CHAPTER 1

BASIC REACTIONS FOR INFLAMMATION & REPAIR

1. **Basic reaction** (**BR**): these are reactions or tissue changes which are repeated in the same way throughout the whole course

2. **Key words**: are important words which describe in brief the reaction or the pathological change being discussed and **will be printed in black**

ACUTE INFLAMMATION

A- LOCALBASIC REACTION (BR) for all types of acute inflammation:

Microscopic:

1-Damage (cell injury) in the form of **necrosis** around injurious agent

2-Reaction around necrotic area in the form of acute inflammation

1-Acute inflammatory cells from connective tissue & inflammatory cellular exudate from the blood = PNLs & macrophages (tissue histiocytes or blood monocytes)
2-**Dilated hyperemic BV**
3-Inflammatory fluid exudate: **edema & fibrin**

NB:The inflammatory exudate is composed of
a) fluid exudate is rich in the protein fibrinogen. This changes into fibrin threads in tissue outside BV).
Fluid in tissue is called edema but if it collects in serous membranes of body cavities e.g. pleura, pericardium & peritoneum, it is called effusion.
b)cellular exudate:PNLs & macrophages

Gross: Redness & swelling

B-GENERAL OR SYSTEMIC REACTION

- **Fever**: from pyrogens released from injurious agent or chemical mediators e.g. prostaglandins. These act on temperature regulating centers in brain stem.
- **Blood changes**

1-Changes in white blood cells (*leukocytosis i.e. ↑ white blood cells in circulation*)
2-Changes in plasma proteins:
3-↑ erythrocyte sedimentation rate (ESR)
4-↑acute phase reactant proteins as C-reactive protein & Alpha1- antitrypsin
5-Immunoglobulins & T lymphocytes

CHRONIC INFLAMMATION

Systemic

-Fever
-Malaise
-Blood changes
tissue:
Lymphocytosis
Plasma cells ↑
Monocytosis
Antibodies

Local reaction

Tissue destruction ⇩ **necrosis** + Chronic inflam ⇩ **lymphocytes** **plasma cells** **macrophages** **+/- giant cells** + Repair(FT) ⇩ fibrous **fibroblasts** **collagen + BV**

+ BV: endarteritis obliterans

NB: In chronic inflammation, **cellular exudate>fluid**. The fluid is minimal as the vessels are very thick walled & have narrow lumen.

PUS: is liquefied necrotic tissue secondary mostly to the pyogenic organism injury
NB pus never contains fibrin since it is liquefied by enzymes
MORPHOLOGY (***Character of pus***)

Gross	**Microscopic**
Yellowish, turbid, opaque	-Fluid exudate + ↑protein (**without fibrin**)
Odorless, alkaline fluid which	-Cellular exudate ↑↑↑**PNLs of** many die and become **pus cells**
toxins	-Bacteria, with its pigments & -RBCs
	-Necrotic host tissue (see basic reaction necrosis)

ACUTE ABSCESS

GROSS

- Small: yellow swollen area surrounded by a zone of redness(congestion)
- Large**: cavity with irregular wall, rough lining** & yellow in color. Its contents are liquid pus (**describe BR above**). The cavity is surrounded by a zone of congestion.

MICROSCOPIC

Early: 2 zones: central necrosis & peripheral zone of acute inflammation
Later: 3 zones

- **Central zone of pus** (see BR of characters of pus, above for description)

- **Pyogenic membrane**: new capillaries, PNLs, macrophages, pus cells, fibrin & few fibroblasts (acute inflammation)
- **Outer zone** of reversible damage or degeneration

CHRONIC ABSCESS

Gross	**Microscopic**
Well defined round cavity Wall is **regular, smooth** &white Cavity contains thick pus Lining smooth as it is formed of fibrous tissue	Central pus(see character in acute inflammation) surrounded by chronic inflammatory cells, endarteritis obliterans & FT

CHAPTER 2

REPAIR

	GROSS	**MICROSCOPIC**
GT	Pink granular, bleeds easily	Fibroblasts+new capillaries (+/-inflammatory cells)
FT	White, firm, smooth tissue causes shrinkage	Fibroblasts+ BV +collagen
Scar	Same as FT	↓fibroblasts +↑collagen (no BV)

Gross Appearance of FT / Scar: depends on site

-Body cavities→adhesions (white firm, smooth, *bands joining visceral to parietal layer*)
-Abscess cavity→smooth thick white wall around cavity
-Hollow structure(intestine – urinary tract etc.) resulting in Stricture, which causes narrowing of lumen i.e. stenosis. If a stricture doesn't form, the whole wall may be thinned out and dilates, producing a pouch, i.e. dilatation or aneurysm (if in a vessel wall). This area is usually weak and may rupture.
-Solid organs e.g. liver: bands or irregular patches of white firm, smooth tissue which shrinks and causes surface depression (*irregularity or nodularity on surface*).

CHAPTER 3 & 4

CELL RESPONSE TO INJURY & MISCELLANEOUS INTRACELLULAR ACCUMULATIONS & EXTRACELLULAR DEPOSITIONS

AMYLOID

GROSS	**MICROSCOPIC**
Specimen: liver, kidney, spleen, any tissue	H&E stain

Size: ↑ size & weight
Surface smooth-capsule stretched
Cut section: sharp edges flat surface
Consistency: firm
Color: pale brown

Gross Stains:
-Lugol's Iodine:amyloid (starch-like): [1]
stains brown & rest yellow
Iodine +H2SO4: stains amyloid blue

Homogenous pink material deposits
on basement membranes & BV
Congo red stain
amyloid appears orange red
Metachromatic stains
e.g. (methyl & cresyl violet)
Amyloid stains rose red & rest of tissue is violet
Immunofluorescence
Amyloid gives apple green color --

Electron microscopy
Extracellular, haphazardly arranged as non-branching fine fibrils 70 A^0

NECROSIS

MICROSCOPIC

- Homogenous dark pink cytoplasm of necrotic cells(**protein denaturation)**
- Swelling of cells(damaged plasma membrane allows Na & H2O into the cell)
- **Nuclear membrane damage** results in

  Karyopyknosis: shrunken dark nucleus due to condensation of chromatin

  Karyorrhexis: fragmentation of nucleus

  Karyolysis: disappearance or lysis of nucleus or simply a pale fading nucleus

- **NECROTIC AREA IS PINK AND GRANULAR CONTAINING NUCLEAR DEBRIS.** The more resistant connective tissue and cells retain some of their outlines and appear as ghosts

CHAPTER 5

CIRCULATORY DISTURBANCES

INFARCTION

GROSS
RECENT:

Shape: pyramidal, as it takes the shape of the distribution of arterial blood supply. The apex is at the site of the occluded vessel while the base is towards the surface. Whole area is **swollen (edema & hemorrhage)**
Surface: bulging & opaque rough (if covered by a serous membrane) due to serofibrinous inflammation
Color: according to type red or pale
HEALED: Healing occurs by organization (GT-FT- scar)
Shape: pyramidal
Surface: depressed (below surface) with adhesions in serous covering
Color: white

MICROSCOPIC
RECENT

- **Protein denaturation**: homogenous dark pink cytoplasm
- The **damaged cell membrane** ⟶ draws Na & H2O into the cytoplasm causing, ↑ osmotic pressure inside cell(swelling of cells)
- **Nuclear membrane damage** results in

-Karyopyknosis: shrunken dark nucleus due to condensation of chromatin
-Karyorrhexis: fragmentation of nucleus
-Karyolysis: disappearance or lysis of nucleus

1- **THE NECROTIC AREA IS PINK AND GRANULAR CONTAINING NUCLEAR DEBRIS. The more resistant connective tissue and cells retain some of their outlines and appear as ghosts. (BR) NB: The necrosis is coagulative in infarctions of all organs except CNS where it is liquefactive in nature**
2- **The rest of the organ appears normal except in lung infarction where there is previous lung congestion**
3- **The area adjacent to the infarction shows a zone of acute inflammation**

NB: a) **Increased enzymes in the blood** are the first signs of necrosis. b) At site of injury, the enzymes & chemical mediators released into the tissue cause irritation of the living tissues, resulting in an **acute inflammatory reaction** (dilated congested BV + edema + PNLs & macrophages + fibrin) and **degenerative** changes in nearby healthy tissue.. c) If there is a serous covering membrane it shows **serofibrinous inflammation**.

HEALED: Pale fibrous tissue causing shrinkage of the lesion GT-FT-scar

CHAPTER 6

IMMUNE RESPONSE

TYPE I HYPERSENSITIVITY

Gross: Picture of acute inflammation

Microscopic (BR):↑<u>eosinophils</u> + macrophages + some PNL, lymphocytes & plasma cells + vasodilatation + ↑ edema

TYPE II HYPERSENSITIVITY

Reaction plasma cells & B lymphocytes + macrophages + VD + edema

TYPE III HYPERSENSITIVITY

Microscopic: Vasculitis & Necrosis with acute inflammation of tissue (<u>PNLs</u>-<u>macrophages</u>-<u>VD</u>-<u>edema</u>)

TYPE IV HYPERSENSITIVITY

GENERAL REACTION IN T CELL responses

A) **<u>Granulomatous</u>**: **Lymphocytes + epithelioid macrophages + giant cells + FT & endarteritis obliterans** OR

B**) <u>Diffuse</u> reaction** e.g. in graft rejection & contact dermatitis
Perivascular lymphocytes & edema

C) **<u>Patchy</u>** e.g. in insect bites

CHAPTER 7

BACTERIAL INFECTIONS

Any infectious disease whether acute or chronic should be described in the following manner:

Etiology & pathogenesis
1-Organism & its description
2-Route of infection
3-Site of lesions
4-Mechanism of lesion production

Manifestations :
- Local:gross & microscopic picture of lesions
- General : e.g. fever & blood changes i.e. clinical picture

Progress & fate
1-Recovery & healing
2-Persistence of organism: Acute changes to chronic (***chronicity***)
3-Complications a) Tissue damage & necrosis with loss of function of organ
b) Spread (no localization)

Direct (***local spread***)
Distant- Lymphatic
-Bloodstream (bacteremia, septicemia etc.……)

c) Complications of healing by fibrous tissue according to site

TB

Tubercle(granuloma)
MICROSCOPIC: The tubercle i.e. the cellular or proliferative tuberculous reaction

- **Central zone of caseous necrosis** which is structureless necrosis occurring as a result of the high lipid content of the bacilli
- Surrounding macrophages become transformed into large pink **epithelioid** cells with foamy cytoplasm and indistinct cell borders. The nucleus is pale, plump oval and vesicular (you can see details of chromatin)
- **Langhan's' giant cells** large pink cells with multiple nuclei arranged in a horse –shoe shaped manner at the periphery of the cell or forming a complete circle.
- Mostly **lymphocytes** (Type IV hypersensitivity reaction to the protein content of the organism) & few plasma cells surround the area
- The outer most zone is composed of fibroblasts & collagen(***FT*)**

Caseation: Exudative reaction is represented by Caseation (a necrosis, resulting from hypersensitivity IV to the TB bacilli body protein)

GROSS

- **Caseation**: yellow, semisolid greasy cheese-like material (due to high lipid content of TB bacilli coat)
- **Fibrosis**: represents the body's ability to heal during a chronic process of tissue destruction (body resistance). It is whitish, firm tissue, which shrinks.

MICROSCOPIC

- Caseation: **pink totally structureless**, granular material. The amount of caseous material depends on dose of organism/ degree of hypersensitivity. ↑ dose & ↑ hypersensitivity results in ↑ caseation. This is counteracted by the body's resistance (ability to localize & form FT).

CHAPTER 8&9

VIRAL & MYCOTIC

CHAPTER 10

BILHARZIASIS

1-**Granuloma(bilharzioma**)+ reticuloendothelial system hyperplasia(lymphadenopathy & splenomegaly)

MICROSCOPIC

Early granulomas are **cellular** (many cells + GT)
Later → **fibrocellular**(cells + FT)
Very late →**fibrotic** or healed (FT or scar tissue)

Granuloma (BR):

- **Central zone contains ovum(oval structures) with a refractile shell.**
- **Ova may contain a living miracidium which is pink & nucleated or a dead miracidium which is pink but with no nuclei. Dead ova in long standing infestations become dystrophicaly calcified & appear blue (H&E stain).**
- **Surrounded by many eosinophils, macrophages, lymphocytes, plasma cells , PNLs & giant cells (this is a mixture of 4 different hypersensitivity reactions).**
- **Outer zone of bilharzial granulation tissue which changes to FT + endarteritis obliterans & later scar tissue with no cells.**

2-**EPITHELIAL or mucosal changes (basic reaction)** NB ova are deposited in the most vascular parts as submucosa, but may also be deposited elsewhere.

MICROSCOPIC	**GROSS**
1. **Epithelial**	
Atrophic epithelium	Thinning (transparent)
Hyperplasia of cells or Metaplasia	Thick mucosa
Cystitis cystica & or glandularis	Cysts
Neoplasia(carcinoma UB)	Mass (complication)
2.**Sandy Patches**	
calcified ova+dense FT seen	Yellowish granular area causing mucosal roughening through atrophic mucosa

Occurs due to a **massive oviposition at the same time** .The ova die become calcified & surrounded by FT & covered by a thin transparent mucosa.

3.**Polyp**	
Cellular + fibrocellular + fibrotic granulomas in mucosa Bilh. granulation tissue & polyp core. Ova are both fresh	Surface protrusion of mucosa + submucosa

& calcified in same
lesion

Occurs due to a **repeated oviposition** of small numbers of ova **at the same site over a long period of time** . This produces a slow rise of mucosa until a finger-like projection or polyp is formed.

4.**Fibrotic lesions**
Fibroblasts + collagen fibers White firm + shrinkage

Few trapped dead ova (mostly Calcified)

5.**Bilh. Ulcers**

-**Superficial**(shallow)
Simple ulcer edges & floor
contain Bil.GT Saucer shaped small
-Rare **deep ulcers**

caused by:1- falling of a polyp / 2- of ova penetrating mucosa / 3- mucosal ischemia due to pressure atrophy of sandy patches
-or **fissure**(tear in UB mucosa) which occurs as a result of
over distention of bladder with urine, in the presence of 2 fixed fibrotic areas along which a tear of mucosa occurs.

CHAPTER 11

VITAMIN DEFICIENCIES

CHAPTER 11

GROWTH DISTURBANCES & NEOPLASIA

General characteristics of Benign & Malignant tumors

	BENIGN	MALIGNANT
Rate & Mode of Growth	Slow rate of growth expansile mode non recurrent	Rapid rate Invasive mode Metastasizes & recurs
Treatment	Lumpectomy	Radical surgery
GROSS		
1-Solid organs(mass=oma)		
Size	Variable	Variable

Shape	well defined Round/oval(capsule)	Ill defined Irregular shape(invasive)
Surface	Smooth capsule of FT Capsule:FT from pressure atrophy on surrounding tissue & produced by tumor	Irregular & adherent to tissue
Cutsection	Homogenous	Mottled (Hge-necrosis)
Color	=original tissue	=original tissue+ red & yellow
Consistency (Necrosis)	=original tissue	Firm to hard + friable areas

2-Surfaces & linings

shapes:	papillary growth (papilloma)	Polypoid fungating Malignant ulcer Diffuse infiltrative Localized infiltrative(stricture)

MICROSCOPIC (**criteria of malignancy**)

Like original tissue		Appearance **Depends on grade or differentiation** GI(well differentiated)=similar GII(moderately diff)can be traced GIII(poorly diff.) very difficult Anaplastic: no resemblance at all (undifferentiated)
1-cell size & shape	same as mother cell	**Pleomorphism**(of size & shape) Small & large cells, variable shape
2-Number	No cell crowding but	↑↑↑**hypercellularity, &** crowding
of cells	mild ↑ in number of cells	
3-Nucleus		
chromatin	Normochromic	**Hyperchromatic**(dark)
-size	Uniform	Small & large(**pleomorphic**)
-shape	Round to oval	**Pleomorphic**
-nucleoli		**Prominent**
-N/C ratio	1/5	**Increased** 1/1 or 1/2
-Mitotic figures(MF)	few normal or none	**Increased & abnormal**

4-Invasion: None (well localized) Cells seen invading healthy tissue
(FT capsule separates tumor from normal tissue)

CHAPTER 17

CYTOLOGY

General features of Benign cells

1. **NUCLEI** :Equal size – same shape(round or oval) – normal size
2. **NUCLEAR MEMBRANE:** Smooth - regular
3. **CHROMATIN:** Fine & uniform diffuse distribution
4. **NO NUCLEOLUS: (few exceptions)**
5. **CLEAN BACKGROUND:** No tumour diathesis
6. **N/C RATIO:** Normal according to the cell type

General features of malignant cells

1. **NUCLEI:** Enlarged – different sizes (pleomorphic) and hyperchromatic
2. **NUCLEAR MEMBRANE:** Irregular with angulations
3. **CHROMATIN:** Angulated - Clumped – irregular distribution
4. **PROMINANT NUCLEOLUS:** may be angulated
5. **DIRTY BACKGROUND (tumour diathesis):** RBCs , necrotic cells and Inflammatory cells . This is a sign of invasion
6. **N/C RATIO:** Increased due to nuclear enlargement