

KUWAIT INSTITUTE OF MEDICAL SPECIALIZATION (KIMS)

RESIDENCY PROGRAM IN DIAGNOSTIC & INVESTIGATIVE IMMUNOLOGY

- CURRICULUM -

Introduction

Diagnostic & Investigative Immunology includes medical immunology, diagnosis of immunodeficiency and autoimmune disorders, allergic diseases, immunity to infection and the immunology of transplantation. This Residency Program focuses on laboratory immunology, residents will therefore develop skills in managing a diagnostic immunology laboratory. Training in this program will allow Residents to obtain the skills, knowledge and experience necessary to provide, interpret and communicate immunological data and other relevant information for use in the diagnosis, management and treatment of patients. The award of the Board Certificate will require evidence of satisfactory completion of training in core aspects of clinical immunology.

Eligibility

Candidates with MBBCh or equivalent and a strong interest in Diagnostic Immunology.

Aim of the Program

The purpose of this program for specialty training in Diagnostic & Investigative Immunology is to meet the standards set by KIMS and for attainment of the award of the KIMS Board Certificate in Diagnostic & Investigative Immunology. Successful graduates of this program will have developed expertise in immunology, clinical immunology, diagnostic immunology and related subspecialties and sciences and will have prepared for responsible positions in Diagnostic & Investigative Immunology laboratories so that they are fully prepared to provide Clinical Immunology and Allergy services.

Learning Objectives:

The residency program is designed to provide education and training to enable the Residents in Diagnostic & Investigative Immunology to meet the stated core objectives.

At the end of the Residency training in Diagnostic & Investigative Immunology, the Resident shall be able to demonstrate knowledge and skills in the following, in terms of (i) working on the bench with, and supervising, technologists involved in the testing procedures and (ii) interacting with physicians in the interpretation of the tests:

- Auto-immune diseases and immunodiagnosis of the individual diseases
- Cellular, serologic and immunophenotyping tests for evaluating immune deficiency diseases and the proper work up for each

- Flow cytometry and the standardization of pertinent procedures required for processing specimens including blood, bone marrow and lymph nodes and the relevance of immunophenotyping to various diseases
- Allergy testing
- Histocompatibility testing by serological, cellular and molecular methods
- Serology of common infectious diseases
- Molecular biology techniques as they pertain to diagnostic immunology

In addition to the laboratory procedures mentioned above, Residents shall also be able to demonstrate the following:

- Basic understanding of principles and practice of Clinical Immunology & Allergy
- Knowledge and ability to handle information management systems available in the clinical laboratory.
- Knowledge and skills in managing and administering a laboratory including budget and space planning, personnel management, quality control and quality assurance, laboratory safety, management of laboratory waste and radioactive materials.
- Skills to develop and conduct a research protocol and describe the methodology, controls and statistical considerations to test a hypothesis proposed as an answer to a basic or applied research problem in immunology and allergy.
- Effective communication skills with colleagues, technologists and physicians regarding specimen collection and testing, interpretation of laboratory data, consultation and implementing policy changes.
- Ability to participate actively in the education of paramedical staff and junior Residents, and supervise their training and day-to-day functioning
- Ability to recognize the role of teamwork and function as an effective member/leader of the team

Learning settings

Training facilities: Health Sciences Centre, Kuwait University and government hospitals where there are designated qualified trainers.

The resident should be able to achieve the training goals and objective through:

- Rotation through laboratories in the Health Sciences Centre
- Rotation in Hamad Al-Essa Transplant Centre
- Rotation in the Al-Rashid Allergy Centre, Al-Sabah Hospital
- Training in other laboratories both inside and outside Kuwait when appropriate
- Participation in outpatient clinics in Clinical Immunology, Allergy, Rheumatology and Nephrology to understand the relevance and application of test results to patient management.
- Attendance and participation in ward rounds and ground rounds

Duration of Training

This is a five-year program and the stages of training will be designated R1 to R5. Residents may not progress to the next stage of training until they have satisfactorily completed the preceding stage.

Time spent in the program will be divided as follows:

- 80% dedicated to laboratory practice
- 10% dedicated to research activity
- 5% dedicated to quality management and safety
- 5% of the program must dedicated to teaching activity (lectures, seminars etc)

Board Certification in Diagnostic and Investigative Immunology will be awarded on the recommendation by KIMS of the following:

- Evidence of satisfactory completion of the requirements of the curriculum of the Diagnostic & Investigative Immunology Residency Program (including workplace-based assessments) and the minimum training period
- Satisfactory outcomes in the requisite number of workplace-based assessments (including multi-source feedback)
- Successfully passing the prescribed final year (R5) examination in Diagnostic & Investigative Immunology

Training methods:

Residents have a service provision role and it is recognized that a large component of training will occur as an apprenticeship, with appropriate supervision. Normally, 60–80% of training would be by in-service training. The environment within the department is expected to encourage independent self-directed learning which will include gaining knowledge in the library and when possible by attending local and/or international conferences. Independent self-directed learning will be encouraged by recommending reference text books. It is the resident's responsibility to seek opportunity for experiential learning. The rotations will be arranged in such a way that residents have

time available for participation in a research project as part of their training. In the case of techniques for which an appropriate laboratory is not available in Kuwait, residents will be required to undertake the training in a foreign laboratory which will be organized by the Residency Board through KIMS.

Workplace-based assessment

Residents will be expected to undertake workplace-based assessment throughout the entire duration of their training in Diagnostic & Investigative Immunology.

- Seminars by residents: Case-based discussion, Review of techniques, Summary of publications: a minimum of 6 seminars per year by each Resident.
- Directly observed practical skills after each rotation (testing of coded samples)
- Continuous observation over the year by Supervisor/s

Marks will be awarded and will be part of the final examination at the end of each year. The final examination at the end of each year shall include:

- A written test
- Laboratory testing of coded samples by techniques covered over the year

There will be Annual Review of Competence Progression which is an opportunity to document the competencies that are being gained by the Resident and progress in the training program. Evidence of competence will be judged based on a portfolio of documentation, including a report from the Supervisor.

External Examiners shall be invited at the end of R1, R3 and R5. Final grades at the end of each year will be based on (i) directly observed practical skills after each rotation, (ii) written test, (iii) seminars (iv) report from Supervisor/s and (v) External Examiner's report at the end of R1, R3 and R5.

Training Periods:

R1:

Basic lab practices, Lab Safety, Specimen collection and Disposal: 4 months

Nephelometry: 2 months

Radial Immunodiffusion: 1 month

Basic molecular biology: 3 months

Training in OPD: 1 month

Didactic Lectures in Immunology

The main objective of this stage is to familiarize the Resident with basic practices in an Immunology laboratory and in a Molecular Biology laboratory. In addition to

familiarization with basic principles of laboratory practices, Residents will also strengthen their knowledge of basic and clinical immunology through lectures and seminars. Didactic lectures will cover structural and functional aspects of the immune system as well as aspects of fundamental aspects of clinical immunology such as autoimmunity and autoimmune diseases, immunodeficiency, hypersensitivity and immunoprophylaxis.

1. **Basic Lab practices: Lab safety, Specimen collection and disposal, Information Systems for sample receipt and registry:** The Resident should be fully aware of and understand the significance of proper collection procedures of specimens for investigation of cells, antibodies and complement. In addition the fellow should be familiar with conditions for preserving the quality of the specimen. The Resident should follow the safety guidelines for biological sample collection and proper disposal of biological samples.
2. **Principles of Precipitation and Nephelometry:** Residents shall understand the principles and procedures for performing precipitation and measurement by nephelometry and shall perform these tests on the bench competently. Nephelometric measurement shall include the detection of C3, C4, C-reactive protein, IgG, IgA, IgM levels, IgG subclasses and rheumatoid factor.
3. **Principles of Radial Immunodiffusion:** Residents shall understand the principles and procedures for performing radial immunodiffusion and shall perform these tests on the bench competently. This will include the detection of C1 inhibitor level and IgD level.
4. **Molecular Biology Techniques:** Residents shall become familiar with basic practices in the Molecular Biology laboratory and shall become familiar with procedures related to the extraction of DNA and RNA and electrophoresis of nucleic acids.

During this period Residents shall strengthen their knowledge of basic immunology and the immunological techniques mentioned above; Resident should be able to achieve these objectives by working in the laboratory and by participation/presentation in seminars, tutorials and self-directed learning.

Residents will be assessed at the end of the year. Residents will have to pass the end of year assessment before they proceed to the next stage.

An external examiner will be invited to assess the Resident and the depth of the training.

R2:

Immunofluorescence Assays: 3 months

ELISA: 3 months

Molecular Biology: 2 months

Allergy: 2 months

Training in OPD: 1 month

During this year the resident's rotation will cover:

1. **Immunofluorescence assays:** The resident should be fully aware of the underlying theory and practice of direct, indirect and competitive immunofluorescence techniques. Immunofluorescence tests shall include the measurement of the following antibodies: anti-ds DNA, anti-adrenal, anti-endomysial, anti-gastric parietal, anti-islet cell, anti-liver kidney microsomal, anti-mitochondrial, anti-neutrophil cytoplasmic, anti-nuclear, anti-ovarian and anti-smooth muscle. Residents shall become familiar with the interpretation of these tests.
2. **ELISA:** Residents shall become fully conversant with the principles different types of ELISA i.e. direct, indirect and competitive and shall perform these tests competently on the bench. Testing by ELISA will include the estimation of the following antibodies: anti- β 2 glycoprotein, anti-cardiolipin, anti-ds DNA, anti-gliadin, anti-glomerular basement membrane, anti-intrinsic factor, anti-microsomal (TPO), anti-mitochondrial (M2), anti-mutated citrullinated vimentin and anti-tissue transglutaminase. Residents shall learn to interpret the various results appropriately.
3. **Molecular Biology Techniques:** Residents shall become familiar with the methodology of molecular biology including Northern blotting, Southern blotting, restriction of fragment length polymorphism (RFLP) and the polymerase chain reaction.
4. **Allergy:** Residents shall become conversant with different types of allergy testing available including RAST. The resident will understand the importance of quantitation of IgE and its relationship to the evaluation of allergic disease, and interpretation of the tests and evaluation of the individual patient.

During this year Residents shall develop knowledge of the spectrum of auto-immune diseases and the diagnostic criteria for each of the individual diseases. The resident will understand the variety of individual tests and understand the different sensitivity and specificity of the tests as well as relevant quality control measures in order to understand the clinical relevance of laboratory testing in the diagnostic and monitoring of autoimmune diseases.

The Resident should become familiar with established diagnostic criteria for autoimmune diseases and should know the autoantibody specificities present in serum

from patients with autoimmune diseases and the methods used for detection of these antibodies and their roles in the monitoring of autoimmune diseases.

The Resident will work at the bench with technologists involved in each of the testing procedures and will interact with physicians in the interpretation of the autoimmune tests. The Resident shall achieve these objectives by working in the laboratory and by participation/presentation in seminars, tutorials and self-directed learning.

By the end of this second rotation in Molecular Biology, Residents will be familiar with the use of nucleic acid probes, PCR amplification methods, plasmid isolation and detection, hybridization and restriction analysis of DNA.

Residents will be assessed at the end of the year. Residents will have to pass the end of year assessment before they proceed to the next stage.

R3:

Infectious disease serology: 1 month

Flow cytometry: 3 months

Complement-related tests: 2 months

Allergy: 1 month

Radioimmunoassay: 1 month

Research proposal: 2 months

Training in OPD: 1 month

The main objective of this stage of training is to expose the residents to further laboratory and clinical training. In addition to time spent in the Health Sciences Centre, Residents will be gain experience in clinical allergy tests such as skin testing and RAST at the Al-Rashid Allergy Centre or at Hamad Al-Essa Transplant Centre in Al-Sabah Hospital.

During this year the resident's rotation will cover:

1. **Complement-related assays:** The resident should be fully aware of the theory and practice of techniques related to the measurement C1q level, C1 inhibitor level, C1 inhibitor function, Complement activation (CH100), Alternative Pathway and mannan-binding lectin. In addition to performing these tests on the bench, Residents shall gain experience in interpreting the data and relating it to immunodeficiency disorders.
2. **Infectious Disease Serology:** The resident should be fully aware of the underlying principles, procedures and interpretation of tests for anti-diphtheria, anti-Haemophilus, anti-tetanus, anti-Saccharomyces cerevisiae and anti-pneumococcus antibodies. They shall also gain knowledge relevant to the analysis of specificity and sensitivity of these tests.

3. **Flow Cytometry:** Residents shall become fully acquainted with the principles underlying Flow Cytometry and the use of Flow Cytometry for immunophenotyping and for the detection of CD3, CD4, CD8, CD11, CD16, CD18, CD19, CD20, CD25, CD40L, CD45, CD69, HLA Class 1 and HLA Class 2 molecules. The Resident should understand the requirements for proper collection, handling, and processing of samples for flow cytometry testing. The Resident should also become familiar with data analysis, interpretation of flow cytometric data and application of this data to immunodeficiency disorders.
4. **Allergy:** In addition to reinforcing their knowledge of IgE testing by RAST, residents shall become familiar with skin testing in allergy and other clinic-based tests.
5. **Radioimmunoassay:** Residents shall become acquainted with RIA techniques at Mubarak Al-Kabeer Hospital.
6. **Research Proposal:** Residents shall use this time to become acquainted with potential research projects available in the Health Sciences Centre and shall identify a suitable project in basic immunology or clinical immunology (autoimmunity, immunodeficiency, immunology of infectious diseases, reproductive immunology etc) or allergy. Residents should prepare a project application that will be assessed by Board members. In preparation for this, Residents should attend pertinent research seminars and journal clubs conducted in the Health Sciences Centre and relevant hospitals during R1-R2.

During this year, Residents will pay particular attention to the diagnosis and monitoring of immunodeficiency disorders; they will develop competence in understanding the laboratory tests for evaluation and determining immunodeficiency disease and the proper work up for each. Residents must understand the application of different assays used in the detection and categorization of immunodeficiency disorders by using a variety of cellular, serologic and immunophenotyping techniques to be able to detect defects affecting different arms of the immune system and will learn to characterize primary and secondary immune deficiency diseases. Residents should understand the role of screening assays for immunoglobulin or cellular deficiency detection.

Residents will also develop expertise in laboratory diagnosis of Allergy; they should understand the immunologic pathways which lead to type 1 hypersensitivity reactions and should know the available laboratory assays which can be used to monitor the likelihood of allergic reactions to a variety of allergic substances. Residents should be familiar with the inflammatory mediators of allergic reactions and the modalities of the clinically available therapies. Residents should know the basis for the IgE-mediated allergic response at both the cellular and molecular level and should know the various mediators of inflammation and their pathologic effects. Residents should know the in vivo skin test methods used by allergists and understand the immunologic response which leads to the positive skin test response in allergic individuals. Residents should know the in vitro methods for measuring levels of IgE and allergen-specific IgE and their interpretation in various clinical conditions.

Residents will be assessed at the end of the year. Residents will have to pass the end of year assessment before they proceed to the next stage.

An external examiner will be invited to assess the Resident and the depth of the training.

R4:

Histocompatibility testing: 2 months

Flow cytometry: 1 month

Western Blotting: 1 month

Cellular immunology: 2 months

Research: 4 months

Training in OPD: 1 month

Histocompatibility testing: 2 months

Flow cytometry: 1 month

Western Blotting: 1 month

Cellular immunology: 2 months

During this year the resident's rotation will cover:

1. **Histocompatibility testing:** Residents shall gain familiarity with methods for histocompatibility testing that will comprise of HLA Class I and Class II antigen typing by serological and molecular methods. The Resident will be able to isolate appropriate cells for typing and interpret the results of typing procedures by microlymphocytotoxicity. The resident will learn cross-matching techniques (both cytotoxicity and flow cytometry techniques) and will be able to compare the utility of these techniques. The resident will use this information to discuss their uses in transplantation, to discuss rationale for tissue typing and transplantation
2. **Flow Cytometry:** Residents shall reinforce their previous knowledge and know-how of flow cytometric methodology, interpretation of data and the application of this information to diagnosis. By the end of this second rotation in the Flow Cytometry Lab, Residents should know the principles of flow cytometry and be familiar with standardized procedures required to correctly analyze and interpret flow cytometry data. The Fellow must understand instrument calibration, compensation, gating, bitmaps, and statistical data analysis. The Resident should also be familiar with the variety of CD surface antigens that are routinely used to categorize and differentiate lymphocytes and bone marrow derived cells.
3. **Western Blotting:** Residents shall become familiar with the principles and performance of Western Blotting in general and for the detection of ENA in particular.

4. **Cellular Immunology:** Residents should become fully conversant with Cellular Immunology techniques including identification of different lymphoid and myeloid cells in peripheral blood, isolation of peripheral blood mononuclear cells, lymphocyte stimulation by mitogens and antigens, and neutrophil function tests (NBT and DHR). Residents shall become familiar with the interpretation of data and relating this information to clinical conditions.
5. **Research Project:** Residents shall use this time to work on their research project with appointed supervisor/s at the Health Sciences Centre. Sample collection and purchase of consumables can be an ongoing activity during the year.

The main objective is to achieve a more advanced training of the residents in clinical competence and laboratory management. During this year, the Resident shall understand the basis of the theory and application of HLA class I and II serologic and molecular based typing methods, know the associations between individual HLA types and some autoimmune diseases, and understand the theories concerning the role of HLA molecules in the development of autoimmune diseases.

Each resident will prepare 2 cases under the supervision of a Clinical Immunologist, Allergist, Rheumatologist or Nephrologist and present them in bound form at the end of the year which will form part of the R4 examinations.

R5:

Review of Nephelometry, Radial immunodiffusion, Immunofluorescence, Flow cytometry, ELISA, Western blotting and Cellular Immunology: 3 months

Information and Quality Management, Budgeting, Costing, Purchasing: 2 months

Research and publication: 5 months

Training in OPD: 1 month

The main objective in this period is to allow the resident to consolidate the knowledge gained in previous years by reviewing all the techniques learned during R1 to R4 and to enable them to ensure that they are fully conversant with:

- Principles, methodology and interpretation. Residents shall confirm that they have the relevant knowledge and experience of Clinical Immunology & Allergy, expertise in laboratory diagnosis and management as well as laboratory investigations.
- Information management, Quality management
- Laboratory safety
- Budget preparation
- Purchasing

- Performance evaluation of members of staff
- Review of relevant government laws
- Interaction with hospital administration and consultants
- Organization of work flow and test reporting
- Problem solving, with relation to tests, results, types of samples, quality control etc.

Towards the objectives listed above, the resident's rotation during R5 will cover:

1. **Review of laboratory techniques:** Residents shall review all immunological techniques they have learned over the previous 4 years and shall ensure that they have gained the necessary bench skills to perform the tests and interpret the data.
2. **Information and Quality Management, Budgeting, Safety etc:** Residents shall review and reinforce their knowledge of Information Management, Quality Management , Laboratory management and Laboratory safety.
 - Residents will become familiar with the use of computers and Laboratory Information System (LIS).
 - Residents must demonstrate the ability to implement a laboratory quality control, quality assurance, and continuous quality improvement program.
 - Residents should know the theory and practice of laboratory safety that includes regulations of the Ministry of Public Health as well as universal regulations, and the implementation of a program that protects the health and safety of all laboratory employees. Residents should understand modes of transmission and acquisition of relatively common laboratory-acquired infections. Residents should understand the principles and practices of biosafety hazards, waste management, including disposal of biohazard material, methods of disinfection and sterilization, management of laboratory accidents and the proper use of biosafety and chemical Hoods
 - Residents shall become familiar with personnel management principles and interpersonal relations, budgeting, workload assessment, space planning and laboratory design, preparation of job descriptions, performance appraisals and medical ethics. They will also gain knowledge on regulations of the Ministry of Public Health as they relate to personnel, finances and purchasing.

This knowledge will be gained via lectures, seminars and self-directed learning.

3. **Research Project:** During this period Residents shall conduct and complete their research projects and prepare a manuscript for publication. Actual publication will not be a pre-requisite to passing, but Residents will have to bring the manuscript to the stage of submission.

The R5 final examination, is an exit examination and successful candidates will be eligible to be appointed as specialists. An external examiner will be invited to assess the Resident and the depth of the training.

RECOMMENDED BOOKS/LITERATURE

A. Textbooks (Latest edition available):

i. Basic:

1. Kuby Immunology by Thomas J. Kindt, Barbara A. Osborne, Richard A. Goldsby. Publisher: WH Freeman.
2. Janeway's Immunobiology by Kenneth Murphy. Publisher: Garland Science

ii. Clinical:

1. Essentials of Clinical Immunology by Helen Chapel, Mansel Haeney, Siraj Misbah, Neil Snowden. Publisher: Blackwell Publishing.
2. Patterson's Allergic Diseases by Leslie C. Grammer, Paul A. Greenberger. Publisher: Williams & Wilkins.
3. Clinical Immunology Principles and Practice by Robert R. Rich, Thomas T. Fleisher, William T. Shearer. Publisher: Mosby.

iii. Practical:

1. Practical Immunology by Frank C. Hay, Olwyn M. R. Westwood, Paul N. Nelson, Leslie Hudson. Publisher: Wiley-Blackwell
2. Clinical Immunology: A Practical Approach by H.C. Gooi, Helen Chapel. Publisher: Oxford University Press.
3. Allergic Diseases: Diagnosis and Management by Roy Patterson, Leslie C. Grammer, Paul A. Greenberger.

B. Journals

1. Journal of Immunology
2. Journal of Clinical Immunology
3. Journal of Allergy and Clinical Immunology
4. Clinical Experimental Allergy
5. Current Opinion in Immunology
6. Clinical Immunology
7. Annals of Allergy, Asthma and Immunology
8. Journal of Immunological Methods
9. Immunological Reviews
10. Reviews in Immunogenetics
11. Tissue Antigens
12. Transplantation