MICR 5051
Introduction to Immunology
FALL 2021

Tuesdays and Thursdays 1:00-3:00 PM Classroom 2.011 Lib

COURSE FACULTY: Keith Krolick, Ph.D.
Course Director

OFFICE HOURS: By appointment; Office 423D/MS Teams
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READ THIS DOCUMENT CAREFULLY - YOU ARE RESPONSIBLE FOR ITS CONTENTS.

CoVID-19 Disclaimer: At the beginning of the summer, as it looked as though we were coming out of the CoVid-19 pandemic, the expectations of the University, designed to keep us safe, changed as circumstances improved. At that time, the new plan was, and for now still is, to hold all lecture and conference discussion sessions in the classroom. This plan also assumed that everyone enrolled in this class was on their way to becoming fully vaccinated against SARS-CoV2. Furthermore, the wearing of masks was to be optional. Recently, however, the pandemic has worsened again, with Texas being one of the hotspots for increasing infections with the very contagious Delta variant. In addition, it is now clear that vaccinated individuals can carry and transmit the virus. Therefore, for the safety of all of us in the class, I insist that we all wear masks while in my class. Furthermore, we will pay close attention in the future to changing expectations and requirements passed down from the University administration. **As of today (August 16), although I still plan to hold class in-person, I am prepared to go virtual, and will do so, if COVID-19 circumstances deteriorate significantly.**

MASTER OF SCIENCE IN IMMUNOLOGY & INFECTION PROGRAM MISSION

The mission of the MSI&I program is to provide classroom and laboratory experiences designed to prepare graduates for professional careers in which they contribute laboratory expertise and problem-solving skills to the biomedical research, educational and healthcare communities.

GENERAL EXPECTATIONS

General expectations of the MICR 5051 course are summarized in a **video recording**, with details provided below.

- Demonstrate respect, collegiality, and support for classmates
- Demonstrate consistent preparation for, and participation in, class activities.
- Complete all assignments and readings on time.
- Demonstrate integrity by completing all assignments and examinations independently.

COURSE DESCRIPTION AND OBJECTIVES

This course presents principles of innate and acquired (adaptive) immunity, including descriptions of the development and functions of cells that participate in immune responses, as well as the role of important soluble mediators. In addition, disorders of impaired or inappropriate immune function are described including autoimmunity, hypersensitivity, immunodeficiency, and transplant rejection. Some laboratory testing for these disorders is described.

The following lists some of the broad objectives of this course. Specific objectives for each individual lesson can be found at the end of this syllabus. ✶**Review the specific lesson objectives routinely.** They provide a direct roadmap to what you are expected to learn and how you will apply them in discussions and on exams.

By the end of this course, each student must be able to define and discuss:

- How host defenses to infection are said to be composed of layers of protection.
- Physical and physiological barriers provided by the host that interfere with initial phases of microbial infection.
- Cells and soluble mediators produced by the host that are involved in non-adaptive (innate) immunity, and how they interfere with early phases of microbial infection.
- Why the antigenic complexity of a potential microbial pathogen and its products often requires multiple adaptive immune mechanisms to insure effective protection of the host.
- Principle hallmarks of the adaptive immune system (diversity, specificity, memory), and how these hallmarks differ from those of non-adaptive (innate) immunity.
- Cells and soluble mediators produced by the host that are involved in adaptive immunity, why this line of defense is considered "adaptive", and how humoral and cell-mediated adaptive immunity interferes with later phases of microbial infection.
- How host immune defenses have "co-evolved" with disease-causing characteristics of pathogenic microorganisms.
- How inappropriate immune responses can lead to pathologies associated with allergy, autoimmunity, immunodeficiency, and graft rejection.

COURSE ORGANIZATION

Three main teaching formats are used to cover the material in this course: **1) Conventional didactic lectures** in which information is delivered to the class; **2) Conference Discussions** which are highly interactive case-based activities, encouraging two-way communication between the instructor and the class, and requiring student active participation in the learning process; and **3) Online review and self-study activities**.

Computer Access – Various materials and assignments will require access to a computer with internet capabilities.

Reading Assignments – Required reading assignments are posted in the schedule of class meetings (shown below) and are never considered optional. Although there will be no attempt to fish out tiny details just to trip up students, anything in the required readings, whether emphasized in class or not, is considered testable on exams. Mandatory readings are primarily found in the required textbook (see below). However, occasionally a reading assignment will be given that is posted online or sent to you via email attachment.

- **Lectures –** Many of the presentations are given in the common lecture format and are accompanied by Pdf-converted PowerPoint slide files posted on the MICR 5051 CANVAS website. The Pdf files are provided to you with active fields that will allow you to type notes on your laptop. You are responsible for all information included in the posted lecture materials, but lecturers may expand and enhance these materials during in-class presentations. Therefore, **take good notes to augment posted content provided because any information discussed in class is considered testable.**

  Animations – You are provided with hyperlinks to a collection of online (YouTube) animated reviews of certain key concepts. These animations will enhance and clarify lecture presentations and give you a sense of the dynamics of immune activities that is sometimes overlooked in static slide presentations. Note that some animations are more detailed than the information provided in the in-class sessions. Although you will not be held responsible for those additional details, **you are highly encouraged to view these excellent animations**.

- **Online Review Activities –** Certain lecture sessions are accompanied by online reviews found on the **MICR 5051 CANVAS website**. **Explicit instructions** for completing these activities are provided online (see "Syllabus and Other Instructions" in the Course Content folder). The online reviews are intended to test your breadth and depth of understanding of the various topics covered in the course. However, they are not intended to represent a thorough coverage of the material, but only as examples of what you might find on examinations and to gauge your level of preparedness. Each online review, when completed, is **worth 0.1 bonus point that will be added to your final exam average at the end of the course** (see grading information below).

- **Conference Discussions (CD) –** These sessions will extend your understanding of basic principles of immunology by discussing patient case histories that describe instances when disease occurs due to inadequate or undesirable immune responsiveness. A **list of strategies and expectations** for these sessions is provided online (see "Syllabus and Other Instructions"). Patient histories to be discussed are found beginning in **Module 3 of the MICR 5051 CANVAS website** and will involve immunopathologies associated with allergy, autoimmunity, immunodeficiency, and transplant rejection.

  To prepare for CD sessions, each student **must become familiar with all cases of the day** (including any test results and images) and relevant background information. Most CD sessions are accompanied by a short introductory video recording that should be viewed prior to class; introductory content will not be reviewed in class.

  Information needed to prepare for discussions is available in introductory **online introductory comments** that accompany each CANVAS session, from **lecture presentations**, and from **text book reading assignments**. Essential information and facts of each case should be inserted and clearly cataloged into **templates** that accompany each case. The templates are designed to help organize information for efficient studying. The more complete the information collected, the less work will be necessary to prepare for exams. Also, each entire set of CD templates that accompany each session, when completed and submitted, is **worth 0.2 bonus point that will be added to your final quiz/exam average at the end of the course** (see grading information below). Templates should be studied prior to class to be prepared for discussion; it is **acceptable to bring templates to class** as an aid during discussions. Finally, although each case history is accompanied by a series of questions that will be the starting point of in-class discussion, students should not assume that simply looking up answers to those few questions is sufficient to fully participate in the discussion. Again, you will be optimally prepared only if you do a thorough job filling in the templates for each case.

  CD sessions are intended to be highly interactive. In order to promote widespread participation, **the instructor will make use of a picture roster for engaging the students**. That is, participation is not voluntary, and students will be called on in class to answer questions. Initially, this may be a bit intimidating for some students, but the CD sessions offer **excellent opportunities to practice skills of interpretation and communication** under circumstances that are meant to foster teamwork and cooperation. You will be allowed to **refer to your information templates during the discussions**; the more thorough and well-organized they are, the more useful they will be to you. Moreover, it is well understood that you are at your initial stages of training, and in-depth expert discussion cannot be expected. However, it is also important to realize that, in your future, considering case presentations such as these may be, in part, the basis for making certain decisions in your research activities.

ATTENDANCE & PARTICIPATION

To achieve the expected level of competency, students must be fully engaged. Therefore, attendance and full participation is expected.

Attendance is defined as being present and ready to begin at the specified class time, and remaining until class ends. If you are unable to attend a session, **NO MATTER THE REASON**, this will be considered an absence. However, certain circumstances may allow you an "excused" absence (see below).

- Attendance is **required** for all Lecture sessions.
- Attendance is **required** for all Conference Discussion sessions.

While obligations to family, friends, work, etc. are important, they are considered "unexcused" absences. Non-urgent care medical appointments should be made for times that do not conflict with class. Absences that result from scheduled appointments will be considered as unexcused.

An absence may be "excused" only if it is the result of a significant illness of the student or dependent, an automobile accident/disablement, or the hospitalization of a student or student's immediate family, or similar urgent events. To request an excused absence for religious holidays, you should follow the guidelines outlined in the UT Health San Antonio Catalog. Whenever possible, prior notification of an absence should be provided to the Course Director.

If you have an excused absence, you will be permitted to make up graded work and exams. If your absence is unexcused, you will not be permitted to make up graded work or exams or to turn in work past the stated deadline for the given work.

It is your responsibility to account for missed information, regardless if an absence is excused or not. The instructor will arrange remediation, if necessary, for missed work to a student with an excused absence. Instructors do not have an obligation to provide remediation for missed work to students with an unexcused absence.

Tardiness. Tardiness is defined as entering a session after the session begins. Furthermore, you are not to leave prior to the conclusion of a session (unless prior arrangements have been made with the instructor). If you arrive late, you should not expect the instructor to provide missed information. If you arrive to class more than **15 minutes** after class has begun, you may be scored as "absent" for that class (see Attendance policy above). It is recognized that a student may occasionally arrive late to class due to unexpected traffic problems or inclement weather. However, chronic lateness is considered an unprofessional behavior that disrupts the learning environment for everyone else in the classroom and will not be tolerated. The consequence of such behavior will be determined by the instructor.

TEXTBOOKS

Mandatory and recommended reading assignments are found primarily in the following two textbooks. Note occasional online reading assignments; links to those sites are also found in the schedule of class meetings.

Required textbook (assignments posted in the schedule of class meetings shown below):

Parham, P. (2014). ***The Immune System, 4th edition*****.** New York: Garland Science. Note that many of the slides used in class are derived from this book.

NOTE: Although a 2021 edition of the Parham textbook will become available later this summer, it is not clear that it will be readily available in time before the school year begins. Therefore, we will continue to use the 2014 edition for this class, and it is more than sufficient for our purposes. If you have the opportunity/wish to purchase the more recent Parham version, you are welcome to do that. However, reading assignments will refer to the pagination of the earlier edition.

Recommended additional textbook:

Sompayrac, L. (2019) ***How the Immune System Works, 6th edition*****.** Blackwell Publishing. An excellent overview of the "big picture" and **very highly** recommended for students who have never had a formal course in immunology. Reasonably priced and worth considering.

GRADING POLICIES AND EXAMINATION PROCEDURES

Testable material comes from 3 main sources: Lecture Presentations, Conference Discussions (**including content provided in the introductory videos; viewing of these videos is not optional)**, and 3) Reading Assignments.

Grading System – Final letter grades are primarily based on your performance on 3 module exams. The first two exams are each worth 25% of your grade; the third exam is **comprehensive** and is worth 50% of your grade. Grading is based on the following scale:

A = 90-100% B = 80-89% C = 70-79% D = 60-69% F = < 60%

Note: Fractions of grades are rounded to the nearest whole number for your final course grade. For example, 89.45 is an A, but 89.44 is a B, or 79.45 is a B, but 79.44 is a C.

Bonus Points – Bonus points may be received in two ways. 1) For each **Online Review** completed and submitted, **0.1 point** will be awarded. 2) For each set of **Conference Discussion templates** completed and submitted, **0.2 point** will be awarded. Bonus points will be added to your 3-exam average at the end of the course.

Examination Format and Protocol – Exams may be composed of multiple choice, short answer, and essay questions. The proportion represented by each question type will vary among the 3 exams. Certain questions will be accompanied by images, so it is **imperative that you study images** (particularly those presented in class).

Brief instructions will be given prior to the start of each exam. No electronic devices, extra paper, books, backpacks, etc. are permitted in the testing area. Hats must be removed. You will **not be allowed to ask questions of the proctor** once the examination has started (except to point out potential typographical errors in the exam).

Exams will be timed. **If you arrive late** to an exam, and are given permission to take the exam, you will not be given additional time to complete your test. If you arrive after another student has finished the exam and has departed the

exam room, you will not be allowed to take the exam. If you miss an exam, you may be eligible for taking a make-up exam (see below).

Exam results will be provided to students as quickly as possible. No "challenges" are allowed. However, a time will be scheduled outside of class so that students can review concepts of concern to them. With regard to multiple choice questions, statistical determinations of question validity will be performed. If flawed questions are identified, and at the Course Director's discretion, appropriate adjustments will be made regarding the grading of those questions. Therefore, grades posted to each student's MICR 5051 CANVAS grade book are to be considered tentative and unofficial until the Course Director contacts the class to indicate the exam grades are final and official.

Make-up Examinations – A student who must miss a scheduled exam for a serious reason must request an excused absence from the Course Director. Acceptable "serious reasons" usually involve serious illness or injury to the student (doctor's excuse may be required) or the student's family member. Examples of unacceptable reasons include: Not prepared or incomplete studying, over-sleeping, hangover, heavy traffic or any travel delays, other appointments or scheduled professional or personal commitments.

If it is determined that missing an exam is justified, a make-up examination will be scheduled. The make-up exam will be given as soon as possible at a time designated by the Course Director. Any student who misses an exam and does not receive an excused absence **will receive a grade of zero for that exam**.

REQUESTS FOR ACCOMODATIONS FOR DISABILITIES

In accordance with policy 4.2.3, **Request for Accommodation Under the ADA and the ADA Amendments Act of 2008 (ADAAA)**, any student requesting accommodation must submit the appropriate request for accommodation under the American with Disabilities Act (ADA, form 100) to the appropriate Associate Dean. In addition, the Course Director should be notified once the paperwork is filed. Additional information may be obtained at http://uthscsa.edu/eeo/request.asp.

ACADEMIC INTEGRITY AND PROFESSIONALISM

Any student who commits an act of academic dishonesty is subject to discipline as prescribed by the UT System Rules and Regulations of the Board of Regents. Academic dishonesty includes, but is not limited to, cheating, plagiarism, collusion, the submission for credit of any work or materials that are attributable in whole or in part to another person, taking an exam for another person, signing attendance sheets for another student, and any act designed to give unfair advantage to a student or the attempt to commit such an act.

The UT Health San Antonio Academic Dishonesty Policy can be found in the UT Health San Antonio 2020-2021 University Catalog and in the University's Handbook of Operating Procedures

A Code of Conduct Statement will accompany each exam; students are expected to be familiar with, and behave according to, the code.

TITLE IX AT UTHSCSA

Title IX Defined:

Title of the Education Amendments of 1972 is a federal law that prohibits sex discrimination in education. It reads "no person in the United States shall, on the basis of sex, be excluded from participation in, be denied the benefits of, or be subjected to discrimination under any education program or activity receiving Federal financial assistance."

University of Texas Health Science Center San Antonio's Commitment:

University of Texas Health Science Center San Antonio (UTHSCSA) is committed to maintaining a learning environment that is free from discriminatory conduct based on gender. As required by Title IX, UTHSCSA does not discriminate on the basis of sex in its education programs and activities, and it encourages any student, faculty, or staff member who thinks that he or she has been subjected to sex discrimination, sexual harassment (including sexual violence) or sexual misconduct to immediately report the incident to the Title IX Director.

In an emergency, victims of sexual abuse should call 911. For non-emergencies, they may contact UPD at 210-567-2800. Additional information may be obtained at http://students.uthscsa.edu/titleix/

EMAIL POLICY

Every student is issued a University e-mail address and account at the time of enrollment. As a matter of University Policy, communications between students and faculty that occur using the student's University e-mail address is considered official business. Therefore, **students are expected to check their university email inboxes frequently** so that any announcements, instructions, or information regarding this course will be received in a timely way. Missed communications due to inadequate monitoring of incoming emails on the University's email server will never be a valid excuse for unsatisfactory academic progress.

USE OF RECORDING DEVICES

Recording of lectures and other learning activities in this course by any means (*e.g.*, photo, video, audio, etc.) is only permitted if approved by the instructor or required for compliance with Americans with Disabilities Act (ADA).

ELECTRONIC DEVICES

Cell phones must be turned off during all class meetings and exams. Computers and electronic tablets are allowed only for participating in classroom activities (*e.g.*, viewing slides presented in lecture or conference materials). No texting, tweeting, emailing, web-surfing, gaming, or any use of electronic devices that is not directly connected with classroom activities is permitted.

MICR 5051

INTRODUCTION TO IMMUNOLOGY

2021 CLASS SCHEDULE

Tuesday-Thursday 1:00-3:00 PM

MODULE 1

WEEK	DATE	TOPIC	Reading Assignment* and relevant CANVAS Reviews	Instructor and Format
Week 1	Aug 24	Overview of Host Defenses Against Infection 1	PAR: Ch1-3 HIW: Ch1, Ch2	Krolick (Lecture)
	Aug 26	Overview of Host Defenses Against Infection 2	[ONLINE REVIEWS 1-4]	Krolick (Lecture)
Week 2	Aug 31	Lymphocyte Receptors for Antigen 1	PAR: Ch4.1-4.12; Ch5.1-5.5	Krolick (Lecture)
	Sept 2	Lymphocyte Receptors for Antigen 2 *** T Cell Development, Antigen Recognition, and Effector Functions 1	PAR: Ch.5.6-5.22; Ch8; 12.1-12.5 HIW: Ch.4, Ch.5, Ch,6 [ONLINE REVIEWS 5-8]	Krolick (Lecture)
Week 3	~~Sept 7~~ Sept 8	T Cell Development, Antigen Recognition, and Effector Functions 2	PAR: Ch7.1-7.2; Ch7.8-7.14	Krolick (Lecture)
	Sept 9	T Cell Development, Antigen Recognition, and Effector Functions 3	PAR: Ch13.6 HIW: Ch.8, Ch.9	Krolick (Lecture)
Week 4	Sept 14	NO CLASS – Voluntary Review		
	Sept 16	Exam #1		

MODULE 2

WEEK	DATE	TOPIC	Reading Assignment* and relevant CANVAS Reviews	Instructor and Format
Week 5	Sept 21	Humoral Immunity 1	PAR: Ch4.13-4.17; Ch6.1-6.8; Ch6.11-6.15 HIW: Ch.3, Ch.7	Krolick (Lecture)
	Sept 23	Humoral Immunity 2	PAR: Ch9 HIW: Ch.10	Krolick (Lecture)
Week 6	Sept 28	Humoral Immunity 3 *** Mucosal Immunity 1	[ONLINE REVIEWS 9-12] PAR: Ch10 HIW: Ch.11	Krolick (Lecture)
	Sept 30	Mucosal Immunity 2	[ONLINE REVIEWS 13-14]	Krolick (Lecture)
Week 7	Oct 5	Flow Cytometry	Flow Cytometry Overview	Krolick (Lecture)
	Oct 7	Serologic Diagnosis	Intro comments in CANVAS Handout and video	Krolick (Conference)
Week 8	Oct 12	NO CLASS – Voluntary Review		
	Oct 14	Exam #2		

MODULE 3

WEEK	DATE	TOPIC	Reading Assignment* and relevant CANVAS Reviews	Instructor and Format
Week 9	Oct 19	**NO CLASS**		
	Oct 21	Hypersensitivity Diseases	Intro Comments in CANVAS and video PAR: Ch14 HIW: Ch.13	Krolick (Conference)
Week 10	Oct 26	**NO CLASS**		
	Oct 28 	Autoimmune Diseases	Intro Comments in CANVAS and video PAR: Ch16 HIW: Ch.13	Krolick (Conference)
Week 11	Nov 2	**NO CLASS**		
	Nov 4	Immunodeficiency Diseases	Intro Comments in CANVAS and video PAR: Ch13.8-13.16; 13.17-13.20; 13.24 HIW: Ch.14	Krolick (Conference)
Week 12	Nov 9	Vaccine Development/Strategies	PAR: Ch.11 HIW: Ch.12 [ONLINE REVIEW 15]	Krolick (Lecture)
	Nov 11	ONLINE SELF-STUDY – Immune Evasion (No in-class meeting) *Vaccine Conference* (Nov 11-12)	PAR: Ch13.1-13.7	
Week 13	Nov 16	**NO CLASS**		
	Nov 18	Transplantation and Graft-versus-Host Disease	Intro Comments in CANVAS and video PAR: Ch5.23; Ch15.1-15.12;	Krolick (Conference)
Week 14	Nov 23	Thanksgiving Break		
	Nov 25	Begin studying for final exam! → Eat-Study-Eat-Study-Eat 		
Week 15	Nov 30	**NO CLASS**		
	Dec 2	Immunopathology Review	Intro Comments in CANVAS Handout and video	Krolick (Conference)
Week 16	Dec 7	**Comprehensive Final Exam**		

* **PAR** = Required readings: Parham, P. (2014). *The Immune System, 4th edition*. New York: Garland Science.
HIW = Recommended readings: Sompayrac, L. (2015) *How the Immune System Works, 5th edition*. Blackwell Publishing.
Certain online readings and review activities are listed.

INTRODUCTION TO IMMUNOLOGY

Lesson Objectives for Individual Sessions

The Lesson Objectives listed below are to be used as a guide to the most essential questions that you should consider in your studies. However, do not view these lists as the "end-all" as you devise your study strategies. Anything covered in reading assignments, online activities, or discussed in class is to be considered "testable".

WEEK	TOPIC	Lesson Objectives
Week 1	**Overview of Host Defenses Against Infection**	Microbial pathogens have many specialized strategies to survive in the host, some that result in highly detrimental and pathological outcomes. This overview briefly describes the diverse repertoire of immunological weapons that we have to neutralize those many specialized microbial strategies. Then, throughout this course, and throughout your career, you will come to appreciate how big this challenge is, and that sometimes, we fail to meet the challenge. Your primary objectives for this overview lecture should be: 1. To familiarize yourself with the various physical and physiological barriers/mechanisms by which the host defends itself from infection. 2. To familiarize yourself with the cells (and their basic functions) that compose the non-adaptive innate and adaptive systems of host defense. 3. To consider relationships between specialized strategies associated with particular types of infections and the immune strategies required to confer resistance to those infections.
Week 2	**Lymphocyte Receptors for Antigen**	Receptors on the surface of lymphocytes are responsible for highly specific recognition of antigens. There is a huge diversity in the receptor specificity repertoire that is the basis for clonal lymphocyte selection and activation. In order to master your understanding of this crucial characteristic of lymphocytes, it is necessary for you to: 1. Know and understand the domain structure of antibodies and what is meant by variable and constant domains. 2. Know and understand the structure and function of the complementarity determining regions (CDRs). 3. Know when functional heavy and light chain genes are generated during B cell development. 4. List the classes and subclasses of antibody present in humans and describe differences in their effector functions. 5. Describe the Fab, Fc, and hinge regions of the antibody molecule and how they relate to antibody function. 6. Know the general structures of the immunoglobulin heavy and light chain genetic loci. 7. Know and understand how VDJ and VJ recombination occurs. 8. Explain how mechanisms resulting in antibody gene rearrangements that dictate antigen binding specificity are "antigen-independent". 9. Explain how a small number of antibody genes can encode for hundreds of millions of antigen-binding specificities.

		10. Explain the importance of allelic exclusion in lymphocyte receptor expression. 11. Explain why B cells are "monospecific" for antigen. 12. Describe how inexact joining during VDJ rearrangements contributes to antigen-binding diversity and why there is greater diversity in CDR3 than in the rest of the variable region. 13. Describe T cell receptor structure and how it functions together with the CD3 complex. 14. Explain how the BCR and TCR are similar. Are different. 15. Explain how T cell receptor antigen-binding diversity is generated and how it resembles the generation of antibody diversity.
Weeks 2-3	**T Cell Development, Antigen Recognition, and Effector Functions**	There are 3 main types of infection, <u>intracellular (cytoplasmic), intracellular (intravesicular), and extracellular</u>. T lymphocytes must specialize in order to effectively contribute to host defenses by guaranteeing the activation of immune responses with effector functions that can reach and destroy the pathogen. Your primary objectives should be to: 1. Understand why appropriate interaction of T cells with antigen presenting cells (APC) is key to effective immune responsiveness. 2. Understand why the nature of particular infections (*e.g.*, intracellular vs. extracellular) dictates which antigen processing pathway is activated in APCs (endogenous vs. exogenous). 3. Understand why the particular antigen processing pathway that is activated dictates which antigen presenting molecules, encoded by the major histocompatibility complex, are engaged. 4. Know the characteristics and genetic origins of major histocompatibility molecules. 5. Explain how, in addition to the T cell receptor, CD3, CD4, CD8, and co-stimulatory molecules are required for T cell activation. 6. Understand why the particular antigen processing/presentation pathway activated dictates which subsets of T cells are activated. 7. Understand why multiple kinds of effector T cells are necessary in order to guarantee complete host defense against infection. 8. Learn to distinguish the multiple types of T cells based on: a) Which membrane molecules that they carry; b) How they recognize antigen; c) Which cytokines that they produce; and d) How they destroy antigen (*i.e.*, effector functions). 9. Be familiar with "unconventional" T cells such as T_{REGS}, NK cells, NKT cells, and $\gamma\delta$ T cells.
Weeks 5-6	**Humoral Immunity**	This series of lectures is intended to provide an understanding of 1) the interactions between B cells and T cell that result in antibody production, and 2) the diversity of antibody structure and function. Again, we can see that the humoral response has evolved in ways intended to guarantee that effector functions are produced that can reach and destroy various biological threats. Important B cell activities that you must master can be divided and studied as 3 topics:

		Development: 1. Correlate B cell developmental stages with the rearrangement and expression of immunoglobulin genes. 2. Describe how antibody expression is dependent on DNA recombination; and when antibody expression is dependent on alternative RNA processing. 3. Be able to explain how a B cell simultaneously expresses IgM and IgD. 4. Understand the roles of the membrane and secreted forms of antibody and the mechanisms by which they are expressed by the B cell. 5. Understand the difference between antigen-independent B cell development in the bone marrow and antigen-dependent differentiation after B cells leave the bone marrow. 6. Understand the process of negative selection of the B cell repertoire during B cell development. Activation: 7. Know that B cell activation requires two independent signals and be able to describe them. 8. Describe the different fates of B cells following activation by antigen. 9. Understand why B cell activation in response to T-dependent antigens (most antigens) requires interaction with helper T cells, while activation in response to T-independent antigens does not. 10. Understand that the immune system is a circulatory one and that antigen-specific B cells and T cells find each other in the secondary lymphoid organs where antigen is concentrated. 11. Be able to describe the germinal center and the events that take place there with regard to B cell-T cell interactions, and B cell activation and function. Effector functions: 12. Describe molecular mechanisms that result in isotype switching in B cells, including: *i)* the role played by helper T cells and how major cytokines regulate this process, *ii)* the effect on antibody binding specificity for antigen, and *iii)* the ultimate importance of being able to switch isotypes. 13. Describe how somatic hypermutation contributes to affinity maturation, a selective phenomenon that increases the ability to neutralize pathogens. Distinguish between affinity and avidity of antigen-antibody interactions and understand how structures of the molecules are related to this distinction. 14. Know the human antibody classes and their major properties and functions relative to immune responses. 15. Know the function of the J chain and with which classes of antibody it associates. 17. Understand the role of Fc receptors in antibody-mediated responses and their association with follicular dendritic cells. 18. Understand the role of the classical pathway of complement activation in host protection.

Weeks 6	**Mucosal Immunity**	The mucosal immune system is often our first line of defense against microbial pathogens. It is of such great importance that it is sometimes considered the third arm of host defense, together with the humoral and cell-mediated arms. Mastery of the information regarding mucosal immunity will require that you: 1. Know the basic organization of the mucosal immune system. 2. Be able to define and distinguish O-MALT and D-MALT. 3. Be able to describe inductive sites of the mucosal immune system including components, anatomical distribution and function. 4. Be able to describe effector sites of the mucosal immune system including components, anatomical distribution and function. 5. Be able to describe how antigen traverses mucosal barriers. 6. Be able to describe Peyer's patches and the activation of IgA secreting B cells. 7. Be able to describe how lymphocytes activated locally in mucosal tissues can mediate immune responses at distant sites. 8. Be able to describe the characteristics of IgA and its major functions. 9. Know and understand how and where mucosal IgA antibodies are produced and how and where they are transported to mucosal surfaces.
Week 7	**Flow Cytometry**	Flow cytometry is an extremely powerful method for evaluating numerous characteristics and activities of individual cells within large populations of cells. Examples of such characteristics include surface membrane molecular architecture, cytoplasmic signaling, proliferation and cell cycle, differentiation and effector functions, production of soluble mediators, and various stages of cell death. In order to master your understanding of flow cytometry, it is necessary for you to: 1. Understand the fundamentals of light scatter (forward scatter and side scatter) and the chemistry of fluorescence. 2. Be familiar with the various probes and fluorochromes used in flow cytometry. 3. Be familiar with the hardware and fundamental methods used in flow cytometry. 4. Understand the basics of data analysis; histograms, dot plots 5. Be familiar with research and clinical applications of flow cytometry presented in class. For example: Cell cycle analysis, surface marker phenotyping, apoptosis, fluxes and pumps, cytoplasmic signaling, cell proliferation, etc.
Week 7	**Serological Diagnosis**	In completing the exercises provided, you are expected to be familiar with the following so as to participate in in-class discussion: 1. Difference between <u>primary</u> vs. <u>secondary</u> antigen-antibody interactions 2. Difference between the acute vs. convalescent phases of infection 3. Relationship between endpoint and titer 4. Utility of "paired" serum samples 5. What an antibody titer can (or cannot) indicate about an active infection 6. Advantages/disadvantages of using monoclonal vs. polyclonal antibodies.

		7. Difference between sensitivity vs. specificity in serological testing. 8. How false positive or false negative test results can be obtained. 9. Describe the principles and interpret the results of selected tests: - Enzyme-Linked Immunosorbent Assay (ELISA or EIA) - Western Blot (immunoblot) - direct and indirect immunofluorescence - RPR Card Test - slide agglutination test - tube agglutination test (what is the Prozone Effect?) - complement fixation (CF) test - neutralization (virus plaque inhibition) assay **Before class, in preparation for Conference Discussion, you must:** 1) perform the assigned readings; 2) study and evaluate the patient case histories provided; and 3) prepare to discuss the cases in class. Questions provided with the cases are intended to be used as a guide to the most important elements of the cases, but it should not be assumed that these will be the only questions asked during the class discussion. Familiarize yourself with the principles and methods of serologic testing described.
Week 9	**Hypersensitivity Diseases**	Hypersensitivity (allergy) is an exaggerated manifestation of normal immune responsiveness and reactivity; reactions exceed healthy limits of intensity and/or are directed at tissues that are particularly sensitive to products of such responsiveness/reactivity. Primary objectives for this lecture include being able to: 1. Distinguish the four main classes of hypersensitivity; be familiar with specific scenarios of clinical interest and mechanisms leading to hypersensitivity diseases. 2. Describe signs and symptoms of hypersensitivity disease occurring in a patient. 3. Distinguish between an allergy-associated immune response and subsequent immune reactions. What is the clinical significance of making this distinction? 4. List characteristics that distinguish Types I-IV hypersensitivity diseases. Name examples of specific pathologic states or diseases that represent each. 5. Be familiar with the specific mechanisms that lead to hypersensitivity diseases presented in class. That would require that you identify the progression of sensitizing and eliciting events for each, name the target tissue and describe the effector mechanism(s) that leads to tissue damage and the onset of symptoms. 6. Describe the main steps leading to degranulation in mast cells during Type I hypersensitivity and name some of the pharmacologically active factors released during this process and therapeutic strategies for interfering with the process. 7. Explain to what late-phase response in IgE-mediated hypersensitivity refers. 8. With regard to Type II and IV allergies, distinguish between the involvement of extrinsic antigens vs. intrinsic antigens. 9. Explain how staining a tissue for the presence of antibody or complement allow you to determine whether a Type II or III hypersensitivity scenario is in progress.

		10. Explain why it is unlikely that complications involving Hemolytic Disease of the Newborn (HDN) would exist during a first-time pregnancy. Why is ABO incompatibility during pregnancy not a more frequent problem? 11. Explain why both kidney and lung involvement may frequently be present in an individual patient with Goodpasture's Syndrome. 12. Explain why is it unattractive (but sometimes necessary) to treat a snake-bite victim with large doses of anti-toxin. 13. Distinguish the 3 variants of delayed-type hypersensitivity. 14. Identify connections between the hypersensitivities described in this session and particular autoimmune diseases. Or blood transfusion reactions? Or organ transplant rejection reactions?
Week 10	**Autoimmune Diseases**	Autoimmune diseases reflect the loss of regulation designed to prevent immune reactivity against the host's own antigens. Your primary objectives for this lecture include being able to: 1. Explain why clonal deletion mechanisms alone, are not sufficient to explain the maintenance of immunologic tolerance to self. 2. Explain the absence of disease in the presence of circulating autoreactive lymphocytes. 3. Explain how mechanisms that result in immune self-tolerance must include both physical deletion of autoreactive lymphocyte clones (central tolerance), together with peripheral tolerance designed to control autoreactive lymphocyte clones that escape central tolerance. 4. Describe mechanisms that can result in a breakdown of self-tolerance that allows autoimmunity. 5. Describe the particular pathologic mechanisms that lead to the autoimmune diseases described. 6. Explain what is meant by an individual having a "genetic predisposition" to a particular autoimmune disease. What factors may be responsible for such a predisposition? 7. Describe how an autoimmune disease may be caused by "antigenic mimicry"; Can you cite clinical examples? 8. Explain what is meant by immunologically privileged cites. Cite clinical examples of how such sites can become targets of autoimmune attack. 9. Describe how chronic infection could lead to autoimmune activities. 10. How could long-term high-dose drug administration lead to autoimmune activities. Can you cite clinical examples? 11.Explain how dysregulated cytokines can influence autoimmune activities**.** 12. List pathologic effector mechanisms that can be involved in autoimmune diseases. Site examples of diseases that involve <u>multiple</u> mechanisms? 13. Describe the specific immune mechanisms that lead to the autoimmune diseases presented in class, and the general characteristics of the diseases presented in the chart included in the introductory materials.

Week 11	**Immunodeficiency Diseases**	Immunodeficiency diseases are the result of missing or impaired components of the immune system. Your primary objectives for this lecture include being able to: 1. Explain how defects in various components of the immune system, or steps in immune developmental pathways, can lead to immunodeficiency diseases. 2. Explain how some immunodeficiency diseases are inherited, while others are transmitted as an infectious disease. 3. Explain how an immunodeficiency disease may be secondary (a sequela) to some other disease. 4. Describe the specific defects that lead to the specific immunodeficiency diseases presented in class. With regard to each disease, describe the expected functional/immunological consequence, predict what forms of infectious disease a patient carrying that defect would become most susceptible, and the phenotypic lymphocyte markers that would allow diagnosis. That is what lymphocyte markers could be used to test for deficient numbers of circulating B and T lymphocytes? How could you test for their ability to function?
Week 12	**Transplant Rejection and Graft-versus-Host Disease**	Your objectives are to become familiar with mechanisms that lead to transplant rejection so as to be able to: 1. Describe the stages and various immune effectors that are associated with the rejection of tissue/organ transplants. 2. Describe the roles played by the MHC molecules acting as antigenic targets of donor transplant rejection, as well as antigen presenting molecules of the transplant recipient. 3. Describe histological signs of allograft rejection. 4. List factors that can influence the rate and intensity of graft rejection. 5. Explain why it is useful to perform <u>both</u> tissue typing and MLC testing prior to transplantation. How is each test performed? 6. Consider potentially detrimental side-effects accompanying immunosuppressive treatments designed to prevent graft rejection. 7. Describe clinical scenarios in which bone marrow/stem cell transplantation would be a useful therapeutic strategy. 8. Describe the process of hematopoiesis. 9. Define circumstances and general pathology are associated with graft-versus-host disease.
Week 13	**Vaccine Development and Strategies**	Microbial pathogens have many specialized strategies to survive in the host, some that out-perform host defenses. In order to survive, the host may need outside help that enhances immune function. Thus, you are expected to demonstrate a mastery of issues regarding vaccination strategies by demonstrating your ability to: 1. Describe the desired results of vaccination. 2. Explain what is meant by herd immunity. 3. Distinguish between passive vs. active immunization

		4. Understand that there are both advantages and disadvantages in choosing live attenuated microbes vs. killed microbes in designing vaccines. 5. Explain what a subunit vaccine is, and what advantages it offers. 6. Explain why toxoids are better suited for vaccination than their corresponding toxins. 7. Understand why immune memory is essential for successful vaccination. 8. Explain how clonal selection is the basis for immune specificity. 9. Define the term "adjuvant", and describe mechanisms that allow an adjuvant to enhance immunization. 10. Explain why T cell-independent antigens create a special challenge, especially in young children. 11. Describe how antigenic variation is an important challenge in designing vaccine, and distinguish between antigenic drift vs. antigenic shift using influenza virus as an example. 12. Understand the global vaccine challenges of the future.
Week 15	**Immunopathology Review**	Immunopathology refers to diseases caused by impaired immune responses that inappropriately cause or allow damage to host tissues. Patient case histories are described that include examples of **exaggerated inflammatory responses, autoimmune and immunodeficiency diseases and hypersensitivity reactions**. In addition, one case involves a patient demonstrating **malignant lymphoproliferative disease**, **multiple myeloma**. Some of the cases discussed involve disease states already described in previous lectures. You will need to review these lectures for necessary information. Some data are derived from techniques that have been described in the previous conference on "Serologic Diagnosis". Review those procedures. New methods of laboratory testing are also presented in the current session including: **immunonephelometry** (for quantification of serum immunoglobulins), **serum protein electrophoresis** (for separation and semi-quantification of major protein fractions of serum), and **immunofixation electrophoresis** (to analyze abnormal patterns of specific immunoglobulins). In completing the exercises provided, you are expected to become familiar with the following so as to participate in in-class discussion: ● Basic immunobiological mechanisms leading to the immunopathologies described in this session ● Basic principles of key serologic and diagnostic tests described in this session.