Chemotherapy

Subcommittee:

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Basic Principles Of Antimicrobial Therapy
Recommended Curriculum Equivalent: 1 hr
Learning Objectives
Define the terms: antibiotics, selective toxicity, therapeutic index, bacteriostatic and bactericidal, chemotherapeutic spectrum. Understand the MIC and MBC values. Describe the terms synergism and antagonism. Discuss the classification of antimicrobial drugs based upon the mechanism of action. Explain the modes of action of various antimicrobial drugs. Define bacterial resistance and illustrate the mechanisms involved in acquiring bacterial resistance. Describe the basic principles of combination therapy with antimicrobial drugs.

Cell Wall Synthesis Inhibitors	
Recommended Curriculum Equivalent: 2 hr	
Drug Classes and Drugs to consider	
Penicillins	Cephalosporins and vancomycin
AMPICILLIN AZTREONAM PENICILLIN G PIPERACILLIN IMIPENEM amoxicillin clavulanic acid cloxacillin indanyl carbenicillin meropenem methicillin mezlocillin nafcillin oxacillin penicillin V sulbactam tazobactam. ticarcillin	CEFTRIAXONE CEPHALEXIN VANCOMYCIN cefaclor cefazolin cefepime cefotaxime cefoxitin ceftazidime cefuroxime fosfomycin
Learning Objectives	
Mechanism of action Describe the structural relationship of the penicillin molecule with antimicrobial activity. Explain the mechanism of action of β-lactam antibiotics Understand the principle of combination of inhibitors of β-lactamase with penicillins (List such combinations). Explain the pharmacological basis for combining imipenem with cilastatin. Describe the structural differences between penicillins and cephalosporins. Explain the mechanism of action of cephalosporins. Discuss the mechanism of action of vancomycin and of fosfomycin.	
Pharmacokinetics Describe the pharmacokinetic properties of penicillins. Describe the repository penicillins. List the penicillinase-resistant penicillins. Describe the four generations of cephalosporins with specific examples and the differences in their antimicrobial spectrum and pharmacokinetic properties. Describe the pharmacokinetic properties of vancomycin.	
Adverse effects and contraindications Describe the principal adverse effects of penicillins. Describe the principal contraindication of penicillins. Describe the adverse effects due to cephalosporins and vancomycin. Explain the terms superinfection and cross-hypersensitivity.	

Therapeutic uses

Discuss primary therapeutic indications for penicillin G.
Describe the indications for broad-spectrum penicillins.
Describe the antimicrobial activity of monobactams and carbapenems.
Describe the main therapeutic indications of cephalosporins and vancomycin.

Clinical Pharmacology

Vancomycin use should be reserved for treatment of MRSA infections. Carbapenems and 3rd and 4th generation cephalosporin antibiotics should be reserved for patients with very serious polymicrobial infections. Carbapenems can reduce the serum concentration of valproate, leading to recurrence of seizures.

Relevance

USMLE topic Cardiovascular System – Abnormal processes	**Principles of therapeutics** Antimicrobials and antiparasitics
AAMC Medical School Objectives Project Report X Patient Safety Table 1	**Topic C** Drug treatment of common conditions and diseases

Protein Synthesis Inhibitors		
Recommended Curriculum Equivalent: 1 hr		
Drug Classes and Drugs to consider		
Aminoglycosides	Macrolides	Streptogramins
GENTAMICIN amikacin neomycin streptomycin tobramycin	AZITHROMYCIN CLARITHROMYCIN ERYTHROMYCIN telithromycin	quinupristin/dalfopristin
Lincosamides	Oxazolidinones	Tetracyclines
clindamycin	LINEZOLID	DOXYCYCLINE TIGECYCLINE minocycline tetracycline
Others		
MUPIROCIN Chloramphenicol		
Learning Objectives		
Mechanism of action Discuss the mechanism of action of each class of protein synthesis inhibitors. Explain the mechanism of acquired drug resistance to aminoglycosides, tetracyclines, and macrolides. Explain the rational basis for combination therapy with an aminoglycoside and a penicillin, cephalosporin, or vancomycin.		
Pharmacokinetics Describe the pharmacokinetic properties of each class of protein synthesis inhibitors, including their routes of administration. Explain the importance of peak and trough levels of aminoglycosides. Discuss the need of and the method of dose adjustment for aminoglycosides in patients with compromised renal function.		
Adverse effects and drug interactions Discuss the main toxicities of each class of protein synthesis inhibitors. Describe the major drug interactions of macrolides due to inhibition of cytochrome P450 enzymes.		
Therapeutic uses Describe the primary therapeutic indications for each class of protein synthesis inhibitors. Discuss the therapeutic options for treating skin and soft tissue infections, and systemic infections due to methicillin-resistant or vancomycin-resistant bacteria.		

Clinical Pharmacology	
Use of macrolide antibiotics in patients receiving cacium channel blockers is associated with an increased risk of hypotension due to inhibition of CYP3A4 activity. Macrolide antibiotics also increase the risk of toxicity to statins metabolized by CYP3A4. Use of linezolid for more than 10 days is associated with bone marrow depression.	
Relevance	
USMLE topic Cardiovascular System – Abnormal processes	**Principles of therapeutics** Antimicrobials and antiparasitics
AAMC Medical School Objectives Project Report X Patient Safety Table 1	**Topic C** Drug treatment of common conditions and diseases

Inhibitors of Nucleic Acid metabolism and Drugs interfering with intermediary metabolism	
Recommended Curriculum Equivalent: 1 hr	
Drug Classes and Drugs to consider	
Fluoroquinolones	Rifamycins
CIPROFLOXACIN levofloxacin	RIFAMPIN rifaximin
Nitroimidazole	Dihydrofolate reductase inhibitors
METRONIDAZOLE	COTRIMOXAZOLE trimethoprim
Sulfonamides	Other Agents
COTRIMOXAZOLE sulfamethoxazole	DAPTOMYCIN FIDAXOMICIN nitrofurantoin
Learning Objectives	
Mechanism of action Explain the mechanism of action of each class of antibiotics. Discuss the synergistic inhibition due to sequential blockade with cotrimoxazole. Learn the adverse effects of ciprofloxacin, including contraindications in children and pregnant women.	
Pharmacokinetics Describe the pharmacokinetics properties of each class of antibiotics. Describe the drug interactions of fluoroquinolones, including the effect of ingested cations on drug absorption.	
Adverse effects Describe the major toxicities of each class of drugs.	
Therapeutic uses Describe the therapeutic indications each class of antimicrobial drugs. List the advantages of newer fluoroquinolones over ciprofloxacin. Describe the major therapeutic indications of sulfonamides alone, and in combination with trimethoprim (cotrimoxazole). Discuss the emergence of microbial resistance to cotrimoxazole and fluoroquinolone drugs, and its implications for the treatment of urinary tract infections and gonorrhea. Describe the role and use of various drugs in the treatment of methicillin-resistant *Staphylococcus aureus* infections. Describe and compare the role of metronidazole, vancomycin, and fidaxomicin in the treatment of *Clostridium difficile* infections. Discuss the therapeutic options for treating traveler's diarrhea.	
Clinical Pharmacology When administered concurrently with warfarin, metronidazole is associated with an increased anticoagulant activity. Caution in using rifampin with other drugs metabolized by CYP3A4 due to its enzyme induction property.	
Relevance	

USMLE topic Cardiovascular System – Abnormal processes	**Principles of therapeutics** Antimicrobials and antiparasitics
AAMC Medical School Objectives Project Report X Patient Safety Table 1	**Topic C** Drug treatment of common conditions and diseases

Antimycobacterial Drugs	
Recommended Curriculum Equivalent: 1 hr	
Drugs to consider	
ETHAMBUTOL ISONIAZID RIFAMPIN PYRAZINAMIDE RIFAPENTINE	azithromycin clarithromycin clofazimine dapsone rifabutin streptomycin thalidomide
Learning Objectives	
Mechanism of action List the first line antitubercular drugs and explain their mechanisms of action. Define the various phases of actively and slow growing *Mycobacterium tuberculosis* and compare the relative effectiveness of various drugs. Describe the drugs used in the treatment of Hansen's disease and their mechanism of action.	
Pharmacokinetics Describe the pharmacokinetic profile of isoniazid and rifampin.	
Adverse effects and drug interactions Describe the adverse effects of isoniazid, rifampin, ethambutol and pyrazinamide. Explain the drug interactions of rifampin with anticoagulants and other drugs, such as oral contraceptives.	
Therapeutic uses Describe the regimen recommended for treatment of latent tuberculosis (formerly prophylaxis) and active tuberculosis. Explain the rationale for newer short-course regimens for latent and active tuberculosis, including the use of isoniazid and rifapentine. Describe the emergence of multidrug-resistant tuberculosis and its implications for the treatment of these infections. Discuss the use of rifabutin, clarithromycin and azithromycin for treatment of *Mycobacterium avium* complex. Describe the drugs used for reversing the lepra reactions and the erythema nodosum leprosum reaction. Explain the WHO regimen for treatment of leprosy.	
Clinical Pharmacology Mostly covered already in other sections of this document. Nothing special to add here.	
Relevance	
USMLE topic Cardiovascular System – Abnormal processes	**Principles of therapeutics** Antimicrobials and antiparasitics

AAMC Medical School Objectives Project Report X Patient Safety Table 1	**Topic C** Drug treatment of common conditions and diseases

Antiparasitic Drugs	
Recommended Curriculum Equivalent: 1 hr	
Drugs to consider	
ALBENDAZOLE IVERMECTIN METRONIDAZOLE MILTEFOSINE NITAZOXANIDE PERMETHRIN PRAZIQUENTAL SPINOSAD TINIDAZOLE	atovaquone diethylcarbamazine diloxanide iodoquinol mebendazole nifurtimox paromomycin pentamidine pyrantel pamoate pyrimethamine/sulfonamide sodium stibogluconate sulfadiazine suramin tinidazole trimetrexate
Learning Objectives	
Mechanism of action Describe the mechanism of action of mebendazole, praziquantel, pentamidine, and atovaquone.	
Therapeutic uses Learn the drugs of choice and alternate drugs available for treatment of diseases due to various helminthes. Learn the broad spectrum anthelminthic drugs and their spectrum of activity. Learn the opportunistic infections commonly known to occur in AIDS patients and the drugs used for their treatment. Learn the drugs of choice for treatment of asymptomatic, mild to moderate and severe intestinal disease and hepatic abscess due to E. histolytica. Learn the drugs used for the treatment of protozoal diseases (giardiasis, trypanosomiasis, and leishmaniasis). Learn the drugs used for toxoplasmosis, an opportunistic infection in AIDS patients.	
Clinical Pharmacology	
Relevance	
USMLE topic Cardiovascular System – Abnormal processes	**Principles of therapeutics** Antimicrobials and antiparasitics
AAMC Medical School Objectives Project Report X Patient Safety Table 1	**Topic C** Drug treatment of common conditions and diseases

Antimalarial drugs	
Recommended Curriculum Equivalent: 1 hr	
Drugs to consider	
ARTESUNATE ARTEMETHER/LUMEFANTRINE CHLOROQUINE DOXYCYCLINE MEFLOQUINE PRIMAQUINE QUININE	atovaquone/proguanil pyrimethamine Sulfadoxine
Learning Objectives	
Mechanism of action Describe the various locations in the life cycle of malarial parasites where the antimalarial drugs are effective. Describe the mechanisms of action of chloroquine, primaquine and pyrimethamine. Discuss the mechanism of resistance to chloroquine. Learn the mechanism of action of artemisinin derivatives.	
Pharmacokinetics Describe the pharmacokinetic properties of chloroquine. Describe the pharmacokinetic properties and metabolism of artesunate and artemether.	
Adverse effects Explain the mechanism of hemolytic anemia induced by primaquine in African-American males. Describe cinchonism. Describe the toxic effects of chloroquine.	
Therapeutic uses List the drugs of choice for treatment of uncomplicated illness and severe illness due to P. vivax, P. ovale, P. malariae and P. falciparum. Describe the regimen for prophylaxis for chloroquine-sensitive and chloroquine-resistant areas. Discuss the drug combination in Fansidar, Coartem, and Malarone and their therapeutic use. Describe the therapeutic indications for artemisinin derivatives.	
Clinical Pharmacology Drug interactions likely in patients with malaria and concurrent HIV infection due to polypharmacy and effects especially on CYP3A4 activity.	
Relevance	
USMLE topic Cardiovascular System – Abnormal processes	**Principles of therapeutics** Antimicrobials and antiparasitics
AAMC Medical School Objectives Project Report X Patient Safety Table 1	**Topic C** Drug treatment of common conditions and diseases

Antifungal Drugs	
Recommended Curriculum Equivalent: 1 hr	
Drugs to consider	
AMPHOTERICIN B CASPOFUNGIN (echinocandins) FLUCONAZOLE ITRACONAZOL TERBINAFINE VORICONAZOLE	flucytosine ketoconazole micafungin posaconazole griseofulvin nystatin sulfamethoxazole-trimethoprim (cotrimoxazole)
Learning Objectives	
Mechanism of action Discuss the mechanism of action of each class of antifungal drugs. Discuss the advantages of liposomal preparations of amphotericin B.	
Pharmacokinetics Describe the pharmacokinetic properties of the various antifungal drugs.	
Adverse effects Describe the important adverse effects of the various antifungal drugs. Discuss the drug interactions of griseofulvin and warfarin; ketoconazole and warfarin.	
Therapeutic uses Describe the major therapeutic indications of the antifungal drugs, including current recommendations for treating aspergillosis, blastomycosis, superficial and systemic candidiasis, coccidioidomycosis, cryptococcosis, histoplasmosis, mucormycosis, and sporotrichosis. Describe the use of trimethoprim-sulfamethoxazole in the treatment of Pneumocystis jiroveci infections. Discuss the appropriate duration of treatment of various fungal infections and the role of surgical debridement in treating subcutaneous mycoses. Describe host factors that predispose patients to fungal infections.	
Clinical Pharmacology Many antifungals are strong inhibitors of CYP3A4 and caution is indicated for patients receiving concurrent drug therapy where CYP3A4 is a prominent drug metabolism pathway.	
Relevance	
USMLE topic Cardiovascular System – Abnormal processes	**Principles of therapeutics** Antimicrobials and antiparasitics
AAMC Medical School Objectives Project Report X Patient Safety Table 1	**Topic C** Drug treatment of common conditions and diseases

Antiviral Drugs	
Recommended Curriculum Equivalent: 1 hr	
Drugs to consider	
ACYCLOVIR BOCEPREVIR FOSCARNET GANCICLOVIR OSELTAMIVIR RIBAVARIN TELAPREVIR TRIFLURIDINE ZANAMIVIR	amantadine idoxuridine peginterferon alfa rimantadine valacyclovir valganciclovir
Learning Objectives	
Mechanism of action Classify antiviral drugs based upon their site of inhibition in the viral replication cycle. Explain the mechanism of action of each antiviral drug.	
Pharmacokinetics Compare pharmacokinetic properties of acyclovir, valacyclovir, and ganciclovir, and valganciclovir.	
Adverse effects List their adverse side effect and therapeutic complications. Describe potential drug interactions.	
Therapeutic uses Describe major therapeutic indications for each antiviral drugs. Compare the drugs and regimens used for prevention and treatment of cytomegalovirus infections. Describe the role and use of oseltamivir and zanamivir in the prophylaxis and treatment of influenza. Describe the emergence and mechanism of influenza virus resistance to amantadine and rimantadine. Describe the use of combination drug therapy in the treatment of hepatitis B and hepatitis C.	
Clinical Pharmacology In drug therapy of hepatitis, polypharmacy is the standard of care. Use of telaprevir, peginterferon and ribavirin as a treatment strategy increases risk for anemia. Telaprevir is both a substrate and inhibitor of CYP3A4 and P-glycoprotein. Thus, drug interactions are predictable, especially with concurrent therapies that have high presystemic elimination by these two mechanisms.	
Relevance	
USMLE topic Cardiovascular System – Abnormal processes	**Principles of therapeutics** Antimicrobials and antiparasitics

AAMC Medical School Objectives Project Report X Patient Safety Table 1	**Topic C** Drug treatment of common conditions and diseases

Antiretroviral Drugs	
Recommended Curriculum Equivalent: 1 hr	
Drugs to consider	
Nucleoside Reverse Transcriptase Inhibitors (NRTI)	Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)
ABACAVIR LAMIVUDINE (3-TC) TENOFOVIR DISOPROXIL ZIDOVUDINE (AZT) EMTRICITABINE didanosine (ddI) stavudine (D4T)	EFAVIRENZ NEVIRAPINE
HIV-1 protease inhibitors	Fusion Inhibitors
ATAZANAVIR RITONAVIR amprenavir indinavir lopinavir nelfinavir saquinavir	ENFUVIRTIDE MARAVAROC
DNA Strand Transfer Inhibitor	
RALTEGRAVIR	
Learning Objectives	
Mechanism of action Classify anti-HIV drugs based upon their site of inhibition in the viral replication cycle. Learn the mechanism of action of individual nucleoside reverse transcriptase inhibitors. Explain the mechanisms of action of each class of anti-HIV drugs. Explain the use of combinations of drugs derived from different drug classes	
Pharmacokinetics Compare pharmacokinetic properties of each class of anti-HIV drugs.	
Adverse effects Learn major side effects of each class of anti-HIV drugs, with emphasis on the metabolic and cardiovascular adverse effects. Describe the major drug interactions of anti-HIV drugs, with emphasis on interactions involving inhibition or induction of cytochrome P450 enzymes.	
Therapeutic uses Describe the various currently preferred drug combinations used for the treatment of HIV infections. Describe the rationale and components of once-a-day formulations for treating HIV infections. Describe the CD4 cell and viral load criteria for the initiation of drug therapy for HIV infection, and the criteria for changing drug therapy due to viral resistance. Describe the use of drugs for treating maternal infections and prevention of maternal-fetal transmission during pregnancy. Describe the use of drugs for the prevention of HIV infection in adults.	

Clinical Pharmacology Present standard of care involves polypharmacy and almost invariably is associated with drug interactions when co-morbidities are also treated with drugs. Extreme caution is advised in choosing drugs for co-morbidities that may affect the elimination mechanisms of the ART drugs prescribed.	
Relevance	
USMLE topic Cardiovascular System – Abnormal processes	**Principles of therapeutics** Antimicrobials and antiparasitics
AAMC Medical School Objectives Project Report X Patient Safety Table 1	**Topic C** Drug treatment of common conditions and diseases

Basic Principles of Cancer Chemotherapy
Recommended Curriculum Equivalent: 1 hr
Learning Objectives
Explain the role of chemotherapy in the management of patients with cancer. Describe the prospects for “cure”, or long term survival in cases of advanced cancer. Compare and contrast the strategies and outcomes from standard cytotoxic chemotherapy and targeted therapies. Describe the various limitations to effective drug treatment. Define and explain the terms: selective toxicity, mass doubling time and growth fraction. Explain the concepts of “total cell kill” and tumor stem cells in cancer treatment. Explain the term *cell cycle specificity* and be able to classify the various anticancer drugs based on the cell cycle specificity. Describe the principles of combination chemotherapy in the treatment of cancer. Explain the mechanisms of resistance to anticancer drugs. Describe adverse effects of anticancer drugs, and approaches to minimizing adverse effects.

Anticancer Drugs		
Recommended Curriculum Equivalent: 3 hr		
Drugs to consider		
Alkylating agents	Antimetabolites	
CYCLOPHOSPHAMIDE MECHLORETHAMINE MELPHALAN NITROSOUREAS (carmustine and lomustine) busulfan dacarbazine ifosfamide	CAPECITABINE CYTARABINE 5-FLUOROURACIL GEMCITABINE METHOTREXATE fludarabine 6-mercaptopurine thioguanine	
Natural products	Tyrosine kinase inhibitors	
BLEOMYCIN CAMPTOTHECIN analogs (irinotecan, topotecan) DAUNORUBICIN DOXORUBICIN DOCETAXEL ETOPOSIDE (VP-16) PACLITAXEL VINBLASTINE VINCRISTINE idarubicin	IMATINIB dasatinib erlotinib gefitinib lapatinib sunitinib	
Monoclonal Antibodies	Hormones	Miscellaneous Agents
TRASTUZUMAB cetuximab rituximab	TAMOXIFEN aromatase inhibitors (anastrozole, letrozole) flutamide glucocorticoids (prednisone) goserelin leuprolide	BORTEZOMIB CISPLATIN all-trans-retinoic acid (ATRA) asparaginase carboplatin hydroxyurea interferon alpha 2a lenalidomide procarbazine sorafenib vorinostat
Learning Objectives		
Mechanism of action Describe the mechanism of action of various individual anticancer drugs under each class. Explain the bioactivation pathways required for the action of cyclophosphamide. Describe the intracellular activation pathways of different antimetabolites. Explain the use of antidote in high dose methotrexate therapy.		

Adverse effects Describe the common toxicities for each class of anticancer drugs. Describe the specific major toxicity of individual anticancer drugs. Describe the cumulative dose-dependent toxicity of anthracyclines.
Therapeutic uses List the major therapeutic indications of various anticancer drugs. Describe the drug combinations that have shown activity against specific types of cancer. Explain the concept of adjuvant chemotherapy and describe various regimens used in the treatment of cancer of different organ systems. Discuss the impact of both patient and tumor genotypes on drug choices and efficacy in cancer chemotherapy.
Clinical Pharmacology Since these treatments are cytotoxic, drug interactions are to be expected, and pretreatment evaluation for possible interactions resulting in toxicity and/or loss of efficacy of drug therapy for co-morbidities is mandatory.

Relevance	
USMLE topic Antineoplastics	**Principles of therapeutics** All organ systems
AAMC Medical School Objectives Project Report X Patient Safety Table 1	**Topic E** How to find and use the most up-to-date info on drugs

Immunomodulatory Drugs	
Recommended Curriculum Equivalent: 1 hr	
Drugs to consider	
AZATHIOPRINE CYCLOSPORINE MYCOPHENOLATE MOFETIL PREDNISONE	antithymocyte globulin cyclophosphamide daclizumab etanercept infliximab interferons (alpha, beta & gamma) lenalidomide methotrexate muromonab-cd3 rho(d) immune globulin sirolimus (rapamycin) tacrolimus thalidomide
Learning Objectives	
Mechanism of action Define the general principles of immunosuppression and immunostimulation. Describe the mechanism of action of immunosuppressants and immunostimulants.	
Adverse effects Describe the toxicities of antibodies and other agents used as immunosuppressants Describe the different types of allergic reactions to drugs	
Therapeutic uses Describe the clinical uses of immunosuppressants.	
Clinical Pharmacology Due to the high first pass elimination of cyclosporine, any additional drug therapy must be evaluated for potential interactions with CYP3A4 and P-glycoprotein that might place the patient's transplanted organ at risk.	
Relevance	
USMLE topic Musculoskeletal System	**Principles of therapeutics** Mechanisms of action and use of drugs for treatment of disorders of the musculoskeletal system
AAMC Medical School Objectives Project Report X Patient Safety Table 1	**Topic C** Drug treatment of common conditions and diseases, using frequently prescribed classes of drugs for the treatment and prevention of disease