HOST DEFENSE
COURSE OBJECTIVES

At the completion of Host Defense, you will be able to describe the immunologic strategies employed by humans to mount an effective immune response and to counter infectious challenge. You will be able to describe the cellular and molecular components of the immune system, how they function in normal and pathologic responses; more importantly, how the basic knowledge in immunology could be used by the clinician to understand better the pathology which leads to a more effective therapeutic approach to benefit the patient.

LEARNING OBJECTIVES

MEDICAL KNOWLEDGE

Identify the functions of the critical components (innate, adaptive and specialized) of the immune system.

Describe the components of the innate system (physical/mechanical and collaborating system of cells, cytokines, chemokines, and cell surface molecules).

Understanding the general histologic characteristics and functions of the cells of the innate and adaptive immune systems including neutrophils, macrophages, basophils/mast cells, eosinophils, natural killer cells, dendritic cells, and various subsets of lymphocytes.

State the clinically relevant growth factors or cytokines (e.g., G-CSF) that drive the development of cells of the innate and adaptive immune systems and the clinical implications of immune deficiencies caused by the lack of these growth factors, cytokines.

Describe the general morphology and organization of primary and secondary lymphoid organs, particularly about antigen transport and processing and the initiation of cellular, cytokine and antibody responses.

Identify the role of Toll and other innate system receptors in the immune response and defense of the host.

Understanding the differential roles of cytokines in driving distinct cellular immune responses and how to take advantage of the knowledge to manipulate cytokine-driven immune response as well as the clinical effect of cytokine abnormalities/deficiencies.

Describe the pro-inflammatory molecules IL-1, 6, 8, and TNF-alpha, the clinical effect of their excess or deficiency (as observed in toxic shock and immunodeficiency states), and their potential targets for pharmacologic manipulation.

Understanding the complement system, how complement proteins are activated and how the system interacts with the immune system. Understanding the consequences of complement system activation in resolving infection or promoting diseases.

State the general characteristics of the adaptive immune system including the concepts of

specificity, clonal expansion, memory, the function of transcription factors, and genes specific to the adaptive and innate immune systems.

Explain the diversity of MHC molecules, and how that diversity differs from immunoglobulin and T cell receptor diversity.

Identify how MHC molecules present antigens, and how antigens are processed for the presentation.

Recognize the primary importance of T lymphocyte activation in facilitating all adaptive immune responses.

Understanding the essential functions of the thymus in T cell development, the recognition of self versus non-self; moreover, the establishing of tolerance.

Recognition and understanding the functional deficiency of the thymus in relating to clinical implications of athymic or thymic dysfunction, autoimmune diseases, and T cell immunodeficiency diseases.

Understand the various types of dendritic cells and their functions the immune response.

Compare the role of cytokines in the five basic T cell pathways:

a. T helper response (Th1 by IL12 and Th2 by IL4)
b. T regulatory response by TGF-β
c. Th17 response by IL6, IL21 and IL23,
d. T cytotoxic response by IFN-γ.
e. Thf response by IL6

Compare the five subsets of T lymphocytes and their respective cytokines:

a. Th1 macrophage cytotoxicity and CD8 antigen-specific cytotoxicity/IFNγ
b. Th2 helper functions for B cells/IL-4, 5, 6, 10
c. CD3, 4, 25, FoxP3 regulatory functions/TGF beta and IL10
d. Th17 mediated chronic inflammation via IL17
e. Thf and B cell response (Il4, 10 and 21)

Be able to Identify distinct types of leukocytes by specific cell surface markers identified by antibodies (CD3, 4, 8, 14, 19, and 56).

Describe the essential functions of B lymphocytes and plasma cells including the concepts of antibody diversity and somatic hypermutation.

Explain the structure and function of the mucosal immune system.

Describe the physiologic significance of communication between the immune system and the microbiota.

Recognize how the effector functions of antibodies (humoral response), T cells, macrophages, neutrophils, and NK cells can eliminate pathogens or lead to pathology.

Explain how cells in both innate and acquired immunity can encounter a pathogen first at one site, and then fight an infection at distal sites.

Describe the classical classification of hypersensitivity syndromes; Type 1 (IgE mediated), Types 2 and 4 (loss of tolerance), Type 3 (immune complex-mediated).

Recognize the strategies used by tumor cells to evade destruction by the immune system, including conceptual mechanisms of inappropriate suppression of cytotoxic responses to tumors, the logic of histologic and array methods to predict clinically response and a general rationale for treatment methods for tumors based on these concepts.

Compare and contrast the clinical implications of specific types of immune response defects-including the rationale for determining the mode of treatment and expected pathophysiology for:

a. Isolated B cell deficiency (e.g., X linked agammaglobulinemia),
b. Isolated T cell deficiency (e.g., thymic aplasia),
c. Combined B and T cell deficiency (e.g., severe combined immunodeficiency or SCID),
d. Stem cell deficiencies, and
e. complement deficiencies and intracellular white cell deficiencies (e.g., chronic granulomatous disease).

Relate the general concepts of how microbial agents can evade the immune system, and certain microbial antigens (super antigens) can excessively activate inflammatory cytokine systems.

Describe and understand the mechanisms by which the MHC system is activated and dictates the intensity of an anti-allograft response.

Discuss the utilization of critical aspects of the immune system in response to an allograft and the implications of each for clinical intervention.

Recognize the importance of maternal/fetal immunology-especially mechanisms of rejection prevention.

Discuss the general concepts of how physicians can exploit their knowledge of the immune system to protect from disease by use of vaccines, modification of immune effector systems (e.g., amplification of T regulatory cells), modulation of immune effector cells, and cytokine/chemokine systems.

Describe the immunological effector mechanisms that are associated with autoimmune disease states.

Organize the utilization of the clinical laboratory to assess immunologic functions and deficiencies including specific immunologic tests:

a. flow cytometry for enumeration and clonality of lymphocytes and other immune effector cells,
b. Serum protein electrophoresis and light chain detection for quantification and clonality of antibodies,
c. Immunofluorescence techniques for antibody detection,
d. Skin testing for in-vivo assessment of T cell function, and
e. the logic of array analysis for detection of specific patterns of immune responses.

INTERPERSONAL AND COMMUNICATION SKILLS

Demonstrate the ability to effectively communicate and work collaboratively together with peers in the small group setting to address problems of immunological significance successfully.

Contribute to the education of peers by actively engaging in small group sessions.

PRACTICE-BASED LEARNING AND IMPROVEMENT

Critically evaluate one's performance in the course to identify strengths and personal limitations in either immunological knowledge or study methods; develop learning goals to address any deficiencies, and actively seek out assistance from appropriate sources to successfully remediate any deficiencies.

Demonstrate an ability to use online resources to objectively identify and evaluate the primary basic scientific and clinical literature relevant to Host Defense small group sessions.

PROFESSIONALISM

Demonstrate professional behavior by completing all course requirements, including course evaluations, in a timely manner.

Demonstrate professionalism by behaving in a professional, courteous, and respectful manner when engaged in course activities or interacting with course faculty and staff.

Demonstrate responsibility and accountability by attending and being punctual at all required course activities.

Demonstrate professional behavior by requesting any excused absence from required course activities well ahead of the scheduled date.

Demonstrate professional behavior by responding to direct communication from the Course Director in a timely fashion, particularly in circumstances when a face-to-face meeting is requested to discuss issues related to academic performance.

Demonstrate professional and ethical behavior by honestly completing course examinations without attempting to seek an advantage by unfair means; and by reporting any unethical behavior of peers to the course administration.