

488. Aminoglycoside antibiotics are useful mainly against which type(s) of microorganisms?
(A) aerobic gram-negative microorganisms
(B) aerobic gram-positive microorganisms
(C) anaerobic gram-negative microorganisms
(D) anaerobic gram-positive microorganisms
(E) both aerobic and anaerobic gram-positive microorganisms

489. Which of the following accurately describe(s) the effect(s) of streptomycin on bacterial ribosomal protein biosynthesis?
(A) It causes misreading of mRNA.
(B) It causes polysomes to break up into nonfunctional monosomes.
(C) It interferes with the initiation complex of peptide formation.
(D) all of the above
(E) none of the above

490. Which of the following best describes the principal type of resistance to aminoglycosides encountered clinically?
(A) adenylvlation, acetvlation, or phosphorylation of the aminoglycoside catalyzed by a transf erase enzyme or enzymes, resulting in inactivation of the antibiotic
(B) deletion or alteration of the receptor protein on the 30S ribosomal subunit
(C) efflux of the aminoglycoside due to an active pump
(D) impairment of the entry of the aminoglycoside into the cell
(E) induction of new proteins that competitively inhibit aminoglycoside binding to the 30S ribosomal subunit

491. Which of the following statements most accurately applies to aminoglycosides?
(A) After intravenous (IV) administration, they are rapidly distributed to most tissues in concentrations ranging from 60 to 90% of plasma levels.
(B) In order to achieve high levels in CSF, they must be administered by intrathecal or intraventricular injection.
(C) It is not necessary to adjust the dosage for patients with renal impairment.
(D) They are rapidly metabolized to inactive products by hepatic enzymes.
(E) They are well absorbed from the gastrointestinal (GI) tract.
492. Which of the following factors is (are) known to increase the likelihood of aminoglycoside-induced nephrotoxicity?
(A) The patient has renal insufficiency.
(B) The patient is elderly.
(C) The patient is receiving concurrent treatment with furosemide.
(D) The patient is receiving concurrent treatment with vancomycin.
(E) all of the above

493. Which of the following adverse reactions is most likely to occur in response to aminoglycosides?
(A) liver toxicity
(B) ototoxicity
(C) Parkinson’s disease-like syndrome
(D) venous thrombosis
(E) visual disturbances

494. High doses of aminoglycosides are most likely to produce which of the following adverse effects?
(A) cardiac arrhythmias
(B) central nervous system (CNS) depression
(C) elevated blood pressure
(D) neuromuscular blockade
(E) stroke

495. What is the most serious toxic effect of streptomycin?
(A) cardiac arrhythmias
(B) CNS depression
(C) cholestatic jaundice
(D) ocular disturbances
(E) vestibular dysfunction

496. Gentamicin belongs to which class of antibiotics?
(A) aminoglycosides
(B) beta-lactam antibiotics
(C) macrolides
(D) quinolones
(E) streptogramins

497. Which of the following mechanisms is (are) known to be part of the reason combination of gentamicin with penicillin or vancomycin produces a potent bactericidal effect against streptococci and enterococci?
(A) The binding site on the 50S ribosomal subunit has enhanced affinity for gentamicin.
(B) The efflux of gentamicin by an active pump is reduced.
(C) The transferase enzyme or enzymes that inactivate gentamicin are inhibited.
(D) The uptake of gentamicin into the cell is enhanced.
(E) all of the above

498. Which of the following antibiotics is least absorbed from the GI tract upon oral administration?
(A) amoxicillin
(B) ampicillin
(C) clarithromycin
(D) doxycycline
(E) neomycin

499. Which of the following antibiotics is most similar to gentamicin in pharmacokinetic properties and antibacterial spectrum?
(A) azithromycin
(B) clarithromycin
(C) moxifloxacin
(D) tobramycin
(E) vancomycin

500. Once-daily aminoglycoside dosing is often preferred over multiple daily dosing for which of the following reasons?
(A) Aminoglycosides have a significant postantibiotic effect against bacteria.
(B) Aminoglycosides have concentration-dependent killing rather than time-dependent killing.
(C) Toxicity tends to depend on the time that the aminoglycoside concentration is above a certain threshold.
(D) all of the above
(E) none of the above

501. The chemical structure of sulfonamides is most similar to which of the following compounds?
(A) Para-aminobenzoic acid (PABA)
(B) pantothenic acid
(C) tetrahydrofolic acid
(D) gamma-aminobutyric acid (GABA)
(E) gamma-carboxyglutamic acid

502. Which of the following statements best describes the antimicrobial activity of sulfonamides?
(A) They are bactericidal for both gram-positive and gram-negative bacteria.
(B) They are bactericidal for gram-negative bacteria only.
(C) They are bactericidal for gram-positive bacteria only.
(TJ) They are bacteriostatic for both gram-positive and gram-negative bacteria.
(E) They are bacteriostatic for gram-positive bacteria only.

503. Which of the following statements accurately reflect(s) the mechanism(s) by which bacteria become resistant to sulfonamides?

(A) Mutations cause a loss of permeability of the cell membrane to sulfonamides.
(B) Mutations cause formation of a folic acid-synthesizing enzyme that has a low affinity for sulfonamides.
(C) Mutations cause overproduction of PABA.
(D) all of the above
(E) none of the above

504. Which of the following sulfonamides has the longest duration of action?
(A)sulfacytine
(B)sulfadiazine
(C)sulfadoxine
(D)sulfamethizole
(E)sulfamethoxazole

505. Which drug or drug combination is administered by the intravenous route most often?
(A) sulfadoxine
(B) sulfamethoxazole
(C) sulfisoxazole
(U) trimethoprim-sulfadoxine
(E) trimethoprim-sulfamethoxazole

506. Which of the following statements LEAST accurately reflects the properties of sulfadiazine?
(A) It crosses the placenta and is distributed to the fetus.
(B) It is absorbed from the stomach and small intestine after oral administration.
(C) It is not distributed in therapeutic levels to the CSF.
(D) It is readily distributed to the lungs.
(E) When combined with pyrimethamine, the combination has synergistic action against toxoplasmosis.

507. Which of the following statements most accurately describes a property of sulfadoxine?
(A) It appears in the plasma mainly as free drug because there is very little binding to plasma proteins.
(B) It is a relatively short-acting sulfonamide.
(C) It is not well absorbed from the intestine after oral administration.
(D) It is rapidly excreted by the kidney.
(E) The free drug undergoes extensive tubular reabsorption in the kidney.
508. Which of the following statements LEAST accurately reflects the properties of sulfasalazine?

(A) It has a therapeutic effect similar to olsalazine, although it may not be as well tolerated.
(B) It is split by intestinal microflora to yield 5-aminosalicylate, which produces a beneficial anti-inflammatory effect.
(C) It is split by intestinal microflora, yielding sulfapyridine as one of its products.
(D) It is useful in treating inflammatory bowel disease.
(E) It is well absorbed from the intestine after oral administration.

509. Which of the following pharmacologic agents is (are) cross-allergenic with sulfonamides?

(A) carbonic anhydrase inhibitors
(B) furosemide
(C) sulfonylurea hypoglycemic agents
(D) thiazide diuretics
(E) all of the above

510. In addition to the administration of fluids, what agent(s) is (are) useful in treating nephrotoxicity caused by sulfadiazine?

(A) folinic acid
(B) probenecid
(C) sodium bicarbonate
(D) sulfinpyrazone
(E) all of the above

511. Where in the body is trimethoprim concentrated when therapeutic doses are given?

(A) adipose tissue
(B) CSF
(C) inner ear
(D) liver
(E) prostatic fluid and vaginal fluid

512. Which of the following toxic reactions would most likely be produced by trimethoprim?

(A) cholestatic jaundice
(B) crystalluria
(C) megaloblastic anemia
(D) tinflitus
(E) venous thrombosis
513. Which of the following alterations is (are) known to occur resulting in resistance to trimethoprim?
(A) decreased bacterial cell permeability
(B) overproduction of bacterial dihydrofolate reductase
(C) production of a modified dihydrofolate reductase with a lower affinity for the drug
(D) all of the above
(E) none of the above

514. To what group of drugs does ciprofloxacin belong?
(A) aminoglycosides
(B) beta-lactam antibiotics
(C) fluoroquinolones
(D) macrolides
(E) sulfonamides

515. Important quinolones are synthetic fluorinated analogs of what compound?
(A) nalidixic acid
(B) PABA
(C) pantothenic acid
(D) tetrahydrofolic acid
(E) GABA

516. The antimicrobial activity of ciprofloxacin is caused by its inhibition of which of the following bacterial enzymes?
(A) dihydrofolate reductase
(B) dihydropteroate synthase
(C) enolpyruvate transf erase
(D) RNA polymerase
(E) topoisomerase II and topoisomerase IV

517. Of the following antibiotics, which one is the most active against gram-negative bacteria?
(A) ciprofloxacin
(B) enoxacin
(C) levofloxacin
(D) lomefloxacin
(E) ofloxacin

518. Which of the following is (are) the most common adverse effect(s) caused by fluoroquinolones?
(A) CNS depression
(B) cholestatic jaundice
(C) nausea, vomiting, and diarrhea
(D) nephrotoxicity
519. Which of the following drugs has the greatest potential for adverse drug interaction if administered concomitantly with fluoroquinolones?
(A) carbamazepine
(B) insulin
(C) metformin
(D) theophylline
(E) warfarin

520. Four of the drugs listed below are first-line agents for treatment of tuberculosis and one is a second-line agent. Which one is the second-line agent?
(A) ciprofloxacin
(B) ethambutol
(C) isoniazid
(D) pyrazinamide
(E) rifampin

521. Which of the following agents can reverse the peripheral neuropathy caused by isoniazid?
(A) ascorbic acid
(B) folic acid
(C) niacin
(D) pyridoxine
(E) thiamine

522. Which of the following is the main cause of resistance of mycobacteria to rifampin?
(A) decreased penetration of rifampin into the bacterial cell
(B) increased efflux of rifampin from the bacterial cell by an active pump
(C) increased formation of an enzyme that inactivates rifampin
(D) mutation preventing the binding of rifampin to RNA polymerase
(E) mutation resulting in overexpression of RNA polymerase

523. Which of the following is the most common serious adverse event associated with use of ethambutol?
(A) bone marrow suppression
(B) hepatitis
(C) nephritis
(D) psychotic reaction
(E) visual disturbance

524. Which of the following antitubercular drugs exerts its antimicrobial activity mainly against intracellular organisms that have been taken up by macrophages?
525. Which of the following drugs exerts its antimycobacterial activity by interfering with the synthesis of mycolic acids, which are essential components of mycobacterial cell walls?
(A) ethambutol
(B) isoniazid
(C) pyrazinamide
(D) rifampin
(E) streptomycin

526. Which of the following drugs exerts its antimycobacterial activity by interfering with the synthesis of arabinoglycan, which is an essential component of mycobacterial cell walls?
(A) ethambutol
(B) isoniazid
(C) pyrazinamide
(D) rifampin
(E) streptomycin

527. Which of the following toxicities represents the most serious toxic reaction to amphotericin B?
(A) hematologic toxicity
(B) liver toxicity
(C) neuropathy
(D) ototoxicity
(E) renal toxicity

528. Which of the following mechanisms accounts for the antifungal activity of amphotericin B?
(A) formation of pores in the cell membrane
(B) inhibition of cytochrome P450 enzymes
(C) inhibition of DNA and RNA synthesis
(D) inhibition of ribosomal protein biosynthesis
(E) inhibition of squalene epoxidase

529. Which of the following mechanisms accounts for the antifungal activity of flucytosine?
(A) formation of pores in the cell membrane
(B) inhibition of cytochrome P450 enzymes
(C) inhibition of DNA and RNA synthesis  
(D) inhibition of ribosomal protein biosynthesis  
(E) inhibition of squalene epoxidase

530. Which of the following mechanisms accounts for the antifungal activity of terbinafine?  
(A) formation of pores in the cell membrane  
(B) inhibition of cytochrome P450 enzymes  
(C) inhibition of DNA and RNA synthesis  
(D) inhibition of ribosomal protein biosynthesis  
(E) inhibition of squalene epoxidase

531. Which of the following drugs is poorly absorbed from the intestine and has the least systemic antifungal activity when administered by the oral route?  
(A) amphotericin B  
(B) flucytosine  
(C) itraconazole  
(D) ketoconazole  
(E) terbinafine

532. Which of the following drugs is available in lipid delivery vehicles to permit the use of effective doses of the drug, but with reduced toxicity to the patient?  
(A) amphotericin B  
(B) flucytosine  
(C) itraconazole  
(D) ketoconazole  
(E) terbinafine

533. Which of the following steps in viral replication is (are) targeted by acyclovir?  
(A) DNA synthesis  
(B) packaging and assembly of the viron  
(C) protein synthesis by host polysome  
(D) uncoating of the viral DNA  
(E) all of the above

534. Which of the following represent(s) mechanism(s) by which resistance to acyclovir develops?  
(A) alteration of neuraminidase  
(B) alteration of proteases  
(C) alteration of reverse transcriptase  
(D) alteration of thymidine kinase  
(E) all of the above
535. An HIV-infected patient is receiving ganciclovir for treatment of cytomegalovirus retinitis. What is the most likely type of drug interaction that may occur if zidovudine is used concomitantly.
(A) accumulation of zidovudine due to cytochrome P450 inhibition by ganciclovir
(B) accumulation of zidovudine due to decreased biliary excretion caused by ganciclovir
(C) additive CNS toxicity
(D) additive myelosuppression
(E) lower systemic levels of zidovudine due to cytochrome P450 induction by ganciclovir

536. Which of the following toxic reactions represents the primary adverse effect of intravenous cidofovir?
(A) CNS symptoms
(B) hepatotoxicity
(C) nephrotoxicity
(D) ototoxicity
(E) skin rash

537. Which of the following represents the primary mechanism targeted by fomivirsen by which the drug inhibits virus replication?
(A) inhibition of DNA synthesis
(B) inhibition of packaging and assembly of the virion
(C) inhibition of protein synthesis
(D) inhibition of uncoating of the virion
(E) inhibition of viral release from the host cell

538. To which of the following groups of drugs does zidovudine belong?
(A) antiherpes and anticytomegalovirus agents
(B) nonnucleoside reverse transcriptase inhibitors
(C) nucleoside reverse transcriptase inhibitors
(D) nucleotide reverse transcriptase inhibitors
(E) protease inhibitors

539. Which of the following represents the major clinical toxicity associated with didanosine therapy?
(A) cardiomyopathy
(B) hepatotoxicity
(C) myelosuppression
(D) nephrotoxicity
(E) pancreatitis

540. Which of the following represents the major clinical toxicity associated with zalcitabine therapy?
(A) hepatotoxicity
(B) myelosuppression
(C) nephrotoxicity
(D) pancreatitis
(E) peripheral neuropathy

541. Which of the following represents the most important limitation to the ease of administration of ritonavir?
(A) effect of food on absorption from the GI tract
(B) interactions with other drugs
(C) nephrotoxicity
(D) pancreatitis
(E) poor bioavailability (<20%)

542. Which of the following protease inhibitors has the highest penetration into the CSF?
(A) amprenavir
(B) indinavir
(C) nelfinavir
(D) ritonavir
(E) saquinavir

543. What is the primary mechanism by which amantadine and rimantadine inhibit the replication of influenza A virus?
(A) inhibition of DNA synthesis
(B) inhibition of packaging and assembly of the virion
(C) inhibition of protein synthesis
(D) inhibition of reverse transcriptase
(E) inhibition of uricoating of the viral RNA

544. What is the primary mechanism by which didanosine inhibits viral replication?
(A) inhibition of RNA synthesis
(B) inhibition of packaging and assembly of the virion
(C) inhibition of protein synthesis
(D) inhibition of reverse transcriptase
(E) inhibition of uncoating of the viral RNA

545. Which of the following is the main reason for giving ritonavir along with saquinavir?
(A) to decrease the development of resistance
(B) to decrease the toxicity of the saquinavir
(C) to increase the concentrations of saquinavir reaching the systemic circulation
(D) to inhibit viral replication by two different mechanisms of action
(E) to reduce GI symptoms associated with saquinavir
546. Which of the following drugs is most effective against extraintestinal infections by *Entamoeba histolytica*?
(A) diloxanide furoate  
(B) iodoquinol  
(C) mefloquine  
(D) metronidazole  
(E) paromomycin sulfate

547. Which of the following drugs or drug combinations is most effective therapy for Pneumocystis carinii pneumonia?
(A) furazolidone  
(B) metronidazole  
(C) paromomycin  
(D) tetracycline  
(E) trimethoprim plus sulfamethoxazole

548. Which of the following represents the greatest limitation in the usefulness of chloroquine for the treatment of Plasmodium falciparum infection?
(A) hepatotoxicity  
(B) nephrotoxicity  
(C) poor absorption of the phosphate salt from the GI tract  
(D) poor distribution of the drug to the tissues  
(E) resistant strains

549. Which of the following is the drug of choice for eradication of dormant hepatic stages of *Plasmodium vivax* and *Plasmodium ovale*?
(A) amodiaquine  
(B) chloroquine  
(C) mefloquine  
(D) primaquine  
(E) quinine

550. Which of the following antimalarial drugs act by inhibition of plasmodial dthydrofolate reductase?
(A) amodiaquine  
(B) artemisinin  
(C) mefloquine  
(D) pyrimethamine  
(E) quinine

551. Which of the following drugs should be avoided during therapy with metronidazole?
(A) alcohol  
(B) diloxanide furoate  
(C) iodoquinol  
(D) paromomycin  
(E) all of the above

552. Which of the following classes of anticancer drugs is cell cycle nonspecific?  
(A) alkylating agents  
(B) antimetabolites  
(C) bleomycin peptide antibiotics  
(D) plant alkaloids  
(E) podophyllin alkaloids

553. P-glycoprotein is a  
(A) cellular glycoprotein that transports foreign molecules  
(B) component of the cell membrane that is primarily structural in function  
(C) component of the endoplasmic reticulum that facilitates drug biotransformation  
(D) glycoprotein involved primarily in cell signaling mechanisms  
(E) glycoprotein that binds to and inhibits certain transcription factors

554. Which of the following toxic reactions represents the major toxicity produced by alkylating agents used for therapy of cancer?  
(A) hepatotoxicity  
(B) nephrotoxicity  
(C) peripheral neuropathy  
(D) reduction of erythrocyte count  
(E) reduction of white blood cell count

555. In which of the following stages of breast cancer is chemotherapy as adjuvant to surgery (e.g., with cyclophosphamide—methotrexate—fluorouracil or fluorouracil—doxorubicin—cyclophosphamide) of most benefit?  
(A) Stage I  
(B) Stage II with one to three involved lymph nodes  
(C) Stage II with four or more involved lymph nodes  
(D) Stage III  
(E) Stage IV

556. Approximately what percentage of patients with nonseminomatous testicular neoplasms enter complete remission in response to combination chemotherapy with cisplatin, vinblastine, and bleomycin?  
(A) 0%  
(B) 10%  
(C) 30%  
(D) 50%
557. Which of the following classes of anticancer drugs is cell cycle specific?
(A) alkylating agents
(B) antibiotics
(C) cisplatin
(D) nitrosoureas
(E) plant alkaloids

558. For which of the following anticancer agents does intracellular formation of polyglutamate derivatives appear to be important?
(A) cytarabine
(B) fluorouracil
(C) mercaptopurine
(D) methotrexate
(E) vinblastine

559. Which of the following anticancer drugs causes cell death mainly by alkylations of DNA in the nucleus as well as alkylations of sulphhydryl, amino, hydroxyl, carboxyl, and phosphate groups of other cellular nucleophiles?
(A) chlorambucil
(B) cytarabine
(C) doxorubicin
(D) methotrexate
(E) vincristine

560. Which of the following anticancer drugs is converted in the body to a metabolite that blocks DNA synthesis by competitive inhibition of DNA polymerase?
(A) cytarabine
(B) etoposide
(C) melphalan
(D) paclitaxel
(E) tamoxifen

561. Which of the following anticancer drugs in
(A) cisplatin
(B) daunorubicin
(C) fluorouracil
(D) gemcitabine
(E) vinbiastine

562. Which of the following anticancer drugs block progression through the cell cycle mainly by inhibition of topoisomerase II?
(A) chiorambucil
(B) dactinomycin
(C) etoposide
(D) methotrexate
(E) procarbazine

563. Which of the following anticancer drugs inhibits DNA-dependent RNA synthesis mainly as a result of its intercalation between adjacent guanine-cytosine base pairs in double-stranded DNA?
(A) dactinomycin
(B) flutarnide
(C) methotrexate
(D) paclitaxel
(E) vinblastine

Answers and Explanations

462. (C) The penicillins that are resistant to staphylococcal beta-lactamase include methicillin, nafcillin, and isoxazolyl penicillins such as oxacillin, cloxacillin, and dicloxacillin.

463. (B) Penicillin G is effective against gram-positive organisms, gram-negative cocci, and non-beta-lactamase-producing anaerobes. However, it has little activity against gram-negative rods. Ampicillin has greater activity against gram-negative organisms than penicillin C.

464. (E) Beta-lactam antibiotics interfere with bacterial cell wall synthesis by blocking the transpeptidation reaction in peptidoglycan synthesis.

465. (C) There are four general mechanisms of resistance to beta-lactam antibiotics, and these are listed in this item. Induction of transpeptidase does not appear to be a mechanism by which resistance is conferred.

466. (E) Use of methicillin has been discontinued because of its nephrotoxicity.

467. (A) The dosage of amoxicillin must be reduced when creatinine clearance falls to 10 mL/min. Nafcillin is cleared primarily by biliary excretion and oxacillin, dicloxacillin, and cloxacillin are cleared by both the kidney and biliary excretion, and therefore the dosages do not need to be adjusted for renal function.
468. (B) Clavulanic acid, sulbactam, and tazobactam are beta-lactamase inhibitors. They are included in combination with ampicillin, amoxicillin, ticarcillin, and piperacillin to extend the activity of these penicillins to include some beta-lactamase-producing strains of bacteria.

469. (D) It is true that hypersensitivity reactions account for most of the adverse reactions to penicillins, that all penicillins are cross-reacting and cross-sensitizing, and that degradation products are the main antigenic determinants.

470. (A) Of the patients who have received penicillin previously without incident, fewer than 1% will have allergic reactions to penicillin.

471. (B) All of the antibiotics listed in this item are orally effective second-generation cephalosporins. Cefaclor is more susceptible to hydrolysis by beta-lactamases than the other agents in this group.

472. (E) Except for cefoperazone, cefixime, ceftibuten, and cefpodoxime proxetil, the third-generation cephalosporins penetrate body fluids and tissues well, including the CSF.

473. (E) Most cephalosporins are excreted through the kidney and need to be dosage adjusted for renal insufficiency. Ceftriaxone and cefoperazone are exceptions to this rule.

474. (E) Beta-lactamase inhibitors are most active against Ambler class A beta-lactamases. Organisms producing this type of beta-lactamase include staphylococci, Haemophilus influenzae, Neisseria gonorrhoeae, Salmonella, Shigella, Escherichia coli, and Klebsiella pneumoniae. These inhibitors are not very effective against class C beta-lactamases produced by Enterobacter, Citrobacter, Serratia, and Pseudomonas.

475. (E) Macrolides interfere with protein biosynthesis by preventing translocation of peptidyl tRNA from the acceptor site to the donor site on the bacterial ribosome.

476. (A) In mammalian cells, there is an active efflux mechanism that prevents intracellular accumulation of tetracycline antibiotics.

477. (D) All three mechanism listed have been described by which bacterial resistance to tetracyclines is produced. The most important of these is efflux of the drug by an active pump.
478. (E) All of the factors listed in this item are known to impair the absorption of tetracyclines. In addition, food can decrease absorption of all the tetracyclines except doxycycline and minocycline.

479. (E) The drugs listed in this item can shorten the half-life of doxycycline 50% by induction of hepatic enzymes.

480. (C) In contrast with other tetracyclines, doxycycline is eliminated by nonrenal mechanisms and therefore requires no dosage adjustment in patients with renal insufficiency.

481. (C) The classification of tetracyclines based on their half-lives is as follows: Short-acting (6 to 8 hours)—chlortetracycline, tetracycline, and oxytetracycline; intermediate-acting (12 hours)—demeclocycline and methacycline; and long-acting (16 to 18 hours)—doxycycline and minocycline.

482. (A) Tetracyclines bind readily to calcium deposited in newly formed bone. When given during pregnancy, it can cause deformity of bone or growth inhibition in the fetus. It also can be deposited in fetal teeth, causing fluorescence, discoloration, and enamel dysplasia.

483. (C) Erythromycin metabolites can inhibit hepatic cytochrome P450 enzymes, causing an increase in plasma concentrations of warfarin and other drugs, including theophylline, cyclosporine, and methylprednisolone.

484. (A) Clarithromycin is a semisynthetic derivative of erythromycin that has better acid stability and oral absorption compared to erythromycin.

485. (E) Linezolid acts by preventing formation of the ribosome complex that initiates protein synthesis. It is not cross-resistant with other drug classes because of its unique binding site located on the 23S ribosomal RNA of the 50S subunit.

486. (E) Quinupristin is a type B streptogramin. These agents block ribosomal protein synthesis by preventing translocation of peptidyl tRNA from the acceptor site to the donor site on the 50S ribosomal subunit. The combination of quinupristin with dalfopristin (type A streptogramin) is bactericidal for most bacteria.

487. (A) Chloramphenicol affects bone marrow in two ways. It can cause a dose related toxicity that results in anemia, leukopenia, or thrombocytopenia. It can also cause aplastic anemia, which is an idiosyncratic reaction unrelated to dose. The latter effect is rare, but it can be fatal.

488. (A) Aminoglycosides are bactericidal antibiotics that are useful mainly against aerobic gram-negative organisms.
489. (D) Streptomycin binds to S12 ribosomal proteins on the 30S subunit and inhibits protein biosynthesis in at least the three ways described in this item.

490. (A) Inactivation of the aminoglycoside is the principal mechanism of resistance encountered clinically. Other mechanisms that have been described include impaired entry of the aminoglycoside into the cell and deletion or alteration of the receptor protein on the 30S ribosomal subunit.

491. (B) Aminoglycosides are highly polar compounds that are not well absorbed from the intestine and are not well distributed to most tissues even after IV administration. Since they are cleared mainly by the kidney, the dose must be adjusted when renal function is impaired.

492. (F) Nephrotoxicity caused by aminoglycosides is more prevalent in patients who are elderly, experiencing renal insufficiency, receiving loop diuretics, or receiving other nephrotoxic antibiotics such as vancomycin or amphotericin.

493. (B) All aminoglycosides can produce ototoxicity. and this adverse reaction is most likely in the elderly, patients receiving high doses, patients receiving continuous therapy for longer than 5 days, and patients with renal insufficiency.

494. (D) High doses of aminoglycosides can produce a neuromuscular blockade that results in respiratory paralysis. The paralysis can usually be reversed by prompt administration of calcium gluconate or neostigmine.

495. (E) The most serious toxic effect of streptomycin is vestibular dysfunction accompanied by vertigo and loss of balance. This effect tends to be irreversible.

496. (A) Aminoglycosides include streptomycin, kanamycin, amikacin, gentamicin, tobramycin, and others.

497. (D) The combination enhances uptake of gentamicin due to inhibition of cell wall synthesis by the penicillin or vancomycin.

498. (E) Neomycin is not well absorbed from the GI tract and is used in preparation for elective bowel surgery to reduce aerobic bowel flora while producing minimal blood levels or systemic toxicity.

499. (D) Gentamicin and tobramycin are both aminoglycosides with similar antimicrobial activities and virtually identical pharmacokinetic properties. They are effective against both gram-positive and gram-negative organisms and are generally given intravenously or intramuscularly because of poor absorption from the GI tract.
500. (D) Concentration-dependent killing means that the higher the concentration of drug, the greater the killing effect. Postantibiotic effect refers to the fact that bacterial killing persists for a significant amount of time after measurable levels of the aminoglycoside have disappeared. Toxicity of aminoglycosides tends to depend on the time that the drug concentrations are above a certain threshold level, although the threshold level may not be precisely defined.

501. (A) The structure of sulfonamides most closely resembles the structure of PABA. They inhibit bacterial growth by blocking folic acid synthesis, which is essential for the production of purines and synthesis of nucleic acids.

502. (D) Sulfonamides inhibit the growth of both gram-positive and gram-negative bacteria by interfering with the formation of dihydrofolic acid, which is essential for production of purines and the synthesis of nucleic acids.

503. (D) Resistance to sulfonamides can be caused by any of the three mechanisms listed in this item.

504. (C) Sulfadoxifile has a half-life of 7 to 9 days. The other sulfonamides listed in this item have short or intermediate half-lives measured in hours.

505. (E) Intravenous trimethoprim-sulfamethoxazole is the agent of choice for moderately severe to severe pneumocystis pneumonia, especially in immunocompromised patients. Oral administration of this combination is also effective against many types of infection.

506. (C) Sulfadiazifile, like other orally effective sulfonamides, is widely distributed to bodily tissues and fluids, including the brain and CSF.

507. (E) Sulfadoxine is a long-acting, orally effective sulfonamide that is excreted slowly by the kidney due to high protein binding and extensive tubular reabsorption.

508. (E) Intestinal microflora split sulfasalazine into sulfapyridine and 5-aminosalicylate (5-ASA). 5-ASA has an anti-inflammatory effect that is beneficial in ulcerative colitis, enteritis, and other inflammatory bowel disease. Because it releases 5-ASA in the intestine, sulfasalazine has a therapeutic effect similar to olsalazine, a dimer of 5-ASA, but it may not be as well tolerated.

509. (E) All of the agents listed in this item are derivatives of sulfonamides and are cross-allergenic with them. Other cross-allergenic agents include bumetanide, torsemide, and diazoxide.

510. (C) Nephrotoxicity due to large doses of sulfadiazine is caused by precipitation of the drug, resulting in crystals in the urine. Since the drug is more
soluble at alkaline than acid pH, sodium bicarbonate may be given to reduce the crystalluria.

511.  (E) Because trimethoprim is a weak base of PKa = 7.2, it concentrates in prostatic fluid and vaginal fluid, which are more acid than plasma.

512.  (C) As a consequence of its antifolate activity, trimethoprim can produce megaloblastic anemia, leukopenia, and granulocytopenia. Use of folinic acid can prevent the hematologic toxicity caused by the combination of trimethoprim and sulfamethoxazole, but its use has been associated with increased morbidity and treatment failures in AIDS patients being treated with trimethoprim-sulfamethoxazole for pneumocystis pneumonia.

513.  (D) All three mechanisms of resistance listed in this item are known to occur in bacteria. Resistance most commonly results from trimethoprim-resistance dihydrofolate reductase encoded by plasmids.

514.  (C) Ciprofloxacin is a fluoroquinolone with excellent activity against gram-negative bacteria and moderate to good activity against gram-positive bacteria.

515.  (A) Nalidixic acid itself can be used for treatment of lower urinary tract infections, but it does not achieve systemic antibacterial levels.

516.  (E) Ciprofloxacin is a fluoroquinolone. This group of antibiotics inhibits bacterial topoisomerase II (DNA gyrase) and topoisomerase IV, thereby interfering with DNA synthesis.

517.  (A) All of the fluoroquinolones in this group have excellent activity against gram-negative bacteria, but ciprofloxacin is the most active against these organisms, especially Pseudomonas aeruginosa.

518.  (C) Fluoroquinolones are extremely well tolerated with the most common adverse effects being GI symptoms. Headache, dizziness, insomnia, skin rash, or abnormal liver function tests are observed occasionally.

519.  (D) Elevated levels of theophylline accompanied by an increased risk of adverse effects, especially seizures, can be caused by concomitant administration of theophylline and fluoroquinolones.

520.  (A) The five first-line agents for treatment of tuberculosis are: isoniazid, rifampin, pyrazinamide, ethambutol, and streptomycin.
521. (D) Isoniazid promotes the excretion of pyridoxine, which leads to a relative pyridoxine deficiency that causes the peripheral neuropathy observed in isoniazid-treated patients.

522. (D) The antimycobacterial activity of rifampin is due to its strong binding to the beta subunit of bacterial DNA-dependent RNA polymerase, which inhibits the enzyme. Resistance is usually caused by one of several possible point mutations in the gene ($rpoB$) encoding for the beta subunit, resulting in prevention of binding.

523. (E) Ethambutol causes a retrobulbar neuritis resulting in loss of visual acuity and red-green color blindness.

524. (C) Pyrazinamide is converted by mycobacterial pyrazinamidase to pyrazinoic acid, which is the active form of the drug. The drug has greater activity against tubercle bacilli at acid pH than at neutral pH. It is taken up by macrophages and exerts its antimycobacterial action mainly against organisms in the acidic intracellular environment.

525. (B) Isoniazid is a prodrug that is converted to its active form by mycobacterial catalase-peroxidase. In its activated form, the drug forms a covalent complex with an acyl carrier protein (AcpM) and a beta-ketoacyl carrier protein synthetase (KasA), resulting in inhibition of mycolic acid synthesis.

526. (A) Ethambutol inhibits mycobacterial arabinosyl transferases which are involved in the polymerization reaction of arabinoglycan.

527. (E) Nearly all patients treated with clinically significant doses of amphotericin B suffer renal impairment. There are reversible and irreversible components of this toxicity. The reversible component is associated with decreased renal perfusion. The irreversible component is caused by renal tubular injury.

528. (A) The amphotericin B molecule may be described as having a double bond-rich side and a hydroxyl-rich side. The double bond-rich side binds to membrane lipids forming the outside of pores, and the hydroxyl-rich side of the drug molecule forms the inside lining of pores in the cell membrane, thus altering cell permeability.

529. (C) Once inside the fungal cell, flucytosine is converted first to 5-fluorouracil, then to 5-fluorodeoxyuridine monophosphate, which inhibits DNA synthesis, and to fluorouridine triphosphate, which inhibits RNA synthesis.

530. (E) Terbinafine inhibits the fungal enzyme squalene epoxidase, thus interfering with the synthesis of ergosterol, and causing accumulation of squalene, which is toxic to the organism.
531. (A) Amphotericin B is poorly absorbed from the intestine and is given by IV injection for treatment of systemic disease. It is widely distributed to most tissues, but it is poorly distributed in the CSF.

532. (A) The lipid vehicle reduces nonspecific binding of amphotericin B to mammalian membranes, thereby reducing the nephrotoxicity of the drug.

533. (A) Acyclovir is an acyclic guanosine derivative that is phosphorylated by multiple steps within the cell to form the triphosphate. The nucleotide analog inhibits DNA synthesis in two ways: (1) It competes with deoxyGTP for the viral DNA polymerase, and (2) it causes chain termination when it is incorporated into the viral DNA.

534. (D) Acyclovir is activated by phosphorylation to the triphosphate, and the nucleotide analog then interferes with DNA synthesis catalyzed by viral DNA polymerase. The first phosphorylation step, yielding the monophosphate, is catalyzed by viral thymidine kinase. Alteration of viral thymidine kinase appears to be the main mechanism of the development of resistance to the drug, and a second mechanism involves alteration of viral DNA polymerase.

535. (D) Both ganciclovir and zidovudine can cause myelosuppression and the toxic effect may be additive when both drugs are administered concomitantly.

536. (C) Probenecid must be administered together with IV cidofovir to block active renal tubular secretion and thereby decrease the nephrotoxicity caused by cidofovir.

537. (C) Fomivirsen inhibits cytomegalovirus replication by an antisense mechanism. The drug is an oligonucleotide that binds to target mRNA, resulting in inhibition of protein synthesis.

538. (C) Zidovudine is a deoxythymidine analog that inhibits HIV-1 reverse transcriptase and can also be incorporated into the growing viral DNA chain, causing termination of the chain.

539. (E) Didanosine is relatively contraindicated in patients with chronic alcoholism or other risk factors for pancreatitis.

540. (E) The peripheral neuropathy associated with zalcitabine can be treatment limiting in 10 to 20% of patients. The neuropathy appears to be slowly reversible if the drug is withdrawn promptly.
(B) Ritonavir is a potent inhibitor of the CYP3A and CYP2D6 isoforms of cytochrome P450 and thus interacts with numerous other drugs. In addition, plasma levels of ritonavir are decreased by drugs that induce the CYP3A isoform.

(B) CSF penetration of indinavir ranges as high as 76% of serum levels.

(E) Both drugs inhibit uncoating of the virion by targeting the M2 protein within the membrane.

(D) Didanosine is a nucleoside reverse transcriptase inhibitor. These agents competitively inhibit HIV-1 reverse transcriptase. They also can be incorporated into the growing viral DNA chain, thereby terminating the chain.

(C) Saquinavir and ritonavir are both protease inhibitors. Saquinavir is extensively metabolized by first-pass effect as it passes through the liver, thereby reducing the levels of drug that reach the systemic circulation. Ritonavir potently inhibits the cytochrome P450 isoform that metabolizes saquinavir (CYP3A4), resulting in less saquinavir being removed by first-pass metabolism and more reaching the systemic circulation.

(D) Metronidazole effectively eradicates intestinal and extraintestinal tissue infections by *E. histolytica*. Iodoquinol, diloxanide furoate, and paromomycin sulfate are effective for therapy of luminal infections, but not extraintestinal tissue infections by this organism. Mefloquine is used for therapy against chloroquine-resistant strains of *P. falciparum*, not *E. histolytica*.

(E) Trimethoprim and sulfamethoxazole block sequential steps in the metabolism of folic acid and thereby produce synergistic effects against *P. carinii* and other organisms.

(E) The phosphate salt of chloroquine is well absorbed from the GI tract, and the drug is well distributed to most tissues. It is generally well tolerated. The emergence of resistant strains of *P. falciparum* since the 1940s has compromised the drug’s utility in the treatment of malaria. It is the drug of choice against sensitive strains.

(D) Most antimalarial drugs do not eradicate the dormant liver forms of *P. vivax* and *P. ovale*, and therefore common therapy includes chloroquine to eradicate erythrocytic forms and primaquine to eradicate liver forms of these parasites.

(D) Pyrimethamine and proguanil inhibit dihydrofolate reductase. Each of these drugs may be used in combination with a sulfonamide or sulfone, which inhibits dthydropteroate synthase, another enzyme in the folate pathway.
551. (A) Metronidazole has a disulfiram-like effect so that if alcohol is ingested during therapy, nausea and vomiting could result.

552. (A) Cell cycle-nonspecific agents include: alkylating agents, antibiotics, cisplatin, and nitrosoureas. Cell cycle-specific agents include: antimetabolites, bleomycin peptide antibiotics, podophyllin alkaloids, and plant alkaloids.

553. (A) P-glycoprotein is a cell surface transport molecule that expels a variety of foreign molecules from the cell and is responsible for multidrug resistance in cancer cells.

554. (E) Toxic reactions to alkylating agents include nausea and vomiting of CNS origin and toxicity in rapidly growing tissues such as bone marrow, GI tract, and gonads. The major toxicity is suppression of myelopoiesis, resulting in a fall in white blood cell count. Erythrocyte counts are affected to only a minor extent due to the long life span of these cells.

555. (B) Adjuvant chemotherapy with the regimens given as examples in this item are of most benefit in stage II with one to three positive lymph nodes. Women with stage II and involvement of four or more lymph nodes receive less benefit, and therapy for women with stage III and stage IV cancer is a major problem.

556. (E) Approximately 95% of the patients described in this item respond to combination chemotherapy, and approximately 90% enter into complete remission. It appears that over half of those patients that enter complete remission are cured.

557. (E) Cell cycle-specific agents include: antimetabolites, bleomycin peptide antibiotics, podophyllin alkaloids, and plant alkaloids. Cell cycle-nonspecific agents include: alkylating agents, antibiotics, cisplatin, and nitrosoureas.

558. (D) Polyglutamate derivatives of methotrexate have greater inhibitory activity against enzymes involved in folate metabolism and are retained longer in cells than methotrexate.

559. (A) Cyclophosphamide, chlorambucil, and other alkylating agents cause cell death mainly as a result of the transfer of their alkyl groups to various cellular constituents, nuclear DNA perhaps being the most important target.

560. (A) Cytarabine (Ara-cytosine) is converted in the body to Ara-CTP, which acts as a competitive inhibitor of DNA polymerase, thereby blocking DNA synthesis without directly blocking RNA or protein synthesis.
561. (E) Vinblastine binds specifically to the microtubular protein tubulin and causes depolymerization of the microtubules that form the mitotic spindle. The result is arrest of mitosis in the metaphase.

562. (C) Etoposide and teniposide are drugs that form a ternary complex of the drug, DNA, and topoisomerase II, resulting in DNA damage through strand breakage.

563. (A) Dactinomycin binds tightly to double-stranded DNA, resulting in interference with RNA synthesis. Ribosomal RNA synthesis is the most sensitive to the blockade, and this results in blockade of protein synthesis.