

## CHAPTER ONE INTRODUCTION TO PATHOLOGY

The literal translation of the word pathology is the study (**logos**) of suffering (**pathos**). It is a discipline that bridges clinical practice and basic sciences. Pathology is concerned with the study of diseases in a scientific way. It comprises a wide foundation of scientific data and investigative procedures that are essential for the practice of modern medicine. In the pathology of any given disease there are structural changes of the relevant tissues that are reflected as functional disturbances, which in turn are perceived as clinical features. The range of the structural changes is from those affecting sub-cellular organelles (molecular pathology) up to alterations seen by the naked eye (gross pathology). Pathology is a dynamic science in that its contents are continuously subjected to changes, revisions and expansions. This is because there are always new findings that shed more light on, add or modify an already established knowledge of various diseases. 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.

### **MORBID ANATOMY (AUTOPSY) (POST-MORTEM EXAMINATION)**

This is one of the scientific ways in pathology to study diseases, and consists of external and internal examination of the body after death. It is through this important investigative technique much information has been gained to help clarify the nature of many diseases. Autopsy comprises both gross (naked eye) as well as microscopic examinations of the diseased organs and tissues. The post-mortem findings enable the pathologist to reach the ultimate pathological diagnosis, to make a clinico-pathologic correlations, and finally to deduce the cause of death. This technique in pathology has enlightened us about the natural history (the expected progress) of many diseases as well as the underlying mechanisms of the relevant clinical features.

#### **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.

## MICROSCOPIC PATHOLOGY

Pathology, and consequently medicine, has been revolutionized by the application of microscopy to the study of diseased tissues from about the year 1800 AC. Before this, it was postulated that diseases are spontaneously generated, independent of any external causes or other influences. This attitude seems

unreasonable to us today, but at that time nothing was known of infectious agents (such as bacteria and viruses, etc.) or cancer causative agents (such as ionizing radiation and carcinogenic chemicals, etc.). 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. At this point it should be emphasized that the contribution of other branches of pathology is unquestionable for e.g. the advances in biochemistry are renovating the knowledge of many diseases at a molecular level; we now have biochemical explanations for many of the cellular and clinical manifestations of disease.

## FIELDS OF PATHOLOGY

Pathology is the foundation of medical science and practice. Without pathology, the practice of medicine would be reduced to legends and traditions.

**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

Pathology/ Third stage

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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. It should be noted that clinical medicine and clinical pathology are complementary and can not be separated: clinical medicine cannot be practiced without an understanding of pathology; pathology is meaningless if it is cut off clinical conclusions.

**Subdivisions of clinical pathology:** in practice the major subdivisions of pathology are **Histopathology**; concerned with the investigation and diagnosis of disease from examination of tissues

**Cytopathology**; concerned with the investigation and diagnosis of disease from the examination of isolated cells

**Hematopathology**; concerned with the study of disorders affecting the cells and the coagulation system of blood

**Microbiology**; concerned with the study of infectious diseases and the organisms responsible for them

**Immunopathology**; concerned with the study of disturbances affecting the defense mechanisms of the body, and their contribution to the disease processes.

**Chemical pathology**; concerned with the study and diagnosis of disease from the chemical changes that occur in tissues and fluids.

**Medical genetics**; concerned with the study of abnormal chromosomes and genes and their relevance to disease processes

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

**Forensic pathology**; concerned with the application of pathology to legal purposes (e.g. investigations of death in suspicious circumstances). Because of the continuous and rapid advances in the above subjects, it is impossible for one pathologist to cover all these branches. Thus each of these branches requires its own team of expert specialists; in fact there are currently specialists in the sub-braches of each of the disciplines mentioned above for e.g. in histopathology there are specialists in liver disease (hepatopathologist),

in skin diseases (dermatopathologist) & in diseases affecting the nervous system (neuropathologist).

## TECHNIQUES OF PATHOLOGY

Our knowledge of the nature and causation of diseases has been revealed by the continuing application of various tools of pathology to their study. Histopathologic techniques include

**1. 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.

**2. 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 or. 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). The microscope can also be used to examine cells derived from fluid.

**3. Histochemistry:** certain cells produce chemical substances the detection of which through treatment with specific reagents (histochemical stains) is of diagnostic value; e.g. PAS stain (for the detection of glycogen), PAS with prior treatment of tissue sections with diastase (for the detection of mucin) Perl's stain (for the detection of iron).

**4. 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.

**5. 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.

**6. Biochemical techniques:** these are applied to the tissues and body fluids and are now one of the principal factors on the growing understanding of pathological processes. The clinical role of biochemistry is exemplified by the importance of monitoring fluid and electrolyte changes that occur in many disorders. Determination of serum enzyme levels are used to assess the integrity and vitality of various tissues; for example, raised levels of cardiac enzymes in the blood indicate damage to cardiac myocytes and thus very helpful in establishing the diagnosis of myocardial infarction.

**7. Hematological techniques:** these are used in the diagnosis and study of blood disorders. They range from relatively simple blood cells counting, which can be performed electronically, to the more sophisticated assays of blood coagulation factors.

**8. Cell cultures:** these are widely used in research and diagnosis. They are an attractive medium for research because of the ease with which the cellular environment can be modified and the responses to it monitored. Diagnostically, cell cultures are used to prepare chromosome spreads for cytogenetic analysis.

**9. Medical microbiology:** this is the study of diseases caused by organisms such as bacteria, fungi, viruses and parasites. Techniques used include direct microscopy of appropriately stained material (e.g. pus), cultures to isolate and grow the organism, and

methods to identify correctly the cause of the infection. In the case of bacterial infections, the most appropriate antibiotic can be selected to treat a given infection by determining the sensitivity of the bacteria to a variety of therapeutic agents (through the use of antibiotic discs)

**10. 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). This powerful technique can reveal new diagnostic and prognostic categories, indistinguishable by other methods. 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.

## DIAGNOSTIC PATHOLOGY

Hospitalized patients are often investigated to diagnose their illness by applying methods to the examination of tissue biopsies and body fluids (including blood). If there are clinical indications to do so, it may be possible to obtain a series of samples from which the course of the disease can be monitored.

## LEARNING PATHOLOGY

Pathology is best learnt in two stages:

**General pathology** is concerned with the causations, mechanisms and characteristics of the major categories of disease (e.g. cell injuries and degenerations, inflammations, healing, neoplasia). The principles of general

pathology must be understood before an attempt is made to study the pathology of various systems of the body (systemic pathology). This is because the former represents the foundation of knowledge that has to be acquired before indulging in the pathology of various organs systems the body.

**Systemic pathology** is the study of various systems that comprise the body such as cardiovascular pathology, gastrointestinal pathology and so on. It includes the descriptions of specific diseases as they affect individual organs (e.g. appendicitis, lung cancer, atheroma etc.). Each specific disease can usually be attributed to the operation of one or more categories featuring in general pathology. Thus, acute appendicitis is acute inflammation affecting the appendix, whereas carcinoma of the lung is a neoplasia that results from carcinogens acting upon cells in the lung.

### **Building knowledge and understanding**

There are two difficulties facing the new student of pathology: language and process. Pathology, like most branches of medicine, has its own special language: this needs to be learnt and understood not just because they are the language of pathology but they are also a major part of the language of clinical medicine. A logical and orderly way of thinking about diseases and their characteristics must be cultivated; for each disease entity the student should be able to list the chief characteristics:

### **Epidemiology**

### **Etiology**

### **Pathogenesis**

### **Pathological and clinical features**

### **Complications and sequelae**

### **Prognosis**

### **Treatment**