Pathophysiology

Dr. Yasser Mufid

Lecture 1

Introduction

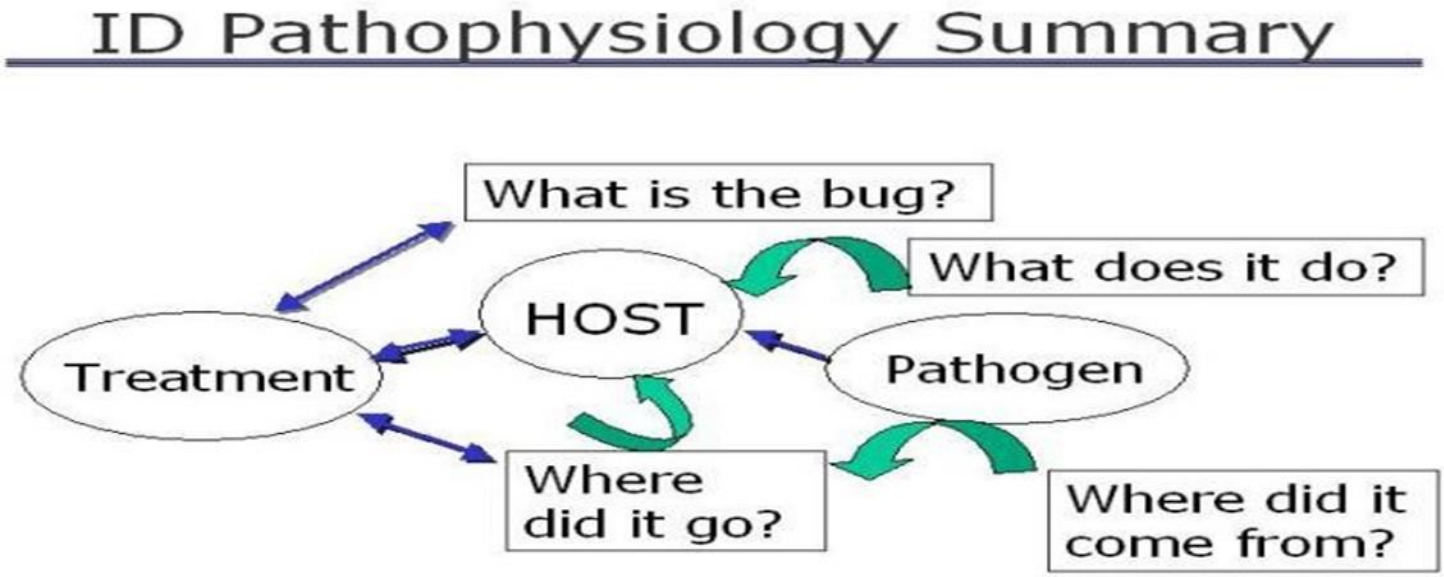
Learning Objectives

Upon completing this Lecture the students should be able to:

1. Define pathophysiology.
2. Discuss the core aspects of disease in pathology.
3. Know the various categories of the causes of diseases.
4. Know the course, outcome of diseases.

Pathophysiology :-

The physiology of altered health, it combines ***Pathology*** :-Greek meaning of disease, literally the study (logos) of suffering (pathos). More specifically, it is abridging discipline involving both basic science and clinical practice and is devoted to the study of the structural and functional changes in cells, tissues, and organs that underlie disease. By the use of molecular, microbiologic, immunologic, and morphologic techniques, pathology attempts to explain the whys and wherefores of the signs and symptoms manifested by patients while providing a sound foundation for rational clinical care and therapy.



Pathophysiology *is the study of the* ***biologic and physical manifestations*** *of disease as they correlate with the underlying abnormalities and physiologic disturbances. Pathophysiology does* ***not deal directly with the treatment of disease****. Rather, it explains the processes within the body that result in the signs and symptoms of a disease.*

A pathologist *is a specialist in pathology; a physician who practices, evaluates, supervises diagnostic tests, using materials removed from living or dead patients, and functions as a laboratory consultant to clinicians, also conducts experiments and other investigations to determine the causes or nature of disease changes.*

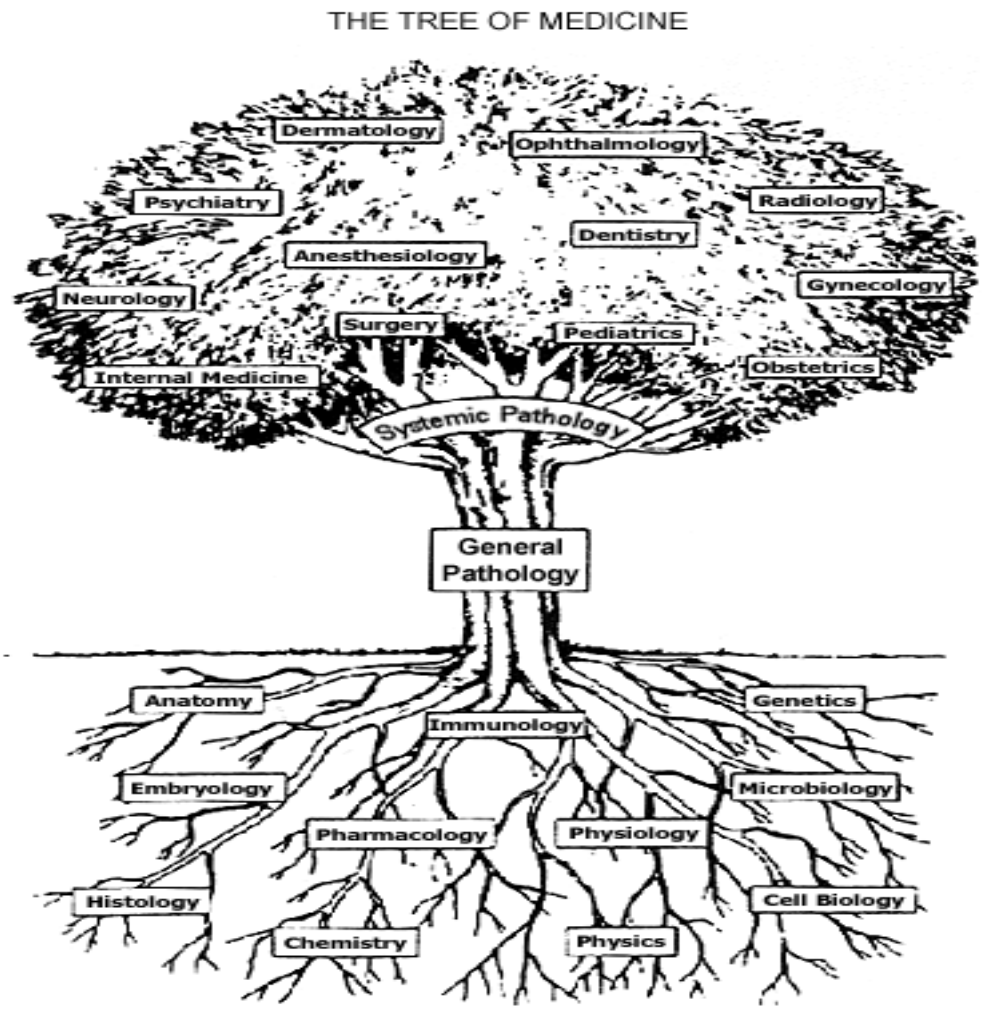
A pathologist is either:

1- **Surgical pathologist:** the study of disease by the analysis of tissue specimens obtained during surgery. The surgical pathologist often examines specimens during surgery to determine how the operation should be modified or completed. The appearance of the specimen is noted. Then, slices of the tissue are prepared by the paraffin or frozen section method and microscopically examined by a physician trained in pathology.
2- **Clinical pathologist:** The laboratory study of disease by a pathologist using techniques appropriate to the specimen being studied. Among the many branches of clinical pathology are hematology, bacteriology, chemistry, and serology.

Pathology is divided into
1- General Pathology.
2- Systemic Pathology.

General Pathology *is concerned with the basic reactions of cells and tissues to abnormal stimuli that underlie all diseases (i.e.) studies inflammation, cell injury adaptation and death, tissue repair, Hemodynamic disorders, diseases of immunity, Neoplasia, genetic and pediatric diseases, environmental diseases and infectious diseases… all in general.*

Systemic Pathology *is the study of the specific responses of specialized organs and tissues to more or less well defined stimuli.*



Disease *is a term for any condition that impairs the normal functioning of an organism or body.*
The aspects of the disease process include:

1. **Etiology.**
2. **Pathogenesis.**
3. **Morphologic changes.**
4. **Clinical manifestations.**
5. **Diagnosis.**
6. **Clinical course.**

1- **Etiology**

The causes of disease are known as etiologic factors.
The recognized etiologic agents are:

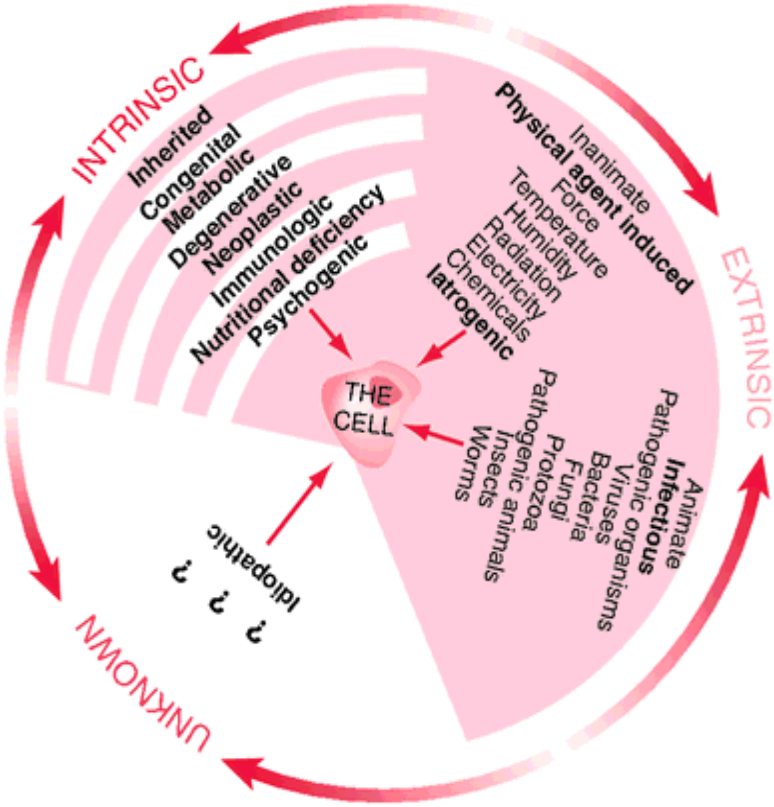
1. Biologic agents(e.g., bacteria, viruses),
2. Physical forces (e.g., trauma, burns, radiation),
3. Chemical agents (e.g., poisons, alcohol), and
4. Nutritional excesses or deficits.

5. At the molecular level, it is important to distinguish between **abnormal molecules and molecules that cause disease**.

Most disease-causing agents are **nonspecific**. and many different agents can cause disease of a single organ. On the other hand, a single agent or traumatic event can lead to disease of a number of organs or systems. Although a disease agent can affect more than a single organ and a number of disease agents can affect the same organ, most disease states do not have a single cause. Instead, the majority of diseases are **multifactorial in origin**. This is particularly true of diseases such as **cancer, heart disease, and diabetes**. The multiple factors that predispose to a particular disease often are referred to as **risk factors**.

The factors that cause disease is to group them into categories according to whether they were present at birth or acquired later in life.

1. **Congenital conditions** are defects that are present at birth, although they may not be evident until later in life. Congenital conditions may be caused by genetic influences, environmental factors (e.g., viral infections in the mother, maternal drug use, irradiation, or intrauterine crowding), or a combination of genetic and environmental factors.
2. **Acquired defects** are those that are caused by events that occur after birth. These include injury, exposure to infectious agents, inadequate nutrition, lack of oxygen, inappropriate immune responses, and neoplasia. Many diseases are thought to be the result of a genetic predisposition and an environmental event or events that serve as a trigger to initiate disease development.



2- **Pathogenesis** *refers to the sequence of events in the response of cells or tissues to the etiologic agent, from the initial stimulus to the ultimate expression of the disease.*
Etiology describes what sets the disease process in motion, and pathogenesis, how the disease process evolves. Although the two terms often are used interchangeably, their meanings are quite different. For example, atherosclerosis often is cited as the cause or etiology of coronary heart disease. In reality, the progression from fatty streak to the occlusive vessel lesion seen in persons with coronary heart disease represents the pathogenesis of the disorder. The true etiology of atherosclerosis remains largely uncertain.

3- **The morphologic changes**
Morphology refers to the fundamental structure or form of cells or tissues. **Morphologic changes** are concerned with both

1. The gross anatomic.
2. Microscopic changes that are characteristic of a disease.

Histology deals with the study of the cells and extracellular matrix of body tissues. The most common method used in the study of tissues is the preparation of histologic sections—thin, translucent sections of human tissues and organs—that can be examined with the aid of a microscope. Histologic sections play an important role in the diagnosis of many types of cancer.
A lesion represents a pathologic or traumatic discontinuity of a body organ or tissue. Descriptions of lesion size and characteristics often can be obtained through the use of radiographs, ultrasonography, and other imaging methods. Lesions also may be sampled by biopsy and the tissue samples subjected to histologic study.

4- **Functional Derangements and Clinical Manifestations.**
The nature of the morphologic changes and their distribution in different organs or tissues influence normal function and determine the clinical features (**symptoms and signs**), course, and prognosis of the disease.
Diseases can manifest in a number of ways. Sometimes the condition produces manifestations, such as **fever**, that make it evident that the person is sick. In other cases, the condition is **silent** at the onset and is detected during examination for other purposes or after the disease is far advanced.
Signs and symptoms *are terms used to describe the structural and functional changes that accompany a disease.*
A symptom *is a subjective complaint that is noted by the person with a disorder*.
A sign *is a manifestation that is noted by an observer.*
Pain, difficulty in breathing, and dizziness are **symptoms of a disease**.
An elevated temperature, a swollen extremity, and changes in pupil size **are objective signs** that can be observed by someone other than the person with the disease.
Signs and symptoms are either:

1. Related to the primary disorder.
2. Represent the body's attempt to compensate for the altered function caused by the pathologic condition.

Many pathologic states are not observed directly—one cannot see a sick heart or a failing kidney. Instead, what can be observed is the body's attempt **to compensate** for changes in function brought about by the disease, such as the tachycardia that accompanies blood loss or the increased respiratory rate that occurs with pneumonia.

A syndrome *is a compilation of signs and symptoms*(e.g., chronic fatigue syndrome) *that are characteristic of a specific disease state.*

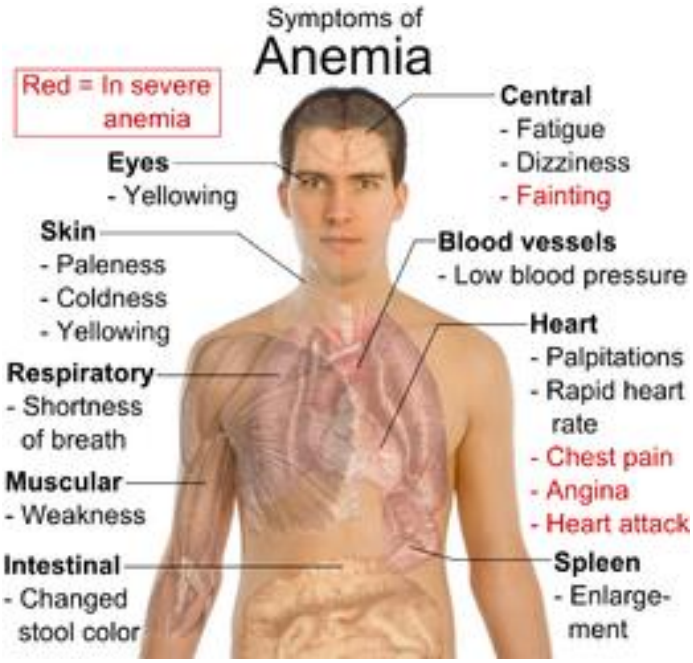
Complications *are possible adverse extensions of a disease or outcomes from treatment.*

Sequelae *are lesions or impairments that follow or are caused by a disease.*

5-**Diagnosis**

In general, diagnosis (plural diagnoses) has two distinct dictionary definitions.

The first definition is: "***the recognition of a disease or condition by its outward signs and symptoms",***



while

The second definition is ***"the analysis of the underlying physiological/biochemical cause(s) of a disease or condition".***

e.g. Iron deficiency anemia

	Normal	Fe deficiency without anemia	Fe deficiency with mild anemia	Fe deficiency with severe anemia
Serum Iron	60-150	60-150	<60	<40
Iron Binding capacity	300-360	300-390	350-400	>410
Saturation	20-50	30	<15	<10
Hemoglobin	Normal	Normal	9-12	6-7
Serum Ferritin	40-200	<20	<10	0-10

The diagnostic process usually requires:

1. **A careful history**. is to obtain a person's account of his or her symptoms and their progression, and the factors that contribute to a diagnosis.
2. **Physical examination**. is done to observe for signs of altered body structure or function.
3. Laboratory tests, radiologic studies, computed tomography (CT) scans, and other tests often are used to **confirm a diagnosis.**

An important factor when interpreting diagnostic test results is the determination of whether they are **normal or abnormal**. Is a blood count above normal, within the normal range, or below normal? What is termed a normal value for a laboratory test is established statistically from test results obtained from a selected sample of people.

The normal values refer to the 95% distribution(mean plus or minus two standard deviations [mean ± 2 SD]) of test results for the reference population.

The diagnosis can be reached

Differential Diagnosis ("rule-outs"): *A list of diagnoses that could account for the history, clinical signs or lesions in a case.*

The diagnostic modalities used by the pathologist

1- **Clinical Diagnosis:** *Diagnosis based on data obtained from the case history, clinical signs, and physical examination.*

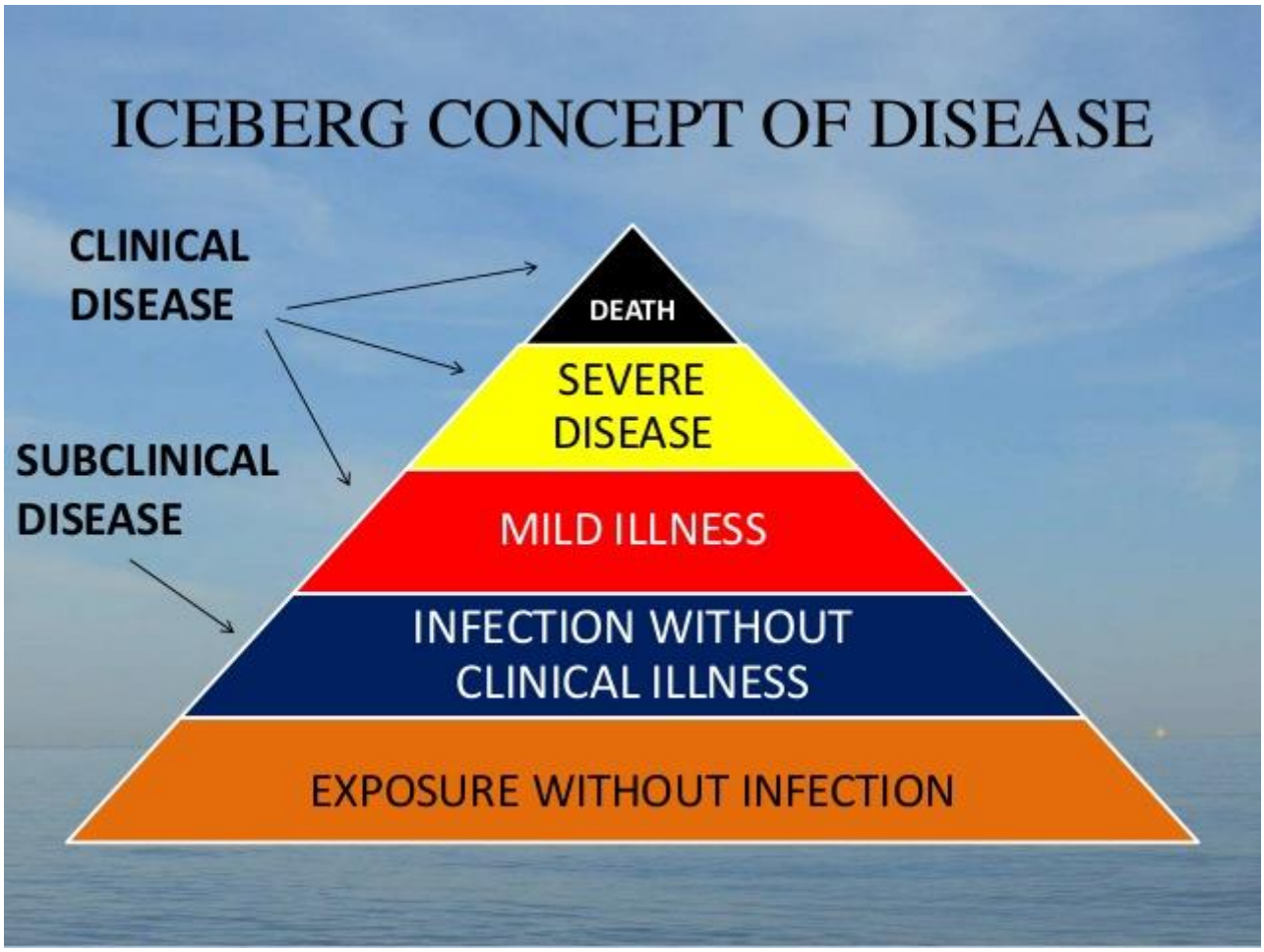
2- **Morphologic Diagnosis (lesion diagnosis):** *A diagnosis based on the predominant lesion(s) in the tissue.* It may be macroscopic (gross) or microscopic (histologic) and describes the severity, duration, distribution, location and nature (eg degenerative, inflammatory, neoplastic) of the lesion. e.g. severe, acute, locally-extensive, fibrinous bronchopneumonia.

3- **Etiologic Diagnosis:** A definitive diagnosis that names the specific (or general) cause of the disease. (eg parvoviral enteritis, parasitic hepatitis)

4- **Disease (Definitive) Diagnosis:** A specific diagnosis that states the "**name of the disease**". eg, an 10-years old child presented to the clinic with severe neck rigidity and vomiting of 2 days duration. The child died prior to complete clinical work up and a necropsy was performed.

Type of Diagnosis		Description
1.	Clinical Diagnosis:	Acute meningitis
2.	Morphologic Diagnosis:	An inflammation of the pia mater & arachnoid layers of the meninges
3.	Etiologic Diagnosis:	Bacterial Meningitis
4.	Disease Diagnosis:	Neisseria Meningitis

6- **The clinical course** *describes the evolution of a disease.*
In other words any disease could be preclinical, acute ,subacute or chronic
Preclinical: a stage in a disease when a specific diagnosis cannot be made because *adequate signs and symptoms have not yet developed*.
Acute a stage in a disease characterized by a relatively *sudden onset of symptoms that are usually severe.* An episode of acute disease results in **recovery** to a state comparable to the patient's condition of health and activity before the disease, in passage into a **chronic phase, or in death**.
Subacute :- An abnormal condition present in a person who appears to be clinically well. Between acute and chronic; denoting the course of a disease of moderate duration or severity.
Chronic a disease that persists over a long period. The symptoms of chronic disease are sometimes less severe than those of the acute phase of the same disease. Chronic disease may be progressive, result in complete or partial disability, or even lead to death. Examples of chronic disease include diabetes mellitus, emphysema, and arthritis.
Carrier one who harbors disease organisms in their body without manifest symptoms, thus acting as a distributor of infection.



Epidemiology and pattern of disease

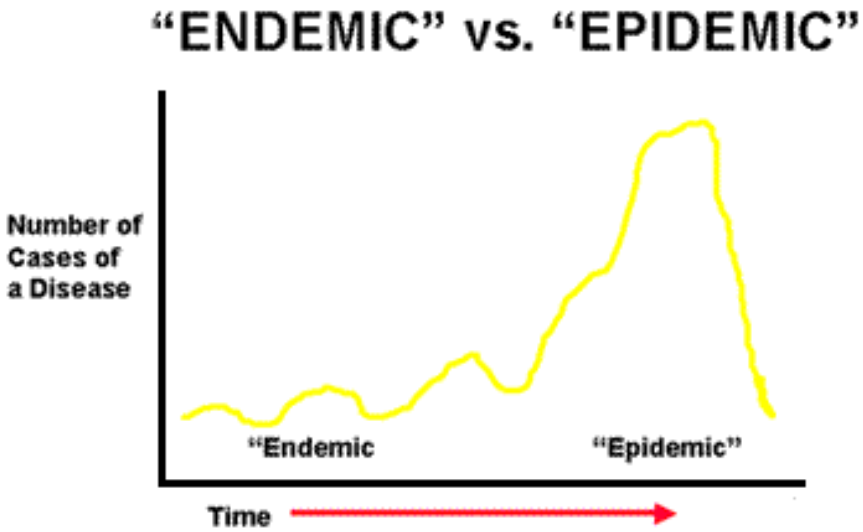
Epidemiology is the *study of the patterns, causes, and effects of health and disease conditions in defined populations.* It is the **cornerstone of public health**, and informs policy decisions and evidence-based medicine by identifying risk factors for disease and targets for preventive medicine.

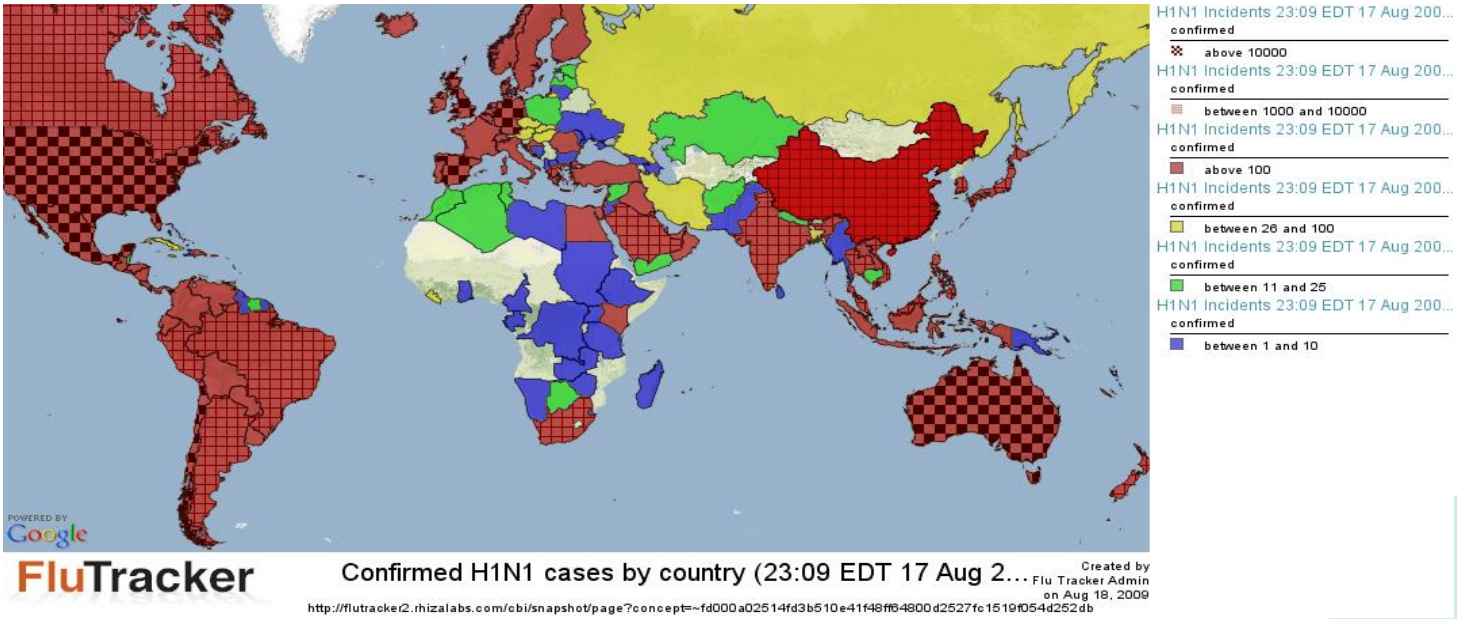
It has emerged as the science that helps to study the risk factor for **multifactorial diseases such as heart diseases and cancer**. It looks for patterns such as age, sex, nutrition, race, habits, lifestyle …..etc in relation to the disease that will help doctors in their diagnosis.

Endemic diseases in a population when that disease is maintained in the population without the need for external inputs.

Epidemic disease any new cases of a certain disease, in a given human population, and during a given period, substantially exceed what is expected based on recent experience.

Pandemic is an epidemic of infectious disease that has spread through human populations across a large region; for instance multiple continents, or even worldwide. E.g. H_1N_1 influenza virus





Exercises

1. What is pathophysiology? What core aspects of disease does it study?
2. Define the following:
   a) Disease.
   b) Sequels of a disease.
   c) Pandemic.
3. What is pathogenesis?
4. What are the diagnostic modalities used by the pathologist?

1- Pathophysiology **does not**

(a) deal with the treatment of disease
(b) explains the signs and symptoms.
(c) cells, tissue and organs changes that result due to a disease.
(d) take the etiology into consideration.

2- The sequence of events in the response of cells or tissues to the etiologic agent is:

(a) Etiology
(b) Disease.
(c) Syndrome.
(d) Pathogenesis.

3- If a diseases was Globally distributed it is called:

(a) Epidemic disease.
(b) Endemic disease.
(c) Pandemic disease.
(d) None of the above.

4- If the pathogen exist in a body without manifest symptoms the patent is regarded as a:

(a) Carrier.
(b) Subacute.
(c) Preclinical.
(d) Chronic.

5- Etiologic Diagnosis is:

(a) A specific diagnosis that states the "name of the disease".
(b) A definitive diagnosis that names the specific (or general) cause of the disease.
(c) A diagnosis based on the predominant lesion(s).
(d) Diagnosis based on data obtained from the case history.

References:

1. Porth. Carol., Kathryn J. Gaspard, Kim A Noble. Essentials of Pathophysiology. Concepts of altered health states. 3rd edition 2011.
2. Sue Huether. Study Guide for Understanding Pathophysiology, Fifth Edition- 2012.
3. Kathryn L. McCance. Pathophysiology - The Biologic Basis for Disease in Adults and Children, 7th Edition 2014