

HOST DEFENSE COURSE GOALS AND OBJECTIVES

At the completion of Host Defense, you will be able to describe the immunologic strategies employed by humans responding to the threat of infection. Specifically, you will be able to describe the cellular and molecular components of the immune system, how they function in normal and pathologic responses and then visualize how a clinician can exploit this knowledge for the benefit of the patient.

LEARNING OBJECTIVES

I. Medical Knowledge

Students will know and be able to discuss/utilize the following concepts about the Immune System:

1. The functions of the major parts (innate, adaptive and specialized) of the immune system;
2. The components of the innate system (physical/mechanical and a collaborating system of cells, cytokines, chemokines and proteins);
3. The components of the physical/mechanical system including the skin, respiratory, gut, tears and saliva and implications of compromised barriers for bacterial infections;
4. The general histologic appearance and functions of the cells of the innate and adaptive systems including neutrophils, macrophages, basophils/mast cells, eosinophils, natural killer cells, dendritic cells and lymphocytes;
5. The clinically relevant growth factors (e.g. G-CSF and Veg F) which drive the development of cells of the innate and adaptive systems and the clinical implications of growth factor deficiencies;
6. The general morphology and organization of primary and secondary lymphoid organs, particularly in relation to antigen transport and processing and the initiation of cellular, cytokine and antibody responses;
7. The general concepts about toll and other innate system receptors and how they dictate types of immune responses and abnormalities in such responses when they are abnormal or missing;
8. The role of cytokines in dictating different types of immune responses-including pharmacologic manipulations of cytokine responses and clinical effects of cytokine abnormalities/deficiencies;

9. The pro-inflammatory tetrad of Il-1, 6, 8 and TNF-alpha, the clinical effects of their excess and deficiency as observed in SIRS or toxic shock and in immunodeficiency states, and their potential for pharmacologic manipulation;
10. The general mechanism and consequences of complement system activation;
11. The kinin/prostaglandin systems-important but learned elsewhere in the curriculum;
12. The general characteristics of the adaptive system including concepts of its specificity, clonal expansion, memory and genes specific to the adaptive and innate systems;
13. The primary importance of T lymphocytes in facilitating all adaptive immune responses;
14. The role of the thymus in T cell development, the recognition of self versus non-self and tolerance, together with the clinical implications of thymus absence or dysfunction, including T cell immunodeficiencies and autoimmunity;
15. The role of dendritic cells in influencing types of immune responses;
16. The role of cytokines, cytokine receptors and cytokine loops in immunological responses, including the specific core cytokines which initiate the four basic T cell pathways –
 - a. T helper response (Th1 by Il-12 and Th2 by Il-4),
 - b. T regulatory response by TGF beta,
 - c. T-17 response by Il 6 and 23, and
 - d. T cytotoxic response by IFN gamma;
17. The four major subsets of T lymphocytes and their respective cytokines –
 - a. Th2 helper functions for B cells/Il-4, 5, 6, 10, and 21,
 - b. Th1 macrophage cytotoxicity and CD8 antigen specific cytotoxicity/IFN gamma and Il-21,
 - c. CD3, 4, 25, foxP3 regulatory functions/TGF beta and IL-10,
 - d. Th17 mediated chronic inflammation/Il-17;
18. The identification of T and B cells by specific cell surface markers (CD3, 4, 8, 19, and 20);
19. The basic functions of B lymphocytes and plasma cells including the concepts of antibody diversity and somatic hypermutation;
20. The structure and functioning of the mucosal immune system including IgA antibodies and antigen processing in the gut;

21. The traditional classification of hypersensitivity syndromes caused by immunologic mechanisms-Type 1 (IgE mediated), Types 2 and 4 (loss of tolerance), Type 3 (immune complex mediated);
22. The concept that Hypersensitivity Diseases are almost always multi-factorial;
23. 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 clinical responses to tumors and a general rationale for treatment methods of tumors based on the above concepts;
24. The clinical implications of specific types of immune response defects-including the rationale for determining the type of infection and its treatment –
 - a. including 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. Chediak-Higashi or chronic granulomatous disease);
25. The general concepts of how microbial agents, especially viruses, can evade the immune system and certain microbial antigens (superantigens) can massively activate inflammatory cytokine systems;
26. The mechanisms of the MHC system in its activation and dictation of intensity of an anti-allograft response;
27. Maternal/fetal immunology-especially mechanisms of rejection prevention;
28. The utilization ,at varying time points, of all arms of the immune system by the host in its response to an allograft and the implications for clinical interventions;
29. The general concepts of how physicians can exploit their knowledge of the immune system to protect hosts from disease including vaccines, modification of immune effector systems(ex-amplification of T regulatory cells), modulation of immune effector cells and cytokine/chemokine systems;
30. Physiologic significance of communication among the nervous, neuroendocrine and immune systems;
31. With respect to the utilization of clinical laboratory to assess immunologic functions and deficiencies, students should know what the following specific immunologic tests measure and when each should be ordered –

- 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.