

# DD

## Disease and Defense

### Course Goals

#### Goals

1. Acquire knowledge of the principles of pharmacology (including prescription writing and drug evaluation, adverse drug reactions and poisoning, pharmacokinetics and pharmacodynamics) for comprehension of the use of anti-infective, anti-neoplastic, and anti-inflammatory agents.
2. Acquire knowledge of the principles of microbiology as a basis for comprehension and application to the study of infectious diseases.
3. Acquire knowledge of the foundational concepts regarding the pathologic basis of disease for comprehension of major categories of general pathology (infection, inflammation, and neoplasia) and as a basis for application to the study of systemic pathology and the diseases of organ systems.
4. Acquire knowledge of the foundational principles underlying the practice of dermatology (including conceptual understanding of the normal structure, histology, physiology and function of the skin and the performance of a thorough skin exam).
5. Apply the basic principles learned from microbiology, pathology, pharmacology and dermatology to the study of infections, inflammatory and neoplastic skin diseases.

# Spring 2019

## Disease and Defense

### Session Learning Objectives

#### **DD - Drug Metabolism and Excretion**

1. Describe the general principles and consequences of drug metabolism.
2. Describe the general characteristics of Phase I and Phase II reactions as related to qualitative and quantitative role in drug metabolism, enzymes involved, genetic polymorphisms, and classifications of reactions.
3. Describe the general characteristics of Phase I and Phase II reactions as related to inducibility-inhibitability and potential for DDIs, general developmental patterns of activity and age-related changes in activity, and relative ease of saturability at high drug substrate levels.
4. Explain the therapeutic consequences of induction and inhibition of metabolism. List the clinically relevant inhibitors and inducers on page 9 of the drug metabolism notes.
5. Describe the general characteristics of drug excretion by the kidney (filtration, secretion, reabsorption and the influence of pH and protein-binding on these processes).
6. Describe the therapeutic implications of enterohepatic recirculation of drugs.

## **DD - Acute and Chronic Inflammation**

1. Differentiate between the temporal, cellular, and local/systemic responses associated with acute and chronic inflammation.
2. Describe the classic clinical signs of inflammation.
3. Identify the major stimuli for acute and chronic inflammation.
4. Describe the mechanisms involved in the cellular events (e.g. recruitment, activation, phagocytosis and antimicrobial activity) and vascular changes (e.g., vasodilation and increased permeability) during acute inflammation.
5. Distinguish between the pathophysiology and constitutional make up of transudates and exudates.
6. Describe Toll-like receptors (TLRs) and the inflammasome and their role in inflammation.
7. List potential outcomes of acute inflammation.
8. Describe the different morphologic patterns of acute inflammation.
9. Describe the processes involved in and give clinical examples of collateral tissue damage associated with inflammation.
10. Identify common causes for defective leukocyte function.
11. Identify the (3) main processes and (3) characteristic clinical setting of chronic inflammation.
12. Describe the biologic responses and functions of inflammatory cells and mediators during chronic inflammation.
13. Identify the distinguishing features of and the clinical etiologies associated with granulomatous inflammation.
14. List four roles of macrophages.
15. Differentiate between classically and alternatively-activated macrophages.
16. List the 3 proteins that can be measured clinically and used to detect and monitor the presence of inflammation.
17. Describe the mechanisms for leukocytosis (increased WBC) early on and after a prolonged period in the inflammatory process.
18. List types of infections associated with: 1) neutrophilia, 2) lymphocytosis, 3) eosinophilia.

## **DD - Antibacterial Agents I - V**

1. Define and/or give examples for selective toxicity, antibiotic spectrum (i.e., narrow vs. extended vs. broad), and resistance (i.e., natural vs. escape vs. acquired).
2. Discuss mechanisms of resistance to antibiotics and implications for therapy.
3. For antibacterial agents in general, classify antimicrobial mechanisms of action, and discuss which mechanisms generally result in bacteriostatic or bactericidal effects, advantages of bactericidal agents, and the important pharmacokinetic and host factors in selection of antimicrobial therapy.
4. For a given drug or drug category, describe their mechanism of action, pharmacokinetics, spectrum of activity, major clinical uses, side effects, and significant drug interactions.

## **DD - Anti-viral Drugs**

1. For each antiviral agent, describe their mechanism of action, pharmacokinetic properties, adverse drug reactions, and role of pharmacotherapy in treatment of viral infections.

## **DD - Bacterial Genetic Variation, Gene Transfer and Evolution of Virulence**

1. Describe the mechanisms that generate genetic diversity within a bacterial species and how these contribute to the evolution of virulence.
2. Discuss how spontaneous mutation and selection can interact to determine the genetic composition of bacterial populations.
3. Distinguish between transformation, transduction and conjugation as mechanisms of gene transfer. Identify the salient features of each mechanism.
4. Discuss the properties of bacterial viruses. Distinguish between the lytic and lysogenic state.
5. Describe how errors in bacteriophage development can lead to phage-mediated gene transfer.
6. Define lysogenic conversion. Distinguish between lysogenic conversion and generalized transduction.

## **DD - Bacterial Structure, Function and Growth**

1. Describe the major structural features of bacteria and explain the principal function(s) of each feature.
2. Define a plasmid and describe how acquisition of a plasmid by a bacterium can increase antibiotic resistance and/or virulence.
3. Describe the similarities and differences between the structures of Gram-positive, Gram-negative and Mycobacterial cell walls.
4. Describe the bacterial structures that underlie the staining properties of Gram-positive, Gram-negative and mycobacterial organisms.
5. Define the terms strict aerobe, facultative anaerobe, aerotolerant anaerobe, strict anaerobe, and microaerophilic organism.
6. Draw a typical bacterial growth curve and explain the characteristics of each growth phase.
7. Identify the principal targets for the major groups of antibiotics used in human medicine.

## **DD - Bacterial Toxins**

1. Define and describe microbial toxins.
2. Explain how a microbial toxin is implicated in pathogenesis of an infectious disease.
3. Explain the mechanisms of action of the microbial toxins described here.
4. Compare the properties of microbial toxins that have different mechanisms of action.
5. Explain the principles of immunization against toxin-mediated diseases.
6. Explain the principles for developing novel therapeutic agents based on toxins.

## **DD - Cancer Therapeutic Strategies and Anti-Cancer Drugs**

1. Contrast and compare differences and purposes of different kinds of chemotherapy - adjuvant, neoadjuvant, and primary chemotherapy.
2. Describe major differences between “targeted therapies” and conventional cytotoxics.
3. Discuss the basis for combining anti-tumor agents.
4. Describe the mechanism of action, major toxicities, and resistance mechanisms of prototypical drugs for each class of anti-tumor agent.
5. Explain basis for therapeutic window allowing conventional cytotoxic drugs that target components such as DNA that are equally important in normal and cancer cells to be used in people.

## **DD - Cell and Tissue Injury**

1. Discuss major causes of cell injury and give examples of how cell injury can contribute to the pathogenesis of disease.
2. Describe pathologic adaptations associated with chronic injury (e.g. hypertrophy, hyperplasia, atrophy, and metaplasia), and give examples of physiologic and pathologic causes of each.
3. Describe the major mechanisms of reversible cell injury (i.e. cell swelling and fatty change).
4. Compare and contrast necrosis and apoptosis (i.e. irreversible cell injury).
5. Describe the major patterns of tissue necrosis seen in human disease.
6. Identify the major mechanisms of cell injury including ATP depletion, influx of calcium, mitochondrial, membrane, and DNA damage, and accumulation of reactive oxygen species.
7. Define free radicals and explain how they arise, how they produce cell injury, and how the body gets rid of them including the enzymatic systems involved.
8. Describe the general pathways which lead to intracellular accumulations and pathologic calcification, and give examples of each.

## **DD - Cell Growth and Neoplasia**

1. Discuss key concepts of normal cell growth and differentiation control.
2. Define and give examples of the following types of abnormal cell growth/ differentiation, including hypertrophy, hyperplasia, metaplasia, dysplasia, neoplasia, and tumor.
3. Define, describe and be able to distinguish between the gross and microscopic features of benign and malignant neoplasms.
4. Discuss key general concepts related to malignant neoplasia (cancer), including etiology, epidemiology, pathology (including tumor grade), and biology.
5. Discuss TNM classification, stage, and relationship to clinical outcome.

## **DD - Clinical Aspects of Common Cancers**

1. List the four basic classes of malignant tumors.
2. List the cell of origin and likely clinical behavior based on the name of a tumor.
3. List the three most common types of cancer in men and women with regard to incidence and mortality.
4. Describe features that determine if a neoplasm has a good or poor prognosis.
5. Use the TNM staging system to describe the extent of tumor spread.

## **DD - Clinical Principles for Antimicrobial Usage**

1. Explain how an antibiogram report may affect empiric antibiotic selection.
2. Describe how broth dilution, disk diffusion, and Etest (gradient diffusion) are performed and how they contribute to antimicrobial susceptibility testing.
3. Define MIC and MBC and their relation in defining bactericidal/bacteriostatic antibiotic activity.
4. Interpret the meaning of antibiotic susceptibility categories (e.g., susceptible, intermediate, and resistant).
5. Describe how local and host factors contribute to appropriate antibiotic selection.
6. Identify clinical indications for which bactericidal therapy may be preferred.

## **DD - Common Bacterial Pathogens Parts I - III**

1. Interpret results of key clinical microbiology laboratory tests (described in lecture or in handout) for the identification of bacterial organisms (e.g., catalase, coagulase, oxidase, lactose fermentation, hemolysis, NaCl tolerance, bile solubility and optochin sensitivity).
2. Describe the Gram stain appearance and the function of key virulence factors produced by each organism.
3. Describe the pathogenesis and epidemiology of diseases associated with each organism.
4. Describe the design/make up and indications for available vaccines discussed.

## **DD - CPC: Hemodynamic Disease**

1. List the causes and clinical features of left and right congestive heart failure.
2. Describe the gross and histologic features of the heart, lung, liver and spleen associated with right versus left sided congestive heart failure and note whether these changes would be considered "acute" or "chronic".
3. List the risk factors, sources, and pathophysiologic effects (e.g. clinical features) associated with pulmonary embolism.
4. Describe the gross and histologic features associated with pulmonary emboli and be able to distinguish acute from chronic changes , including "organization" of pulmonary embolus.
5. List several sources of arterial versus venous emboli and potential organs affected.
6. Distinguish between emboli from blood clot, tumor, and bone marrow.
7. Distinguish between thrombus, infarct and hemorrhage and categorize the gross and histologic findings as acute or chronic changes.
8. Interpret the State of Colorado Certificate of Death form given a clinical scenario especially as it relates to 1) immediate and underlying cause of death as well as 2) manner of death.
9. List some common causes of sudden death based on various organ systems.

## **DD - CPC: Inflammation, Infection and Repair**

1. Develop an organ-based differential diagnosis for chest pain and abdominal pain.
2. Describe the gross and histologic features of a normal appendix.
3. List the gross and microscopic findings seen in the various components of the appendix (lumen, epithelium, muscularis, serosa) in acute versus chronic appendicitis.
4. Describe the pathophysiology of appendicitis.
5. Describe the complications associated with a ruptured appendix in cases of acute appendicitis.
6. Describe the gross and histological features of a normal gallbladder.
7. Distinguish chololithiasis from cholecystitis.
8. Describe the pathophysiology of cholecystitis.
9. List the gross and microscopic findings (including inflammatory cell type) seen in the various components of the gallbladder (lumen, epithelium, muscularis, serosa) in acute versus chronic cholecystitis.
10. Describe the gross and histologic features of a normal heart.
11. Describe the histologic features of normal coronary arteries and those associated with atherosclerosis.
12. Describe and distinguish between gross and histologic findings associated with acute/subacute and chronic myocardial infarcts.

## **DD - CPC: Neoplasia (Required)**

1. Describe the histologic and biologic features that distinguish between "benign" and "malignant" neoplasms with respect to the degree of differentiation, rate of growth, mitotic activity, local invasion, and metastasis.
2. Distinguish between hypertrophy and hyperplasia.
3. Define metaplasia and give an example that might occur in the respiratory tract in the setting of smoking.
4. Name the most common histologic type/category of neoplasm associated with cigarette smoking.
5. Describe the gross and histologic features associated with benign versus malignant neoplasms of the lung, uterus and skin (melanocytes).
6. Recall correct nomenclature of benign and malignant neoplasms.

## **DD - Dermatology Histopathology**

1. Describe the various reasons for which a skin biopsy might be performed.
2. Describe the 4 major types of biopsies that are commonly performed in dermatology practices.
3. Describe at least two types of fixatives that are commonly employed in dermatology and the circumstances in which each are utilized.
4. Outline 6 major steps that occur at a dermatopathology lab to take a biopsy specimen and make an histology slide that can be read by a dermatologist/dermatopathologist.
5. Name the single most common tissue stain performed in dermatology and its two major components.
6. Compare and contrast the general histologic features of skin of the palms and soles, as compared to the skin of the eyelids and ears, as compared to the skin of the scalp, as compared to the skin of the mucosa.
7. Describe what an "error of representation" is and characterize two different steps that can be done by the clinician to minimize this type of error.
8. List three additional studies/steps that can be done to provide additional diagnostic data when interpreting a biopsy specimen by light microscopy.

## **DD - Dermatology Small Group Session #1 (Required)**

1. Develop a practical clinical approach to the full body skin exam (skin cancer screening exam).
2. Describe morphology of different skin lesions and rashes.
3. Practice skin biopsy technique (punch and shave).

## **DD - Dermatology Small Group Session #2 (Required)**

1. Recognize and provide basic treatment options based on etiology (i.e. infectious vs inflammatory, benign vs malignant) for different skin presentations including rashes and skin lesions.

## **DD - Dermatology Small Group Session #3 (Required)**

1. Develop an approach to rashes and skin lesions.
2. Initiate proper workup and initial treatment for clinical vignette.

## **DD - Dermatology Therapeutics**

1. Describe the properties of the skin that affect the efficacy of topical therapies.
2. Describe topical steroids of three different potencies and potential adverse events from topical steroid use.
3. Learn about one part of the light spectrum that can be harnessed to treat dermatologic conditions.
4. Become familiar with 3 different surgical techniques used in dermatology.

## **DD - Dermis and Adnexal Structures**

1. Describe the physiology, histology and function of and be able to recognize the structural components of the dermis.
2. Describe the synthesis of and distinguish between the types of collagen relevant to the skin.
3. List the components and describe the function of the ground substance of the dermis.
4. Describe the pathophysiology of and identify disorders associated with defects in collagen and elastin.
5. Describe the pathophysiology and recognize the clinical manifestations associated with disorders of the vascular supply and innervation of the skin.
6. Describe the physiology, histology and function and be able to identify the major adnexal structures of the skin.
7. Describe the pathophysiology and identify disease processes that occur with dysfunction or deficiency of proteins and structural components of the dermis.

## **DD - Drug Eruptions**

1. Describe the clinical morphology of common drug eruptions.
2. Identify features suggestive of a "complicated" cutaneous adverse drug reaction.
3. Compare typical timing of each drug eruption in relationship to time since drug initiation.

## **DD - Drug Regulation**

1. Describe the role of federal, state and local governments in regulating the prescription writing process.
2. Summarize the preclinical and clinical phases (1-4) of the new drug approval process of the FDA with respect to number and types of subjects, approximate time involved, and limitations in pronouncing a new drug as "safe".
3. Compare and contrast FDA regulation of prescription drugs vs. dietary supplements (DSHEA 1994).
4. Distinguish the different categories of FDA drug equivalency (pharmaceutical, biologic, and therapeutic) with regards to comparison of generic vs brand name products.
5. Describe the major elements of the Controlled Substances Act
  - Distinctions between prescription drugs and controlled substances
  - Explain the special requirements for prescribing controlled substances and their schedules I-V
  - Explain how prescribing controlled substances in Colorado differs from other states
6. Describe the legal components of a written prescription in Colorado.
7. Convert apothecary/avoirdupois/household measures to metric equivalents (and vice-versa).
8. List the Latin and English abbreviations for common medical terms or phrases.
9. Give examples of suggestions for improved prescription writing.

## **DD - Glucocorticoids**

1. Describe the regulation of glucocorticoid secretion by the hypothalamic-pituitary-adrenal gland axis.
2. Describe the metabolic and mineralocorticoid effects associated with glucocorticoids and explain how these effects can result in serious adverse effects when they are used as pharmacotherapeutic agents.
3. For glucocorticoid agents used as anti-inflammatory and immunosuppressive drugs, describe their mechanisms of anti-inflammatory and immunosuppressive actions, metabolic pathways - activating vs. inactivating, clinical uses, dosing considerations/formulations, and toxicities (distinguish acute vs. chronic vs. withdrawal).
4. For glucocorticoid agents used as anti-inflammatory and immunosuppressive drugs, compare and contrast their relative salt-retaining vs. anti-inflammatory activities vs. ACTH suppression and their routes of administration.
5. Explain the rationale for alternate day therapy and the necessity for tapered withdrawal following chronic therapy with glucocorticoids.

## **DD - Hemodynamic Basis of Disease**

1. Define edema, effusion, hyperemia, and congestion.
2. List disturbances in fluid balance that lead to edema and effusions.
3. Distinguish the features of exudate and transudate (don't need to memorize specific numbers).
4. List defects that lead to hemorrhage.
5. Name the key factors (Virchow's Triad) that are involved in thrombosis.
6. Compare and contrast types of emboli and clinical outcomes for blockage of right/venous and left/arterial sided circulation.
7. Recognize the features of disseminated intravascular coagulation.
8. Contrast the gross morphology and pathophysiologic differences of red and white infarcts.
9. Differentiate the pathophysiology of common causes/categorizations of shock: cardiogenic, hypovolemic, septic.

## **DD - Herpes Viruses**

1. Define shared properties of all herpesviruses.
2. Describe general lytic replication cycle of herpesviruses.
3. Compare lytic and latent infection.
4. Understand the classification of herpesviruses and identify the human viruses of each sub-family and associated diseases.

## **DD - Host Response and Viral Pathogenesis**

1. List effects of viruses on infected cells, such as CPE, syncytia, growth, apoptosis.
2. Explain the interferon response and “anti-viral state”.
3. Compare the efficacy of antibody versus cell-mediated immunity in the anti-viral response.
4. Explain means of virus evasion/manipulation of host defenses by various viruses.
5. Explain the effects of tissue tropism, virulence and host responses on the nature of viral disease.
6. Compare and contrast acute local disease versus acute systemic disease in incubation periods, virus shedding and transmission, host responses, and likelihood of re-infection.
7. List the potential outcomes and types of viral diseases, with contributing factors.

## **DD - Host-Microbe Interactions**

1. Define and describe infection, infectious disease, pathogen, and commensal.
2. Describe typical stages in pathogenesis of an infectious disease and list some of the microbial defenses against host clearance.
3. Describe the roles that pathogens and the host can play in causing host damage.
4. Describe the composition and importance of the microbiome of the body.

## **DD - Inflammatory Mediators**

1. Distinguish mediators of inflammation in regards to their site of production (e.g., locally by cells vs those derived from circulating inactive precursors).
2. Describe mechanisms of activation, major biologic activity, and major sources for the chemical mediators of inflammation (e.g., vasoactive amines, arachidonic acid metabolites, platelet activating factor, cytokines, reactive oxygen species, nitric oxide, lysosomal enzymes, neuropeptides, complement and the coagulation and kinin systems).
3. Describe how restricted tissue distribution of activating enzymes helps to locally regulate the inflammatory response due to targeted production of different chemical mediators of inflammation.
4. Distinguish between cytokines generally important for acute versus chronic inflammation as well as those active mainly locally versus those capable of affecting a systemic response.
5. Distinguish complement components associated with opsonization, enhanced vascular permeability, cellular chemotaxis, and formation of the membrane attack complex.
6. Describe the role of Hageman factor in the coagulation system, complement system, fibrinolytic system and the kinin system and their respective contributions to inflammation.
7. Describe molecules and mechanisms that limit and/or terminate inflammatory reactions.

## **DD - Inflammatory Skin Disease (Rashes)**

1. Identify common causes of irritant and allergic contact dermatitis.
2. List common clinical associations and clinical presentation of atopic dermatitis.
3. Recognize the clinical presentations and different patterns of psoriasis.
4. Compare and contrast the clinical presentations of atopic dermatitis and psoriasis.
5. Recognize the common clinical location of seborrheic dermatitis and stasis dermatitis.
6. Identify the causes of seborrheic dermatitis and stasis dermatitis.
7. Compare and contrast the clinical presentations of cellulitis and stasis dermatitis.
8. Recognize the similarity of drug eruptions and viral exanthems.
9. Acknowledge the difference between immediate type hypersensitivity reactions and delayed type hypersensitivity reactions in the skin (urticaria vs. ACD).

## **DD - Influenza and RSV**

1. For Influenza and RSV, list the basic structure, important proteins, and describe the roles they play in pathogenesis.
2. Describe how Influenza and RSV cause disease - including outlining routes of viral entry and cells/organs infected, mechanisms of infection, and the consequences of infection on clinical disease presentation.
3. Describe transmission and effective prevention strategies for Influenza and RSV.
4. Outline basic principles of vaccine strategies, including listing the different stages of vaccine development for Influenza and RSV, the differences between the types of influenza vaccines, and the differences in populations in terms of who can and cannot receive certain types of vaccine.
5. Describe antigenic drift (point mutation) and antigenic shift (reassortment of genome segments) of influenza and recognize that antigenic drift does NOT change the subtype of the virus (i.e. H2N2).
6. Describe the origin, as well as the basic epidemiology and morbidity/mortality of Pandemic H1N1 influenza virus, recognizing that it has caused a human pandemic.
7. Discuss newly-emerging influenza viruses including the type (H5N1), including an outline of its geographic occurrence and its importance to public health.
8. Describe the necessary qualities in an influenza virus strain to potentially cause a pandemic (new gene segment from another species or ability of a non-human strain to bind to human receptors), stages of a pandemic, and stages leading up to a pandemic.

## **DD - Introduction to Clinical Microbiology**

1. Name the 4 general types of cultures that can be set up on most patient specimens sent to the microbiology laboratory (in other words – what are the 4 general types of “cultures” that you can order on most specimens”).
2. Briefly explain what constitutes a routine blood, urine and sputum culture and how they are processed/performed in the lab.
3. Distinguish between streaking for isolation vs streaking for quantitation.
4. Quantitate a urine culture based on bacterial growth on a Sheep Blood Agar plate.
5. Briefly describe the procedures for the Gram stain and acid-fast stain and recall the bacterial structures that determine whether organisms stain Gram positive/negative and Acid Fast positive/negative.
6. Compare and contrast the selective and/or differential properties of Chocolate, Sheep Blood Agar, and MacConkey Agar.
7. Identify alpha, beta and gamma hemolysis on Sheep Blood Agar.
8. Identify lactose and non-lactose fermenting colonies on MacConkey agar.
9. Describe how the following biochemical tests are used in the identification/classification schema of Gram-positive and Gram-negative bacterial organisms (catalase, coagulase, oxidase, lactose-fermentation, NaCl tolerance, bile solubility and optochin sensitivity).

## **DD - Introduction to Dermatology and Epidermis**

1. Identify the structure and list the functions of the skin.
2. Identify Fitzpatrick skin types.
3. Differentiate between melanin in dark and light skin.
4. Identify the functions of the different layers of the epidermis and cells in this region.
5. Describe the proteins involved in cell attachments.
6. Distinguish regional variation of skin with regard to skin thickness and adnexal structures.
7. Recognize how abnormal structure and function of the epidermis is reflected in disease.
8. Perform a skin exam and describe skin lesions using proper terminology.

## **DD - Introduction/Overview of Pharmacologic Principles**

1. Recognize basic pharmacology principles.

## **DD - Lumps and Bumps of the Skin**

1. Diagnose common benign skin tumors in infants and adults.
2. Identify the cell type of origin for each of the skin growths included in this lecture.
3. Differentiate between skin tumors that are benign and those that are malignant or have malignant potential.
4. Describe clinical features of these benign skin tumors.

## **DD - Mechanisms of Antimicrobial Resistance**

1. Describe the difference between intrinsic and acquired antibiotic resistance and list ways a bacterium may acquire antibiotic resistance.
2. Recognize the role of porins and efflux pumps in mediating antibiotic resistance and for which types of bacteria they can be important.
3. Distinguish between types of beta-lactamases (e.g., narrow spectrum, ESBLs, carbapenemases) based on their spectrum of activity and sensitivity to inhibition.
4. Describe the enzymatic activity and gene regulation of the beta-lactamase, AmpC and distinguish between inducible and constitutive expression based on antibiotic susceptibility data.
5. Compare and contrast the mechanisms that result in modified penicillin-binding proteins (PBPs) and their impact on resistance to beta-lactam antibiotics.
6. Describe the mechanism of vancomycin resistance mediated by VanA/VanB, and recall which organisms might house these genetic elements.
7. Describe the process of target modification that leads to fluoroquinolone resistance and recall in which types of organisms this may occur.
8. Recall the aminoglycoside-modifying enzymatic reactions associated with antibiotic resistance.

## **DD - Microbiology Team Based Learning Session 1 (Required)**

1. Interpret alpha, beta and gamma hemolysis on Sheep Blood Agar.
2. Describe the role of catalase, coagulase, lactose fermentation, oxidase, optochin susceptibility, bile solubility and NaCl tolerance as aids to identifying bacterial isolates.
3. Describe the selective and differential properties for MacConkey agar.
4. Describe the procedure, and interpret and provide a rationale for the results for the Gram stain.
5. Quantitatively report a urine culture based on growth on Sheep Blood Agar.
6. Identify bacterial organisms based on clinical presentation and/or key clinical microbiology characteristics/tests.
7. Describe the acid-fast stain and list organisms associated with a positive result.

## **DD - Microbiology Team Based Learning Session 2 (Required)**

1. Identify common bacterial pathogens given a clinical presentation, Gram stain, culture characteristics and/or biochemical testing.
2. Choose appropriate antibiotics based on their spectrum of activity and/or appropriateness for a given clinical presentation.
3. Identify important virulence factors associated with common bacterial pathogens.
4. Describe the mechanism of action for each of the antibiotic classes.
5. Describe the process for performing minimal inhibitory concentration testing and interpret the results.
6. Describe the key steps necessary for performing antibiotic susceptibility testing and susceptibility interpretation.

### **DD - Microbiology Team Based Learning Session 3 (Required)**

1. Identify common bacterial pathogens given a clinical presentation, Gram stain, culture characteristics, biochemical testing and/or antibiotic resistance.
2. Choose appropriate antibiotics based on their spectrum of activity and/or appropriateness for a given clinical presentation.
3. Identify important virulence factors associated with common bacterial pathogens.
4. Describe the mechanism of action, special pharmacokinetic parameters, and metabolism for each of the antibiotic classes.
5. Interpret the results of antibiotic susceptibility reports that may suggest the presence of antibiotic resistance mechanisms.
6. Describe common antibiotic resistant mechanisms that mediate resistance to beta-lactams, vancomycin, fluoroquinolones, and aminoglycosides and in which organisms they may be observed.

### **DD - Neoplasia: Invasion and Metastasis**

1. Define metastasis.
2. Describe how the conditions in a growing primary tumor can contribute to metastasis and relate this to the "Hallmarks of Cancer".
3. List the 4 major steps in the invasion-metastasis cascade.
4. Define key features of the 3-step model for invasion of cancer cells.
5. Define the main characteristics of EMT, including the main transcription factors driving the phenotype.
6. Define metastatic niche and describe three mechanisms by which cancer cells can colonize distant niches.
7. Explain the role of metastases in death by cancer and give an example of one of the three most common ultimate causes of cancer related mortality.

## **DD - NSAIDs**

1. Describe the biosynthetic pathways for production of prostaglandins, prostacyclin, thromboxane, and leukotrienes, including the source of the precursor arachidonic acid and the specific enzymes involved.
2. Compare and contrast the biochemistry and physiology of cyclooxygenase-1 and cyclooxygenase-2 with regards to expression, tissue locations, physiologic role, inducers, and inhibitors.
3. List the effects of prostaglandins on vascular smooth muscle, platelets, GI tract smooth muscle and secretory cells, kidney cells, uterus, and inflammatory cells and be able to relate these actions to side effects that occur from use of drugs that block their synthesis.
4. Describe the effects of leukotrienes on inflammatory cell function and pulmonary / vascular smooth muscle.
5. Describe the functional interaction of prostacyclin and thromboxane A2 with relation to physiologic effects on vascular smooth muscle and platelets.
6. Compare and contrast the effects of aspirin, acetaminophen, NSAIDs, and COX-2 selective inhibitors on the cyclooxygenase enzymes 1 and 2 as the relation to therapeutic uses and adverse reactions.
7. Describe the mechanism whereby low-dose, but not high-dose, aspirin is able to exert an anti-thrombotic / cardioprotective effect. Relate this effect to potential cardiovascular toxicity associated with use of COX-2 selective agents.
8. For aspirin, acetaminophen, ibuprofen/naproxen/ketorolac, and celecoxib, describe similarities and distinctions in their therapeutic uses, metabolism and excretion, common side effects at therapeutic doses, overdose toxicities and their treatment, contraindications to use, and drug-drug interactions.

## **DD - Pathology: Introduction and Terminology**

1. List reasons why specimens are collected from patients for analysis by pathology.
2. List and describe common subdivisions of pathology.
3. Interpret medical terms listed on the Terminology slide.

## **DD - Pharmacodynamics**

1. Describe the drug-receptor concept and its consequences for pharmacotherapy.
2. Explain the theoretical aspects and therapeutic consequences of the hyperbolic shape of the dose-response curve.
3. Describe the advantages of the log dose-response curve versus the dose-response curve.
4. Explain the terminology of log dose-response curves and their use to compare potency and efficacy of different drugs, including: potency (affinity/ $K_d$ / $EC_{50}$ ), efficacy (power/ $E_{max}$ ), and agonist - partial agonist - antagonist.
5. Distinguish between characteristics of the different types of antagonism (pharmacological [competitive reversible and noncompetitive irreversible], physiological, chemical) and provide examples.
6. Compare and contrast graded dose-response curves and population dose-response curves and explain the use of population dose-response curves to evaluate drug safety (Therapeutic Index and Standard Safety Margin).

## DD - Pharmacokinetics - Drug Absorption

1. Summarize the therapeutic advantages and disadvantages of the various routes of drug administration, especially with regards to bioavailability and rate of onset of effect.
2. Explain the derivation and clinical relevance of the pharmacokinetic parameter bioavailability (F) and describe its use in designing dosage regimens->adjustment of dose for oral vs. parenteral administration.
3. Identify the factors that determine a given drug's ability to cross biological membranes.
4. Describe the mechanisms by which drugs cross biological membranes (diffusion, transport, etc.).

## DD - Pharmacokinetics - Drug Distribution

1. Explain the influence of pH on the ionization of weak acid/weak base drugs.
2. Use the Henderson-Hasselbach equation to qualitatively predict the ratio of ionized to unionized species of a weak acid or weak base drug in various body compartments.
3. Explain the therapeutic consequences of anatomic "barriers" (GI mucosa - blood-brain barrier - renal tubule cells) to distribution and selective accumulation of drugs.
4. Describe how drug binding to plasma proteins can effect drug distribution and elimination as well as being a potential source of drug-drug interactions.
5. Explain the derivation and clinical relevance of the pharmacokinetic parameter volume of distribution (Vd). Describe its use in designing dosage regimens -> converting drug dose to Cp, selecting loading dose (LD), implications of high or low values.

## DD - Pharmacokinetics of Elimination

1. Explain the derivation and clinical relevance of pharmacokinetic parameters and be able to use them in designing dosage regimens and predicting changes in drug plasma levels and drug response, including: bioavailability (F), volume of distribution (Vd), clearance (CL), half-life ( $t_{1/2}$ ), elimination rate constant (ke), and first-order and zero-order kinetics.
2. Describe the relevance of pharmacokinetic concepts to clinical drug actions including: first-order elimination, zero-order elimination, volume of distribution, steady-state plasma concentration, clearance, and bioavailability.

## DD - Skin Cancer: Malignant Tumors of the Skin

1. Recognize common types of skin cancer including basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma.
2. Describe the incidence of skin cancer in the US.
3. Identify risk factors for skin cancer.
4. Recognize that actinic keratoses (AKs) are precursors to squamous cell carcinoma (SCC).
5. Describe common mutations leading to skin cancer and chemotherapeutic interventions, including patch1 mutation and vismodegib (basal cell carcinoma) and BRAF mutation, vemurafinib (melanoma).
6. Differentiate between Breslow depth and Clark's level used in staging of melanoma as important prognostic factors of melanoma.
7. Identify treatment options for premalignant and malignant skin tumors.
8. Review methods of skin cancer prevention.

## **DD - Skin Infections and Infestations**

1. For common cutaneous bacterial infections, including impetigo, and cellulitis - recognize the clinical characteristics and identify the etiologic agent.
2. For common cutaneous fungal infections, including dermatophyte infections, candidiasis, and tinea (pityriasis) versicolor - recognize the clinical characteristics and identify the etiologic agent.
3. For common skin infections, including scabies, lice infestation, and cutaneous larva migrans - recognize the clinical characteristics and identify the etiologic agent.
4. Explain the clinical utility and indications for the following diagnostic procedures in dermatologic patients: tzanck smear, gram stain, KOH prep, Wood's light exam, and mineral oil (wet prep) for scabies.
5. Describe the morphology and growth characteristics of common fungi and their role in dermatologic disease.

## **DD - Skin Signs of Systemic Disease I**

1. Skin findings may indicate an underlying systemic disorder.
2. Recognize disorders may be a sign of underlying thyroid disease and a screening TSH should be evaluated in patients with vitiligo, alopecia areata, exophthalmos and pretibial myxedema.
3. Identify dermatitis herpetiformis as the skin rash associated with gluten sensitivity and celiac disease and the treatment is a gluten free diet or dapsona.
4. Identify pyoderma gangrenosum as a skin sign of inflammatory bowel disease.
5. Acknowledge that ulcers of pyoderma gangrenosum should not be treated with debridement.
6. Acanthosis nigricans (thickening of the skin of the axilla, neck and knuckles) is most commonly associated with obesity and insulin resistance, but may also be a sign of underlying malignancy (especially gastric carcinoma) when associated with weight loss.
7. Erythema nodosum is a panniculitis (inflammation of the subcutaneous fat) which is often associated with underlying infection, medication, sarcoidosis, or inflammatory bowel disease.
8. Clubbing is a nail finding which may be present in patients with underlying cardiopulmonary disease.
9. Recognize the clinical presentation of Lichen planus as purple, polygonal, pruritic papules on the skin or as erosions in the oral mucosa.
10. Note that patients with lichen planus should be screened for hepatitis C virus infection.

## **DD - Skin Signs of Systemic Disease II**

1. Identify skin findings of bacterial endocarditis.
2. Describe the most common cutaneous presentations of sarcoidosis.
3. List the two organ systems that can be involved in digital clubbing.
4. Differentiate between the three most common skin eruptions seen in systemic lupus erythematosus.
5. Compare and contrast the skin findings of systemic lupus erythematosus and dermatomyositis.

## **DD - Tissue Repair and Wound Healing**

1. Describe the temporal and cellular relationship between tissue repair and inflammation.
2. List the various components and features of the repair process and the cells responsible.
3. Define and give a specific example of "granulation tissue" and its components.
4. Define and describe the process of repair with respect to the epithelium (i.e., re-epithelialization) and organs such as the liver (i.e., regeneration).
5. Define and describe normal scar formation and pathologic scar formation (e.g., hypertrophic scar, keloid, contracture).
6. List local factors and systemic factors that might adversely influence the repair/regeneration process.

## **DD - Toxicology and Poisoning**

1. List the pharmacokinetic (decreased absorption, inhibition of toxication, enhancement of detoxication, or enhanced elimination) interventions that are available for treatment of drug overdoses and poisoning and the limitations and contraindications for each.
2. Compare and contrast the concepts of toxicokinetics and toxicodynamics and the important differences seen with toxic amounts of drugs relative to therapeutic doses and therapeutic plasma levels to "normal" pharmacokinetics and pharmacodynamics.
3. Describe the mechanism of acetaminophen overdose toxicity and its treatment with N-acetylcysteine (role of hepatic bioactivation to toxic metabolite and depleted hepatic glutathione in hepatocellular injury).
4. Describe the basic pharmacokinetics and pharmacodynamic actions of methanol and ethylene glycol that underlie their toxicities: rapid oral absorption, metabolism by common hepatic enzyme systems.

## **DD - Viral Structure and Function**

1. Define the basic properties of viruses.
2. List the strategies viruses employ for survival.
3. Describe two means of classifying viruses.
4. Describe basic methods for studying viruses.
5. Identify the main structural characteristics of virus particles.
6. Describe the seven basic virus genomes, protein expression strategies and replication strategies of each.
7. Describe the typical, generalized replication cycle of a virus.