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.
Detailed Learning Objectives

• 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. lepraе, 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. Tuiss’ 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. Tuiss’ 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 (Kalliolas)
• 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.
Detailed Learning Objectives

Wednesday (5-25)

**PBL: MR. ACHES’ JOINT PAIN**

**Lecture:** Tolerance, dependence and withdrawal (Szeto)
- Define tolerance, dependance, 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 enterobacteriace 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: Viruses 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
 Detailed Learning Objectives

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.
Detailed Learning Objectives

- 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