Adaptations

Relative volumes of intracellular organelles (hepatocyte)

Compartment	% total volume	number/cell	role in the cell
Cytosol	54%	1	metabolism, transport, protein translation
Mitochondria	22%	1700	energy generation, apoptosis
Rough ER	9%	1*	synthesis of membrane and secreted proteins
Smooth ER, Golgi	6%	1*	protein modification, sorting, catabolism
Nucleus	6%	1	cell regulation, proliferation, DNA transcription
Endosomes	1%	200	intracellular transport and export, ingestion of extracellular substances
Lysosomes	1%	300	cellular catabolism
Peroxisomes	1%	400	very long-chain fatty acid metabolism

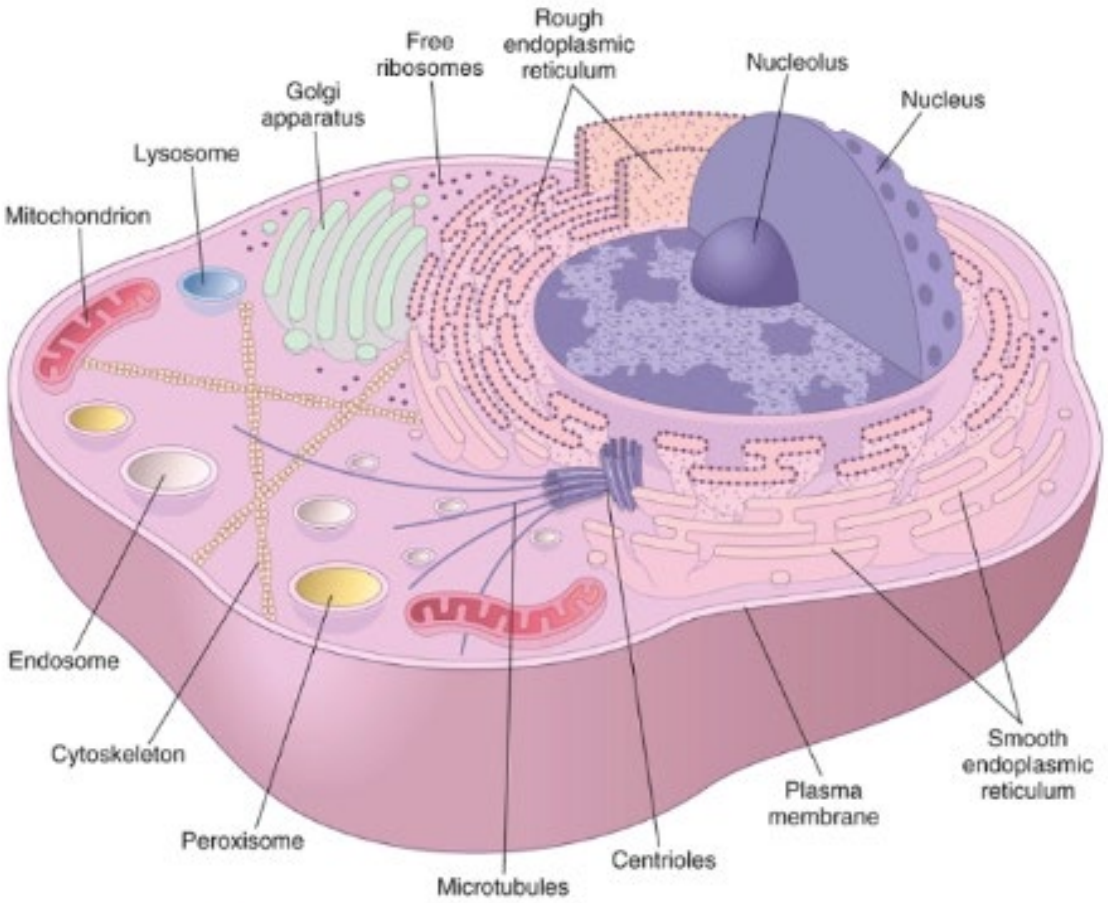


FIG. 1.6 Basic subcellular constituents of cells. The table pr…

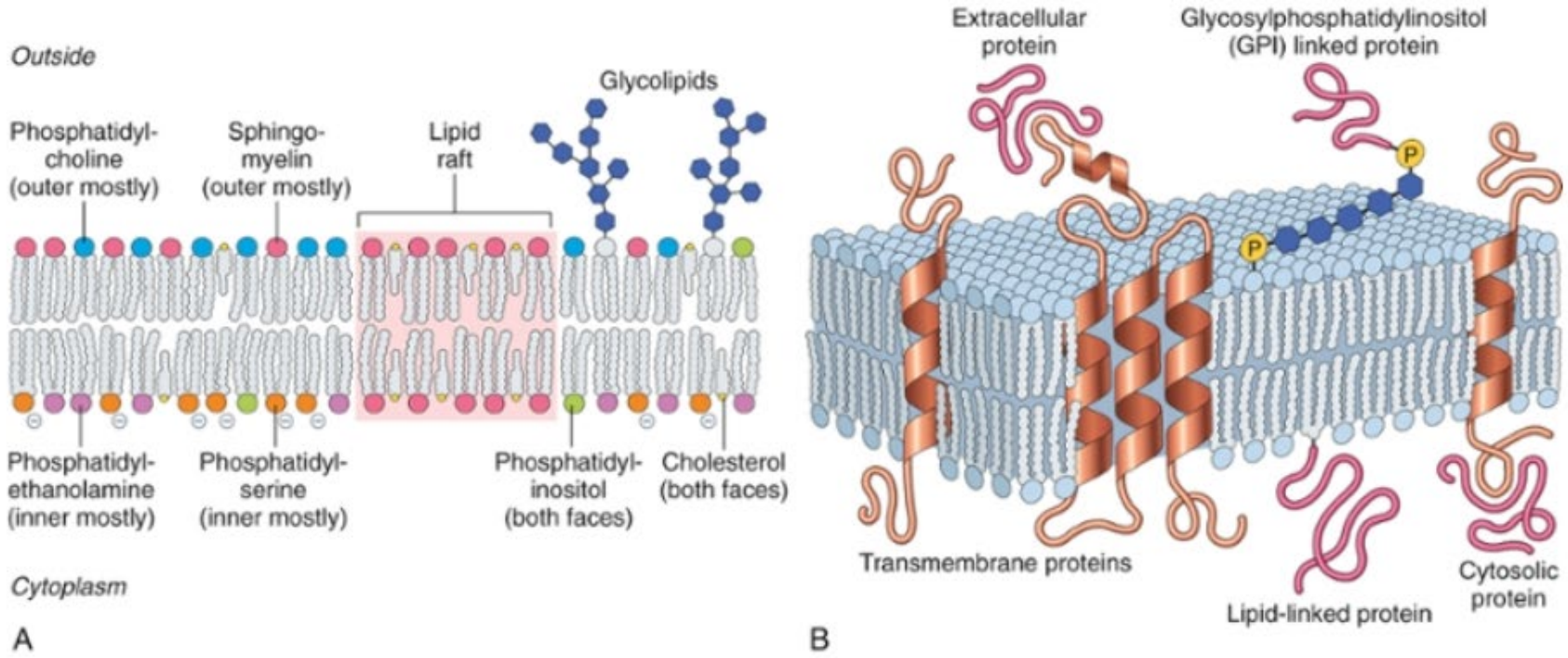


FIG. 1.7 Plasma membrane organization and asymmetry. (A) The plasma membran…

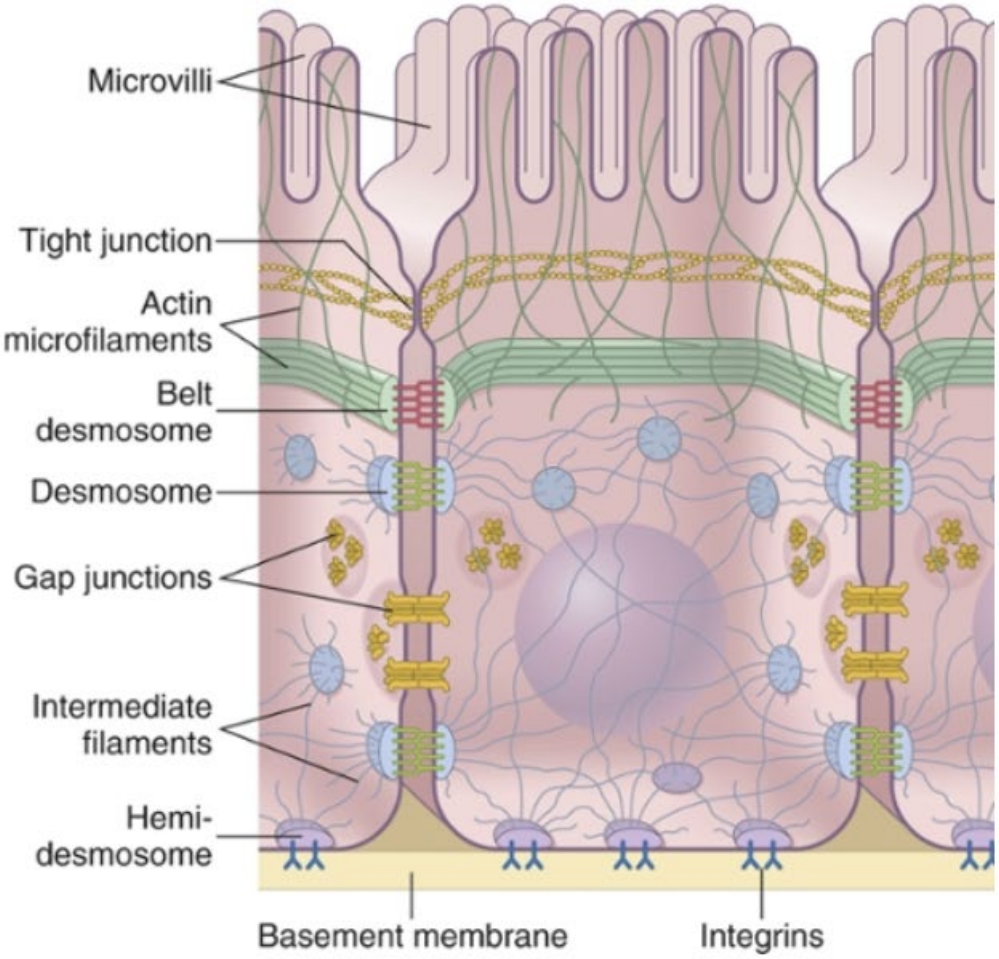
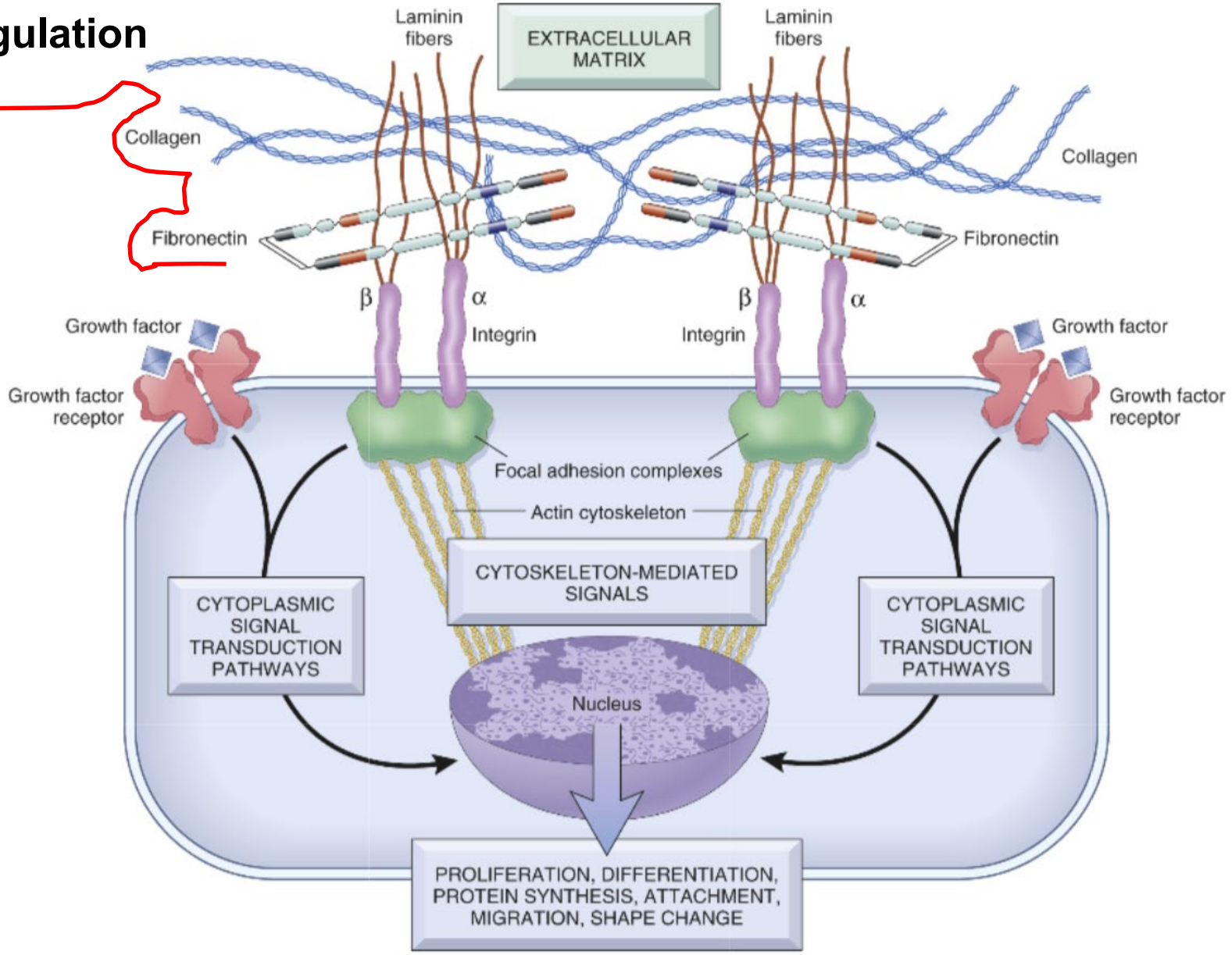
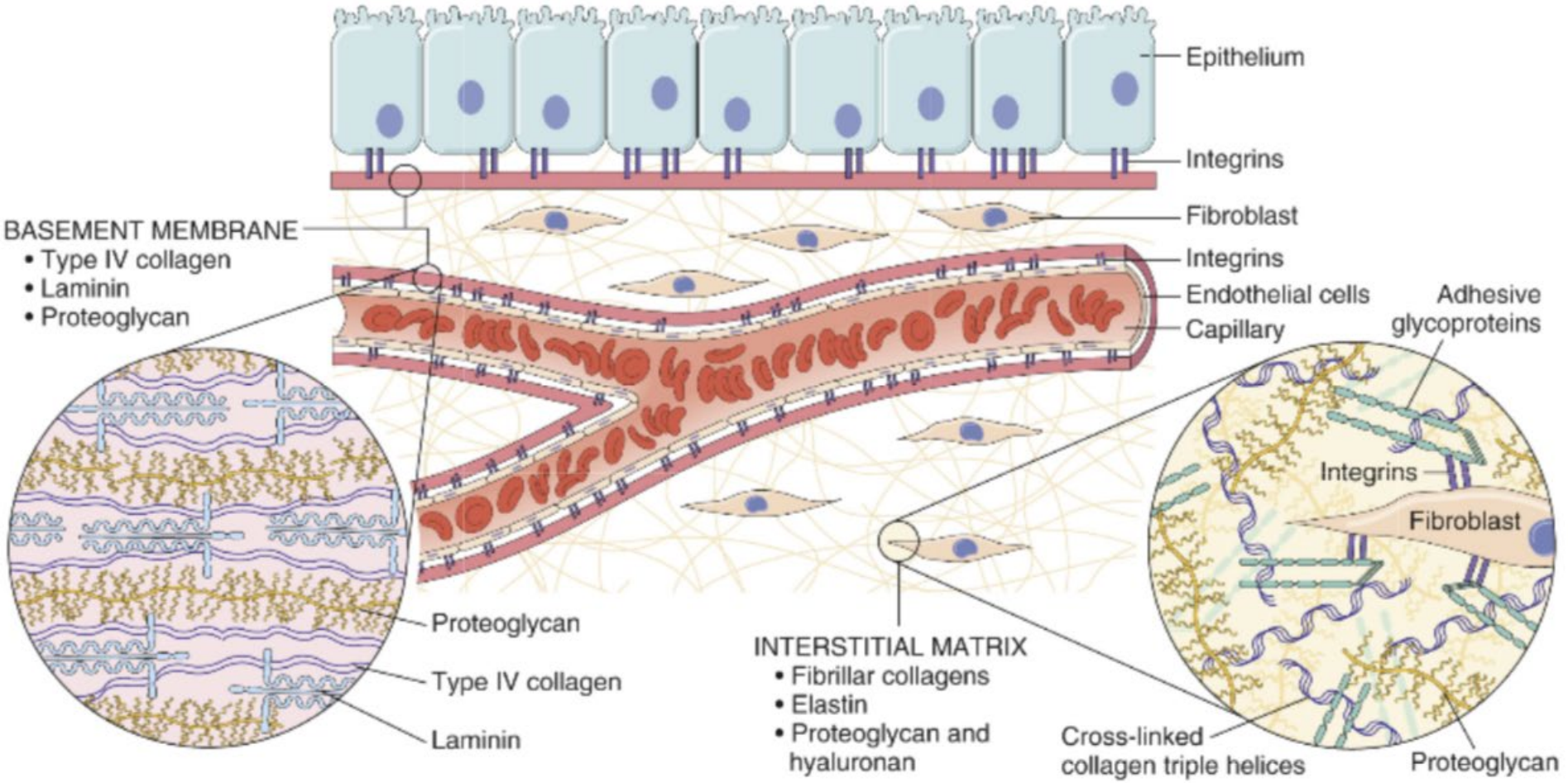


FIG. 1.9 Cytoskeletal elements and cell–cell interactions. Interepithelial adhesion in…

Coagulation



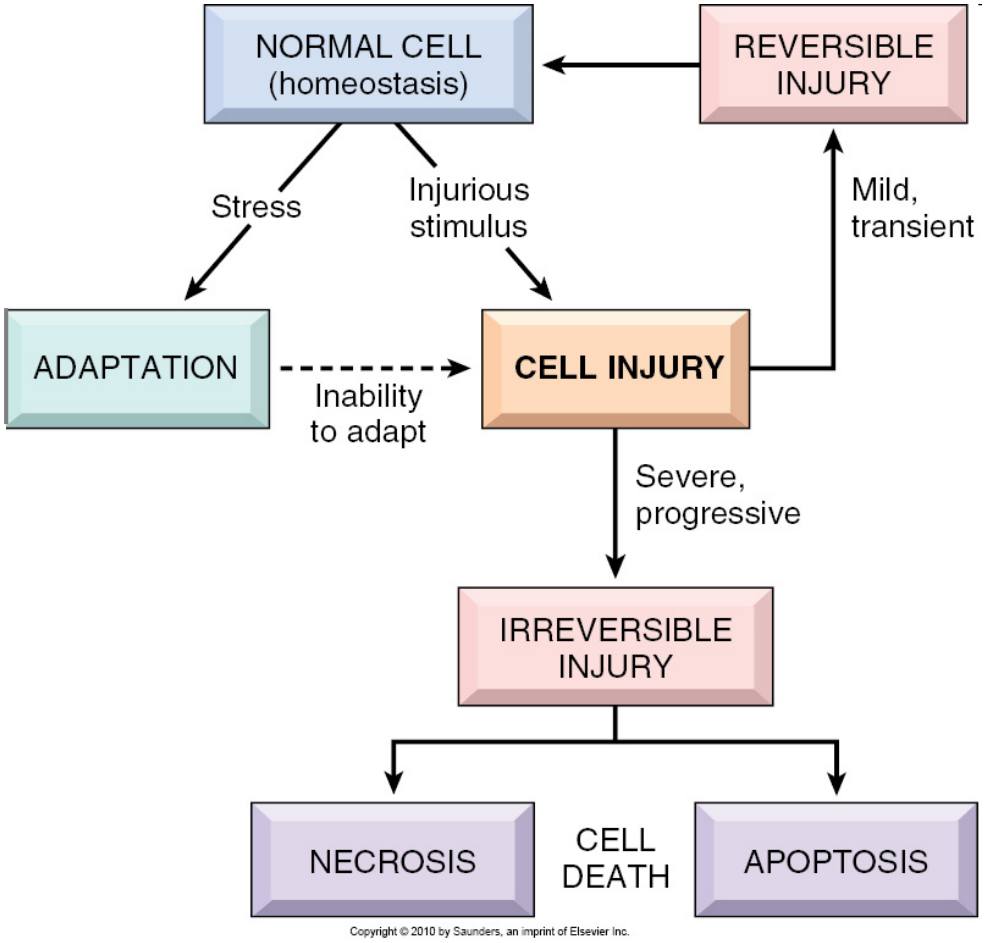
Robbins Basic Pathology



Robbins Basic Pathology

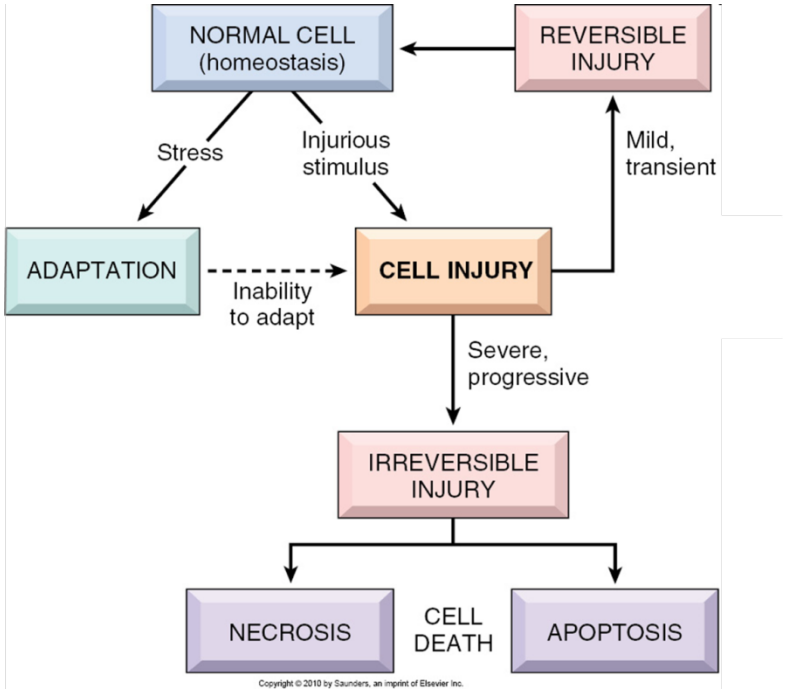
Homeostasis

- Maintenance of a steady state



Adaptations

- Reversible functional and structural responses to physiologic stress and some pathogenic stimuli
- New altered “steady state” is achieved



Adaptive responses

- Hypertrophy
  - *hyper* = above, more
  - *trophe* = nourishment, food
- Hyperplasia
  - *plastein* = (v.) to form, to shape; (n.) growth, development
- Dysplasia
  - *dys* = bad or disordered
- Metaplasia
  - *meta* = change or beyond
- Hypoplasia
  - *hypo* = below, less
- Atrophy, Aplasia, Agenesis
  - *a* = without
  - nourishment, form, begining

- Altered demand (muscle activity)
- Altered stimulation (growth factors, hormones)
- Altered nutrition (including gas exchange)

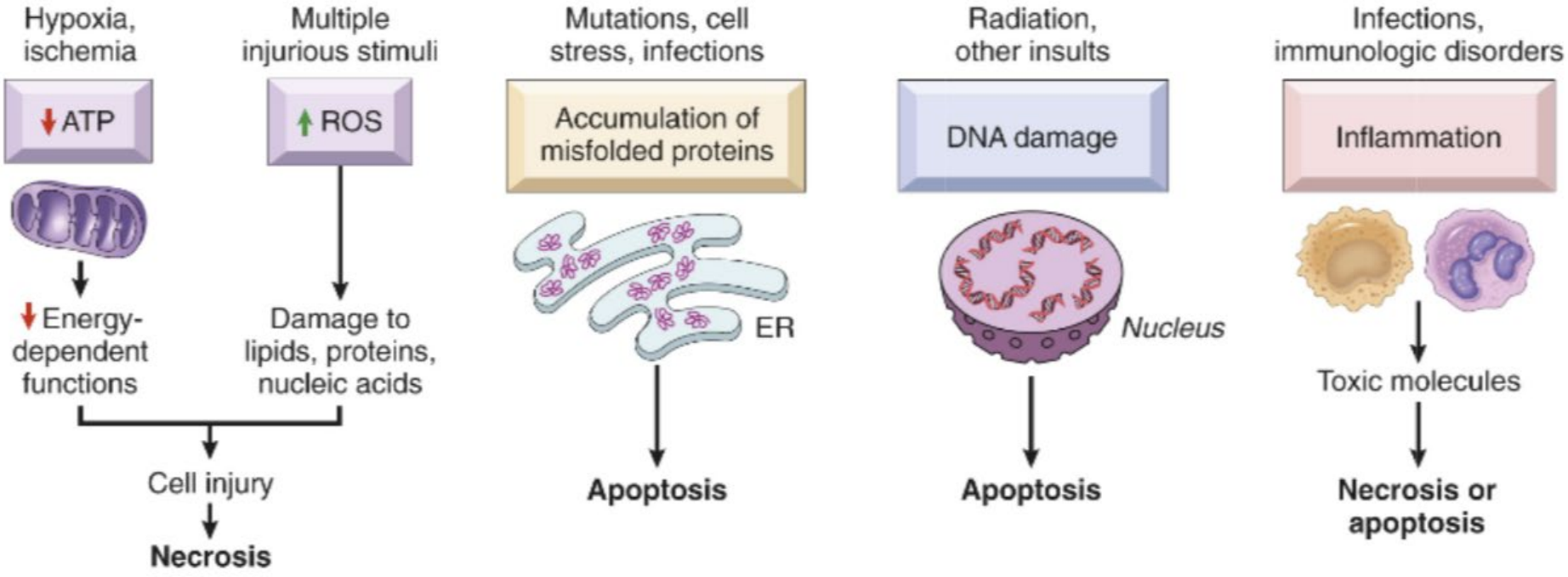


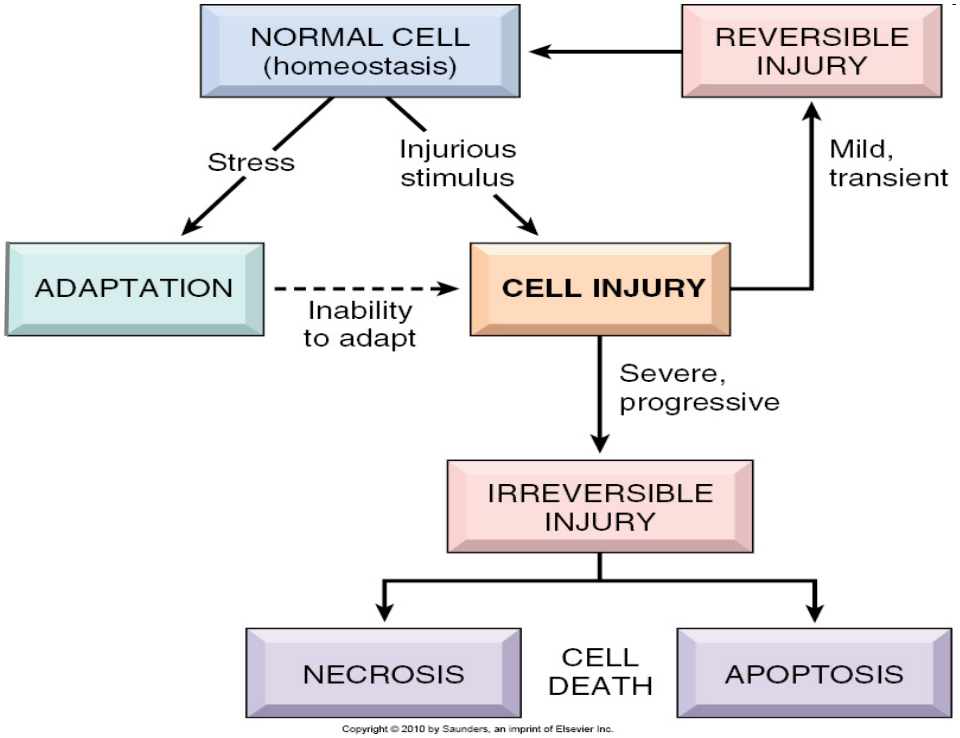
TABLE 1-1 -- Cellular Responses to Injury

Nature of Injurious Stimulus	Cellular Response
ALTERED PHYSIOLOGICAL STIMULI; SOME NONLETHAL INJURIOUS STIMULI	CELLULAR ADAPTATIONS
• Increased demand, increased stimulation (e.g., by growth factors, hormones) • Decreased nutrients, decreased stimulation • Chronic irritation (physical or chemical)	• Hyperplasia, hypertrophy • Atrophy • Metaplasia
REDUCED OXYGEN SUPPLY; CHEMICAL INJURY; MICROBIAL INFECTION	CELL INJURY
• Acute and transient • Progressive and severe (including DNA damage)	• Acute reversible injury Cellular swelling fatty change • Irreversible injury → cell death Necrosis Apoptosis
METABOLIC ALTERATIONS, GENETIC OR ACQUIRED; CHRONIC INJURY	INTRACELLULAR ACCUMULATIONS; CALCIFICATION
CUMULATIVE SUBLETHAL INJURY OVER LONG LIFE SPAN	CELLULAR AGING

Cell death, the end result of progressive cell injury, is one of the most crucial events in the evolution of disease in any tissue or organ. It results from diverse causes, including ischemia (reduced blood flow), infection, and toxins. Cell death is also a normal and essential process in embryogenesis, the development of organs, and the maintenance of homeostasis.

Two principal pathways of cell death, *necrosis* and *apoptosis*.

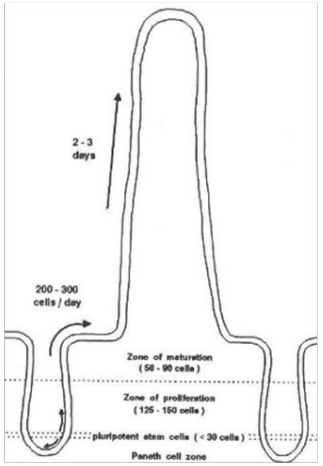
Nutrient deprivation triggers an adaptive cellular response called *autophagy* that may also culminate in cell death.



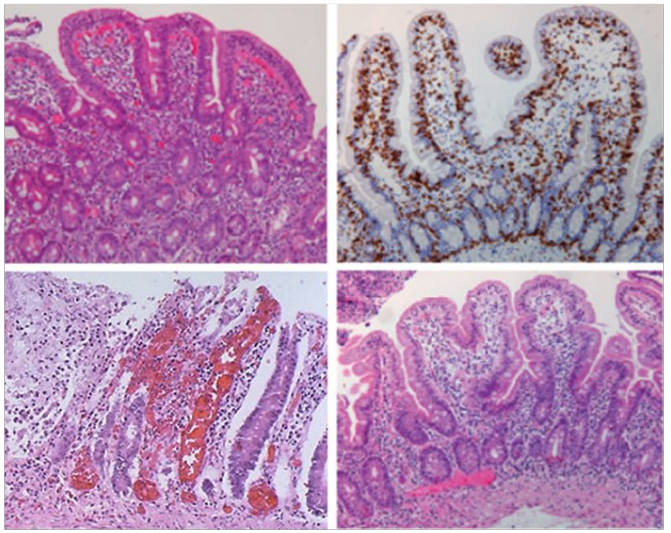
Adaptations

- Hypertrophy
- Hyperplasia
- Atrophy
- Metaplasia

A



B



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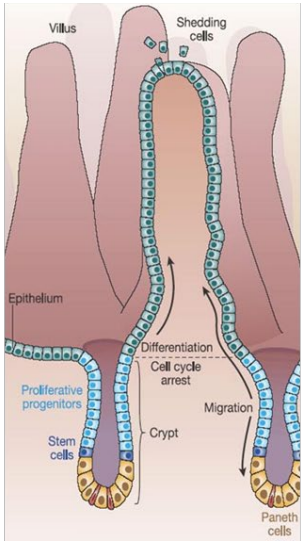

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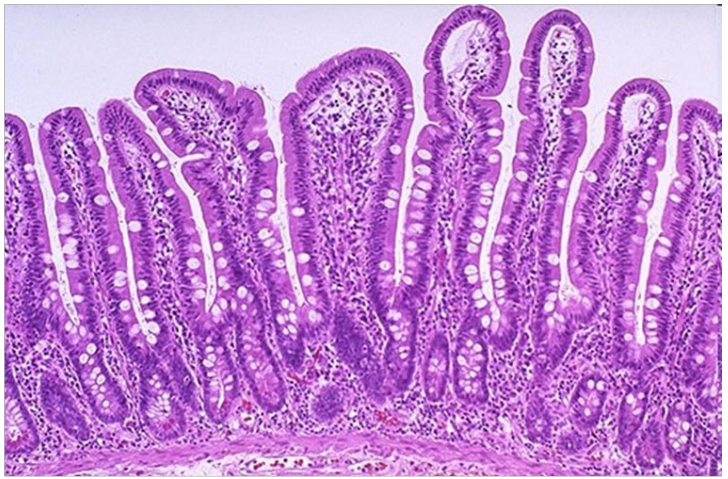


HYPERTROPHY

Hypertrophy refers to an increase in the size of cells, resulting in an increase in the size of the organ

No new cells, just larger cells. The increased size of the cells is due to the synthesis of more structural components of the cells usually proteins.

Cells capable of division may respond to stress by undergoing both hyperrtophy and hyperplasia

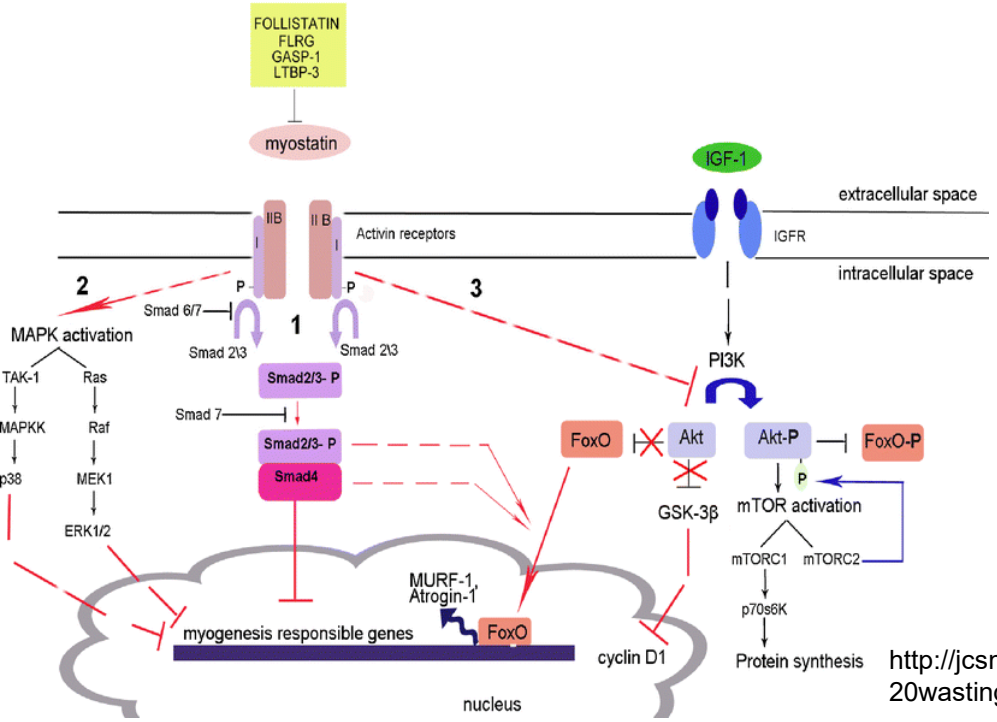
Non-dividing cell increased tissue mass is due to hypertrophy.

Physiological hypertrophy—normal?

The Belgian Blue has been bred to be predisposed towards myostatin blocking.

Wendy the whippet is the Schwarzenegger of dogs.

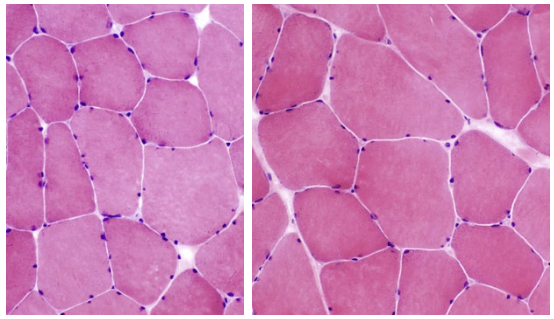
http://thevoiceofnetizen.blogspot.com/2012/04/genetic-factors-myostatin-and-size-of.html



http://jcsm.info/documents/0311/The%20role%20of%20myostatin%20in%20muscle%20wasting-Dateien/13539_2011_35_Fig2_HTML.gif

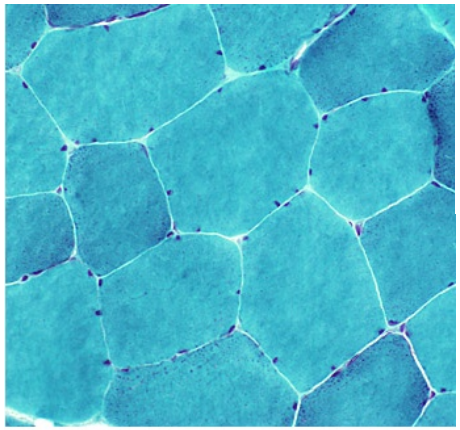
Exercise hypertrophy

http://neuromuscular.wustl.edu/pathol/hypertrophy.htm

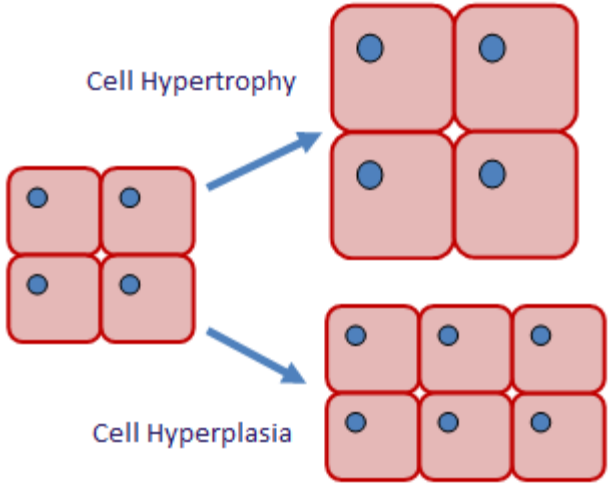


ATPase pH 9.4

Cytochrome oxidase stain



Gomori trichrome stain

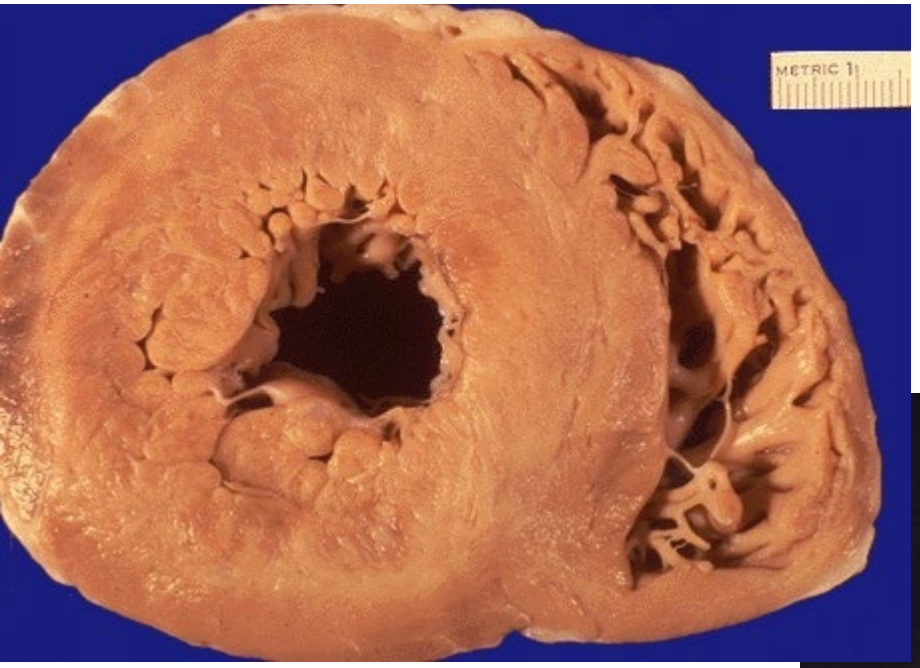


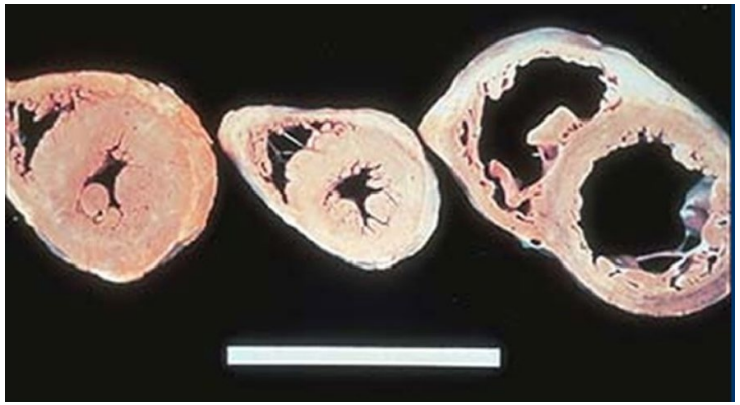
http://www.expert-nutrition.com/image-files/hypertrophy.png

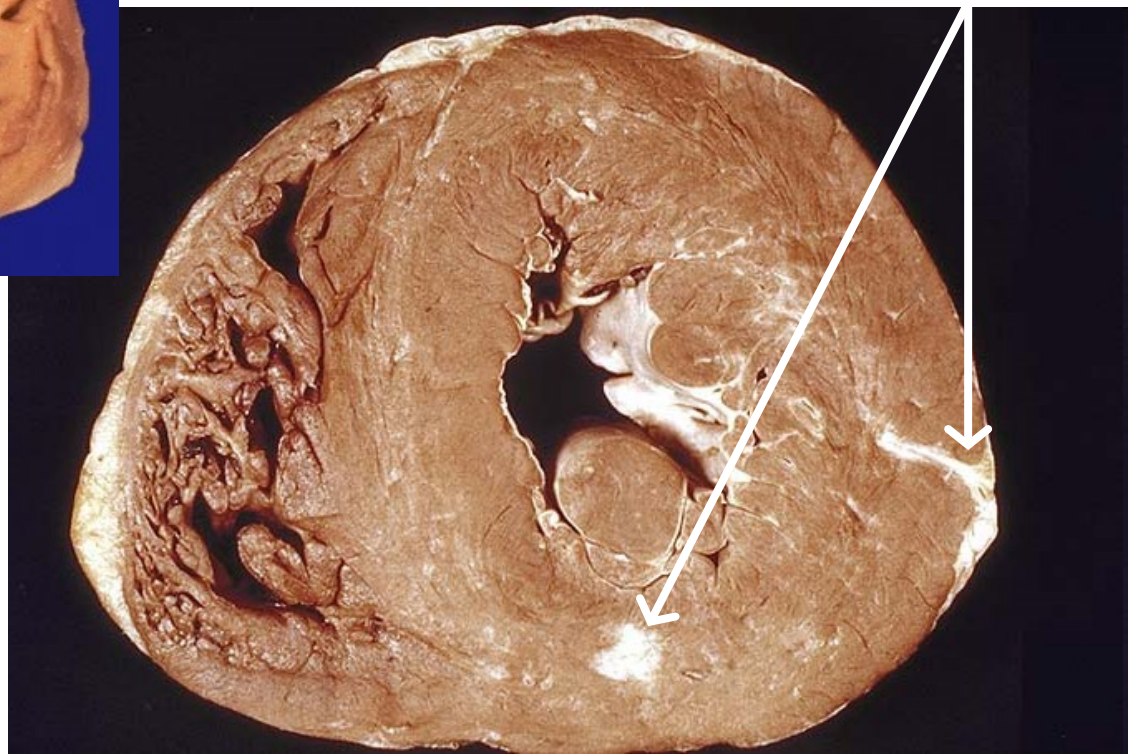
Microscopic views of muscle hypertrophy. Enlarged type 2 (fast twitch) fibers stain dark with ATPase at pH 9.4. Enlarged fast twitch fibers stain pale with cytochrome c oxidase. Hypertrophied fibers with less sarcoplasmic reticulum relative to fiber proteins stain paler with the trichrome stain.

http://neuromuscular.wustl.edu/pathol/hypertrophy.htm

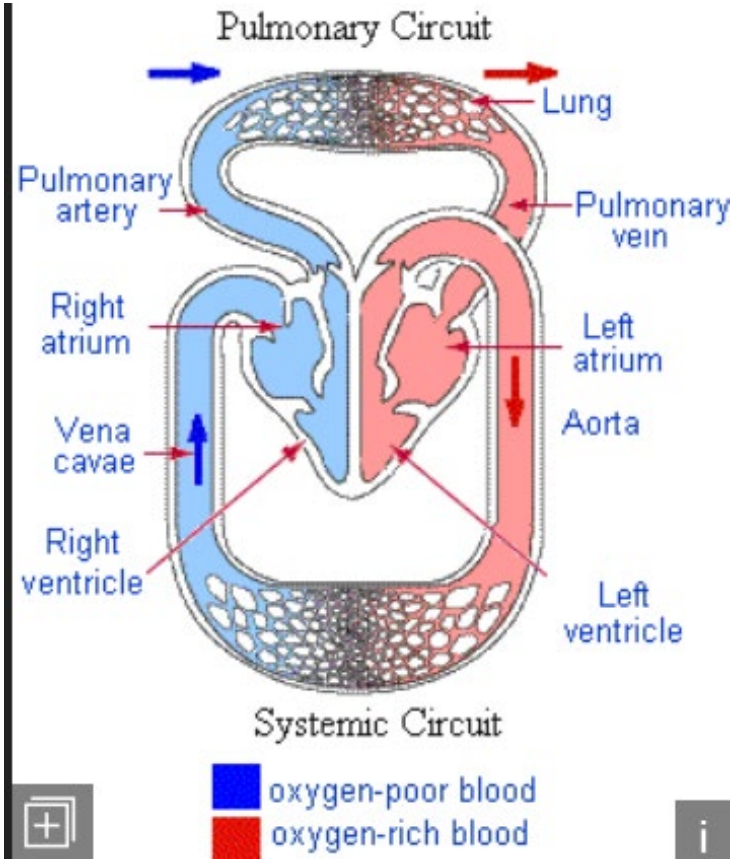
Hypertrophy resulting from pathological injury (hypertension)







Circulation as a Circut



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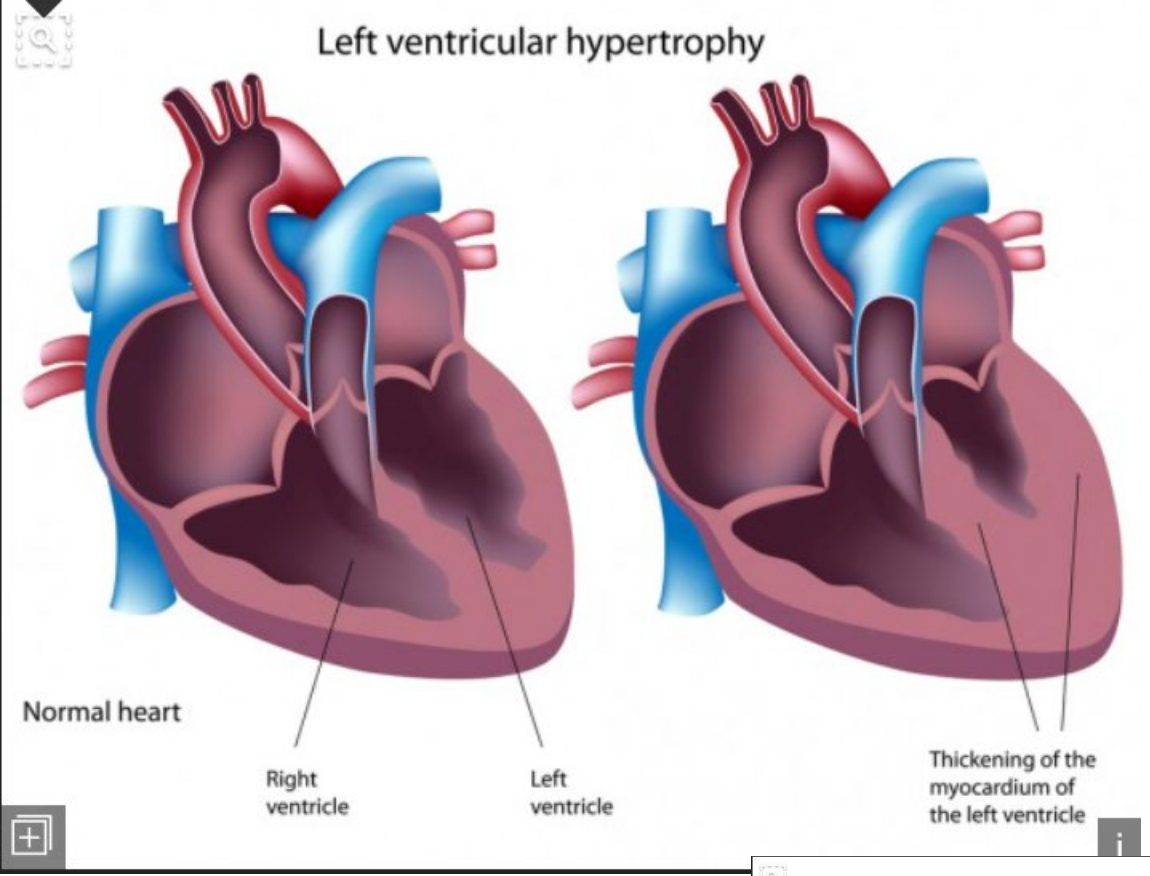
VH



https://www.bing.com/images/search?q=hypertension+and+cardiac+hypertrophy&view=detailv2&&id=C2A390B5E541DE9EE23884852AB9CF8150D8D7FE&selectedIndex=56&ccid=ge%2ftspqQ&simid=608040351063936810&thid=OIP.M81efedb29a90bf54dbef49a423ec3706H0&ajaxhist=0

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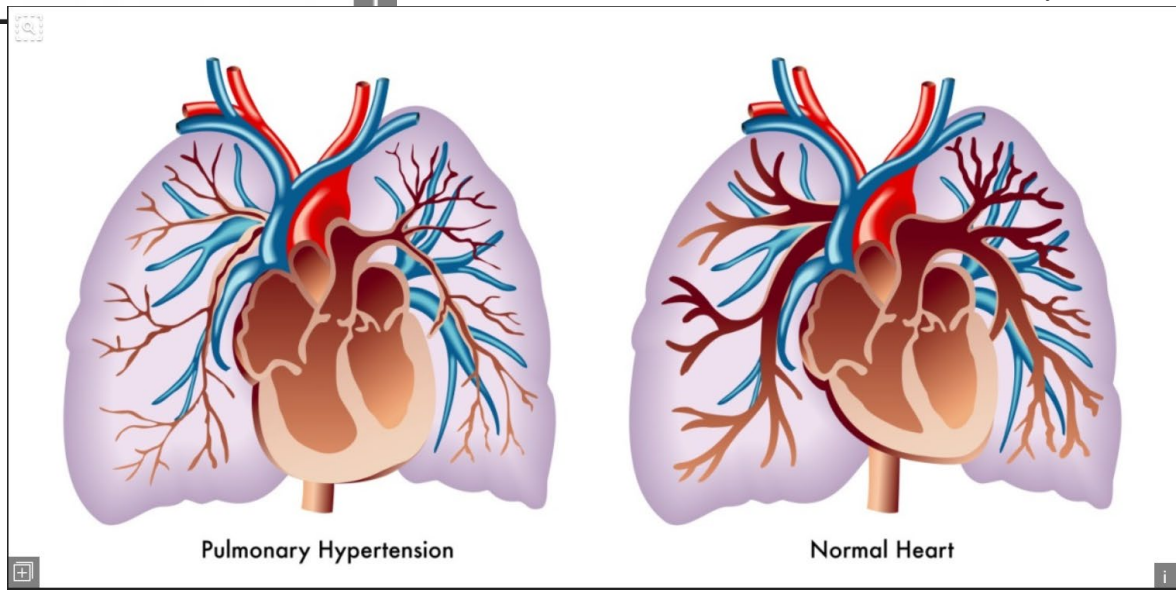
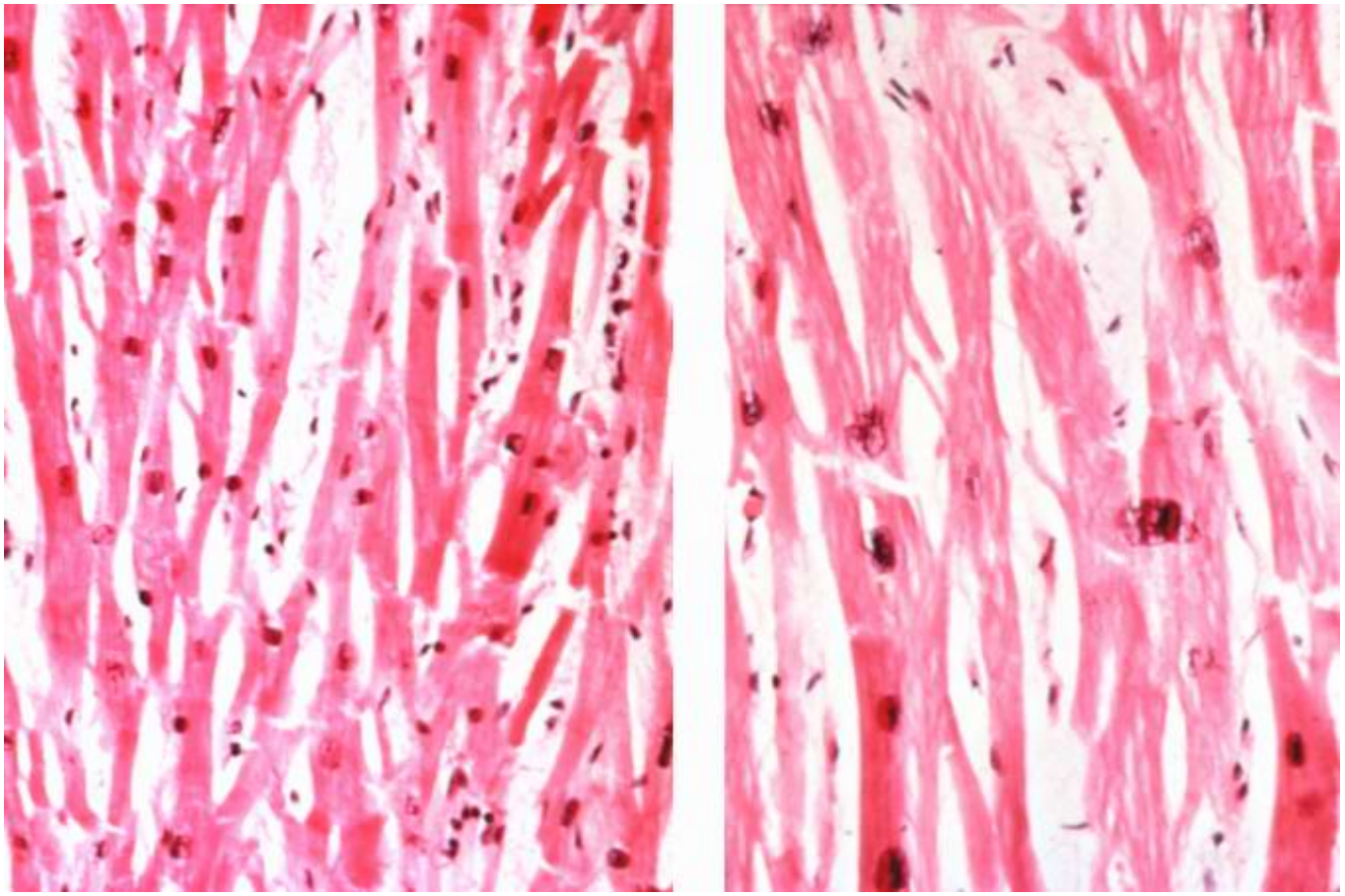
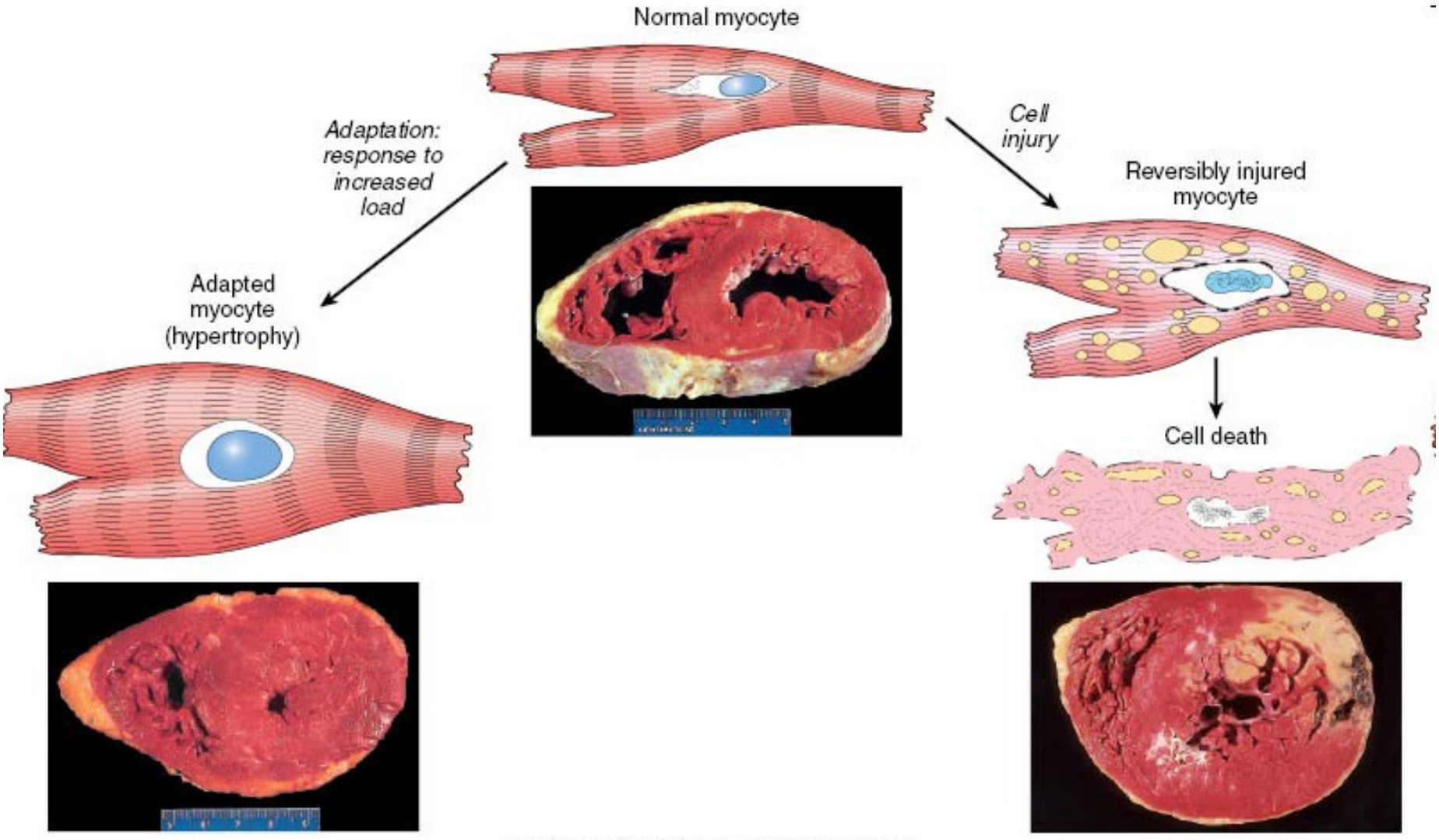


Cardiac Muscle Hypertrophy

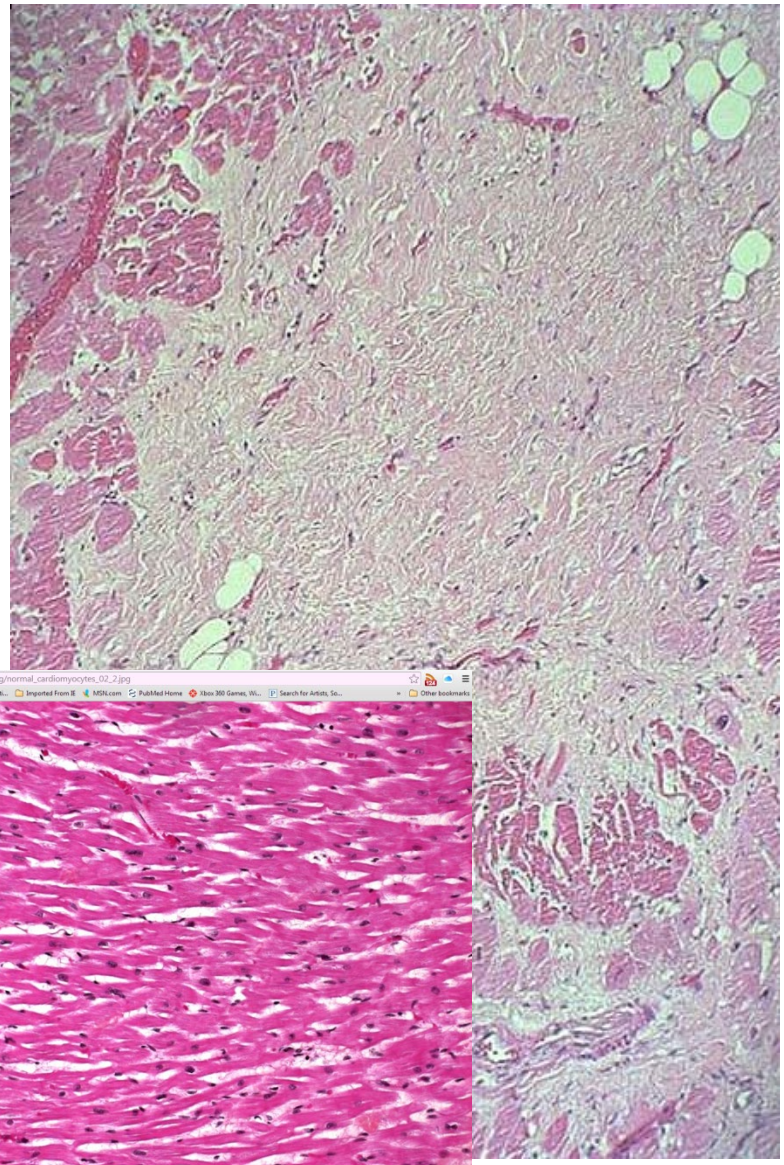


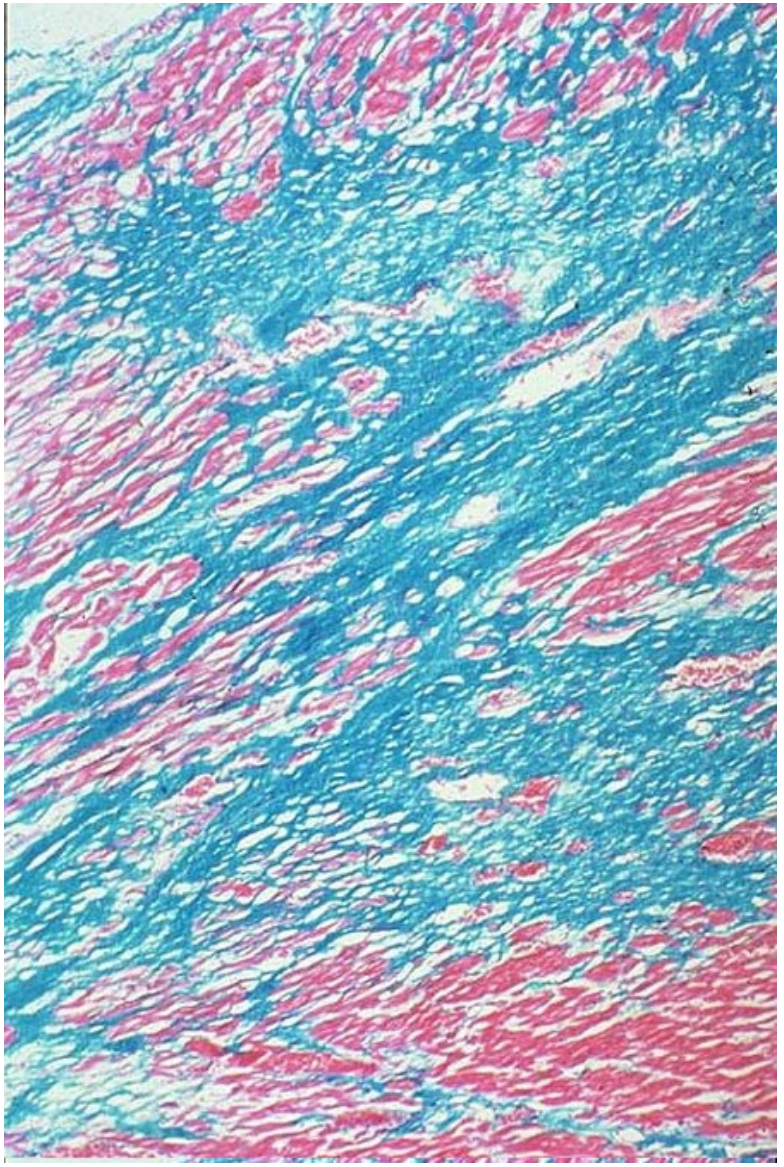
http://static.wikidoc.org/a/a8/Comparison_of_hypertrophy_and_normal_myocardial_micro_2.JPG

Physiologic adaptation vs. pathology

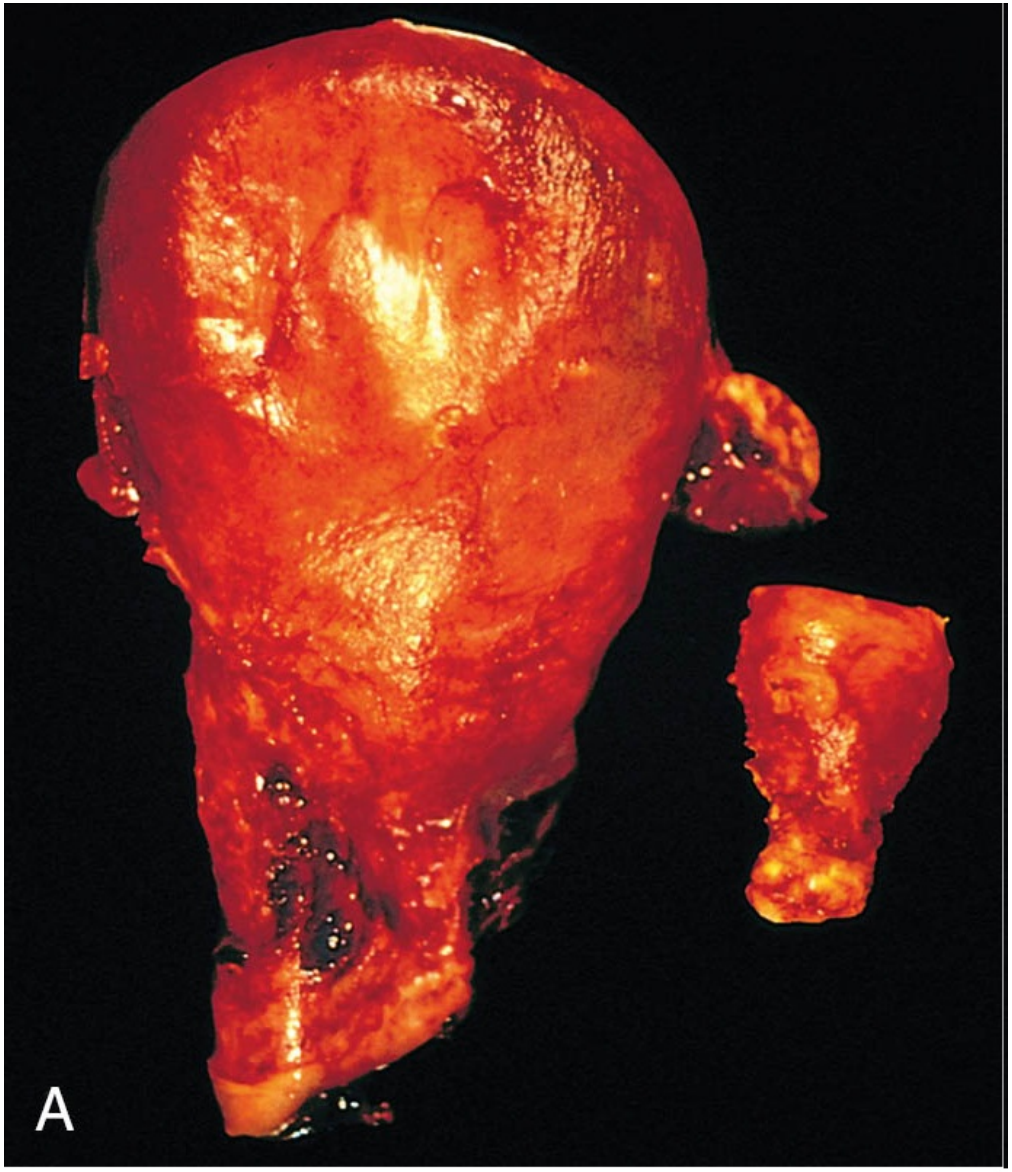


Scarred necrosis



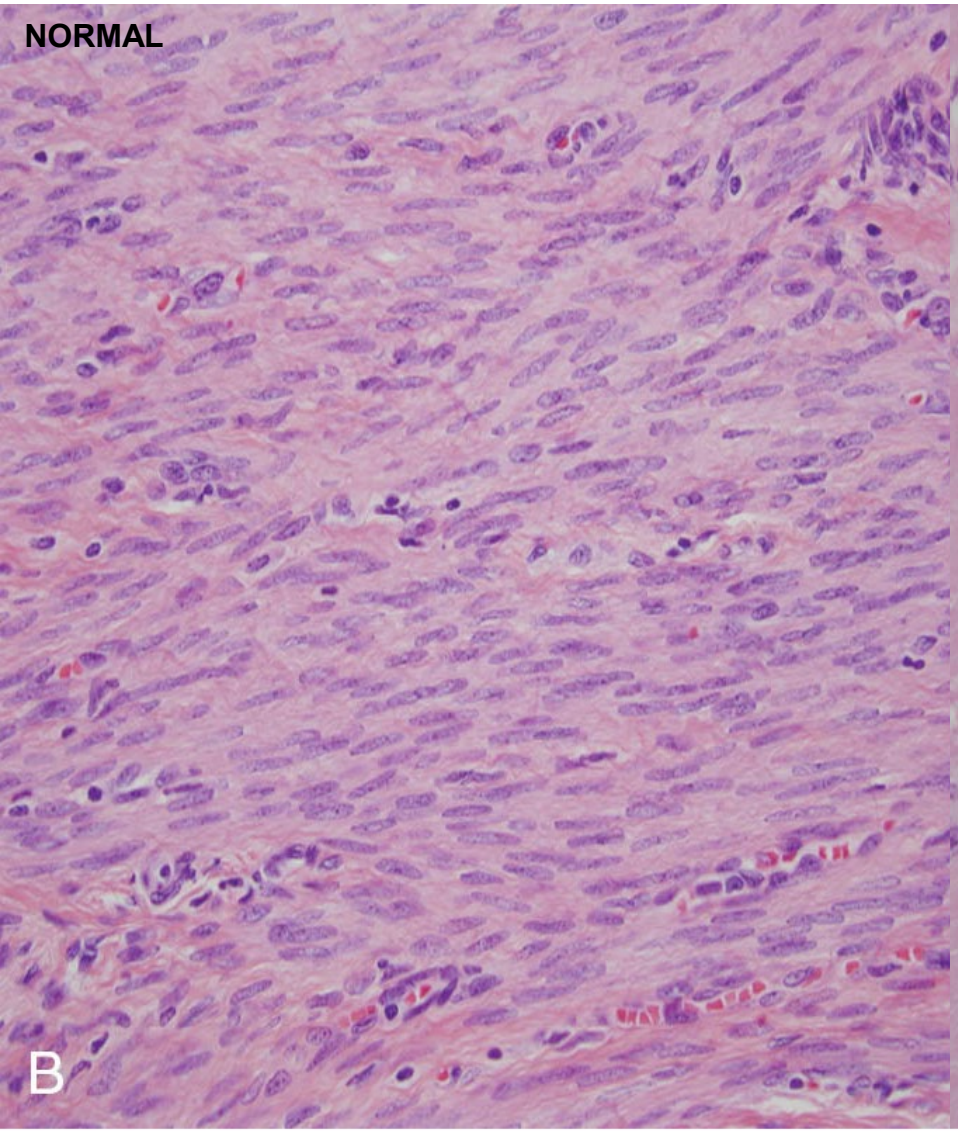


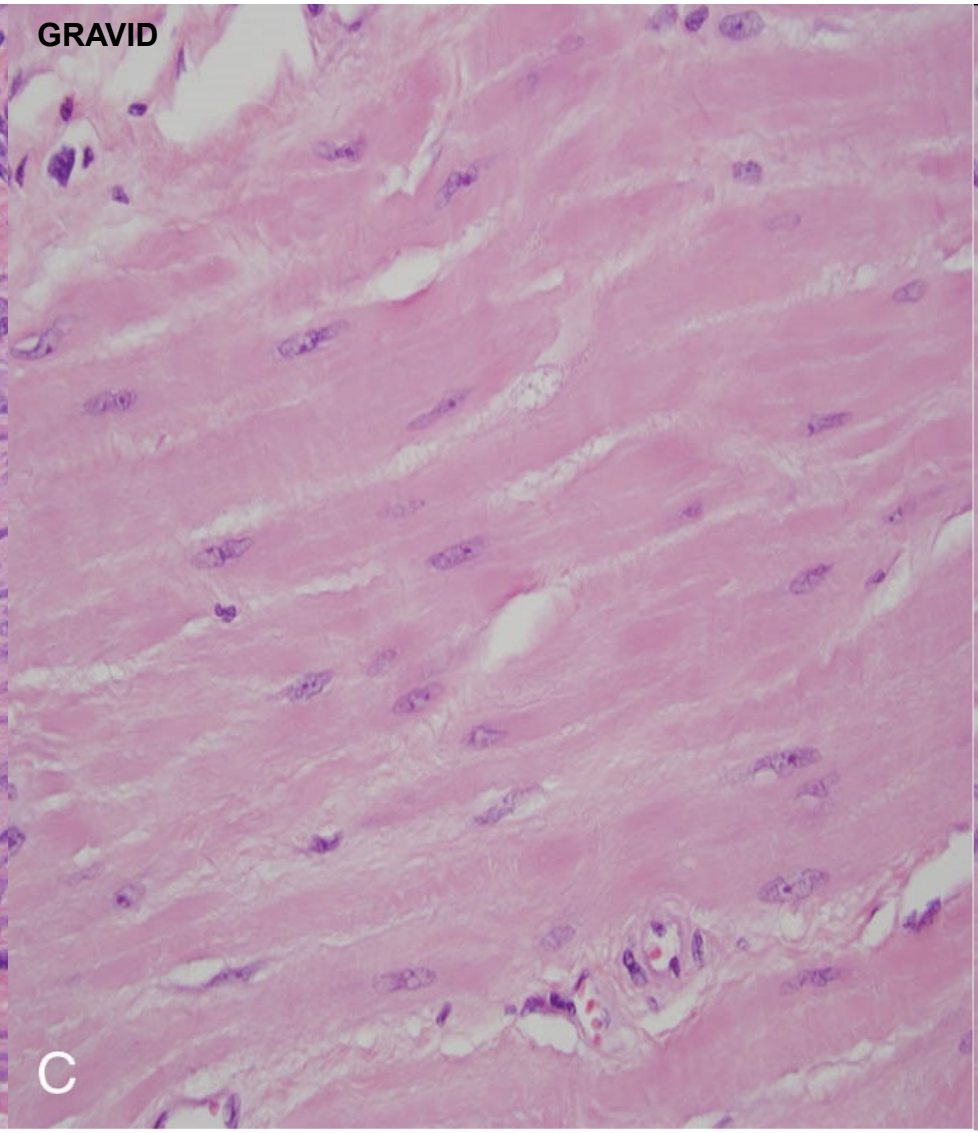
Physiological hypertrophy—normal



Estrogen acting on smooth muscle during pregnancy

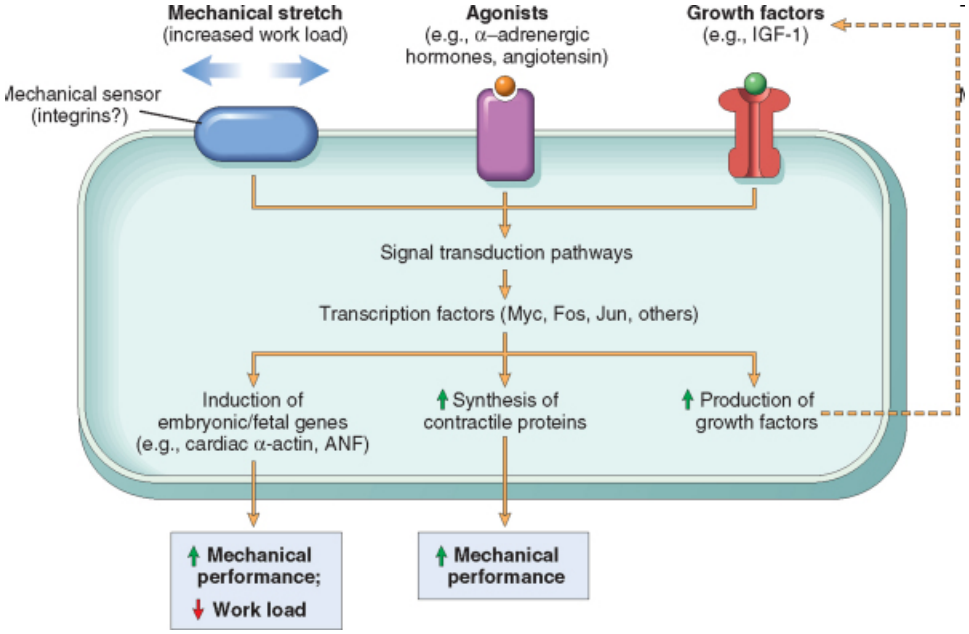
Microscopic physiological hypertrophy

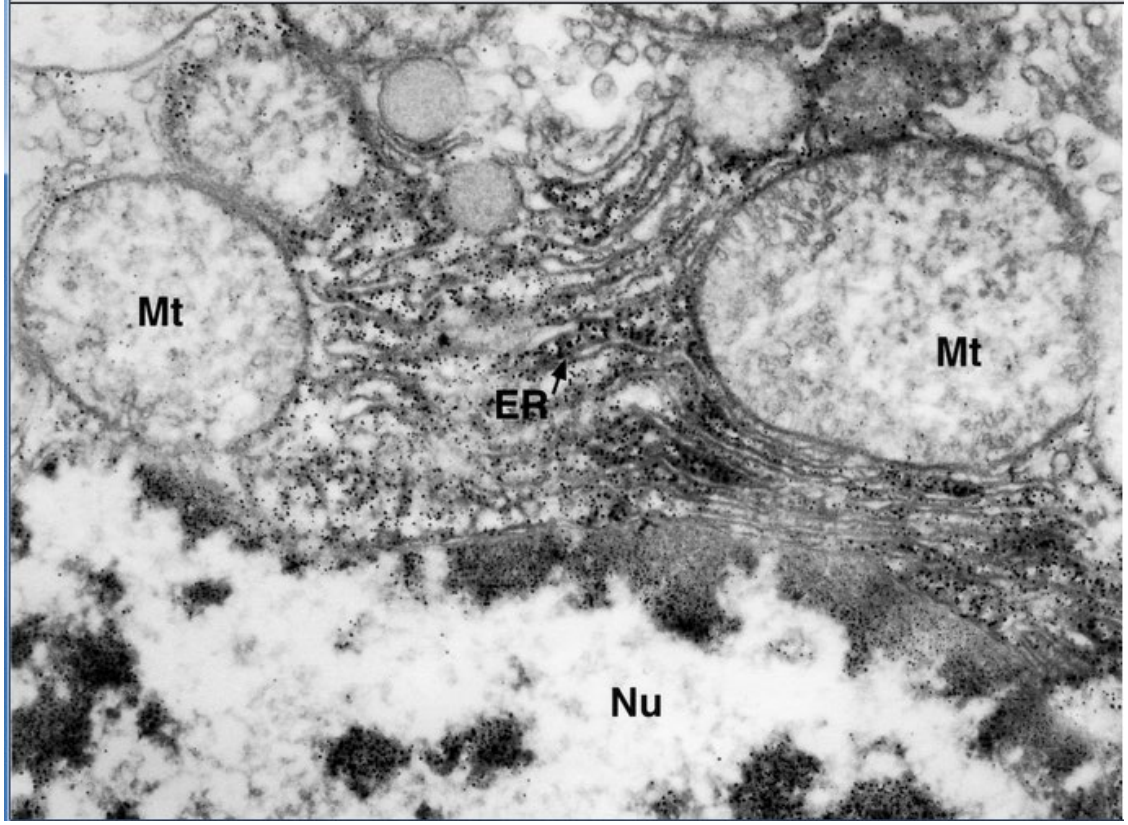




Mechanisms of muscle hypertrophy

- Increased protein synthesis →increased cell size → increased organ size
- Nondividing cells produce more protein and membrane without division
- Mechanosensors, PI3K /Akt signaling pathway important in exercise-induced growth
- Growth factors, vasoactive agents, hormones mediate stress-induced response
- Unrelieved stress eventually results in irreversible injury





Subcellular organelle may undergo selective hypertrophy

As example, individuals treated with drugs such as barbiturates show hypertrophy of the smooth endoplamic reticulum (ER) in hepatocytes, which is an adaptive response that increases the amount of enzymes (cytochrome P-450 mixed function oxidases) available to detoxify the drugs.

HYPERPLASIA

Hyperplasia is an increase in the number of cells in an organ or tissue, usually resulting in increased mass of the organ or tissue

Hyperplasia and hypertrophy are distinct processes but frequently occur together

Both can triggered by the same external stimulus

Hyperplasia takes place if the cell population is capable of dividing resulting in increased cell numbers

HYPERPLASIA

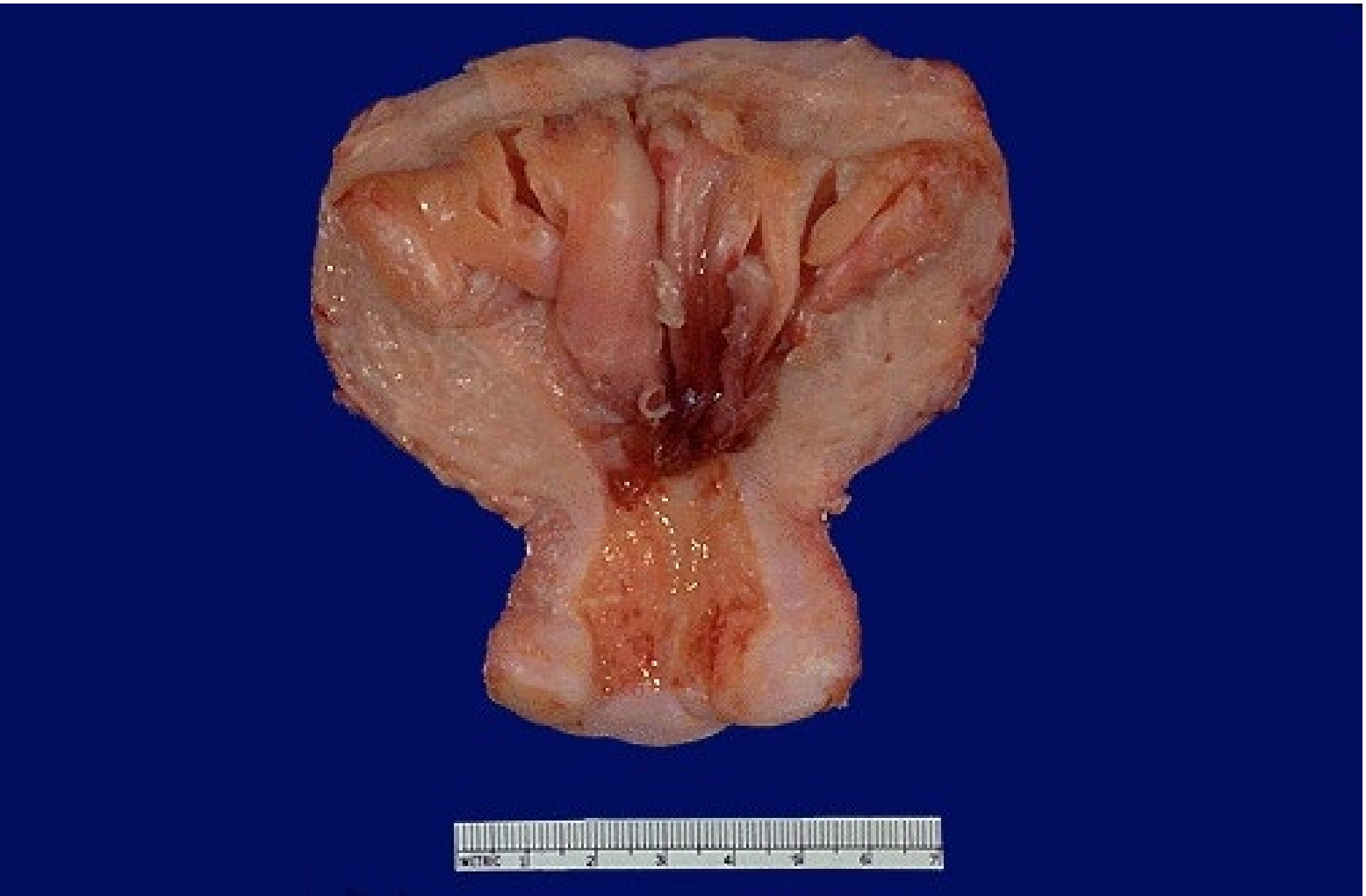
Physiologic vs Pathologic

Physiologic

hormonal vs compensatory

Artrenewal.org

Physiological, hormonal hyperplasia

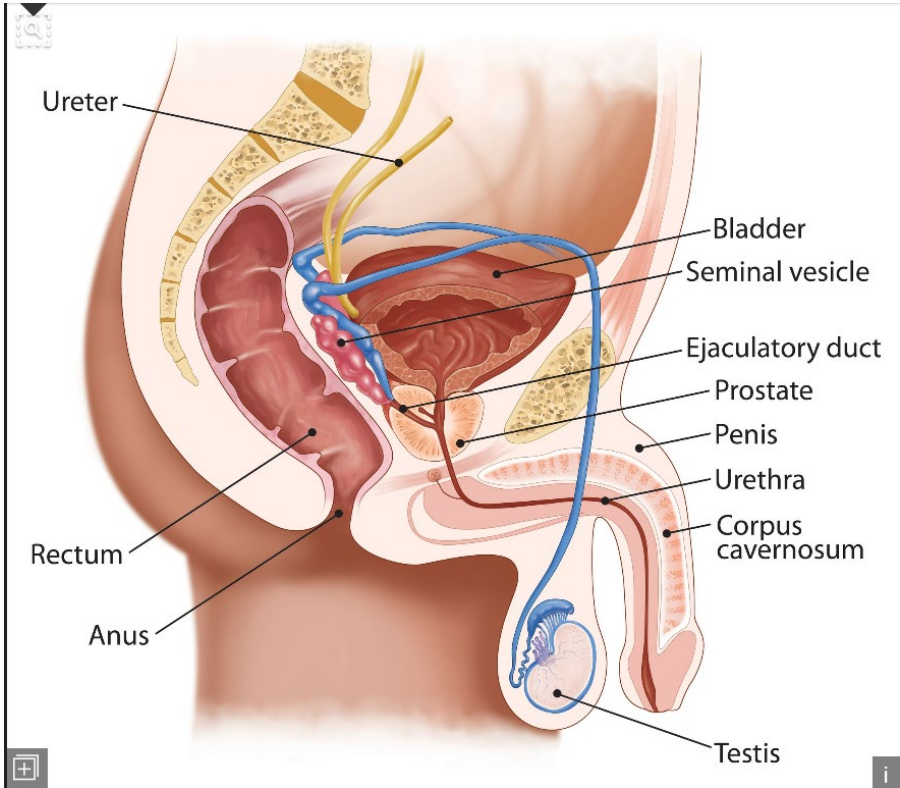


https://c1.staticflickr.com/3/2840/11359744405_50a0c0ce4a_b.jpg

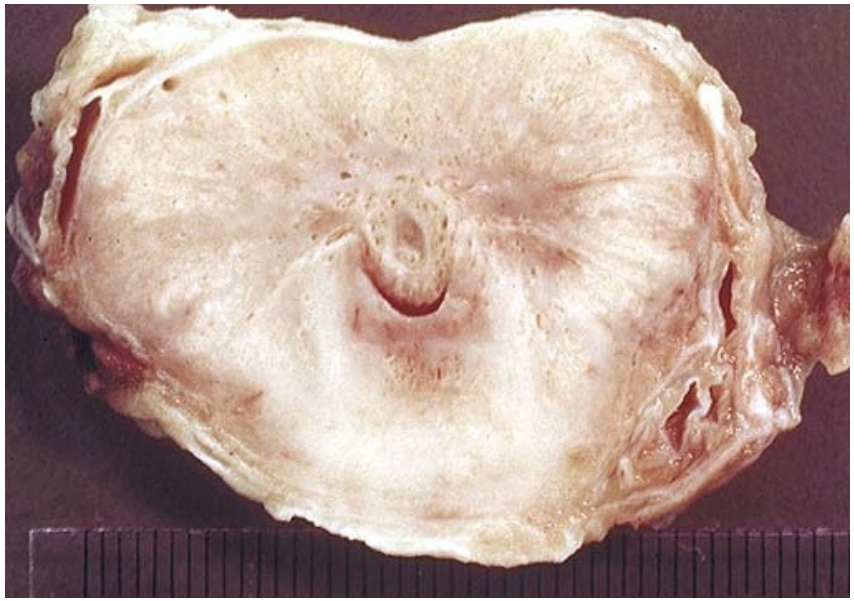
Pathological hormomal hyperplasias

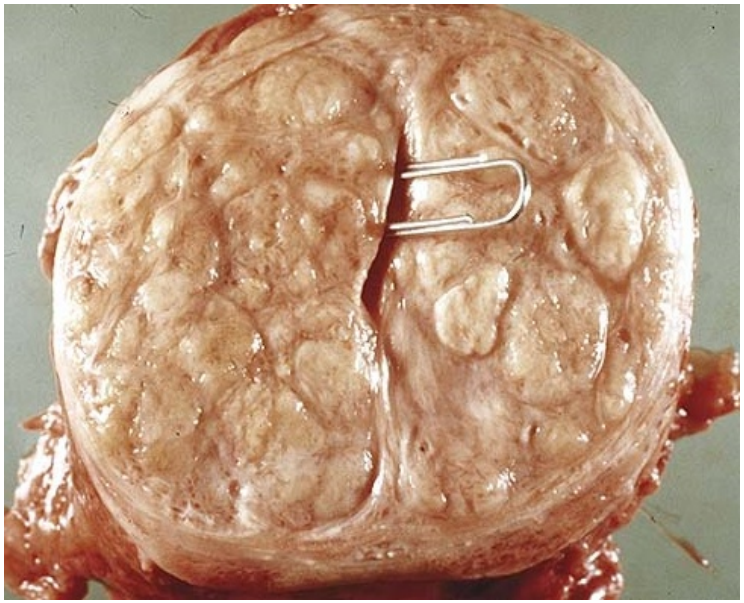
- Hyperplasia reversible with appropriate treatment

- Benign Prostate Hyperplasia
  - BPH from accumulation of stable DHT-AR complexes
  - Androgen-driven up-regulation of fibroblast growth factor (FGF) and TGF-beta
  - FGF stimulates proliferation of stroma



Prostate normal vs. hyperplasia



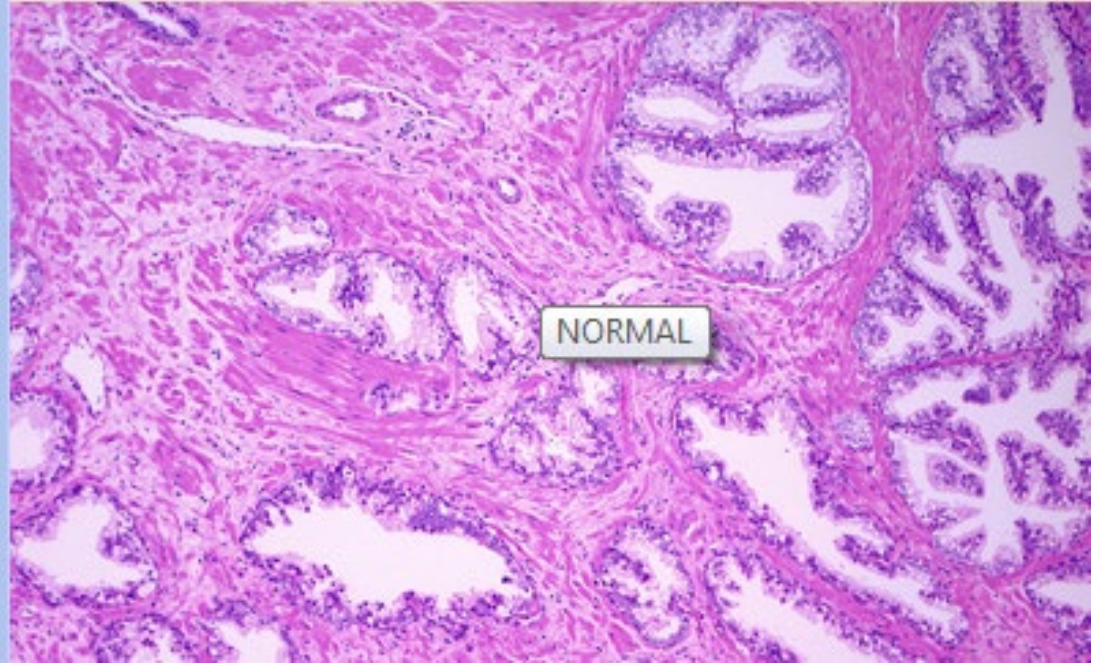


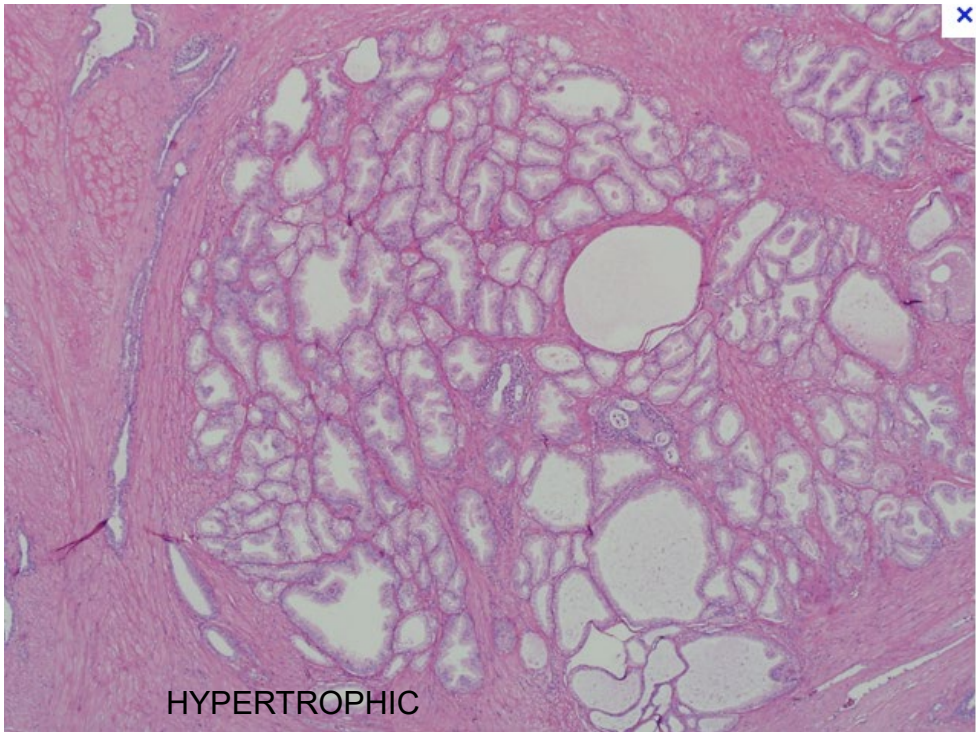
Benign prostatic hyperplasia androgens

Hyperplasia regresses if the hormonal stimulation is eliminated

Hyperplasia is distinct from cancer, but cancerous proliferation may arise

Prostate





ATROPHY

Atrophy is reduced size of an organ or tissue resulting from a decrease in cell size and number

Physiologic or Pathologic.

Physiologic atrophy is common during normal development.

Some embryonic structures, such as the notochord and thyroglossal duct, undergo atrophy during fetal development.

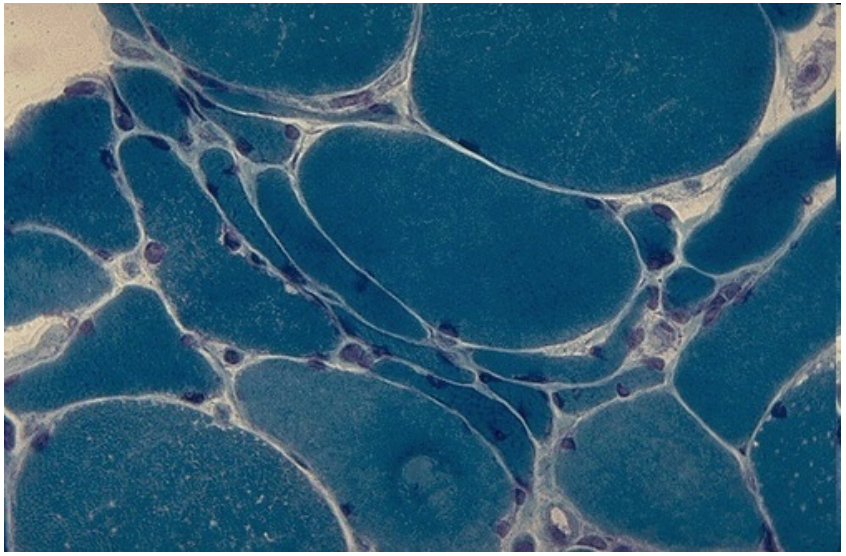
The uterus decreases in size shortly after parturition.

Pathologic

Decreased workload (atrophy of disuse)

When a fractured bone is immobilized in a plaster cast or when a patient is restricted to complete bedrest, skeletal muscle atrophy ensues

The initial decrease in cell size is reversible once activity is resumed., leading to osteoporosis of disuse

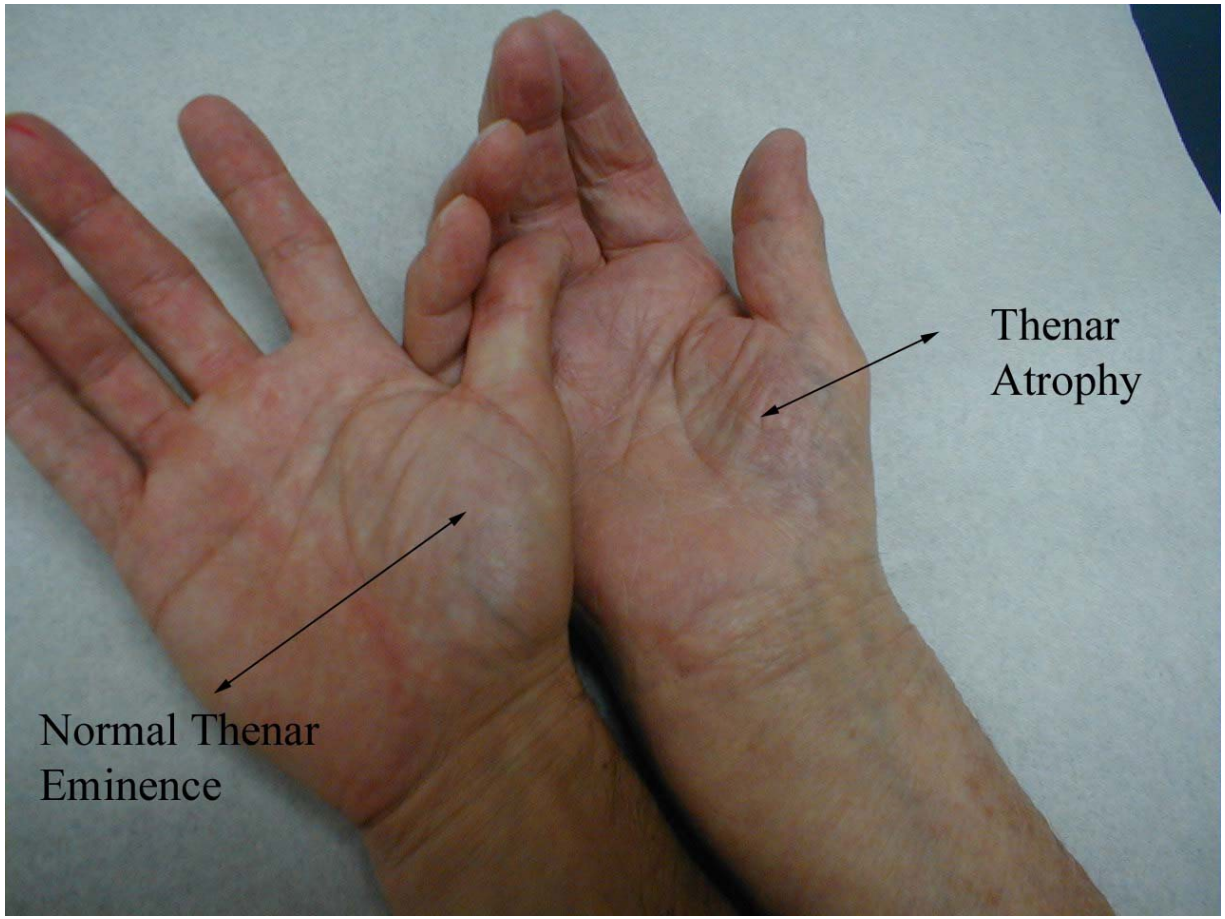


Some of these skeletal muscle fibers here show atrophy, compared to normal fibers. The number of cells is the same as before the atrophy occurred, but the size of some fibers is reduced. This is a response to injury by "downsizing" to conserve the cell. In this case, innervation to the small, atrophic fibers was lost. (This is a trichrome stain.)

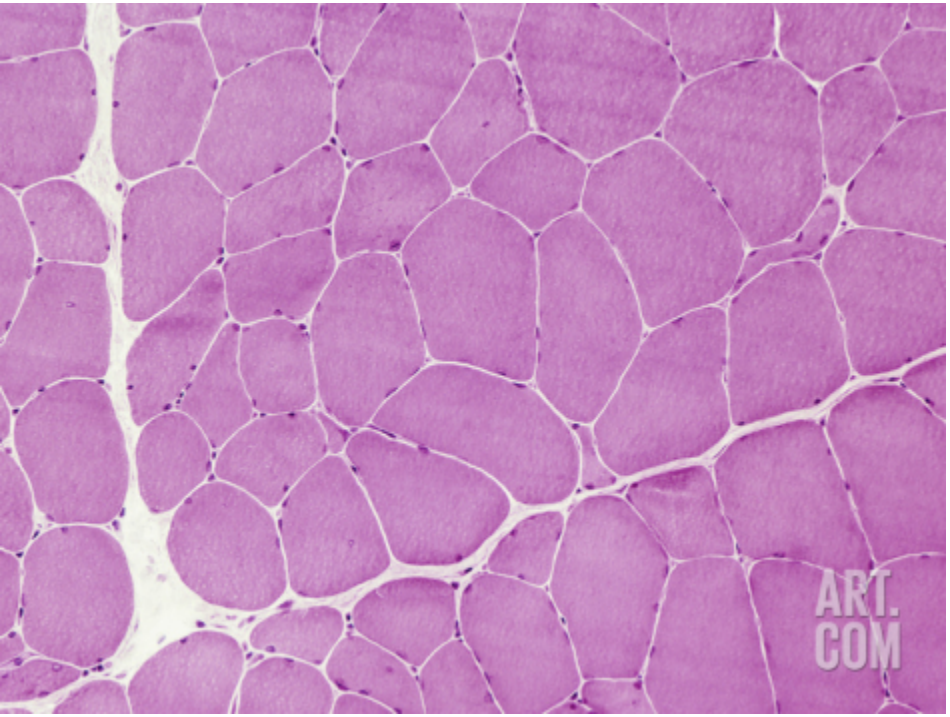
Pathologic

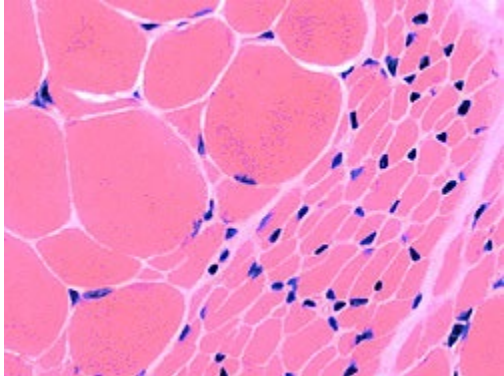
Loss of Innervation (denervation atrophy)

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

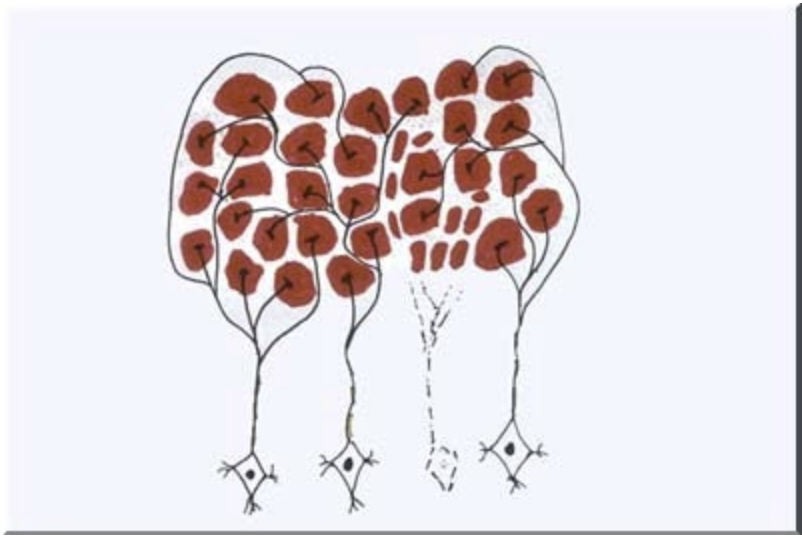


Loss of Innervation (denervation atrophy)



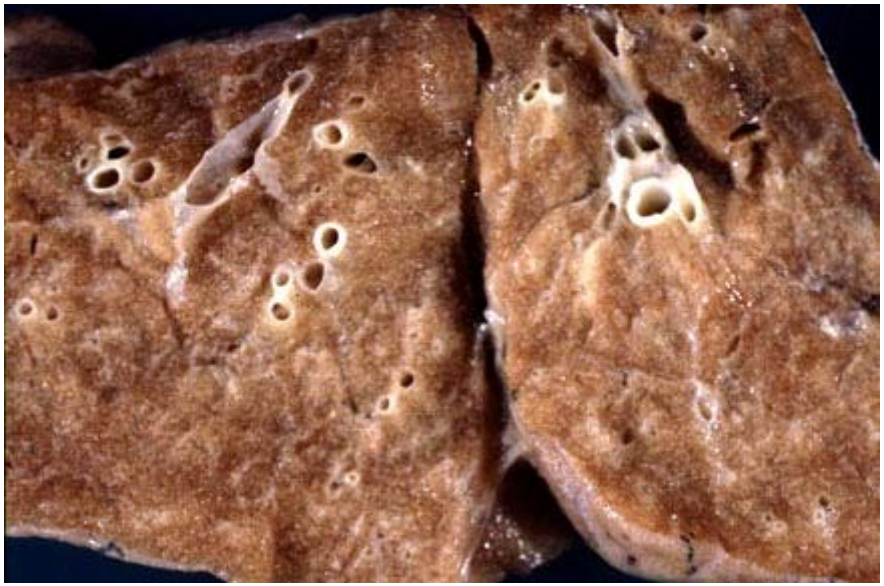


http://neuromuscular.wustl.edu/pics/smahe3.jpg

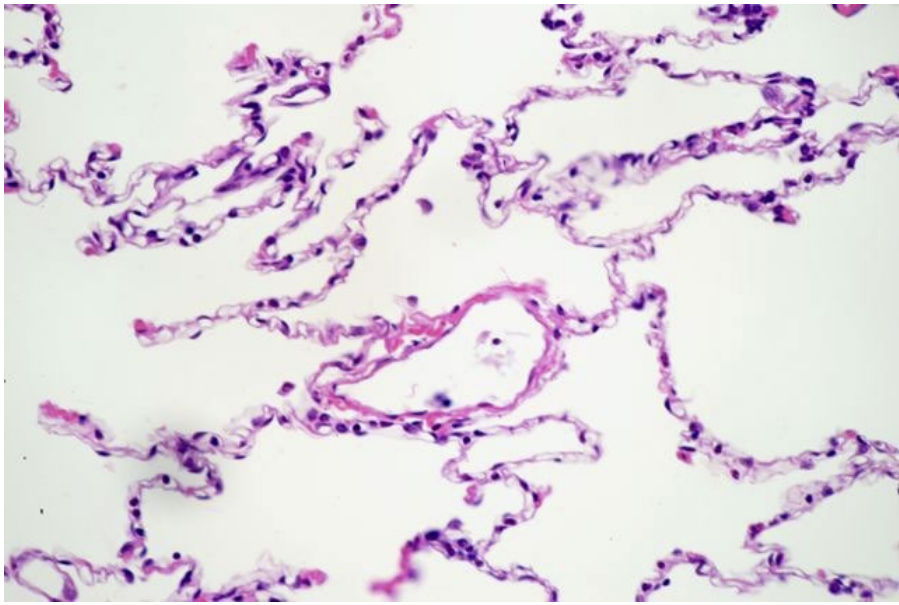


http://www.pathology.vcu.edu/WirSelfInst/neuro_medStudents/image/04.jpg

Normal Lung

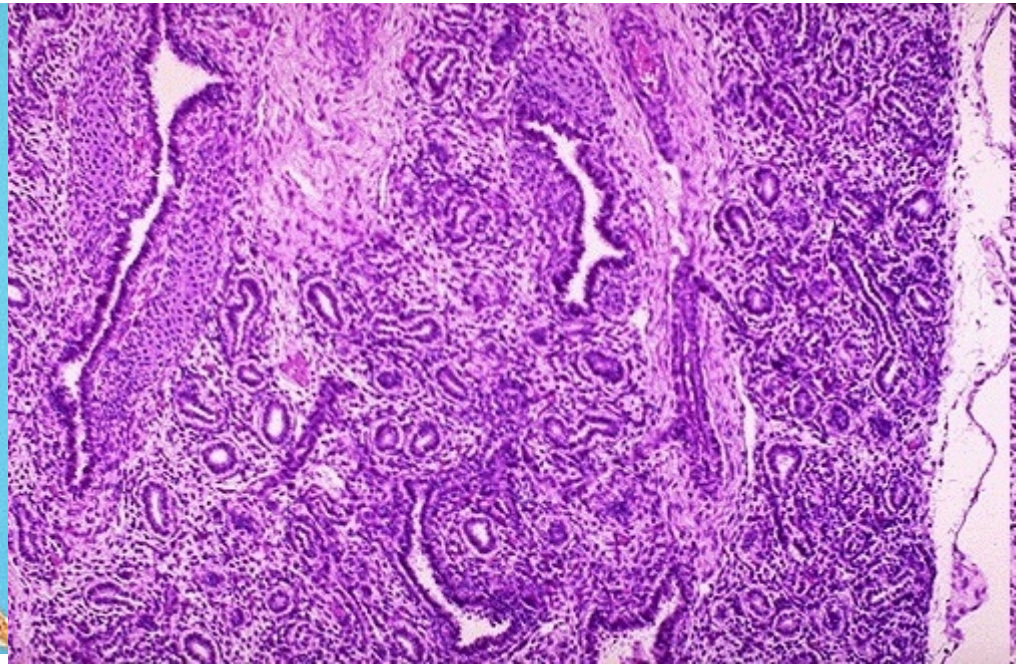


http://www.meddean.luc.edu/lumen/bbs/p/pulpathi/pulpath3.jpeg



http://www.microscopy-uk.org.uk/mag/imgsep08/Apocap4.jpg

Hypoplastic lung



Microscopic examination of the lung reveals no alveolar development, only tubular bronchioles incapable of significant gas exchange, in this premature baby with pulmonary hypoplasia from oligohydramnios. This results in insufficient gas exchange from respiration following birth.

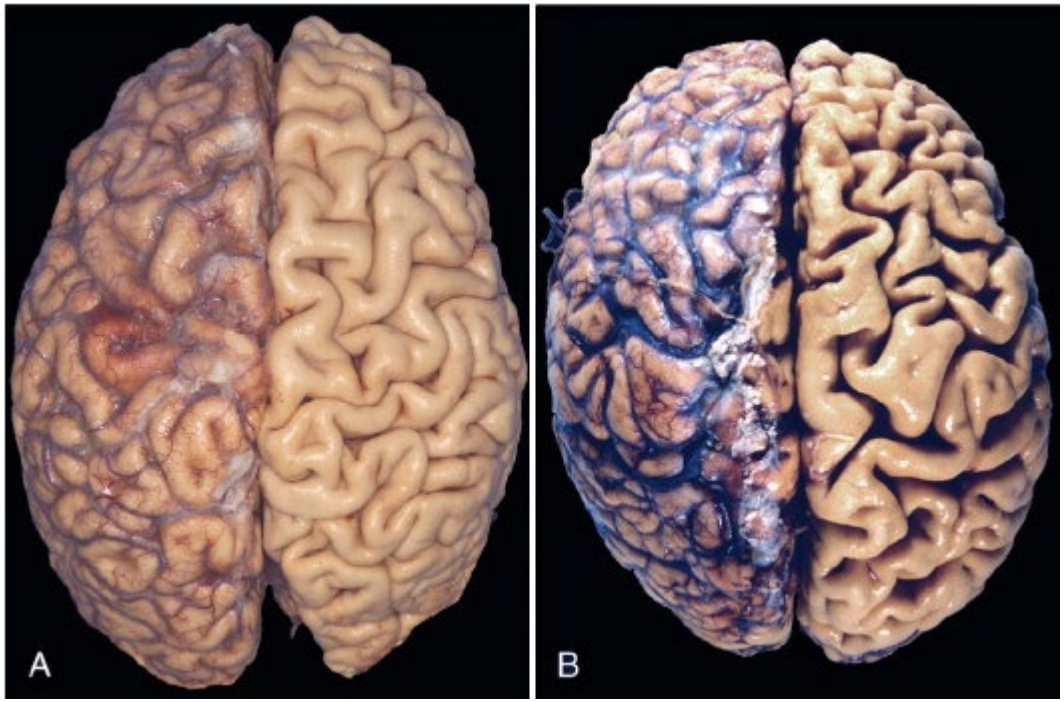
Pathologic

Diminished Blood Supply

A decrease in blood supply such as ischemia

The brain may undergo progressive atrophy, mainly because of reduced blood supply as a result of atherosclerosis

This is called senile atrophy; it also affects the heart



Pathologic

Pressure

Tissue compression for any length of time can cause atrophy.

Atrophy in the setting below is likely the result of ischemic changes caused by compromise of the blood supply by the pressure exerted by the mass

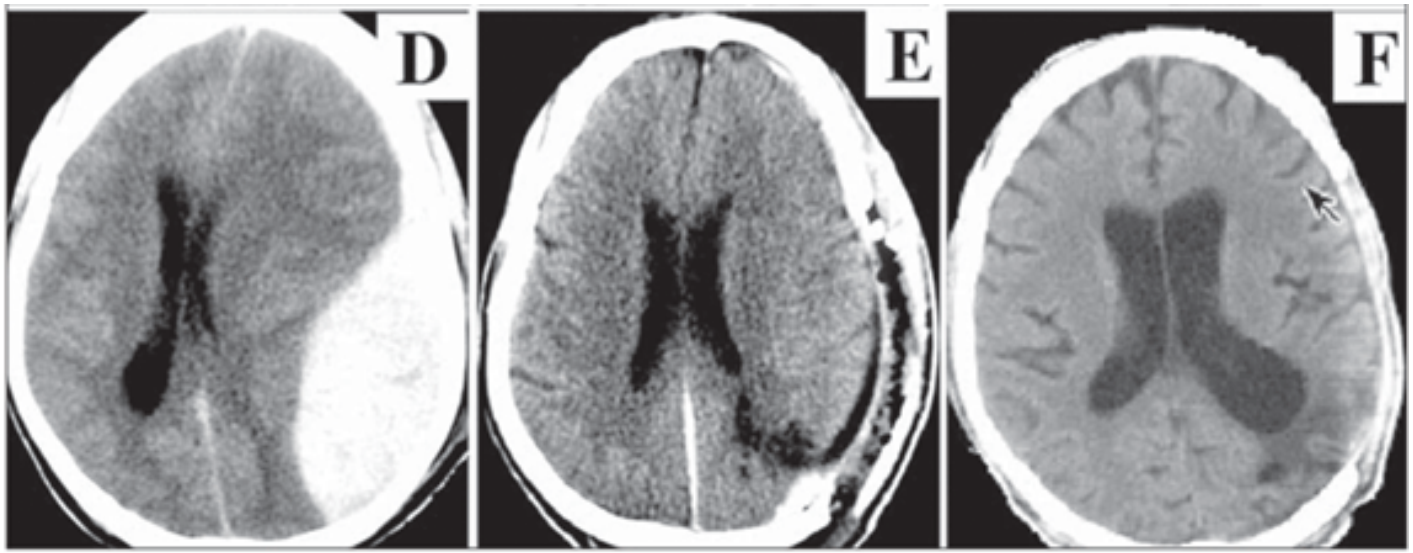


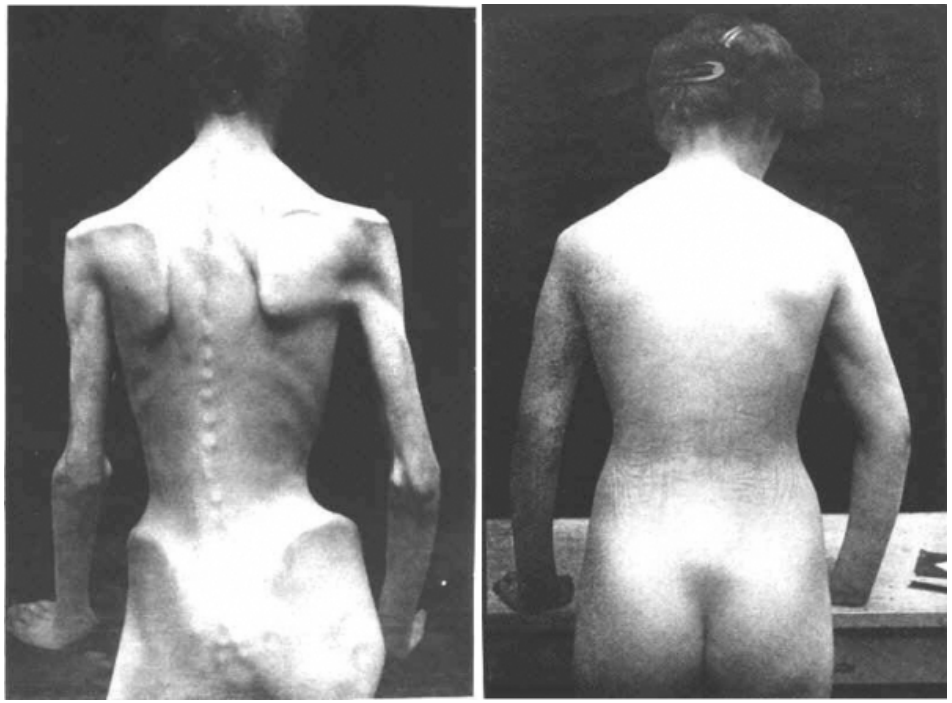
Fig 1. CT scans showing large parietal left extradural hematoma (A and D). B and E, immediate post op CT scan: complete evacuation of the lesion by craniectomy. C and F, delayed cerebral atrophy in the exam performed about four months after surgery.

http://www.scielo.br/img/revistas/anp/v65n4b/a29fig1d.gif

Inadequate Nutrition

Profound protein-calorie malnutrition (marasmus) is associated with the use of skeletal muscle as a source of energy after other reserves such as adipose stores have been depleted.

Cachexia is also seen in patients with chronic inflammatory diseases and cancer. In the former, chronic overproduction of the inflammatory cytokine tumor necrosis factor (TNF) is thought to be responsible for appetite suppression and lipid depletion, culminating in muscle atrophy.



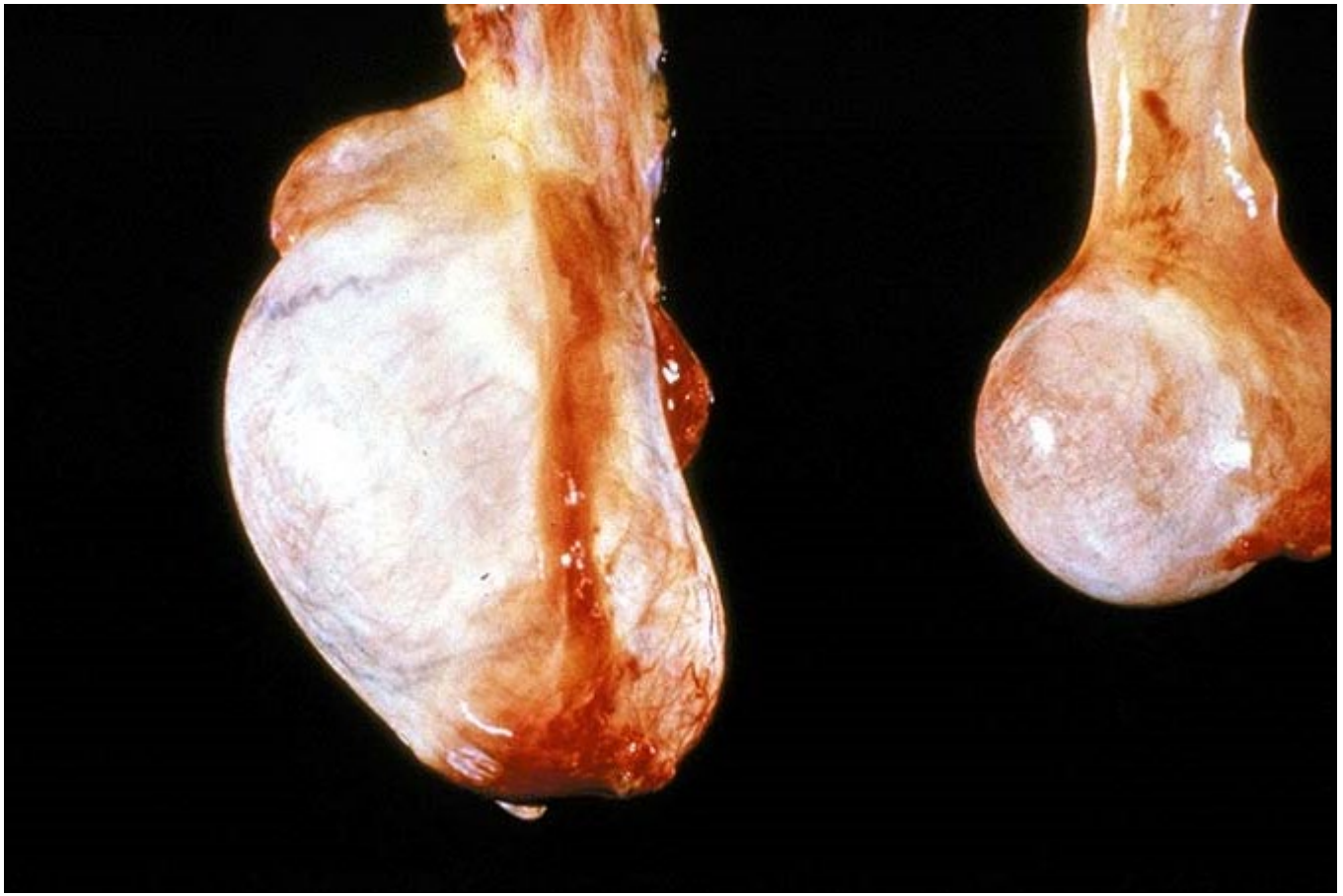
http://oceanplasma.org/documents/cases_1.php?iid=8&category=Cases&page=&action=item&title=Case%20

Pathologic

Loss of Endocrine Stimulation

Many hormone-responsive tissues, such as the breast and reproductive organs, are dependent on endocrine stimulation for normal metabolism and function

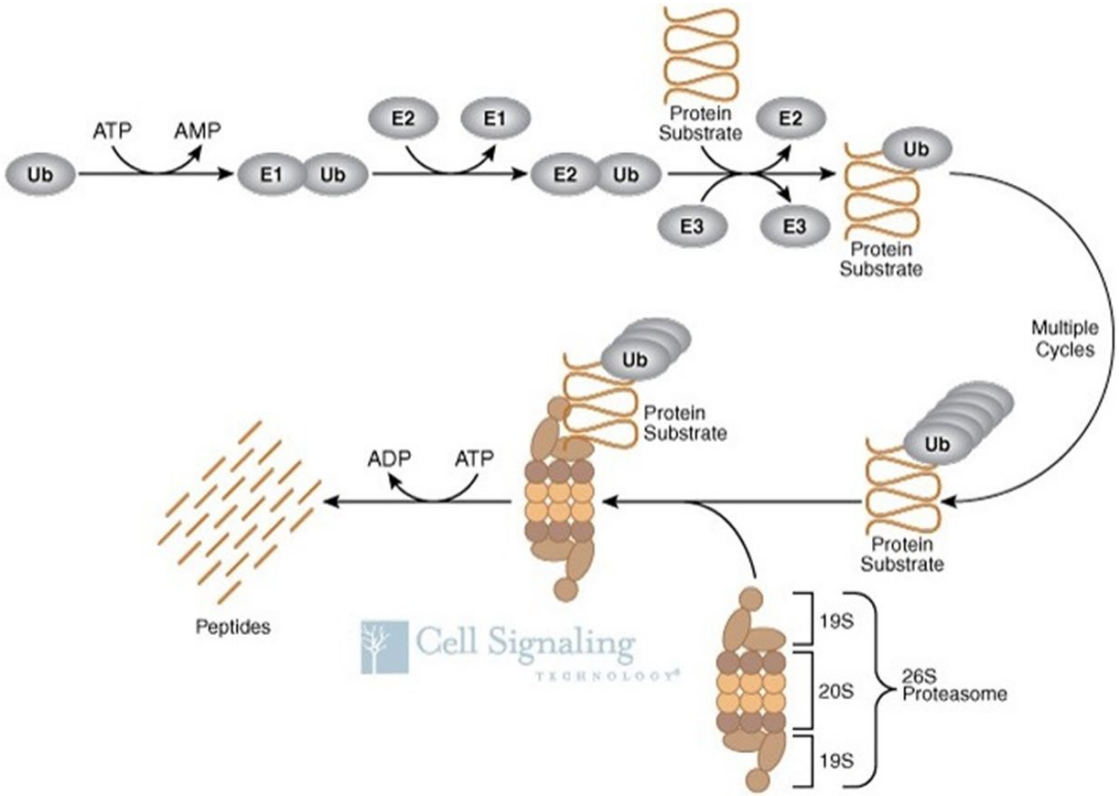
testicular atrophy



MECHANISMS of ATROPHY

Decreased protein synthesis and increased protein degradation in cells because of reduced metabolic activity.

The degradation of cellular proteins occurs mainly by the ubiquitin-proteasome pathway.



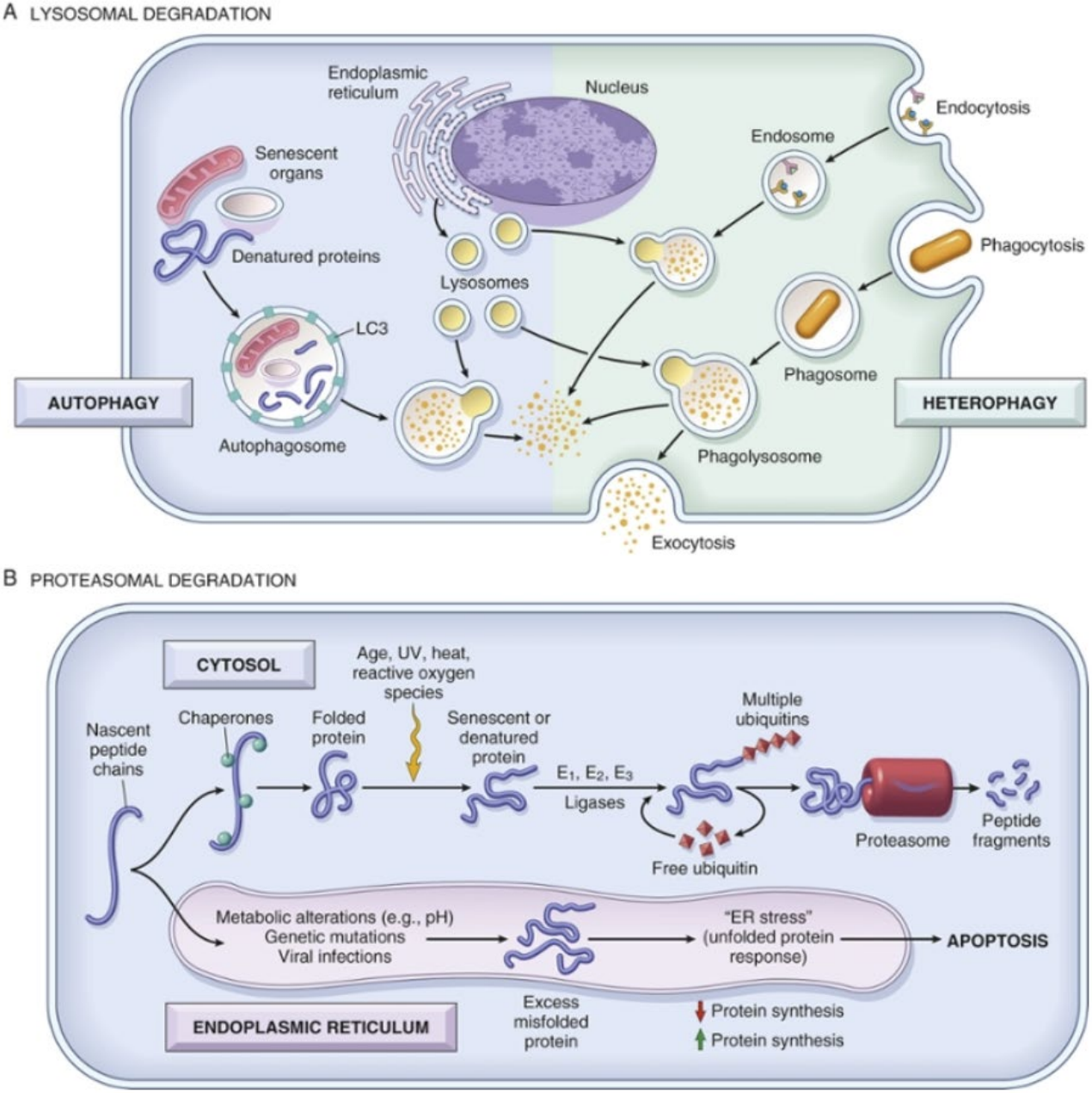
Autophagy

Atrophy can be accompanied by increased autophagy

Autophagy ("self eating") is the process in which the starved cell eats its own components

Autophagic vacuoles are membrane-bound vacuoles that contain fragments of cell components

The vacuoles ultimately fuse with lysosomes, and their contents are digested by lysosomal enzymes

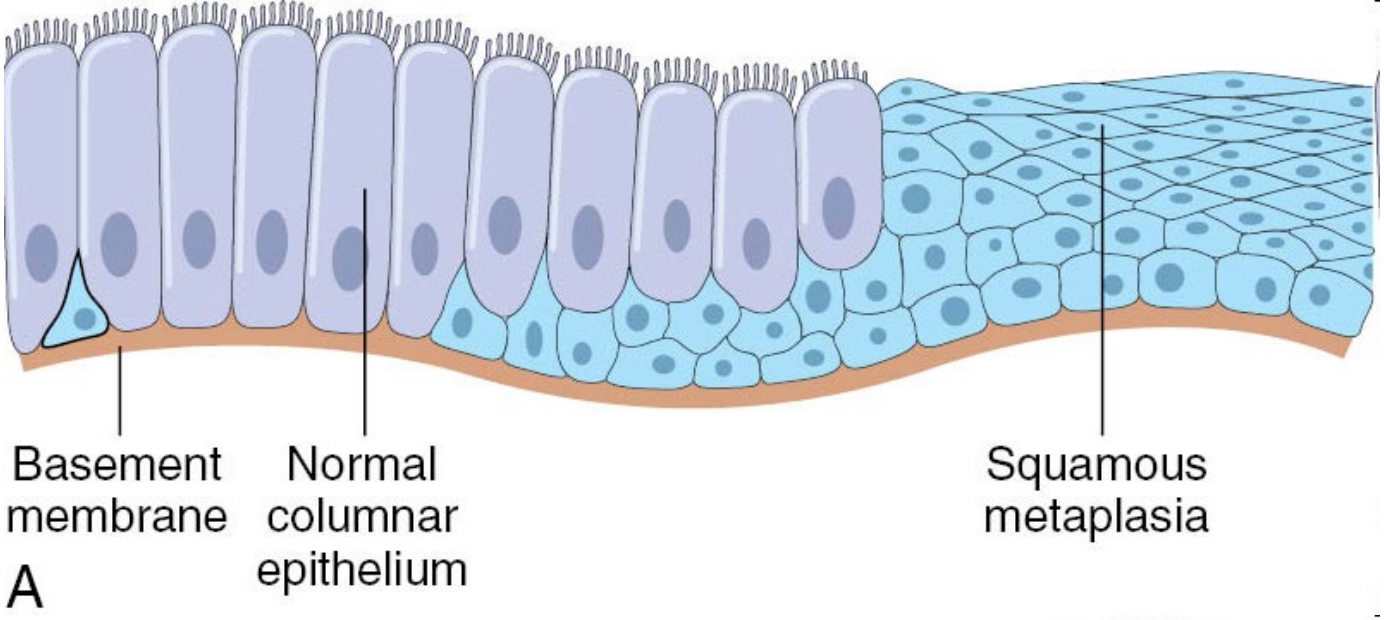


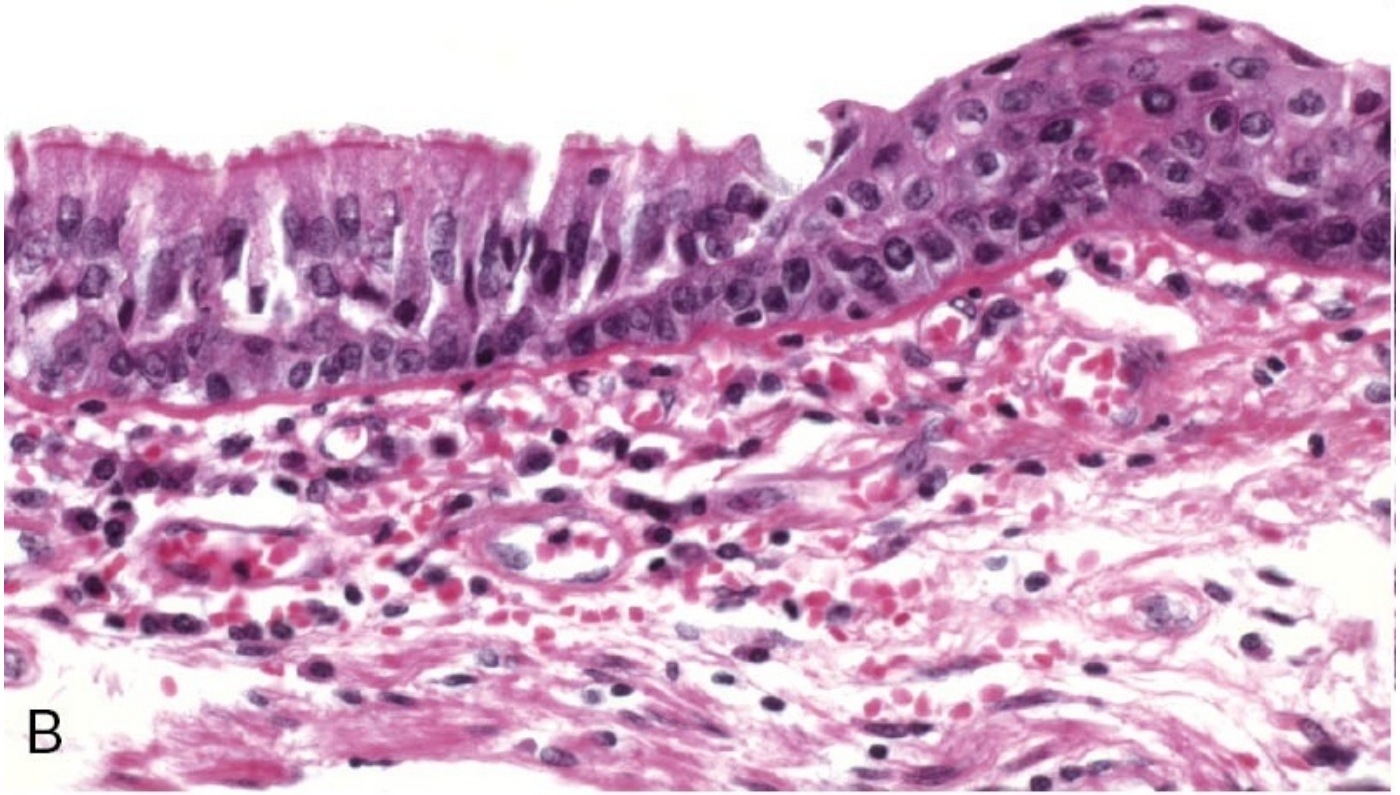
Robbins Basic Pathology

METAPLASIA

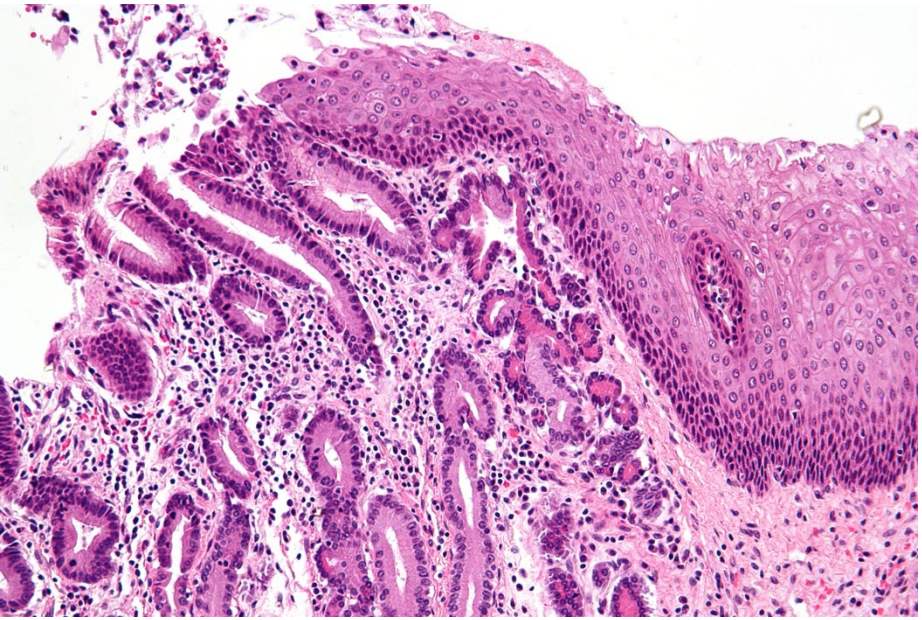
Reversible change in which one differentiated cell type is replaced by another cell type.

It may represent an adaptive substitution of cells that are sensitive to stress by cell types better able to withstand the adverse environment

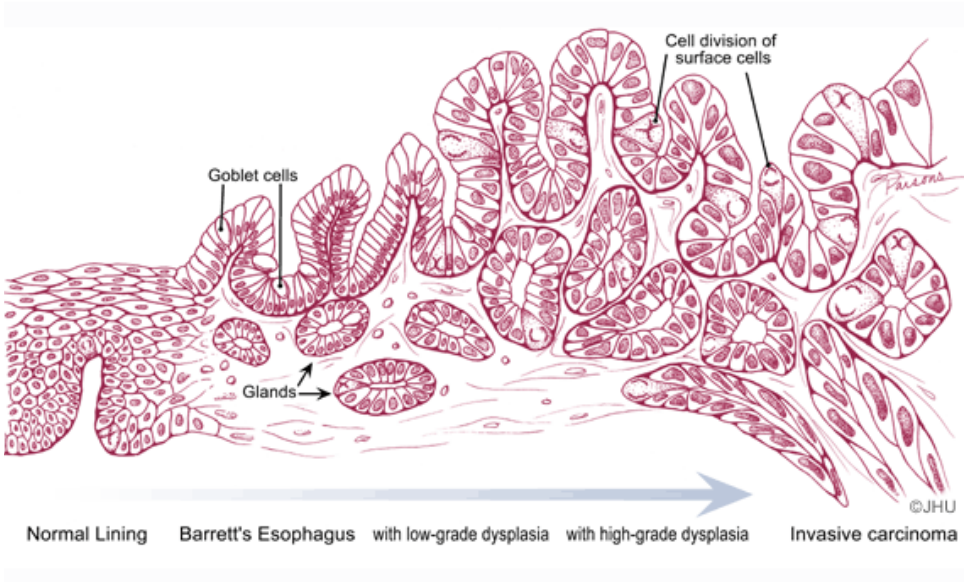




Metaplasia of esophageal epithelium



http://upload.wikimedia.org/wikipedia/commons/1/17/Pancreatic_acinar_metaplasia_-_high_mag.jpg



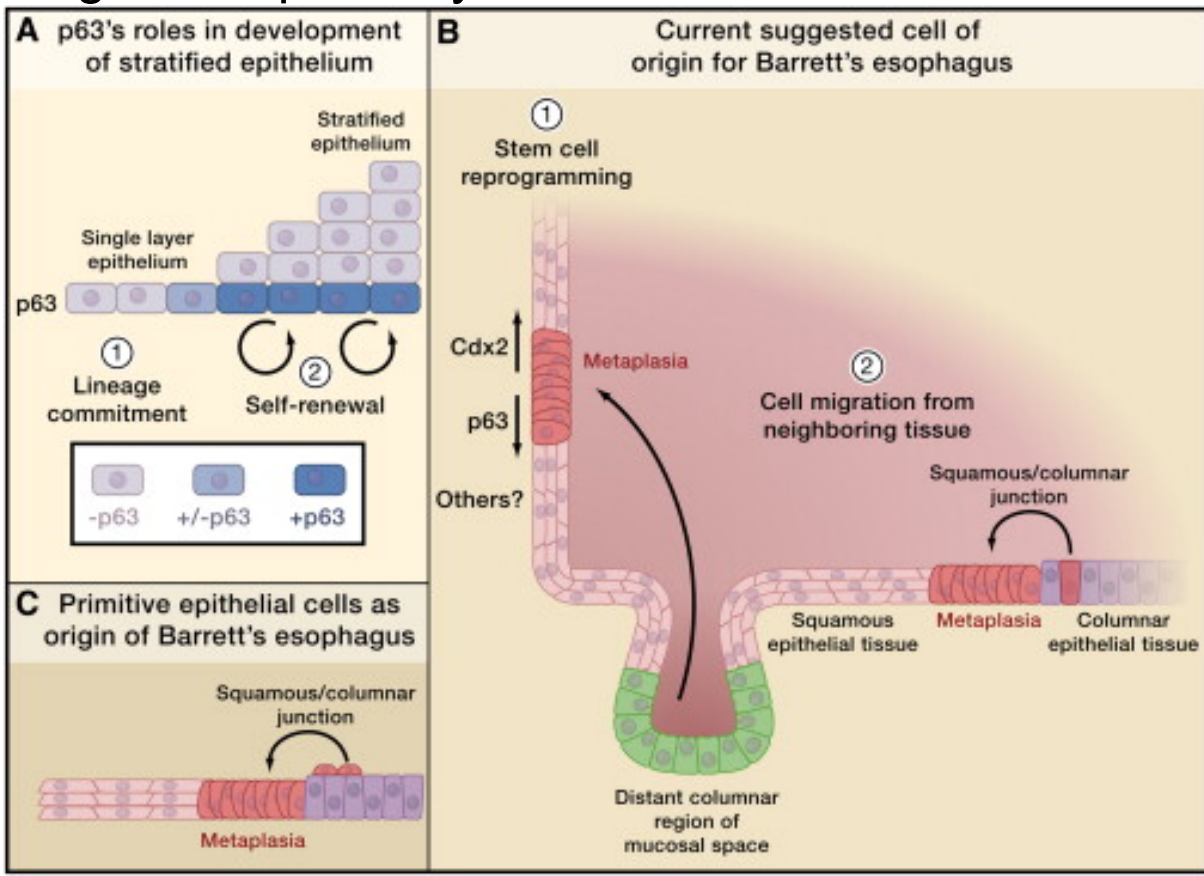
Glandular, or Barrett's,metaplasia of the normal esophageal squamous mucosa has occurred here, with the appearance of gastric type columnar mucosa, secondary to gastric reflux.

Mechanisms of Metaplasia

Result of a reprogramming of stem cells that are known to exist in normal tissues, or of undifferentiated mesenchymal cells present in connective tissue

Precursor cells differentiate along a new pathway

The differentiation of stem cells to a particular lineage is brought about by signals generated by cytokines, growth factors, and extracellular matrix components in the cells' environment



http://mahendrasinghphd.blogspot.com/2011/07/molecular-dissection-of-barretts.html