Lecture 1 General pathology

Introduction to pathology

Pathology: The study of diseases by scientific method.

Pathology as a word means the study (*logos*) of suffering (*pathos*).

Pathology involves the investigation of:

1- Etiology: The causes of disease.

2- Pathogenesis: The underlying mechanisms that result in the presenting signs and symptoms of the disease.

3- Morphology: Identify changes in the gross or microscopic appearance of cells, tissues and organs.

The ultimate goal of pathology is the identification of the cause or causes of a given disease (etiology) that can eventuate in disease prevention &/or successful therapy.

The primitive light microscope of Rudolf Virchow (1821-1902), a German pathologist, enabled him to see changes in diseased tissues at a cellular level. His observations have had a profound influence on the understanding of many diseases

Pathology is divided into:
a- General pathology: Study of cellular and tissue responses to pathologic stimuli.
b- Systemic pathology: study of the particular responses of specialized organs.

Disease: Abnormal variation in structure or function of any part of the body.
Causes of diseases:
A- Genetically determined diseases: Abnormality in the DNA of the fertilized ovum that is inherited from one or both parents.
B- Acquired diseases: occurs due to environmental factors like:

1- Deficiency disease: iron deficiency anemia.

2- Physical agents: mechanical injury, heat, cold, irradiation.

3- Chemical and drugs: cyanide, strong acids and alkalis.

4- Infectious microorganism: bacteria, fungi and viruses.

5- Immunological factors: immunity has protection effects against microbes but it also has harmful effects due to reaction of antibodies and lymphocytes with microbes and their toxic products.

6- Pscyhologic factors: schizophrenia, depression.

7- Diseases of addiction (alchohol, tobacco and various drugs).

Experimental pathology refers to the observation of the effects of manipulations on animal models or cell cultures regarding researches on human diseases.

Clinical pathology: the approach to the patient's illness clinically is based on the following sequence of steps;
Patient's history _Examination_Investigations _Diagnosis _Treatment

Clinical pathology is more concerned with analysis of the disease itself that include;
§ its cause (etiology),
§ the mechanisms of its evolution (pathogenesis),
§ its effects on various organs and systems of the body.

Methods used to study pathology:

1- Histopathology: Examination of the diseased tissues by light or electron microscope.

2- Cytopathology: Examination of isolated cells for diagnosis of the disease.

3- Biochemistry: Examination of the metabolic disturbances of diseases by evaluation of various compounds in body fluids.

4- Microbiology: Identification of the causative microorganism of the disease by examination of body fluids, mucosal surfaces and excised tissues using microscopical, cultural and serological techniques.

5- Haematology: Microscopical examination of blood.

6- Cytogenetics: Examination of chromosomal abnormality.

7- Histochemistry: Detection of cells and tissues constituents using special immunohistochemical techniques.

8- Forensic pathology: Examination of tissues taken from autopsy (dead body).

9- Toxicology; concerned with the study of the effects of known or suspected poisons on the body.

Techniques in Pathology

1-Anatomic Pathology
- a-Gross pathology
- b-Light Microscopy
- c-Immunohistochemistry & immunofluorescence
- d-Electron microscopy
- e-Molecular pathology

2-Biochemical techniques
3-Hematological techniques
4-Medical microbiology
5-Serology 6-Flowcytometry

Gross pathology (macroscopic pathology):

This refers to the changes affecting various organs and tissues in diseases as evident to the naked eye. Much of these changes have been derived from autopsy (postmortem) examinations, which is still an important investigative method.

The gross pathology of many diseases is so characteristic that an experienced pathologist can give a fairly confident diagnosis of the disease before further investigations are carried out.

Light microscopy:

Advances in light microscopic examination have resulted in a wealth of new information about the structure of tissues and cells in health and disease.

If solid tissues (e.g. liver, kidney etc.) are to be examined by light microscopy, the sample must first be thinly sectioned to permit the transmission of light and to minimize the superimposition of tissue components.

These sections are routinely cut from tissue hardened by permeation with and embedding in wax

For some purposes (e.g. histochemistry, or when very urgent diagnosis is needed) sections have to be cut from tissue that has been hardened rapidly by freezing (frozen section technique).

The sections are stained to help distinguishing between different components of the tissue (e.g. nuclei, cytoplasm, and other structures such as collagen).

Stains used in pathology:

1- Haematoxylin and eosin stain (H&E): It is the primary stain used in sectioned slides to reveals their histological details. Haematoxylin has strong affinity for nuclear chromatin giving blue discoloration, while eosin has strong affinity for proteins presents in the cytoplasm giving pink discoloration.

2- Periodic acid Schiff stain (PAS): Special stain used to demonstrate glycogen, neutral mucosubstances, basmement membrane and most types of fungi and parasites.

3- Stain for microorganism: used to demonstrate gram-positive and gram-negative bacteria, acid fast bacteria, fungi and parasites. e.g: Gram stain and zeihl-Neelsen stain.

4- Amyloid stain: e.g. congo red for detection of amyloid.

5- Reticulin stain: used to demonstrate both reticular fiber (type III collagen presents in the connective tissue throughout the body) and basement membranes (type IV collagen and laminin). The main use of this stain is in tumor pathology.

6- Giemsa stain: used to demonstrate lymphoreticular elements.

7- Perl's stain (for the detection of iron).

Immunohistochemistry and immunofluorescence

These techniques employ antibodies (with antigen specificity) to visualize substances (for e.g. cellular proteins or surface receptors) in tissue sections or cytological cell preparations.

To visualize the reaction sites; these antibodies are connected **chemically to enzymes (Immunohistochemistry) or fluorescent dyes (Immunofluorescence) are used.**

In immunohistochemistry the end product is a deposit of colored material that can be seen with a conventional light microscope. The list of substances detectable by these techniques has been greatly enlarged by the development of monoclonal antibodies.

Electron microscopy: this has extended the range of pathology to the study of disorders at an organelle (subcellular) level and the demonstration of viruses in tissue samples from some diseases.
The most common diagnostic use of electron microscopy, however, is the interpretation of renal biopsies i.e. helps establish the diagnosis of various glomerular diseases.

Electron Microscopes (EM) are scientific instruments that use a beam of highly energetic electrons to examine objects on a very fine scale

Application of EM to diagnostic Pathology
1. Tumor pathology (histogenesis)
2. Renal pathology (deposits and classification)
3. Skin vesicular disorder

Molecular pathology:
Many important advances are now coming from the science of molecular pathology for e.g. the disclosure that defects in the chemical structure of molecules are in fact the result of errors in the genomic DNA, and precisely, in the sequence of the DNA bases that directs amino acid synthesis.
Through the use of in situ hybridization technique, it is possible to make the presence of specific genes or their messenger RNA visible in tissue sections or cell preparations.
Minute quantities of nucleic acids can be amplified by the use of the polymerase chain reaction (PCR) using oligonucleotide primers specific for the genes being studied.

DNA microarrays can be used to determine patterns of gene expression (mRNA).
Molecular pathology applications include the study, for example, of abnormal hemoglobin molecules, such as in sickle cell disease and the alterations in the genome that control cell growth, which is important part in the development of neoplasms

MORBID ANATOMY (AUTOPSY)
An autopsy, also known as a post-mortem examination or necropsy
itis a procedure that consists of a thorough examination of a dead body to determine the cause and manner of death and to evaluate any disease or injury that may be present. It is usually performed by a specialized medical doctor called a pathologist.

Autopsies are useful
1- For the determination of the cause of death
2- The evaluation of the accuracy of clinical diagnosis (and hence management) before death; thus, postmortems act as a quality control for the medical practice.
3-Education tool for medical students (both undergraduates and postgraduates) to learn pathology. It is an opportunity to correlate clinical signs with their underlying pathological changes.
4-As a source of research into the causes and mechanisms of different diseases
5-For accurate statistics about disease incidence.