Necrosis

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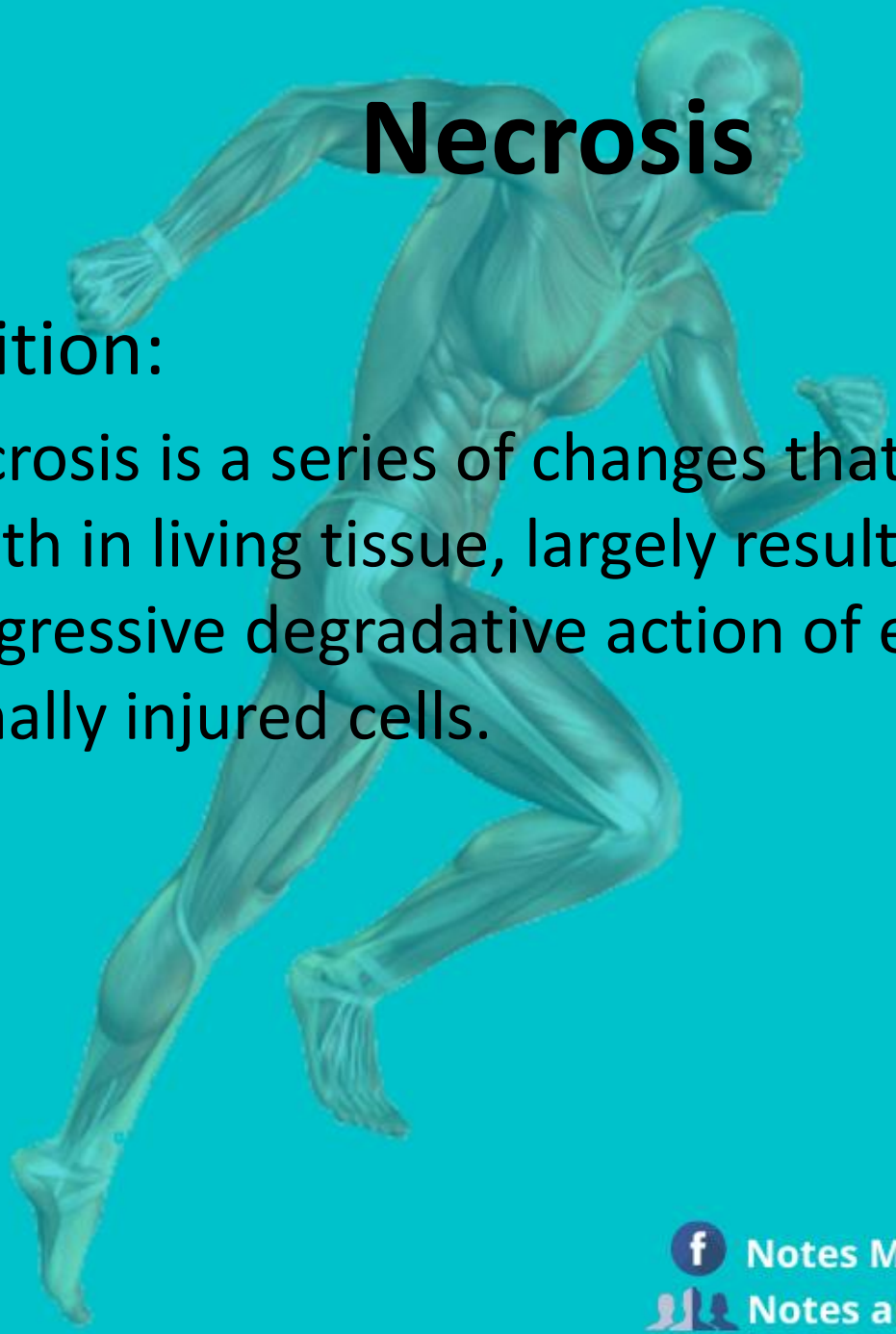
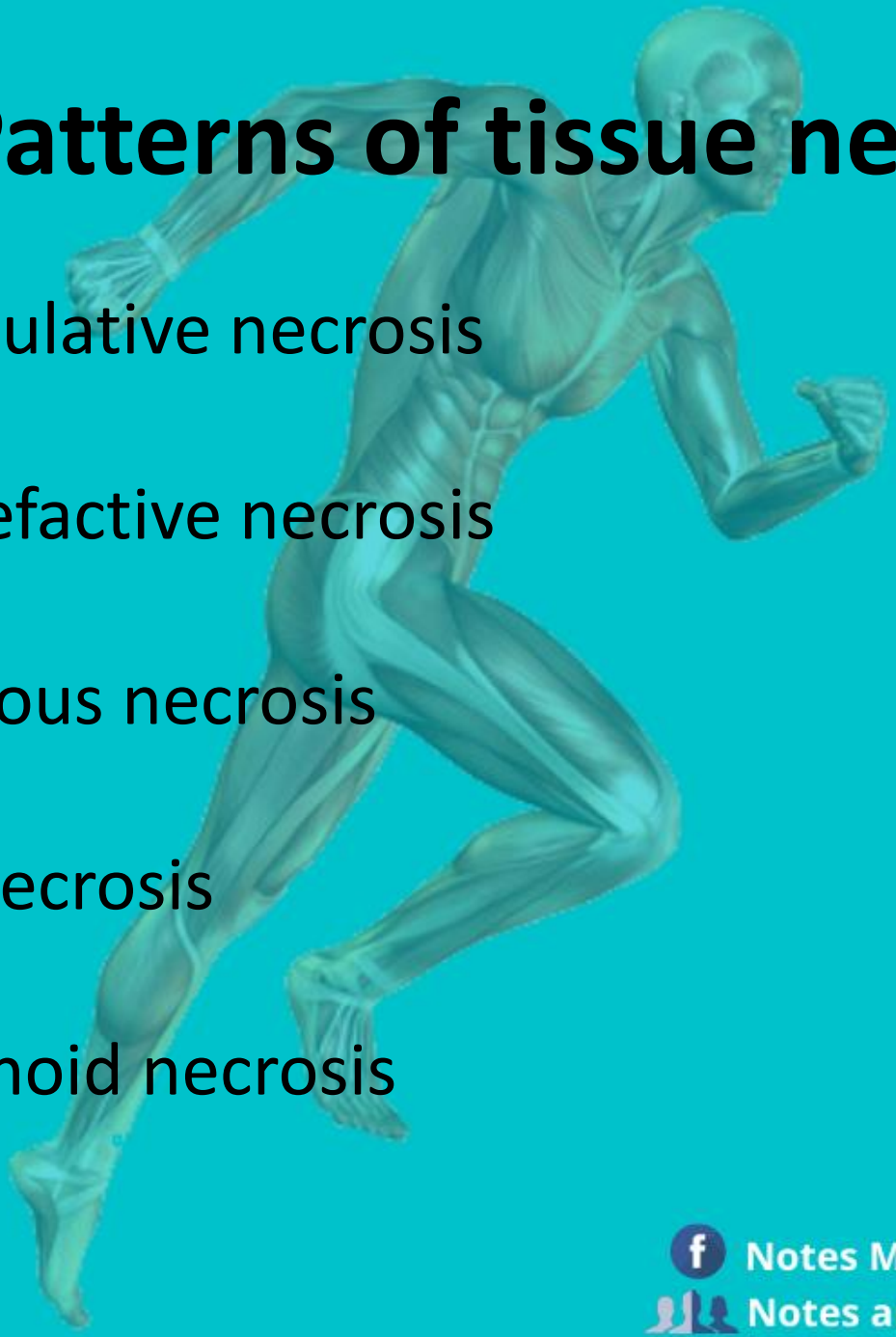


- Definition:
  - Necrosis is a series of changes that accompany cell death in living tissue, largely resulting from the progressive degradative action of enzymes on lethally injured cells.

Patterns of tissue necrosis



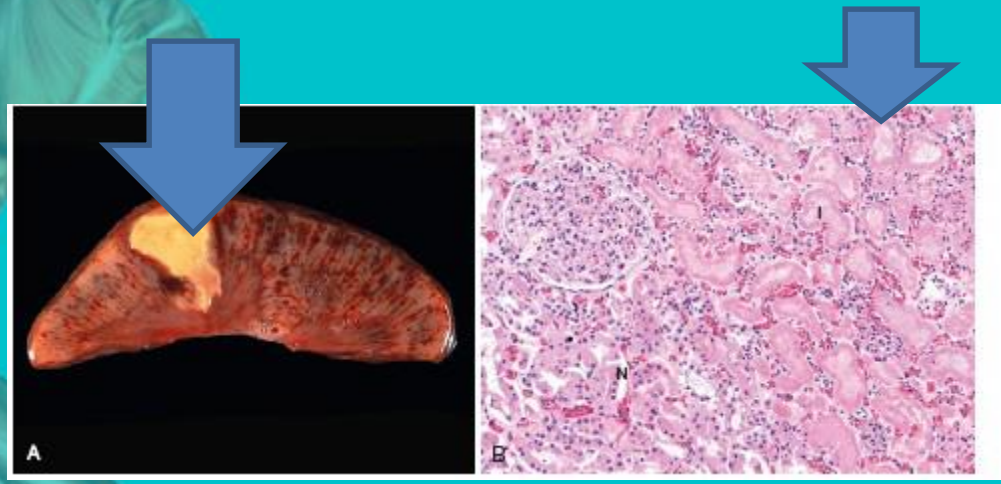
1. Coagulative necrosis
2. Liquefactive necrosis
3. Caseous necrosis
4. Fat necrosis
5. Fibrinoid necrosis

Coagulative necrosis

- Coagulative necrosis is characteristic of **infarcts (areas of ischemic necrosis) in all of the solid organs except the brain.**
- Mechanism : Denaturation of enzymes and structural proteins.
- **Preservation of the structural outline of dead cells.** (Inactivation of intracellular enzymes prevents dissolution (autolysis) of the cell.)

Morphology of coagulative necrosis

- **Gross :**
  - The affected tissues take on a firm texture.
- **Microscopic examination :**
  - **Eosinophilic, anucleate cells may persist**
  - Leukocytes are recruited to the site of necrosis.



Gangrenous necrosis

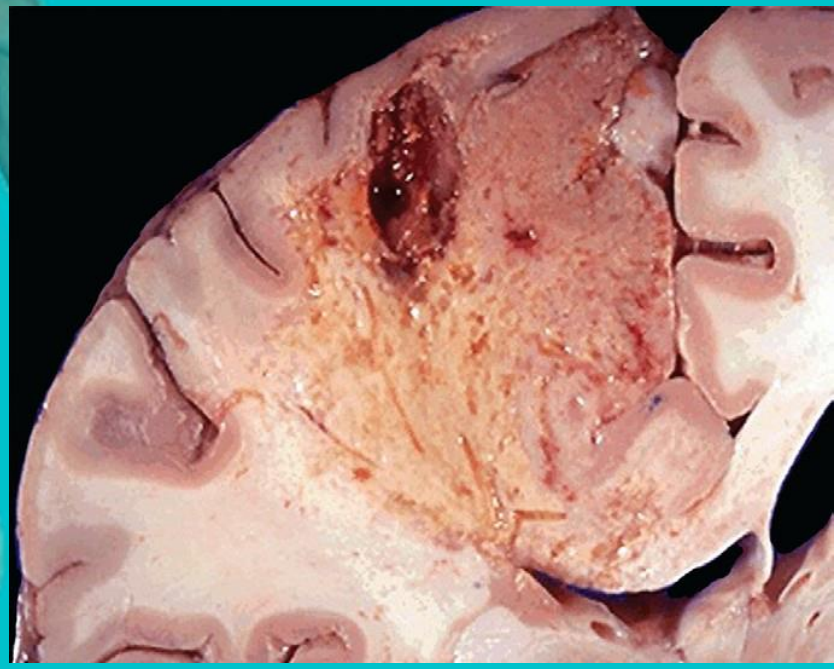
- It usually refers to the condition of a limb, generally the lower leg, that has lost its blood supply and has undergone coagulative necrosis involving multiple tissue layers.
- When bacterial infection is superimposed, coagulative necrosis is modified by the liquefactive action of the bacteria and the attracted leukocytes (resulting in so-called **wet gangrene).**

Gangrenous necrosis

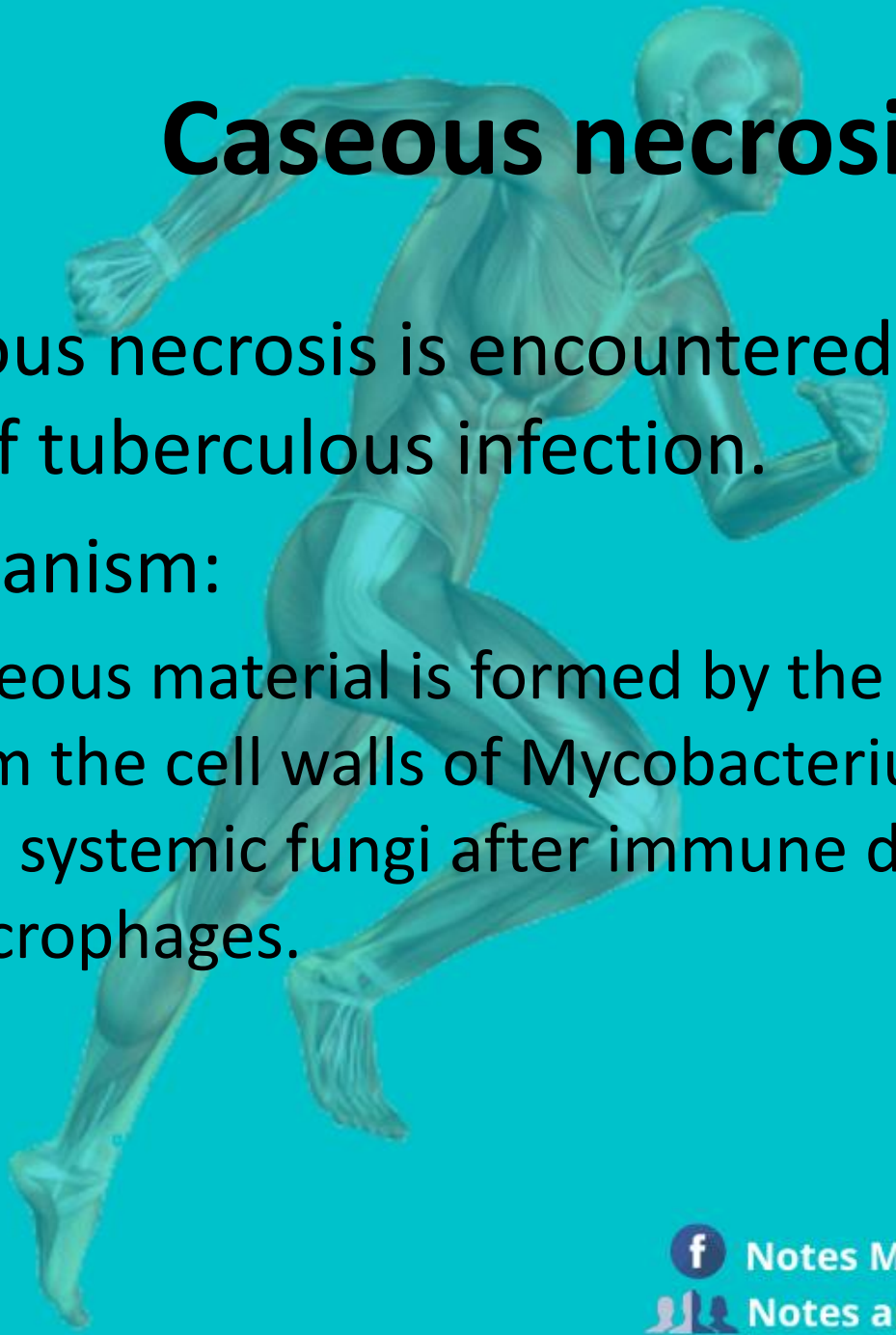
- Dry gangrene
  - Dry gangrene predominantly consists of a coagulative type of necrosis.
  - The affected site is dry shrunken (shriveled) dark brown or black resembling the foot of a mummy.
  - In this dry gangrene, the line of demarcation is clear and spread slowly but the prognosis is fair.
  - Dry gangrene is caused by ischemia due to arterial obstruction and the rate of obstruction is slow.

Liquefactive necrosis

- **Causes:**
  I. **Focal bacterial or, occasionally, fungal** infections.
  II. Hypoxic death of cells within the central nervous system.
- Mechanism:
- The dead cells are completely digested by the lysosomal enzymes released by neutrophils or dead cells, transforming the tissue into a **liquid viscous mass (Pus in case of acute inflammation).**



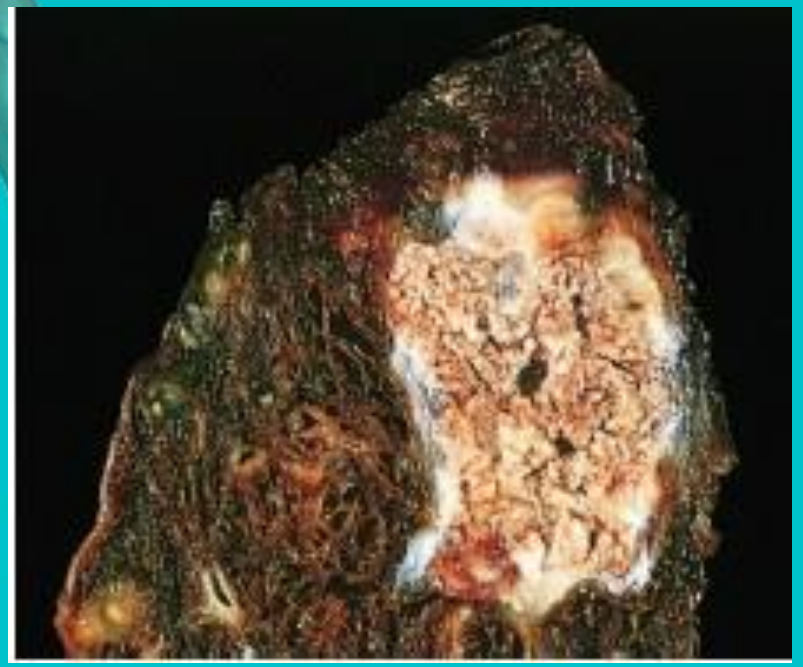
Caseous necrosis



- Caseous necrosis is encountered most often in foci of tuberculous infection.
- Mechanism:
  - Caseous material is formed by the release of lipid from the cell walls of Mycobacterium tuberculosis and systemic fungi after immune destruction by macrophages.

Morphology of **Caseous necrosis**

- **Grossly - Friable yellow-white** appearance of the area of necrosis (**Caseous means "cheese-like,")**
- On **microscopic examination: the** necrotic focus appears as a collection of fragmented or lysed cells with an amorphous granular pink appearance

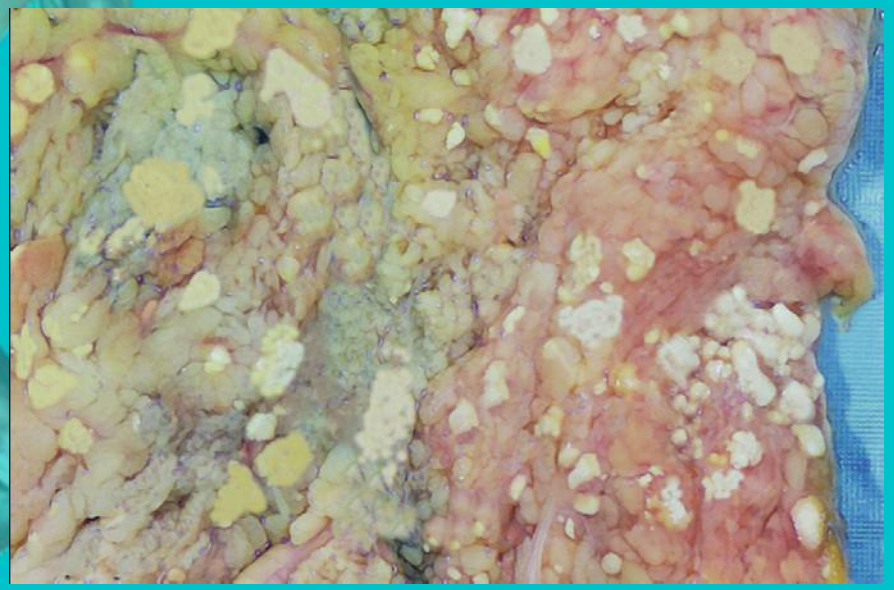


Enzymatic Fat necrosis

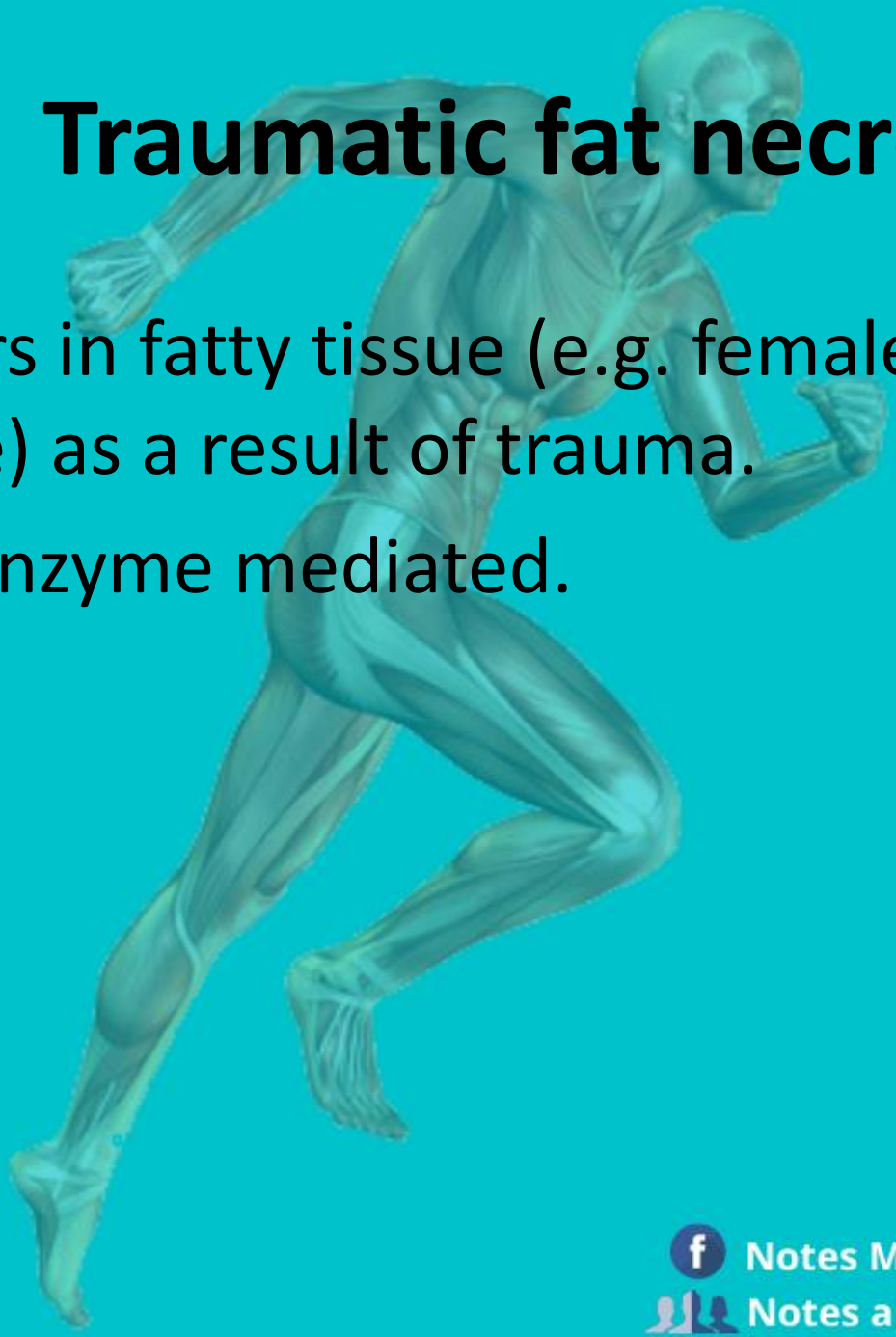
- **Fat destruction,** typically resulting from release of activated pancreatic lipases into the substance of the pancreas and the peritoneal cavity.
- **Mechanism:**
  - Activation of pancreatic lipase (e.g. alcohol excess) causing hydrolysis of triglyceride in fat cells with release of fatty acids.
  - Conversion of fatty acids into soap (Fatty acid+soap) (***saponification)***

Morphology of Enzymatic Fat necrosis

- **Grossly:**
  - Chalky white areas of saponification.
- **Histologic examination:**
  - Foci of necrosis contain shadowy outlines of **necrotic fat cells with** basophilic **calcium deposits,** surrounded by an **inflammatory** reaction.



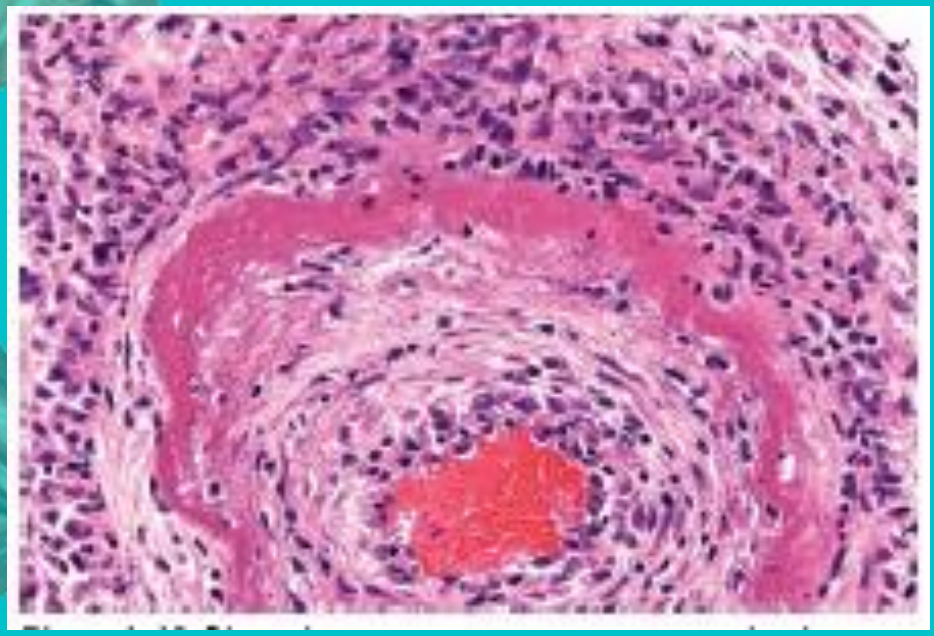
Traumatic fat necrosis



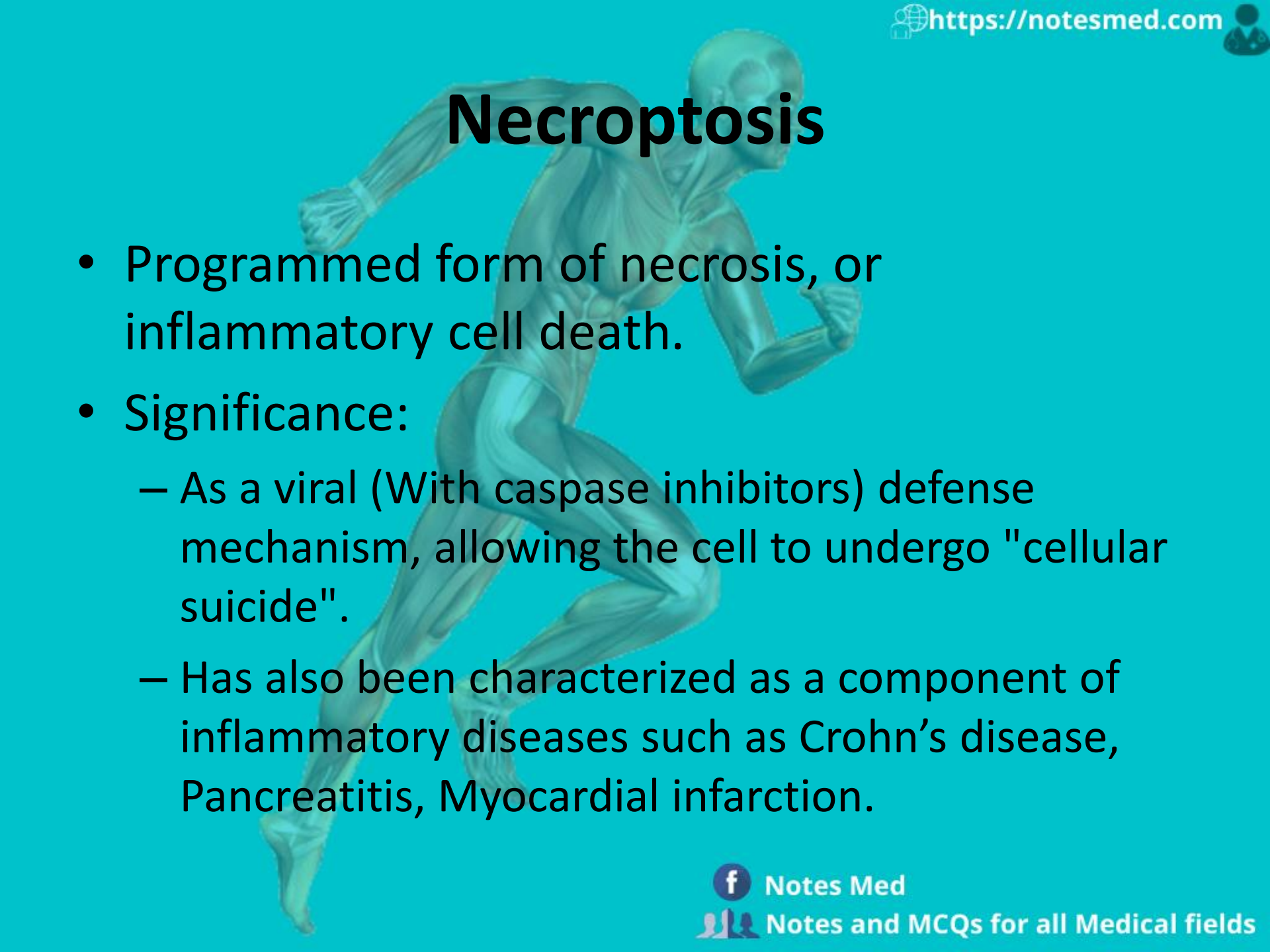
- Occurs in fatty tissue (e.g. female breast tissue) as a result of trauma.
- Not enzyme mediated.

Fibrinoid necrosis

- Seen in immune reactions.
- The deposited immune complexes, together with fibrin that has leaked out of vessels, produce a bright pink and amorphous appearance on H&E preparations called **fibrinoid (fibrin-like) necrosis.**



Necroptosis

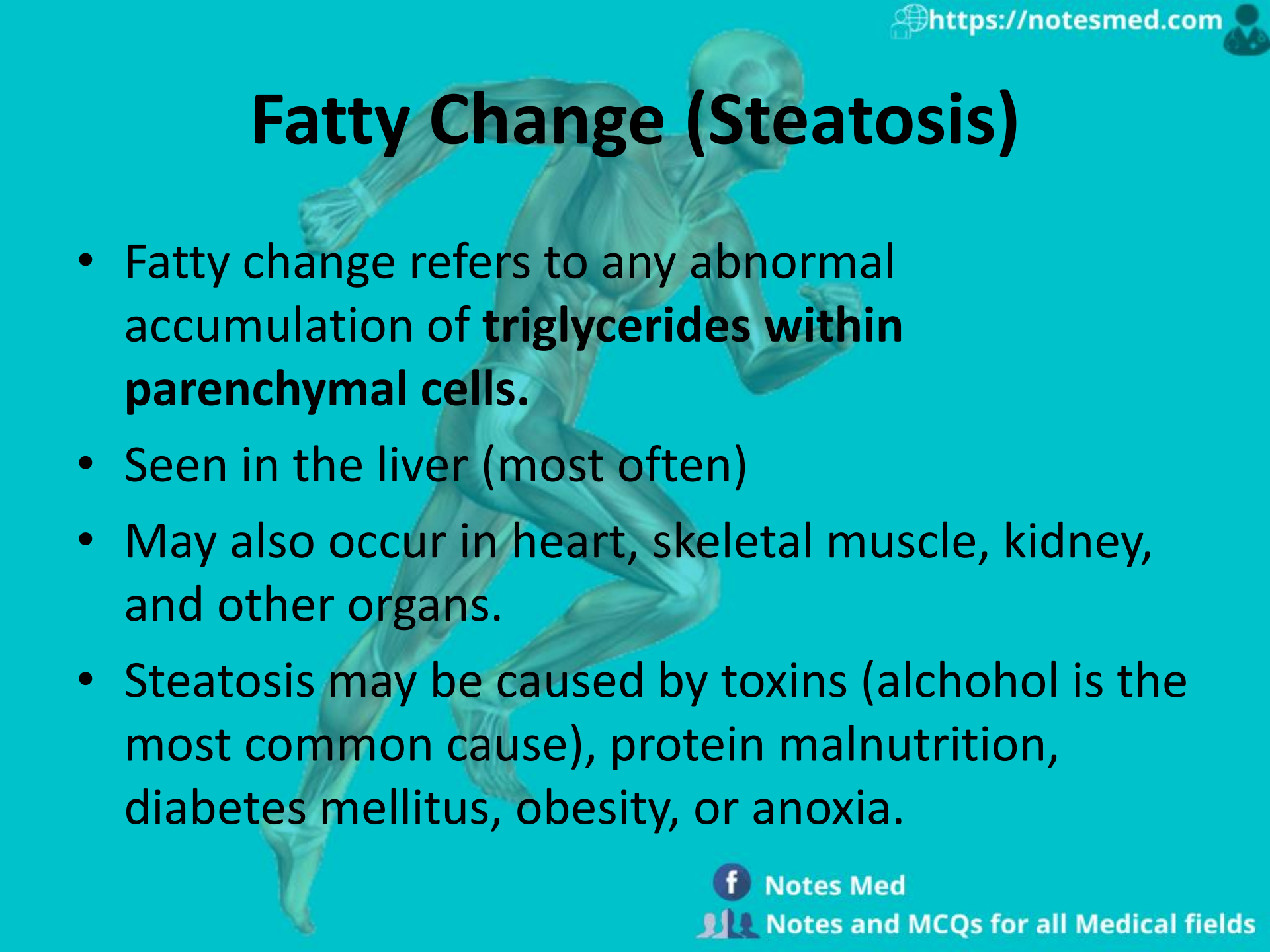


- Programmed form of necrosis, or inflammatory cell death.
- Significance:
  - As a viral (With caspase inhibitors) defense mechanism, allowing the cell to undergo "cellular suicide".
  - Has also been characterized as a component of inflammatory diseases such as Crohn’s disease, Pancreatitis, Myocardial infarction.

Intracellular accumulations

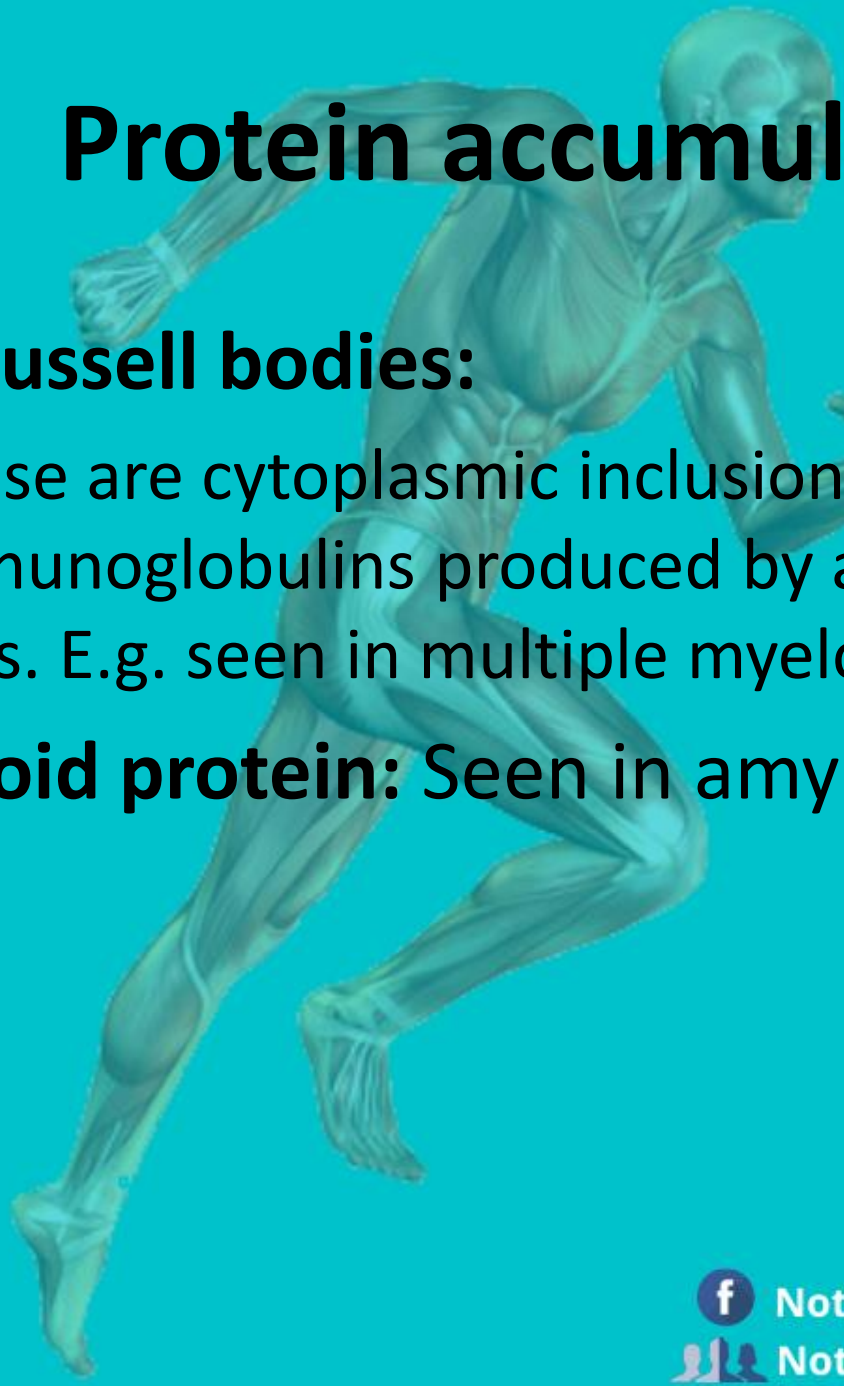
- Cells may accumulate abnormal amounts of various substances located in the **cytoplasm,** within organelles (typically lysosomes), or in the **nucleus.**
- The substance may be synthesized by the affected cells or may be produced elsewhere.
- The various types of accumulation or changes are:
  - **Fatty accumulation**
  - **Protein accumulation**
  - **Cholesterol accumulation**
  - **Hyaline change**
  - **Glycogen accumulation**
  - **Pigment accumulation**

Fatty Change (Steatosis)



- Fatty change refers to any abnormal accumulation of **triglycerides within parenchymal cells.**
- Seen in the liver (most often)
- May also occur in heart, skeletal muscle, kidney, and other organs.
- Steatosis may be caused by toxins (alchohol is the most common cause), protein malnutrition, diabetes mellitus, obesity, or anoxia.

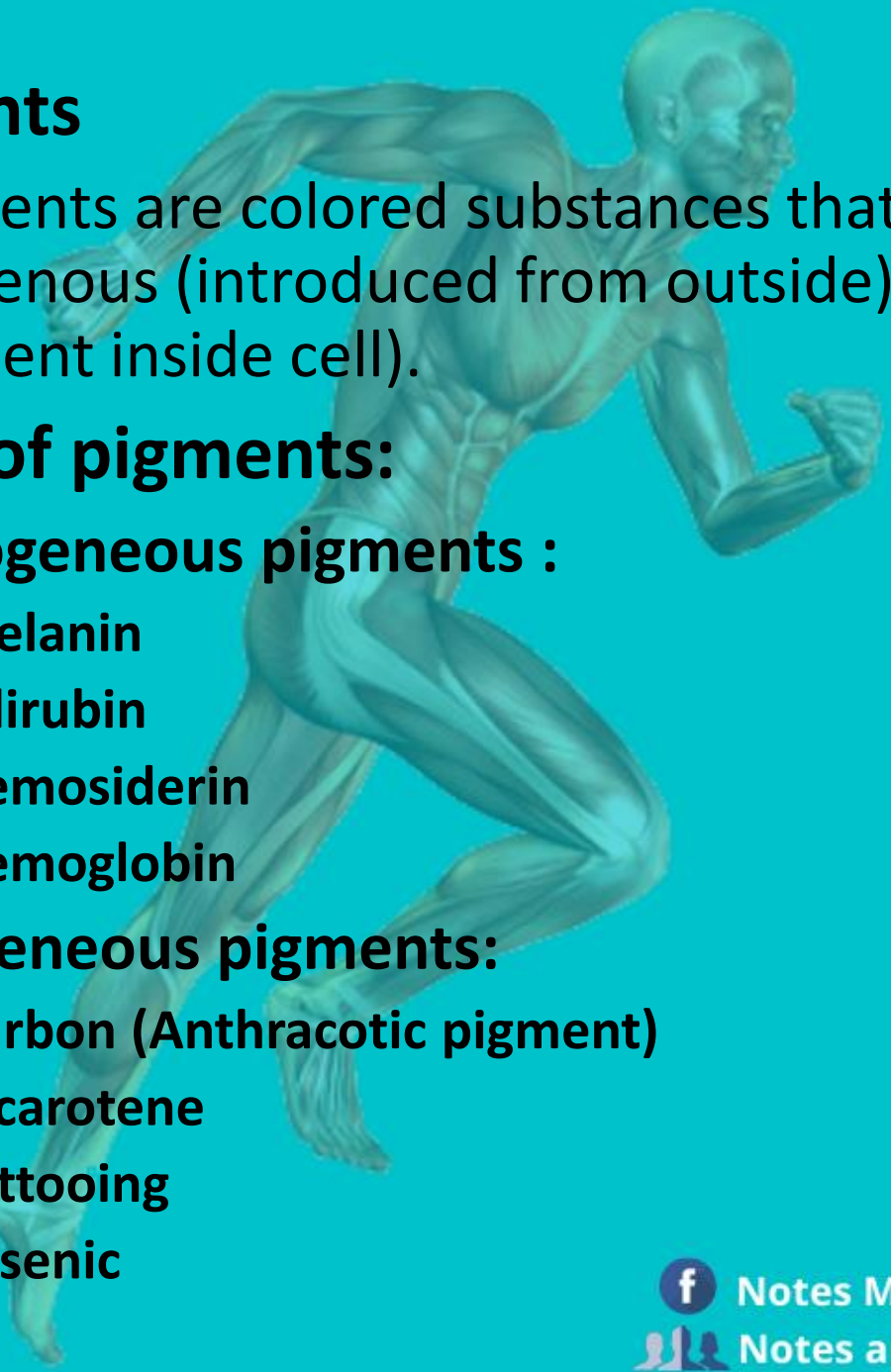
Protein accumulation



- E.g. **Russell bodies:**
  - These are cytoplasmic inclusions of immunoglobulins produced by activated plasma cells. E.g. seen in multiple myeloma.
- **Amyloid protein:** Seen in amyloidosis

Glycogen accumulation

- Seen in glycogen storage diseases.
  - Diabetes mellitus



- **Pigments**
  - Pigments are colored substances that are either exogenous (introduced from outside) or endogenous (present inside cell).
- **Types of pigments:**
  - **Endogeneous pigments :**
    - **Melanin**
    - **Bilirubin**
    - **Hemosiderin**
    - **Hemoglobin**
  - **Exogeneous pigments:**
    - **Carbon (Anthracotic pigment)**
    - **b-carotene**
    - **Tattooing**
    - **Arsenic**

Melanin

- The melanin producing melanocytes are derived from neural crest cells during embryogenesis.
- Distribution of melanin pigment: Skin, hair, adrenal medulla, nerve cells, substantia nigra.

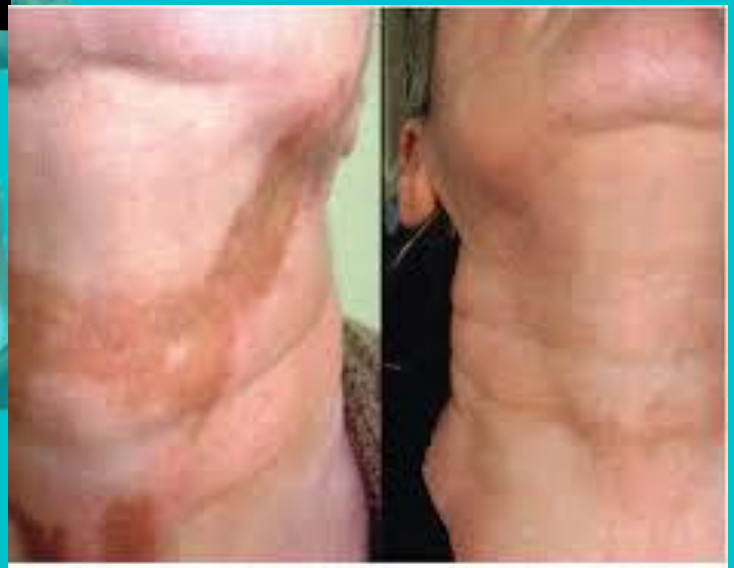
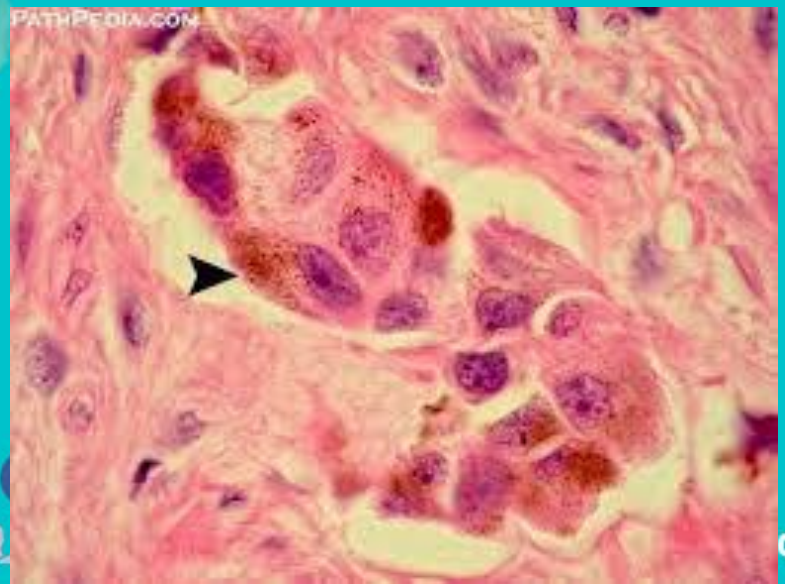
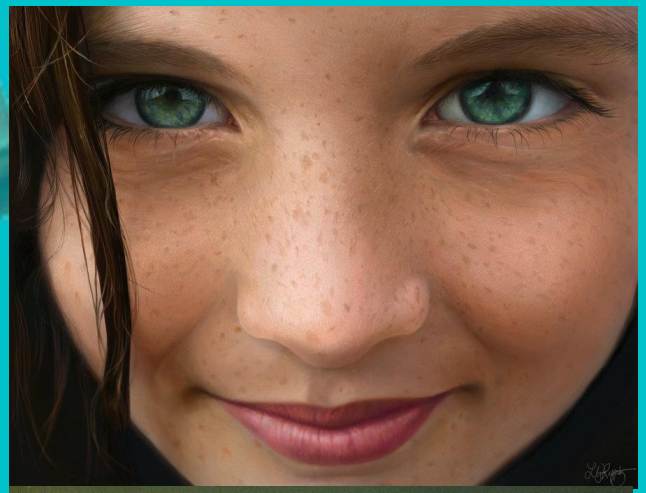


FIGURA 1: Pescoço. À esquerda, vitiligo generalizado com área normal de pigmentação. À direita, após oito meses de fenol 88% tópico



Melanin
Abnormalities in pigmentation

- **Hyperpigmentation**
  - Cushing's syndrome
  - ACTH producing tumors
  - Addison's disease
  - Freckles
- **Hypopigmentation**
  - Vitiligo
  - Leprosy
  - Following burn

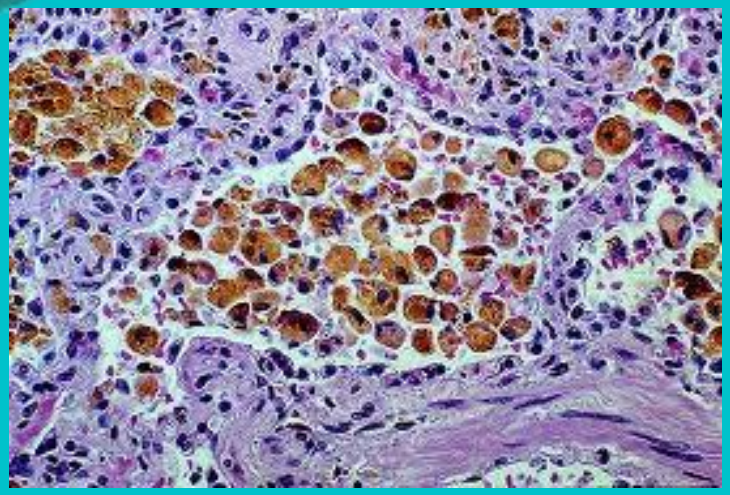


Hemosiderin

- **Hemosiderin** is a **hemoglobin-derived granular pigment that is golden** yellow to brown and accumulates in tissues when there is a local or systemic excess of iron.
- Hemosiderin pigment represents large aggregates of these **ferritin micelles.**
- The iron can be identified by the Prussian blue histochemical reaction.

Hemosiderin

- Small amounts of this pigment are normal in the mononuclear phagocytes of the bone marrow, spleen, and liver, where aging red cells are normally degraded.
- Pathologic conditions:
  - Hemosiderosis
  - Hemochromatosis
  - Hemorrhagic conditions, Blood transfusion, Fracture, Ectopic pregnancy



Lipofuscin

- Also known as ***"wear-and-tear pigment,"*** is an insoluble brownish-yellow granular endogenous material.
- It is a marker of **past free radical injury.**
- Accumulates in a variety of tissues (particularly the
- heart, liver, and brain) as a function of age or atrophy.
- Lipofuscin represents complexes of lipid and protein that derive from the free radical–catalyzed peroxidation of polyunsaturated lipids of subcellular membranes.
- The brown pigment, when present in large amounts, imparts an appearance to the tissue that is called ***brown atrophy.***