INFLAMMATON

Dr. Rafal Al-Saigh

MBChB, PhD, FIBMS Pathology

Specialist Doctor (Clinical Microbiologist)

Inflammation

reaction of tissues to various injurious stimuli

a protective response → remove the initial cause of cell injury, necrotic cells and tissues

have harmful effects like anaphylactic shock, rheumatoid arthritis and atherosclerosis

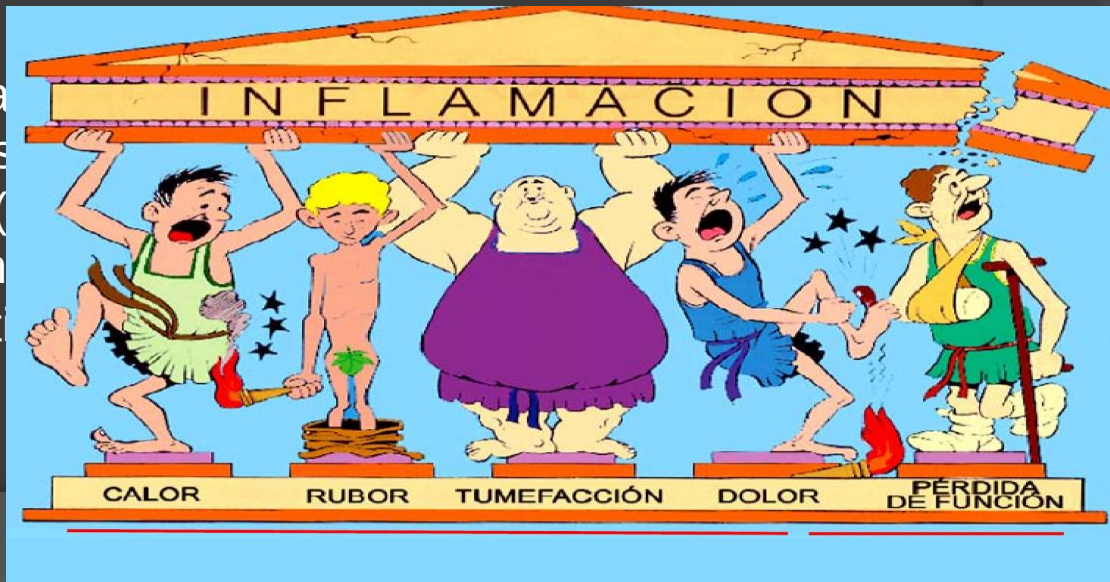
Acute inflammation

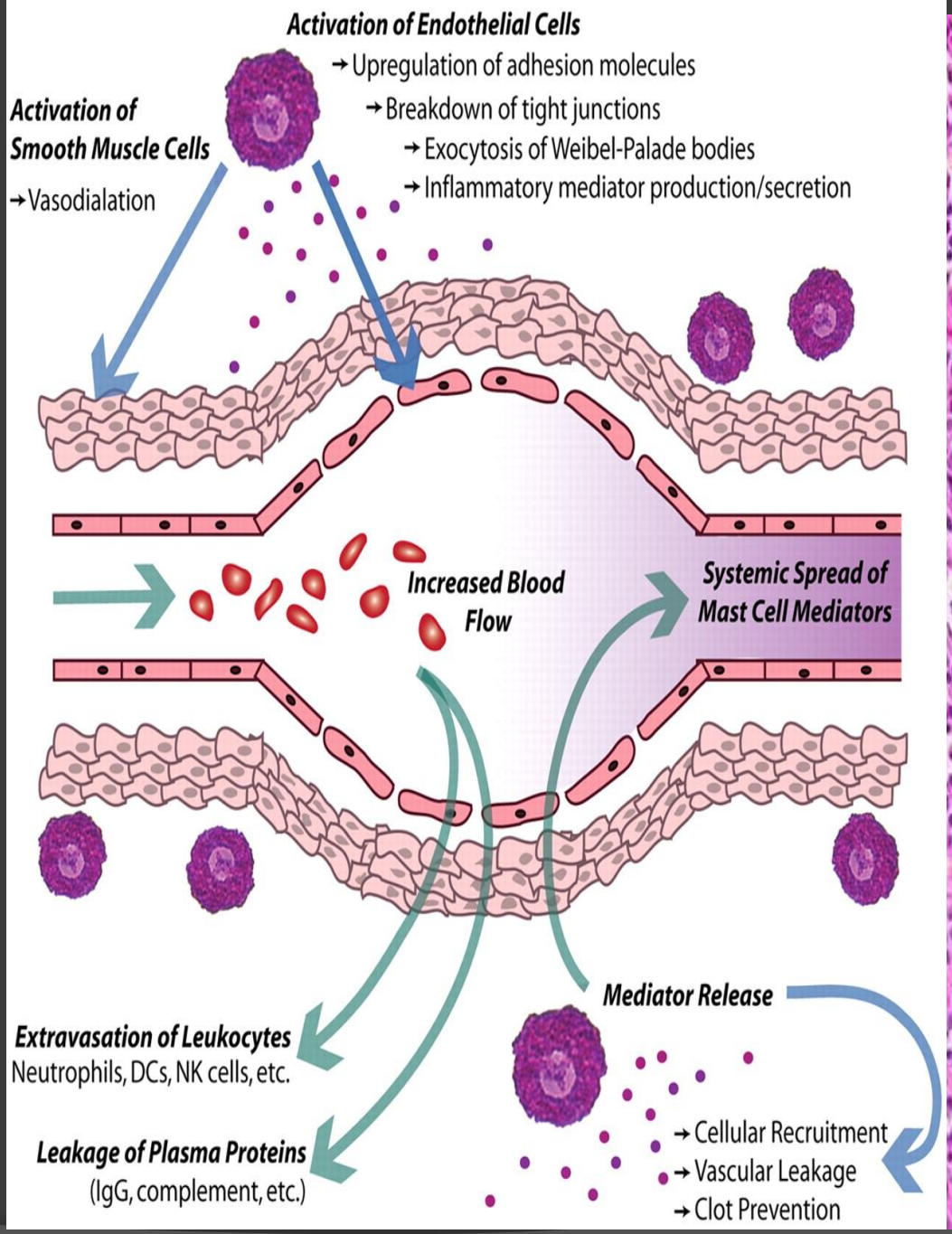
short duration (few minutes - few days)

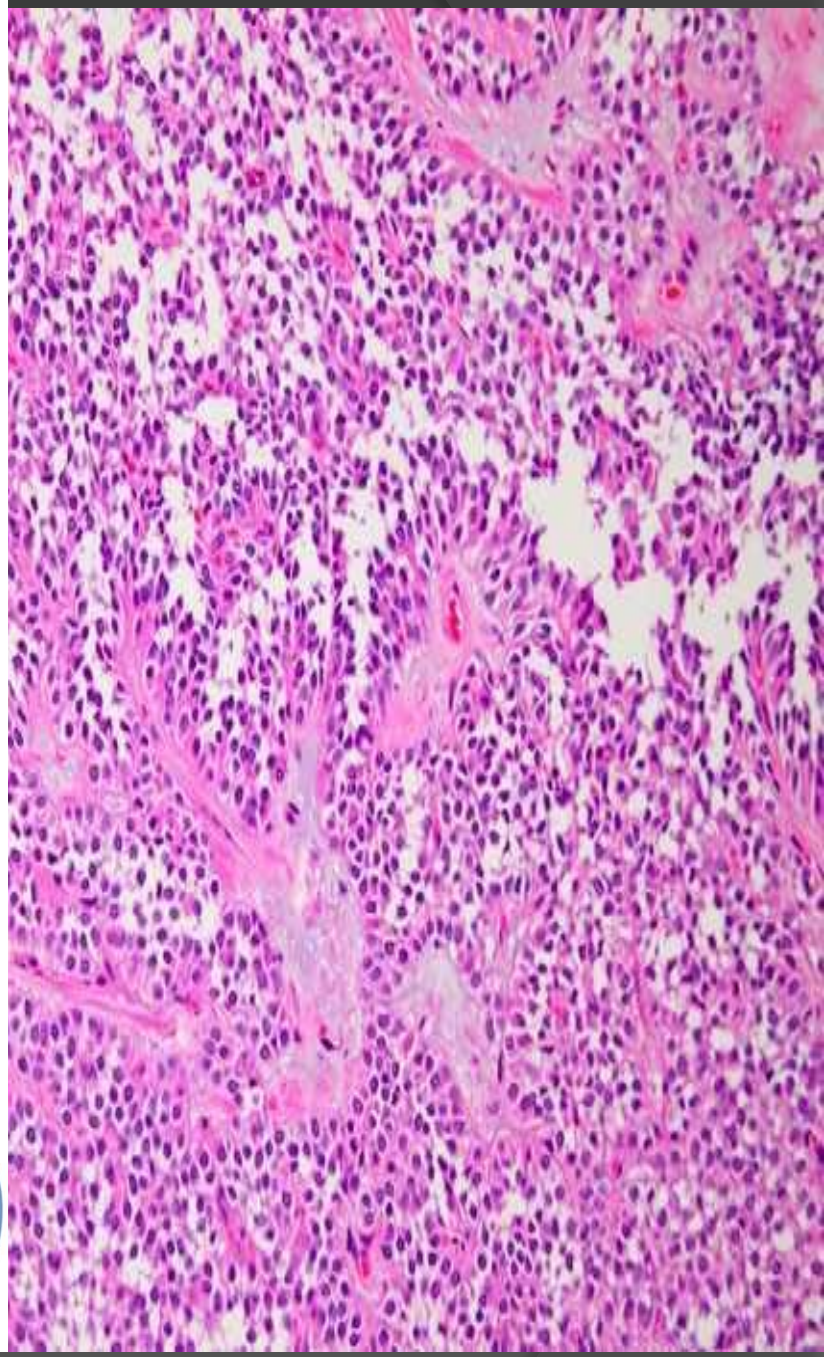
1. Vascular changes leading to increased blood flow (hyperæmia).
2. Microvascular structural changes leading to leakage of plasma proteins (exudation).

Emigration of leukocytes (neutrophilic) towards the site of injury..٣

hea
redness
swelling (
pain
loss of function (funct




Activation of Endothelial Cells
→ Upregulation of adhesion molecules
→ Breakdown of tight junctions
→ Exocytosis of Weibel-Palade bodies
→ Inflammatory mediator production/secretion
Activation of Smooth Muscle Cells
→ Vasodialation
Increased Blood Flow
Systemic Spread of Mast Cell Mediators
Mediator Release
Extravasation of Leukocytes
Neutrophils, DCs, NK cells, etc.
Leakage of Plasma Proteins
(IgG, complement, etc.)
→ Cellular Recruitment
→ Vascular Leakage
→ Clot Prevention



Benificial Effects of Acute Inflammation

1. Dilution of toxins.
2. Exudation of protective antibodies.
3. Fibrin formation which delays bacterial spread.
4. Exudation of plasma mediators (complement, coagulation, fibrinolytic and kinin).
5. Exudation of nutrient materials.
6. Promotion of immunity.

Outcomes of Acute Inflammation

1. Complete resolution to histologic and functional normality.
2. Fibrosis: Occurs in
   - When inflammation in tissues that do not regenerate..A
   - After substantial tissue destruction..B
   - Extensive fibrinous exudates. .C
3. Abscess formation in pyogenic infection.
4. Progression to chronic inflammation

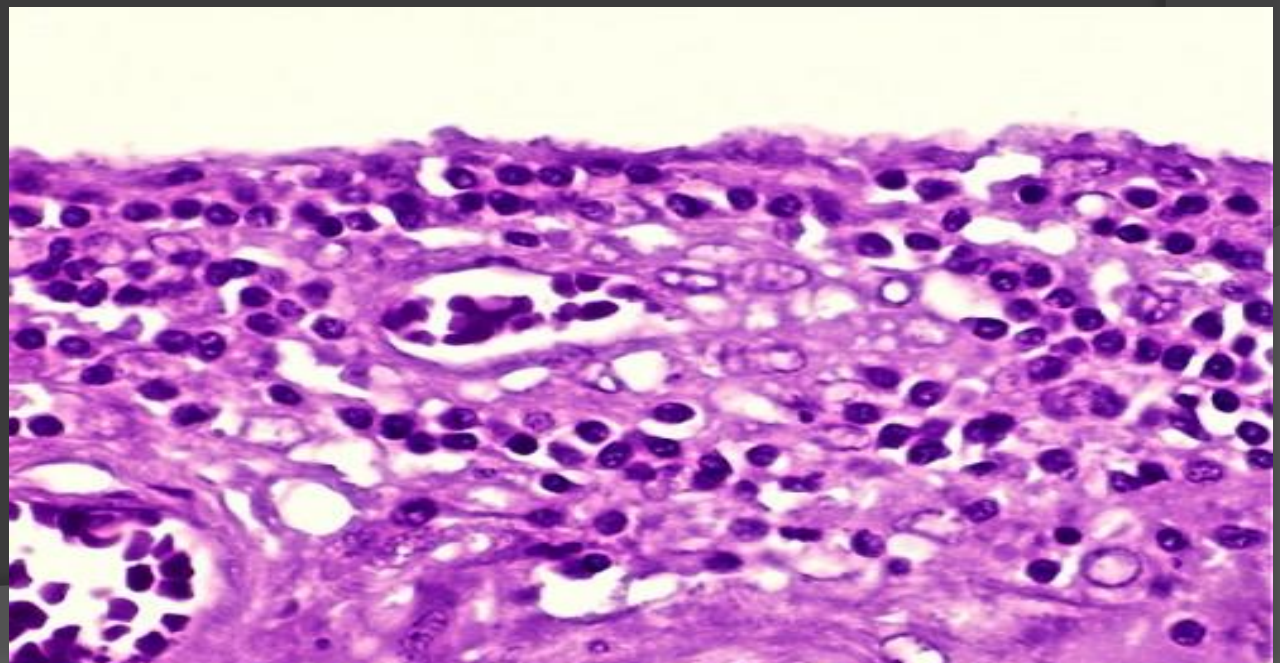
Chronic inflammation

longer duration (days or years)

- Infiltration by mononuclear cells (monocytes, lymphocytes & macrophages .
- Tissue destruction.
- Tissue repair. (vascular proliferation and fibrosis).

Causes

١. Persistent infections like tuberculosis, syphilis..
٢. Prolonged exposure to potentially toxic agents..
٣. Autoimmune disorders..



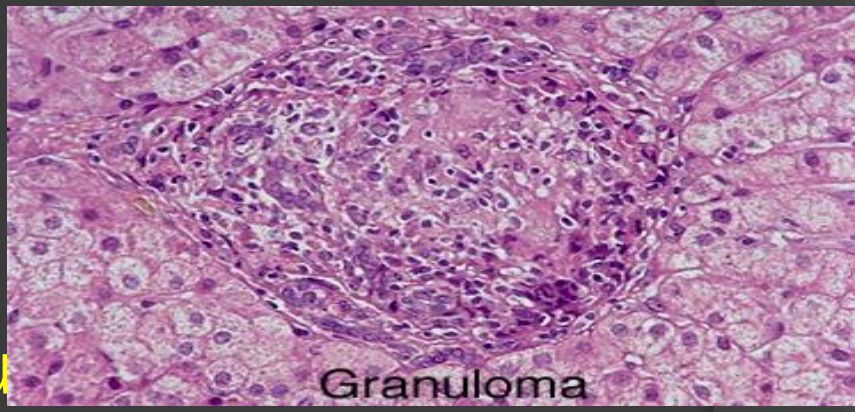
Cells

- Macrophages derived from monocytes → increasing in size, contents of lysosomes and more active metabolism.

lymphocytes,
plasma cells
eosinophils

- Activation signals include IFN-γ secreted from T lymphocytes,
- Macrophages secrete:

1) Acid and neutral proteases.
2) Complement components.
3) Oxygen-free radicals and nitric oxide.
4) Cytokines (IL-1, TNF).



Granu

aggregation of activated macrophages as (epithelioid) appearance.

Bacterial infection: e.g. tuberculosis, leprosy, syphilis, cat scratch disease..١

Parasitic: Bilharziasis..٢

Fungal: Histoplasmosis..٣

Inorganic metals: Silica, berylliosis..٤

Foreign body..٥

Unknown: Sarcoidosis.

Morphologic Patterns of Acute And Chronic Inflammation

1.Serous Inflammation: Effusions of watery, protein-poor fluid derived from serum or mesothelial cells, lining peritoneal, pleural or pericardial cavities.

2.Fibrinous Inflammation: Occurs in severe injuries, appearing as a meshwork of threads or as an amorphous coagulum. Fibrinous exudates is either removed by macrophages or fibrinolysis or replaced by fibrosis (organization).

3.Suppurative (Purulent) Inflammation: Manifested by the presence of a large amount of purulent exudates (pus), consisting of neutrophils, necrotic cells and fluid, caused by bacteria (pyogenic) like staphylococci. Abscess is a focal collection of pus caused by deep seeding of MO in tissues or by secondary infection of necrotic areas, having large central necrotic region rimmed by preserved neutrophils and surrounded by dilated blood vessels and proliferated fibroblasts.

4.Ulceration: This refers when an epithelial surface becomes eroded by necrosis with associated subepithelial acute and chronic inflammation.

- Toxic or traumatic, e.g. peptic ulcer.
- Vascular e.g. foot ulcers of diabetes.

Neoplasia (Benign and malignant tumour)

Dr. Rafal Al-Saigh

MBChB, PhD, FIBMS Pathology

Specialist Doctor (Clinical Microbiologist)

Neoplasia

Is a new growth or an abnormal outgrowing mass of tissue and uncoordinating with the normal tissue, which may persist after the cessation of the stimuli.

General Charachteristics of Neoplasms

1. Unresponsive to the normal growth factors controlling cell division (continue to replicate).
2. Competing with the normal cells and tissues for their metabolic needs.
3. Have degree of autonomy steadily increasing in size regardless of their local environment and the nutritional status of the host.
4. Require endocrine stimulatory signals for their growth.

Neoplasm is **“a tumour OR swelling”**.

Tumours can be subdivided into

1. Benign considered innocent: remaining localized, not spreading to other sites, may produce local effects.

2. Malignant tumours, cancers, which can invade and destroy adjacent structures and spread to distant sites (metastasize).

Benign tumours

- Resemble their normal cells of origin morphologically and functionally
- Well differentiated cells
- Mitoses are very scanty in number and are of normal configuration
- Grow slowly, localized, not infilterate.

Acquired preneoplastic disorders

1. Persistent regenerative cell replication, e.g. long standing skin ulcer, and hepatic cirrhosis.
2. Hyperplastic and dysplastic proliferations, e.g. endometrial hyperplasia and dysplastic changes of the bronchus.
3. Chronic atrophic gastritis.
4. Chronic ulcerative colitis.
5. Leukoplakia of the oral cavity.
6. Villous adenomas of the colon.

Nomenclature of Benign tumours

- Cell type from tumour arises + suffix “-oma” , e.g. fibroma, chondroma, leiomyoma.

- according to cells of origin, e.g.:

Adenoma: glandular pattern.

Papilloma: epithelial surfaces, producing microscopic or macroscopic finger-like structure.

Polyp: Is a mass projects above the mucosal surface to form a macroscopically visible structure.

Cystadenomas: Hollow cystic masses (in the ovary).

Fibroadenoma of the breast and benign mixed tumour of salivary glands (pleomorphic adenoma): Mixed type

Malignant tumours

1. **Pleomorphism:** variation in size and shape.
2. **Hyperchromasia:** Increased nuclear pigmentation.
3. **High nuclear/ cytoplasmic (N/C) ratio**.
4. **Giant cells** may be formed containing several nuclei.
5. **Nuclear pleomorphism**, with coarse and clumped chromatin.
6. Numerous **mitoses** with atypical forms.
7. **Loss of polarity:** cells fail to form a recognizable pattern of orientation.
8. **Dysplasia:** loss in the uniformity of individual cells and their architectural orientation (partial or the entire thickness of the epithelium (carcinoma in situ)).

- **Rapidly growing tumour with progressive infiltration, invasion, destruction and penetration of the surrounding tissue.**

- ***Metastasis:*** secondary implants discontinuous with the primary tumour.

Pathways:

1. Seeding within body cavities.
2. Lymphatic spread typical for carcinomas.
3. Hæmatogenous spread for sarcomas, but carcinomas also metastasize by this route. The **liver and lungs** →most secondary sites.

Mechanisms of Local And Distant Spread

1. Invasion of ECM: reach to the basement membrane, then invade the interstitial connective tissue and then penetrate the blood vessels' basement membrane; As four stages:

A. **Detachment of tumour cells from each other by loss of surface E-cadherins.**
B. **Attachment of tumour cells to matrix components.**
C. **Degradation of ECM by production and induction of fibroblasts to produce proteases, especially metalloproteinases including gelatinases, collagenases and stromelysins.**
D. **Migration of tumour cells by cell-derived cytokines, cleavage products of matrix components and some growth factors.**

2. Vascular dissemination:

- **Intravasation:** by degradation of blood vessels' basement membrane, forming tumour emboli by aggregation with leukocytes and platelets, hiding tumour cells from the immune system.

- **Extravasation** of free tumour cells involves adhesion to the endothelium followed by transgression through the basement membrane by a similar mechanism to intravasation.

Nomenclature of Malignant tumours

- **Mesenchymal origin**→ sarcomas e.g. fibrosarcoma, chondrosarcoma, leiomyosarcoma.

- **Epithelial origin** (endo, meso and ectoderm) →carcinomas, e.g. squamous cell carcinoma, adenocarcinoma.
- **Two components** (mesenchymal and epithelial) e.g. Teratomas → divergent differentiation into all embryonic layers, commonly seen in the ovaries and testicles, being benign or malignant.

Tumour antigens (tumour markers):

1. **Tumour-specific antigens:** unique antigens for tumours.

- melanoma associated antigen-1 (MAGE-1)
- some pancreatic and breast carcinoma (CA-125, CA-119).

2. Tumour-Associated Antigens: shared by normal untransformed cells, t

-prostate-specific antigens (PSA

-alfa-fœtoprotein (AFP) in hepatocellular carcinoma

- carcinoembryonic (CEA) antigen in colorectal carcinomas.

Grading And Staging

Grading: based on cytological differentiation of tumour cells and the number of mitoses within the tumour. Graded I, II, III or IV in order of increasing anaplasia.

Staging: is based on:

1. The size of the primary lesion.
2. Extent of spread to regional lymph nodes.
3. Presence or absence of metastases.

TNM staging system:

T: tumour size,

N: Lymph node metastases,

M: Distant metastases.