MICR 5051
Introduction to Immunology
FALL 2020

Tuesdays and Thursdays **1:00-3:00 PM** **Provider: CANVAS and MS Teams**

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

OFFICE HOURS: By appointment; Office 423D/MS Teams
For appointment, contact instructor by email.

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READ THIS DOCUMENT CAREFULLY - YOU ARE RESPONSIBLE FOR ITS CONTENTS.

CoVID-19 Disclaimer: In light of expectations from the University designed to keep us safe during the CoVID-19 pandemic, many of our usual activities have been transformed into remote learning strategies. It will be necessary for each student to have access to a computer with Internet/WiFi and audio/video capability. The following describes the expectations and mechanics of the 2020 MICR 5051 course during the current circumstances. Additional addenda to this syllabus will be provided as needed.

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

- Demonstrate academic professionalism by consistently and fully preparing for, and participating in, class activities.
- Demonstrate a commitment to learning by completing all assignments and readings by or before due-dates.
- 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 those specific lesson objectives routinely.** They provide a direct roadmap to what you are expected to learn and how you are likely going to be asked to apply them in discussions and on exams.

By the end of this course, each student should 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 to 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.
- the principle hallmarks of the adaptive immune system (diversity, specificity, memory), and how these hallmarks differ from those of non-adaptive (innate) immunity.
- the 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**.

- **Reading Assignments** – Required reading assignments for any of these activities are posted in the schedule of class meetings (shown below) and are never considered optional. Anything in required readings is considered testable on exams, although there will be no attempt to fish out tiny details just to trip up students. Mandatory readings are primarily found in required textbooks (see below). However, certain reading assignments are found on websites; links to those sites are found in the schedule of class meetings.
- **Lectures –**Because of our unusual circumstance and the requirement to provide remote delivery of class material, lectures will be provided as recorded video presentations using the MP4 file format. The rationale for recording lectures is to 1) avoid technical glitches that sometimes accompany real-time streaming, and 2) to ensure that "disconnects" between you and the lecture content can be minimized; that is, you can stop, start and rewind recordings at will, and will have the opportunity to review the lectures as often as desired. Lecture videos will remain available for the duration of the course. Periodic online class meetings via MS Teams will be scheduled for reviews of the lecture material. Lecture videos will be available and should be viewed on the weekly schedule shown in the class schedule below; you must keep up with that schedule. Last minute "video cramming" is a very bad idea. To counter any technical issues, the lecture videos can be accessed in either of two ways. First, links to lectures are posted on the MICR 5051 CANVAS site directly embedded in the relevant modules. Or links to a cloud site (MicrosoftStream) are inserted into the class schedule found in the syllabus (also found on CANVAS).

  Pdf slides. To enhance the use of the lecture videos, each lecture will be accompanied by Pdf-converted PowerPoint slides posted in the Course Content folder on the MICR 5051 CANVAS website. The Pdf files should be downloaded onto your computer. These Pdf files are provided with active fields that will allow you to type notes (side-by-side windows containing the video and the Pdf slides is recommended). Note that you are responsible for all information in the lecture materials. You should not assume that all testable information is found only in posted Pdf slides. Lecture videos may expand and enhance information in the slides. **So, take good notes because any information discussed in the videos, whether or not included in the slides, is considered testable.**

  Animations – ** You are provided with a collection of online animated reviews to enhance and clarify lecture presentations and to give a sense of the dynamics of immune activities sometimes overlooked in presentations of static slides. Some animations are more detailed than information presented in lectures. Although watching these excellent animations is **highly encouraged, students will not be held responsible for those additional details.
- **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). Online Reviews are not intended to represent a thorough coverage of the material, but only as examples of what you might find on examinations and to allow you to gauge your level of preparedness. Each online review, when completed on time, 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. An **explicit 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, you **must become familiar with all cases of the day** (including any test results and images) and relevant background information. Information needed to prepare for discussions is available in **textbook** reading assignments, introductory **online comments** that accompany each session, and from **lecture presentations**. While collecting information from readings etc, **students should fill in and submit templates** that accompany each case. Each entire set of CD templates that accompany each session, when completed and submitted on time, is **worth 0.2 bonus point that will be added to your final exam average at the end of the course** (see grading information below). Templates should be studied prior to the conference session to be prepared for discussion; it is acceptable to use/view templates during the conference session as an aid during discussions. Although each case history is accompanied by a series of questions that will be the starting point for our discussions, you should not assume that simply looking up answers to those few questions is sufficient to fully participate in the discussion. Again, you will be adequately prepared only if you fill out the information templates for each case.

  CD sessions will be highly interactive. Due to current circumstances that prevent us from meeting face-to-face, discussions will occur using the **MS Teams platform**. Detailed instructions regarding the mechanics and logistics of these sessions will be provided as we get closer to the dates of those discussion later in the semester.

  In general, to promote widespread participation, **the instructor will make use of a picture roster for engaging the students**. That is, participation is not voluntary, and you may 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. 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 and Participation

In order to achieve the expected level of competency, students must be fully engaged. Therefore, attendance when appropriate and full participation is expected.

It is expected that all lecture videos will be viewed during the weeks in which they are scheduled.

Attendance is **required** for all Conference Discussion and laboratory sessions. Attendance is defined as being present and ready to begin at the specified class time. If you are unable to attend a session, **NO MATTER THE REASON**, this will be considered an absence.

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 an unexcused absence.

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 students with an excused absence. Instructors do not have an obligation to provide remediation for missed work to students with an unexcused absence.

Tardiness. For synchronous class meetings (live streaming), 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). Repeated tardiness 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.

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 if you 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, conferences, and 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. Note that in addition to being helpful study aids, credit for the numerous submissions adds up to a substantial number of bonus points that may significantly affect your final course grade.

Examination Protocol – In light of the unusual nature of remote/virtual examinations, and in order to ensure the integrity of this course for all students, each student will be expected to sign an Official Code of Conduct agreement at the time of each examination.

Exams will be composed of multiple choice, short answer, and essay questions. Certain questions will be accompanied by images, so it is **imperative that you study images** (particularly those presented in lectures and class discussions).

Brief instructions will be given via MS Teams by the instructor prior to the start of the exam. You will not be allowed to ask questions of the instructor **once the examination has started** (except to point out potential typographical errors in the exam).

Late arrival to exams - Exams will be timed and will begin at a predetermined time. **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 miss an exam, you may be eligible for taking a make-up exam (see below).

Grading procedures – Exam results will be provided as quickly as possible. With regard to multiple choice portions of the exams, statistical determination 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. Grades will be posted in each student's MICR 5051 CANVAS grade book. No "challenges" are allowed. However, a time will be scheduled so that students may review concepts of concern to them.

Make-up Examinations – If you must miss a scheduled exam for a serious reason you must request an excused absence (see above) from the Course Director. Acceptable "serious reasons" usually involve serious illness or injury to you (doctor's excuse may be required) or a 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

Information regarding accommodations for disabilities is available in the UTHSCSA Catalog. If you wish to request an accommodation, you must submit the appropriate request for accommodation under the American with Disabilities Act (ADA, form 100) to the GSBS Associate Dean of Student Affairs. 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

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

You have been issued a University e-mail address and account at the time of your 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, **you are expected to check your university email inboxes on a regular basis** 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.

ELECTRONIC DEVICES

Cell phones or other potentially disruptive devices must be turned off during all synchronous/streaming class meetings and exams.

MICR 5051

INTRODUCTION TO IMMUNOLOGY

2020 CLASS SCHEDULE

Tuesdays and-Thursdays 1:00-3:00 PM

MODULE 1				
WEEK	**DATE**	**TOPIC (linking to lectures will require login)**	**Reading Assignment* and relevant CANVAS Reviews**	**Instructor and Format**
Week 1	Aug 25	Overview of Host Defenses Lecture Video – Overview 1 Lecture Video – Overview 2	PAR: Ch1-3 HIW: Ch1, Ch2	Krolick (Lecture)
	Aug 27	Lecture Video – Overview 3 Lecture Video – Overview 4	[ONLINE REVIEWS 1-4]	Krolick (Lecture)
Week 2	Sept 1	Lymphocyte Receptors for Antigen Lecture Video – Lymphocyte Receptors 1 Lecture Video – Lymphocyte Receptors 2	PAR: Ch4.1-4.12; Ch5.1-5.5	Krolick (Lecture)
	Sept 3	Lecture Video – Lymphocyte Receptors 3 T Cell Development, Antigen Recognition Lecture Video – T Cell Development/Function 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 8	Lecture Video – T Cell Development/Function 2 Lecture Video – T Cell Development/Function 3 and 3a	PAR: Ch7.1-7.2; Ch7.8-7.14	Krolick (Lecture)
	Sept 10	Lecture Video – T Cell Development/Function 4 Lecture Video – T Cell Development/Function 5	PAR: Ch13.6 HIW: Ch.8, Ch.9	Krolick (Lecture)
Week 4	Sept 15	NO CLASS – Voluntary Review		
	Sept 17	Exam #1		

MODULE 2

WEEK	DATE	TOPIC (linking to lectures will require login)	Reading Assignment* and relevant CANVAS Reviews	Instructor and Format
Week 5	Sept 22	Humoral Immunity Lecture Video – Humoral Immunity 1 Lecture Video – Humoral Immunity 2	PAR: Ch4.13-4.17; Ch6.1-6.8; Ch6.11-6.15 HIW: Ch.3, Ch.7	Krolick (Lecture)
	Sept 24	Lecture Video – Humoral Immunity 3	PAR: Ch9 HIW: Ch.10	Krolick (Lecture)
Week 6	Sept 29	Lecture Video – Humoral Immunity 4	[ONLINE REVIEWS 9-12]	Krolick (Lecture)
	Oct 1	Mucosal Immunity Lecture Video - Mucosal Immunity 1 Lecture Video - Mucosal Immunity 2	PAR: Ch10 HIW: Ch.11 [ONLINE REVIEWS 13-14]	Krolick (Laecture)
Week 7	Oct 6	Flow Cytometry 1 and 2	Flow Cytometry Overview	Gorena (Lecture)
	Oct 8	Serologic Diagnosis 1 and 2 Video Intro/MS Teams Discussion	Intro comments in CANVAS Handout	Krolick (Conference)
Week 8	Oct 13	NO CLASS – Voluntary Review		
	Oct 15	Exam #2		

MODULE 3

WEEK	DATE	TOPIC (linking to lectures will require login)	Reading Assignment* and relevant CANVAS Reviews	Instructor and Format
Week 9	Oct 20	NO CLASS		
	Oct 22	Hypersensitivity Diseases 1 and 2 Video Intro/MS Teams Discussion	Intro Comments in CANVAS PAR: Ch14 HIW: Ch.12	Krolick (Conference)
Week 10	Oct 27	NO CLASS		
	Oct 29	Autoimmune Diseases 1 and 2 Video Intro/MS Teams Discussion	Intro Comments in CANVAS PAR: Ch16 HIW: Ch.12	Krolick (Conference)
Week 11	Nov 3	NO CLASS		
	Nov 5	Immunodeficiency Diseases 1 and 2 Video Intro/MS Teams Discussion	Intro Comments in CANVAS PAR: Ch13.8-13.16; 13.17-13.20; 13.24 HIW: Ch.13	Krolick (Conference)
Week 12	Nov 10	Vaccine Development and Strategies Lecture Video - Vaccines 1 Lecture Video - Vaccines 2	PAR: Ch.11 HIW: Ch.14 [ONLINE REVIEW 15]	Krolick (Lecture)

	Nov 12	**ONLINE SELF-STUDY – Immune Evasion** **(No in-class meeting)** ***~~Vaccine Conference~~*** **~~(Nov 12-13)~~**	**PAR: Ch13.1-13.7**	
Week 13	**Nov 17**	**NO CLASS**		
	Nov 19	**Transplant Rejection and Graft-versus-Host Disease 1 and 2** **Video Intro/MS Teams Discussion**	**Intro Comments in CANVAS** **PAR: Ch5.23; Ch15.1-15.12;**	**Krolick (Conference)**
Week 14	**Nov 24**	**Thanksgiving Break**		
	Nov 26			
Week 15	**Dec 1**	**NO CLASS** **Begin studying for final exam!**		
	Dec 3	**Immunopathology Review 1 and 2** **Video Intro/MS Teams Discussion**	**Intro Comments in CANVAS Handout**	**Krolick (Conference)**
Week 16	**Dec 8**	**Comprehensive Final Exam**		

* **PAR** = Required readings: Parham, P. (2014). *The Immune System, 4th edition*. New York: Garland Science.

HIW = Recommended readings: Sompayrac, L. (2019) *How the Immune System Works, 6th 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).
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: <u>Development</u>: 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. <u>Activation</u>: 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. <u>Effector functions</u>: 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 the 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.