

Training Program Director's Allergy & Immunology Core Curriculum Outline 2005

The Training Program Directors' (TPD) Core Curriculum Outline is updated every three years by the Core Curriculum Subcommittee of the TPD and is consistent with the requirements of the Residency Review Committee for training in allergy and immunology. The TPD Core Curriculum outline serves as a guide for: (1) TPD and trainees in meeting the requirements of the Residency Review Committee, (2) the Reading List Subcommittee, (3) the In-Training Examination Subcommittee. The intent of this outline is to provide a framework for training programs to design an individualized course of study that supplements the diverse strengths and weaknesses of each fellowship training program and faculty.

I. Basic Immunology

Strategies and resources for acquiring the body of knowledge within the Basic Science Core Curriculum might include structured didactic programs, TPD-recommended textbooks, TPD reading list, and regional or national seminars. The knowledge obtained through the basic science curriculum serves as the foundation for diagnosis and therapy for immunologic and allergic disorders.

A. Overview of the Immune System

1. Organization and Function of the Immune System
 - a. Thymic development and shaping peripheral systemic T-cell immunity
 - b. Cutaneous Immunity
 - c. Intestinal/Mucosal Immunity
 - d. Primary Immune Function of Cellular Elements of the Immune System
 - i. T-cells
 - ii. B cells
 - iii. Neutrophils
 - iv. Eosinophils
 - v. Mast cells
 - vi. Basophils
 - vii. Antigen presenting cells
 - viii. Natural Killer Cells
 - ix. Platelets

B. Immune Mechanisms

1. Innate versus adaptive immunity
 - a. complement and the innate immune response
 - b. Pattern Recognition Receptors (MBP, Toll-like Receptors, CD14 etc.)
 - c. Natural Antimicrobial Agents
 - i. Reactive Oxygen Species
 - ii. Releasable granule proteins (defensins, lactoferrin, cathelicidins)
2. The major histocompatibility complex – molecular structure and function
3. Immunogenetics – Gene rearrangements in the generation of immune system diversity
4. Antigen-presenting cells – processing and presentation of conventional and superantigens
5. Gell and Coombs Classification of Immune Responses
 - a. Type I –Immediate Hypersensitivity Response
 - i. IgE binding and signal transduction

- iii. preformed and newly synthesized mediator release
 - iv. late phase reactions
 - b. Type II – Antibody induced reactions Response
 - c. Type III – Immune-Complex mediated reactions
 - d. Type IV – Cell mediated /Delayed Hypersensitivity Response
- 6. T cell mediated immunity
 - a. T cell activation – T cell receptor structure and function, epitope recognition and accessory molecules in signal transduction
 - b. Cytokines and co-stimulatory molecules in T cell activation
 - c. T cell mediated immune responses – participating cells. Properties and functions of antigen presenting cells.
 - d. T cell subsets
 - e. Regulatory T cells and memory cells
 - f. NK T cells
- 7. B cell mediated immunity
 - a. B cell activation – cytokines and signal transduction
 - b. Epitope recognition and immunoglobulin production
 - c. Maturation of B lymphocytes
 - d. Maturation of the antibody response
 - e. Biologic process initiated by antibody: opsonization, complement fixation, antibody dependent cell mediated cytotoxicity
 - f. IgE mediated immediate and late phase reactions
 - g. Immune complexes – immunologic properties and mechanisms of clearance
- 8. Other immune and inflammatory mechanisms
 - a. Natural killer cells, their CD markers and functions
 - b. Lymphokine activated killer cells and their effects
 - c. Cutaneous basophil hypersensitivity
 - d. Kinin mediated inflammation
 - e. Arachidonic Acid Metabolites and Inflammation
 - f. Cytokines/Chemokines and their receptors
 - g. Growth factors
- 9. Receptor ligand interactions in immune functioning – Signal transduction resulting from receptor ligand interaction. Genetic polymorphisms producing gain or loss of function.
- 10. T & B cell Immunologic Memory(Including CD markers of cells involved in immunological memory)

C. Mucosal Immunity

Mucosal Barrier Function

1. Innate defenses
 - a. Barrier function and local enzyme systems
 - b. Normal Flora
 - c. Complement
 - d. Defensins
2. Antigen transport
3. Adaptive Immunity
 - a. Responses to bacteria viruses and parasites
 - b. Mucosal Immunoglobulins

- i. Secretory IgA
 - ii Ig Transport
 - iii FcγRII function
 - iv Mucosal associated lymphoid tissue (MALT)
4. Passive immunization

D. Transplantation Immunology

1. Allograft rejection
2. Graft versus host reactions (GVHR)
3. Maintenance of tolerance

E. Tumor Immunology

1. Tumor specific and tumor associated antigens
2. Oncogenes, translocations and tumor suppressor genes

F. Immunoregulatory Mechanisms

1. Tolerance
2. Idiotypic networks
3. Apoptosis
4. Anergy

G. Laboratory Measurements

1. Principles and methodology of:
 - a. measurements of immunoglobulin levels, immunoglobulin classes and subclasses
 - b. serologic testing
 - i. ELISA, immunoblot
 - ii. autoimmune serology
 - iii. in vitro testing techniques for specific IgE
 - iv. RAST Inhibition techniques
 - v. serologic testing for infectious disease
 - c. flow cytometry -cell surface marker and intracellular techniques
 - d. Cellular functional responses
 - i. Chemotaxis and adhesion
 - ii. mitogen or antigen induced proliferation and activation
 - iii. phagocytosis and intracellular killing
 - iv. cellular cytotoxicity
 - e. measurement of immune complexes, cryoprecipitable proteins, total serum complement activity, complement components and C1 Inhibitor assays.
 - f. histocompatibility typing
 - g. genetic techniques including TRECs, PCR and use of probes.
 - h. hybridoma and monoclonal antibody technology
 - i. cytokine and mediator measurement
2. Test-performance characteristics: principles of sensitivity, specificity, predictive value, and ROC analysis
3. Unproven and inappropriate diagnostic tests for allergic and immune deficiency diseases.

II. Anatomy and Physiology

A. Normal anatomy and physiology

1. Upper airway -nose, sinuses, middle ear
2. Lower Airway
3. Skin
4. Gastrointestinal Tract
5. Lymphoid Tissue

B. Pathology of primary atopic disorders

1. Asthma (including airway remodeling)
 - a. Children
 - b. Adults
2. Rhinitis and rhinosinusitis
 - a. Allergic
 - b. Infectious
 - c. Nonallergic
 - d. Nasal polyps
3. Atopic Dermatitis
4. Early and late responses to allergen challenge
 - a. nasal
 - b. bronchial challenge
 - c. cutaneous challenge
5. Role of structural cells
 - a. epithelium
 - b. endothelium
 - c. smooth muscle
 - d. fibroblasts
 - e. mucociliary cells

C. Measurements and interpretation of lower airway function

1. Spirometry: FVC, FEV1, FEV/FVC, FEF 25-75, Flow volume loop, pre-and post-bronchodilator values
2. Provocative challenges (exercise, methacholine, allergen, other): indications, performance, and interpretation, predictive value of asthma

III. Pharmacology

A. Pharmacology and pharmacokinetics of drugs used in allergy/immunology

1. Glucocorticoids
2. Beta-Agonists and Antagonists
3. Mast Cell Active Agents (Cromolyn / Nedocromil)
4. Cyclooxygenase and Leukotriene Pathway Modulators
5. Anticholinergics
6. Theophylline
7. Antihistamines
8. Immunosuppressive Agents (calcineurin inhibitors, methotrexate, azathioprine etc.)
9. Immunomodulatory Medications (see section V.G)
10. Agents and Principles of Aerosolized Respiratory Treatments
11. Topical Dermatologic and Ophthalmic Therapy

12. Vaccines against transmissible agents
13. Drug Interactions

B. Allergenic Proteins and Extracts for Diagnosis and Treatment

1. Inhalant Allergenic Protein Sources
 - a. Pollen and Mold/Fungi
 - b. Insects and Arachnids
 - c. Animals
 - d. Aerobiology and environmental assessment of allergens, irritants and pollutants
2. Allergen Extract Preparation and Standardization Methods
3. Clinical Use of Allergenic Extracts as Therapeutic Agents

IV. Research Principles

- A. Research ethics
- B. Experimental design
- C. Data analysis, biostatistics and use of computer database, spreadsheet and statistical analysis applications.
- D. Epidemiology
- E. Informed Consent (ABAI content added)
- F. Adverse Event Reporting (ABAI content added)
- G. Grant Writing

V. Clinical Sciences

The subspecialty of allergy and immunology encompasses three major clinical areas: allergic diseases and asthma, immunoregulatory disorders, and immunodeficiency diseases. It is the intention of allergy and immunology training programs to train residents as expert consultants and accomplished practitioners in these areas. Moreover, the scholastic approaches to maintain understanding of recent advances and current concepts of the specialty over a professional lifetime must be instilled during the training program.

The following is an outline of the diseases about which allergy and immunology fellows must be knowledgeable. Training programs may vary their emphasis on the basis of mission, expertise, and resources. It is expected that all residents be trained in the physiology, pathology, differential diagnosis, and treatment of such diseases with understanding of the use therapeutic modalities including mechanisms of action, dosing, adverse effects, and costs of therapy. Explicit instruction should also be given on the importance of behavioral studies and bioethics in regard to clinical trials and appropriate use of diagnostic and therapeutic techniques.

A. Allergic Diseases and Related Disorders

1. Upper airway disease
 - a. Rhinitis, sinusitis, nasal polyposis, otitis (bacterial and serous), and laryngeal disorders
 - b. Clinical skills and interpretive strategies for diagnosis of upper airway diseases: skin testing (epicutaneous and intracutaneous); cytology of nasal secretions; understanding of indications for and methodology of nasal challenges; rhinoscopy; nasal and ear examination; gross assessment of upper airway imaging studies.

2. Eye Disease
 - a. Allergic and vernal conjunctivitis, iritis, iridocyclitis
 - b. Clinical skills: eye examination
3. Dermatologic disease
 - a. Urticaria, angioedema, dermatographia, atopic dermatitis, contact dermatitis, urticaria pigmentosa, bullous disease, drug rashes, erythema multiforme and toxic epidermal necrolysis, erythema nodosum, and other immunologic skin diseases.
 - b. Clinical skills: proper cutaneous examination, patch testing, drug skin testing (immediate and delayed type hypersensitivity skin tests), testing for physical urticaria/angioedema, and an understanding of dermatopathology and immunofluorescent tests.
4. Lower respiratory tract disease
 - a. Asthma and related disorders (exercise-induced, allergic bronchopulmonary aspergillosis, sulfite-related, and intrinsic); including assessment of severity and control; hypersensitivity pneumonitis; chronic obstructive pulmonary disease; bronchitis, croup & RSV; cystic fibrosis, immotile cilia syndrome, sarcoid, occupational lung disease, chronic cough
 - b. Specific skills and interpretative strategies to be acquired: chest exam, interpretation of pulmonary function testing, bronchial challenges, sputum and exhaled breath analysis, and gross interpretation of imaging studies.
5. Drug Allergy (See dermatologic disorders and anaphylaxis)
 - a. Distinction between hypersensitivity and intolerance
 - b. Cytotoxic, immune complex and delayed hypersensitivity reactions
 - c. Aspirin and NSAID reactions
 - d. Reactions to Vaccines
 - e. Photoallergy, phototoxicity, drug fever, and serum sickness reactions
 - f. Clinical skills – specific testing and provocative challenges
6. Adverse reactions to ingestants
 - a. Food sensitivities-IgE mediated, food intolerance, gluten sensitivity
 - b. Food-additive reactions
 - c. Eosinophilic esophagitis and gastroenteritis
 - d. Clinical skills mastered: set up double blind placebo controlled food challenge, interpretation of skin prick and in vitro testing to foods
7. Anaphylaxis and Anaphylactoid Reactions
 - a. Causes (ingestants, exercise, allergy immunotherapy, latex, radiocontrast media) case definition and common presentations.
 - b. Laboratory evaluation of anaphylactic episode, allergy testing, tryptase
 - i. Acute treatment
 - ii. Patient education, use of Epi-pen, Epi-pen Jr.
 - c. Treatment of Anaphylaxis including Cardiopulmonary Resuscitation
8. Insect Hypersensitivity
 - a. Classes of insects associated with hypersensitivity
 - b. Skin prick, intradermal and in vitro testing to stinging insects
 - c. Predictive value of clinical history and testing for adult and pediatric population
 - d. Algorithm for history positive, test negative, stinging insect reactive patient

- e. Venoms, formulation, schedule and duration of immunotherapy.
- 9. Economic costs of diagnosis and treatment of allergic diseases
- 10. Psychosocial aspects of allergic disease and chronic illness, failure of adherence to therapy

B. Immunodeficiency Diseases

- 1. Primary immunodeficiency diseases (including clinical presentation, diagnostic approach, cellular profile, genetic basis, prognostic factors and therapeutic options)
 - a. Combined immunodeficiencies syndromes
 - b. Predominant antibody deficiencies
 - c. Other well defined immunodeficiency syndromes
 - d. Complement deficiencies including hereditary acquired C1 inhibitor deficiency
 - e. Congenital defects of phagocytic number, function and adhesion
 - f. Clinical skills for diagnosis and treatment
- 2. Acquired immunodeficiency diseases
 - a. Due to infection, AIDS and other
 - b. Nutrition and metabolic related
 - c. Associated with malignancy and infectious processes
 - d. Iatrogenic immunodeficiency
 - e. Clinical skills for diagnosis and treatment

C. Immunoregulatory Disorders

Interpretation of physical findings, diagnostic tests and management of:

- 1. The Vasculitides (Small, Medium and Large vessels)
- 2. Immune rheumatic disorders
- 3. Immune renal disorders
- 4. Immune endocrine and reproductive disorders
- 5. Immune pulmonary disorders
- 6. Immune gastrointestinal and hepatobiliary disorders
- 7. Immune neurologic and neuromuscular disorders
- 8. Immune hematologic disorders
- 9. Immune ocular disorders
- 10. Immune skin disorders

D. Transplantation Medicine

- 1. Recognition of alloantigens
- 2. Alloreactive T cell activation
- 3. Allograft rejection
 - a. Hyperacute
 - b. Acute
 - c. Chronic
- 4. Prevention and treatment of allograft rejection
 - a. Immunosuppression
 - b. Methods to reduce allograft immunogenicity
 - c. Methods to induce allograft host tolerance
- 5. GVHD: Acute and Chronic
 - a. Prevention

b. Treatment

E. Immune System Related Malignancies and Cellular Disorders

1. B cell and plasma cell neoplasms
2. T cell neoplasms
3. Monocyte/macrophage neoplasms
4. Mast Cell Dyscrasias
5. Eosinophilic Disorders
6. Cryopathies (amyloid)
7. Clinical skills: Physical findings associated with neoplasms, interpretation of serum protein electrophoresis and immunoelectrophoresis, interpretation of serum immunoglobulin levels, and interpretation of lymphocyte subset data.

F. Established and Evolving Immune-based Treatment Modalities

1. Glucocorticoids and Immunosuppressants (see Section III. A.)
2. Modified Allergen Immunotherapy
3. Cellular immune reconstitution including stem cell and bone marrow transplant
4. Immunoglobulin replacement therapy
5. Nucleic Acid Based Therapies (DNA vaccines, CpG, gene insertion, antisense nucleotides)
6. Cytokine receptors and receptor antagonists (IFN, antiTNF, etc)
7. Recombinant molecules and humanized monoclonal antibodies (imatinib, infliximab,omaluzimab, rituximab)
8. Plasmapheresis and cytopheresis
9. Probiotics
10. Unproven and Controversial therapies

VI. Basics of ACGME Core Competencies

- A. Professionalism
- B. Communication Skills
- C. Practice Based Learning
- D. Systems-Based Practice