

INTRODUCTION: PATHOLOGY

Pathology

- study of disease
- Devoted to the study of structural, biochemical and functional changes in cells, tissues and organs that underlie the disease.
- Attempts to explain the signs and symptoms manifested by patients while providing a rational basis for clinical care and therapy.
- serves as bridge between the basic sciences and clinical medicine
- Scientific foundation for all of medicine.
- The study of pathology is divided into:
 1. General Pathology
 - Concerned with the:
 - a. reactions of the cells and tissues to abnormal stimuli and
 - b. to inherited defects, which are the main causes of disease.
 2. Systemic Pathology
 - Examines the alterations in specialized organs and tissues that are responsible for disorders that involve in these organs.

FOUR ASPECTS OF DISEASE

- forms the core of pathology
 1. Etiology - cause of disease
 2. Pathogenesis - mechanisms of its development
 3. Molecular and Morphological Changes - the biochemical and structural alterations induced in the cells and organs of the body
 4. Clinical Manifestations - functional consequences of the different changes

Etiology

- two major classes of etiologic factors:
 1. genetic (inherited mutations and disease associated gene variants or polymorphisms)
 2. acquired (infectious, nutritional, chemical, physical)
- The idea that one etiologic agent is the cause of one disease is not applicable to majority of disease is not applicable.
- Most of the common afflictions are multifactorial and arise from the effects of various external triggers on a genetically susceptible individual.
- The relative contribution of inherited susceptibility and external influences varies in different disease.

Pathogenesis

- Pathogenesis refers to the sequence of events in the response of cells or tissues to etiologic agents.
- from the initial stimulus to the ultimate expression of the disease.

Molecular and Morphologic Changes

- Morphologic changes refer to the structural alterations in cells or tissues that are either characteristic of a disease or diagnostic of an etiologic process.
- Diagnostic pathology is devoted to identifying the nature and progression of disease by studying morphologic changes in tissues and chemical alterations in patients.
- Molecular analysis by techniques such as DNA microarrays has begun to reveal genetic differences that predict the behavior of the tumors as well as their responsiveness to different therapies.

Functional Development and Clinical Manifestation

- End result of genetic, biochemical and structural changes in cells and tissues are functional abnormalities, which lead to the clinical manifestations of disease as well as its progress.
- All forms of disease start with molecular or structural alterations in cells.
- Injury to cells and to the extracellular matrix ultimately leads to tissue and organ injury, which determine the morphologic and clinical patterns of disease.

OVERVIEW: CELLULAR RESPONSES TO STRESS AND NOCIOUS STIMULI

- The normal cell is confined to a fairly narrow range of function and structure:
 - by its state of metabolism, differentiation and specialization
 - by constraints of neighboring cells
 - by availability of metabolic substrates
- The normal cell can handle physiologic demands, maintaining a steady state called homeostasis.
- Adaptations

- Are reversible functional and structural responses to more physiologic stress and some pathologic stimuli.
- new but altered steady states are achieved
- Allow the cell to survive and continue to function.
- the adaptive response may consist of:
 - a. increase in size of cells (hypertrophy) and functional activity
 - b. increase in number of cells (hyperplasia)
 - c. decrease in the size and metabolic activity of the cells (atrophy) or
 - d. a change in the phenotype of the cell (metaplasia)
- When the stress is eliminated, the cell can recover to its original state without having suffered any harmful consequences.

CELLULAR RESPONSES TO INJURY

Nature of Injurious Stimulus	Cellular Response
Altered Physiological Stimuli	Cellular Adaptations
Neofunctional injurious Stimuli	
• increased demand, increased stimulation (GF/Hormones) • decreased nutrients, decreased stimulation • Chronic irritation	• Hyperplasia, hypertrophy • Atrophy • Metaplasia
Reduced Oxygen Supply, Chemical Injury, Microbial Infection	Cell Injury
• Acute and transient • Progressive and severe	• Acute reversible injury, cellular swelling, fatty change • Irreversible injury → cell death, necrosis, apoptosis
Metabolic alterations, genetic or acquired; chronic injury	Intracellular accumulations, calcification
Cumulative sublethal injury over long life span	Cellular aging

CELL INJURY

- Cell injury occurs:
 - a. if the limits of adaptive responses are exceeded
 - b. if the cells are exposed to injurious agents or stress
 - c. if the cell is deprived of essential nutrients
 - d. if the cell becomes compromised by mutations that affect essential cellular constituents
- Cell injury is reversible up to a certain point.
- If the stress or noxious stimuli persists, or it is severe enough from the beginning, the cell suffers irreversible injury and ultimately cell death.
- Adaptation, reversible cell injury and cell death may be the stages of progressive impairment following different types of insults.

CELL DEATH

- Cell death
 - the end result of progressive cell injury
 - Most crucial events in the evolution of disease in any tissue or organ.
 - Results from diverse causes including ischemia (reduced blood flow), infection and toxins.
 - Is a normal and essential process in embryogenesis, the development of organs and maintenance of homeostasis.
- there are two principal pathways for cell death:
 1. Necrosis
 2. Apoptosis
- Nutrient deprivation triggers an adaptive cellular response call autophagy and may also culminate in cell death
- Stresses of different types may induce changes in cells and tissues other than typical adaptations, cell injury and cell death:
 - Metabolic derangements in cells and sub lethal, chronic injury may be associated with intracellular accumulations of a number of substances, including proteins, lipids and carbohydrates
 - Calcium is often deposited at the sites of cell death resulting in pathologic calcification
 - Aging is accompanied by characteristic morphologic and functional changes in the cell.
- Three other processes that affect cells and tissues are
 1. intracellular accumulations
 2. pathologic calcification
 3. Cell Aging

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