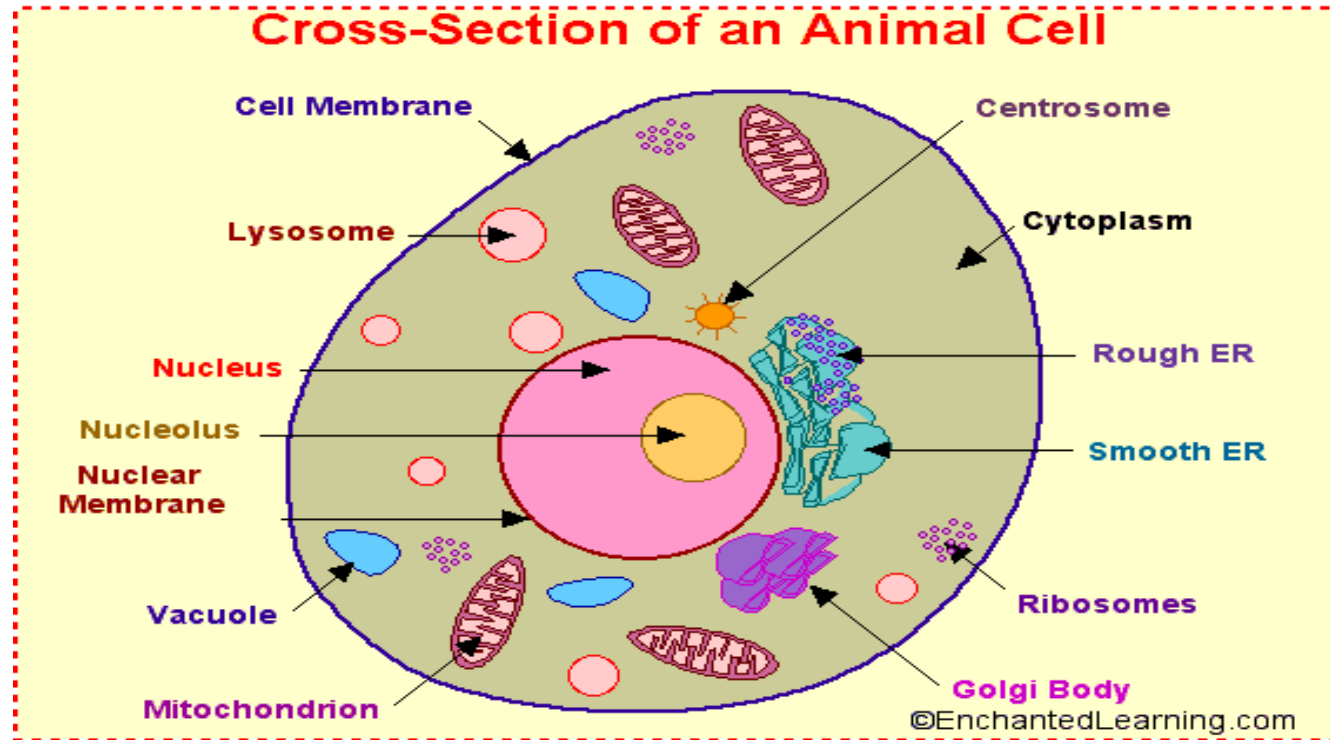
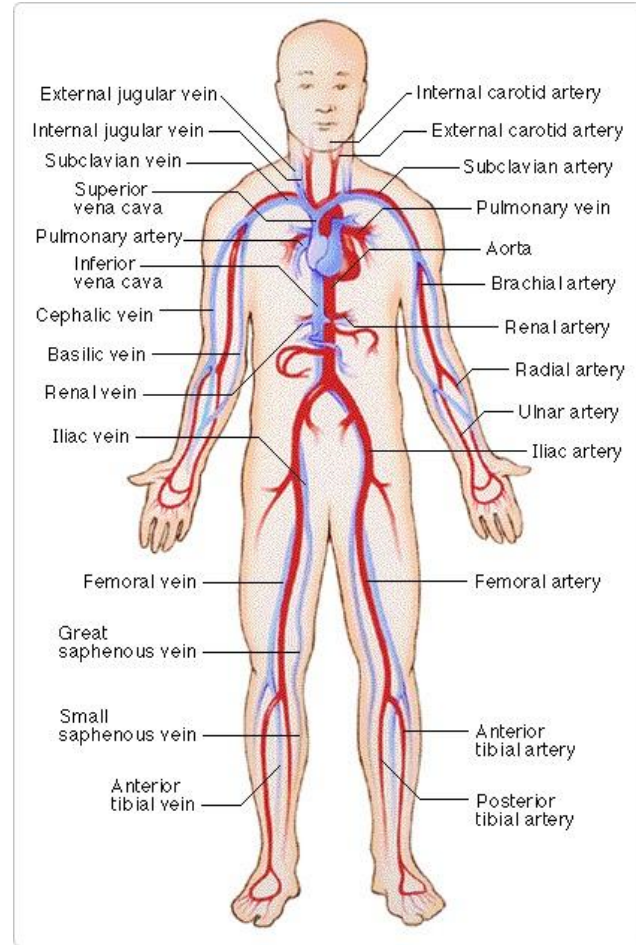
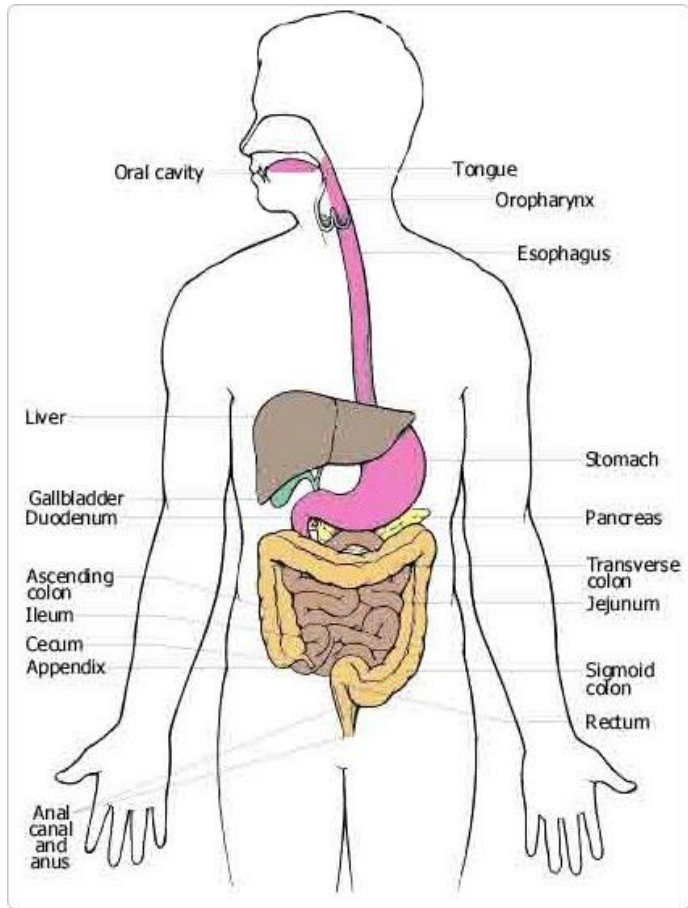


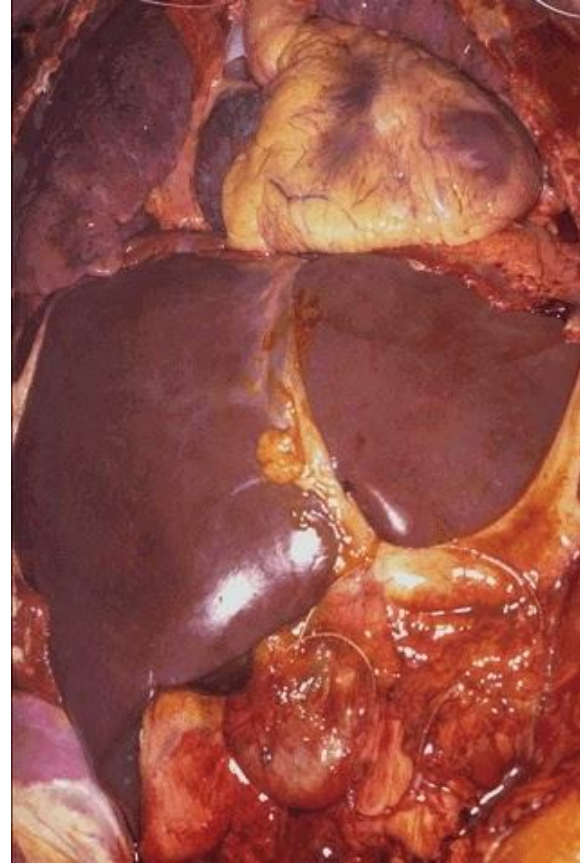
When Cells Die
MIT ESP Splash 2013
Andrew Thompson

typical cartoon cell



cartoon anatomy man





When homeostasis can't be achieved=injury

Cells can

- 1) Adapt
- 2) reversible injury
- 3) Irreversible injury

Adaptation

hyperplasia -more cells

hypertrophy -bigger cells

atrophy -fewer, smaller cells

metaplasia- change to different cell type

Reversible injury

lack of ATP, switch to anaerobic respiration.
Cytosol more acidic, ion pumps start to fail

Cell swelling -ion & water balance

detachment of ribosomes from rough ER

less protein synthesis

What's a cell to do?

Decreased ATP leads to more glycolysis -more acid. pH down

Decreased ATP lets ion pumps fail -water and ions flow freely

in this environment, ribosomes detach from endoplasmic reticulum , limiting protein production-*no membrane proteins?

the cell swells with water as osmoregulation is lost.

organelles swell

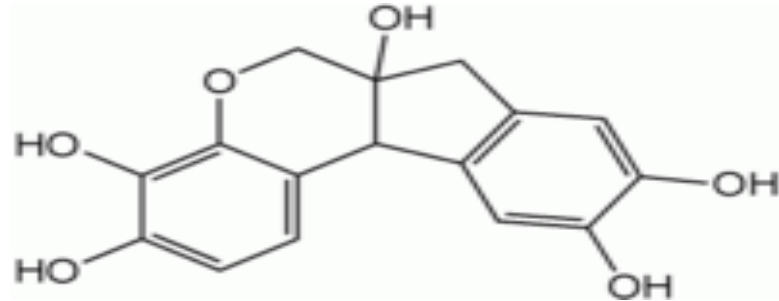
the cell membrane develops "blebs"

Hematoxylin&Eosin stains

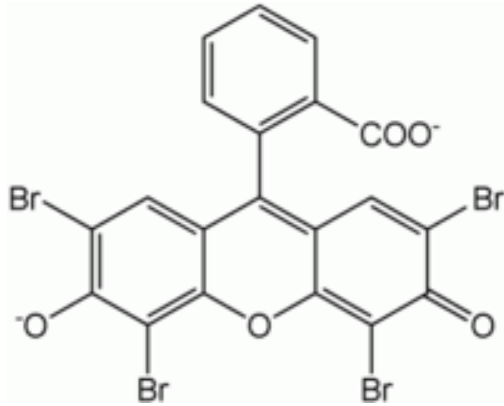


<http://waynesword.palomar.edu/ecoph4.htm>

Heartwood from logwood tree
A basic dye-basophilic



hematoxylin/eosin 2

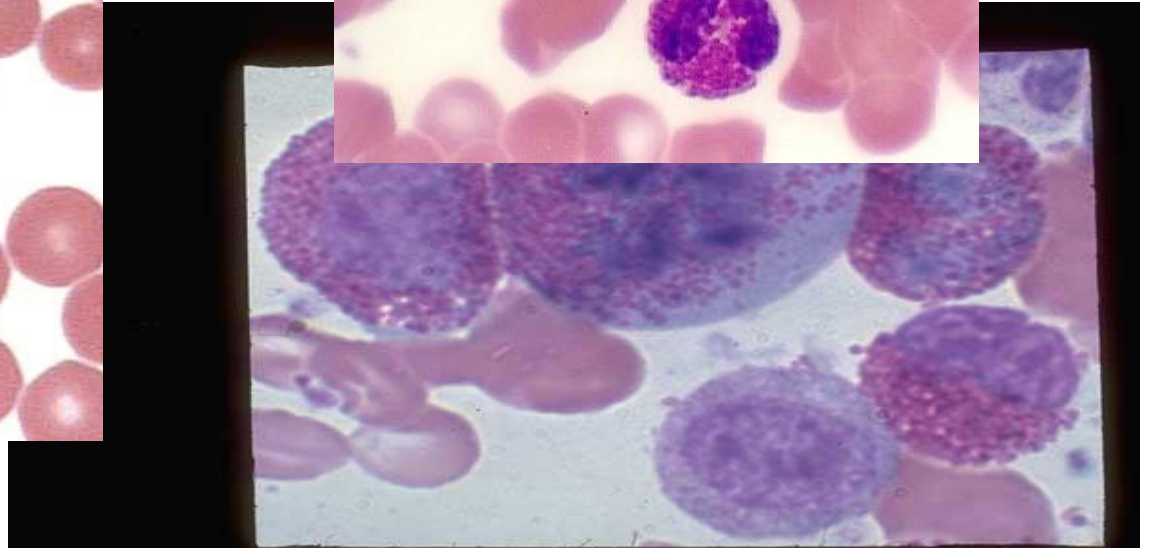
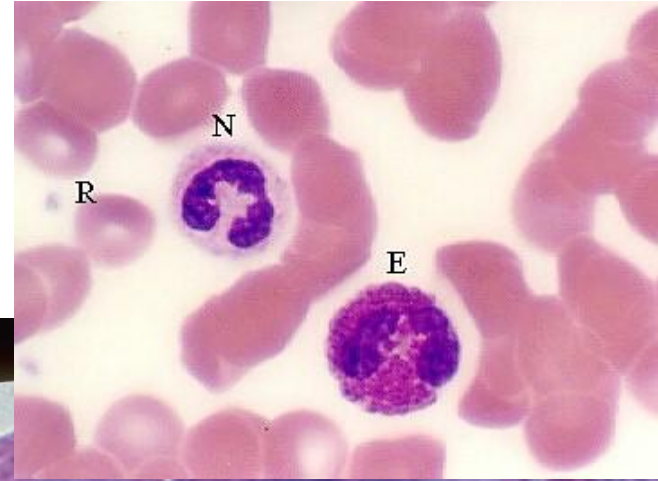
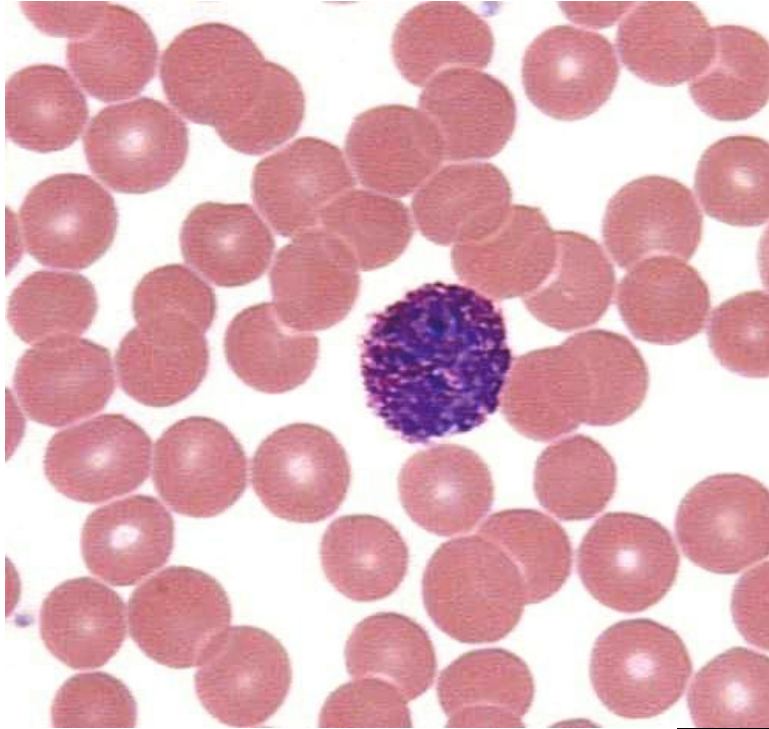


Eosin- fluorescent dye made from fluorescein.

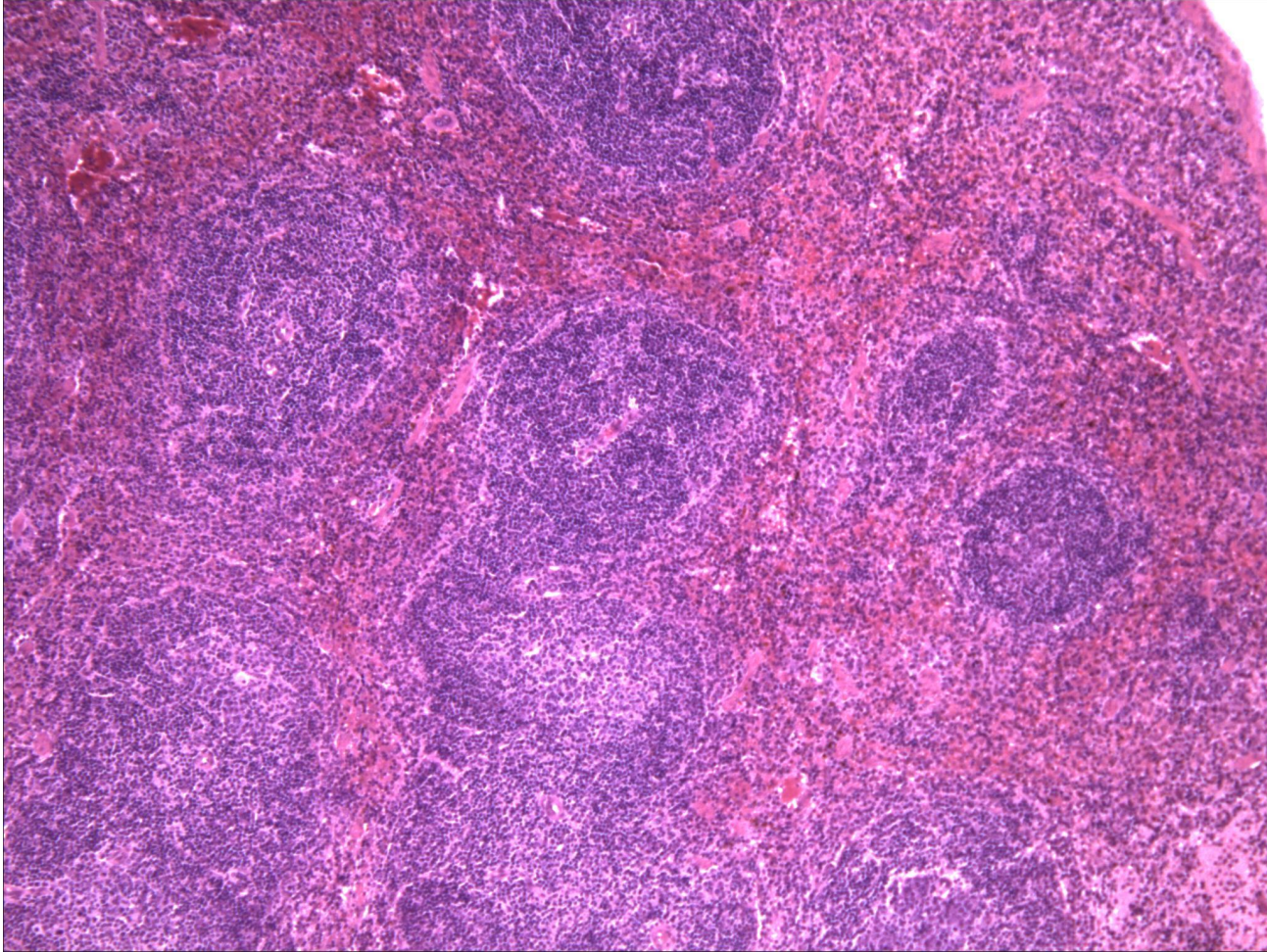
Fluorescein fully synthetic from phthalic anhydride+resorcinol

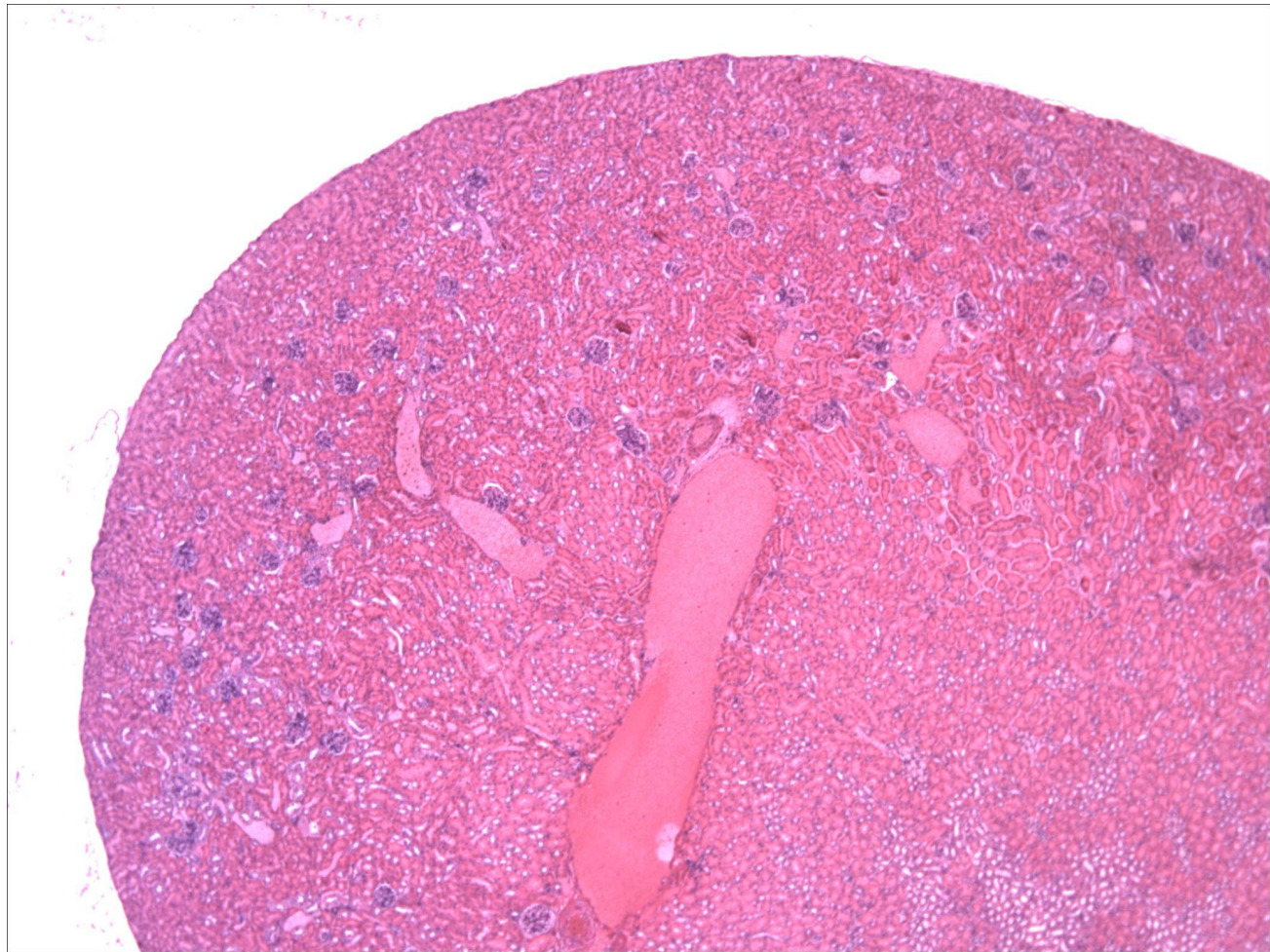
An acidic dye- acidophilic or eosinophilic

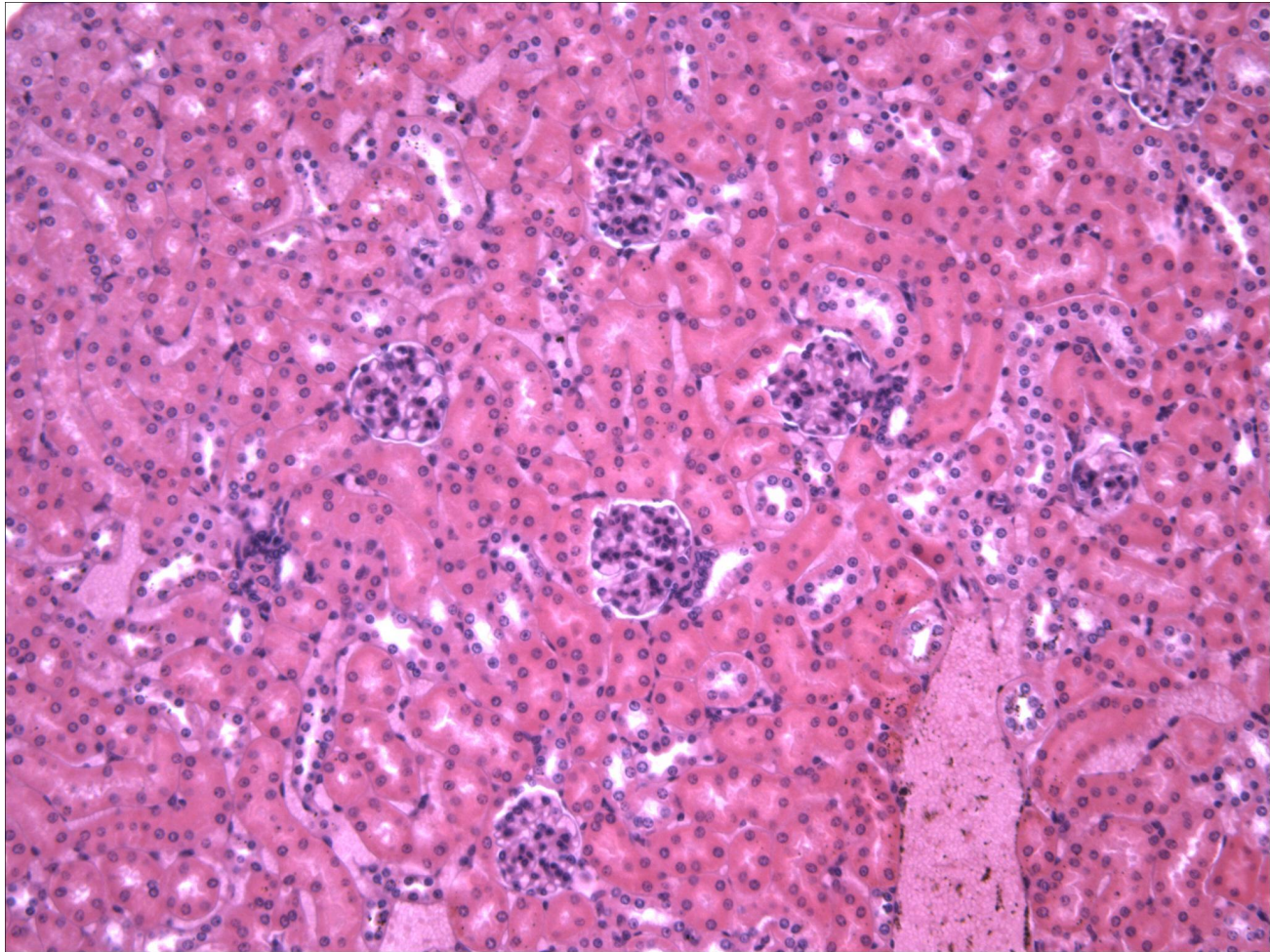
Basophilic vs. Acidophilic (eosinophilic)

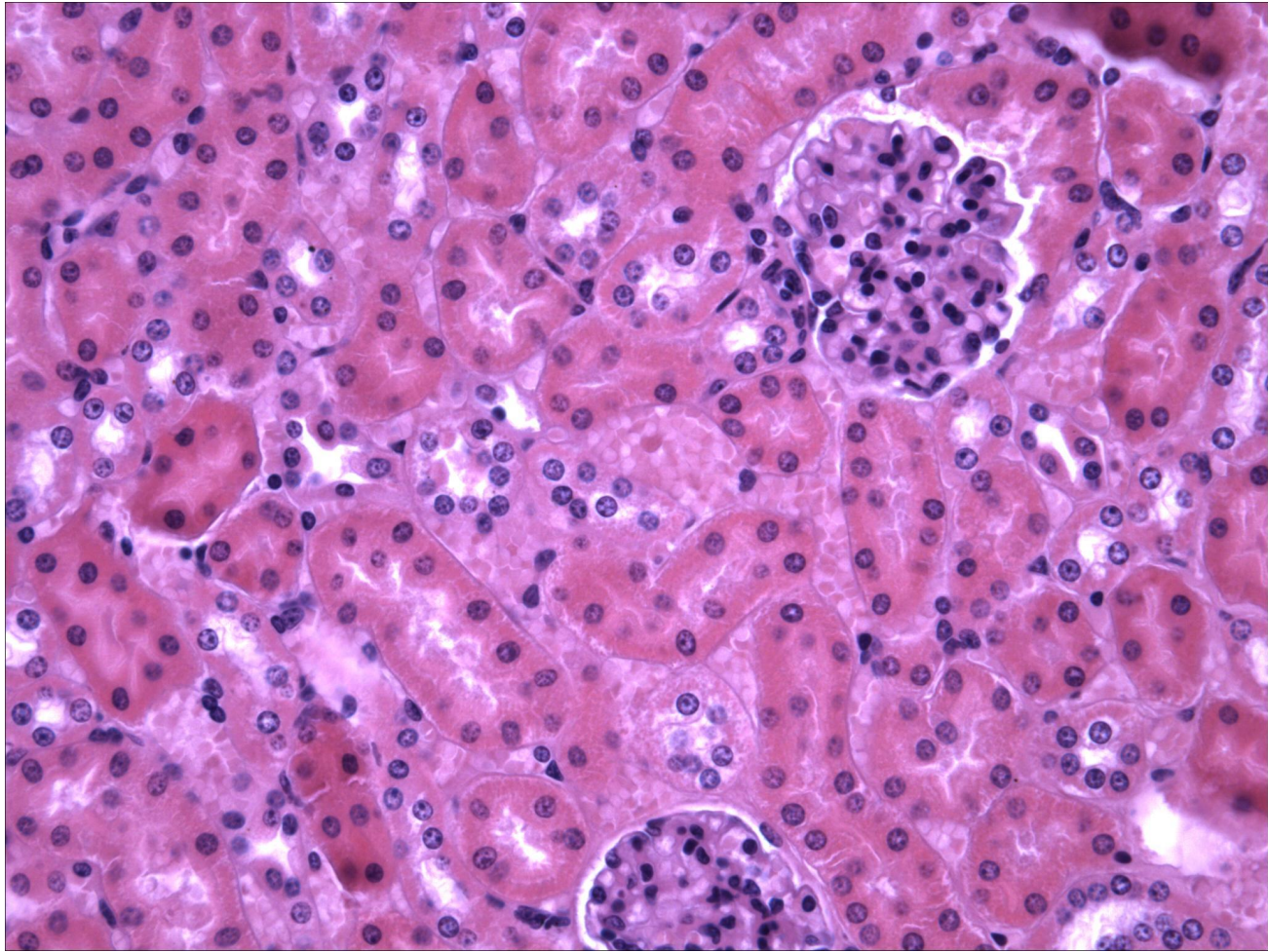


spleen







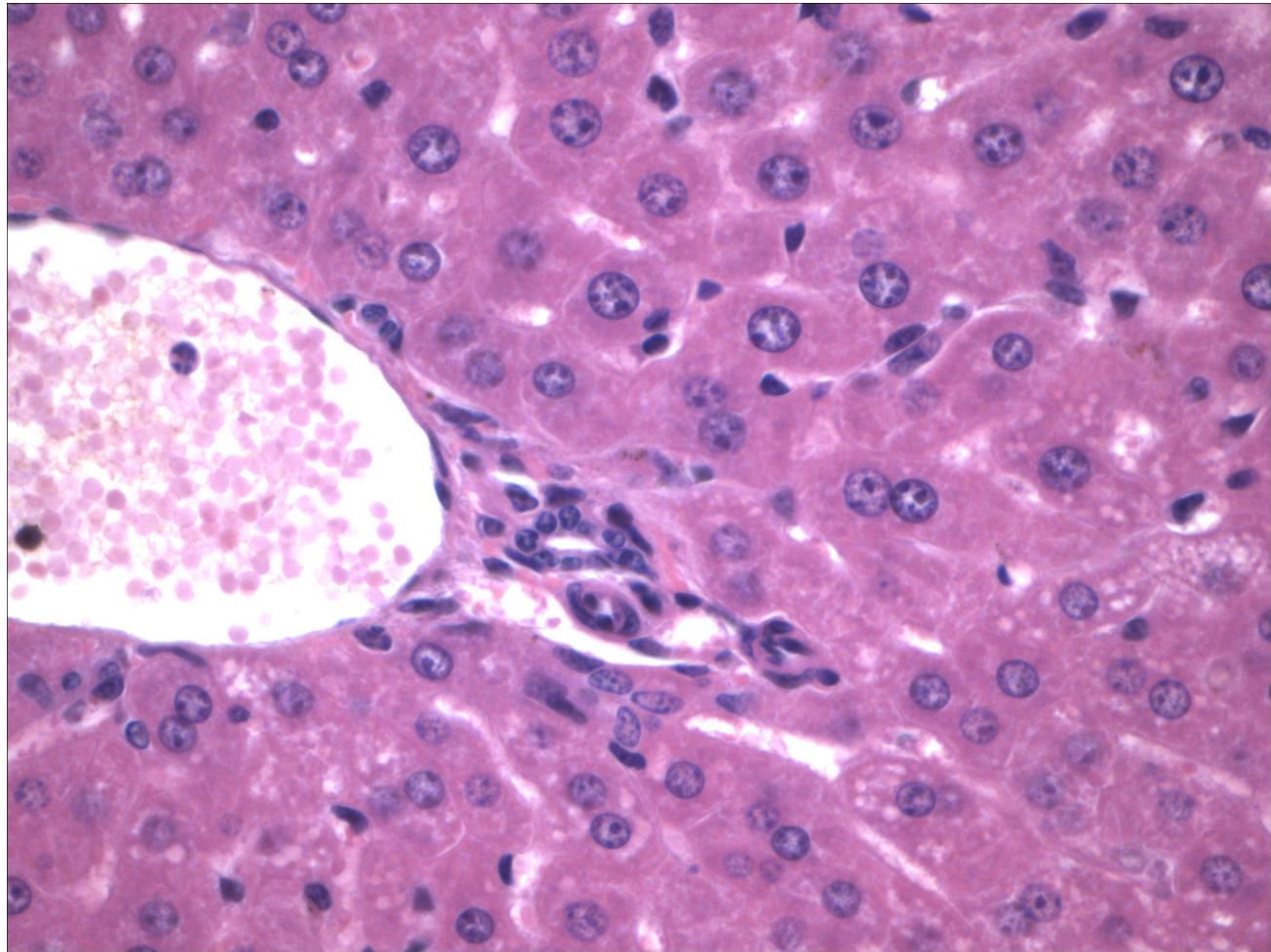


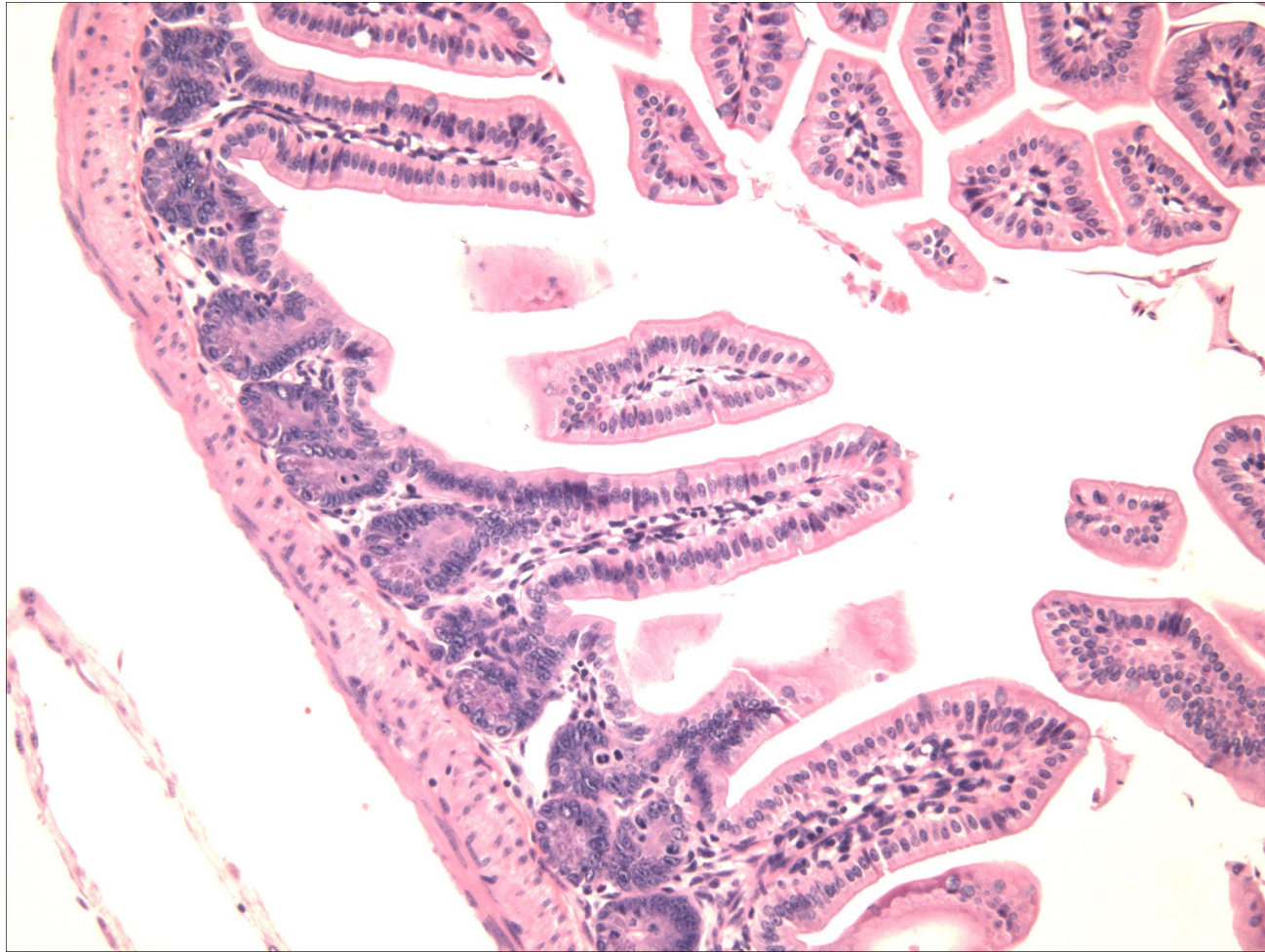
active vs "quiet" cells vs dividing cells

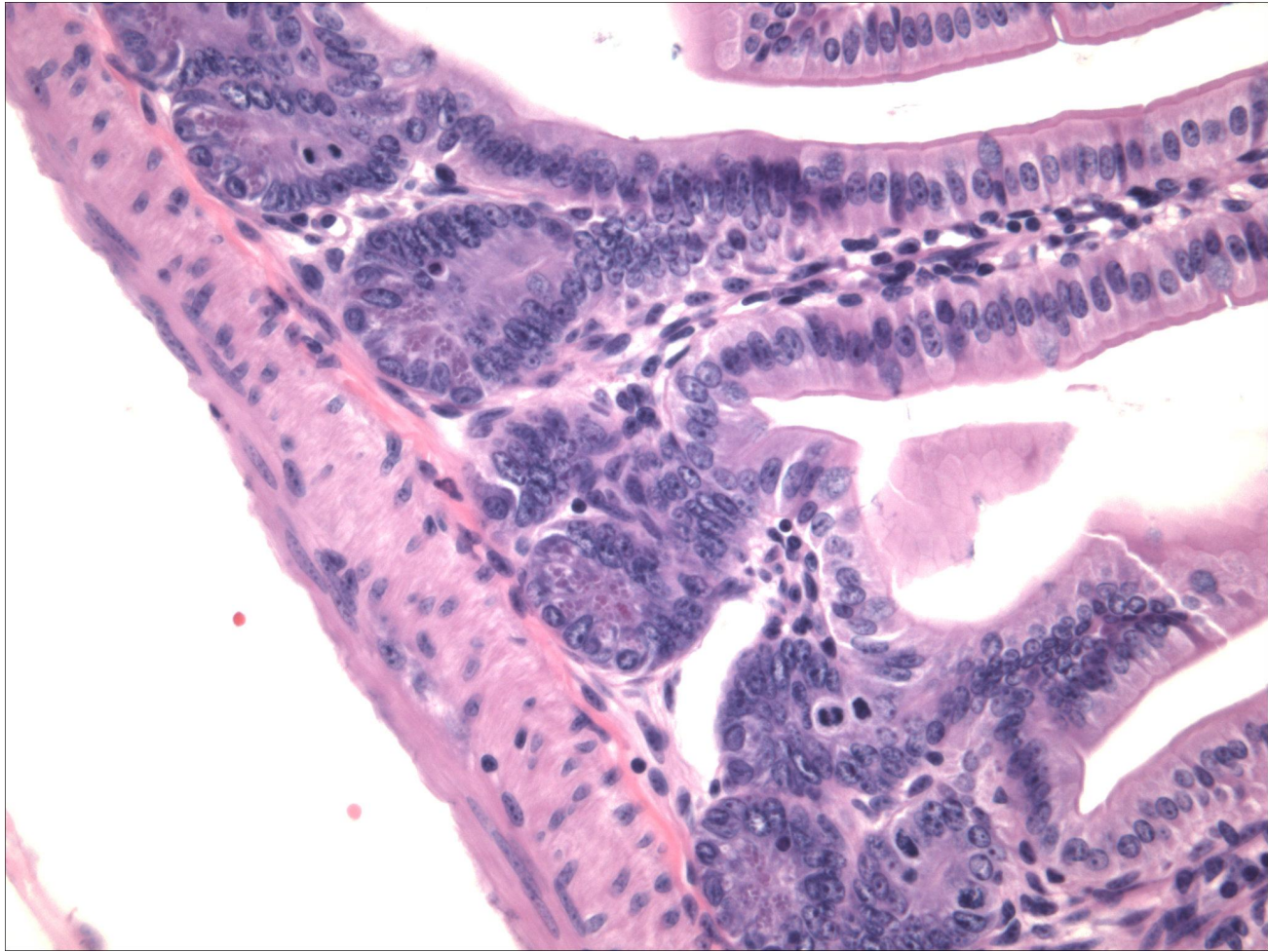
active -euchromatin. Unwound, pale staining, nucleolus,

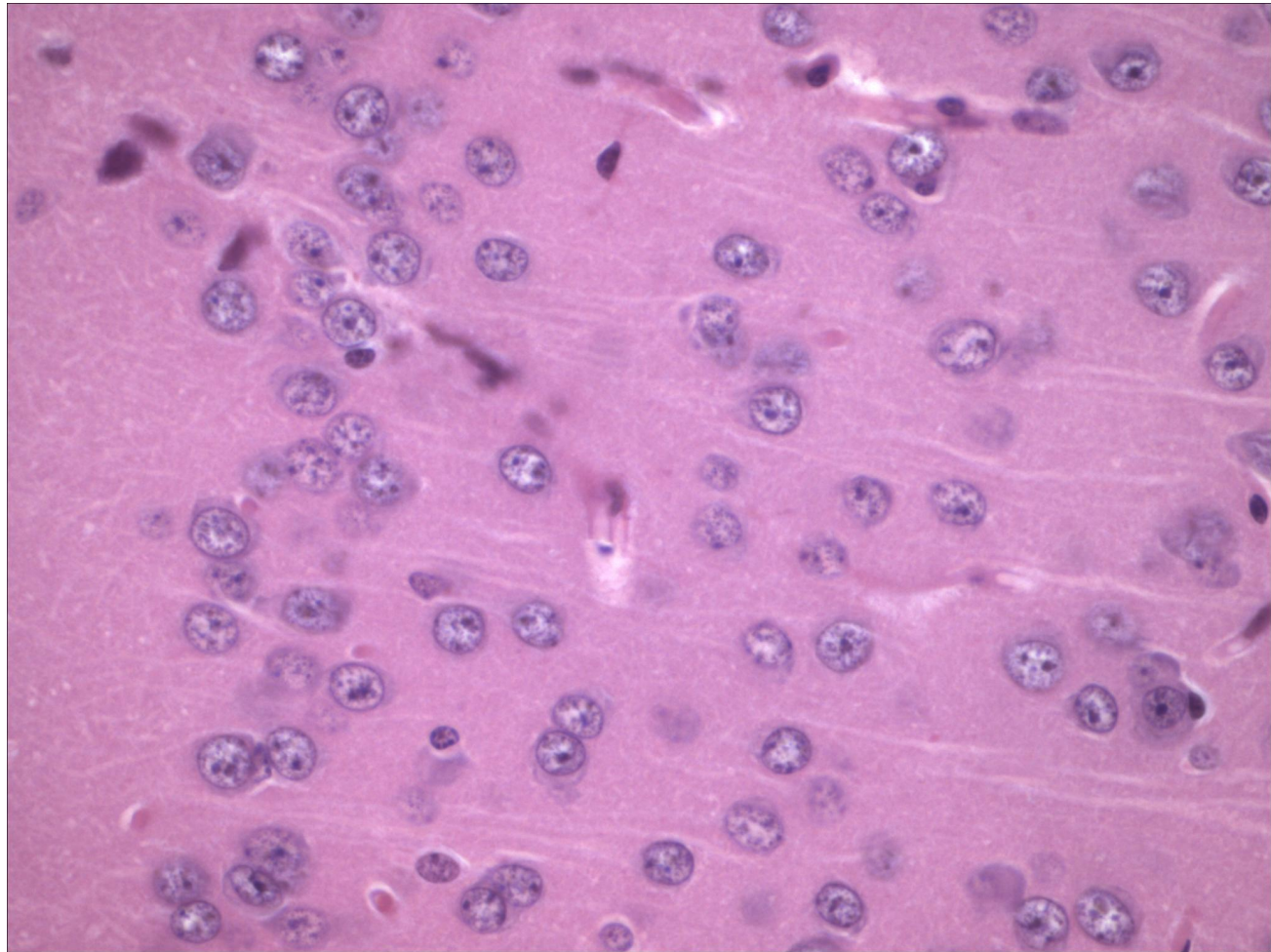
dividing -heterochromatin DNA condensed, wound tightly around histone proteins

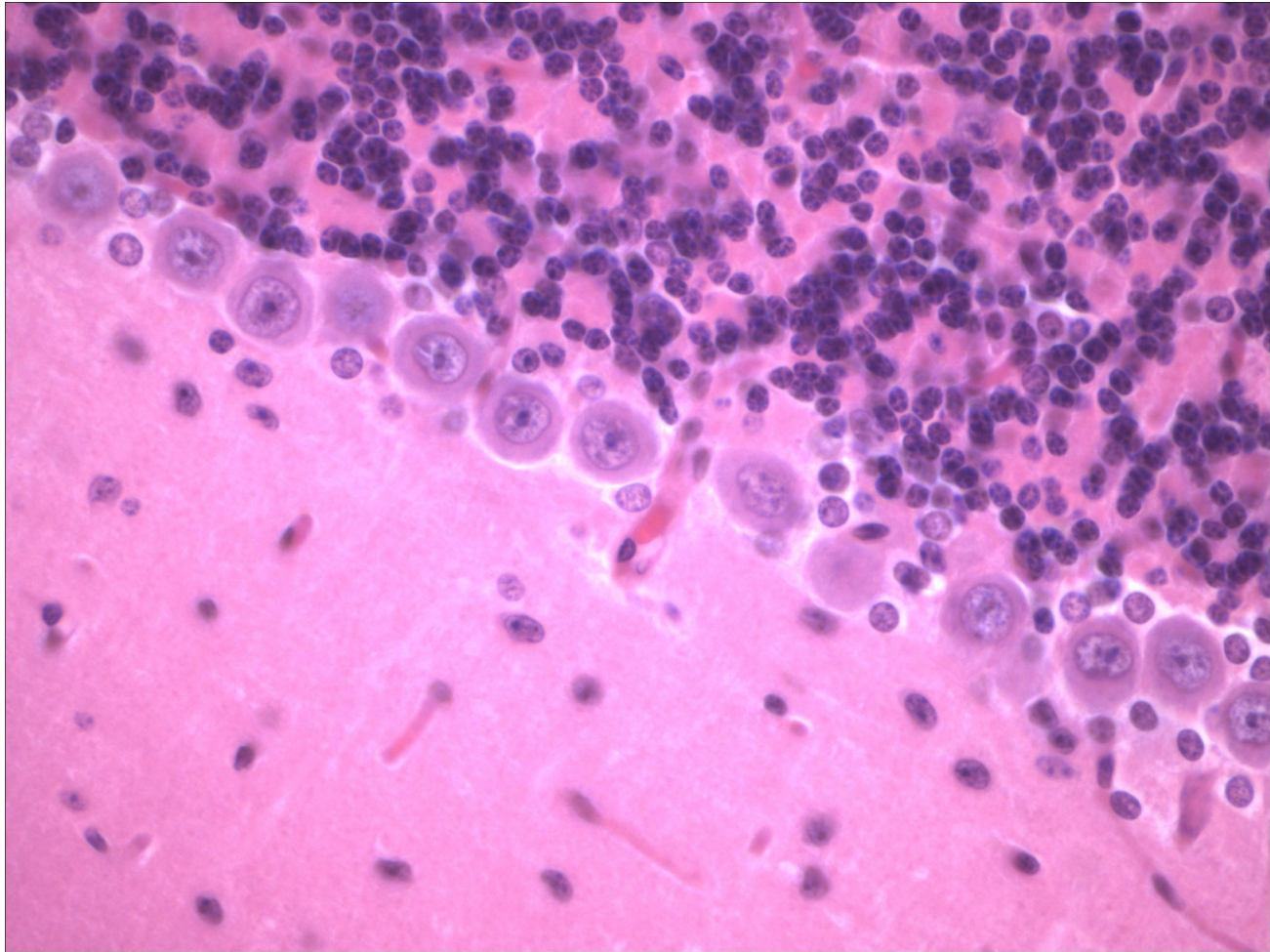
"quiet"?











Cell injury patterns

Reversible adaptation:

hyperplasia-increase in cell number

hypertrophy-increase in cell size

metaplasia-change in cell type

atrophy-change in cell size

Irreversible: cell death and necrosis

coagulative: cell death in setting of ischemia

liquifactive: cell death in setting of bacterial infection

caseous: combination of coagulative and

liquifactive.

Often seen in tuberculosis

fatty necrosis: cell digestion and release of fatty

acids

and calcium. In setting of pancreas

Ischemia & ions

Less/no ATP

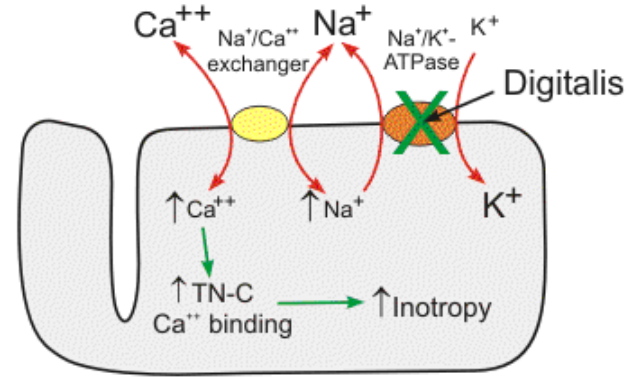
ATPase ions pumps fail

cell swells

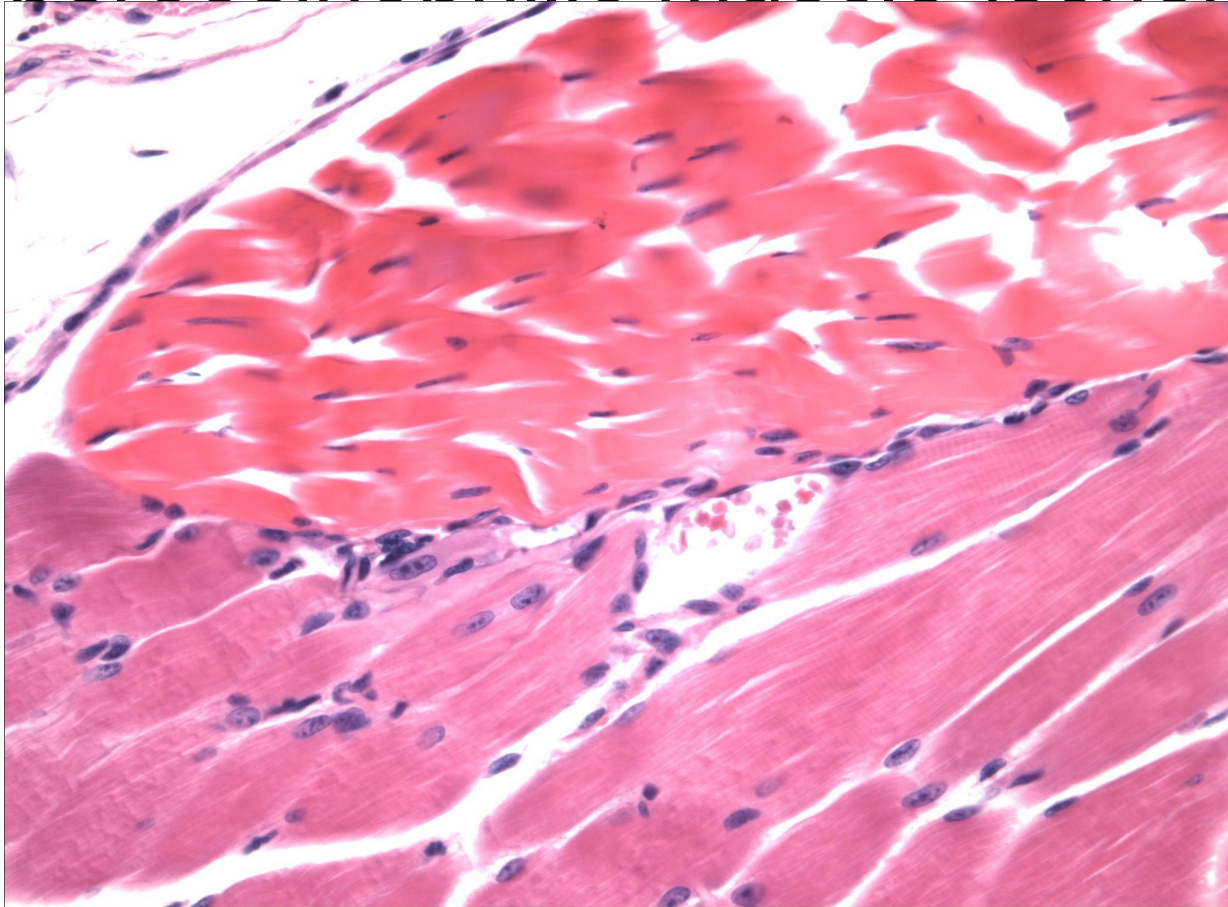
calcium escapes sequestering

glycolysis lowers pH lysosomes degrade cytosol-eosinophilia,
autodigestion

reperfusion injury- "tourniquet shock"?



hypereosinophilic muscle-ischemic



hydropic change

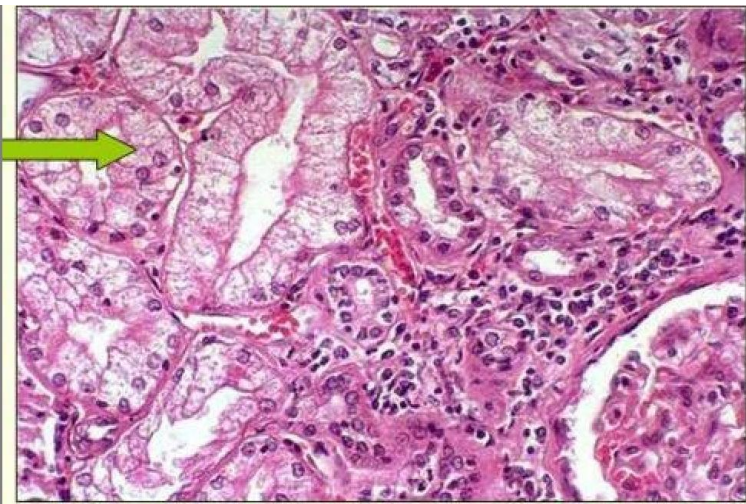
cell swelling

membrane blebs

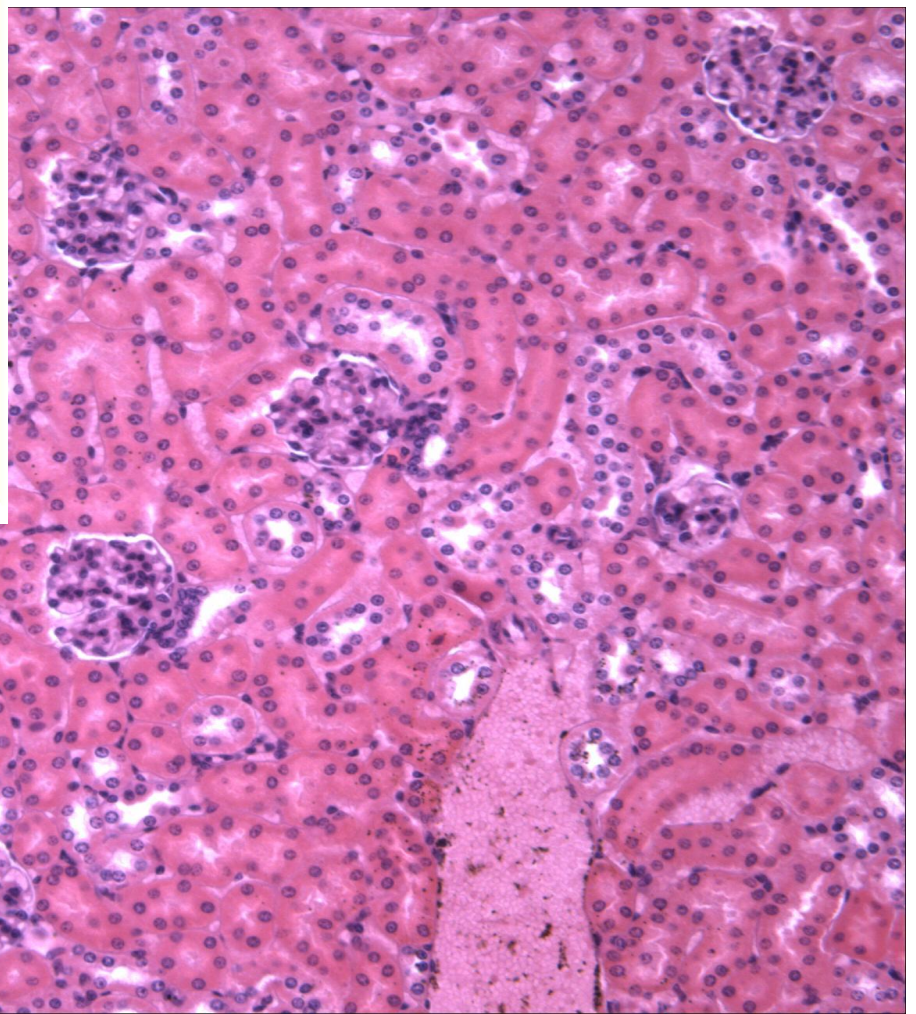
organelle swelling

detachment of ribosomes- pale hematoxylin staining

eventually vacuoles form within cell.



http://ocw.tufts.edu/data/51/551831/552071_xlarge.jpg

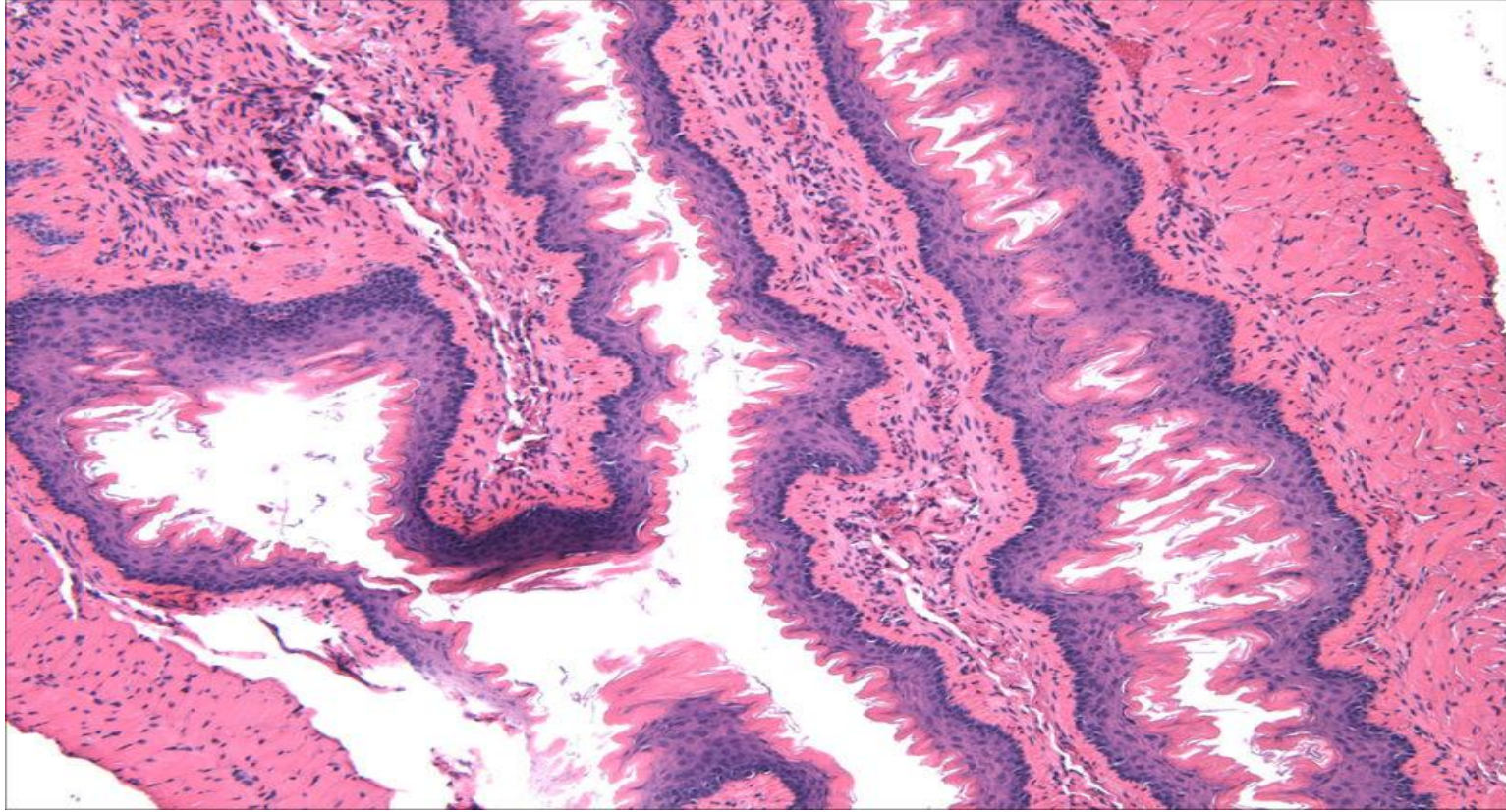


metaplasia

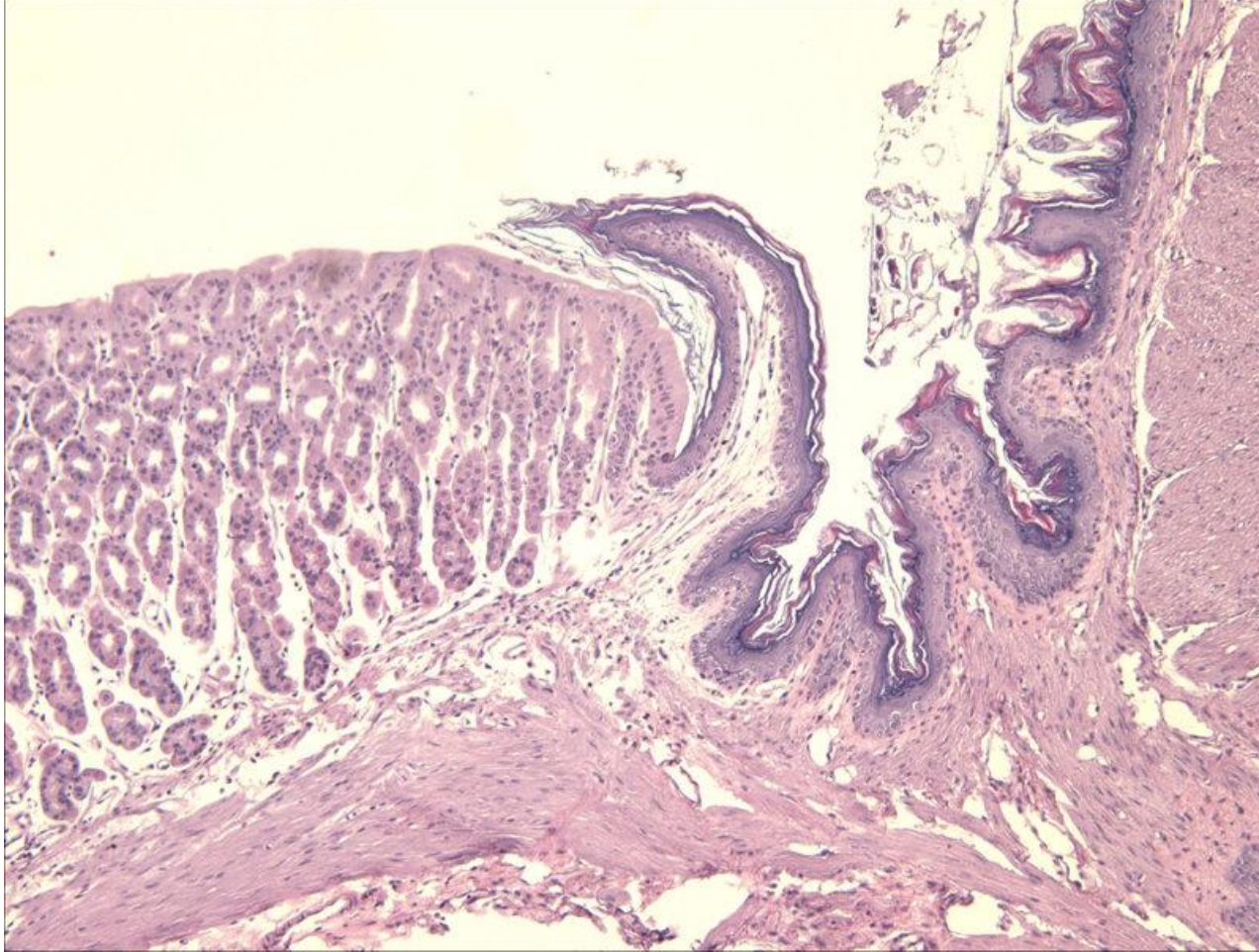
esophageal gastric junction



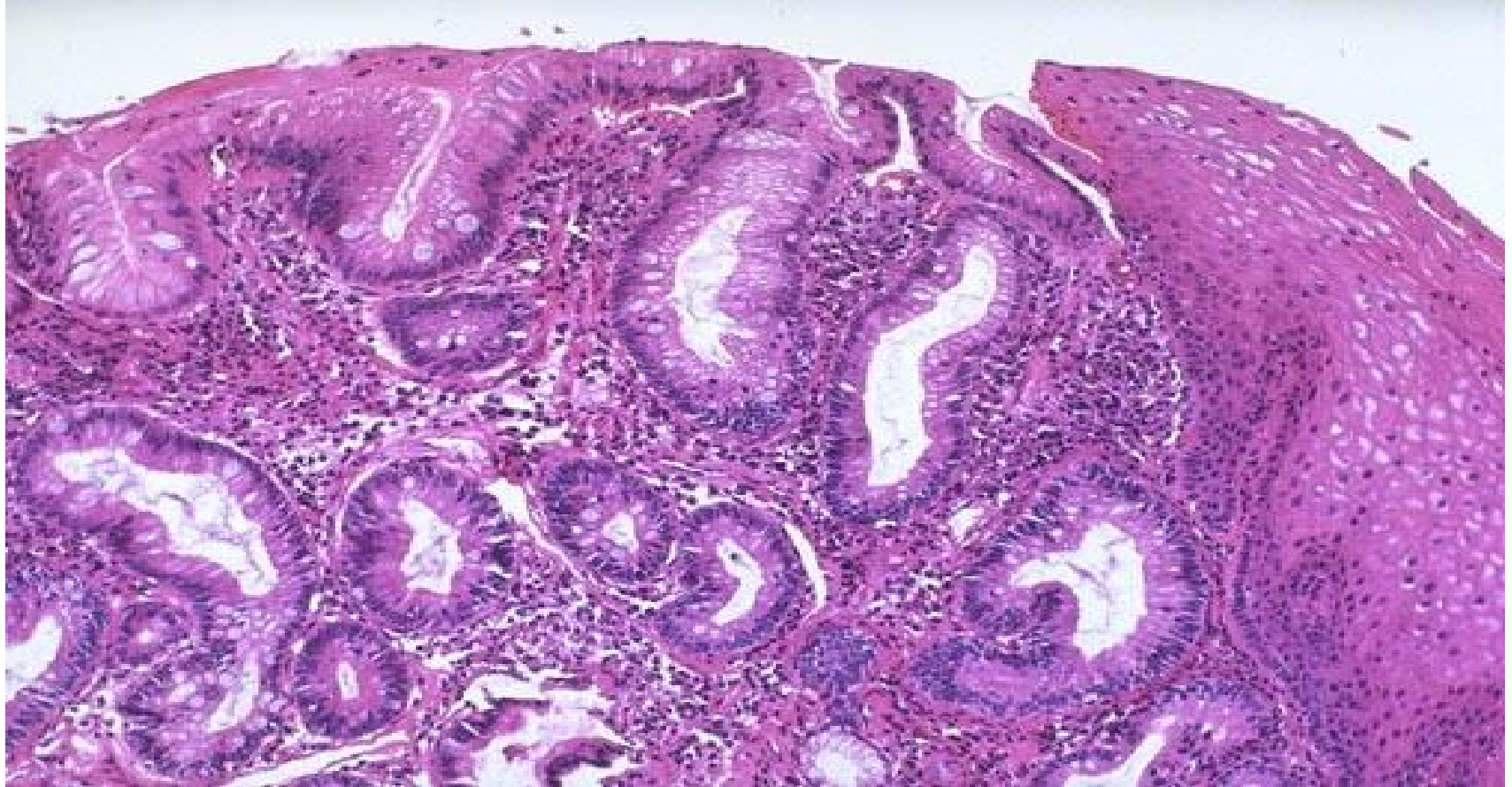
esophagus



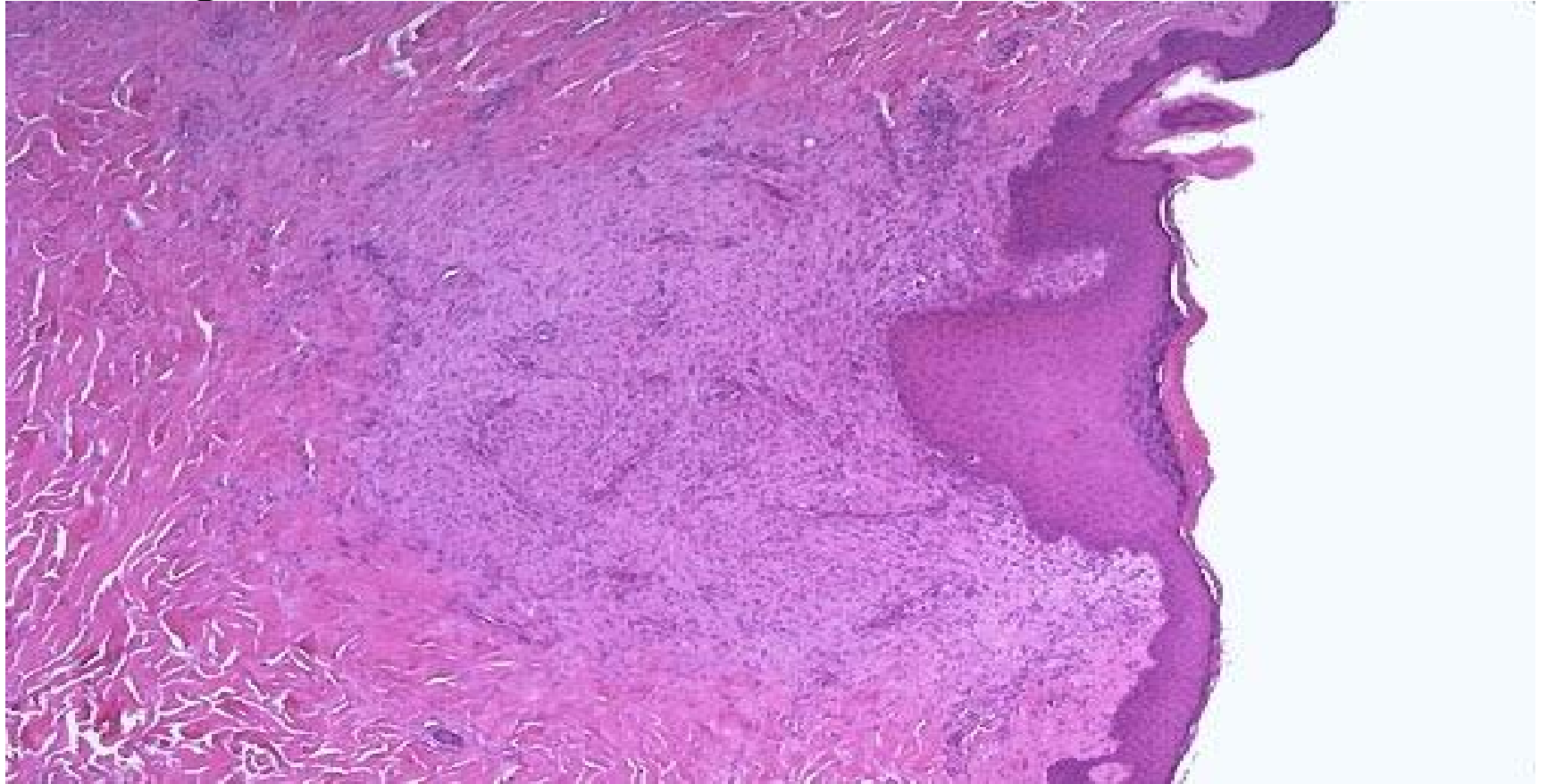
gastric esophageal junction- 100x



Barrett's esophagus

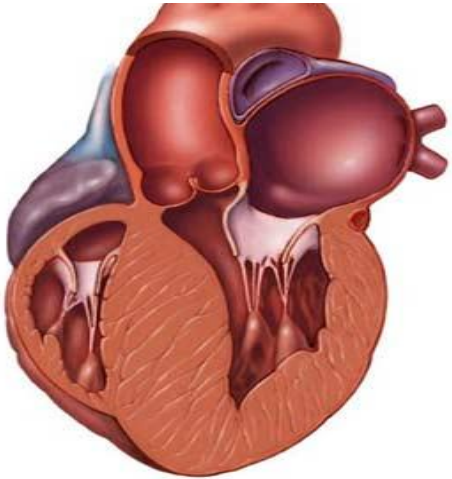
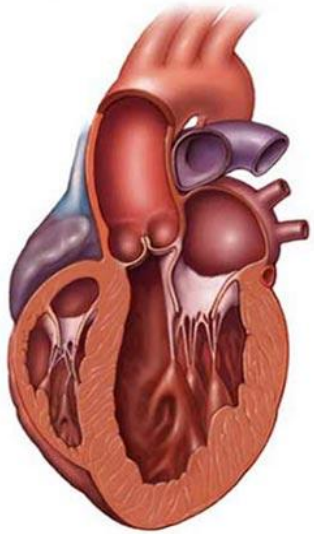


healing skin wound



Hypertrophy

heart hypertrophy



hypertrophy



Hyperplasia

Hyperplasia-cell proliferation



http://www.australianprescriber.com/upload/issue_files/2601_ging_02.gif



<http://img.tfd.com/mosby/thumbs/500099-fx5.jpg>

phenytoin (Dilantin)-anticonvulsant

Cyclosporine-immunosuppressant

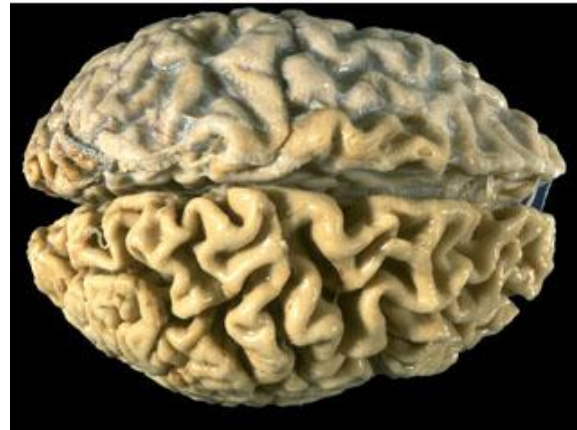
Nifedipine-calcium channel blocker

cause of drug induced gingival hyperplasia not well understood

atrophy



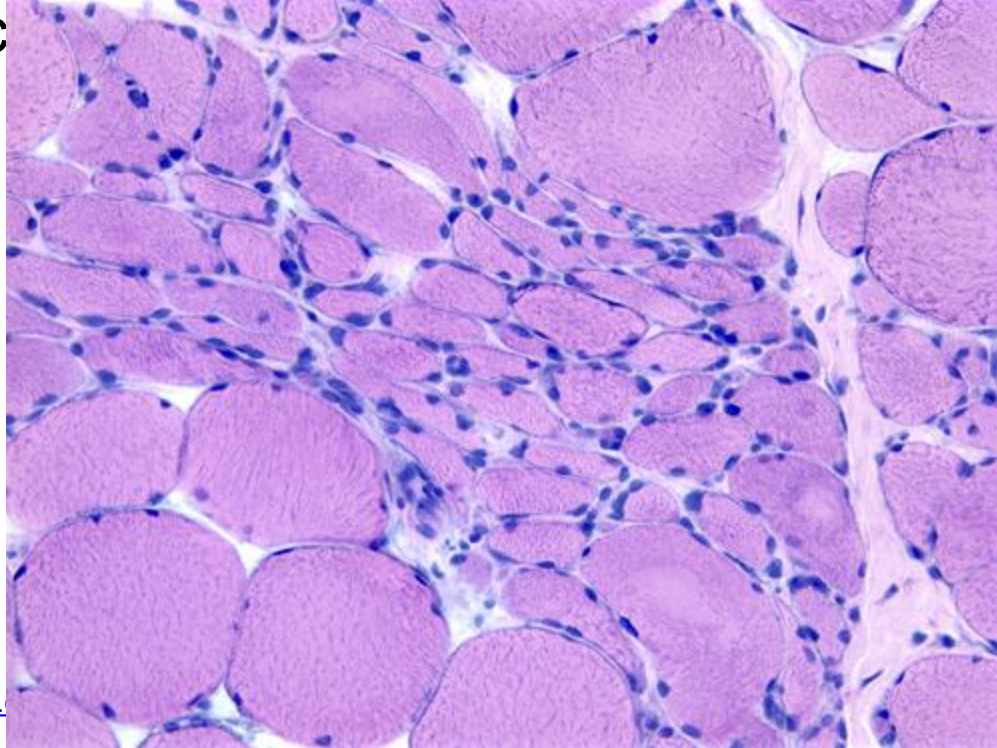
.jpg



<http://library.med.utah.edu/WebPath/jpeg5/CNS178.jpg>

<http://library.med.utah.edu/WebPath/jpeg5/CNS013.jpg>

denervation atrophy in
skeletal muscle



[http://neuropathology-web.
jpg](http://neuropathology-web.jpg)

What's a cell to do?

Decreased ATP leads to more glycolysis -more acid. pH down

Decreased ATP lets ion pumps fail -water and ions flow freely

in this environment, ribosomes detach from endoplasmic reticulum , limiting protein production-*no membrane proteins?

the cell swells with water as osmoregulation is lost.

organelles swell

the cell membrane develops "blebs"

Intracellular accumulations, extracellular depositions

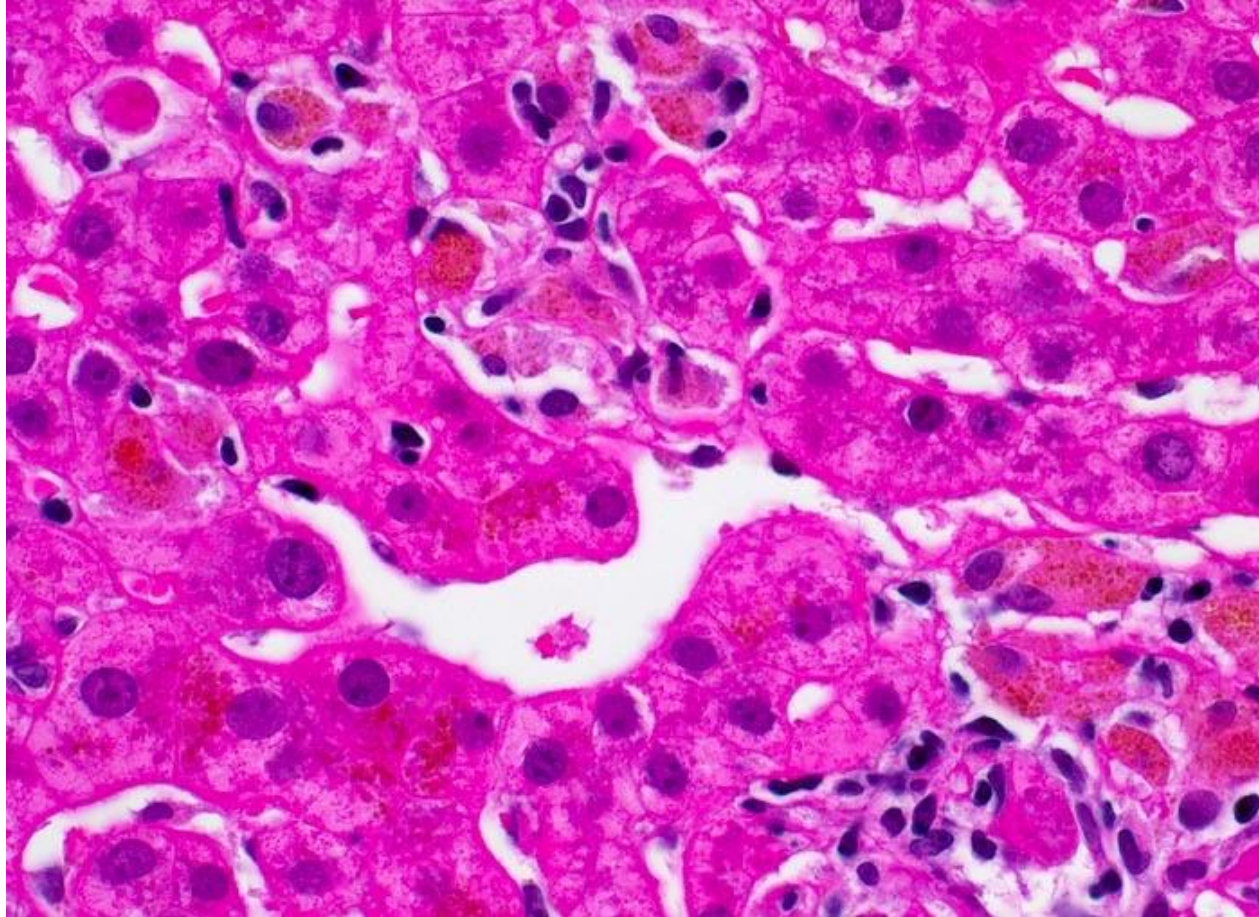
fatty change -steatosis

glycogen

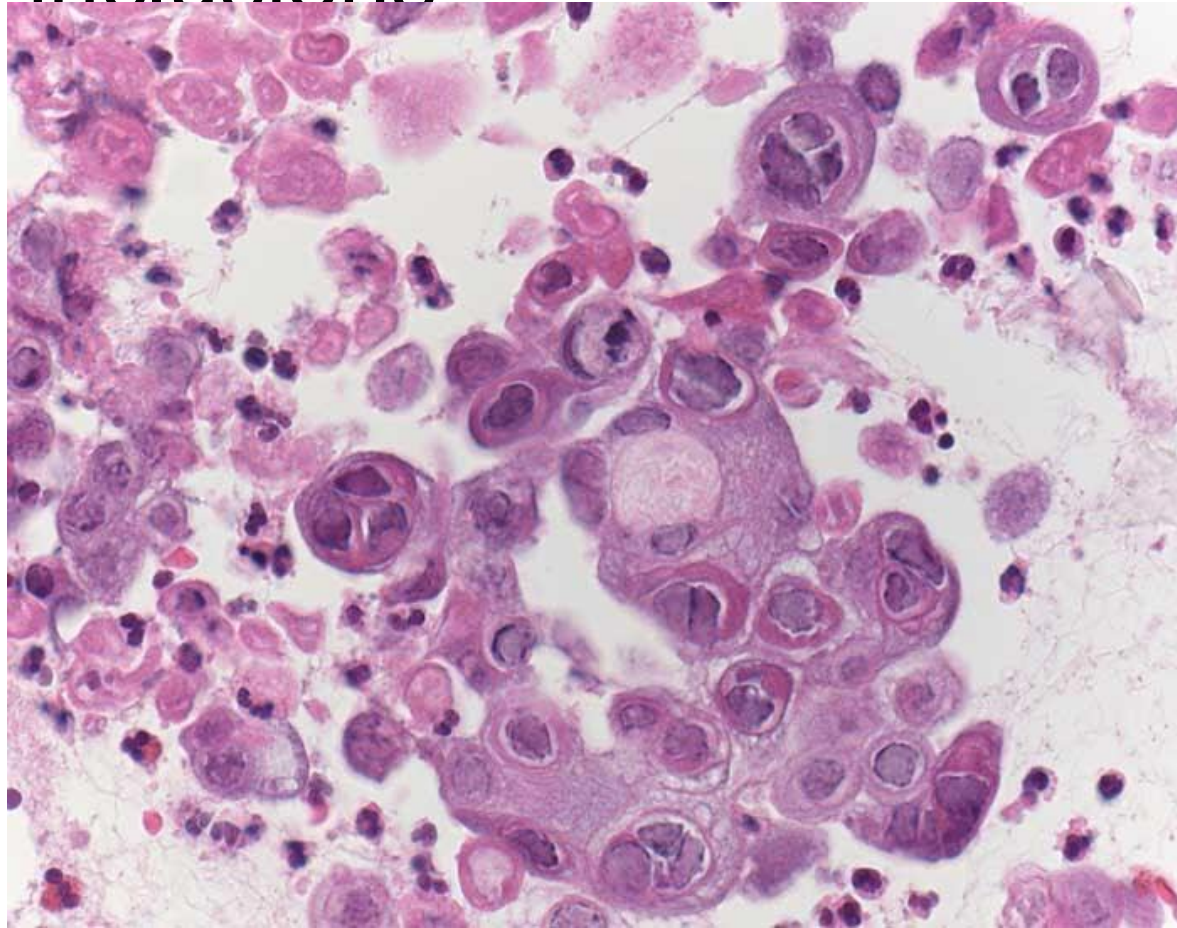
pigment- carbon anthracosis, tattooing,
hemosiderin, lipofuscin, melanin

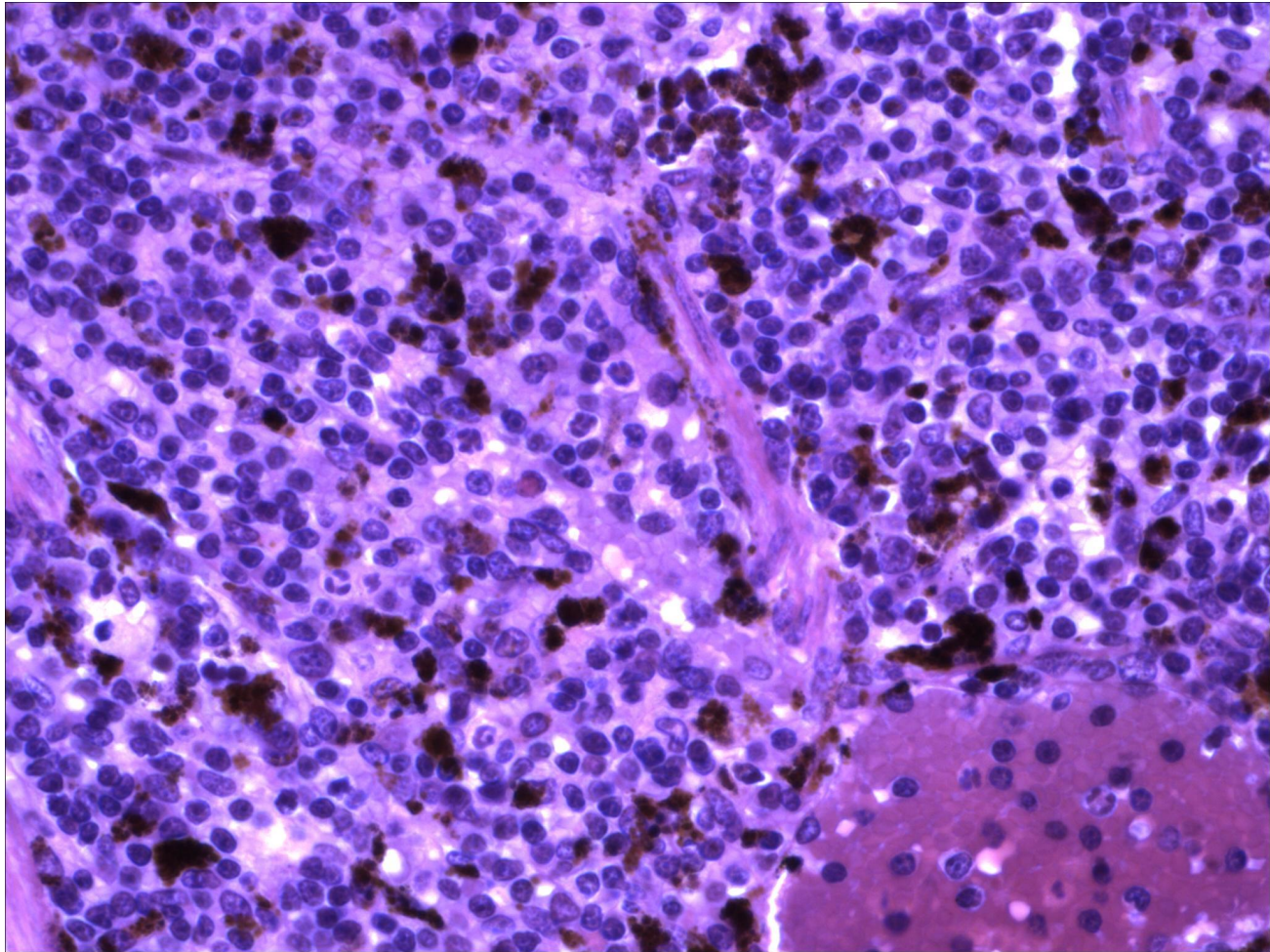
Viral inclusions, Russell bodies, lewy bodies,
amyloid

viral inclusions 2

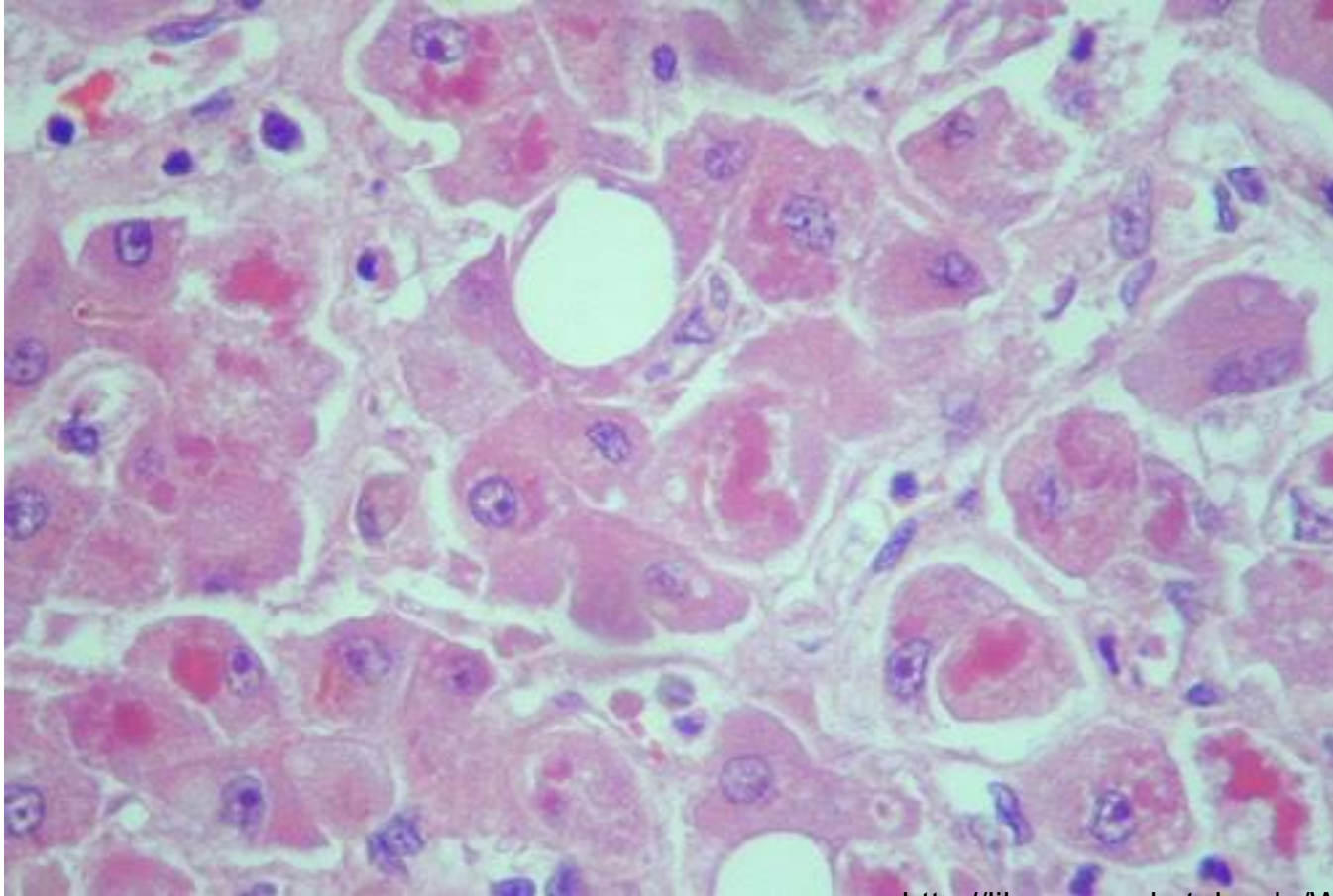


viral inclusions

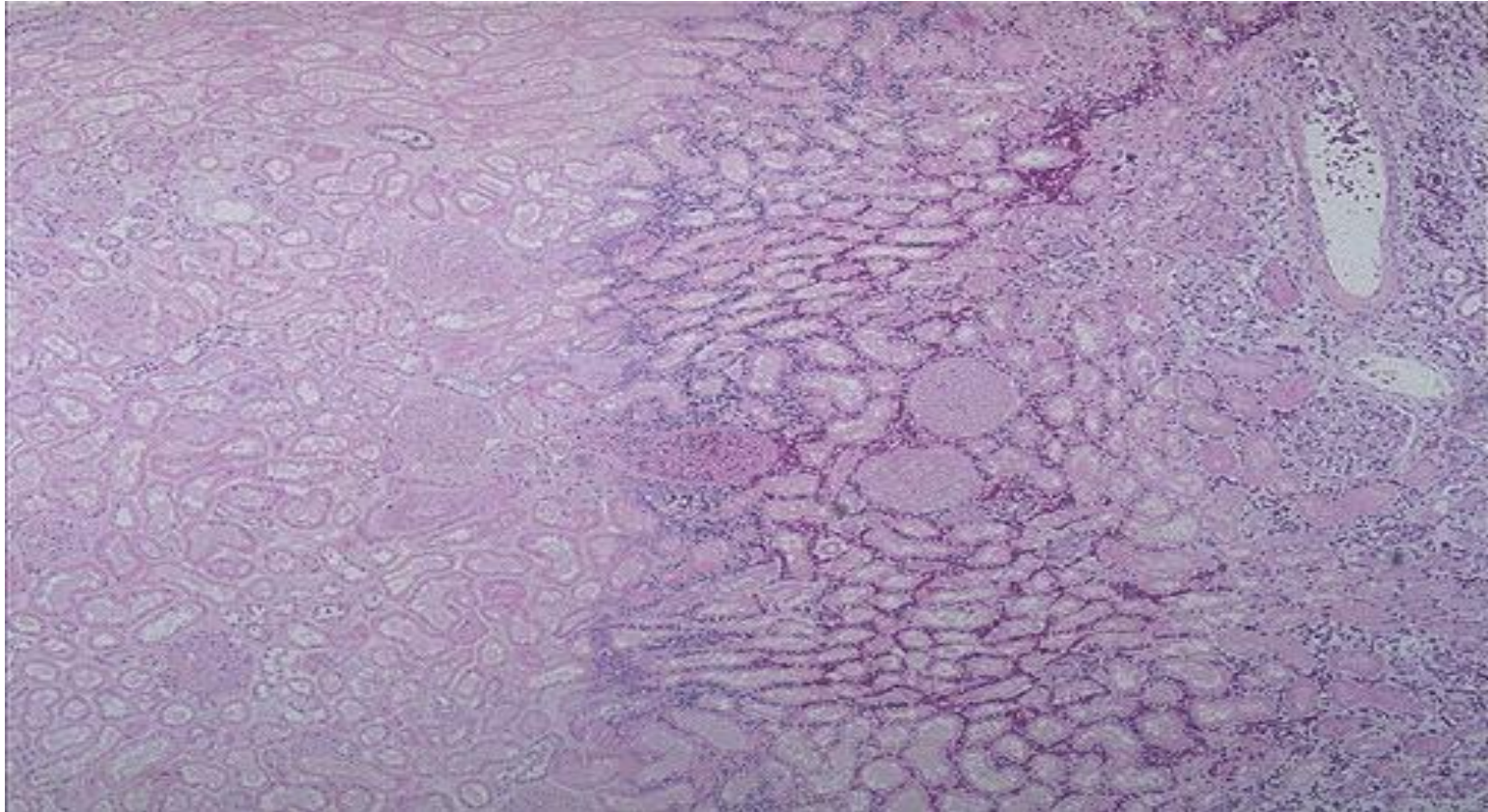




mallory hvaline



infarct border



<http://library.med.utah.edu/WebPath/webpath.html>

From adaptation to failure.
Crossing the threshold into
"When Cells Die"

Irreversible injury - cell death

necrosis- coagulative, liquifactive, caseous

apoptosis-

(reperfusion injury)

pyknosis, karyorrhexis, karyolysis inflammatory

Calcium escape

calcium dependent lipases - destroy cell membrane, pancreas

proteases -destroy enzymes and structural proteins

endonucleases -destroy DNA and RNA

many enzymes are controlled/activated by calcium.

adipocere formation-

Necrotic cell changes

Karyolysis -destruction of nucleus contents, DNA degraded

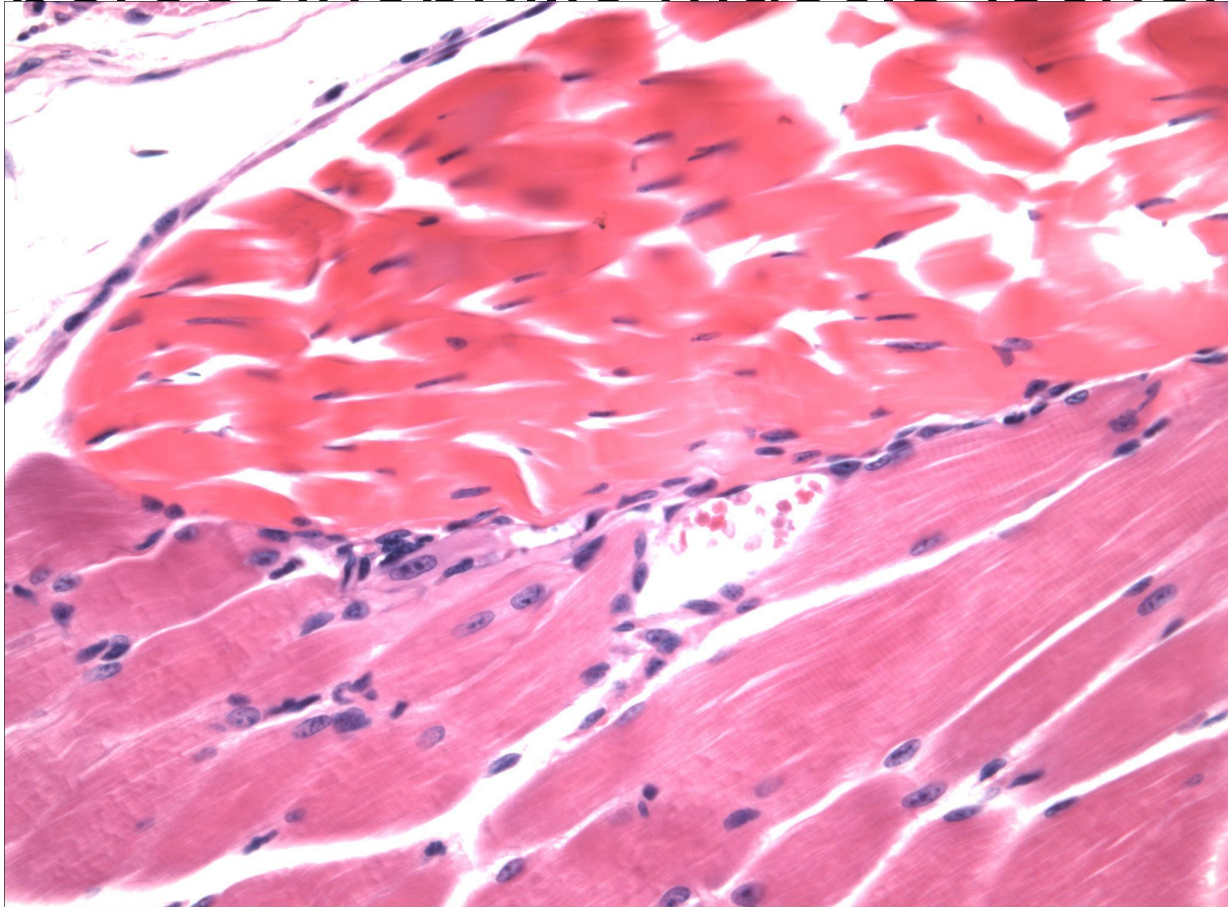
Pyknosis -condensation of chromatin

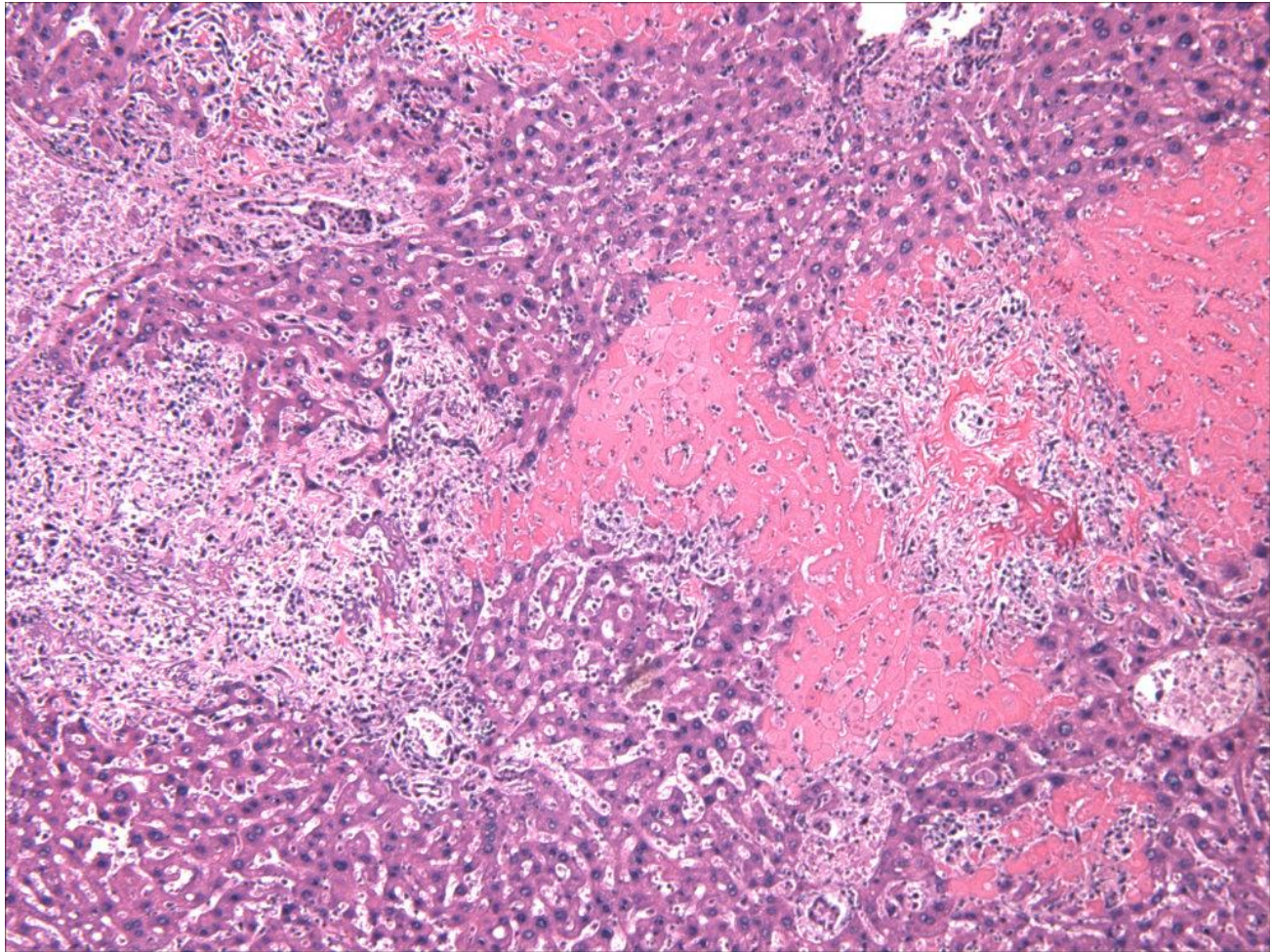
Karyorrhexis -fragmentation of nucleus

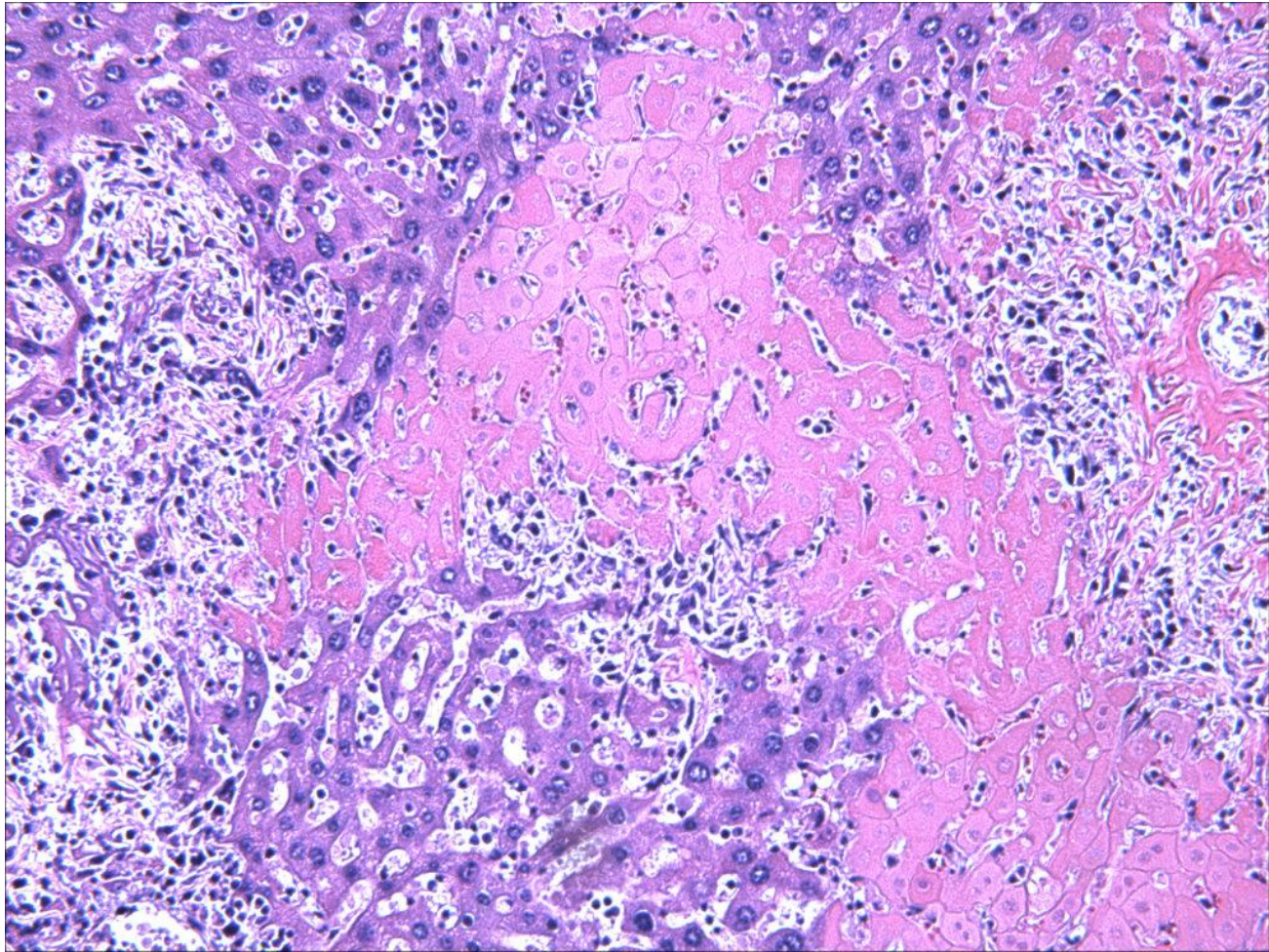
Loss of basophilia -no DNA to stain, ribosomes dispersed . Blue staining is paler.

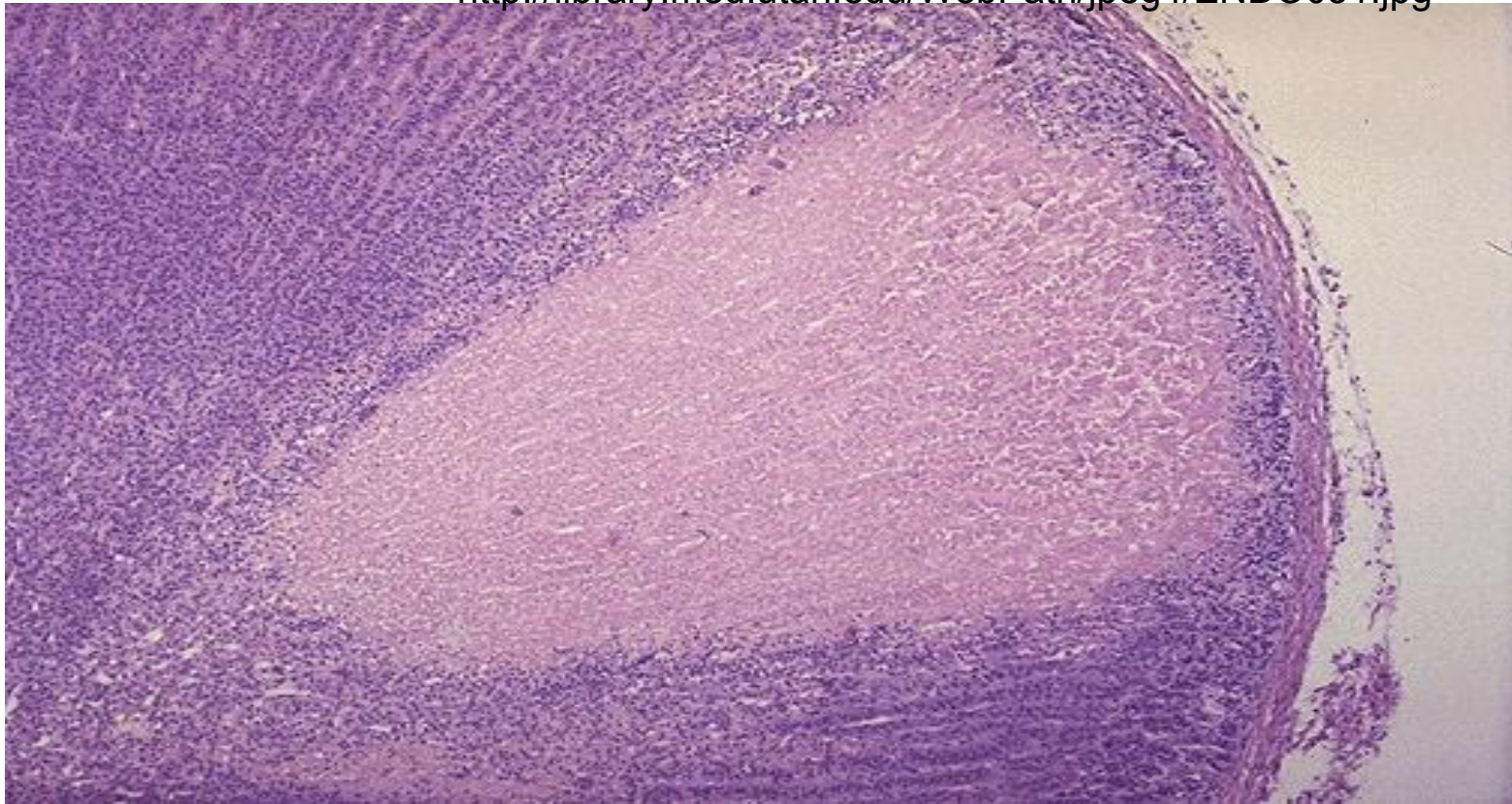
increased acidophilia/eosinophilic -proteins denatured. Red/pink staining brighter/darker

hypereosinophilic muscle-ischemic

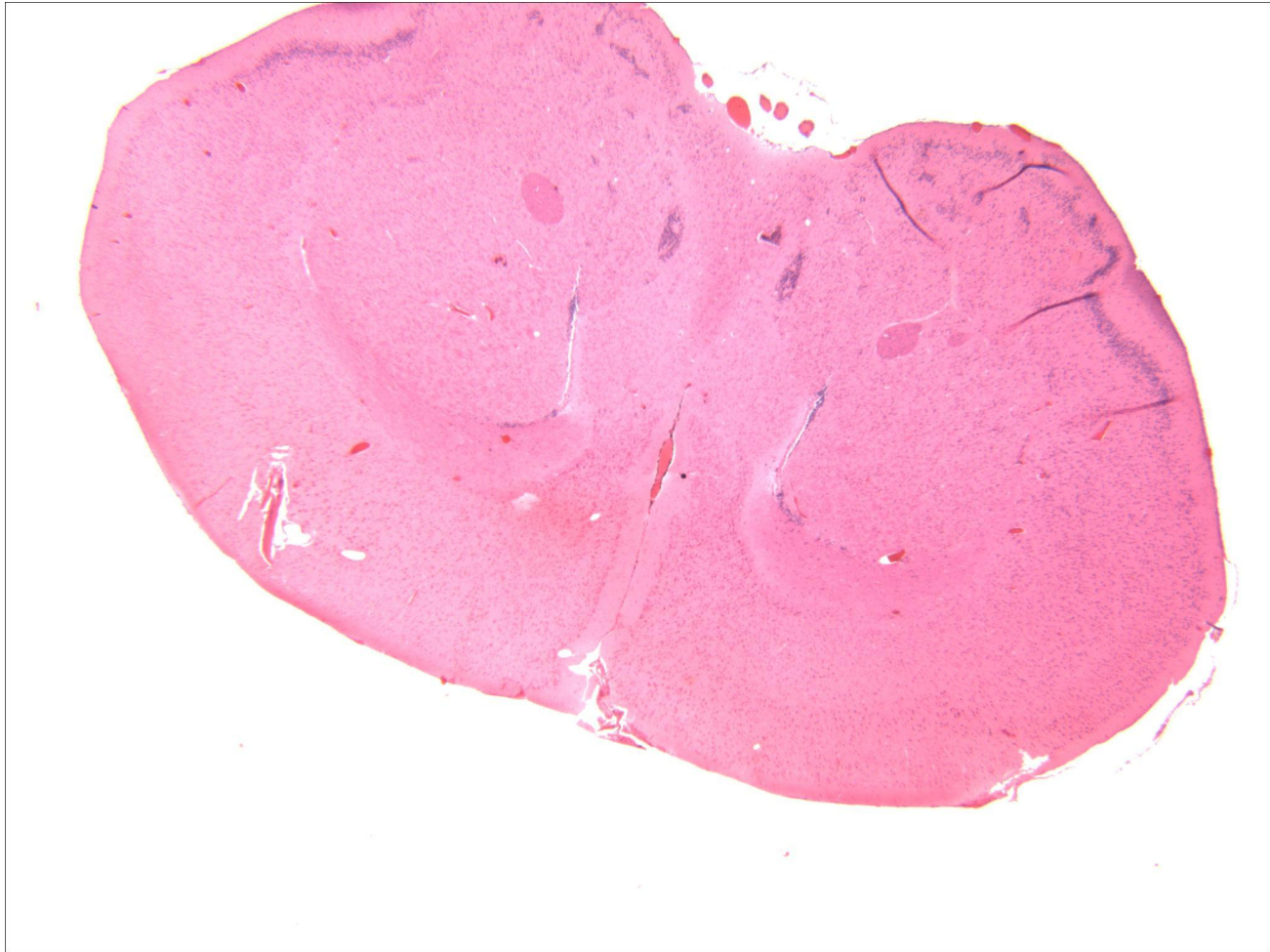


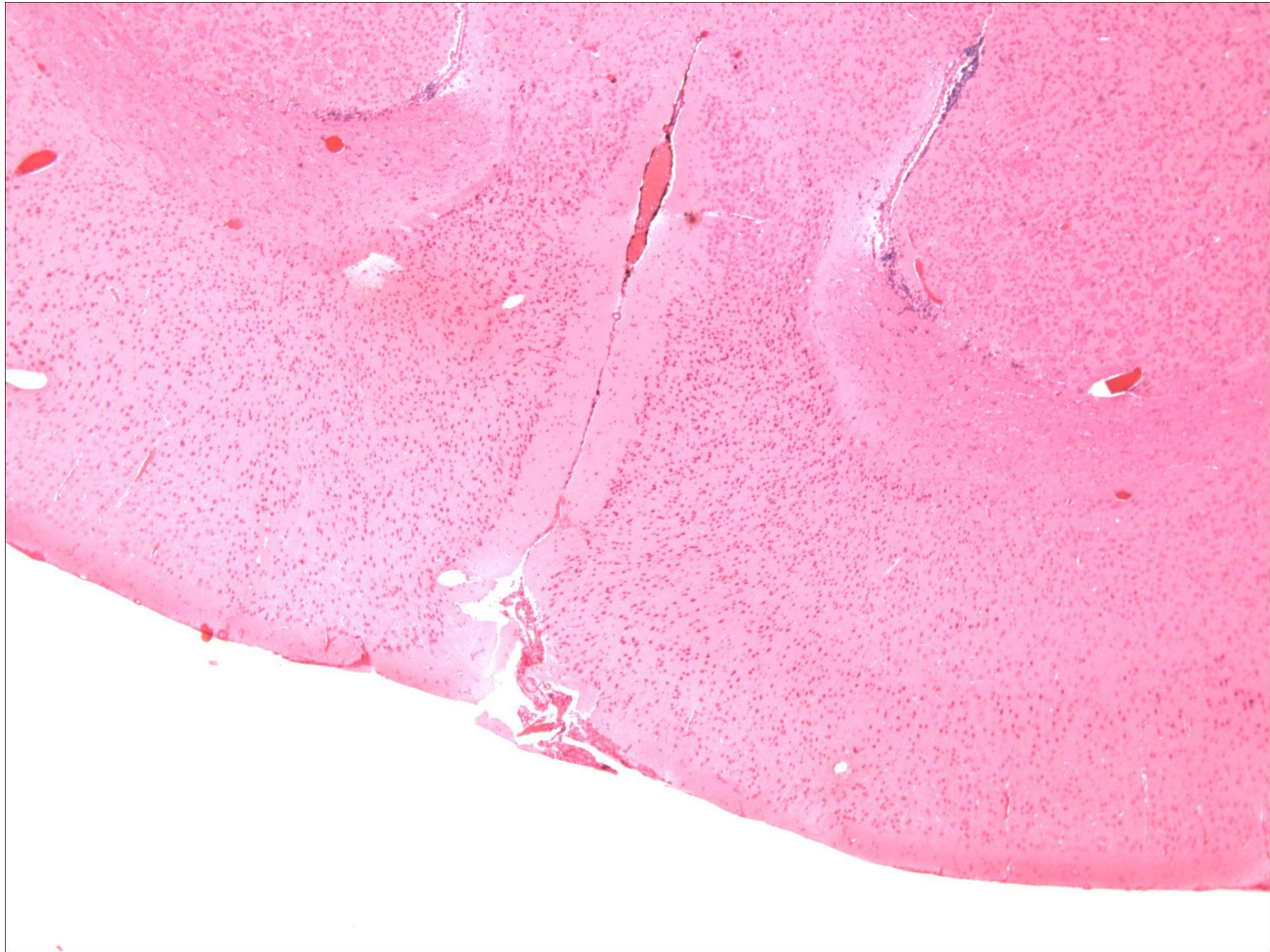


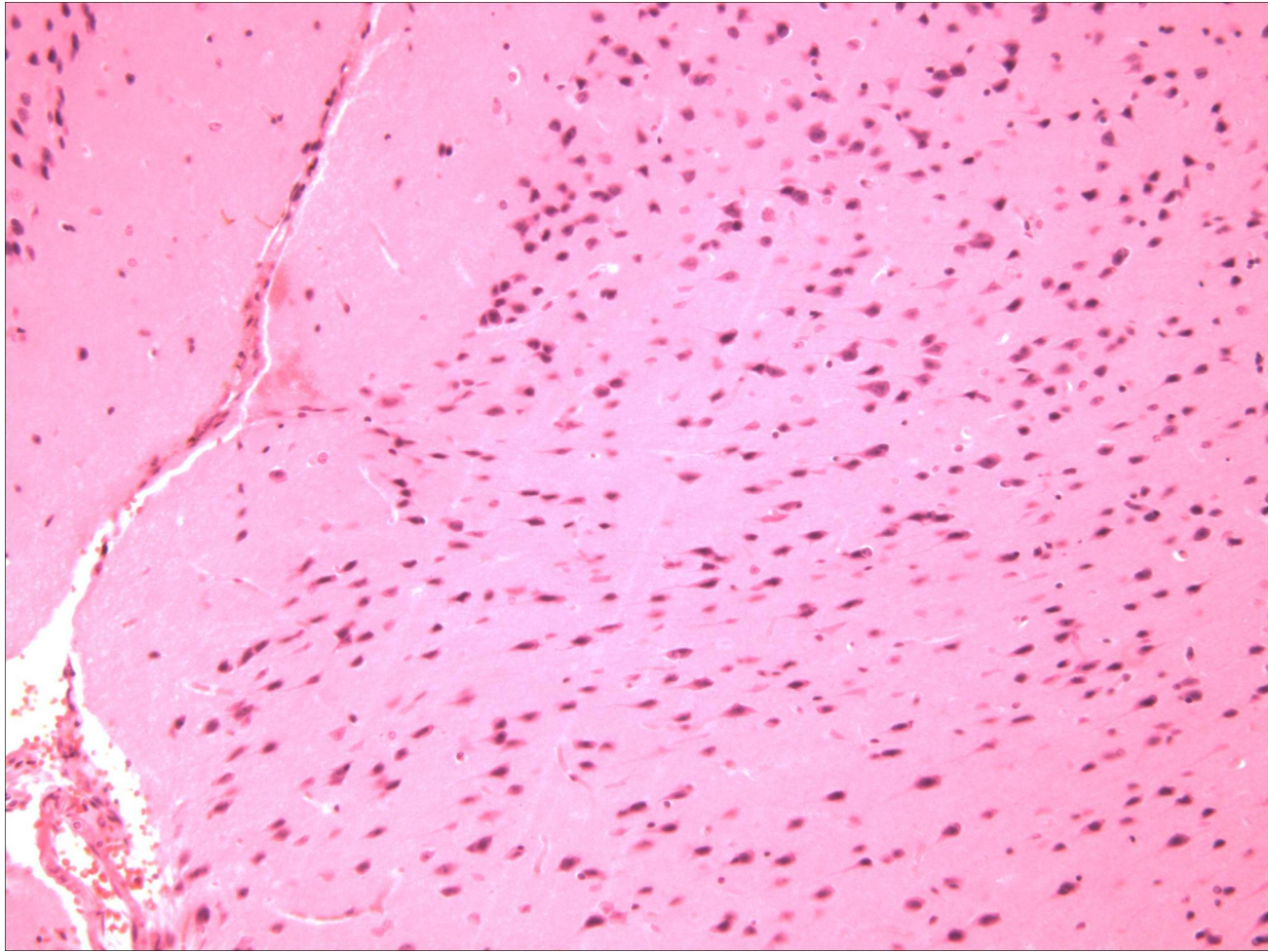


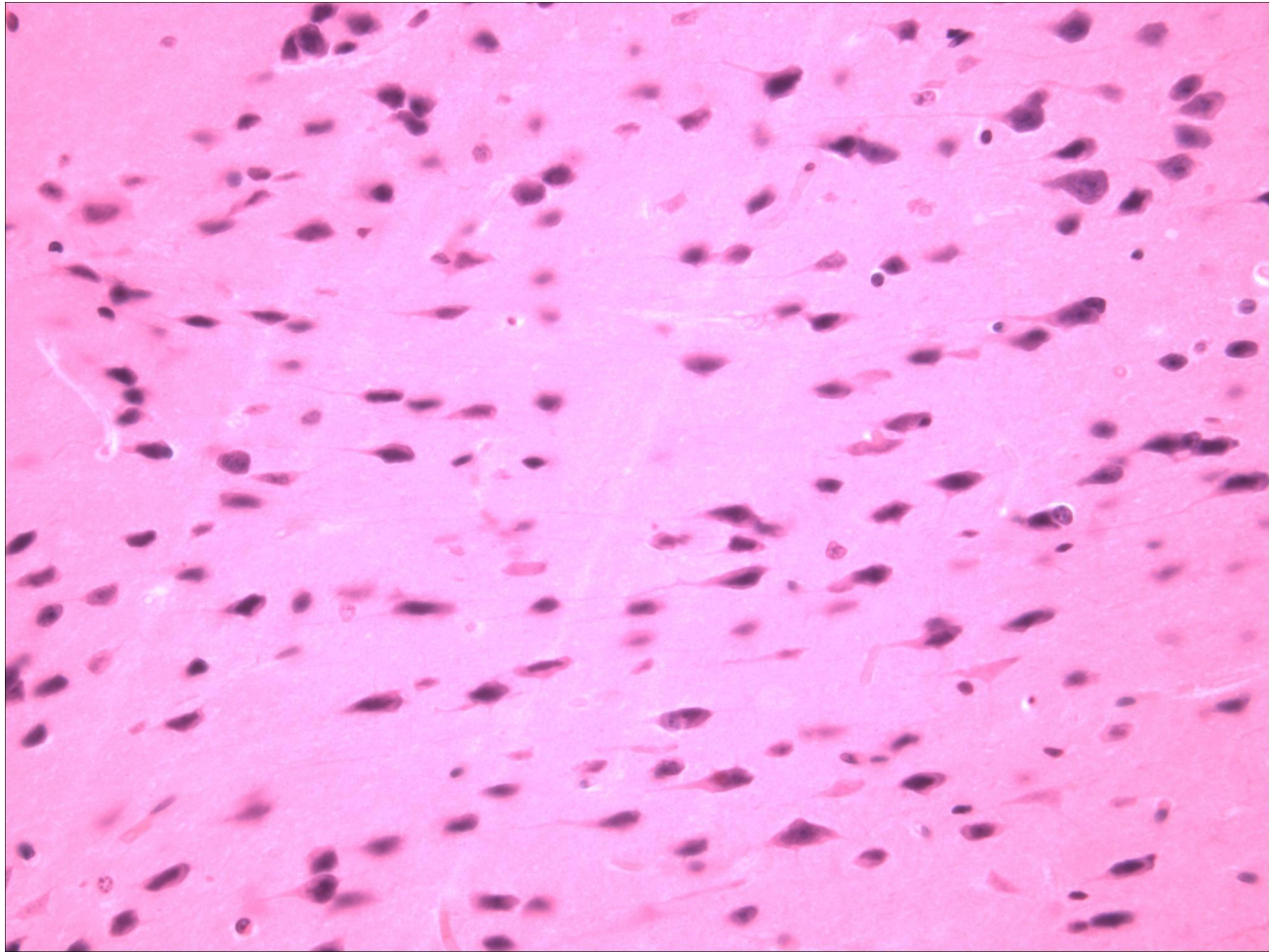


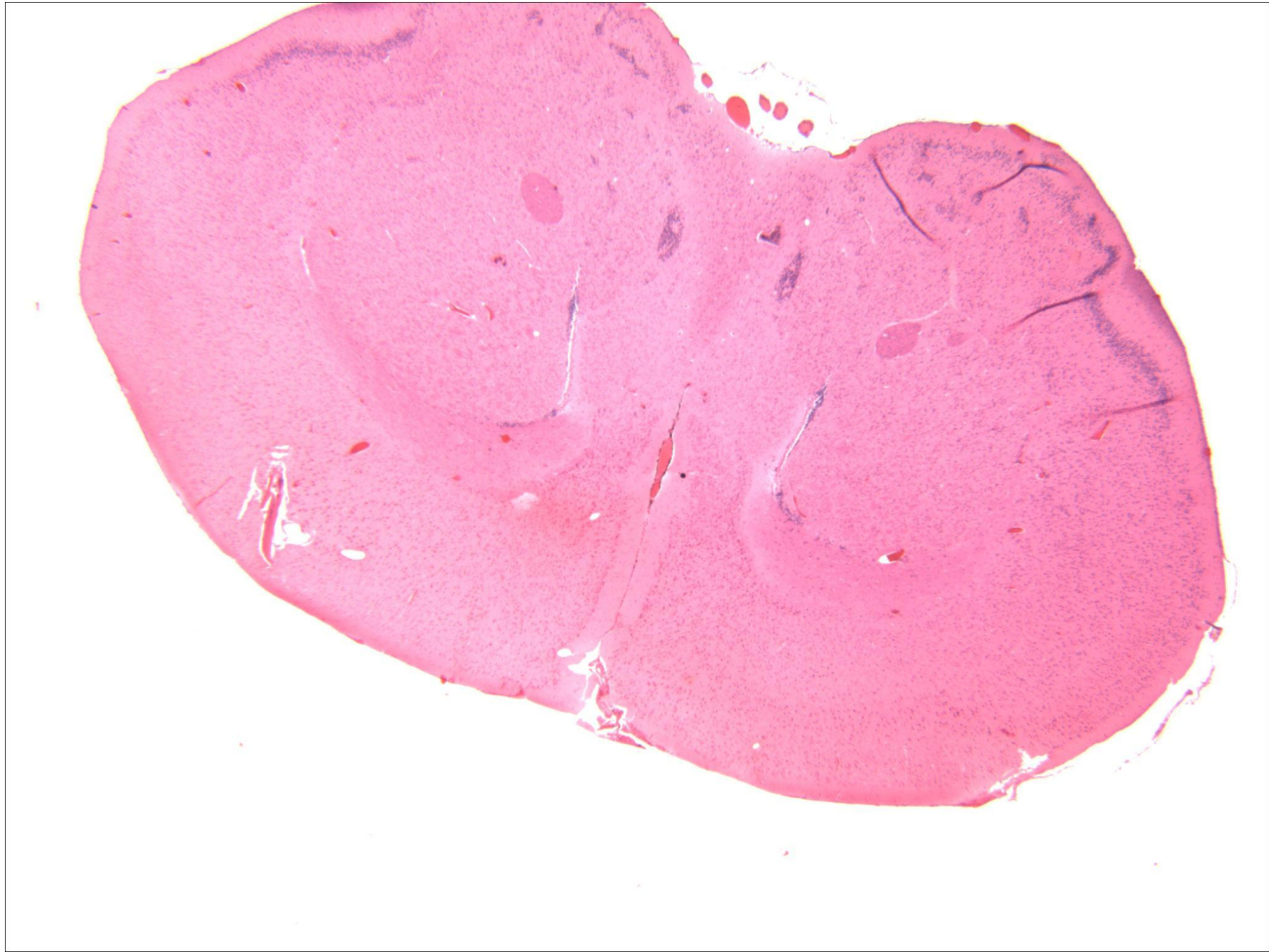
Adrenal cortex infarct- coagulative
necrosis







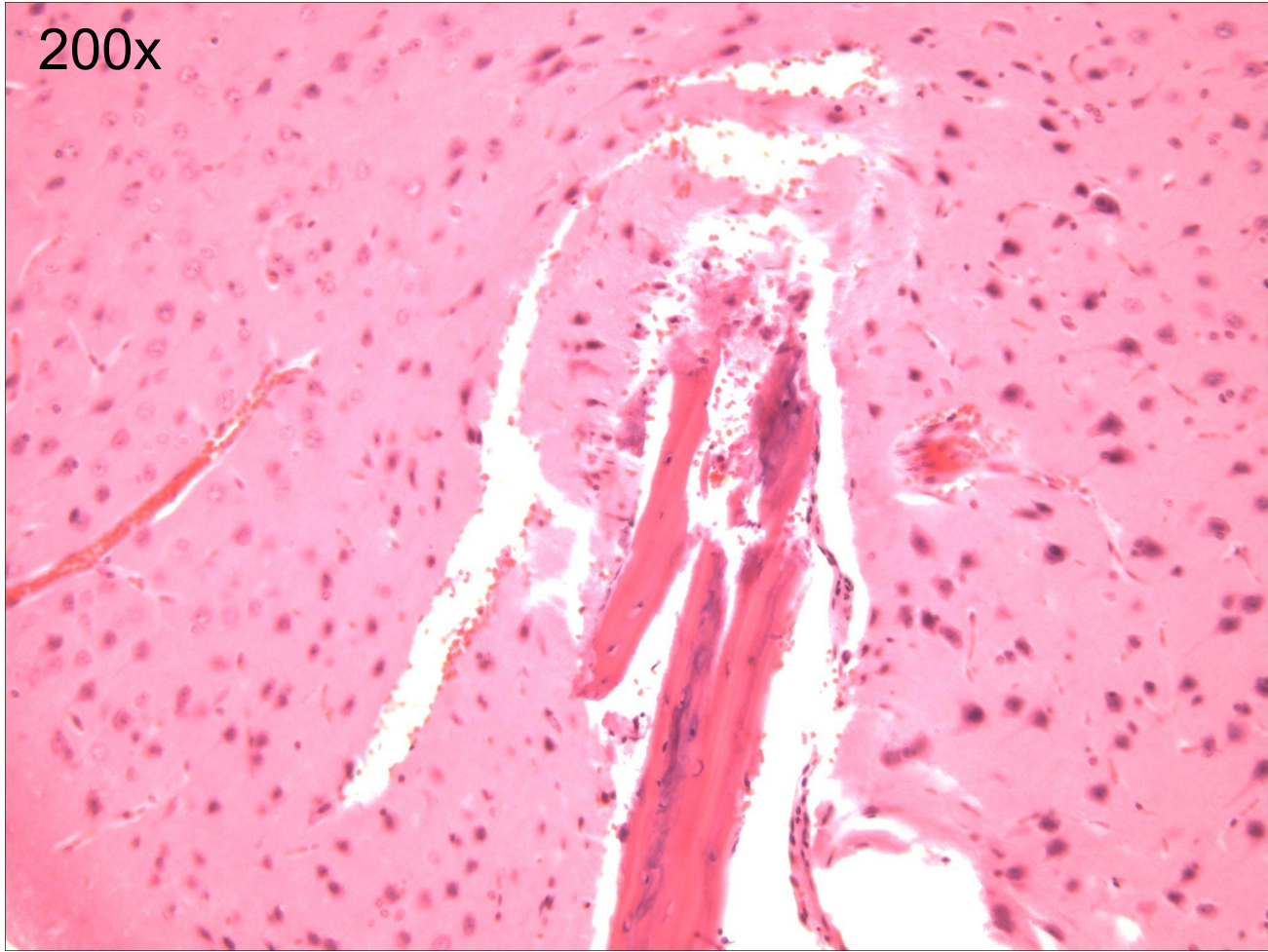




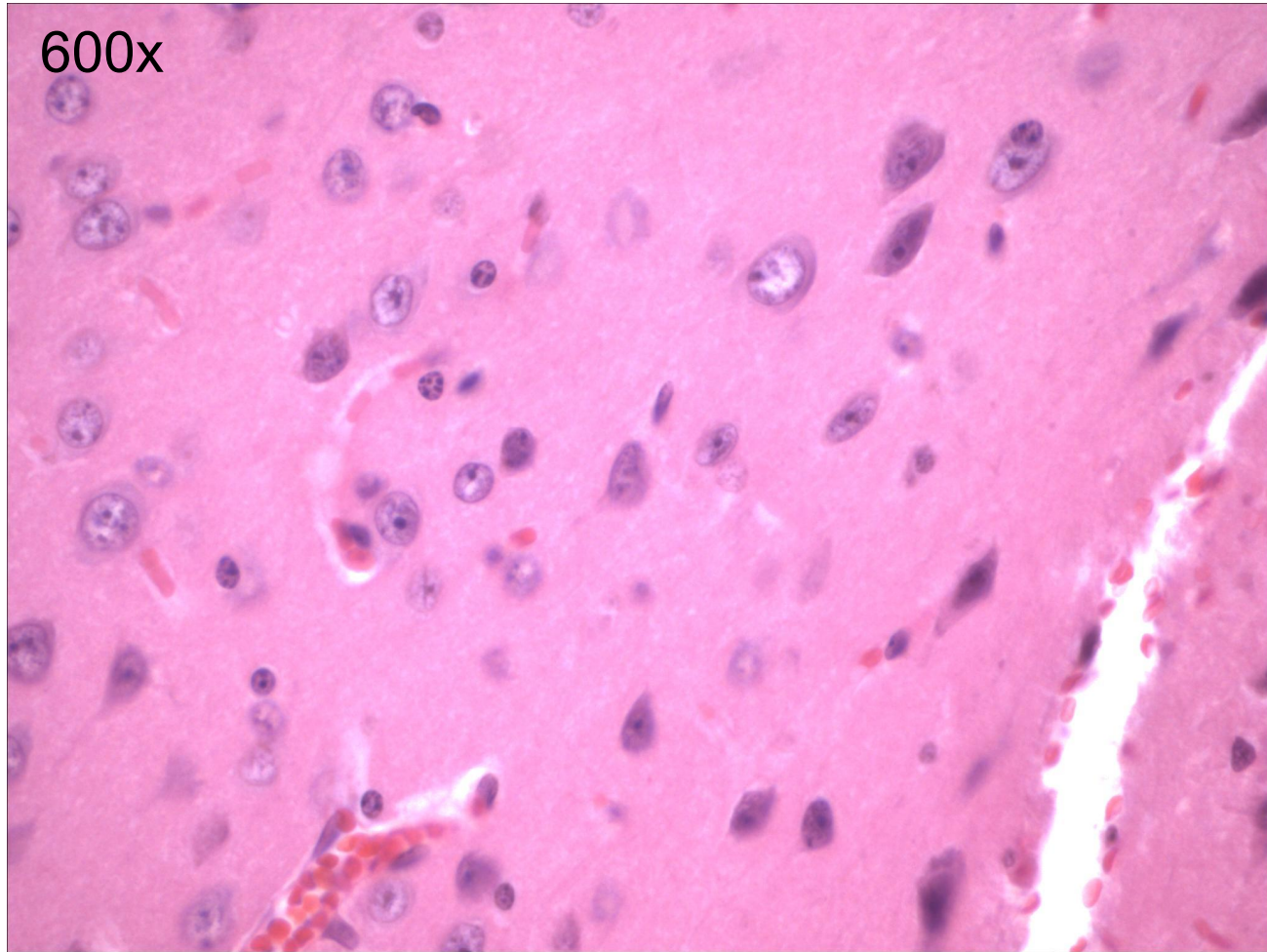
100x



200x



600x



Apoptosis

deliberate cell "suicide"

requires energy

certain genes activated (caspases) and controlled
cascade of events leading to apoptosis

Most notable-DNA fragmentation

normal development -webs of fingers and toes

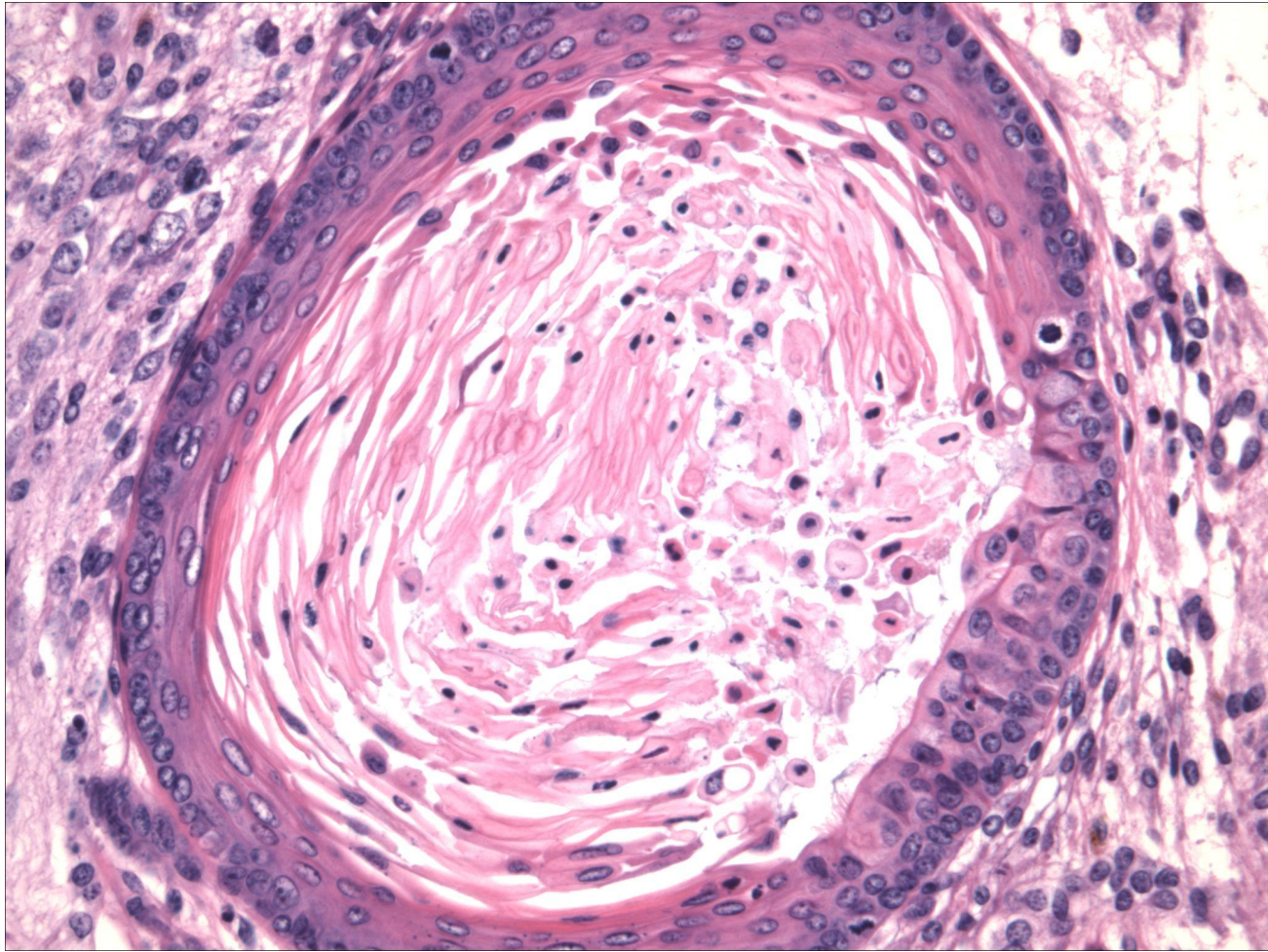
thymus, immune system-involution

sebaceous glands

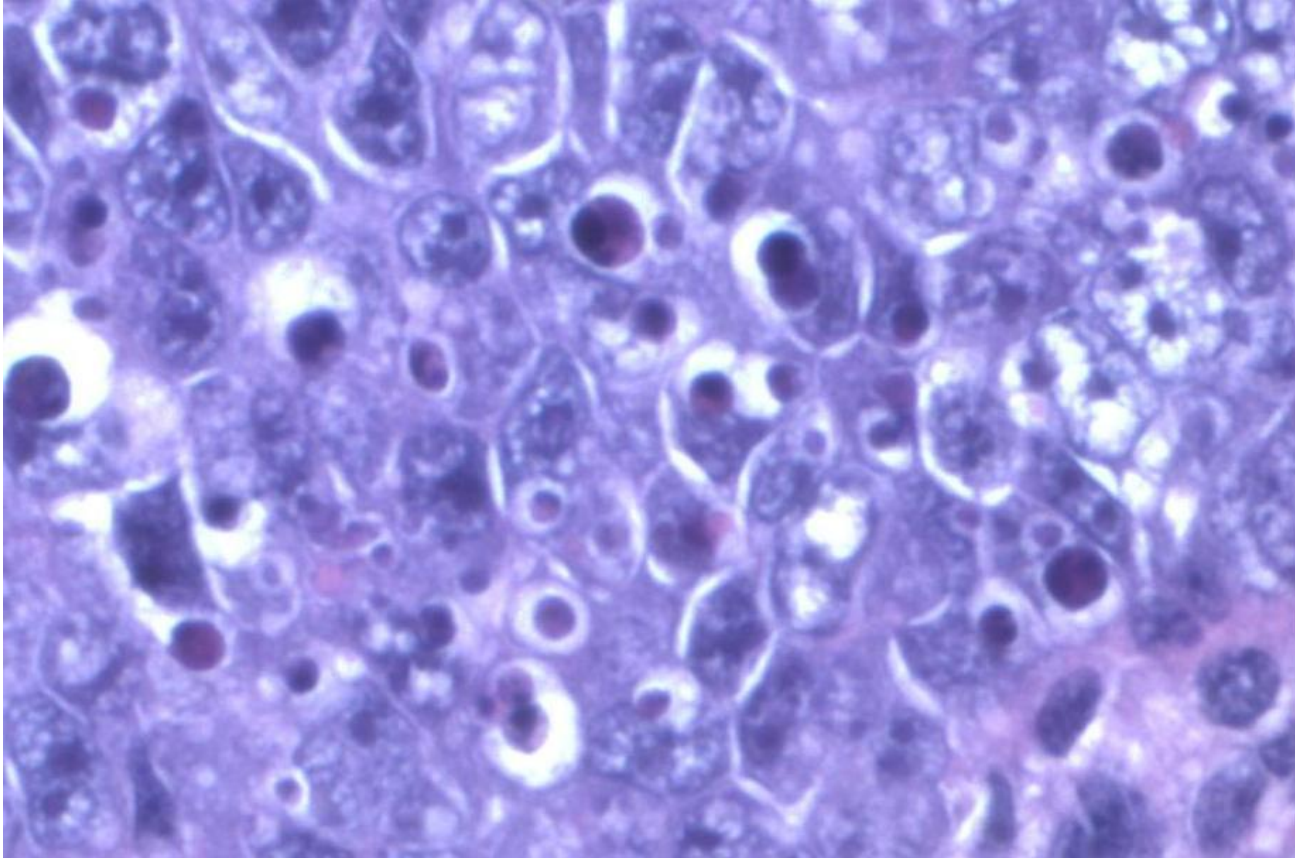
viral infection

cancer

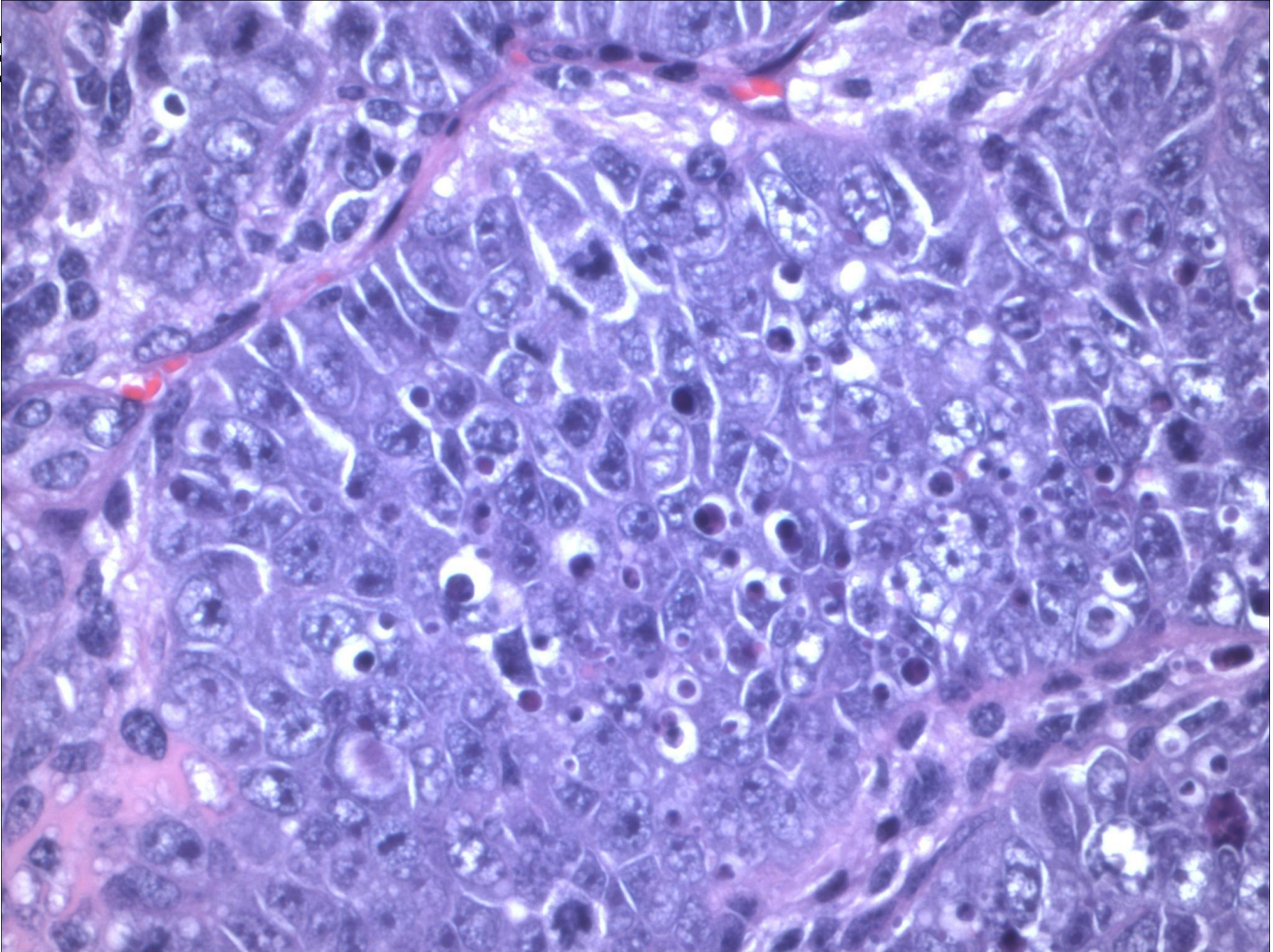
radiation injury



apop 2



02

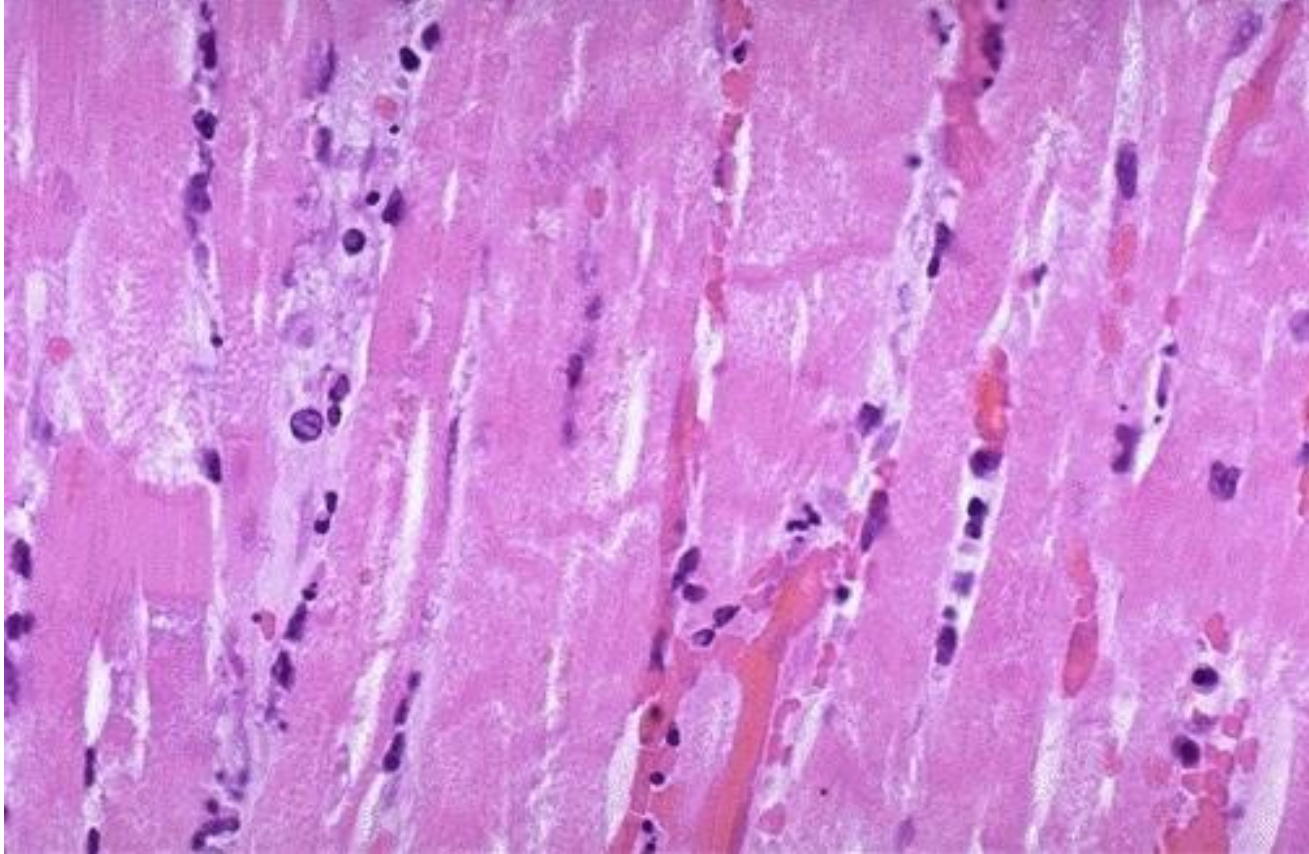


interventricular septum

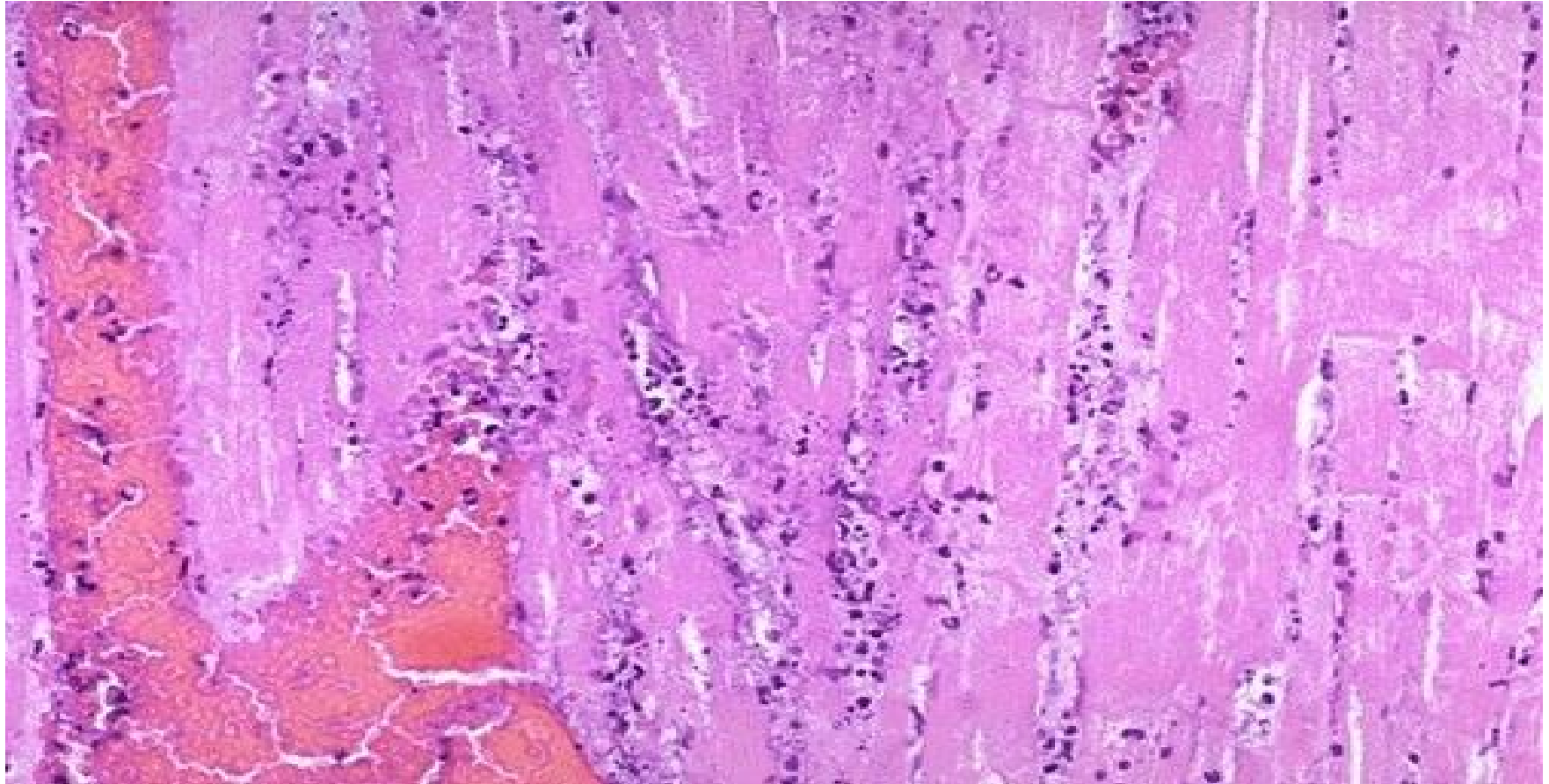


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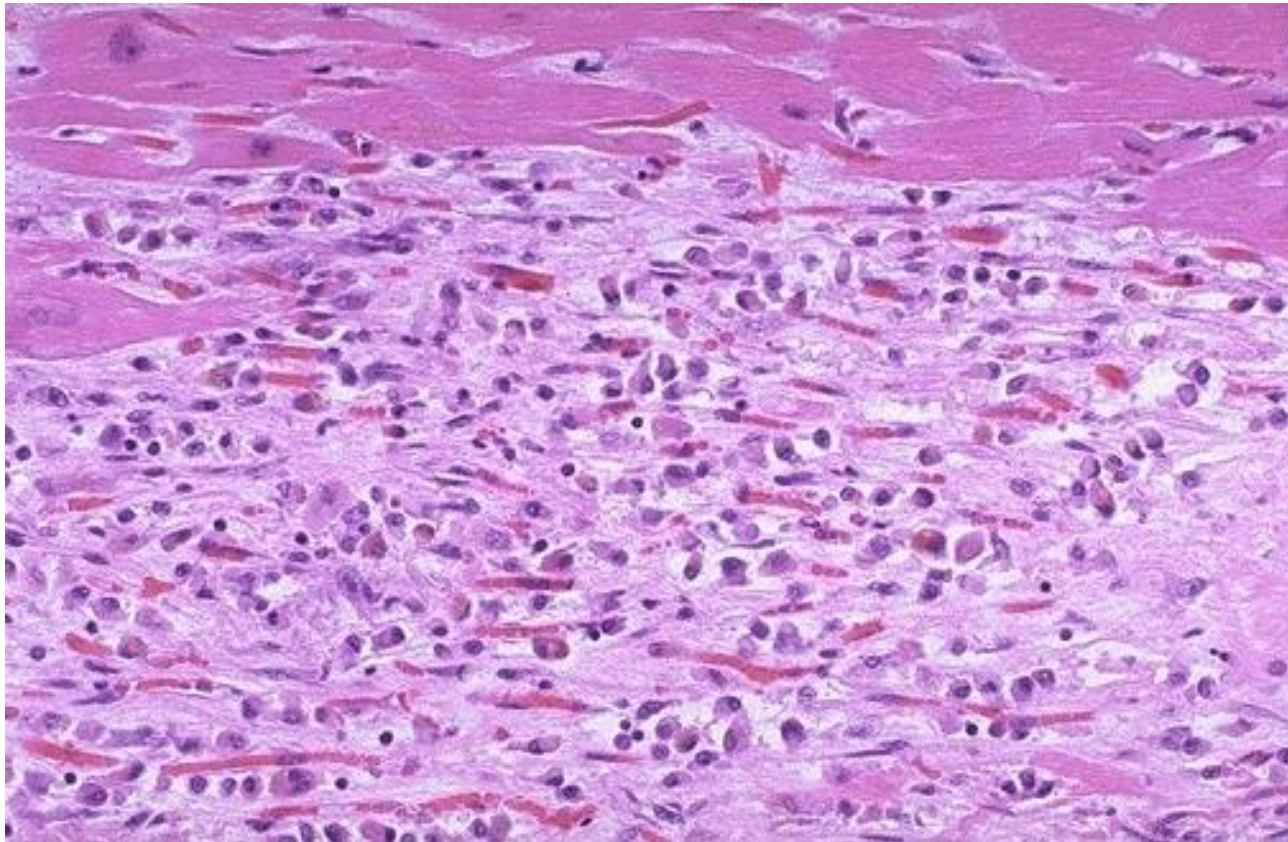
myocardial infarction day 1 or 2 with contraction bands



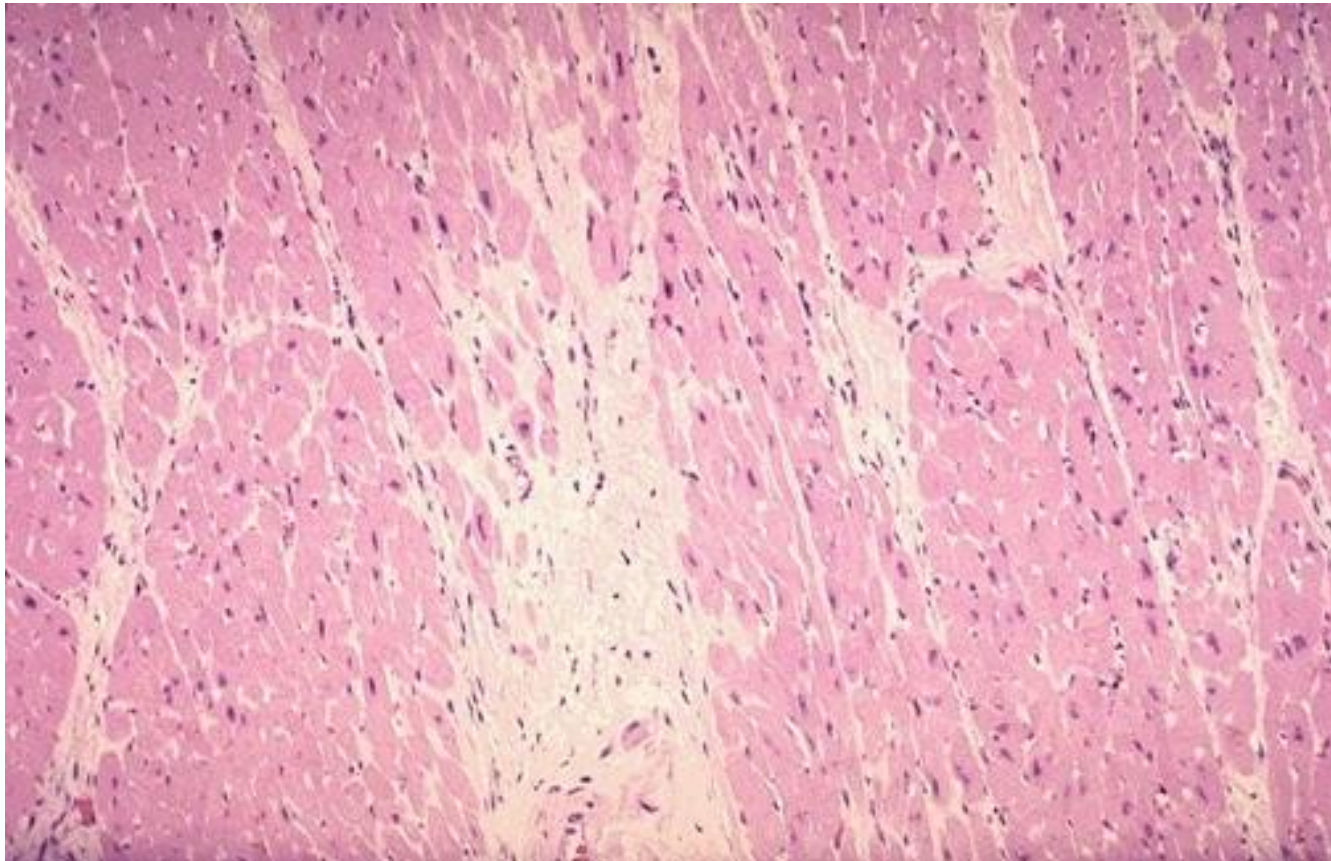
mi day 4



mi week 2

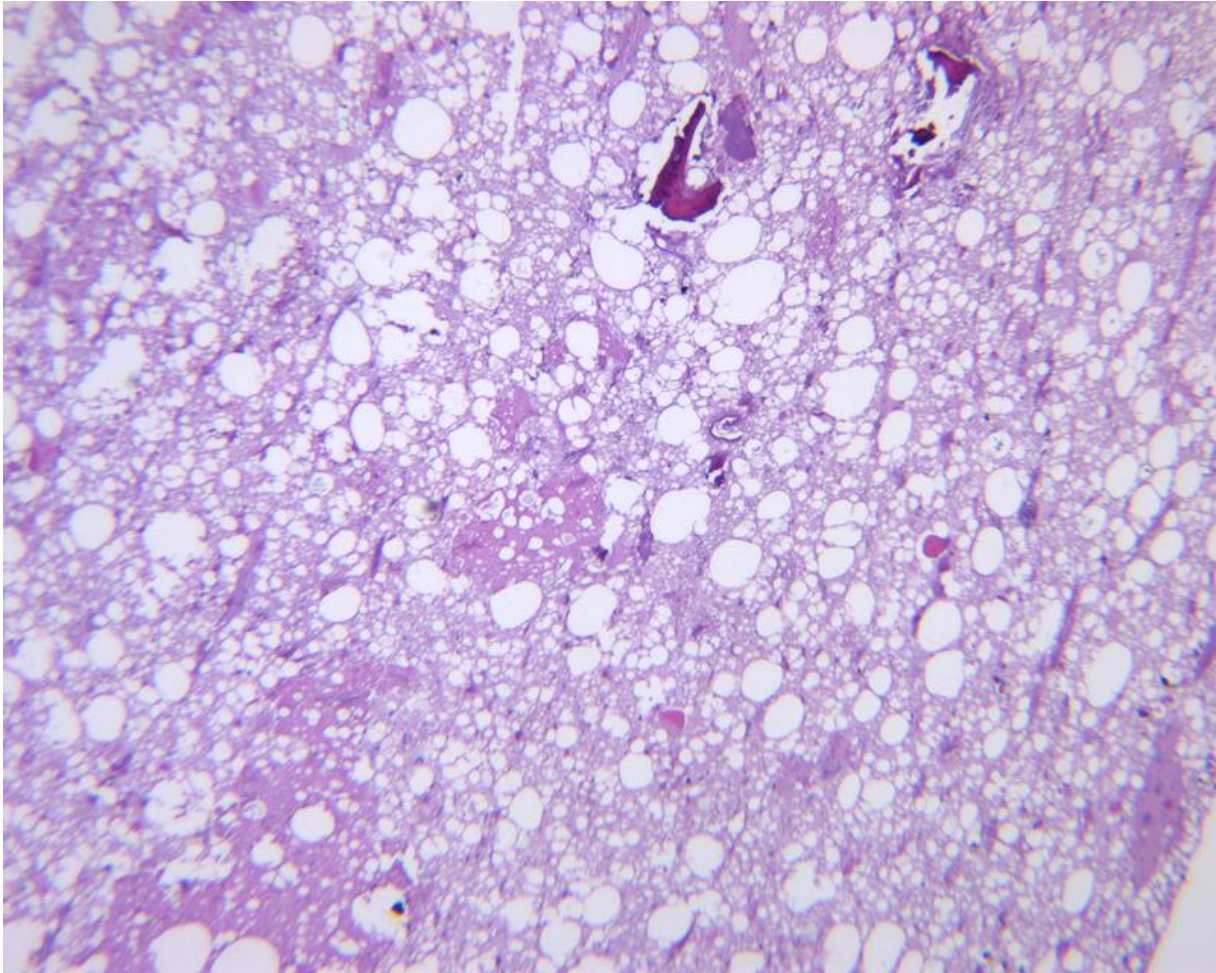


old mi scar



<http://library.med.utah.edu/WebPath/webpath.html>

40x



Cardinal Signs Inflammation

tumor -swelling

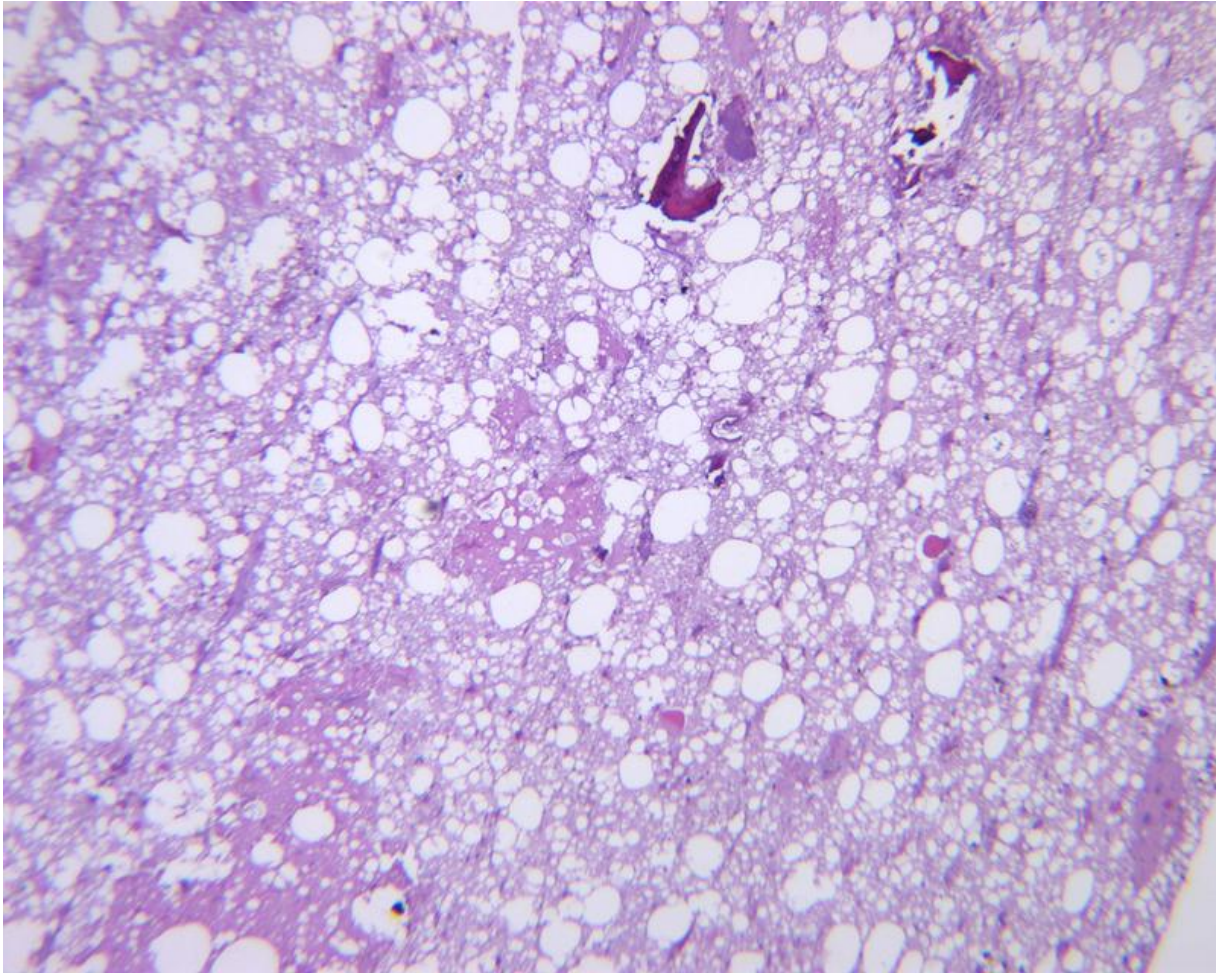
rubor -redness

dolor -pain

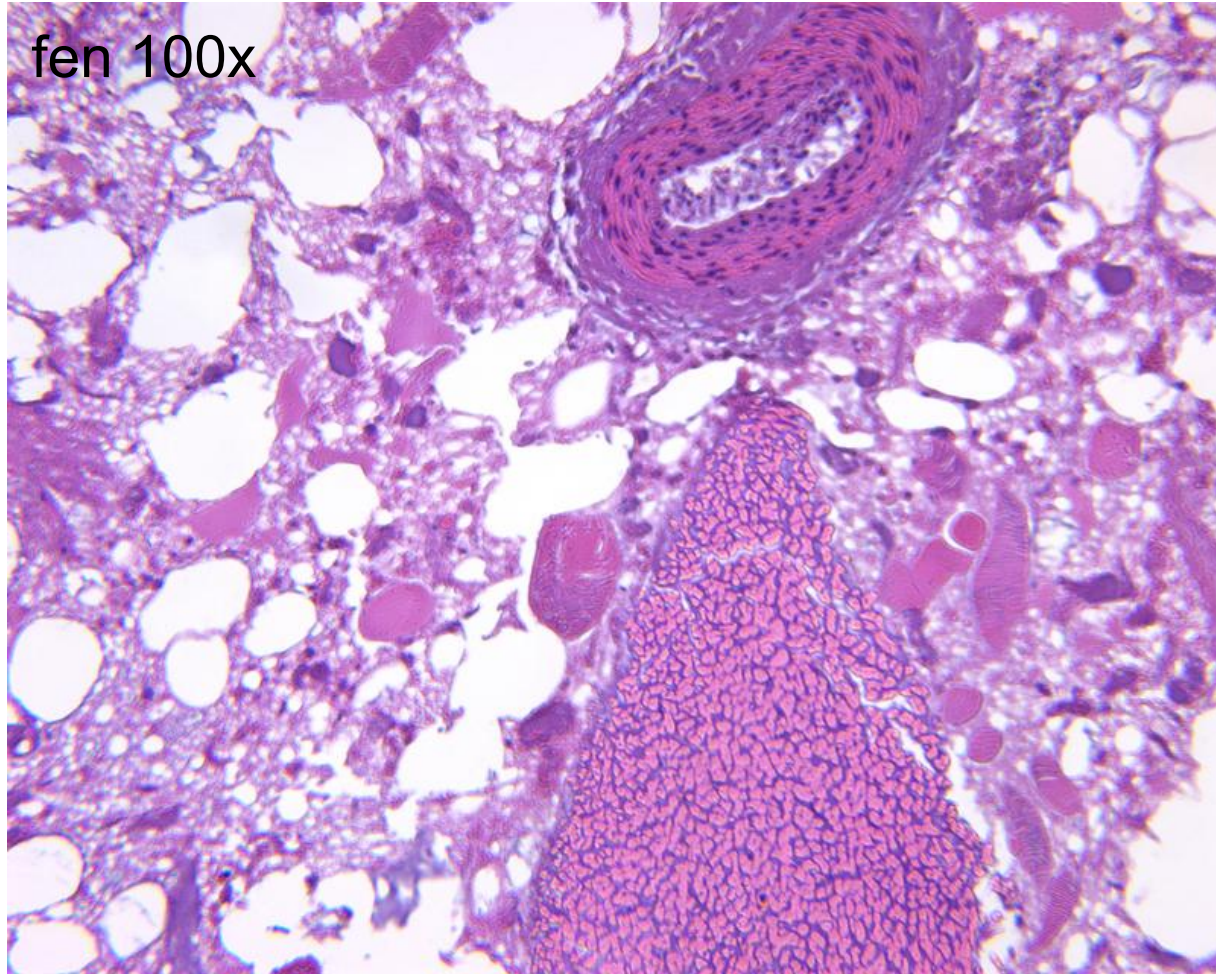
calor -increased heat/warmth of injury site

functio laesa "Loss of function" (Virchow ~1870)

40x



fen 100x



neurovascular bundle



cheap 100x

