CURRICULUM

DM CLINICAL IMMUNOLOGY

2009-10

JAWAHARLAL INSTITUTE OF POSTGRADUATE MEDICAL
EDUCATION & RESEARCH (JIPMER),

PUDUCHERRY-605 006

CONTENTS

JIPMER, Puducherry

Curriculum outline and syllabus for DM Clinical Immunology

Duration of the course: Three years

Frequency of admission: Once a year through an all India entrance examination

Eligibility for admission: MD Medicine, MD Pediatrics

Preamble

Immunology can be broadly defined as a science that deals with the body's defense system (immune system) against various pathogens. The application of the knowledge of immunology and the immune system to human health can be defined as **clinical immunology**. Clinical immunology is a relatively new specialty of medicine. It encompasses the laboratory diagnosis and clinical management of various diseases caused by disorders of the immune system either due to its failure (immunodeficiency), aberrant action (autoimmunity, allergy) or malignant growth of cellular elements (leukemia, lymphoma). It also encompasses the diseases of other systems, where immune reactions play a part in the pathogenesis such as multiple sclerosis, diabetes etc.

Thus, Clinical Immunology can be grouped into the following six distinct divisions:

1. Autoimmunity
2. Immunodeficiency
3. Allergy
4. Immune malignancies
5. Transplantation Immunology and Immunogenetics
6. Infectious disease immunology and vaccinology

Program objectives

The aim of the DM program is to provide advanced training in Immunology to produce competent sub-specialists who are able to provide clinical care of the highest order to patients and serve as future teachers, trainers and researchers in the field.

Specific Learning Objectives

At the end of the course, the student should be able to:

A. Clinically diagnose, investigate and manage a whole spectrum of immune-mediated disorders
B. Practically perform and interpret the common laboratory techniques used in the Immunology Laboratory

C. Plan and undertake research in Clinical Immunology in the clinic, laboratory and community

D. Competent to understand and critically analyze the new literature in the field of Immunology

E. Teach the subject to undergraduates and postgraduates in Medicine and Pediatrics

DM Training Curriculum

Theoretical training

A. Understanding of Basic Immunology

I. Structure and function of the immune system

a. The human immune response
b. Cells and tissues of the immune system, T and B cell development, lymphocyte trafficking
c. Immunoglobulin genes and proteins
d. TCR genes, gene products and co-receptors
e. The HLA major histocompatibility complex
f. Antigens and antigen presentation, superantigens
g. Cytokines, cellular adhesion and interactions
h. Immune regulation
i. Tolerance

II. Host defense mechanisms and inflammation

a. Immunoglobulin function
b. Regulatory and effector functions of CD4+ T lymphocytes
c. Cytotoxic T cell function, cytotoxic function of macrophages, NK cell function
d. Mucosal defense mechanisms
e. Tumor immunity
f. Pro-inflammatory and inhibitory cytokines
g. Complement
h. Function of phagocytes, mast cells, basophils and eosinophils
i. Immunopathology of inflammation

III. Infection and immunity

a. Immune response to microbes
b. Infections in the immuno-compromised host
c. Vaccines

IV. Immunodeficiency

a. Approach to evaluation of the immunodeficient host
b. Primary immunodeficiency disorders
c. HIV/AIDS
d. HIV vaccine development
e. Ageing and immune system
f. Secondary immunodeficiency (excluding AIDS)

III. Allergic diseases

a. Allergic response in host defense
b. Anaphylaxis
c. Pathogenesis of allergic asthma and rhinitis including environmental aspects
d. Pharmacotherapy and immunotherapy of allergic disorders

IV. Systemic immune diseases

a. Mechanisms of autoimmunity
b. Serum sickness and pathology of immune complex mediated diseases
c. Systemic Lupus erythematosus
d. Rheumatoid arthritis
e. Juvenile rheumatoid arthritis (JRA/JIA)
f. Rheumatic fever
g. Spondyloarthropathies
h. Systemic sclerosis
i. Polymyositis/dermatomyositis
j. Systemic necrotizing vasculitis
k. Sjogren's syndrome
l. Overlap syndromes
m. Others (PMR, panniculitis, relapsing polychondritis, erythema nodosum)
n. Behcet's disease
o. Sarcoidosis
p. Amyloidosis
q. Goodpasture syndrome

V. Organ-specific immuno-inflammatory diseases

a. Immune-mediated cytopenias and coagulation disorders
b. Autoimmune skin diseases
c. Demyelinating CNS diseases, myasthenia gravis and autoimmune peripheral neuropathies
d. Immunological disorders of the gut and hepatobiliary system
e. Autoimmune thyroid disease
f. Immunology of diabetes mellitus
g. Polyglandular autoimmune disease
h. Reproductive immunology

VI. Organ transplantation

a. Concepts and challenges in transplantation
b. Solid organ (Renal etc) transplantation

VII. Treatment of immunological diseases

a. Bone-marrow transplantation
b. IVIG therapy
c. Cancer vaccines
d. Cytokine-modulatory therapies
e. Therapeutic antibodies
f. Gene therapy
g. Anti-inflammatory medications: steroids, NSAIDs and antihistamines
h. Immunosuppressive therapy
i. Plasmapheresis and experimental immunotherapies for immune diseases

VIII. Immunodiagnostics

a. Evaluating immunological functions
b. Detection of specific antibodies
c. Flowcytometry
d. HLA typing and matching
e. Lymphoproliferation assays
f. Molecular methods

Practical Knowledge

I. Laboratory techniques (hands-on experience)

a. Indirect immunofluorescence method for detection of (i) anti-nuclear, anti-smooth muscle, anti-parietal cell and anti-mitochondrial antibodies by using rat liver, stomach and kidney sections as substrates (ii) ANA and anticentromere antibodies on Hep-2 cell line and (iii) ANCA
b. Nephelometry for the estimation of serum complements (C3, C4) and immunoglobulins (IgG, IgM, IgA, IgE)
c. ELISA technique for the estimation of ANA, anti-ds-DNA, ACLA and ANCA

d. Immunoblot for ANA profile

e. Serum electrophoresis and immunofixation for myeloma screening

f. Polarizing microscopy for detection of crystals in synovial fluid

g. Lupus anticoagulant assay

h. HLA typing (serological and molecular)

i. Multitest CMI testing

j. NBT test for evaluation of phagocytic function

k. Enumeration of lymphocyte subsets in peripheral blood using flow cytometry

l. Lymphoproliferation assay

m. PCR standardization and optimization

II. Management of patients with autoimmune rheumatic disorders, allergic diseases and immunodeficiency (including HIV/AIDS)

III. Practical skills in Clinical Immunology

a. Clinical examination with special reference to immunological diseases

b. Rational use and interpretation of immunological tests

c. Diagnostic synovial fluid aspiration and examination including polarized light microscopy

d. Joint and soft-tissue injections with steroids

e. Diagnosis of allergic diseases by skin prick test (SPT) / patch test

f. Proficiency in the use of immunomodulators and immunosuppressive agents

g. Practical experience in immunotherapeutic procedures (immunosupression, Plasma exchange, immunoglobulin therapy, allergen immunotherapy (SCT/SLIT) and treatment with monoclonal antibodies and cytokines

h. Basic physiotherapy and rehabilitation skills

i. Tissue biopsies like bone marrow, synovial, skin, liver, kidney, muscle, minor salivary gland, sural nerve etc.

j. Clinical evaluation of primary and secondary Immunodeficiency

k. Handling of Flow-cytometer, PCR, Electrophoresis, Gel documentation, Nephelometer, ELISA, Polarising and Florescence microscope and Scintillation counter

C. Training Program

1. Clinical attachment: Two years, to work in Immunology ward, OPD etc
2. Laboratory attachment: Six months in two parts of 3 months duration each
3. Posting in other departments (12 weeks): Four weeks in Pediatrics, Two weeks each in Orthopedics, Physical medicine and Rehabilitation, DTCD and Dermatology
4. External rotation: (12 weeks)

   Six weeks to CMC, Vellore, Dept of Hematology for Stem Cell training

   Four weeks to Dept of Rheumatology, MMC, Chennai for Rheumatology training

   Two weeks to VP Chest Institute, New Delhi for Allergy training
5. Academic Activities:
   - Journal Club (once a week)
   - Seminar (once a week)
   - Subject Review (once a week)
   - Clinical case presentation and discussion (once a week)
   - Clinical grand rounds (once a week)
   - Interdepartmental discussions (Radiology, Pathology etc)
   - Basic training courses in Biostatistics, Research methodology, Scientific writing, Laboratory Immunology and Molecular biology.
   - Conferences/Workshop/symposia in the relevant areas
   - Guest lectures by external subject specialists
6. Maintenance of log book/portfolio

D. Research work: Proof of research work done during the period of training in the form of papers published / submitted for publication in National or International Journals / peer reviewed and found suitable for publication duly certified by the Head of the Department should be submitted to the department before the examination. This will be presented to the external examiners at the time of the final examination for evaluation.

E. Performance evaluation during the period of training:

Performance of the student will be evaluated continuously during the course of the DM training program. This will include evaluation of the clinical skills through assessment of

proficiency acquired in patient management, therapeutic procedures, clinical case presentations and laboratory work**.** It will include the following:

1. Regular internal assessment of the performance in teaching programs.
2. Assessment of day to day clinical activities by log book evaluation. This Log Book would be scrutinised and certified by the Head of Department and other Consultants and presented to the external examiners at the time of the final examination.
3. The seminars and the subject reviews presented by the candidate during the training would also be scrutinised and certified by the Head of the Department and other Consultant and presented to the External Examiners at the time of the final examination.
4. Feedback from the external training institutes during external rotation.
5. Six monthly evaluation of academic and clinical competence by theory and practical examination

F. <u>Final Examination at the end of three years</u>:

I. ***Theory Examination*** (Maximum marks 400)

1. The three theory papers would be as follows:

Paper-I:	Basic Sciences related to Clinical Immunology
Paper-II:	Principles and practice of Clinical Immunology including pediatric immunology
Paper III:	Diagnostic Immunology, prevention and therapy of immunological disorders
Paper-IIV:	Recent advances in Clinical Immunology, Epidemiology of Immunological disorders, research methodology

2. Each theory paper will be of three hour duration.
3. Each theory paper will consist of 10 short note questions.
4. Each theory paper will carry a maximum of 100 marks.
5. To obtain a pass in theory examination the candidate will be required to obtain a minimum of at least 40% marks in each theory paper and 50% marks in aggregate.

II. Practical and Viva-voce examination (Maximum marks 400)

The practical and viva-voce examination will be conducted over a period of two days

Day 1: Clinical Examination

The clinical examination will be based on structured and objective evaluation of history taking, examination skills, data interpretation and synthesis of the overall clinical case and its discussion. It will include at least four semi long cases.

Day 2: Practical and Viva voce Examination

This will be an objective assessment based on proficiency in diagnostic and therapeutic procedures, laboratory data interpretation, radiology spots, histology slides, clinical photographs as well as observed laboratory skill assessment.

The viva-voce would cover different areas of the specialty to assess the depth and breadth of knowledge of the student in the specialty.

1. The practical examination will consist of the following three components

I. Clinical Competence (4 semi-long cases):	200 marks
II. Practical skills (lab immunology and therapeutic procedures):	100 marks
III. Viva voce (spots and viva):	100 marks

2. The candidate will be required to obtain at least 50% in each component of the practical Examination.
3. To obtain a pass in the practical examination the candidate will be required to obtain at least 50% in aggregate.

SAMPLE MARKS SHEET

Theory:	Paper I.	100 Marks	
	Paper II.	100 Marks	
	Paper III	100 Marks	
	Paper IV	100 Marks	
Total Theory :		**400 Marks**	**Pass 200/400 (50%)**
Clinics:			
	Clinical Cases:	200 Marks	
	Practical skills:	100 Marks	
	Total Clinics:	**300 Marks**	
Viva-Voce:		**100 Marks**	
Total of Clinics and Viva-Voce:		**400 Marks**	**Pass 200/400(50%)**

G. Final Result:

1. The candidate will be required to obtain a pass in theory and practical separately.
2. The candidate will be declared pass only if he/she scores a minimum of 50% in aggregate.
3. If any candidate fails either in theory or practical, he/she has to re-appear for both theory and Practical/Clinical/Viva examination.

LEARNING RESOURCE MATERIALS

RECOMMENDED TEXT BOOKS AND JOURNALS

The following is only a partial recommended list of the prevailing text books and journals at the time of the compilation of the syllabus. As and when New Text Books or Journals become available, the candidates would be appraised accordingly.

A. Text books

1. Rheumatology by Hochberg (Mosby)
2. Oxford Textbook of Rheumatology
3. Primer on the Rheumatic Diseases
4. Kelley's Textbook of Rheumatology
5. Kuby's Immunobiology
6. Samter and Rich: Clinical Immunology
7. Middleton's Allergy: Principles and Practice
8. A clinical guide to AIDS and HIV by Wormser (Raven Press)
9. Advances in Chemotherapy of AIDS by Robert B Diasio (Elsvier Science)
10. MHC: A practical approach by Fernandez Butcher (Oxford University Press)
11. Hematopoietic stem cell transplantation by Champlin, Richard (Marcel Dekker)

B. Journals

1. Journal of Immunology
2. Clinical and experimental Immunology
3. Current opinions in Immunology
4. Journal of Clinical Immunology
5. Journal of Experimental Medicine
6. Journal of Autoimmunity
7. Infection and immunity
8. Current advances in Immunology and Infectious diseases
9. Arthritis and Rheumatism
10. Annals of Rheumatic diseases
11. Current opinions in Immunology

12. Current Opinion in Rheumatology
13. Rheumatic Disease Clinics of North America
14. Seminars in Arthritis & Rheumatism
15. Journal of AIDS
16. Journal of Allergy and Clinical Immunology
17. Transplant Immunology
18. Journal of transplantation
19. Bone Marrow Transplantation
20. Journal of Immunotherapy
21. NEJM
22. Annals of internal medicine

The Student should also be familiar with Internet browsing for online Journals, Special Articles, Review Articles and other recent recommendations of International Societies like the ACR, AAAAI etc.

Model question paper (theory) for DM Clinical Immunology

Paper I: Basic Sciences related to Clinical Immunology

Time: 3 Hours **All Questions Carry Equal marks** **Max Marks: 100**

Write short notes on:

1. Toll Like Receptors
2. Th 17 cells
3. Murine models of Lupus
4. Anti CCP antibodies
5. Airway remodeling in Bronchial asthma
6. NOS pathway in autoimmune and inflammatory diseases
7. MALT
8. Immune dysregulation in HIV infection
9. Oral tolerance
10. Abzymes

Paper-II: Principles and practice of Clinical Immunology including Pediatric Immunology

Time: 3 Hours **All Questions Carry Equal marks** **Max Marks: 100**

Write short notes on:

1. Classification criteria for JIA
2. Disease assessment in Ankylosing Spondylitis
3. CGD
4. Autoimmune polyglandular syndrome
5. Catastrophic APS
6. Management of refractory lupus nephritis
7. ANCA associated vasculitis
8. Macrophage Activation Syndrome
9. IRIS
10. Treatment of Sarcoidosis

Paper-III: Diagnostic Immunology, prevention and therapy of immunological disorders

Time: 3 Hours **All Questions Carry Equal marks** **Max Marks: 100**

Write short notes on:

1. Describe methods for qualitative assessment and characterization of immunoglobulins.
2. Natalizumab
3. Tumor vaccines
4. Immunoprevention of Type 1 Diabetes
5. In vivo provocation tests for allergic disorders
6. Approach to diagnosis of primary immunodeficiency disorders
7. Oral tolerance
8. IVIG: Mechanism of action and uses
9. Gene transfer therapy of immunological disorders
10. SEGRAS

Paper-IV: Recent advances in Clinical Immunology, Epidemiology of Immunological disorders, research methodology

Time: 3 Hours **All Questions Carry Equal marks** **Max Marks: 100**

Write short notes on:

1. Tocilizumab
2. Autologous mesenchymal stem cell transplantation
3. Genetic epidemiology of RA
4. Immunomodulatory properties of Vitamin D
5. Antigen specific immunotherapy in allergic respiratory disorders
6. TNF inhibitors
7. Biomarkers of osteoporosis
8. Tregs in autoimmunity
9. Immunodeficiency of IFNγ / IL12 axis
10. Autoinflammatory syndromes