21.02.2023

PATOLOGIA GENERALE E FISIOPATOLOGIA ANIMALE

- Cellular Adaptation -

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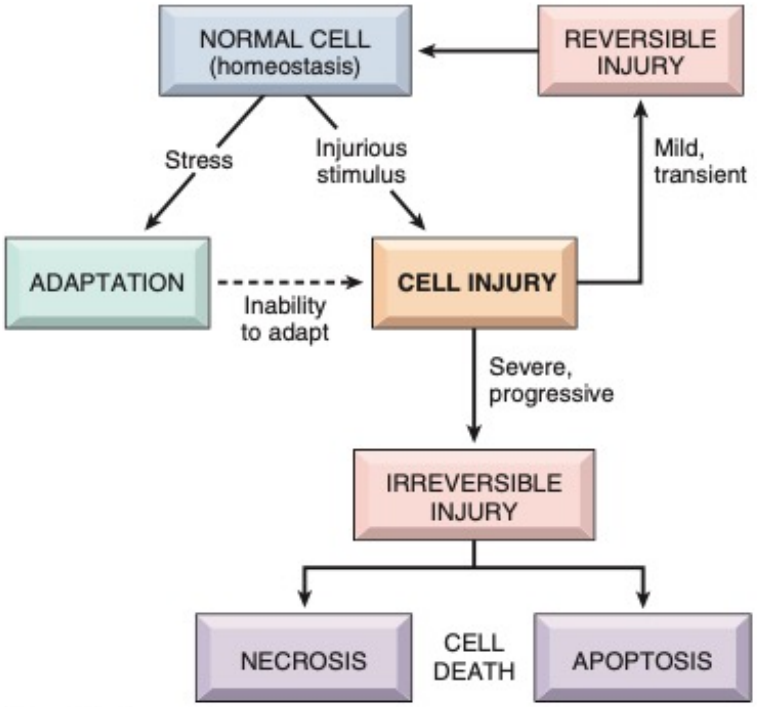
OBJECTIVES

PATHOLOGY

"The study of the structural, biochemical, and functional changes in cells, tissues, and organs that underlie disease"

GENERAL PATHOLOGY

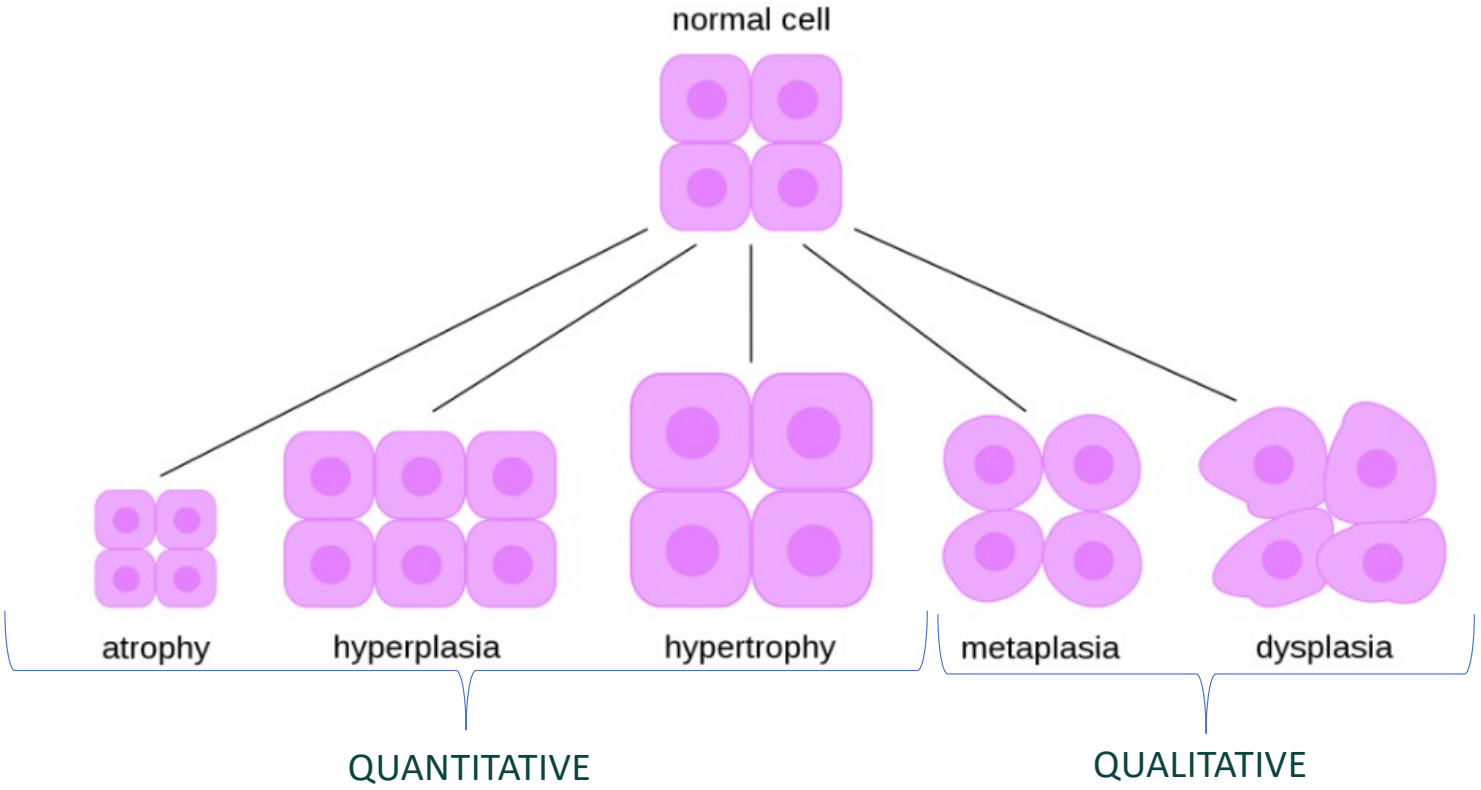
"Reactions of cells and tissues to injurious stimuli. Such reactions are often not tissue specific (acute inflammation in response to bacterial infections produces a very similar reaction in most tissues)"



ADAPTATION TO CELLULAR GROWTH AND DIFFERENTIATION

Adaptations → *"Reversible changes in the size, number, phenotype, metabolic activity or functions of cells in response to changes in their environment"*

Such adaptations may take several distinct forms

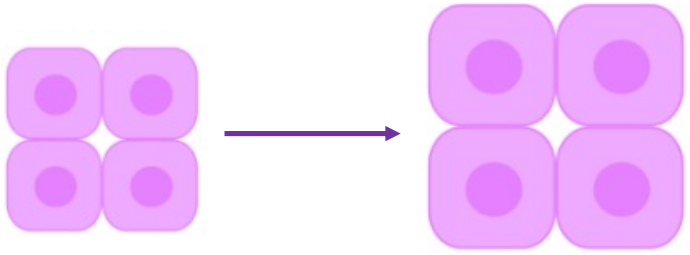


HYPERTROPHY

"An increase in the size of cells, that results in an increase in the size of the affected organ"

≠ PSEUDO-HYPERTROPHY

- No new cells
- Larger cells
- Histologic architecture of the organ is normal
- Synthesis and assembly of additional intracellular structural components
- STRESS → Cells capable of division → both hyperplasia and hypertrophy
- STRESS → Non dividing cells (e.g., myocardial fibers) → increased tissue mass due to hypertrophy



Hypertrophy

PHYSIOLOGICAL
increased functional demand or by stimulation by hormones and growth factors

PATHOLOGICAL

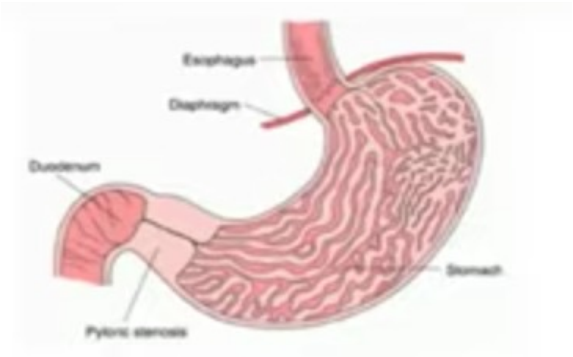
IN MUSCLES:

- Most common stimulus for hypertrophy – increased workload
  → enlargement of individual muscles fibers

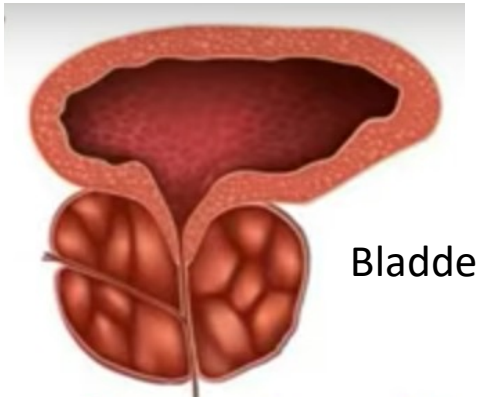
Chronic hemodynamic overload – Hypertension, Valve incompetence

IN MUSCLES:

- Smooth muscle hypertrophy - Obstruction to the outflow

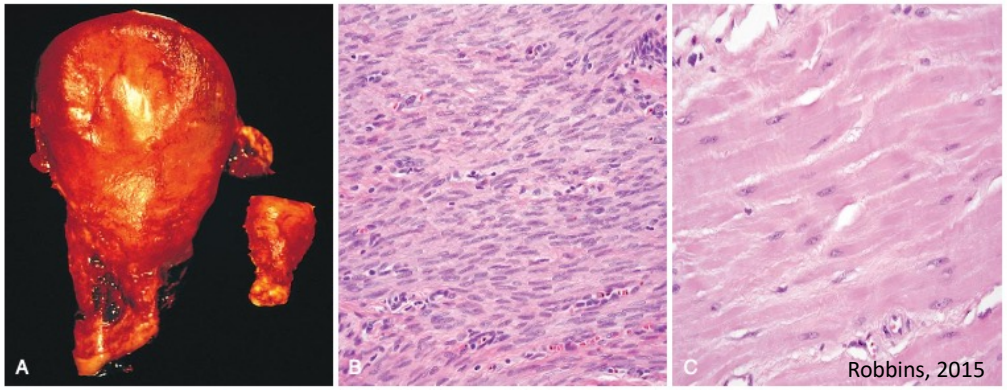


Stomach – Pyloric Stenosis



Bladder – Prostatic Hyperplasia

- Hormone induced hypertrophy



Pregnancy – Massive growth of the uterus

COMPENSATORY

→ Compensatory hypertrophy is a response to the loss of a part of an organ or one of the paired organs.

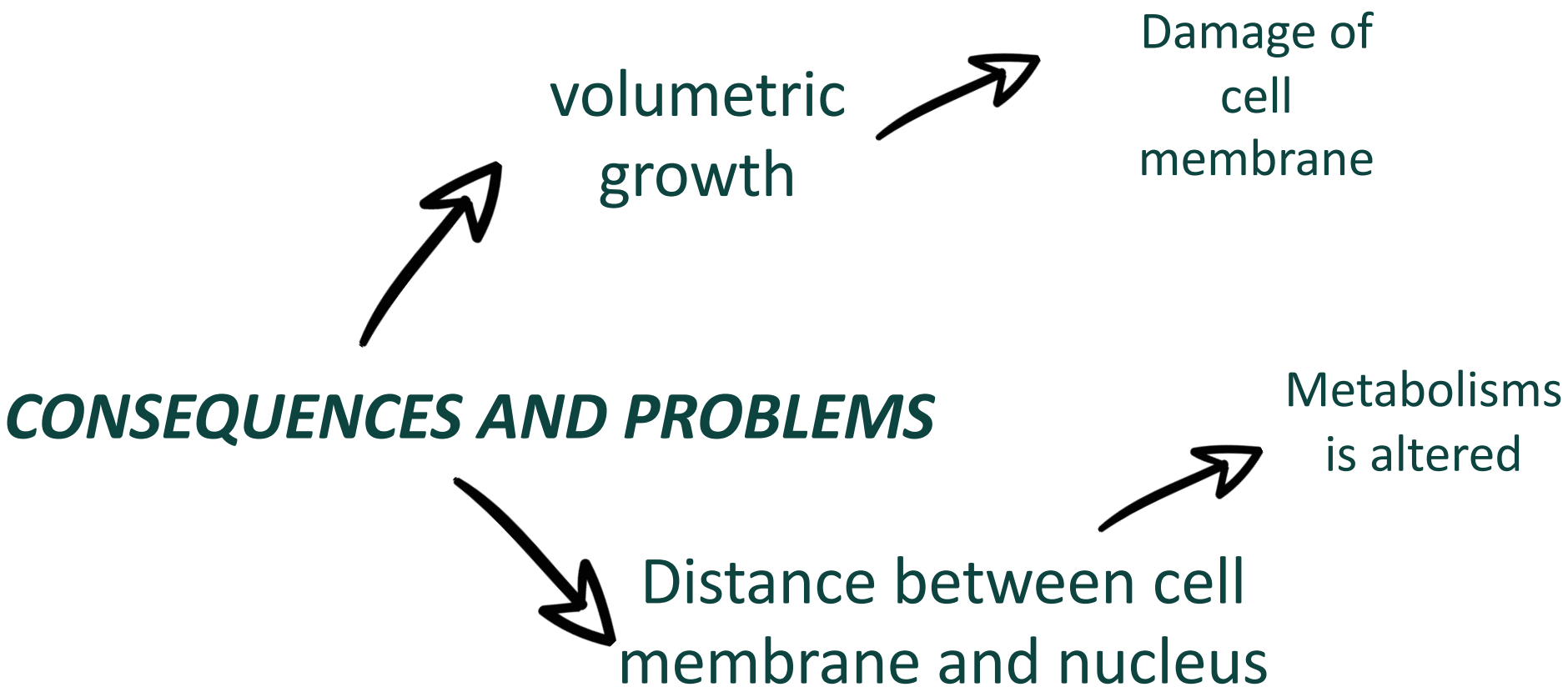
CAUSES OF HYPERTROPHY

CONGENITAL

- Pyloric hyperplasia
- Mega-colon
- Mega-esophagus

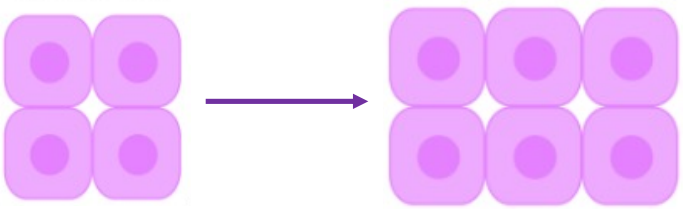
ACQUIRED

- Physical activity
- Pregnancy
- Hormonal stimulation



Stroma is not altered → problem of nutrition

HYPERPLASIA



"An increase in the number of cells in an organ or tissue in response to a stimulus"

- USUALLY (not always: I.E. COMPENSATORY)→ INCREASE SIZE OF THE ORGAN OR TISSUE
- HYPERPLASIA AND HYPERTROPHIA CAN OCCUR TOGETHER
- HYPERPLASIA OCCURS ONLY IF THE CELL POPULATION IS CAPABLE OF DIVIDING

Labile cells (that routinely proliferate in normal circumstances) → those of the epidermis, intestinal epithelium, and bone marrow cells → readily become hyperplastic

Permanent cells (neurons and cardiac and skeletal muscle myocytes) → very little capacity to regenerate or become hyperplastic

Stable cells (bone, cartilage, and smooth muscle) → are intermediate in their ability to become hyperplastic.

Hyperplasia

PHYSIOLOGICAL PATHOLOGICAL

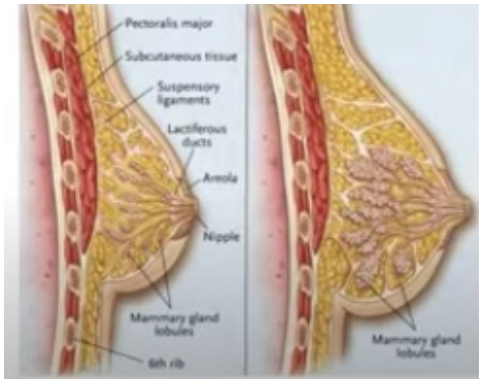
PHYSIOLOGICAL HYPERPLASIA

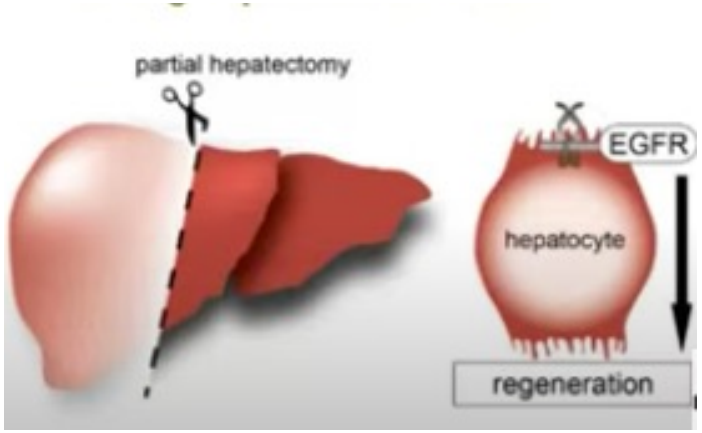
HORMONAL

- *Increases the functional capacity of the organ*

COMPENSATORY

- *Increases the tissue mass after damage/partial resection*



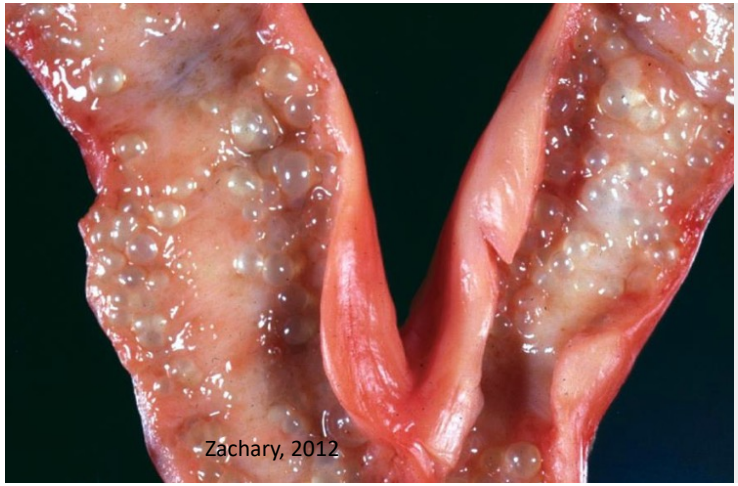


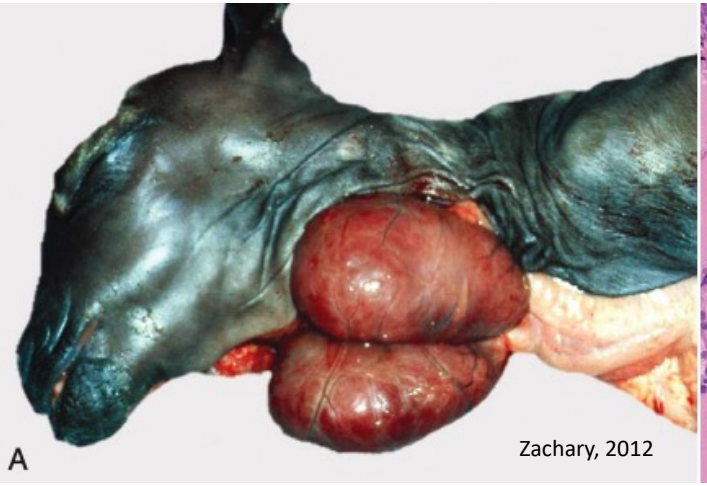
PHATOLOGICAL HYPERPLASIA

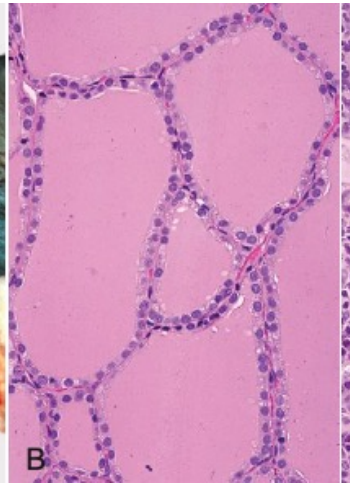
Mostly caused by excessive or inappropriate actions of hormones or growth factors acting on target cells or by a chronic stimulus

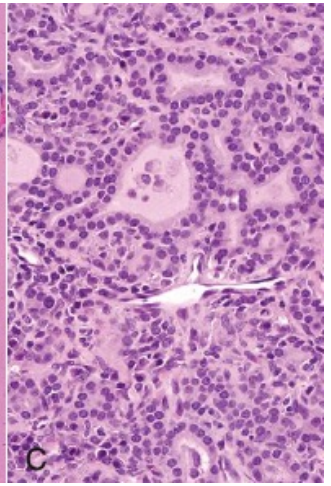
- ***Cystic endometrial hyperplasia*** of the ***canine uterus*** as a result of ***prolonged progesterone influence*** is common. The process is reversible if the stimulus is removed

- Hyperplasia of the thyroid gland









HYPERPLASIA

ENDOCRINE GLANDS

- Hyperparathyroidism
- Adrenal Cortex Hyperplasia
- Thyroid Hyperplasia

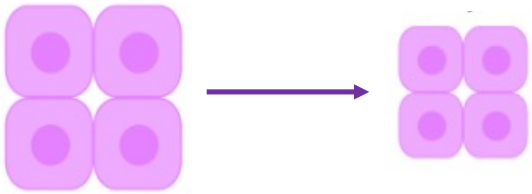
ENDOCRINE GLANDS TARGETED ORGANS

- Breast
- Prostate
- Endometrium

OTHER TISSUES

- Bone marrow
- Liver
- Kidney
- Lymphoid tissue

ATROPHY



"A reduction in the size of an organ or tissue due to a decrease in cell size and number, after normal growth has been reached"

Atrophy

PHYSIOLOGICAL PATHOLOGICAL

≠ HYPOPLASIA

Physiologic Atrophy → common during normal development

- Some **embryonic structures**, undergo atrophy during fetal development.
- The **decrease in the size of the uterus** that occurs shortly after parturition is another form of physiologic atrophy
- Thymus involutes with age

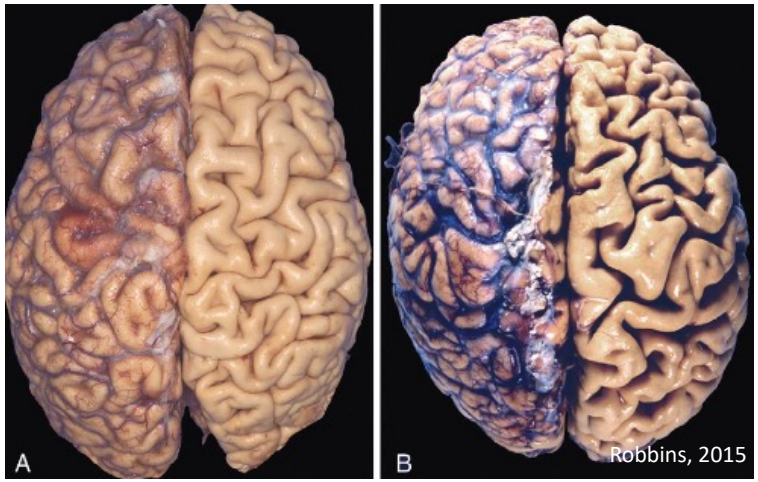
Pathologic Atrophy → several causes; local or generalized

Common causes of atrophy:

- ***Decreased workload*** *(atrophy of disuse)*
  Fractured bone → skeletal muscle atrophy.
  The initial decrease in cell size is reversible once activity is resumed.
  With more prolonged disuse → skeletal muscle fibers decrease in number (due to apoptosis) as well as in size

- ***Loss of innervation*** *(denervation atrophy)*
  The normal metabolism and function of skeletal muscle are dependent on its nerve supply. Damage to the nerves leads to atrophy of the muscle fibers supplied by those nerves.

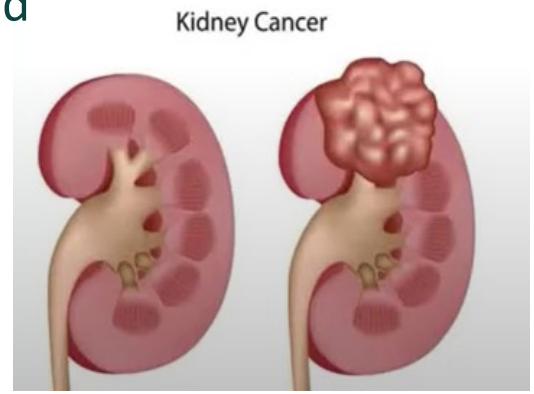
- ***Diminished blood supply***
  A gradual decrease in blood supply (ischemia) to a tissue as a result of slowly developing arterial occlusive disease results in atrophy of the tissue.
  In late life, the brain may undergo progressive atrophy, mainly because of reduced blood supply as a result of atherosclerosis. This is called *senile atrophy,* which also affects the heart



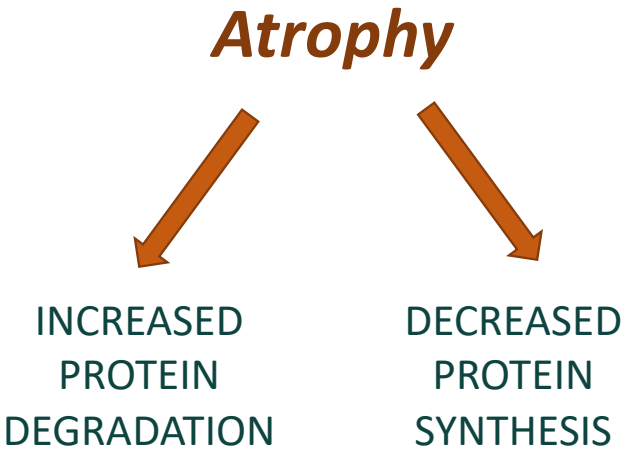
- ***Inadequate nutrition***
  Profound malnutrition (marasmus) → utilization of skeletal muscle proteins as a source of energy after other reserves such as adipose stores have been depleted. This results in marked muscle wasting *(cachexia)*. Cachexia is also seen in patients with chronic inflammatory diseases and cancer

- ***Loss of endocrine stimulation***
  Many hormone-responsive tissues (breast and reproductive organs), are dependent on endocrine stimulation for normal metabolism and function. Atrophy of the zona fasciculata of the adrenal follows prolonged steroid therapy

- ***Pressure***
  Tissue compression for any length of time can cause atrophy.
  Enlarging benign tumour → atrophy in the surrounding uninvolved tissues

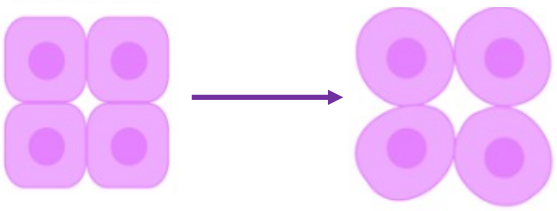


MECHANISMS OF ATROPHY



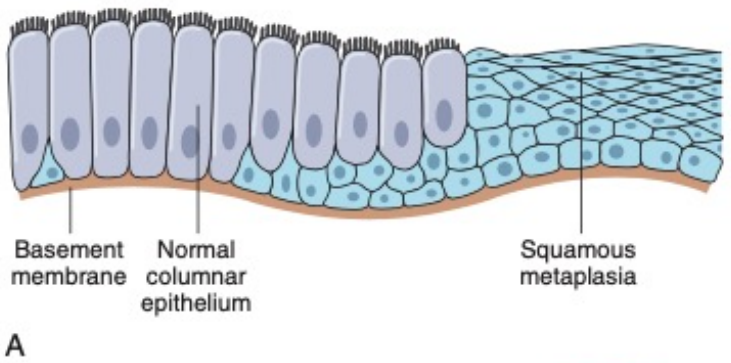
- Decrease in protein synthesis - due to the reduced metabolic activity
- Degradation of cellular proteins
- Increased autophagy - starved cells eat their own cellular components

METAPLASIA



"A reversible change in which one differentiated cell type (epithelial or mesenchymal) is replaced by another cell type"

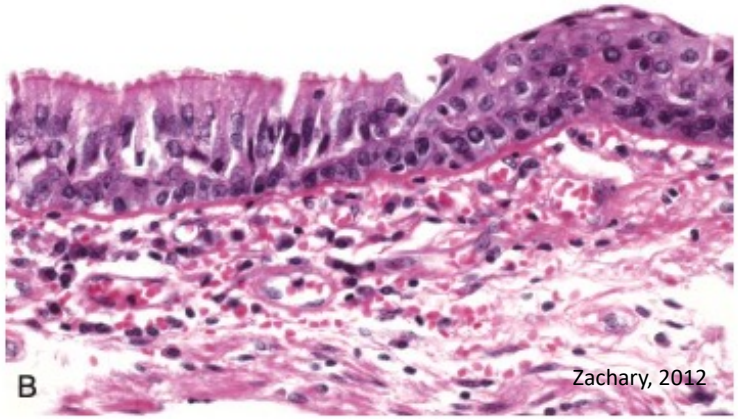
One cell type that is sensitive to a particular stress is replaced by another cell type that is better able to with stand the adverse environment. Metaplasia is reversible (usually) if the cause is withdrawn.



Columnar to Squamous

(the most common epithelial metaplasia)

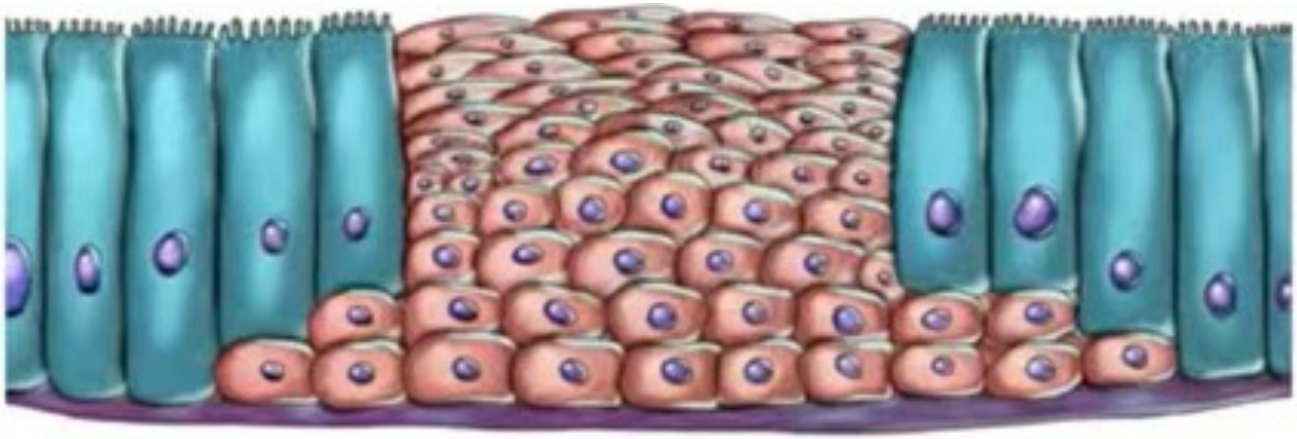
- Respiratory tract in response to chronic irritation or in case of deficiency of vitamin A (retinoic acid).
- More rugged stratified squamous epithelium → able to survive under circumstances in which the more fragile specialized columnar epithelium might have succumbed.



→ important mechanisms of protection against infection (mucus secretion and the ciliary action of the columnar epithelium) are lost.

→ The influences that predispose to metaplasia, if persistent, can initiate **malignant transformation in metaplastic epithelium**.

A common form of cancer in the respiratory tract is composed of squamous cells, which can arise in areas where the normal columnar epithelium has been replaced by squamous epithelium.



Squamous to columnar

Barrett Esophagus → esophageal squamous epithelium is replaced by intestinal-like columnar cells under the influence of refluxed gastric acid.
Cancers may arise in these areas.

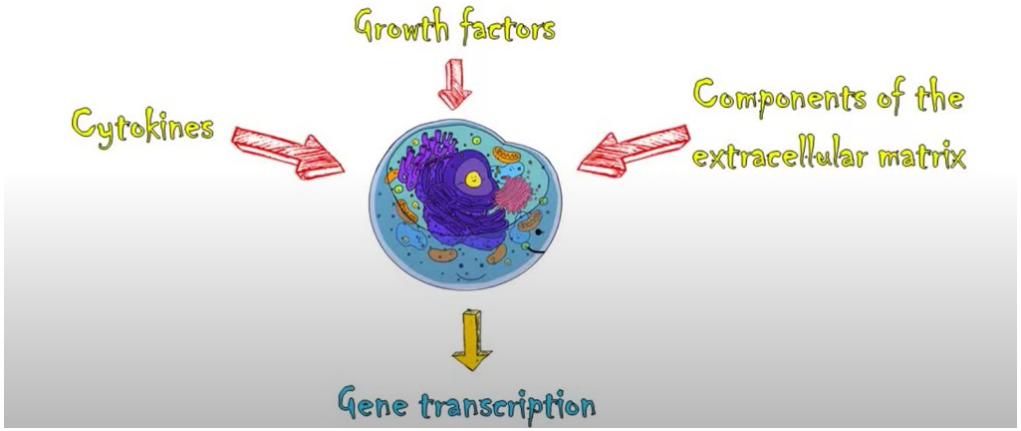
Connective tissue metaplasia

Formation of cartilage, bone, or adipose tissue (mesenchymal tissues) in tissues that normally do not contain these elements.
(bone formation in muscle - *myositis ossificans* - after intramuscular hemorrhage).

MECHANISMS OF METAPLASIA

- Does not result from changes of the phenotypes of an already differentiated cell
- Reprogramming of stem cells along a new differentiation pathway

→ differentiation into a new type of cell



FALSE METAPLASIE

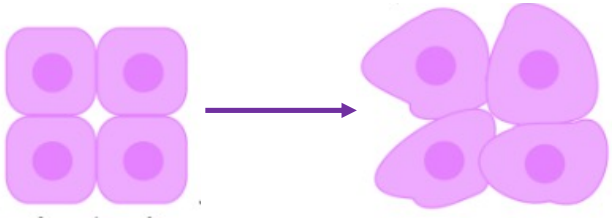
Eteroplasie

- *T. tiroideo alla base del cuore*
- *T. pancreatico nella parete gastrica*
- *T. pancreatico nella cistifellea*
- *T. splenico nel mesentere*

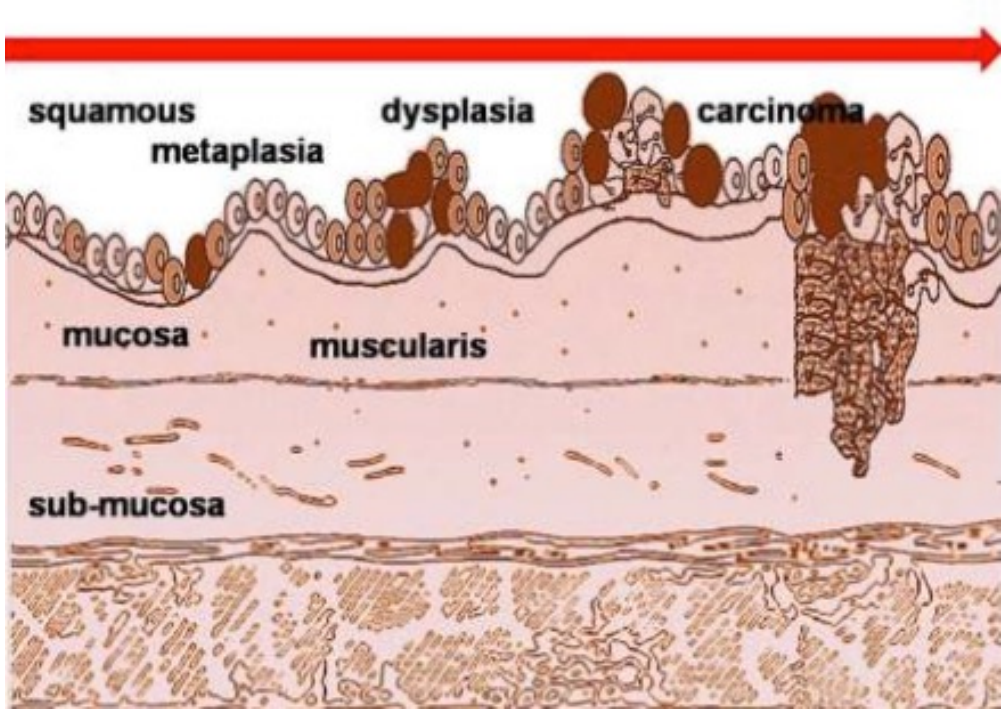
Dismorfie

- *Appiattimento dell'epitelio tiroideo per compressione (accumulo di colloide)*
- *Appiattimento dell'epitelio alveolare fetale*

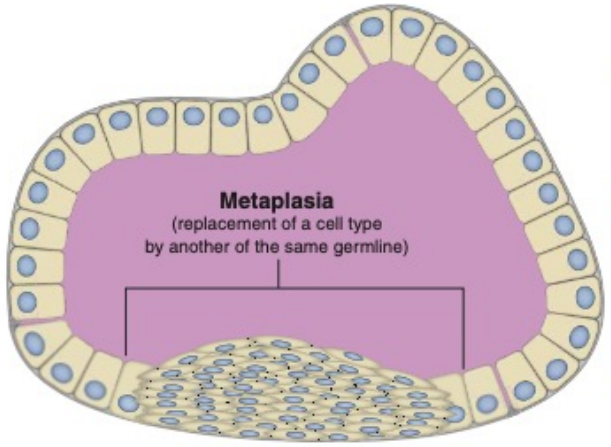
DISPLASIA

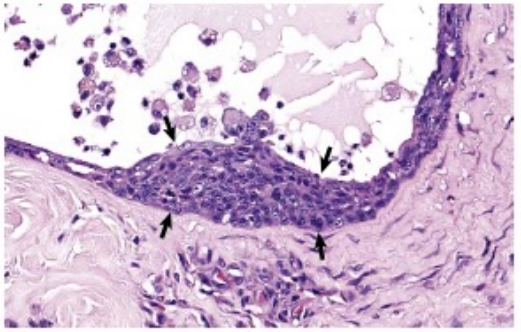


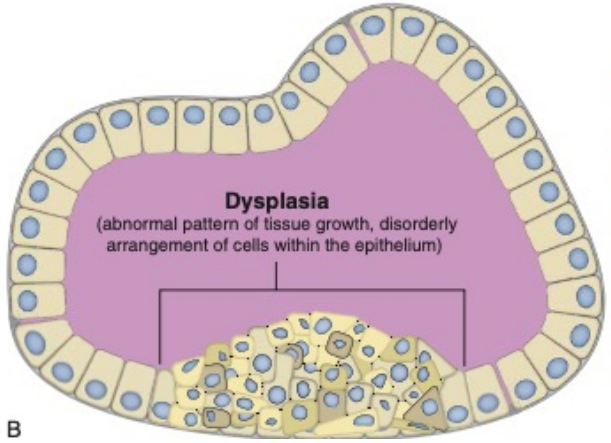
"The failure or impair differentiation of a tissue"

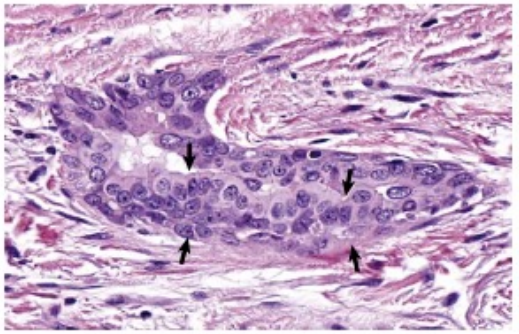


- La displasia può rappresentare l'evoluzione di una metaplasia
- La displasia, a lungo andare, può evolvere in **Carcinoma in Situ** (formazione neoplastica che non ha ancora superato la membrana basale)
- N.B. Metaplasia, displasia e carcinoma NON sono sempre e necessariamente legate tra loro: possiamo anche osservare la presenza di un carcinoma senza che prima si sia verificata una displasia.




Squamous metaplasia in an ectatic mammary duct




Dysplasia (atypical ductal cell hyperplasia)

Zachary, 2012

23.02.2023

PATOLOGIA GENERALE E FISIOPATOLOGIA ANIMALE

- Accumuli Intracellulari -

- Degenerazioni Cellulari -

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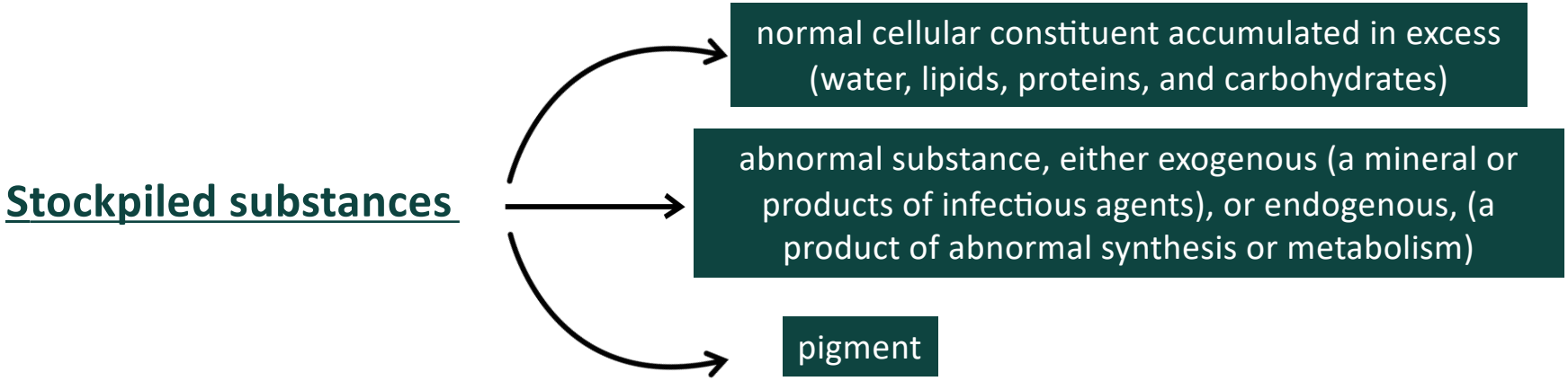
UNITE

INTRACELLULAR ACCUMULATION

"Presence of abnormal amounts of various substances in cells as manifestations of metabolic derangements "



- Transient **or** permanent accumulation
- Harmless to the cells **or** severely toxic
- In the cytoplasm (frequently within phagolysosomes) **or** the nucleus

Many processes result in abnormal intracellular accumulations, but most accumulations are attributable to

A normal endogenous substance is produced at a normal or increased rate, but the ***rate of metabolism is inadequate to remove it***

An abnormal exogenous substance is deposited and accumulates because the cell has ***neither the enzymatic machinery nor the ability to transport it*** to other sites

A normal or abnormal endogenous substance accumulates because of ***genetic or acquired defects in the metabolism, packaging, transport, or secretion of these substances***

Accumulation is reversible BUT
→ cells so overloaded as to cause secondary injury
→ death of the tissue

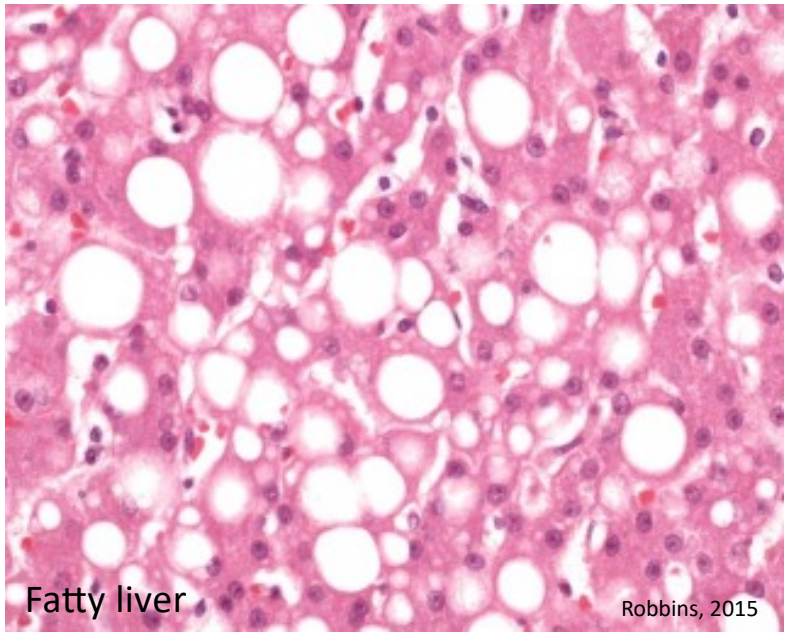
… AUMENTO DI VOLUME …

Accumuli intracellulari

- **Di norma limitata a singoli organi**
- **Raramente generalizzata**

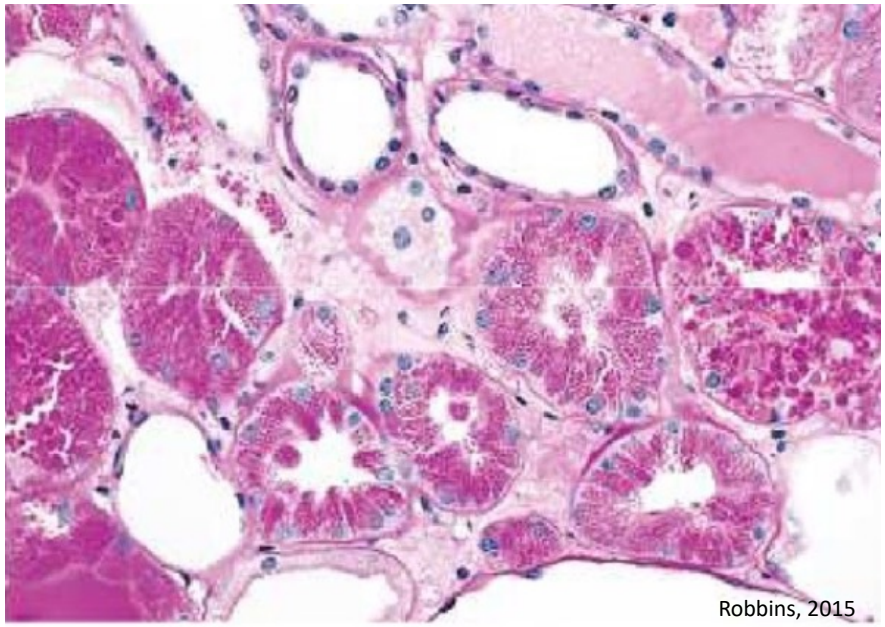
SOSTANZE CHE POSSONO ESSERE ACCUMULATE

LIPIDI
(trigliceridi, colesterolo, fosfolipidi)



PROTEINE
(gocce eosinofiliche, Vacuoli, Aggregati)

es. aumento del riassorbimento di proteine a livello renale



SOSTANZE CHE POSSONO ESSERE ACCUMULATE

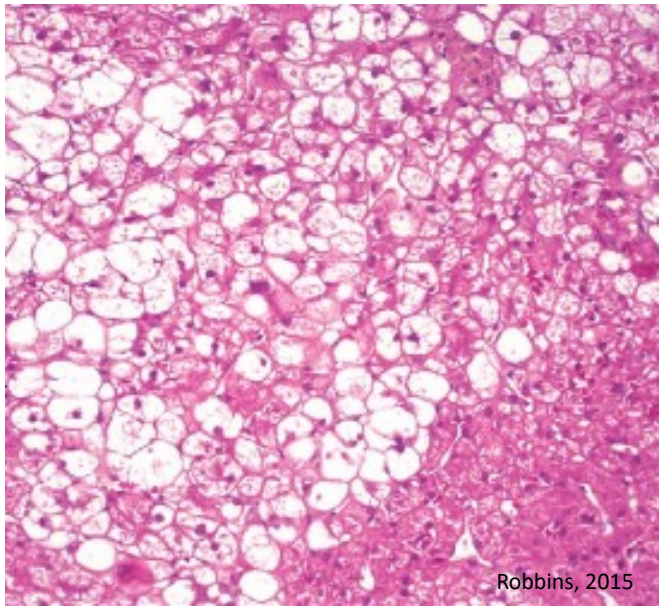
GLICOGENO

risorsa di energia normalmente presente nelle cellule

Alterazione del metabolismo del glucosio o del glicogeno

→ Accumulo

Es. Accumulo nelle cellule epiteliali dei tubuli renali o nel fegato nei pazienti diabetici



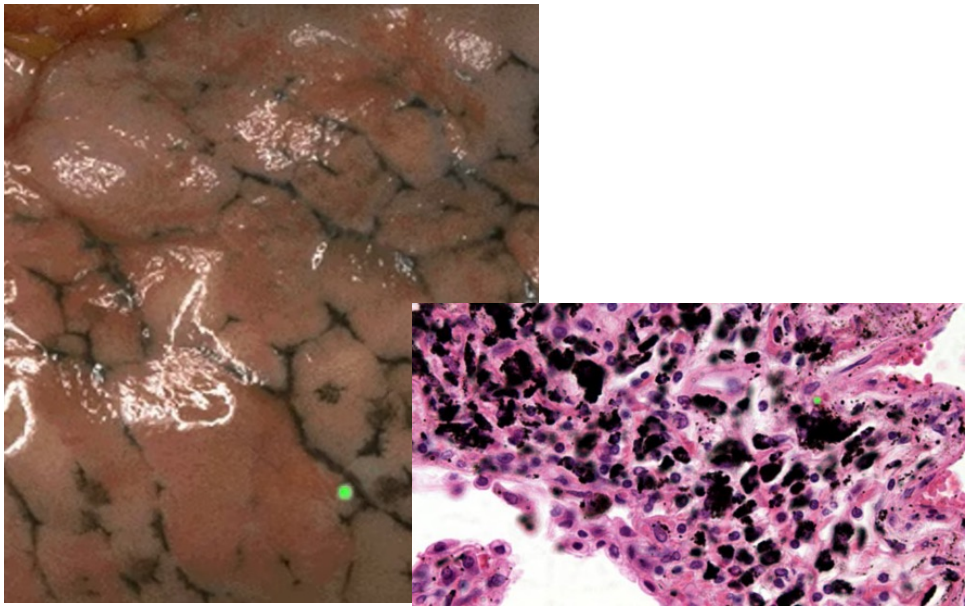
Robbins, 2015

PIGMENTI

Sostanze con una colorazione

Esogeni (carbone)

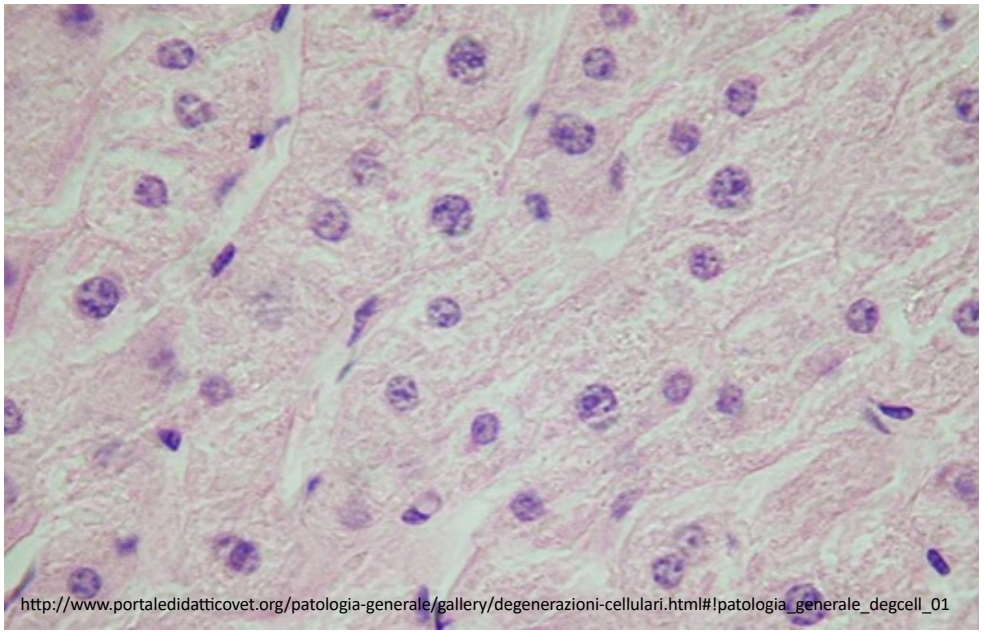
Endogeni (lipofuscine/melanina/emosiderina)



DEGENERAZIONI CELLULARI

"Accumulo all'interno delle cellule di sostanze che si rendono morfologicamente evidenziabili, ma che il più delle volte o non vi sono contenute oppure lo sono, ma in quantità non aprezzabili"

RIGONFIAMENTO TORBIDO



http://www.portaledidatticovet.org/patologia-generale/gallery/degenerazioni-cellulari.html#!patologia_generale_degcell_01

Aumento del numero dei ribosomi e dei mitocondri

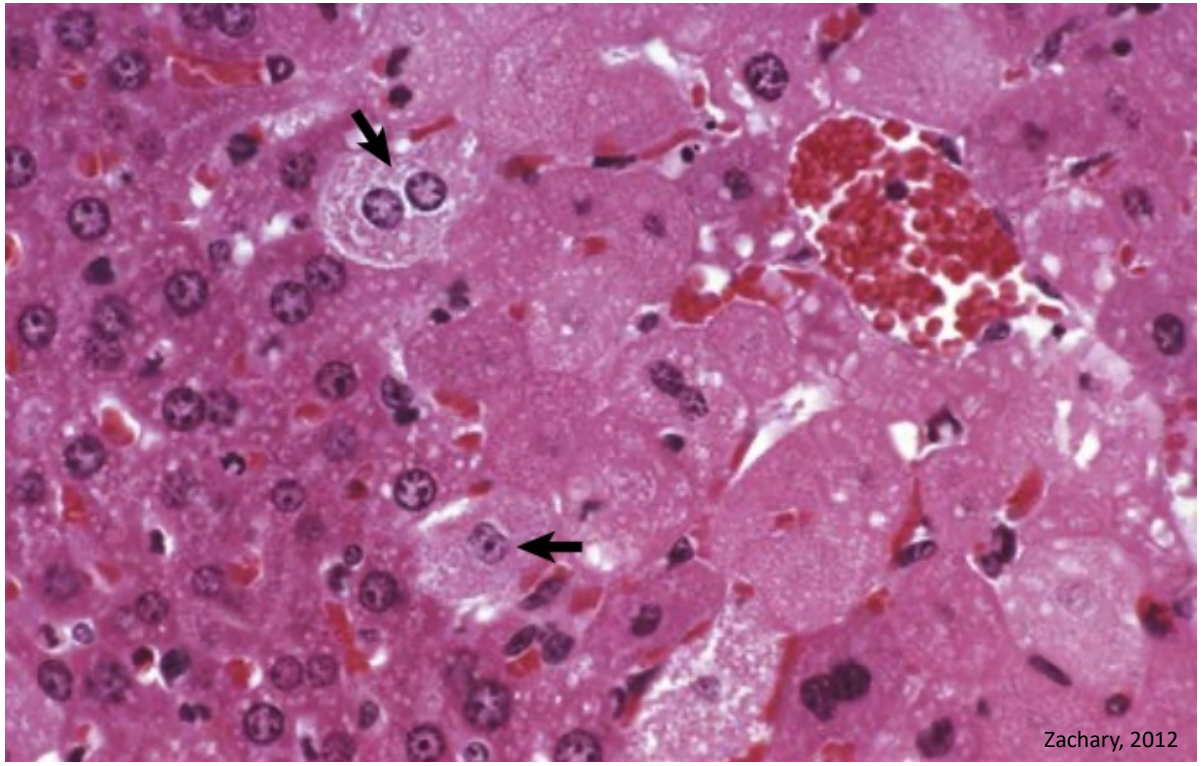
→ Il citoplasma appare finemente granulare

→ cellule in sofferenza e difficoltà metabolica

→ Fase iniziale di ogni tipo di difficoltà funzionale cellulare

→ In un primo momento può anche essere positivo, ma non a lungo termine.

DEGENERAZIONE IDROPICA

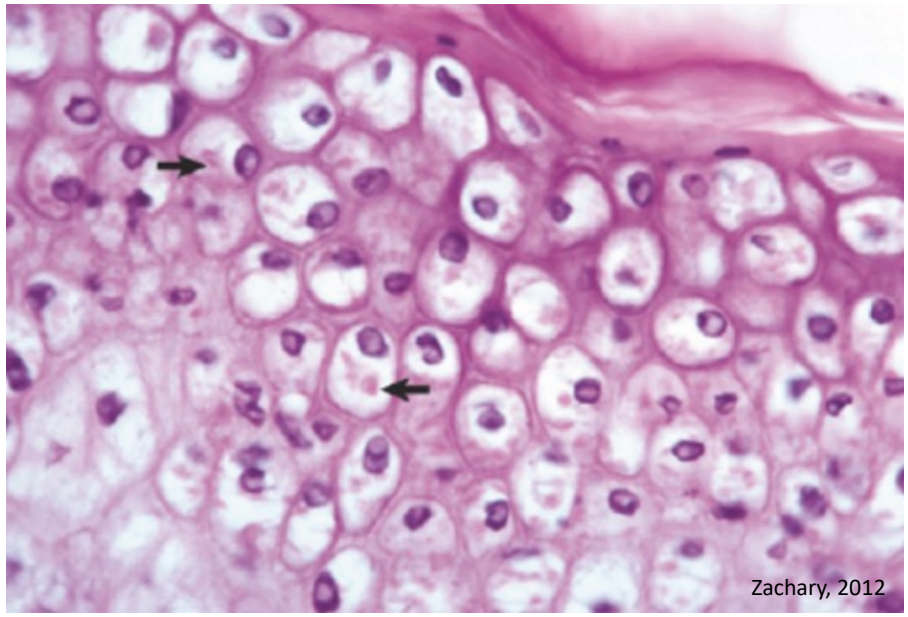


Accumulo di **acqua** dentro la cellula (le cellule degenerate sono indicate dalle frecce)

Causa:
Riduzione dell'apporto di ATP (mancato funzionamento delle pompe ioniche)

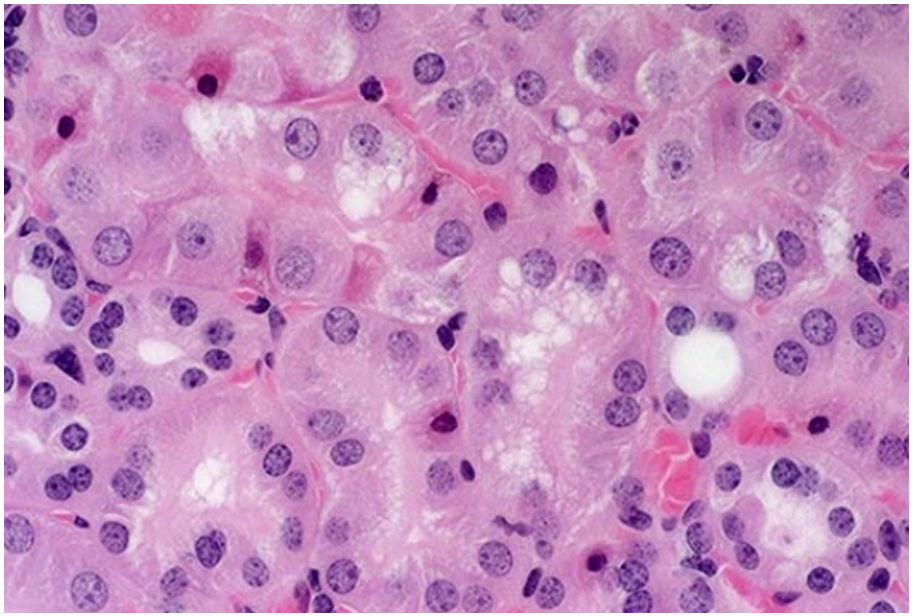
Il termine degenerazione idropica è comunemente usato quando la degenerazione si verifica in certi tipi cellulari, come epatociti (cellule del fegato) o cellule epiteliali dei tubuli renali

DEGENERAZIONE BALLONIFORME



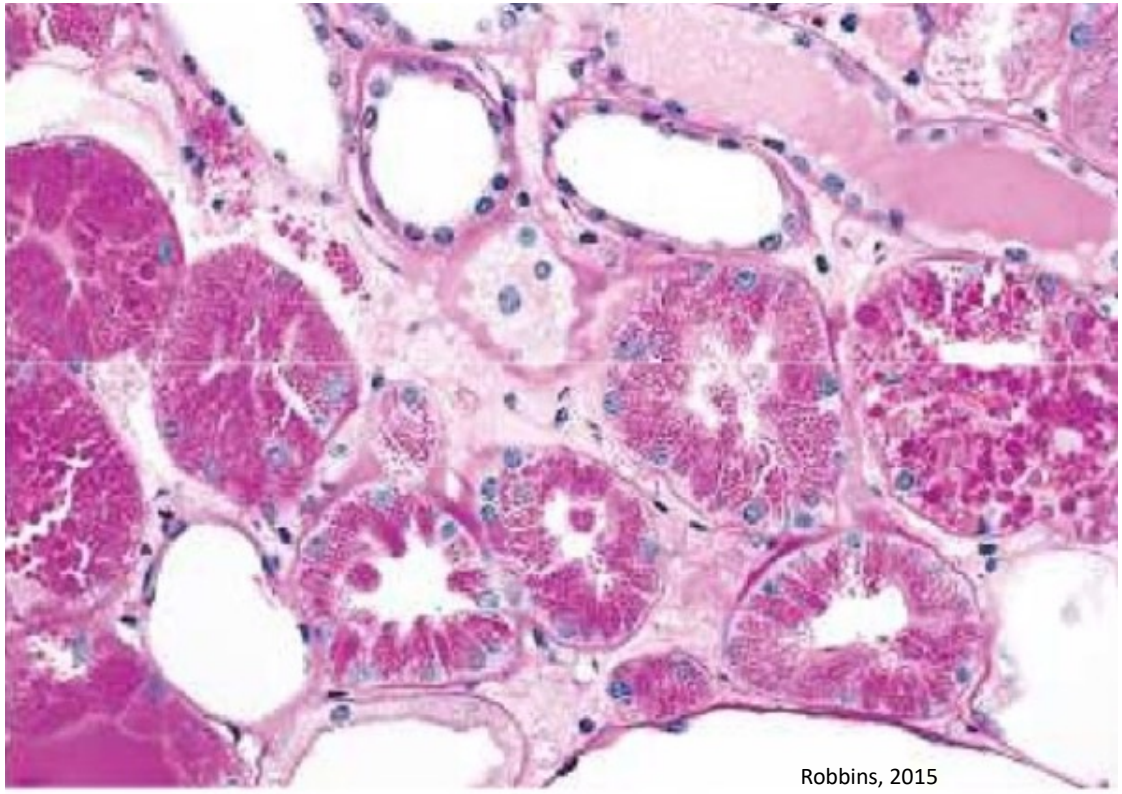
Degenerazione non reversibile (l'unica)
È l'equivalente delle degenerazione idropica, ma che si verifica in altre tipologie cellulari (es. cheratinociti dell'epitelio pluristratificato squamoso).
Causa: virus (creano un danno e la cellula si riempie di lesioni vescicolose che una volta rotte lasciano aree ulcerate).
Aumento delle dimensioni della cellula per accumulo di acqua all'interno.

DEGENERAZIONE VACUOLARE



Alterazione del sistema fagolisosomiale con accumulo nel citoplasma di vacuoli di varie dimensioni.
Il materiale di accumulo può provenire o dalla cellula stessa (materiale indigerito) o dal plasma.
Cause: ipossia, mancanza di un enzima, farmaci (gentamicina)

DEGENERAZIONE A GOCCE IALINE



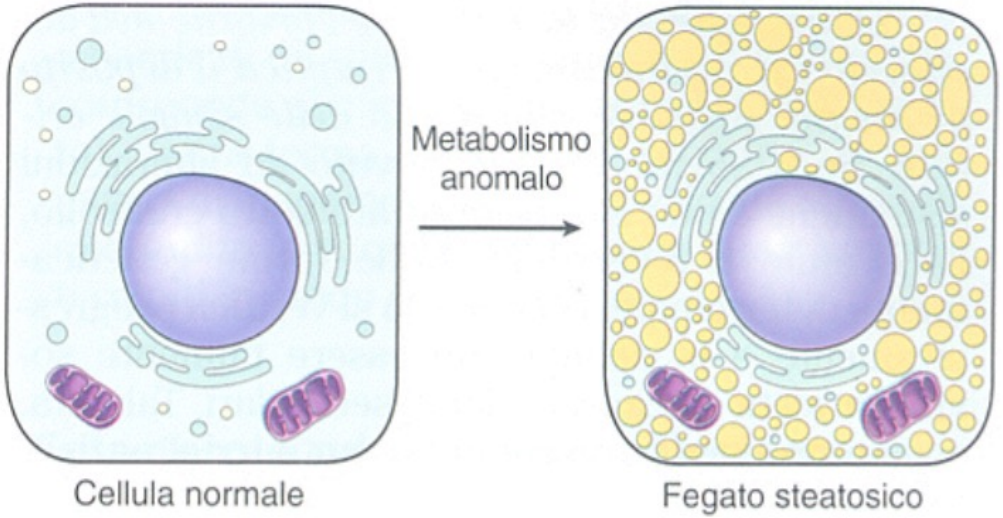
Robbins, 2015

Gocciole omogenee contenenti materiale proteico o glicoproteico che si accumula nelle cellule a livello citoplasmatico.

Molto comune nei tubuli renali (riassorbimento da parte dei tubuli prossimali renali di materiale proteico)

Se c'è un danno a carico del glomerulo si ha un danno a gocce ialine.

STEATOSI

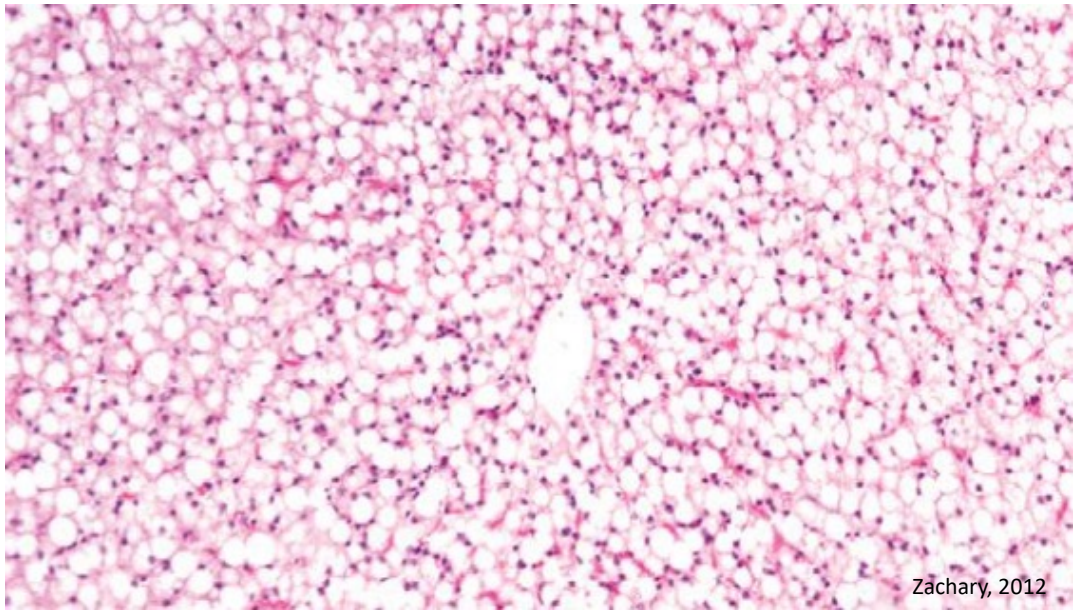


Accumulo di lipidi (generalmente trigliceridi) in cellule che normalmente non ne contengono quantità evidenziabili

- Condizione piuttosto frequente
- Gocciole lipidiche nelle cellule (epatociti+++).
- Non sono steatosi → cellule adipose o le lipomatosi (accumulo localizzato di tessuto adiposo e quindi di lipidi)
- Tessuti interessati: rene, fegato, cuore e muscoli
- Se perdura → apoptosi o necrosi.

Steatosi Epatica

Asintomatica se non l'epatomegalia (che può avere anche altre cause).
Minore efficienza complessiva della funzione metabolica del fegato

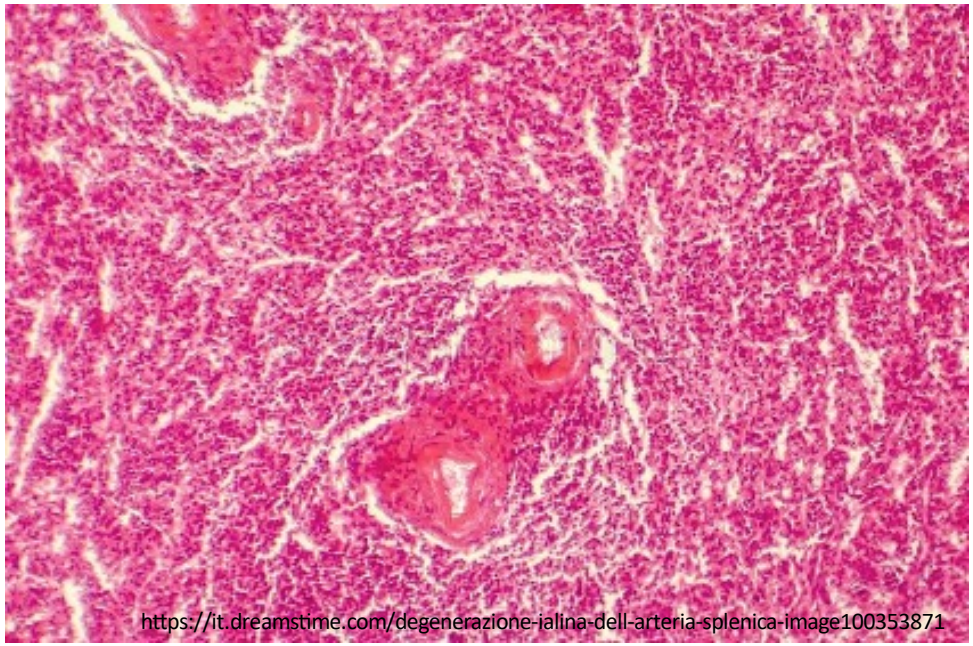


DEGENERAZIONE IALINA

Degenerazione extracellulare di materiale proteico, ialino

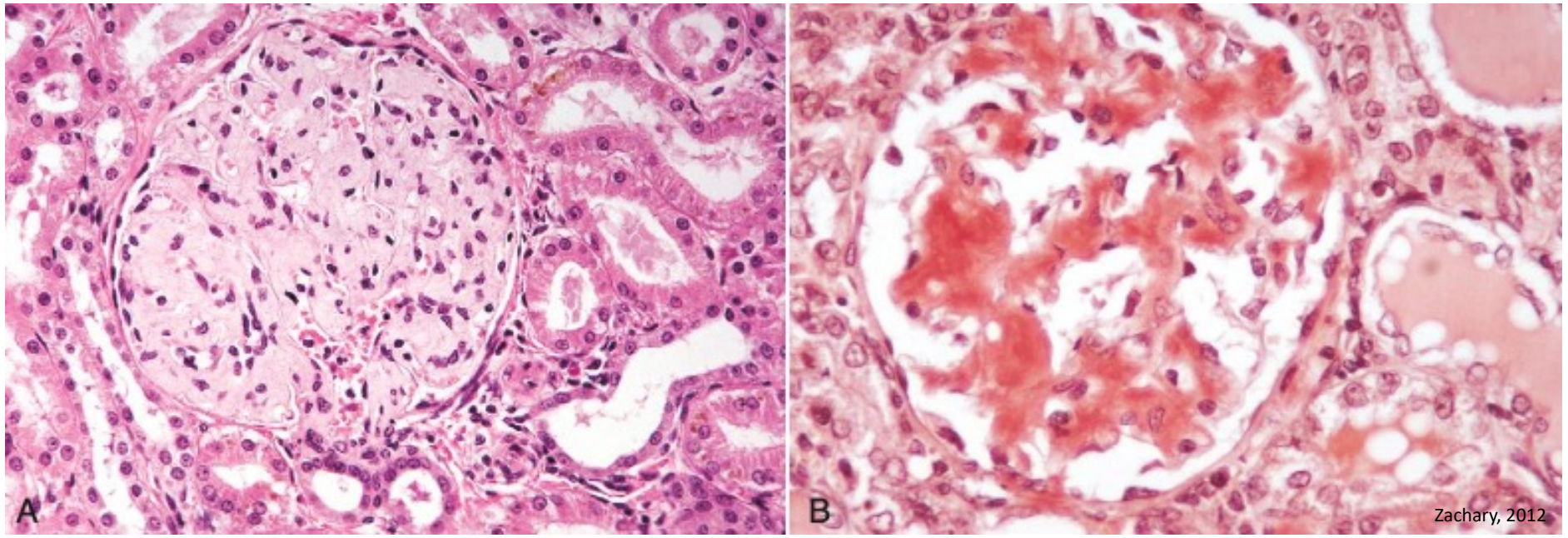
Localizzazione:

- Vascolare → accumulo con perdita della funzione → indurimento delle strutture vascolari
- Renale: accumulo della sostanza a livello della capsula del Bowman (glomerulo renale)



https://it.dreamstime.com/degenerazione-ialina-dell-arteria-splenica-image100353871

AMILOIDOSI



Deposito di amiloide (materiale di natura proteica) nello spazio extracellulare (nell'interstizio)

Conseguenza → atrofia

CALCIFICAZIONI PATOLOGICHE

Deposizione di Sali di Calcio nei tessuti che normalmente non ne contengono (visibile radiograficamente)

DISTROFICA

non correlata ad ipercalcemia ma associata ad aree necrotiche o tessuti in sofferenza.
Detta distrofica perché il tessuto coinvolto è in sofferenza

METASTATICA

correlata ad ipercalcemia

Localizzazione:
- Setti polmonari
- Tubuli renali
- Vasi sanguigni

- **Eccessiva vit. D**
- **Distruzione diffusa di tessuto osseo (tumori primitive all'osso o metastasi ossee)**

23.02.2023

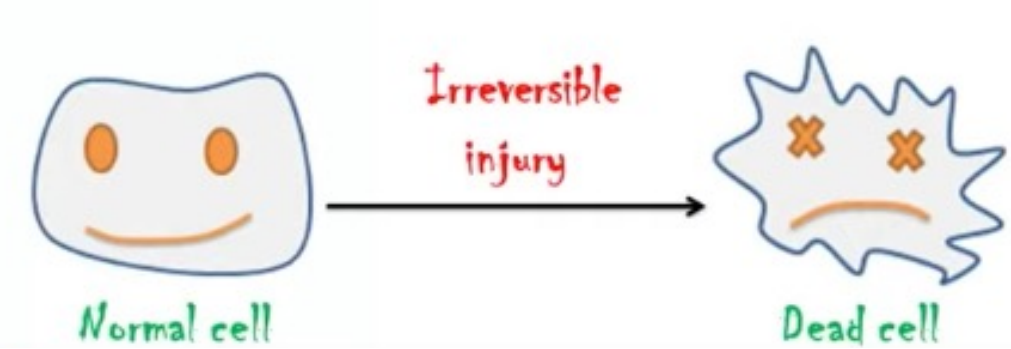
PATOLOGIA GENERALE E FISIOPATOLOGIA ANIMALE

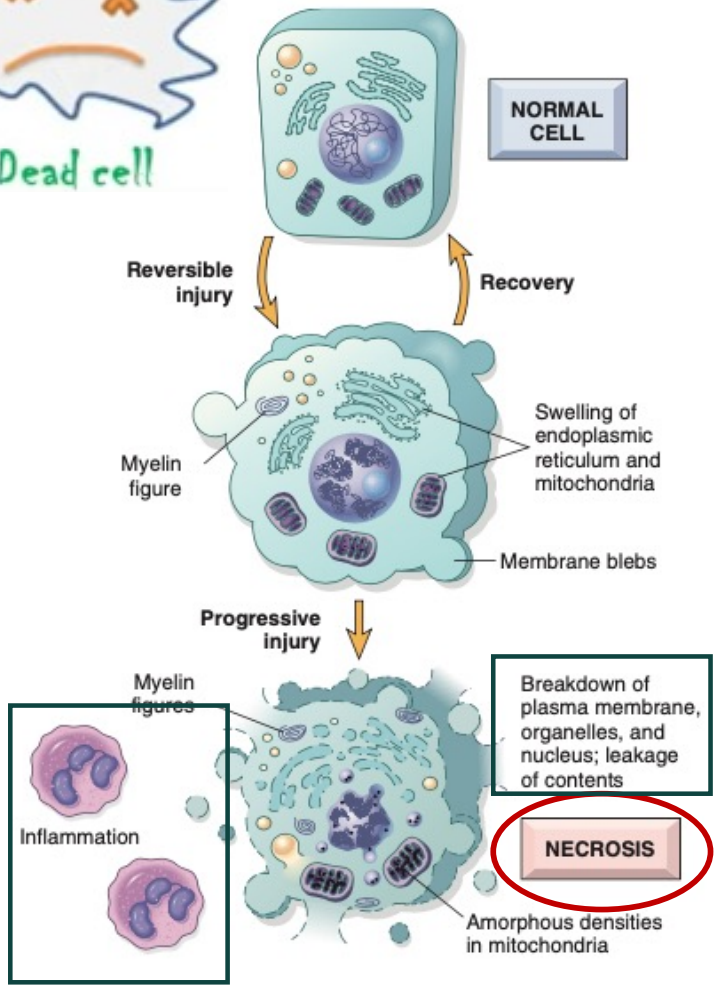
- Cell Death -

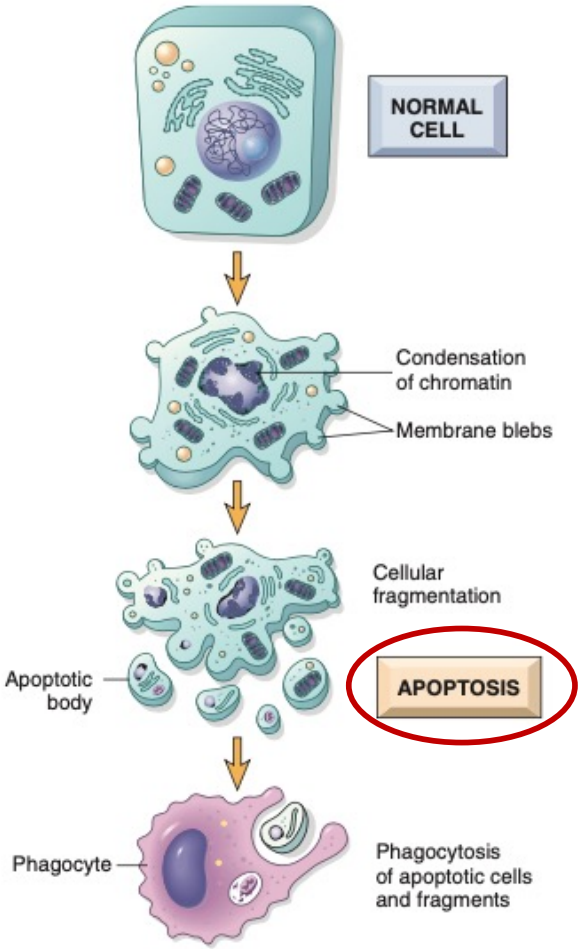
ALICE MUSI, DVM, PhD student

University of Teramo, Teramo, Italy

Supervisor Prof. Laura Bongiovanni


Irreversible
injury
Normal cell
Dead cell

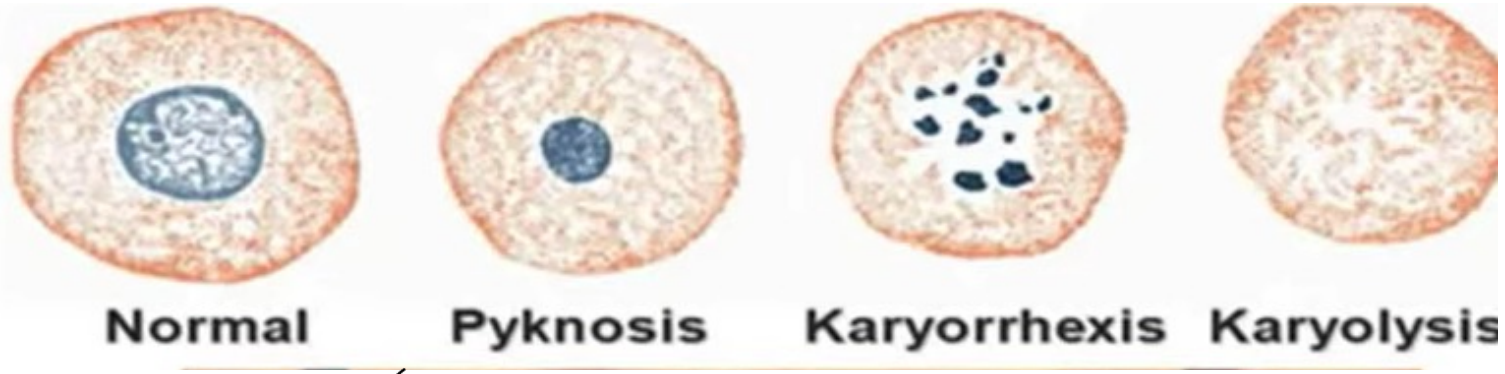

NORMAL CELL
Reversible injury
Recovery
Myelin figure
Swelling of endoplasmic reticulum and mitochondria
Membrane blebs
Progressive injury
Myelin figures
Inflammation
Breakdown of plasma membrane, organelles, and nucleus; leakage of contents
NECROSIS
Amorphous densities in mitochondria


NORMAL CELL
Condensation of chromatin
Membrane blebs
Cellular fragmentation
Apoptotic body
APOPTOSIS
Phagocyte
Phagocytosis of apoptotic cells and fragments

NECROSI

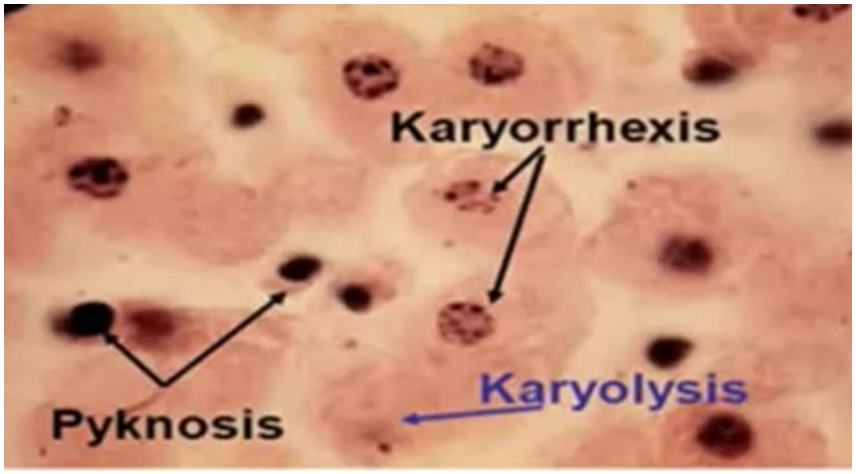
Cambiamenti morfologici e digestione nucleare durante la necrosi

Rottura del nucleo in piccolo frammenti per azione di endonucleasi



Completa digestione del nucleo da parte dello endonucleasi

La cromatina si addensa e aggrega e il nucleo si restringe. Un nucleo picnotico è più piccolo rispetto ad un nucleo normale. Di fronte a questo evento si può affermare che la morte cellulare è avvenuta



Rimozione del tessuto necrotico

Autolisi

Digestione per opera di enzimi propri della cellula colpita da necrosi

Eterolisi

Digestione per opera di enzimi secreti da alter cellule (es. neutrofili o macrofagi)

CLASSIFICAZIONI delle NECROSI

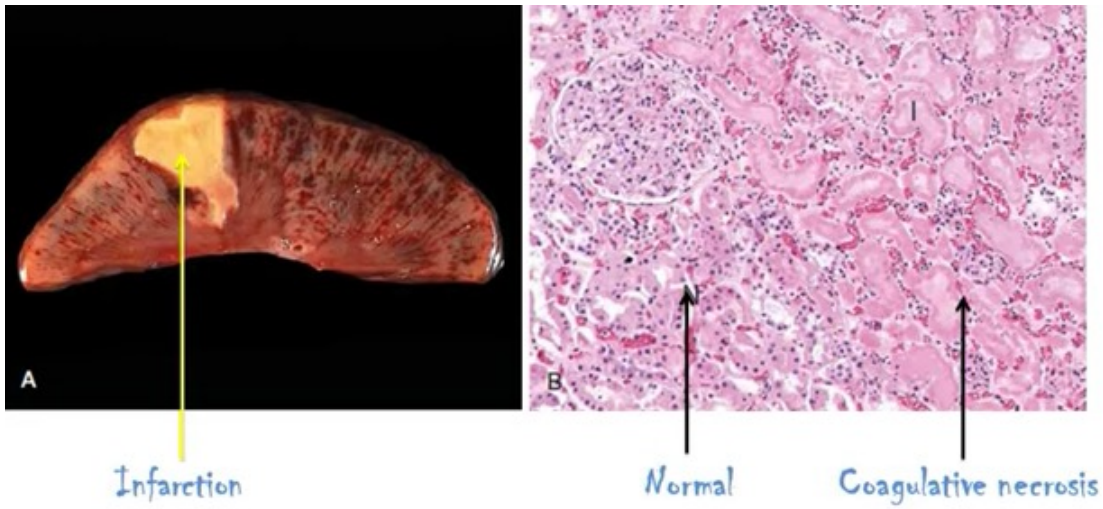
- STRUTTURATA: la struttura del tessuto è ancora riconoscibile
- NON STRUTTURATA: non c'è struttura e il tessuto di origine non è riconoscibile

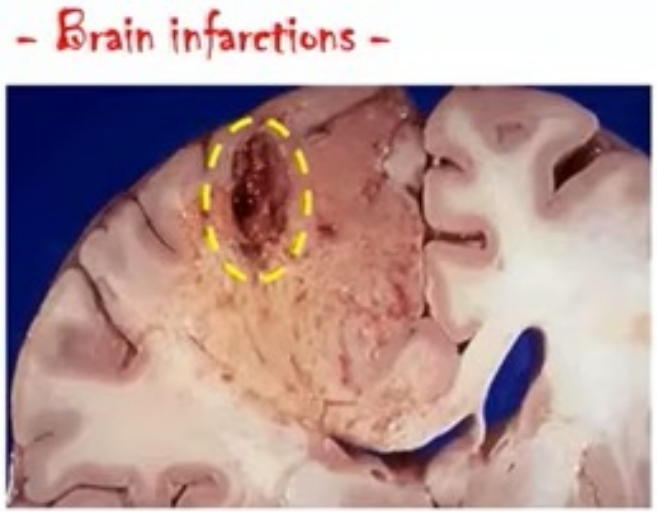
IN BASE ALLA CLASSIFICAZIONE MORFOLOGICA:

- COAGULATIVA: si mantiene e si conferma completamente la struttura (es. uovo cotto)
- COLLIQUATIVA: si perde la struttura del tessuto che si sta "fluidificando". Spesso rappresenta l'esito finale delle alter necrosi. Tipica nel tessuto nervosa o quando c'è un'intense reazione infiammatoria.

Immagini → https://www.youtube.com/watch?v=P2rAeaR_zuY&list=PLKUo9R_tDXYT_1U1nZXo7-NHgUoaf4csu&index=10

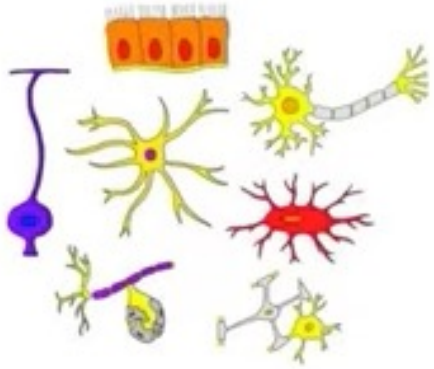
Necrosi coagulativa





Necrosi colliquativa

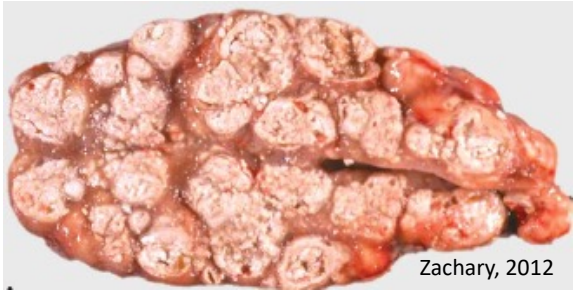
- High level of lysosomal enzymes in glial cells



NECROSI “SPECIALI”

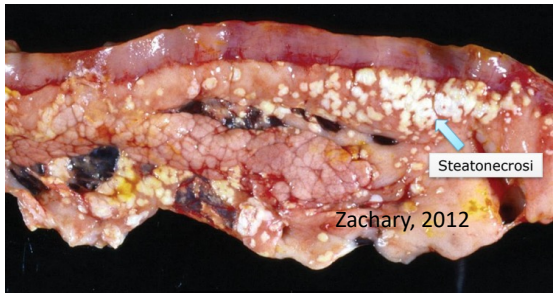
Necrosi caseosa

- Tipo di necrosi coagulativa
- Mycobatterium Tuberculosis



Steatonecrosi

- Necrosi del tessuto adipose
- Di origine traumatica o da pancreatite



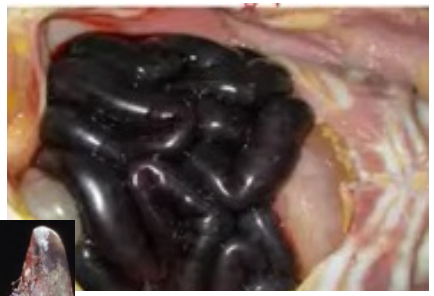
Necrosi cerea/di Zenker

- Necrosi del muscolo striato
- Necrosi strutturata
- Aspetto di cera, asciutto, omogeneo, opaco, fermo
- Carenza di vit. E o Selenio

GANGRENA

Disfacimento putrefattivo di tessuto in necrosi.

Area di tessuto necrotico in un organismo ancora vivente, caratterizzato da una colorazione scura.



UMIDA +++

Tipica di aree umide, ricche di acqua

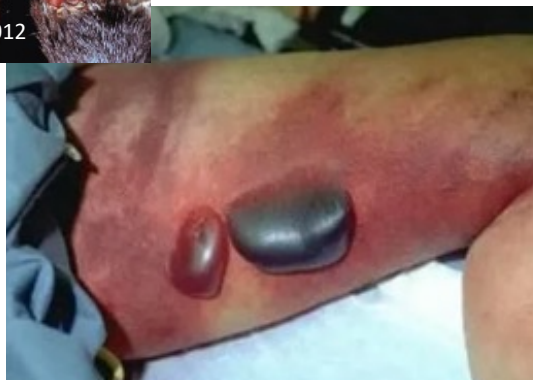
Colorazione scura per azioni di germi saprofiti che intaccano il tessuto necrotico.

Si verifica dove c'è la presenza di batteri anaerobici.

Intestino in Corso di torsioni intestinali.

SECCA

Coinvolge le strutture periferiche dell'organismo (coda, orecchie, arti)



GASSOSA

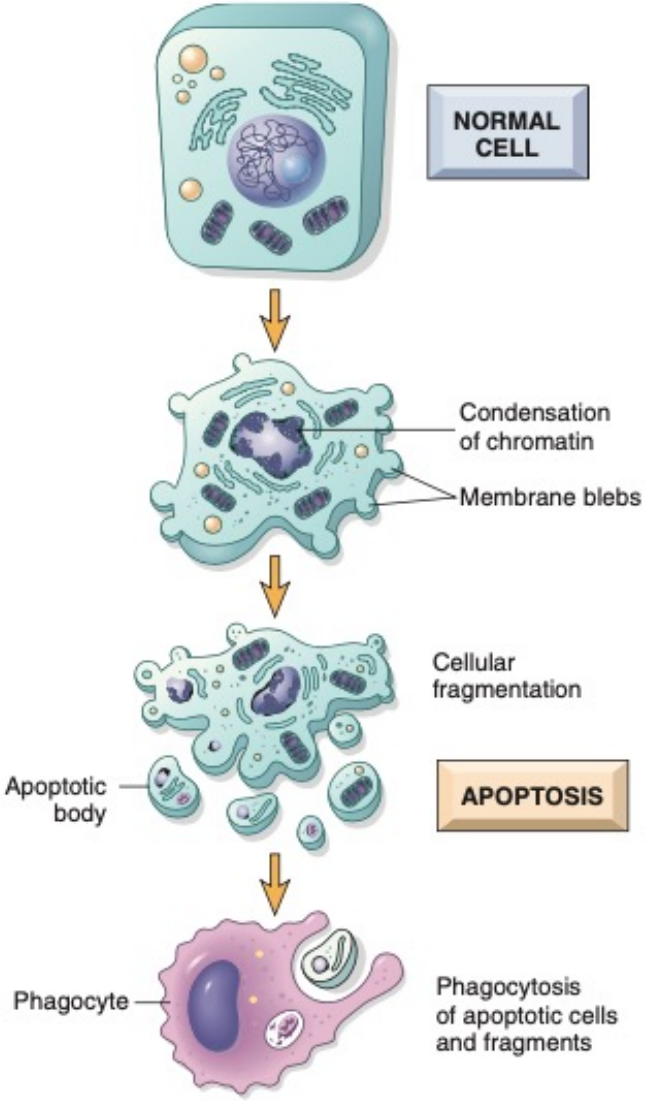
Aree aumentate di volume che, se palpate, danno una sensazione di crepitio

Aree tumefatte per accumulo di gas

Clostridium perfringens

Spesso porta a setticemia → febbre

APOPTOSI



- **Morte cellulare programmata**

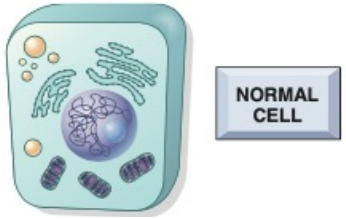
- **Meccanismo fisiologico di morte cellulare**
  - **a. Embriogenesi**
  - **b. Involuzione di organi per azione ormonale**
    (es. Involuzione tessuto mammario dopo la lattazione)
  - **c. Eliminazione di cellule con mutazioni durante la divisone cellulare**
  - **D. Normale turn-over tissutale**

- **In alcune circostanze: apoptosi patologica**

Frammentazione cellulare → Formazione di corpi apoptotici → Fagocitosi dei corpi apoptotici da parte di cellule con attività fagocitaria (es. macrofagi)

"SUICIDIO ALTRUISTA" → EVITARE INFIAMMAZIONE

Non c'è materiale cellulare che fuoriesce dalla cellula



Risulta dall'attivazione di enzimi detti ***caspasi***
(proenzimi inattivi → clivaggio → attivazione)

1. *Fase di inizializzazione:* alcune caspasi diventano cataliticamente attive
2. *Fase esecutiva:* altre caspasi iniziano la degradazione di componenti cellulari

APOPTOSI

Via Estrinseca

- **Si attiva grazie a sistemi esterni alla cellula**
- **Attivazione di "recettori di morte cellulare"**
- **Sostanze esterne alla cellula si legano a questi recettori andando ad attivare l'apoptosi**

Via Intrinseca +++

- **Sistema basato sul danno mitocondriale**
- **Aumentata permeabilità della membrana mitocondriale esterna con rilascio di molecole pro-apoptotiche nel citoplasma**

Anche se questi pathway **possono convergere**, sono in genere attivati da cause differenti, coinvolgono molecole diverse e presentano **ruoli distinti** sia in processi fisiologici che patologici

KEEP CALM
and
STUDY HARD
FOR EXAM