

Week 1, May 2 - 6

Monday (5-2)

LECTURE: COURSE INTRODUCTION (FALCONE)

- Overview of course objectives, schedule and resources.

LECTURE: THE IMMUNE SYSTEM: CHALLENGE & COMPONENTS (MA)

- Cells (APC, B, T) and organs of the immune system and nomenclature of major CD molecules; BCR and TCR and encoding genes, and the definition of cytokines.
- Principles of innate and adaptive immunity; dynamics of the immune response; concept of primary and secondary response;
- Concept of terminal B and T cell differentiation; concept of memory and vaccination; concept of innate and acquired immunodeficiency.

LECTURE: GENERAL BACTERIOLOGY AND NORMAL FLORA (LARONE)

- Understand the basics of bacterial classification.
- Learn the principles of bacterial colonization and human infection.
- Define the physiological and clinical relevance of normal flora.

MICROBIOLOGY LAB EXERCISE: NORMAL FLORA (PART 1)

- Describe the nature and diversity of the human normal flora.
- Learn the fundamental techniques of microbiology.
- Learn the procedures and principles by which microorganisms are isolated, characterized and identified, a major component in the diagnosis of infectious diseases.

Tuesday (5-3)

LECTURE: CELLULAR RESPONSE TO INJURY: ADAPTATION, INJURY AND DEATH (FALCONE)

- Define cellular adaptations and describe the morphologic characteristics by which they are distinguished.
- Describe the pathogenesis and morphologic characteristics of reversibly and irreversibly injured cells.

LECTURE: THE INNATE RESPONSE I (RHEE)

- Learn the main cellular elements of and distinctions between innate and adaptive immunity.
- Learn how polymorphonuclear leukocytes and macrophages kill antigen.
- Learn how the adaptive immune system increases the killing power of the innate immune system.
- Learn how the innate immune system sets up the adaptive immune system.

LECTURE: BACTERIAL PHYSIOLOGY (LUE)

- Explain the structure and function of key components of bacteria, including both the cytoplasmic and surface structures (nucleoid, ribosomes, granules, plasma membrane, flagella, pili, and capsules).
- Understand the structure and synthesis of the major chemical components of bacterial cell walls: peptidoglycan, teichoic acids and lipopolysaccharides.
- Discuss the nutrients needed to sustain bacterial growth and environmental factors that influence bacterial growth.
- Understand the concept of bacterial communication (quorum sensing and biofilm) and the notion of human microbiome.

MICROBIOLOGY LABORATORY EXERCISE: NORMAL FLORA (PART 2)

- See the objectives listed for Part 1.

Wednesday (5-4)

PBL: THE BAKER'S WOUND**LECTURE: THE INNATE RESPONSE II (RHEE)**

- Learn the main cellular elements of and distinctions between innate and adaptive immunity.
- Learn how polymorphonuclear leukocytes and macrophages kill microbes.
- Learn how the adaptive immune system increases the killing power of the innate immune system.
- Learn how the innate immune system sets up the adaptive immune system.

HISTOPATHOLOGY LABORATORY EXERCISE: CELLULAR ADAPTATIONS, INJURY AND DEATH

- Define hypertrophy, hyperplasia, atrophy, and review the morphologic characteristics by which they are distinguished.
- Review the pathogenesis and morphologic characteristics of reversibly and irreversibly injured cells.

Friday (5-6)

PBL: THE BAKER'S WOUND**LECTURE: INTRODUCTION TO PHARMACOLOGY: DOSE RESPONSE AND SELECTIVE TOXICITY I (GROSS)**

- Understand pharmacological principles that relate drug concentration to receptor occupancy and bioactivity as they relate to in vitro reactions.
- Define the following terms: agonist, partial agonist, competitive antagonist, non-competitive antagonist, potency, efficacy, dose-response, receptor selectivity/specificity, therapeutic index, margin of safety, LD50, ED50.
- Understand the factors governing dose-response relationships for therapeutic and toxic

effects of drugs in vivo.

LECTURE: THE COMPLEMENT SYSTEM (JANE SALMON)

- Outline the components of the complement system
- Define the pathways of complement activation
- Define the biological effects of complement activation in the defense to infection and tissue injury

LECTURE: BACTERIAL GENE STRUCTURE, REPLICATION AND TRANSCRIPTION (BARANY)

- Describe genomic structure of bacterial chromosomes and plasmids.
- Describe the basic molecular machinery of DNA replication and how they are useful targets for drug therapy.
- Explain the control mechanisms used by bacteria to turn genes on and off: positive control, negative feedback, attenuation control and translational control.

Week 2, May 9-13

Monday (5-9)

PBL: TOO MANY INFECTIONS**LECTURE: ANTIBODY STRUCTURE & FUNCTION, B-CELL DIVERSITY (PAPAVASILIOU)**

- Define the key structural elements of immunoglobulins, including heavy and light chains as well as variable and constant regions.
- Outline the main processes involved in antibody diversification, including V(D)J recombination, V(D)J somatic hypermutation, and heavy chain class switching.
- List the functions associated with the variable and constant regions of immunoglobulins and how these functions are modulated by V(D)J recombination, somatic hypermutation, and class switching.
- Discuss the effector functions of different immunoglobulin isotypes.
- Identify the role and main features of T cell-independent and T cell-dependent antibody responses.
- Describe the most common antibody deficiencies, including common variable immunodeficiency, selective IgA deficiency, and IgG subclass deficiency.

LECTURE: INTRODUCTION TO PHARMACOLOGY: DOSE RESPONSE AND SELECTIVE TOXICITY II (GROSS)

- See Friday, May 6.

Tuesday (5-10)

LECTURE: THE LYMPHOID ORGANS (LU)**LECTURE: B-CELL DEVELOPMENT (PAPAVASILIOU)**

- Outline B cell development: antigen-independent and antigen-dependent B cell differentiation
- Define the mechanisms that underlie antibody and clonal B cell diversity, specificity and affinity maturation.
- Define the mechanisms directing the generation of memory B cells and plasma cells.
- Determine the role played by B cells and antibodies in the adaptive immune response to microbial antigens.
- Natural antibodies and affinity mature antibodies

LECTURE: DRUG ABSORPTION, DISTRIBUTION AND EXCRETION (INTURRISI)

- Understand the pharmacokinetic and pharmacodynamic processes that can affect drug disposition.

- Understand the terms: Bioavailability, First Pass Effect and Absorption Limited Kinetics and how they can influence drug disposition.
- Understand how pH partition and lipid solubility can affect the absorption, distribution and elimination of a drug.

MICROBIOLOGY LABORATORY EXERCISE: RESPIRATORY INFECTIONS (PART 1)

- Distinguish between the normal flora of the oropharyngeal region and the bacteria commonly responsible for respiratory tract infections.
- List the primary characteristics of streptococcal infections.
- Discuss group A beta hemolytic strep infections and the diseases caused by these infections.
- Identify the features of bacterial pneumonia and the associated pathogens.
- Understand techniques used to isolate and identify specific strains of gram-positive bacteria and the drug sensitivity of different gram-positive bacteria.

Wednesday (5-11)

PBL: TOO MANY INFECTIONS**LECTURE: THE HOST'S RESPONSE TO INJURY: ACUTE INFLAMMATION (NICHOLSON)**

- Recognize and describe the vascular and cellular manifestations of acute inflammation.
- List the mediators of vasodilation and increased permeability.
- List the adhesion molecules and describe the molecular events involved in the attachment of inflammatory cells to the vascular endothelium and movement into the tissues.

LECTURE: BIOTRANSFORMATION (RIFKIND)

- Define phase I and phase II metabolism.
- Understand the role of cytochrome P450 in phase I metabolism, and the major types of reactions catalyzed by cytochrome P450.
- Name the major cytochrome P450 enzymes involved in human drug metabolism.
- Understand the processes of P450 induction and inhibition, and their consequences for biotransformation and drug levels.

MICROBIOLOGY LABORATORY EXERCISE: RESPIRATORY INFECTIONS (PART 2)

- See the objectives listed for Part 1.

Friday (5-13)

PBL: TOO MANY INFECTIONS**LECTURE: RESPIRATORY INFECTIONS (SOAVE)**

- Understand the clinical presentations and the pathogenesis of pulmonary infections.
- Using pneumonia as a paradigm - understand the etiological determinants of respiratory

- infections (host characteristics, environmental factors and pathogen characteristics).
- Understand the different classes of pneumonia and the related etiologic agents.

HISTOPATHOLOGY LABORATORY EXERCISE: ACUTE INFLAMMATION

- Recognize the vascular and cellular manifestations of acute inflammation.
- Know the mediators of vasodilation and increased permeability.
- Know the adhesion molecules and understand the molecular events involved in the attachment of inflammatory cells to the endothelium and movement into the tissues.

Week 3, May 16-20

Monday (5-16)

PBL: MR. TUSSIS' PERSISTENT COUGH**LECTURE: DRUG INTERACTIONS IN PATIENTS (REIDENBERG)**

- Know how the processes of absorption, distribution, biotransformation and excretion can affect dose-response relationships for drugs in patients
- Know how to adjust dose to allow for these factors and bring response to desired intensity of effect

LECTURE: T CELLS: T-CELL RECEPTORS, MHC & ANTIGEN RECOGNITION (SADELAIN)

- T cell receptor (TCR) diversity is generated by gene rearrangement
- Two classes of T cells, CD8⁺ and CD4⁺, are specialized to respond to intracellular and extracellular sources of infection
- Two classes of MHC molecules present antigen to CD8⁺ and CD4⁺ T cells.
- Peptides generated in two different intracellular compartments are presented to T cells by MHC class I and class II molecules respectively
- The two classes of MHC molecules are expressed differentially on cells
- The diversity of MHC molecules in the human population is due to multigene families and genetic polymorphism, and is selected by infectious agents
- MHC polymorphism affects the binding and presentation of peptide antigens to T cells

Tuesday (5-17)

LECTURE: BACTERIAL GENETICS AND ANTIMICROBIAL RESISTANCE (BARANY)

- Describe the mechanisms used by bacteria to obtain new genes (transformation, conjugation, and transduction)
- Apply the consequences of bacterial genetics and drug resistance to the management of antibiotic use.

LECTURE: T-CELLS: DEVELOPMENT & EFFECTOR FUNCTION (PAMER)

- Characterize CD4 T cell differentiation.
- Th1 versus Th2 T cells in immune defense against infection.
- Effector functions of CD8 T cells.
- Th17 cells in immune defense.

MICROBIOLOGY LABORATORY EXERCISE: MYCOBACTERIUM AND OTHER ACID FAST ORGANISMS

- Understand the characteristics of mycobacterium tuberculosis and the complex clinical

disease associated with infection by this organism.

- Learn about the other clinically important mycobacteria, including *M. leprae*, *M. avium-intracellulare* complex, *M. kansasii*.
- Discuss the clinical importance of *Nocardia*.
- Understand the significance of cording and the interferon-gamma release assays.

Wednesday (5-18)

PBL: MR. TUSSIS' PERSISTENT COUGH**LECTURE: CHRONIC INFLAMMATORY (FALCONE)**

- Understand the causes of chronic inflammation.
- Describe the morphologic presentations of chronic inflammation.
- Contrast chronic inflammation and granulomatous inflammation.

LECTURE: ANTIBIOTICS (GUDAS)

- Learn the mechanisms of action of the major classes of antibiotics
- Understand the problem of drug resistance and the mechanisms by which bacteria become resistant to antibiotics.
- Be familiar with the side effects of prototype antibiotics.

LECTURE: PHARMACOKINETIC ANALYSIS (SZETO)

- Understand the relationship between absorption, distribution and elimination of a drug and its concentration at its site of action.
- Describe drug distribution and elimination in mathematical and graphical terms.
- Use pharmacokinetic parameters to design suitable dosing regimens
- Apply pharmacokinetic principles in dosage adjustments during therapeutic drug monitoring.

Friday (5-20)

PBL: MR. TUSSIS' PERSISTENT COUGH**LECTURE: CHRONIC INFECTIOUS DISEASES: MALARIA AND TB (TEMPLETON AND SCHNAPPINGER)**

- List the factors of TB and malaria that allow them to cause chronic infections and that contribute to their success as parasitic organisms.
- Understand the concepts of drug resistance, drug tolerance and how they pose challenges to drug development.
- Identify the issues involved in controlling widespread persistent infections in third world environments.

HISTOPATHOLOGY LABORATORY EXERCISE: CHRONIC INFLAMMATION AND GRANULOMATOUS DISEASE

- Know the causes of chronic inflammation.

- Recognize the morphologic presentations, effector cell populations and mediators of chronic inflammation.
- Contrast chronic inflammation and granulomatous inflammation.

Week 4, May 23-27

Monday (5-23)

LECTURE: HYPERSENSITIVITY REACTIONS AND TOXIC SYNDROME (KALLIOLIAS)

- Outline the triggers and effectors of the four (or five) types of hypersensitivity reactions.
- Define the role of the different hypersensitivity reactions in immunopathology.
- Describe the initiators and effectors modalities and the mechanisms of the toxic shock syndrome.

PHARMACOLOGY CONFERENCE: CASES REQUIRING PHARMACOKINETIC ANALYSIS (SZETO)

- Describe how changing renal function affects steady state levels of drugs excreted by the kidney.
- Describe how to calculate the dose of a metabolized drug for an elderly patient in whom it has an extended half-life when the usual dose was determined in young men who had a shorter half-life.
- Determine how a drug should be given to achieve a steady state in as short a time as possible and how long would it take to reach steady state.

Tuesday (5-24)

PBL: MR. ACHES' JOINT PAIN**LECTURE: AUTOIMMUNITY & AUTOIMMUNE DISEASES (CROW)**

- To describe contributions of the innate and adaptive immune system to induction of autoimmunity
- To discuss genetic and environmental contributions to autoimmune disease
- To describe mechanisms of tissue damage in autoimmune disease

LECTURE: THE PLACEBO EFFECT (GUDAS)

- To learn more about how clinical trials are designed.
To learn the differences between placebos and the placebo effect.
- To discuss the biochemical basis for the placebo effect re pain.

MICROBIOLOGY LABORATORY EXERCISE: WOUND INFECTIONS PART 1

- Describe types and characteristics of bacteria involved in wound infections.
- List the characteristics of anaerobic bacteria that are often the primary pathogens in wound infections.
- Discuss complex issues involved in characterizing and treating polymicrobial infections.

Wednesday (5-25)

PBL: MR. ACHES' JOINT PAIN

LECTURE: TOLERANCE, DEPENDENCE AND WITHDRAWAL (SZETO)

- Define tolerance, dependence, withdrawal, and addiction
- List factors related to drug administration that affect the degree of tolerance and dependence.
- Describe the relationships between the pharmacokinetics of a drug, the degree of tolerance and the severity of withdrawal.

HISTOPATHOLOGY LABORATORY EXERCISE: IMMUNOPATHOLOGY: THE HOST'S DELETERIOUS RESPONSE

- Review the pathogenesis and morphologic presentations of hypersensitivity reactions.

Friday (5-27)

PBL: MR. ACHES' JOINT PAIN

LECTURE: BONE AND SOFT TISSUE INFECTIONS (BRAUSE)

- List the characteristic types of skin and soft tissue infections.
- Identify the elements of bacterial pathogenesis in these infections.
- Define the factors that contribute to bacterial spread in soft tissue infections and the treatment options.

LECTURE: ALLOGRAFT & REJECTION (MUTHUKUMAR)

- Understand the immunological mechanisms underlying organ rejection.
- Understand graft-versus-host disease and post-transplant immune deficiency

MICROBIOLOGY LABORATORY EXERCISE: WOUND INFECTIONS (PART 2)

- See the objectives listed for Part 1.

Week 5, May 30- June 3

Monday (5-30)

MEMORIAL DAY

Tuesday (5-31)

PBL: THE DISTINGUISHED SCIENTIST

PHARMACOLOGY CONFERENCE: REVIEW OF PHARMACOLOGY PRINCIPLES (INTURRISI)

MICROBIOLOGY LABORATORY EXERCISE: URINARY TRACT INFECTION AND ENTERIC BACTERIA (PART 1)

- Describe the normal flora of the GI tract and factors which can contribute to urinary tract infections.
- Characterize the enterobacteriaceae family of bacteria, and describe the diseases associated with infections by these organisms, and how these bacteria are identified.

Wednesday (6-1)

PBL: THE DISTINGUISHED SCIENTIST

LECTURE: INTERFERONS, CYTOKINES AND INTERLEUKINS (IVASHKIV)

- Identify the cells producing interferon, cytokines, and interleukins.
- Define the mechanisms whereby interferons, cytokines, and interleukins activate lymphocytes and mono/macrophages.
- Outline the impact of these activation mechanisms on host defenses.

LECTURE: HEMOSTASIS AND THROMBOSIS: MAINTENANCE OF VASCULAR INTEGRITY (PEERSCHKE)

- Describe the components and regulation of the coagulation system.
- Contrast thrombosis and hemostasis.
- Describe the etiology and morphologic characteristics of venous and arterial thrombi.

MICROBIOLOGY LABORATORY EXERCISE: UTI AND ENTERIC BACTERIA (PART 2)

- See the objectives listed for Part 1.

Friday (6-3)

PBL: THE DISTINGUISHED SCIENTIST

LECTURE: BACTEREMIA (HARTMAN)

- List the classifications of bacteremia.

- Identify the bacterial and host factors that contribute to endocarditis.
- Consider the infectious complications of catheter-related infections.

HISTOPATHOLOGY LABORATORY EXERCISE: HEMOSTASIS, THROMBOSIS AND SHOCK

- Contrast thrombosis and hemostasis.
- Review the etiology and morphologic characteristics of venous and arterial thrombi.
- Review the etiology and morphologic characteristics of disseminated intravascular coagulation.
- Contrast acute and chronic congestion.
- Review the pathogenesis and morphologic characteristics of shock.

MICROBIOLOGY LABORATORY EXERCISE: UTI AND ENTERIC BACTERIA (PART 3)

- See the objectives listed for Part 1.

Week 6, June 6-10

Monday (6-6)

PBL: MRS. ENZA'S RESPIRATORY PROBLEM**LECTURE: ANTI-NEOPLASTIC DRUGS (GUDAS)**

- Describe the fractional kill hypothesis and explain how it is the underlying principle of much current anti-neoplastic therapy.
- Describe three mechanisms by which tumors become resistant to anti-neoplastic therapy.
- Understand the principles of combination chemotherapy and the reasons why this therapy is so widely used.
- Learn the differences between cytotoxic cancer chemotherapy and tumor “targeted” chemotherapy.
- Learn the major side effects associated with cytotoxic cancer chemotherapy and the reasons why side effects are a problem with this type of chemotherapy.

MICROBIOLOGY LABORATORY EXERCISE: ANTIBIOTIC SUSCEPTIBILITY TESTING (PART 1)

- Understand the principles of antibiotic susceptibility testing (E test, K-B disk and beta-lactamase disk).
- Understand the roles of these tests in the management of infectious diseases .

Tuesday (6-7)

LECTURE: VIRUSES I: INTRODUCTION TO VIROLOGY DNA VIRUSES (FALCK-PEDERSEN)

- Understand the major classes of viruses and the structural characteristics of each class.
- List pathways of virus entry and general features of virus replication and spread.
- Understand the most frequently encountered effects of virus on host cells.
- Explain the mechanisms by which virus infections cause immune activation, and the mechanisms used by viruses to evade host defenses.

LECTURE: VIRUS II: VACCINES AND RNA VIRUSES (FALCK-PEDERSEN)

- Describe the biology of oncogenic RNA virus (including infection, replication, and latency).
- Explain the influence of virus infection on the host, including the molecular mechanisms of transformation and the targeting of the immune system.
- Discuss the diseases caused by these viruses.

LECTURE: HERPESVIRUSES (CESARMAN)

- Know the eight human herpesviruses and disease associations.
- Understand the basic structure and basic features of replication.
- Understand latency and lytic reactivation.
- Review the sites of latency and relationship with pathogenesis for the different classes of

herpesviruses.

- Review the mechanisms of oncogenic transformation for the gamma herpesviruses (EBV and KSHV).
- Discuss therapeutic approaches based on viral biology.

LECTURE: NEOPLASIA: HOSTS RESPONSE TO ACQUIRED (ENVIRONMENTAL) AND INHERITED MUTATIONS (STANEK)

- Contrast benign and malignant neoplasms.
- Describe the morphologic characteristics of neoplastic cells.

Wednesday (6-8)

PBL: MRS. ENZA'S RESPIRATORY PROBLEM

LECTURE: ANTI-VIRAL DRUGS (SAUVE)

- Identify reverse transcriptase inhibitors;
- Identify HIV protease inhibitors;
- Identify neuraminidase inhibitors;
- Describe molecular mechanism of action of these compounds;
- Describe mechanisms of resistance;
- Describe pharmacologic properties of these compounds.

LECTURE: NATURAL KILLER CELLS (DUPONT)

- Define the developmental lineage of natural killer cells relative to other cells of the immune system
- Describe the major functions of natural killer cells
- Describe the "missing self" recognition paradigm
- Describe the "induced self" recognition paradigm
- Discuss how natural killer cells participate in early response to pathogens

MICROBIOLOGY LABORATORY EXERCISE: ANTIBIOTIC SUSCEPTIBILITY TESTING (PART 2)

- See the objectives listed for Part 1.

Friday (6-10)

PBL: MRS. ENZA'S RESPIRATORY PROBLEM

LECTURE: OPPORTUNISTIC INFECTIONS (SOAVE)

- Understand the concepts and able to give examples of emerging pathogens and opportunistic pathogens.
- Understand the immunologic elements of host defense that are compromised in opportunistic infections.
- Understand the impacts of neutropenia on infections.

- Review the determinants and characteristics of infections in the immunocompromised host.
- Review the risk factors and the mechanisms that contribute to the development of opportunistic infections in transplant patients.

LECTURE: HIV AND VACCINE STRATEGIES (MOORE)

- Understand the basic virology and immunology of HIV-1 infection. Outline the mechanisms, both viral and host-derived that lead to the persistence of HIV, rather than its eradication by host defenses.
- Understand the requirements for a successful HIV-1 vaccine and the challenges of meeting the requirements.
- Understand the basic characteristics of killed, live-attenuated and subunit vaccines.
- List the various strategies being deployed for the development of an effective HIV-1 vaccine.

LECTURE: DRUG USE IN PREGNANCY (RIFKIND)

- Apply the principles concerning drug absorption, metabolism, and excretion to the maternal-fetal unit.
- Learn how the age of the fetus affects the sensitivity of the fetus to adverse effects of drugs.
- Learn the major human teratogens.

Week 7, June 13-17

Monday (6-13)

LECTURE: MEDICAL MYCOLOGY (LARONE)

- Discuss general characteristics: morphology, reproduction.
- List host fungal interactions.
- Describe clinical syndromes associated with fungal infections.

LECTURE: HOW ARE DRUGS APPROVED (B. REIDENBERG)

- Explain the process of drug approval.
- Explain the different types of clinical trials used for drug approval.
- Explain safeguards to protect the public from potentially unsafe drugs.
- Discuss the criteria for approval of generic and over-the-counter drugs.
- Explain the role of the FDA in drug approval. Discuss ethical issues associated with clinical trials.

LECTURE: NEOPLASIA II: HOSTS RESPONSE TO ACQUIRED AND INHERITED MUTATIONS (STANEK)

- Describe the pathogenesis of neoplastic change
- Describe the mechanisms of tissue invasion and metastasis.

HISTOPATHOLOGY LABORATORY EXERCISE: NEOPLASIA

- Contrast benign and malignant neoplasms.
- Review the morphologic characteristics of neoplastic cells.
- Review the mechanisms of tissue invasion and metastasis.

Tuesday 6-14

LECTURE: ANTI-FUNGAL DRUGS (LEVIN).

- Describe the four classes of antifungal agents along with their mechanisms of action.
- Explain the mechanisms of resistance found for each class.
- Explain why they exhibit different spectrums of action and different levels of toxicity to the host.
- List the considerations used to determine which antifungal agent should be prescribed.

LECTURE: TUMOR IMMUNOLOGY (CHEN)

- Define cancer antigens
- Outline the link between infection and immunity to cancer
- Describe how cancer escape the immune response
- Discuss how to use the immune system to treat cancer