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Aids To Undergraduate Pathology

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Foreword by
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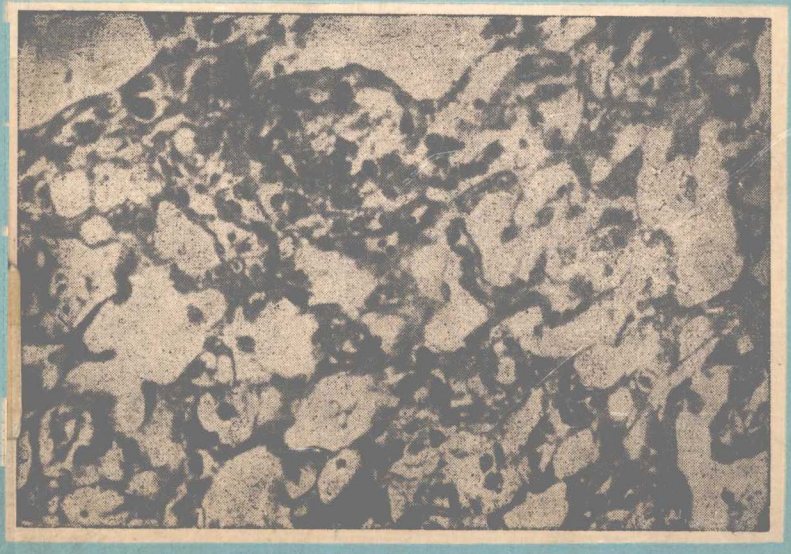

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By

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Foreword

Pathology is the scientific study of disease and follows the course of the disease process from its inception to its termination. History of medicine is inseparable from the history of developments in the science of Pnthology. Roots of Pathology go back into antiquity when human beings first started discerning their natural environment through penetrating and analytical observation.

Recent developments in various aspects of the subject have been responsible for explosion of the knowledge in the field of medicine as a whole. It can safely be said that if medical education is the leading of humans to excellance then serious study of Pathology is the foundation of that education.

Pathology texts, available to students of medicine, have gradually become too huge to form a ready reference to a student studying the clinical applications of the subject at the bedside of the patient. It is welcome to find that an attempt at presenting a concise volume giving an outline of general principles and systemic pathology has been made available by Dr. Uma Chaturvedi. She has put in a good amount of industry and ability to prepare a carefully organised and tabulated material incorporating maximum amount of information in minimum amount of space.

It gives me tremendous pleasure to introduce "Aids to undergraduate pathology" and recommend it to students of medical and para-medical sciences. I can claim satisfaction that one of my students Dr. K. Uma Chaturvedi has presented the subject for the benefit of a still younger generation in a competent, yet simple manner.

I wish her success.

GAURI BAZAZ MALIK
Professor and Head, Department of Pathology, Lady Hardinge Medical College, New Delhi.

Preface to the Second Edition

A second edition so soon after the first has been necessiated primarily by the very good response that this book has received from the readers.

A few illustrations and clarifications have been added but the theme remains the same—an overall coverage of the subject with an emphasis on brevity and clarity.

K. Uma Chaturvedi

Preface to the First Edition

Knowledge regarding the basis of disease processes is in rapid progress. This necessiates text books in Pathology to be voluminous in order to cover this vast subject fully and in depth.

As an undergraduate student and more so as an undergraduate teacher, I have felt the need for a simpler version of the subject which would help in easy initiation into the understanding of Pathology and also in quick revision prior to examinations. This book is the result of an effort in that direction. I have gleaned the matter from several sources and presented it in a manner which is simple to understand and easy to remember.

I claim this book to be not a substitute but a supplement to text books. General Pathology has received an overall uniform coveage. Systemic Pathology including haematology is discussed with greater stress laid on the commoner diseases.

A list of general reference books is included and so is a list of further references for the more avid reader.

My sincere gratitude is expressed to Dr. Gauri Bazaz Malik for her suggestions towards improvements and for consenting to write the foreword.

My heartfelt thanks are also due to my friends and family who have directly or indirectly contributed to the genesis of this book.

Dr. K. Uma Chaturvedi

Contents

CHAPTER 1

Cell Response to Injury

THE NORMAL CELL

This cytological unit of tissues has 3 main components.

1. The cell membrane
2. The nucleus
3. The Cytoplasm with its organelles.

Cell Membrane

Structure. Trilaminar unit membrane made up of 2 electron

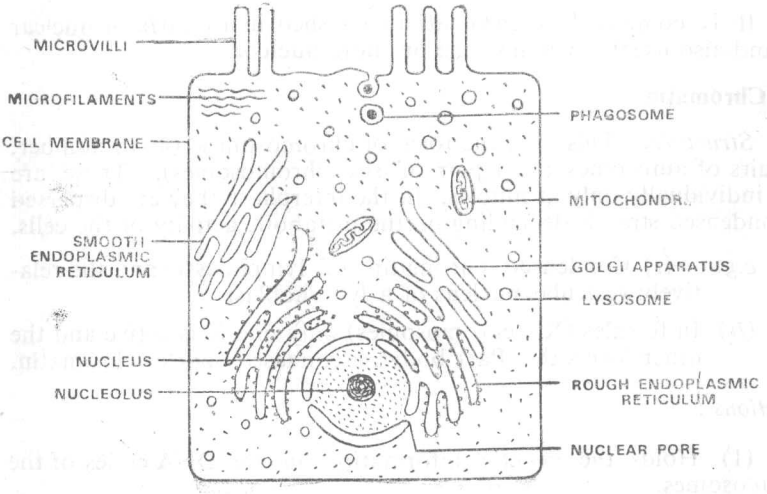


Fig. 1.

dense lipoprotein layers with a clear space in between. The bilayer is made up of phospholipids, with the proteins embedded in it.

Functions

(1) Boundary for the cell.

(2) Cell movement—aided by cilia.

(3) Contact and adhesion with neighbouring cells.

(4) Cell recognition (surface antigens).

(5) Receptor function for stimuli from outside (cyclic-AMP).

(6) Transfer function :

(*i*) Diffusion of ions.

(*ii*) Exocytosis of secretions.

(*iii*) Endocytosis including phagocytosis and pinocytosis. Absorptive surface is increased by microvilli on cell surface.

(7) Energy dependant sodium pump.

Nucleus

It is bounded by the nuclear membrane which is bilaminar with pores 50 nm. in diameter.

It is composed of chromatin enmeshed in a matrix or nuclear sap and also usually contains one or more nucleoli.

A. Chromatin

Structure. This is in the form of chromosomes (46 in number, 22 pairs of autosomes and 1 pair of sex chromosomes). These are seen individually only at mitosis. In the interphase they are dispersed or condensed strands depending on the metabolic activity of the cells.

e.g. :—(*i*) Condensed chromatin of lymphocyte and the relatively vesicular nucleus of a lymphoblast,

(*ii*) In females (XX chromosomes) only one X is active and the other forms the 'Barr body', a condesed spot of chromatin.

Functions :

(1) Holds the genetic information in the DNA codes of the chromosomes.

(2) DNA replication.

(3) Production of messenger RNA for coding protein synthesis in cytoplasm.

(4) Synthesis of proteins of nuclear sap.

B. **Nucleolus**

Structure. These are dense basophylic structures in the nucleus. They are more prominent in cells which are active metabolically. They are made up of RNA.

Function :

Not known ? Pass on information for protein synthesis in cytoplasm.

Cytoplasm

This is made up mostly of water with organelles, proteins and ions dispersed in it. It has more protein, potasssium, magnesium and phosphate and less sodium and bicarbonate than the extracellular fluid. The sodium is kept out by the energy dependant Sodium pump.

Cytoplasmic organelles

(1) **Mitochondria**

Structure. Oval to rod shaped structures, abundant in active cells. These have a smooth outer membrane and an inner membrane with septae (cristae).

Function

They contain the Kreb's cycle enzymes and are responsible for oxidative phosphorylation of ADP to ATP (which is the stored form of cellular energy).

(2) **Lysosomes**

Structure. Round membrane bound bodies, containing lytic enzymes active at low PH.

These enzymes are produced in the endoplasmic reticulum and secreted into lysosomes via golgi apparatus.

Functions :

(*i*) Intracellullar digestion. Material to be digested may be :

(*a*) Exogenous material, when ingested, forms a membrane bound phagosome.

(*b*) Damaged cytoplasmic organelles, get membrane bound to form an autophagic vacuole.

These vacuoles fuse with a primary lysosome to be known as a secondary lysosome, where digestion takes place. Undigested material may be exocytosed or remain in the cell as residual body.

(*ii*) Secretion of enzymes for extracellular digestion.

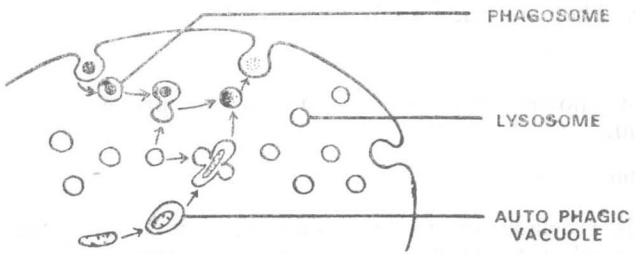


Fig. 2.

(3) Rough Endoplasmic Reticulum (RER)

Structure. A complex system of layers of membranes, enclosing channels and vesicles. They are rough because of the presence of ribosomes (RNA) on their surface.

Functions

RER is abundant in cells manufacturing protein for secretion (glandular cells, liver cells, plasma cells etc).

Free ribosomes are prominent in cells synthesising protein for their own use (actively growing cells).

(4) Smooth endoplasmic reticulum (SER)

Structure. Similar to RER except that that the ribosomes are absent. This communicates with the RER and the cell membrane.

Functions

(*i*) Glycogen synthesis.
(*ii*) Triglyceride formation from free fatty acids.
(*iii*) Steroid and cholesterol metabolism.
(*iv*) Drug detoxification.

(5) Golgi Apparatus

Structure. It is a series of membrane bound flat sacs, vacuoles and vesicles, richly present in secretory cells.

Function

(*i*) Material produced in the RER is transported via the golgi apparatus. At the secretory end of the cell, vacuoles containing the packaged material are pinched off and secreted.

(*ii*) Lysosomes for intracellular action are also formed in the same way.

(6) Microtubules and Microfilaments

Structure. Bundles of filaments and tubules of contractile material in the cytoplasm, anchored to cell membrane.

Functions

(*i*) Forming a cytoskeleton for cell shape.

(*ii*) Movement af material within the cell.

(*iii*) Anchoring of surface receptors.

(*iv*) Spindle formation in mitosis.

(*v*) Cell movement.

CELL RESPONSE TO INJURY

Alteration in cell function and structure can be caused by many extraneous agents and intracellular causes :

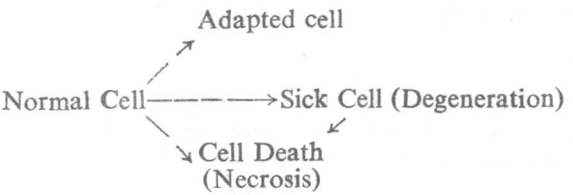
Causes

1. Physical agents
2. Chemical agents
3. Hypoxia
4. Immunological derangements
5. Genetic enzyme defects
6. Infections
7. Nutritional imbalances.

In response to these, the cell may :—

1. Adapt itself to the altered situation and maintain a new equilibrium.

2. Show reversible changes indicative of cell sickness.
3. Die with or without going through the changes of sickness.



Mechanisms of cell injury

(1) Damage to sodium pump.
(2) Defect in oxidative phosphorylation.
(3) Lysosomal rupture or overloading.
(4) Ribosomal and mitochondrial disintegration.
(5) Membrane lysis.

DEGENERATION

Definition : Reversible cell injury.

(1) **Water accumulation in the form of :**

(*i*) Cloudy swelling.
(*ii*) Vacuolar degeneration.
(*iii*) Hydropic degeneration.

This change is commonly seen in parenchymal cells *e.g.* kidneys.

This is the effect of initial or mild injury, causing failure of the energy dependent sodium pump. There is resultant increase in intracellular sodium and water.

Gross appearance

The organ is swollen, soft and pale.

Microscopic appearance

Cells show varying degrees of swelling. Cytoplasm may be granular, vacuolated, homogenously pale and ballaooned out.

(2) **Fatty change.** An excessive, demonstrable accumulation of fat is common in parenchymal cells of liver and heart. In the liver, it can be due to :

(*i*) Excess fat entry into the liver as occurs in starvation and in steroid excess due to mobilisation from stores.
(*ii*) Excess triglyceride formation.
(*iii*) Reduced phosphorlyation of fat.
(*iv*) Decreased release as lipoprotein due to protein deficiency.

Causes

(*i*) Hypoxia as in severe anaemia and venous stasis.
(*ii*) Protein malnutrition.
(*iii*) Hepatotoxins like CCl_4.
(*iv*) Alcoholism.
(*v*) Metabolic defects like Diabetes mellitus.
(*vi*) Infections.

Gross appearance

The organ is enlarged, soft and greasy, with a pale yellowish colour. It may involve the organ uniformly or patchily (thrush breast or tabby cat heart).

Microscopic appearance

The cells contain clear vacuoles (stainable by fat-sudan-stains on frozen sections). These may be small and dispersed or large, displacing the nucleus peripherally. Several such cells may fuse to form fat cysts.

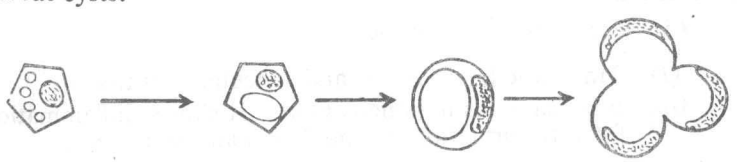


Fig. 3.

(3) Hyaline degencration. In alcoholic liver damage, the cytoplasmic organelles are damaged and give the cytoplasm a deep eosinophillc staining—Mallory hyaline.

NECROSIS

This implies structural changes indicative of cell death.

These changes are due to autolysis. The cellular changes of necrosis *i.e.* death of circumscribed group of cells in continuity with living tissues are similar to changes in tissues following somatic death, except that in the former, there is leucocytic infiltration in reaction to the dead cells and the lytic enzymes partly come from the inflammatory cells also. (Heterolysis).

Cell death occurs in the normal situation of cell turnover also and this is called apoptosis—single cellular dropout.

Nuclear changes in necrosis

As cytoplasmic changes are a feature of degeneration, similarly nuclear changes are the hallmark of necrosis. These changes are :

(*i*) Pyknosis (condensation of chromatin)
(*ii*) Karyorrhexis (fragmentation).
(*iii*) Karyolysis (dissolution).

Types of necrosis

(1) *Coagulative necrosis.* Seen in infarcts. The architectural outlines are maintained though structural details are lost.

(2) *Caseous necrosis.* A variant of coagulative necrosis seen in tuberculosis. The architecture is destroyed, resulting in an eosinophilic amorphous debris.

(3) *Colliquative* (*liquifactive*) necrosis seen in cerebral infarcts and in suppurative necrosis.

In addition to the above 3 main forms of necrosis, other variants may be :

(4) *Gangrenous necrosis.* It is the necrosis with superadded putrefaction.

(5) *Fat necrosis.* May be :

(*i*) Traumatic (as in breast and subcutaneous tissue).
(*ii*) Enzymatic (as in pancreatitis). It shows inflammation of fat with formation of lipophages and giant cells.

This is often followed by deposition of calcium as calcium soaps.

(6) *Hyaline necrosis.* Seen in skeletal muscles in typhoid and in liver cells in some forms of hepatitis.

(7) *Fibrinoid necrosis.* In hypertension and in immune based diseases.

Sequelae

(1) Secondary infection
(2) Healing by regeneration or scarring
(3) Calcification.

CHAPTER 2

Inflammation

Definition. Response of living tissue to injury, involving neural, vascular and cellular response.

ACUTE INFLAMMATION

The immediate and early response to most injuries is nearly similar. It involves the formation of a protein rich and cellular exudate and the cardinal signs are calor, dolor, tumour, ruboi and functiolaesa.

The basic components of the response are :

(1) Haemodynamic changes.
(2) Permeability changes.
(3) Leucocyte events.

1. Haemodynamic Changes :

(*i*) Transient vasoconstriction followed by dilatation.
(*ii*) Increased blood flow in arterioles.
(*iii*) More open capillary bed.
(*iv*) Venous engorgement and congestion.
(*v*) Packing of microvasculature by RBC (due to fluid outpouring).
(*vi*) Vascular stasis.
(*vii*) Change in axial flow (resulting in margination of leucocytes).

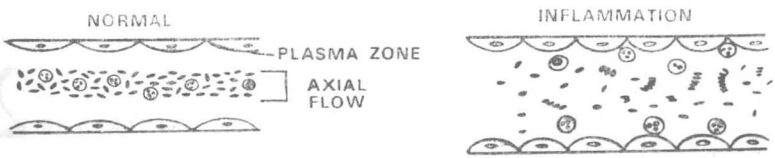


Fig. 4

2. Permeability Changes :

Causes :

(*i*) Increased intravascular hydrostatic pressure.

(*ii*) Breakdown of tissue proteins into small molecules resulting in increased tissue osmotic pressure.

(*iii*) Increased permeability due to chemical mediators, causing an immediate transient response.

(*iv*) Sustained response due to direct damage to microcirculation.

3. White Cell Events :

(*i*) *Margination*—due to vascular stasis and change in axial flow.

(*ii*) *Pavementing*—due to

(*a*) endothelial cells swollen and more sticky.
(*b*) leucocytes more adhesive.
(*c*) binding by a plasma component (? calcium, ? complement).

(*iii*) *Emigration* of leucocytes by amoeboid movement between endothelial cells and beyond the basement membrane. The passive movement of RBCs through the gaps created during emigration is called '*diapedesis*'.

(*iv*) *Chemotaxis*. This is a directional movement, especially of polymorphs and monocytes towards a concentration gradient resulting in aggregation of these cells at the site of inflammation. Chemotactic agents may be :

(*a*) Complement components. (c_3 and c_5 fragments and c_{567})
(*b*) Bacterial products.
(*c*) Immune complexes, especially for monocyte.
(*d*) Lymphocytic factor, especially for monocyte.