

Lecture 1

# General pathology

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## INTRODUCTION

Pathology also referred to as histopathology, anatomical pathology or morbid anatomy, is the study of abnormal or diseased tissues and organs.

**Pathology** literally translates as the *study of suffering*

(Greek *pathos* = suffering, *logos* = study);

and as applied to modern medicine, it is the *study of disease*.

the foundation of modern pathology is understanding the *cellular and molecular* aberrations that give rise to diseases.

Traditionally, the study of pathology is divided into

1. General pathology is concerned with the common reactions of cells and tissues to injurious stimuli.
2. systemic pathology examines the alterations and underlying mechanisms in diseases of particular organ systems.

*Pathology is fundamental to the study, understanding and diagnosis of disease and therefore to successful treatment.*

**Disease:** Abnormal variation in structure or function of any part of the body.

Micro-organisms that have the capability of producing a disease are referred to as *pathogenic organisms, or pathogens*, as opposed to those that cannot cause illness or disease, which are called *non-pathogens*.

When pathogens attack the body, they may have several effects on the body cells and tissues, causing any of the following reactions:

- **Infection** – the actual invasion of the body cells by the pathogens, resulting in an inflammatory response of the cells, which produces the five signs of inflammation: heat, swelling, pain, redness and loss of function.
- **Ulcer** – a shallow break in the skin or mucous membrane, leaving a raw and painful circular base that may bleed when touched.
- **Cyst** – an abnormal sac of fluid that develops within the body tissues over a period of time.
- **Tumor** – a swelling within any body tissue due to an uncontrolled and abnormal overgrowth of the body cells; when the swelling causes no harm other than displacing any surrounding structures it is called benign, but when the swelling invades and damages the surrounding structures it is called malignant, and is usually referred to as cancer.

### Response of the body to attack by pathogens

The body has three natural lines of defense against attack by pathogens, which in fit and healthy individuals are often enough to prevent the development of a serious illness:

- *Intact skin and mucous membrane*, which acts as a physical barrier against the pathogens, preventing them from entering the body.
- *Surface secretions* that help to dilute and neutralize the pathogens and their poisons (toxins), such as:

- **Saliva in the mouth**
  - **Gastric juice in the stomach**
  - **Sweat on the skin**
  - **Tears in the eyes**
- ***Inflammatory response*** if the body tissues are breached and they have to actively fight off the pathogens

**The four aspects of a disease process that form the core of pathology:**

1. causation (*etiology*).
2. biochemical and molecular mechanisms (*pathogenesis*).
3. the associated structural (*morphologic changes*).
4. functional alterations in cells and organs, and the resulting clinical consequences (*clinical manifestations*)

***1. Etiology is the initiating cause of a disease.***

factors that cause disease can be grouped into two broad classes:

**a. Genetic** (e.g., inherited or acquired mutations, and disease-associated gene variants, or polymorphisms)

**b. Environmental or acquired** (e.g., infectious, nutritional, chemical, physical, Immunological factors, Psychologic factors, Diseases of addiction).

Most likely *atherosclerosis* and *cancer*, arise from the effects of various environmental insults on a genetically susceptible individual and hence are referred to as being multifactorial.

2. **Pathogenesis** refers to the sequence of molecular, biochemical, and cellular events that lead to the development of disease.

The study of pathogenesis is a central focus of pathology. Even when the initial cause is known (e.g., infection or mutation), it is many steps removed from the expression of the disease.

3. **Morphologic changes** refer to the structural alterations in cells or tissues that are characteristic of a disease and hence diagnostic of an etiologic process.

4. **Clinical manifestations**. The end results of genetic, biochemical, and structural changes in cells and tissues are functional abnormalities that lead to the clinical manifestations (symptoms and signs) of disease, as well as its progression (clinical course and outcome). Hence, clinicopathologic correlations are very important in the study of disease.

### **Basic histology techniques:**

*Histopathology* works with tissue samples and *cytopathology* with cell samples. Both end up with the examination of biological material from a patient on a glass slide using a microscope. Before the specimen can be examined in this way a number of steps are usually needed. In the case of a histopathology specimen, after removal from a patient, the tissue undergoes the following steps:

- *Fixation* (which may take up to 48 hours)
- *Macroscopic (gross) examination* and selection of the parts to be submitted for microscopic examination (depending on the size of the specimen)
- *Processing* – takes from 2 hours to overnight
- *Embedding* in paraffin wax
- *Microtomy* (cutting very thin slices) and placing sections onto a glass slide
- *Staining and cover-slipping*

## **Diagnostic techniques used in pathology:**

The pathologist uses the following techniques to the diagnose diseases:

- a. Histopathology
- b. Cytopathology
- c. Hematopathology
- d. Immunohistochemistry
- e. Microbiological examination
- f. Biochemical examination
- g. Cytogenetics
- h. Molecular techniques
- i. Autopsy

### **A. Histopathological techniques**

studies tissues under the microscope. During this study, the pathologist looks for abnormal structures in the tissue.

Tissues for histopathological examination are obtained by biopsy. *Biopsy* is a tissue sample from a living person to identify the disease. Biopsy can be either incisional or excisional.

Once the tissue is removed from the patient, it has to be immediately fixed by putting it into adequate amount of 10% Formaldehyde (10% formalin) before sending it to the pathologist.

The purpose of fixation is:

1. to prevent autolysis and bacterial decomposition and putrefaction
2. to coagulate the tissue to prevent loss of easily diffusible substances
3. to support the tissue against the harmful effects of the various stages in the preparation of sections and tissue processing.
4. to leave the tissues in a condition which facilitates differential staining with dyes and other reagents.

Once the tissue arrives at the pathology department, the pathologist will examine it macroscopically (i.e. naked-eye examination of tissues).

Then the tissue is processed to make it ready for microscopic examination. The whole purpose of the tissue processing is to prepare a very thin tissue (i.e. five to seven  $\mu\text{m}$  or one cell thick tissue) which can be clearly seen under the microscope.

The tissue is processed by putting it into different chemicals. It is then impregnated (embedded) in paraffin, sectioned (cut) into thin slices, & is finally stained. The stains can be Hematoxylin/Eosin stain or special stains such as PAS, Immunohistochemistry, etc...

The Hematoxylin/Eosin stain is usually abbreviated as H&E stain. The H&E stain is routinely used. It gives the nucleus a blue color & the cytoplasm & the extracellular matrix a pinkish color. Then the pathologist will look for abnormal structures in the tissue. And based on this abnormal morphology he/she will make the diagnosis. Histopathology is usually the gold standard for pathologic diagnosis.

## **B. Cytopathology techniques**

Cytopathology is the study of cells from various body sites to determine the cause or nature of disease.

### **Applications of cytopathology:**

#### **1. Screening for the early detection of asymptomatic cancer**

For example, the examination of scrapings from cervix for early detection and prevention of cervical cancer.

#### **2. Diagnosis of symptomatic cancer**

Cytopathology may be used alone or in conjunction with other modalities to diagnose tumors revealed by physical or radiological examinations.

It can be used in the diagnosis of cysts, inflammatory conditions and infections of various organs.

### **3. Surveillance of patients treated for cancer**

For some types of cancers, cytology is the most feasible method of surveillance to detect recurrence. The best example is periodic urine cytology to monitor the recurrence of cancer of the urinary tract.

#### **Advantages of cytological examination**

it is cheap, takes less time and needs no anesthesia to take specimens.

#### **There are different cytopathologic methods including:**

##### **1. Fine-needle aspiration cytology (FNAC)**

In FNAC, cells are obtained by aspirating the diseased organ using a very thin needle under negative pressure. Virtually any organ or tissue can be sampled by fine-needle aspiration. The aspirated cells are then stained & are studied under the microscope. Superficial organs (e.g. thyroid, breast, lymph nodes, skin and soft tissues) can be easily aspirated. Deep organs, such as the lung, mediastinum, liver, pancreas, kidney, adrenal gland, and retro- peritoneum are aspirated with guidance by fluoroscopy, ultrasound or CT scan. FNAC is cheap, fast, & accurate in diagnosing many diseases.

##### **2. Exfoliative cytology**

Refers to the examination of cells that are shed spontaneously into body fluids or secretions. Examples include sputum, cerebrospinal fluid, urine, effusions in body cavities (pleura, pericardium, peritoneum), nipple discharge and vaginal discharge.

##### **3. Abrasive cytology**

Refers to methods by which cells are dislodged by various tools from body surfaces (skin, mucous membranes, and serous membranes). E.g. preparation of cervical smears with a spatula or a small brush to detect cancer of the uterine cervix at early stages. Such cervical smears, also called *Pap smears*, can significantly reduce the mortality from cervical cancer.

### **C. Hematological examination**

This is a method by which abnormalities of the cells of the blood and their precursors in the bone marrow are investigated to diagnose the different kinds of anemia & leukemia.

### **D. Immunohistochemistry**

This is a method is used to detect a specific antigen in the tissue in order to identify the type of disease.

### **E. Microbiological examination**

This is a method by which body fluids, excised tissue, etc. are examined by microscopical cultural and serological techniques to identify micro-organisms responsible for many diseases.

### **F. Biochemical examination**

This is a method by which the metabolic disturbances of disease are investigated by assay of various normal and abnormal compounds in the blood, urine, etc.

### **G. Clinical genetics (cytogenetics),**

This is a method in which inherited chromosomal abnormalities in the germ cells or acquired chromosomal abnormalities in somatic cells are investigated using the techniques of molecular biology.

### **H. Molecular techniques**

Different molecular techniques such as fluorescent in situ hybridization (FISH), polymerize chain reaction (PCR), etc... can be used to detect genetic diseases.

### **I. Autopsy**

Autopsy is examination of the dead body to identify the cause of death. This can be for forensic or clinical purposes.