Study & Evaluation Scheme

of

Doctor of Medicine
MD (Pathology)
2011-12
P.G. Curriculum
M.D. Pathology

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PG Curriculum
MD Pathology

The infrastructure and faculty in the department will be as per MCI guidelines..

1. Goals
The goal of MD course in Pathology is to produce a competent pathologist who:
- Has acquired the competence pertaining to basic instrumentation and procedures required for the practice of Pathology in the community and at all levels of health care system.
- Has acquired skills effectively in communicating the diagnosis to the patients especially cancer patients. He should be able to demonstrate empathy and have a humane approach towards patients and their families and respect their sensibilities.
- Demonstrate communication skills of a high order in explaining management and prognosis, providing counseling and giving health education messages to patients, families and communities.
- Practice the specialty of Pathology in keeping with the principles of professional ethics.
- Function as a productive member of a team engaged in health case, research and education.

2. Objectives
- Has the competence to diagnose important pathological conditions in various fields like histopathology, cytopathology, haematology & Immunopathology.
- Has acquired skills in effectively interpreting all laboratory reports.
- Develops skills as a self-directed learner, recognize continuing educational need, use appropriate learning resources, and critically analyze published literature in order to practice evidence-based pathology.
- Demonstrates competence in basic concepts of research and epidemiology.
- Can organize and supervise the desired managerial and leadership skills.
3. Syllabus
3.1. Theory
  _ General Pathology
  _ Cellular adaptation cell injury and cell death
    _ Mechanism, morphology and examples of cell injury, necrosis and apoptosis.
    _ Subcellular and cellular responses and adaptation to injury
      _ Intracellular accumulations, pathological calcification and cell aging.
  _ Acute and chronic inflammation
    _ Vascular and cellular events in acute inflammation, chemical mediators, outcome and morphological patterns of acute inflammation.
    _ Chronic inflammation with special reference to granulomatous inflammation.
    _ Systemic effects and effects of deranged inflammation.
  _ Tissue renewal and repair: Regeneration healing and fibrosis.
    _ Control of normal cell proliferation and tissue growth, mechanism of tissue regeneration, repair by healing and fibrosis.
    _ Extracellular matrix and cell matrix interactions.
  _ Hemodynamic disorders, thromboembolic disease and shock.
    _ Edema, hyperemia, congestion and haemorrhage.
    _ Normal Hemostasis, thrombosis, DIC, embolism, infarction and shock.
  _ Genetic Disorders
    _ Principles of genetics, normal karyotyping.
    _ Mutations, Mendelian disorders, disorders with multifactorial inheritance cytogenetic disorders involving autosomes and sex chromosomes.
    _ Single gene disorders with nonclassic inheritance.
    _ Diagnosis of genetic disorders involving molecular and genetic techniques.
  _ Neoplasia
    _ Definition, nomenclature and biology of tumor growth.
    _ Molecular basis of cancer with special reference to carcinogenic agents and molecular basis of multistep carcinogenesis.
    _ Epidemiology and clinical features of tumors.
    _ Grading, staging and laboratory diagnosis of cancer.
  _ Infectious Diseases
    _ General principles of microbial pathogenesis, bacterial, fungal, parasitic and viral infections.
  _ Environmental and nutritional pathology
    _ Common environmental and occupational exposures leading on to diseases.
    _ Nutritional deficiencies and obesity related disorders.
  _ Disease of Infancy and Childhood
    _ Congenital anomalies, birth injuries, diseases of neonates, inborn errors of metabolism, tumor and tumor like lesions of infancy and childhood.
**Systemic Pathology**

**Blood vessels, lymphatic and veins**
- Normal morphology, congenital anomalies, atherosclerosis, hypertensive vascular disease.
- Inflammatory and neoplastic diseases of all the vessels.

**Heart**
- Normal morphology, its blood supply and effect of aging on heart.
- Ischemic, hypertensive, valvular, congenital heart diseases and cardiomegaly
- Pericardial diseases.
- Tumors of the heart.

**Lungs**
- Congenital anomalies
- Obstructive and restrictive pulmonary diseases.
- Diseases of vascular origin.
- Infections and tumors of lung
- Lung transplantation
- Diseases of pleura.

**Head and Neck**

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- Oral cavity: - inflammatory disease and tumors
- Diseases of teeth and supporting structures.
- Upper airways and ear – congenital anomalies, infections and tumors.
- Salivary glands – Infections autoimmune disorders and tumors.
- Thymus – Developmental autoimmune and inflammatory disorder and tumors.

**Gastro Intestinal Tract**
- Congenital anomalies, infections inflammatory and vascular disorders and tumors of esophagus, stomach, small and large intestines, appendix and anal canal.
- Diseases of the peritoneum

**Liver**
- Normal morphology with general features of hepatic disease including LFTs.
- Infectious, autoimmune drug induced, metabolic and circulatory disorders of liver.
- Hepatic diseases associated with pregnancy, neonates organ and bone marrow transplantation.
- Liver transplantation
- Nodules and tumors of liver.

**Biliary tract**
- Congenital anomalies, injuries, Gallstones, cholecystitis and tumors of gall bladder and extra hepatic bile ducts.

**Pancreas**
- Congenital anomalies, pancreatitis and neoplasms of pancreas.

**Kidney**
- Clinical manifestations of renal diseases
- Congenital anomalies
Diseases affecting glomeruli, tubules, interstitium and blood vessels.
- Cystic diseases of kidney.
- Tumors of kidney

**Lower urinary tract and male genital system.**
- Congenital anomalies, inflammation and tumors of ureter, urethra, penis, testis and epididymis.
- Inflammation, enlargement and tumors of prostate.

**Female genital tract**
- Embryology, Anatomy, Physiology and histology of female genital tract.
- Congenital anomalies, inflammation and tumors of vulva, vagina, cervix, uterus, fallopian tubes and ovaries.
- Gestational and placental disorders.

**Breast**
- Inflammations, benign epithelial lesions and tumors of the breast.
- Diseases of male breast.

**The Endocrine System**
- Normal hormonal levels and functions of all the endocrine glands.
- Hypo and hyperactivity of glands of endocrine system i.e. pituitary, thyroid, parathyroid, pancreas, adrenals and pineal gland.
- Autoimmune diseases, inflammations and tumors affecting these glands.

**Skin**
- Disorders of pigmentation and melanocytes
- Inflammatory, vesiculobullous and infectious disease
  Tumors of the epidermis, dermis and skin appendage.

**Musculoskeletal system**
- Bones
  Modelling, growth and development, genetic and acquired abnormalities in bone cells, matrix and structure, features necrosis and infections of bones, tumors and tumor like lesions.
- Joints
  Arthritis, tumor and tumor like lesions.
- Soft tissue
  Tumors and tumor like lesions

**Peripheral nerves and skeletal muscles**
- General reactions of motor units.
- Inflammatory, infectious, hereditary, metabolic and traumatic neuropathies
- Atrophy, dystrophy, myopathies of the skeletal muscles.
- Diseases of neuromuscular junction
- Tumors of peripheral nerves and skeletal muscle bundles

**Central Nervous System**
- Degenerative, metabolic, toxic, demyelinating, infectious, cerebrovascular malformations and traumatic injuries of skeletal muscle bundles.
- Tumors

**Eye**
- Infections, inflammatory, congenital diseases and neoplasms of orbit, eyelid, conjunctiva sclera, uvea, cornea, retina and optic nerves

**Cytopathology**
- General Cytology
Origin & principles with stress on basic structure of a mammalian cell.
Recognition and classification of different cell types.
Fundamental concepts of neoplasia – Benign & malignant.
**Cytology of Female Genital Tract**
Normal FGT
Cytologic evaluation of menstrual disorders and hormonal abnormalities
Benign disorders of uterus, cervix and vagina.
Intraepithelial lesions and squamous carcinoma of the uterine cervix
Adenocarcinoma and related lesions of the uterine cervix.
Proliferative disease and carcinoma of the endometrium.
Disease of vagina and vulva.
Tumorous and non-tumorous conditions of ovary and fallopian tubes.

**CYTOLOGY**

**Cytology of Respiratory tract**
Non-cancerous and cancerous lesions including conventional and aspiration cytology.

**Cytology of GIT**
Lesions of oral cavity, salivary glands, oesophagus, stomach, small intestine, colon and rectum.

**Cytology of kidney & lower urinary tract**
Cancerous & non-cancerous lesions, conventional cytology, aspiration cytology, urine & brushings.

**Breast cytology**
Cytological diagnosis of all breast lesions on FNA.

**Cytology of thyroid, lymph nodes, neck masses.**
Aspiration cytology of all common lesions.
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**Cytology of Skin, Bone & Soft tissue**
Cytology of common lesions
**Cytology of Liver, Spleen, Pancreas, Retroperitoneum, Abdominal lumps**
Cytology of neoplastic and non-neoplastic lesions
**Cytology of Testis & Prostate.**
**Miscellaneous**
Lesions of eye, orbit
Mediastinum
CNS – Touch smears

**Cytology of all effusions & fluids in the absence as well as presence of cancer.**
HAEMATOLOGY

Clinical Correlation
Signs & Symptoms, General & Systemic examination) with various haematological disorders.

Biology of stem cell & disorder of Haematopoiesis.
- Overview of stem cell biology and cellular biology of haematopoiesis.
- Transcription factors and humoral regulation in normal and malignant haematopoiesis.
- Interaction between haematopoietic stem cells, progenitor cell and stromal compartment of bone marrow.
- Stem cell homing & mobilization.

Erythroid maturation, differentiation and abnormality.
- Pathobiology of human erythrocyte & Haemoglobin.
- Anaemias
  - Approach to anaemia in adults and children in: Clinical correlation & diagnostic modalities.
  - Classification of anaemias (Morphological, pathophysiological and based on erythropoiesis ie Proliferative vs non-proliferative)
  - Iron deficiency anaemia including iron metabolism and differential diagnosis from other microcytic hypochromic anaemias.
  - Disorder of iron metabolism including iron overload.
  - Anaemia of chronic disorders with special reference to infections, collagen vascular disorders, inflammation etc.
  - Megaloblastic anaemia and other causes of megaloblastosis.
  - Definition, lab diagnosis of Haemoglobin disorders like Thalassemia, sickle cell anaemia, Haemoglobin associated with altered Oxygen affinity.
  - Red blood cell enzymopathy, membrane disorder, autoimmune hemolytic anaemia, non immune hemolytic anaemia, paroxysmal nocturnal haemoglobinuria.
  - Approach to Pancytopenia

WBC disorders, complement and immunoglobin biology
- Normal granulopoiesis
- Acquired and congenital disorders of phagocytosis (neutrophil, monocyte, eosinophil and macrophages)
- Disorder of lymphocyte function
- Storage disorder.
- Lymphocyte response to the various viral disorders like infectious
  - Mononucleosis, Hepatitis & Dengue
- Hematological responses to Viraemia and parasitic infections

Haematological malignancies:-
- Conventional & molecular cytogenetic and immunohistochemical basis of haematological malignancies.
- Classification (FAB, WHO). Their basis and diagnostic approach to various haematological malignancies.
- Pathophysiology, prognostic factors, cytochemistry, cytogenetics of various acute myeloid and lymphoblastic leukaemias
Pathophysiology and classification of MDS, MPD/MDS, myeloproliferative disorders

Plasma cell dyscrasias & Mastocytosis especially with reference to practical aspects of the clinical approach to patient.
Role of chemotherapy and antineoplastic agents based on molecular mechanism of haematological malignancies, clinical use of haematopoietic growth factors.
Late complications of Haematological disorders.

Haematopoietic stem cell transfusion

Gene transfer for haematological disorders.

Haemostasis & Thrombosis.

Megakaryocyte and platelet structure. Molecular basis of platelet function, activation. Role of blood vessel, coagulation system and fibrinolytic system in haemostasis.
Clinical evaluation of bleeding disorder.
Clinical & diagnostic aspects of:
  - Haemophilia,
  - Coagulation factor deficiency,
  - Von Willebrand disease,
  - Thrombotic and non thrombotic purpura,
  - Hereditary and acquired platelet disorders
Factors effecting coagulation, Venous Thromboembolism and role of lupus anticoagulant.

Human blood group antigen and antibody.

Haematological manifestations of various diseases like liver disorders, renal disorders, infections, cancers, AIDS and Parasitic diseases.

Haematological problem in surgical patients.

Spleen and its disorders.

Current topics and recent advances.

Immunopathology

Innate immunity

Role of phagocytic cells, complement, mast cells & humoral mechanisms.

Specific Acquired Immunity-

Details about antibody production & action, Brief principles about memory,
Ag specificity & vaccination

Cell involved in Immune response-

T- lymphocytes, B-lymphocytes, macrophages, dendritic cells and natural-killer cells, Natural killer Cells

Cytokines with details about their properties and functions

Structure and function of histocompatibility molecules and disease association

Disorders of the immune system
- All hypersensitivity reactions
- Autoimmune disorders with special reference to SLE, Rheumatoid arthritis, Sjogren’s syndrome, systemic sclerosis, polyarteritis nodosa and other vasculitides, Mixed connective tissue disorders and inflammatory disorders.
- Immunodeficiency syndrome – Acquired with emphasis on AIDS

Amyloidosis including pathogenesis, special stains & clinical correlation.

Transplant rejection in detail

Graft Vs Host Disease

Practical
Histopathology

Histological techniques

- Principles of grossing
- Fixation and fixatives.
- Tissue processing and microtomy
- Theory of staining and its implications
- Details of haematoxylin and eosin stain
- Principles of special stains used in histopathology with their practical applications.
- Processing of bones
- Immunocytochemical, enzyme, histochemistry,
- Details, techniques and uses of immunohistochemistry.
- Internal and external quality control and management of laboratory.
- Principles & application of all types of microscopes e.g. light, electron, fluorescence etc.
- Block cutting,
- Staining - routine (H & E),
- Mounting and labelling of slides
- Special stains
- PAS stain
- ZN stain
- Reticulin stain
- Masson’s trichrome stain

Cytopathology

- Fixation & staining of smears
- Processing of fluid specimens
- Cyto centrifugation
- Filtration procedures
- Liquid based cytology
- Preparation of cell blocks
- Stains
- Pap stain
- Ziehl Neelsen stain
- Giemsa stain
- H & E stain

Haematology

- Interpretation of a Hemogram
_ Preparation & examination of blood & Bone marrow with relevant special stains
_ Bone marrow aspiration & biopsy procedure
_ ESR
_ Reticulocyte count preparation & interpretation of smear for Reticulocyte count
_ Hemoglobin electrophoresis
_ Osmotic fragility,
_ BT, CT, PTI, PTTK, FDP, Fibrinogen
_ G6PD
_ Plasma Hb
_ Fetal Hb
_ Coomb’s test
_ Sickling test
_ LE cell phenomenon

_ Clinical Pathology
_ Complete urine examination with reference to its physical, chemical and special tests.
_ Semen examination – Physical, chemical (pH, Liquefaction time) and microscopic examination.
_ Stool examination – Physical and microscopic examination

_ Immunopathology
_ Agglutination Reactions- Principle, Techniques & practical Applications
_ All tests based on ELISA – Principle, Techniques & practical Applications
_ Protein electrophoresis – Principle, Technique & practical applications
_ Immunoelectrophoresis
_ Immunohistochemistry Principle, Techniques & Practical Applications

4. Teaching Programme
4.1. General Principles

Acquisition of practical competencies being the keystone of postgraduate medical education, postgraduate training is skills oriented.

Learning in postgraduate program is essentially self-directed and primarily emanating from clinical and academic work. The formal sessions are merely meant to supplement this core effort.

4.2. Teaching Schedule
1. Journal Club-Once a week
2. Subject seminar-Once a week
3. Slide discussion-Once a week
4. Central sessions-Once a week(CPC)
5. Formal lecture/interactions-Once a week

5. Postings
Residents will be posted in all the sections – Histopathology, Cytopathology, Hematology, Clinical Pathology and Immunology during all the 3 years. There will also be postings in Microbiology and Biochemistry once during the 3 year period.

6. Thesis
6.1. Every candidate shall carry out work on an assigned research project under the guidance of a recognized Postgraduate Teacher, the project shall be written and submitted in the form of a Thesis.

6.2. Every candidate shall submit thesis plan to the University within the time frame set by the university.

6.3. Thesis shall be submitted to the University six months before the commencement of theory examination i.e. for examination May/June session, 30th November of the preceding year of examination and for November/December session 31st May of the year of examination.

6.4. Identify a relevant research question; (ii) conduct a critical review of literature; (iii) formulate a hypothesis; (iv) determine the most suitable study design; (v) state the objectives of the study; (vi) prepare a study protocol; (vii) undertake a study according to the protocol; (viii) analyze and interpret research data, and draw conclusions; (ix) write a research paper.
7. Assessment

All the PG residents are assessed daily for their academic activities and also periodically.

7.1. General principles

- The assessment is valid, objective, and reliable.
- It covers cognitive, psychomotor and affective domains.
- Formative, continuing and summative (final) assessment is also conducted in theory as well as practicals/clinicals. In addition, thesis is also assessed separately.

7.2. Formative Assessment
The formative assessment is continuous as well as end-of-term. The former is based on the feedback from the senior residents and the consultants concerned. End-of-term assessment is held at the end of each semester (upto the 5th semester). Formative assessment will not count towards pass/fail at the end of the program, but will provide feedback to the candidate.

7.3. Summative Assessment
- Ratio of marks in theory and practicals will be equal.
- The pass percentage will be 50%. Candidate will have to pass theory and practical examinations separately.

A. Theory examination (Total = 400 marks)
Title Marks
Paper 1: Patho-physiology and General principles of Pathology including Applied Pathology
100
Paper 2: Immunopathology, Molecular Biology, Cytogenetics and Experimental Pathology including Cancer Research
100
Paper 3: Histopathology - Cytology including recent advances in the concerned Topics.
100
Paper 4: Haematology, ImmunoHaematology & Blood Transfusion with Recent advances in the concerned topics.
100

B. Practical & viva voce examination (Total = 400 marks)
Splitting of marks: Total 300
Practical Examination (300 marks) is conducted over two days and the student evaluated out of 300 marks which is distributed as follow:
1. Clinical case with routine and special haematology test (25 marks)
2. Haematology slides 10 slides (100 marks)
3. Cytology slides 5 slides (50 marks)
4. Histopathology slides – 10 slides (100 marks)
5. Grossing and histopathological techniques (20 marks)
6. Spots (5 marks)

**Oral: 100**

8. **Job Responsibilities**
   - Reporting in Clinical Pathology
   - Routine hemograms.
   - Routine urine examination
   - Routine Stool examination.
   - Cytology of fluids like CSF, Pleural fluid etc.
   - Perform procedures
   - Grossing
   - Bone marrow aspiration & Biopsy
   - Fine needle aspiration
   - Attend reporting sessions with consultant in 1\textsuperscript{st} year. Independent screening and discussion with reporting consultant 2\textsuperscript{nd} year onwards.
   - Histopathology
   - Cytopathology
   - Haematology
   - Interpret under supervision all Immunopathology techniques & special haematology techniques.
   - Assist in undergraduate teaching especially practical classes and tutorials.
9. **Suggested Books**

9.1 Core books

- Basic Pathology by Robin’s
- Surgical Pathology by Ackerman
- Cytopathology Atlas (McKee)
- Diagnostic Cytopathology (Gray)
- Wintrobe’s Clinical Hematology
- Practical Hematology (Dacie)
- Essential immunology (Roitt)

9.2 Reference Books

- WHO Fascicles
- Silverberg’s Principles and practice of Surgical
- Diagnostic Cytopathology (Koss)
- Comprehensive cytopathology (Bibbo)
- Cytopathology (Naib)
- Diagnostic cytopathology (Orell) Pathology & Cytopathology
- Greenfield’s Neuropathology
- Heptinstall’s pathology of kidney
- Lever’s histopathology of skin
- Primer of Dermatopathology
- Pathology of Placenta (FOX)
- Schiffer’s Brain Tumors
- Liver biopsy interpretation (Scheuer)
- Tumors of Fetus and Newborn (Isaacs)
- Dahlin’s Bone tumors
- Urological Pathology (Murphy)
- Spencer’s Pathology of Lung
- Cardiovascular Pathology (P Chopra)
- Williams Pathology of GIT
- Clinical diagnosis and management by Laboratory methods
- Postgraduate hematology (Hoffbrand)
- Immunopathology – Lobo & Stites.
- Blood Cells – A Practical Guide (Barbara Bains)

9.3 Journals

- Indian Journal Of Pathology & Microbiology
- Indian Journal Of Haematology & Transfusion Medicine
- Indian Journal Of Cytology
- Cytopathology
- Acta Cytologica
10. Model Test Papers

MD (Pathology)

Paper-I
Pathophysiology and General Principles of Pathology including Applied Pathology
Max. Marks: 100
Time: 3 hrs

Attempt ALL questions
Answer each question & its parts in SEQUENTIAL ORDER
ALL questions carry equal marks
Illustrate your answer with SUITABLE DIAGRAMS

I Discuss the molecular events leading on to apoptosis and give examples.
II Give a diagrammatic representation of the various signal transduction pathways. Discuss in detail the role of tyrosine kinase pathway in neoplasia.
III Discuss in detail the pathogenesis of septic shock.
IV Give an account of the various oncogenes, their mode of action and association with human tumors.
V Describe the tissue response to fungal infections in humans.
VI Elaborate the pathogenesis and complications of obesity.
VII Explain the Pathophysiology of uraemia.
VIII Discuss cystic disease of kidney under the following headings:
a. Pathogenesis
b. Morphology
IX Outline the role of adhesion molecules in acute inflammation.
X Discuss the various aspects of telepathology.
MODEL QUESTION PAPER

MD (Pathology)

Paper-II

Immunopathology, Molecular biology, Cytogenetics and experimental Pathology including cancer research

Max. Marks: 100 Time: 3 hrs

Attempt ALL questions

Answer each question & its parts in SEQUENTIAL ORDER

ALL questions carry equal marks

Illustrate your answer with SUITABLE DIAGRAMS

I Discuss in detail the diagnostic and therapeutic applications of immunohistochemistry.
II Elaborate the mechanisms involved in renal transplant rejection.
III Discuss FISH under the following headings – principles, applications and diagnostic pitfalls.
IV Enumerate the various hypersensitivity reactions and discuss in detail type III hypersensitivity reaction.
V Outline the laboratory diagnosis of autoimmune diseases.
VI Describe the normal structure, function and disease association of the HLA system.
VII Discuss the various aspects of proteomics.
VIII Write a note on the role of immunofluorescence as a diagnostic tool in pathology.
IX Explain the process of serum protein electrophoresis and immunofixation and its clinical applications.
X What is the role of tissue microarray in the diagnosis of malignancy?
MODEL QUESTION PAPER

MD (Pathology)

Paper-III
Histopathology – Cytology including Recent Advances in the concerned topics

Max. Marks:100 Time: 3 hrs

Attempt ALL questions

Answer each question & its parts in SEQUENTIAL ORDER

ALL questions carry equal marks

Illustrate your answer with SUITABLE DIAGRAMS

I Discuss the differential diagnosis of neonatal cholestasis.
II Enumerate the Premalignant lesions of breast. Give their morphology and risk of progression to invasive cancer.
III List the various giant cell lesions of bone and discuss their differential diagnosis.
IV Highlight the role of transbronchial lung biopsy in the diagnosis of interstitial lung disease.
V Describe the pathogenesis and morphology of childhood renal tumors.
VI Discuss the role of IHC as an aid to morphology in the differential diagnosis of grey zone lesions of the prostate.
VII Discuss the principles, advantages and disadvantages of liquid based cytology.
VIII Elaborate the role of endoscopic ultra sound guided FNA in lesions of pancreas.
IX Explain the various aspects of quality control in histopathology laboratory.
X Write a note on the recent concepts in the pathogenesis of atherosclerosis.
MODEL QUESTION PAPER

MD (Pathology)

Paper-IV

Haematology, Immunohaematology & Blood Transfusion & Recent Advances in the concerned topics

Max. Marks:100 Time: 3 hrs

Attempt ALL questions

Answer each question & its parts in SEQUENTIAL ORDER

ALL questions carry equal marks

Illustrate your answer with SUITABLE DIAGRAMS

I Discuss the procedures for maintenance of precision in automated electronic cell counters.

II Elaborate WHO classification of AML with its merits and demerits.

III Describe the molecular methods for the diagnosis of red cell membrane disorders.

IV Enumerate the haematological complications of HIV with their pathogenesis.

V Discuss in detail the role of bone marrow trephine biopsy in haematolymphoid malignancies.

VI Outline the laboratory diagnosis of platelet function disorders.

VII Give an overview of the recent concepts in stem cell transplantation.

VIII Discuss Waldenstrom’s macroglobulinemia under the following headings – clinical features, morphology and diagnosis.

IX Give an account of the Pathophysiology of Acquired Aplastic Anaemia.

X Discuss in detail the lab diagnosis of DIC.