



MASTER OF PATHOLOGY (CLINICAL IMMUNOLOGY)

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TRAINING CURRICULUM FOR TRAINEES AND SUPERVISORS
UNIVERSITI SAINS MALAYSIA

MASTER OF PATHOLOGY (CLINICAL IMMUNOLOGY)

1. AIM

A four-year post-graduate training program in Immunology.

2. BACKGROUND

The Master of Pathology (Clinical Immunology) programme is to produce immunopathologists whom are knowledgeable in theoretical and practical aspect of laboratory diagnoses, helping in management of immune-mediated diseases and in managing the laboratory (staff, quality, troubleshooting, safety and training). The specialists produced are competent and able to provide consultations on patients' management, hence provide a communication link between the Immunology laboratory and the clinician.

3. STRUCTURE OF COURSE

This program is a 4-year programme and is divided into two stages, Stage 1 (Year 1) and stage 2 (Year 2-4). The stage 1 conjoint programme was started from year 2004/2005 intake. At the moment, the Stage 2 MPath (Immunology) is only offered in USM.

Modes of training include lectures, seminar/journal presentation, bench-working, clinical and laboratory attachment and consultation. The knowledge in laboratory quality management is acquired throughout the training period by taking part in QMS activities.

3.1 STAGE 1: CLINICAL IMMUNOLOGY MODULE

3.1.1. INTRODUCTION

In USM, Clinical Immunology input is delivered in a well-structured program for 2 weeks (i.e. lectures, laboratory attachment, seminars). For bench rotation in the laboratory, students are required to achieve certain level of competency. At the end of posting the students will be assessed.

3.1.2. LEARNING OBJECTIVE

GENERAL OBJECTIVE:

1. To acquire knowledge of basic immunology and immunopathology

SPECIFIC OBJECTIVES:

1. To acquire knowledge on components of immune system and immune response
2. To acquire knowledge on various mechanisms of immune mediated diseases (e.g., autoimmunity, hypersensitivity, immunodeficiency, tumour immunology) and transplantation immunology
3. To understand the principles of various immunological tests and their clinical significance

3.1.3. COURSE CONTENT

THEORETICAL ASPECTS

1. Organization of the immune system
2. Antigen and antibody reactions
3. Complement & Cytokines
4. Major Histocompatibility Complex
5. Immune Response
6. Hypersensitivity
7. Immunodeficiency
8. Autoimmunity and autoimmune disease
9. Tumour immunology
10. Transplantation immunology

PRACTICAL ASPECTS

Level of competence	
Level 0	: No skills
Level 1	: Observer status only
Level 2	: Assistant status
Level 3	: Able to perform under close and direct supervision
Level 4	: Able to perform under indirect supervision
Level 5	: Able to perform unsupervised

Practical skill to be acquired	Level of competence
1. Agglutination: - Rheumatoid Factor/ C-Reactive Protein/ RPR	5
2. Immunofluorescence: - Anti-Nuclear Antibody/Anti-dsDNA / Anti-Smooth Muscle Antibody / Anti- Mitochondrial Antibody / Anti- Neutrophil Cytoplasmic Antibody	1
3. Turbidometry/nephelometry: - C-Reactive Protein - Immunoglobulin G, Immunoglobulin A, Immunoglobulin IgM, Complement 3, Complement 4	1
4. Immunoassay: -ELISA/EIA/FEIA fluoroenzyme immunoassay (FEIA)/ Immunoblot -Anti-Cardiolipin Antibody -Extractable Nuclear Antigen -Alpha-Feto Protein -Allergen Specific IgE Test	1
5. Immunophenotyping -Lymphocyte subsets	1

3.1.4. TEACHING PROGRAMME

It is student-centered and teacher-centered consisting of

1. Lectures for the theoretical 10 topics
2. Seminars which involve case presentation, theoretical aspect of the disease and immune-diagnosis and principle of management
 - Seminar 1 – Autoimmunity
 - Seminar 2 – Immunodeficiency
 - Seminar 3 – Hypersensitivity
3. Laboratory attachment

3.1.5. LEARNING OUTCOMES

At the end of the posting the candidate should be able to:

1. Describe the components of the immune system ie. organs, cells and their functions and mediators (antibody, cytokines, TNF, IFN and complement)
2. Define the innate and acquired immune system
3. Understand general principles of agglutination, precipitation, turbidometry, immunofluorescence, and immunoassay techniques
4. Describe the complement activation pathways
5. Describe types and functions of cytokines
6. Describe the structure and biological functions of MHC class I and II molecules
7. Describe the-acquired immune response
8. Describe primary and secondary phases of the immune response and its application.
9. Explain various mechanisms, laboratory investigations and principle of management of immunodeficiency, hypersensitivity and autoimmunity
10. Describe cancer antigens, mechanisms of the immune response against cancers, immune evasion and cancer immunotherapies
11. Understand the principles of transplantation and HLA test

3.2 STAGE 2: CLINICAL IMMUNOLOGY MODULE

3.2.1 INTRODUCTION

The Stage 2 programme is of three years duration in the sub-discipline of Clinical Immunology. This programme may only be undertaken in USM as a closed system.

It is a guided self-learning module where knowledge acquisition is emphasized during seminar/journal club presentations, performing test, reporting and validating laboratory results, clinical consultations and ward/clinic visits. Throughout the module, students have to participate in laboratory quality management system.

1. During the Stage 2 programme the candidate shall undertake a research project and submit a research project report. At the end of the Stage 2 programme the candidate must sit and pass Part 2 examination in order to be awarded the degree of Master of Pathology (Clinical Immunology). After completing Stage 2, the graduates are competent in their knowledge and skills as Immunopathologist.

3.2.2 LEARNING OBJECTIVES:

GENERAL OBJECTIVE:

1. To acquire knowledge of advanced immunology, diagnostic and immunopathology

SPECIFIC OBJECTIVES:

1. To acquire knowledge of advanced immunology
2. To acquire knowledge and practical skills in conducting the laboratory tests
3. To acquire competence for administering and interpreting laboratory tests associated with clinical conditions
4. To acquire experience, knowledge and skill for diagnosis and consultation of immune-mediated diseases
5. To acquire knowledge/skills in the laboratory quality management system
6. To acquire skills in providing specialist assistance to clinical colleagues
7. To acquire knowledge in quality teaching in immunology
8. To be able to conduct research and thesis writing

3.2.3 COURSE CONTENT

THEORETICAL ASPECTS

I. Advanced Immunology:

1. Immune response
2. Cytokines and complement
3. Immunomodulators and immunoregulation
4. Hypersensitivity reactions
5. Tolerance and autoimmunity
6. Transplantation immunology
7. Tumor immunology
8. Immunotherapy

II. Immunopathology:

1. Immunodeficiency diseases
2. Allergic diseases
3. Systemic Autoimmune Diseases
4. Immune mediated respiratory diseases
5. Immune mediated musculoskeletal diseases
6. Immune mediated endocrine diseases
7. Immune mediated hematological diseases
8. Immune mediated neurological diseases
9. Immune mediated gastrointestinal diseases
10. Immune mediated renal diseases
11. Neoplastic diseases and the immune system
12. Immunologic diseases involving other organ systems (vascular, skin, reproductive, etc)
13. Cancer immunotherapy
14. Organ and bone marrow transplantation

PRACTICAL ASPECTS

Level of competence	
Level 0	: No skills
Level 1	: Observer status only
Level 2	: Assistant status
Level 3	: Able to perform under close and direct supervision
Level 4	: Able to perform under indirect supervision
Level 5	: Able to perform unsupervised

Practical skill to be acquired	Level of competence
1. Agglutination - Rheumatoid Factor, C-Reactive Protein	5
2. Immunofluorescence - Anti-Nuclear Antibody/ Anti-dsDNA, Anti-Smooth Muscle Antibody/Anti-Mitochondrial Antibody, Anti-Neutrophil Cytoplasmic Antibody and others	5
3. Turbidometry/nephelometry - C-Reactive Protein - Immunoglobulin G, Immunoglobulin A, Immunoglobulin IgM, Complement 3, Complement 4 - Specific antibody response: <ul style="list-style-type: none"> • Pre and post pneumococcal vaccination • Pre and post tetanus vaccination 	5
4. Immunoassay : ELISA/EIA/FEIA fluoroenzyme immunoassay (FEIA)/ Immunoblot - Anti-Cardiolipin Antibody - Extractable Nuclear Antigen - Alpha-Feto Protein - Allergen Specific IgE Test	5

5. Flowcytometry <ul style="list-style-type: none"> - Immunophenotyping (Lymphocyte subsets) - CD40 Ligand Assay - BTK function test - Switch Memory B cells - Lymphocyte Transformation Test - Dihydrorhodamine (DHR) 	3
6. Lymphocyte proliferation Test	3
7. Phagocytic Function Test: <ul style="list-style-type: none"> - Chemiluminescence - nitro blue tetrazolium test (NBT) 	3
12. HLA Test: <ul style="list-style-type: none"> - HLA typing - Cross matching - HLA antibody Test 	2

RESEARCH ASPECTS

The student is expected to have general knowledge on conducting research and should be able to come out with research proposal. This proposal needs to be presented in the department and submitted to local human/animal ethical committee for approval. The student has to conduct the research within the candidature and submit the dissertation at least six months before final examination as prerequisite.

3.2.4. COURSE STRUCTURE

Postings at various clinical disciplines are compulsory in order to gain knowledge and experience related to immunology.

ACTIVITIES/POSTINGS

YEAR 2

Orientation-LQMS 1 week	Research Methodology Workshop & Biostatistics, Good Clinical Practice, Critical Appraisal & Bioethics, Communication Skills 2 weeks	Proposal preparation & Research Protocol presentation 4 weeks	Laboratory Immunology postings 37 weeks	Blood bank/Haematology posting 4 weeks	Leave 4 weeks (2 weeks every 6 months)
Research Project					

YEAR 3

Postings at various clinical disciplines: <ul style="list-style-type: none"> Clinical & Paediatrics (Immunodeficiency diseases; HRPZ II), Haemato Oncology, HUSM Haematopoietic Stem Cell Transplantation (Ampang Hospital). 20 weeks	Laboratory postings: <ul style="list-style-type: none"> Allergy & Immunology Research Center (IMR), Medical Microbiology & Immunology Department (UKM), Immunology Laboratory (IPPT, Bertam), Human Genome Centre, HUSM Molecular Technology-Vaccinology (PPSK) Laboratory Immunology postings 28 weeks	Leave 4 weeks (2 weeks every 6 months)
Research Project		

YEAR 4

Postings at various clinical disciplines at HUSM: <ul style="list-style-type: none">• Nephrology• Rheumatology• Respiratory• Skin• ENT 20 weeks	Laboratory postings at HUSM: <ul style="list-style-type: none">• Serology (Microbiology Department)• Endocrine Laboratory• Tissue Bank Unit 20 weeks	Study Leave 6 weeks	Examination 2 weeks	Leave 4 weeks (2 weeks every 6 months)
Research project				

* This program schedule is flexible in terms of time and duration.

To be eligible for sitting Part II Examination, the candidates must submit:

- 3 case reports in publishable format
- log book
- dissertation

3.2.5. TEACHING PROGRAMME

1. The lecturer: student ratio is 1:1
2. No formal teaching. The emphasis is on knowledge acquisition through selfdirected learning, daily laboratory activities, including reporting of laboratory results under supervision, writing up case reports, presentations in journal club and seminars.
3. Various postings in laboratory and ward/clinic with supervision.
4. Candidates are expected to assist in teaching of undergraduates.
5. Candidates are required to attend and take part in clinico-pathology/immunology conferences and research presentation.

3.2.6. LEARNING OUTCOMES

At the end of the posting the candidate should be able to:

1. Recall immune system and immune response
2. Recall the complement system (understand the components, activation pathways and biological activities and diseases)
3. Describe immunogenetics: polymorphism, generation of diversity and rearranging gene families
4. Describe T cell receptors: structure, function and antigen binding.
5. Describe receptor-ligand interactions: adhesion molecules, complement receptors, Fc receptors and signal transduction.
6. Describe the cytokines: for each cytokine, understand the origin, structure, effect, site of action (receptor), metabolism, regulation and gene activation.
7. Describe the inflammatory mediators (e.g. leukotrienes, prostaglandins and PAF: for each, understand the origin, structure, effect, site, metabolism and regulation).
8. Describe immunomodulation and immunoregulation (tolerance: clonal selection, suppression and antigen paralysis, cell-cell interactions, idiotype networks: inhibition and stimulation and mechanism of autoimmunity)
9. Describe hypersensitivity reactions: types, mechanisms/pathogenesis, and disease examples
10. Describe histocompatibility complex: major and minor antigens and principles of cross- matching, allograft rejection mechanism, graft-versus-host reaction mechanism and HLA-Typing
11. Describe tumor immunology (tumor markers, oncogenes, principles of cancer therapy.
12. Describe immunotherapy (drug, antibodies, and recombinant molecules)
13. Describe immunodeficiency diseases (primary immunodeficiency, secondary immunodeficiency: HIV infection and AIDS, cancer, leukemia, malnutrition and etc.)
14. Describe allergic diseases eg. eczema/allergic dermatitis/ allergic rhinitis, asthma etc (types of allergens, mechanisms/pathogenesis, laboratory investigations and management- eg. allergen immunotherapy etc.)
15. Describe systemic autoimmune diseases (systemic lupus erythematosus, Sjogren syndrome, systemic sclerosis, rheumatoid arthritis, polymyositis/dermatomyositis, mixed connective tissue disease).

16. Describe immune mediated respiratory diseases (Allergic rhinitis/hay fever, asthma, hypersensitivity pneumonitis, pulmonary fibrosis and related disorders)
17. Describe immune mediated musculoskeletal disease and vasculitis
18. Describe immune mediated endocrine diseases (autoimmune thyroiditis, autoimmune diabetes mellitus (Type 1), autoimmune primary adrenal Insufficiency, autoimmune polyendocrinopathy)
19. Describe immune mediated haematological diseases (autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura, pernicious anemia, plasma cell disorders, amyloidosis etc)
20. Describe immune mediated neurological diseases (multiple sclerosis, Guillain-Barre syndrome, myasthenia gravis etc)
21. Describe immune mediated renal diseases (IgA nephropathy, Goodpasture syndrome, glomerulonephritis etc.)
22. Describe immunologic diseases involving other organ/systems (immune mediated dermatoses, immune mediated gastrointestinal diseases, immune mediated reproductive diseases)
23. Describe neoplastic diseases and the immune system (leukemia/lymphomas, and neoplasia associated with immunodeficiencies)
24. Describe cancer immunotherapy
25. Describe organ and haematopoietic stem cell transplantation

3.2.7. RESEARCH DISSERTATION

A research dissertation is compulsory for Clinical Immunology Stage 2 programme and the candidate have to pass the research dissertation as a prerequisite for the part 2 examination. The purpose of the dissertation is to allow assessment of the practical ability of candidates and of ability to report and assess the significance of their findings. It is a test of the ability to analyse, criticise and present raw data. The overall standard of the project should be such that it is suitable for publication in a professional scientific journal.

A proposal describing the background, the research questions, the objective of the intended study, the details of the proposed experimental work and the expected outcomes must be presented and submitted for the approval by the committee. The project and the writing of the dissertation should be carried out under the supervision of a designated lecturer.

The dissertation must be written in English and should be submitted according to Guide to The Preparation & Submission of Dissertation: Applicable for Master of Medicine, Master of Surgery & Master of Pathology, School of Medical Sciences Universiti Sains Malaysia.

The candidate can submit the dissertation in traditional format or manuscript ready format [for publication in peer-reviewed journal] as stated in the guidelines.

The dissertation will be examined by designated examiners and will be marked by assigning to it one of four scales:

- | | |
|----------|---|
| Scale 1: | The candidate's dissertation is acceptable unconditionally as partial fulfillment of the requirement for the Masters Degree. |
| Scale 2: | The candidate's dissertation is acceptable as partial fulfillment of the requirement for the Masters Degree subject to the candidate making such changes/corrections as listed by examiner. |
| Scale 3: | The candidate should be permitted to resubmit the dissertation after the candidate has made changes/corrections as listed by examiner for re-examination |
| Scale 4: | The candidate's dissertation is not acceptable as partial fulfillment of the requirement for the Master of Medicine degree. |

Candidates will be informed of the Scale awarded following approval by the Examiners' Sub-committee. A candidate awarded a Scale 4 will be barred from taking the Part 2 final examination.

4. MODE OF TEACHING AND LEARNING

4.1 STAGE 1

It is student-centered and teacher-centered consisting of:

1. Lectures for the theoretical 10 topics
2. Seminars which involve case presentation, theoretical aspect of the disease and immune-diagnosis and principle of management
3. Laboratory attachment

4.2 STAGE 2

1. The lecturer: student ratio is 1:1
2. No formal teaching. The emphasis is on knowledge acquisition through self-directed learning, daily laboratory activities, including reporting of laboratory results under supervision, writing up case reports, presentations in journal club and seminars.
3. Various postings in laboratory and ward/clinic with supervision.
4. Candidates are expected to assist in teaching of undergraduates.
5. Candidates are required to attend and take part in clinico-pathology/immunology conferences and research presentation.

5. SUPERVISION AND PROGRESS REPORTS

The department will appoint a qualified Immunopathologist to be a supervisor for each candidate. The supervisor is responsible for the progress report of the candidate.

6. EXAMINATION AND ASSESSMENT

The Stage 2 examination will be held at the end of Year IV and will comprise of:

Theory papers
Practical Papers
Viva-voce

Allocation of Marks:

1. Continuous assessment/Dissertation – Prerequisites
2. Professional examination II (end of Stage 2).....100%
 - i) Theory.....45%
 - MCQ 50%
 - Essay 1 & 2 50%
 - ii) Practical45%
 - OSPE 50%
 - Long Practical 50%
 - iii) Viva-voce..... 10%

Criteria:

1. Overall score must be 50% and above.
2. Must pass each component with a score of 50% and above
 - a) Theory
 - b) Practical
3. Must attend viva session.

Note: Viva component can be used to assess candidates with borderline marks.

7. ENTRANCE CRITERIA

- 7.1 Candidate must hold a recognized medical degree.
- 7.2 Candidates are required to pass the entrance exam and interview.

8. DURATION OF TRAINING

The minimum duration of training is four (4) years with a maximum of seven (7) years.

9. CURRICULUM AND SYLLABUS

Syllabus that will be used is attached (appendix II & III). However, the syllabus will be updated from time to time in view of the progress in this field of specialty.

10. ACADEMIC AND TEACHING STAFFS

All academic and laboratory staffs in the Department of Immunology will be involved in teaching activities and laboratory postings.

11. ADMINISTRATIVE COMMITTEE

The Department of Immunology will be responsible in organizing and monitoring the program, preparing teaching schedule and organizing seminars pertaining to the program.

12. ADMINISTRATION OF EXAMINATION

The Medical School will coordinate and execute all examination. The result will be discussed at the Examination Board before approval by the Medical School Board and the Post-graduate University Board.

Appendix I

Programme Structure

Stage	Year	Curriculum
1	1	* Lectures * Seminars * Laboratory attachment
Professional Examination I		
2	2, 3 & 4	* Case reports * Log book * Dissertation * Elective posting * Annual assessment
Professional Examination II		

Appendix II

SYLLABUS FOR STAGE 1 (YEAR 1)

At the end of the posting the candidate should be able to:

1. Describe the components of the immune system ie. organs, cells and their functions and mediators (antibody, cytokines, TNF, IFN and complement)
2. Define the innate and acquired immune system
3. Understand general principles of agglutination, precipitation, turbidometry, immunofluorescence, and immunoassay techniques
4. Describe the complement activation pathways
5. Describe types and functions of cytokines
6. Describe the structure and biological functions of MHC class I and II molecules
7. Describe the-acquired immune response
8. Describe primary and secondary phases of the immune response and its application.
9. Explain various mechanisms, laboratory investigations and principle of management of immunodeficiency, hypersensitivity and autoimmunity
10. Describe cancer antigens, mechanisms of the immune response against cancers, immune evasion and cancer immunotherapies
11. Understand the principles of transplantation and HLA test

Appendix III

SYLLABUS FOR STAGE 2 (Year 2, 3 and 4)

At the end of the posting the candidate should be able to:

1. Recall immune system and immune response
2. Recall the complement system (understand the components, activation pathways and biological activities and diseases)
3. Describe immunogenetics: polymorphism, generation of diversity and rearranging gene families
4. Describe T cell receptors: structure, function and antigen binding.
5. Describe receptor-ligand interactions: adhesion molecules, complement receptors, Fc receptors and signal transduction.
6. Describe the cytokines: for each cytokine, understand the origin, structure, effect, site of action (receptor), metabolism, regulation and gene activation.
7. Describe the inflammatory mediators (e.g. leukotrienes, prostaglandins and PAF: for each, understand the origin, structure, effect, site, metabolism and regulation).
8. Describe immunomodulation and immunoregulation (tolerance: clonal selection, suppression and antigen paralysis, cell-cell interactions, idiotypic networks: inhibition and stimulation and mechanism of autoimmunity)
9. Describe hypersensitivity reactions: types, mechanisms/pathogenesis, and disease examples
10. Describe histocompatibility complex: major and minor antigens and principles of cross-matching, allograft rejection mechanism, graft-versus-host reaction mechanism and HLA-Typing
11. Describe tumor immunology (tumor markers, oncogenes, principles of cancer therapy.
12. Describe immunotherapy (drug, antibodies, and recombinant molecules)
13. Describe immunodeficiency diseases (primary immunodeficiency, secondary immunodeficiency: HIV infection and AIDS, cancer, leukemia, malnutrition and etc.)

14. Describe allergic diseases eg. eczema/allergic dermatitis/ allergic rhinitis, asthma etc (types of allergens, mechanisms/pathogenesis, laboratory investigations and management- eg. allergen immunotherapy etc.)
15. Describe systemic autoimmune diseases (systemic lupus erythematosus, Sjogren syndrome, systemic sclerosis, rheumatoid arthritis, polymyositis/dermatomyositis, mixed connective tissue disease).
16. Describe immune mediated respiratory diseases (Allergic rhinitis/hay fever, asthma, hypersensitivity pneumonitis, pulmonary fibrosis and related disorders)
17. Describe immune mediated musculoskeletal disease and vasculitis
18. Describe immune mediated endocrine diseases (autoimmune thyroiditis, autoimmune diabetes mellitus (Type 1), autoimmune primary adrenal Insufficiency, autoimmune polyendocrinopathy
19. Describe immune mediated haematological diseases (autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura, pernicious anemia, plasma cell disorders, amyloidosis etc)
20. Describe immune mediated neurological diseases (multiple sclerosis, Guillain-Barre syndrome, myasthenia gravis etc)
21. Describe immune mediated renal diseases (IgA nephropathy, Goodpasture syndrome, glomerulonephritis etc.)
22. Describe immunologic diseases involving other organ/systems (immune mediated dermatoses, immune mediated gastrointestinal diseases, immune mediated reproductive diseases)
23. Describe neoplastic diseases and the immune system (leukemia/lymphomas, and neoplasia associated with immunodeficiencies
24. Describe cancer immunotherapy
25. Describe organ and haematopoietic stem cell transplantation