Ischaemia & Infarction

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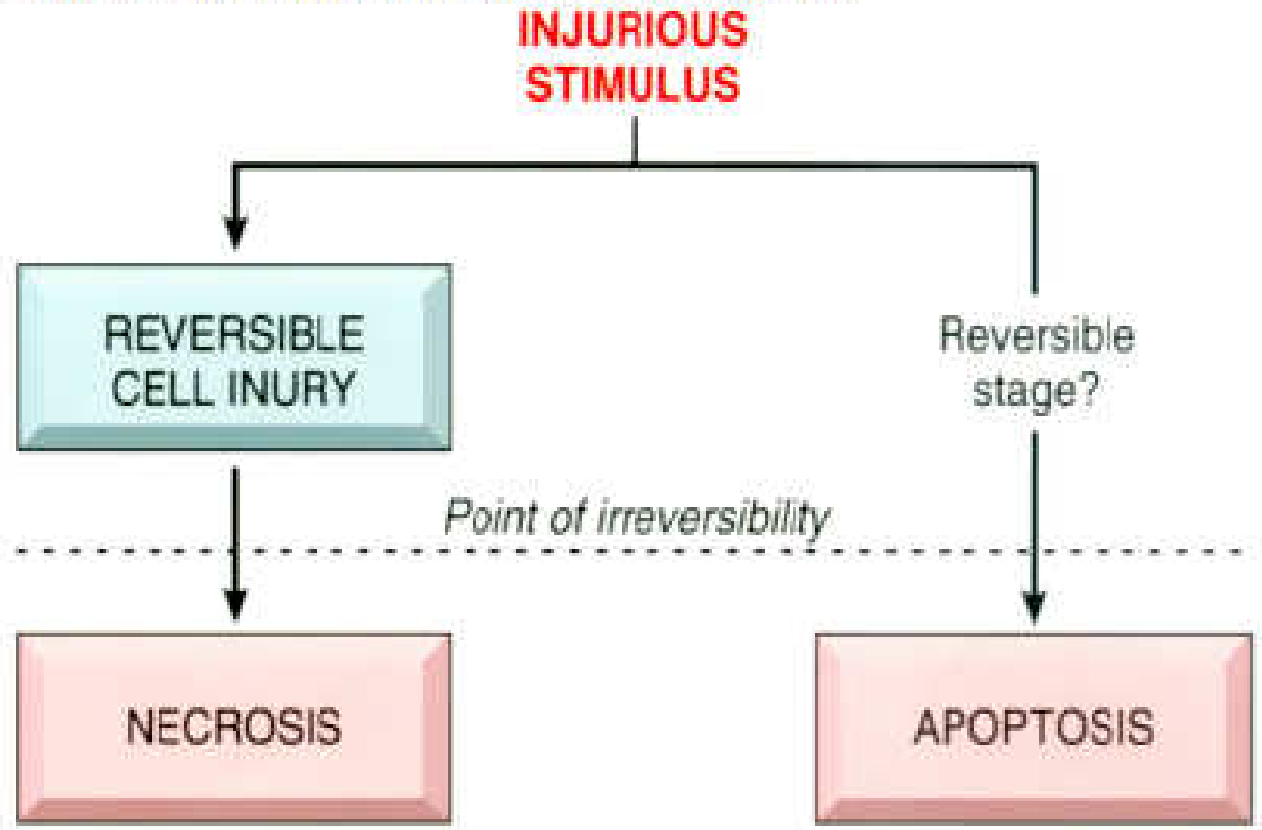
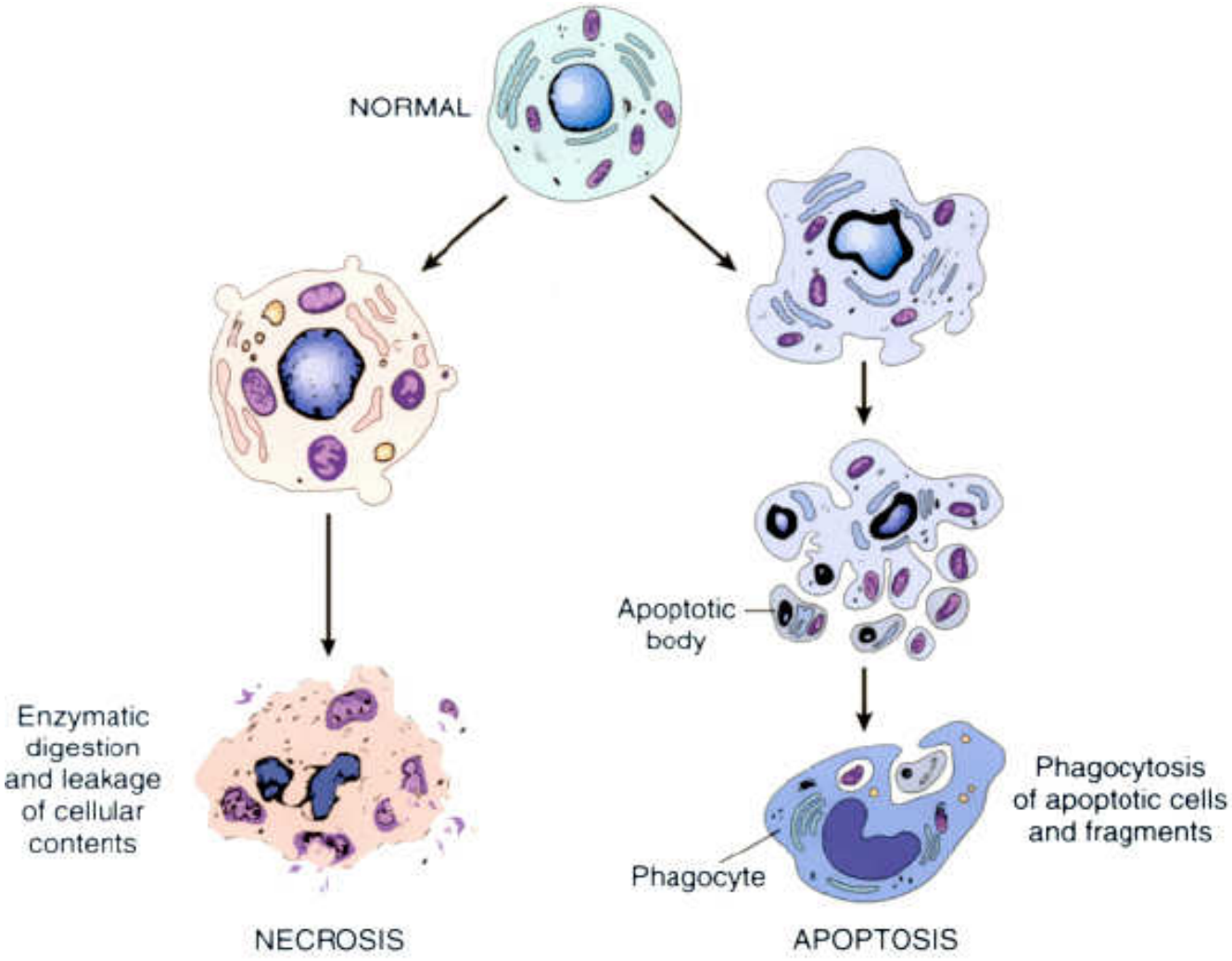
Evolution of Cell Injury

Figure 1-7 Stages in the evolution of cell injury and death.



Cell Death: Necrosis vs Apoptosis

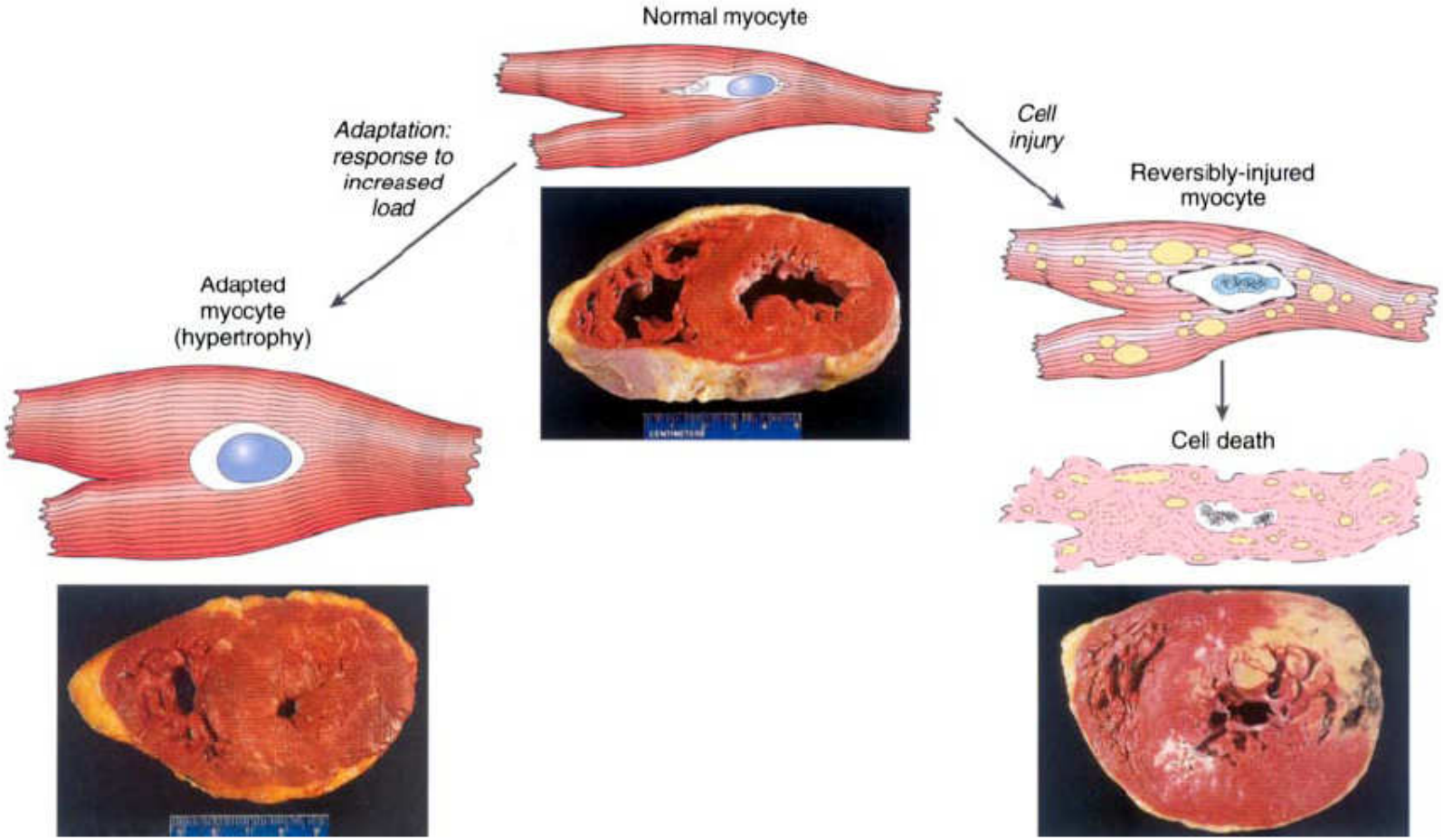


Cellular Reaction To Injury

Adaption to Environmental Stress

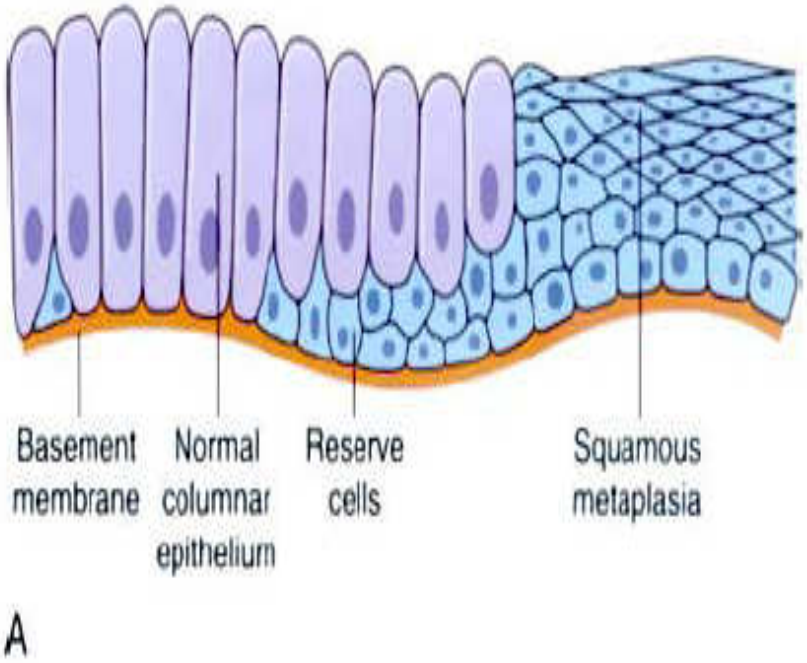
- Hypertrophy – increase in organ or tissue size due to increase in cell size.
- Hyperplasia – increase in organ size or tissue due to increase in cell number.
- Aplasia – failure in cell production resulting in agenesis (in-utero) or permanent loss of precursor cells (e.g. bone marrow failure).
- Hypoplasia – decrease in cell production (less extreme than aplasia).
- Atrophy – decrease in organ or tissue size from decrease in mass of preexisting cells.
- Metaplasia – replacement of one differentiated tissue/cells by another.

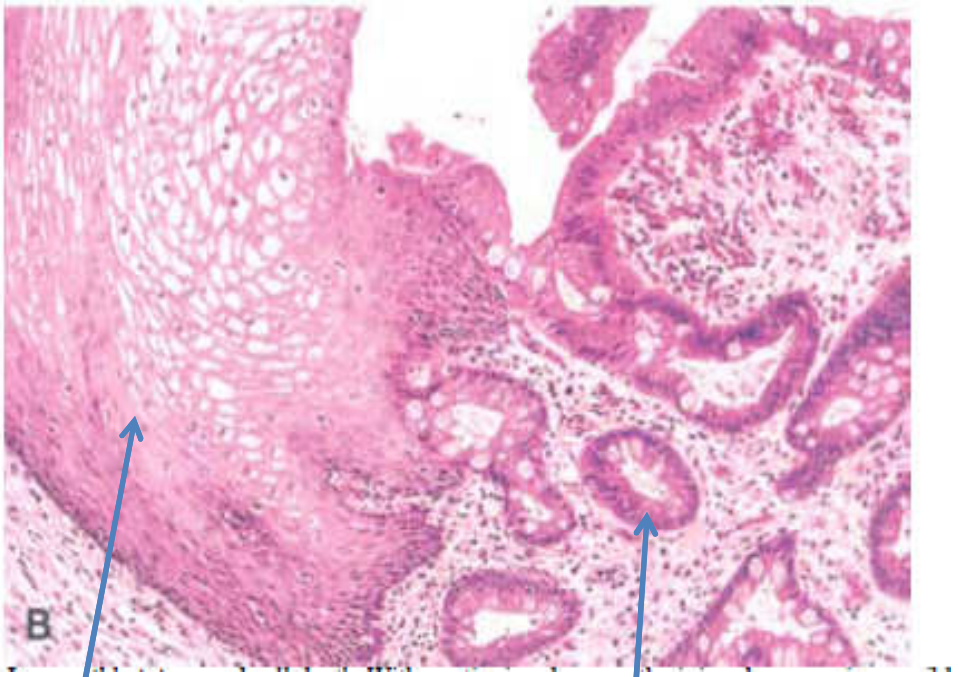
E.g. of Cell Adaption



E.g. of Metaplasia

Columnar metaplasia of esophagus





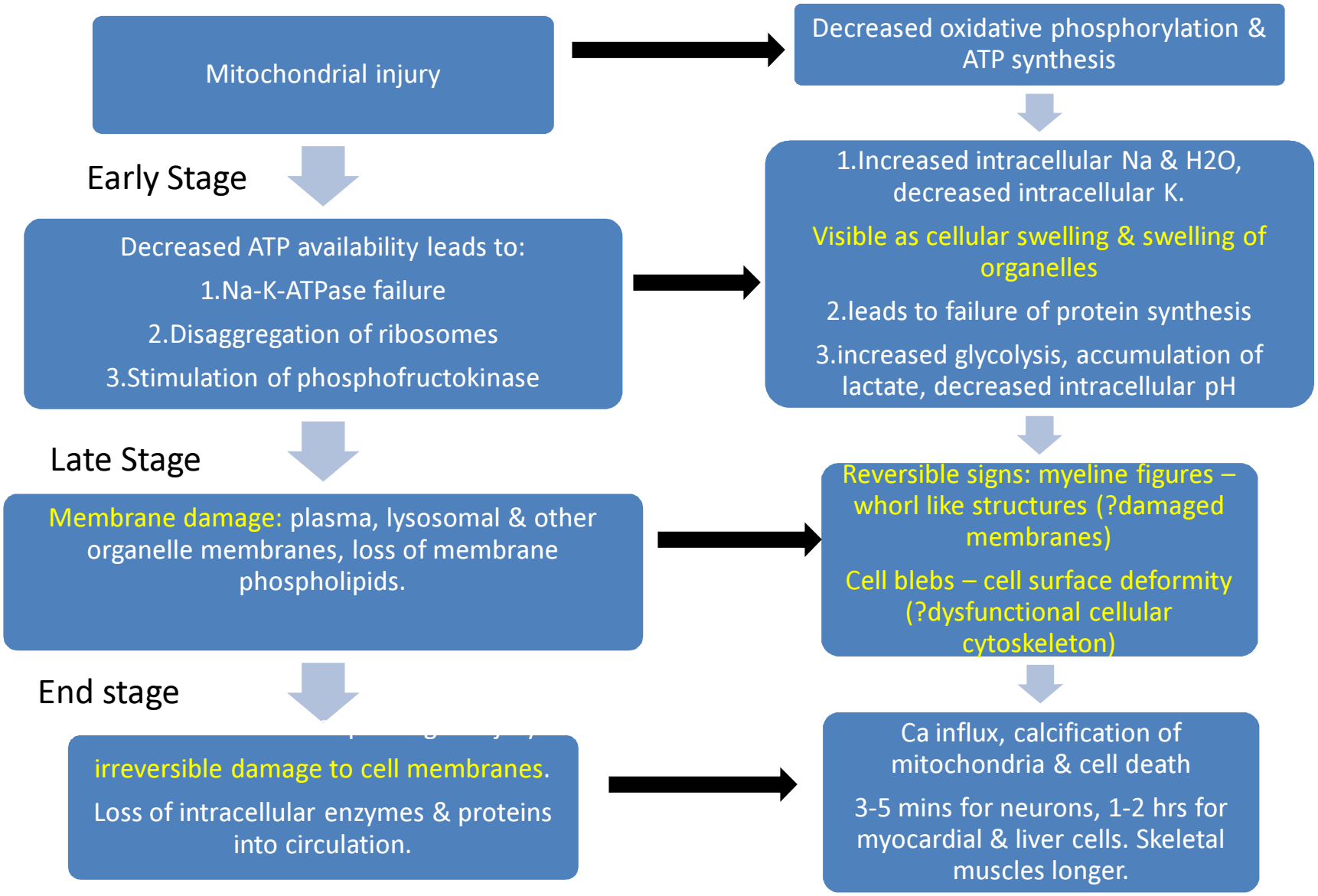
Stratified squamous cells

Columnar cells with glands

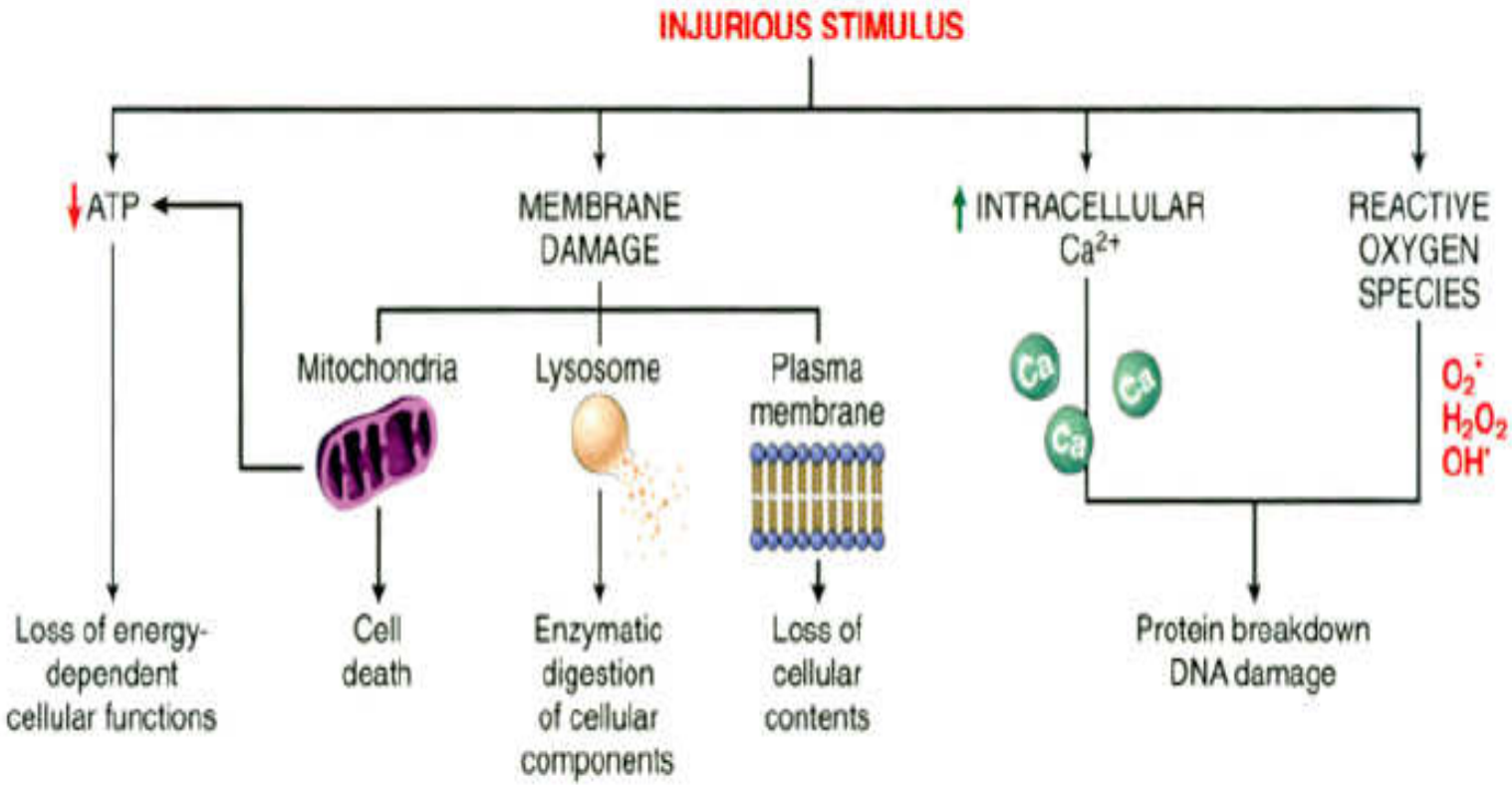
Hypoxic Cell Injury

- Hypoxic cell injury results from several mechanisms
  - **Ischaemia**
  - Anemia
  - Carbon monoxide poisoning
  - Decreased perfusion of tissues by oxygen-carrying blood (e.g. cardiac failure, hypotensive shock)
  - Poor oxygenation of blood (e.g. pulmonary diseases)

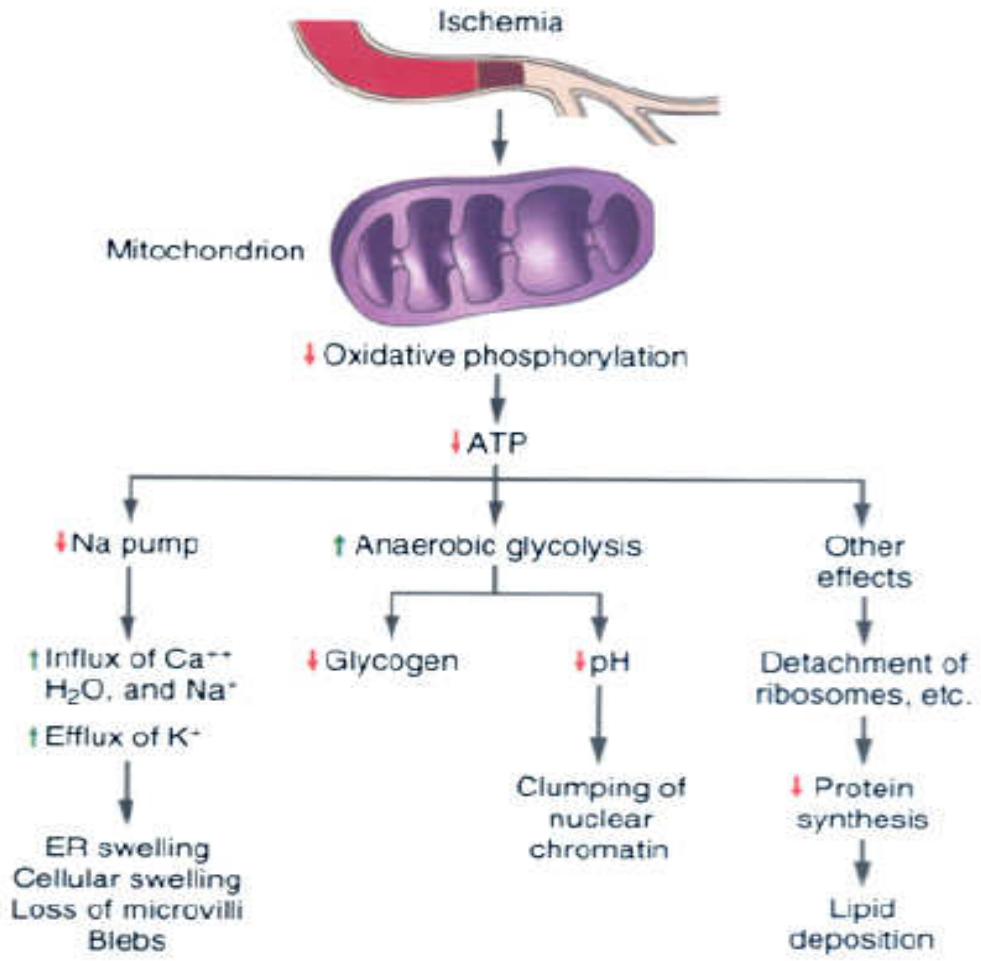
Stages in hypoxic cell injury



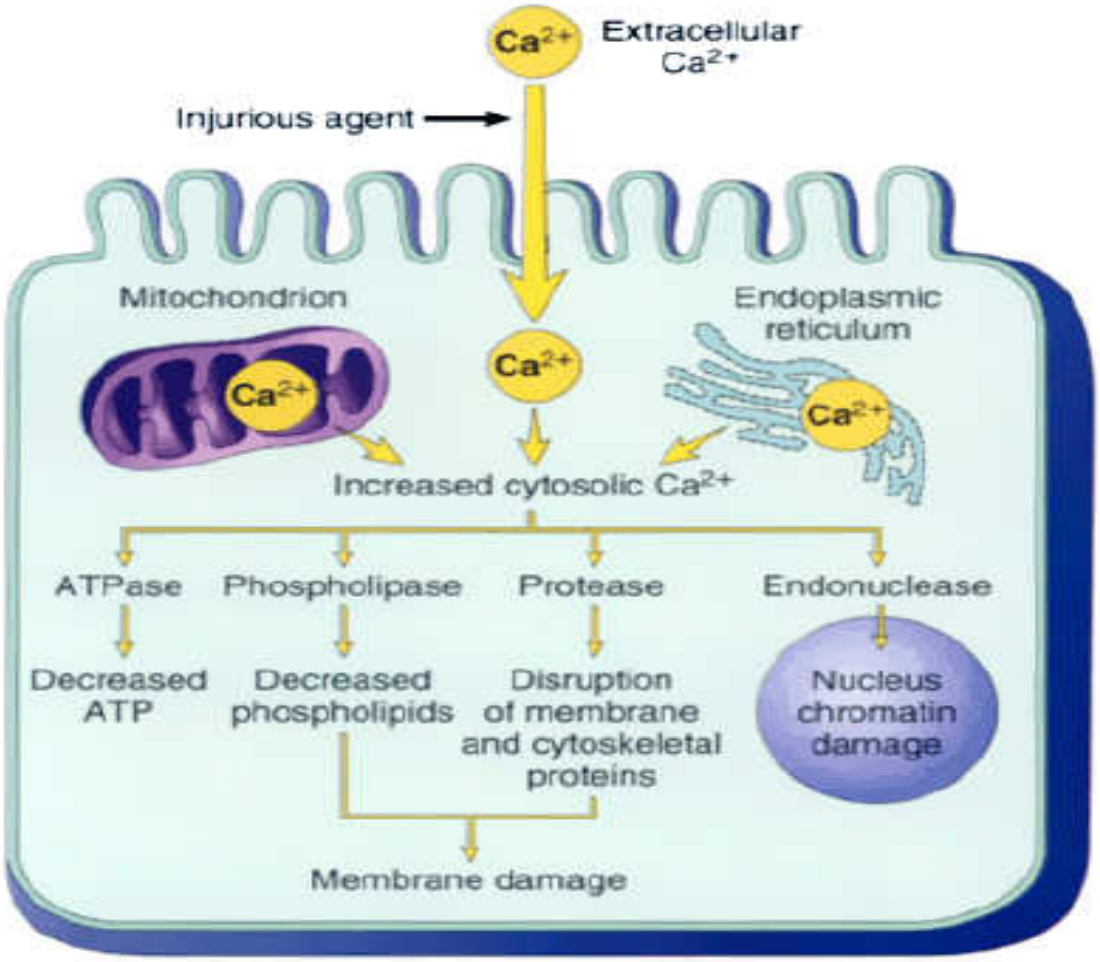
Molecular Sites of Cell Injury



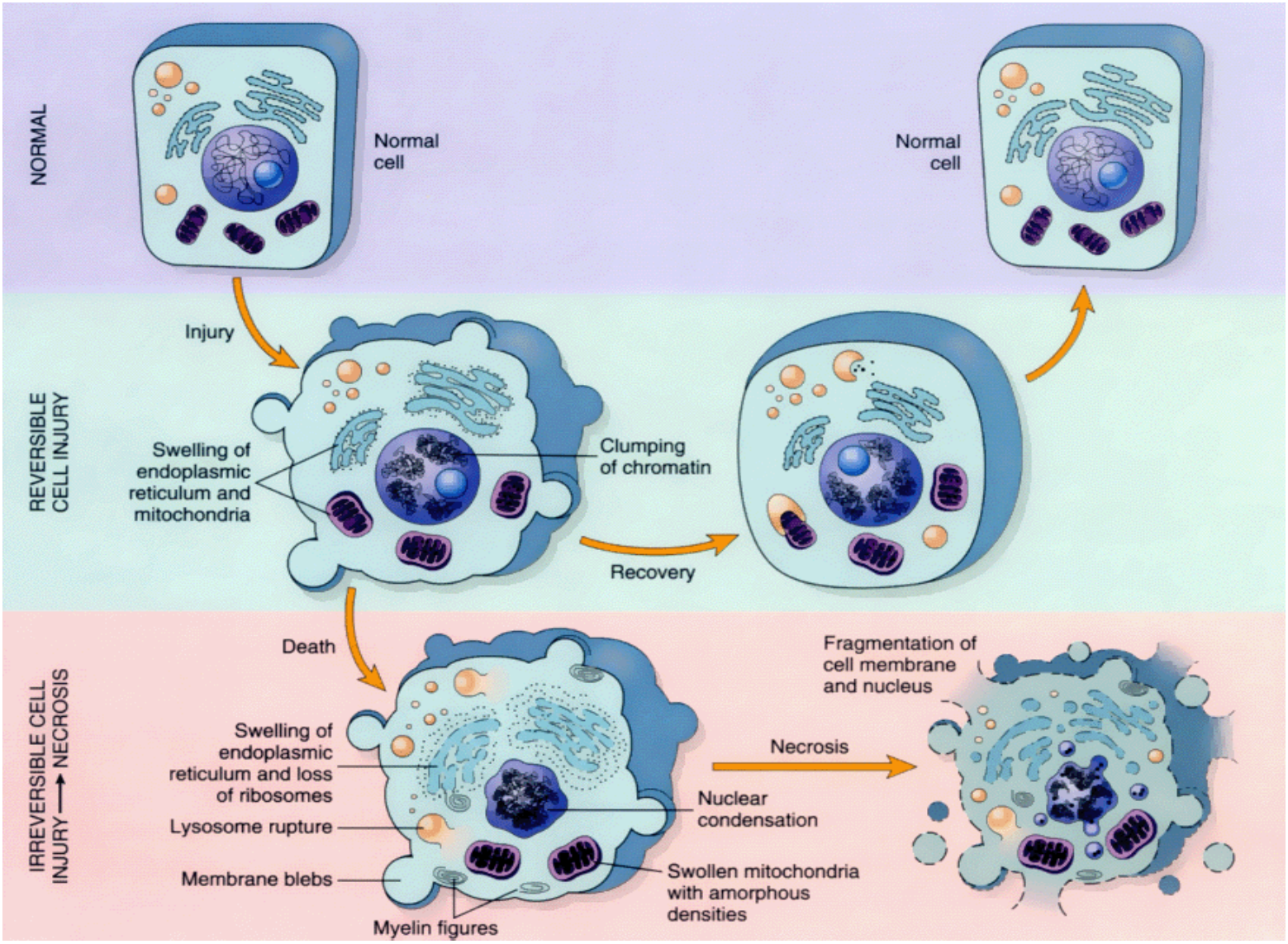
Consequences of decreased intracellular ATP



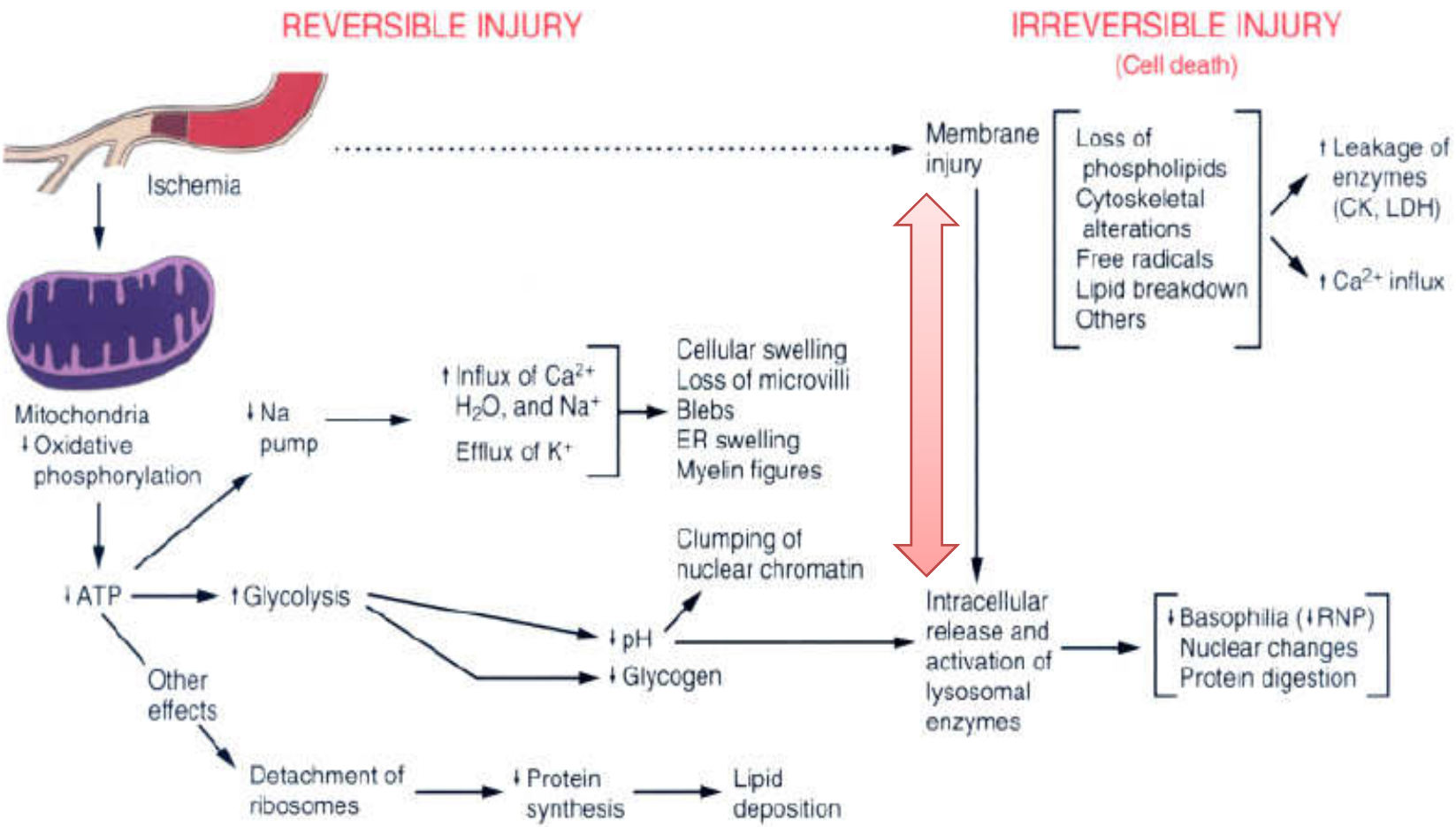
Consequences of increased intracellular Ca



Reversible & Irreversible Cell Injury



Where is the point of no return?



Infarction

- Definition: Tissue necrosis due to ischaemia.
- In the myocardium – coagulative necrosis

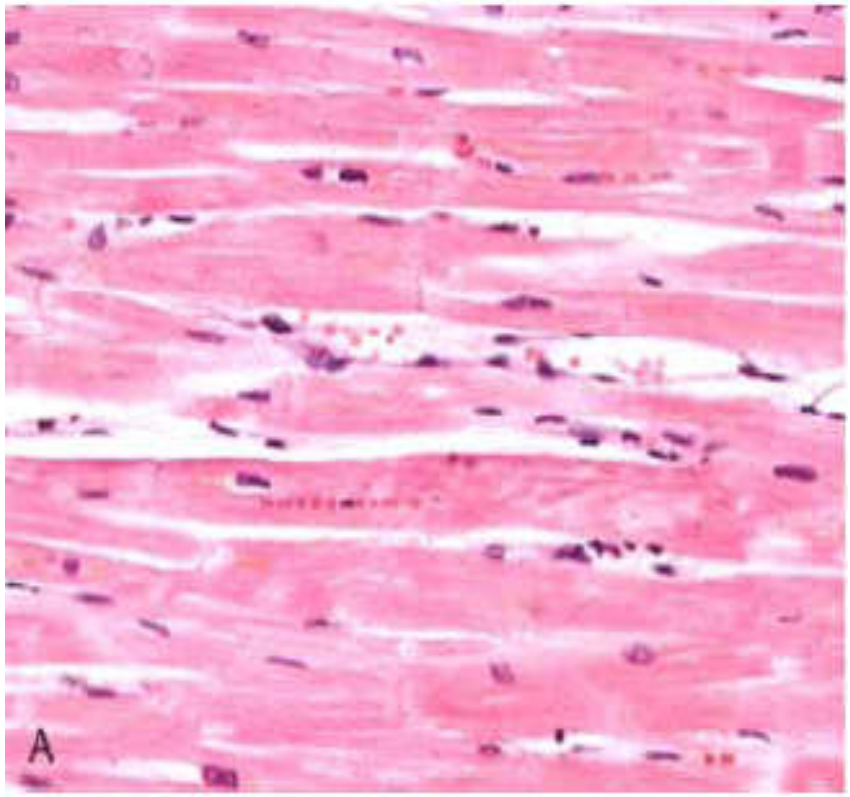
Feature	Necrosis	Apoptosis
Cell size	Enlarged (swelling)	Reduced (shrinkage)
Nucelus	Pyknosis → karyorrhexis → karyolysis	Fragmentation into nucleosome size fragments
Plasma membrane	Disrupted	Intact; altered structure, especially orientation of lipids
Cellular contents	Enzymatic digestion; may leak out of cell	Intact; may be released in apoptotic bodies
Adjacent inflammation	Frequent	No
Physiologic or pathologic role	Invariably pathologic (culmination of irreversible cell injury)	Often physiologic, means of eliminating unwanted cells; may be pathologic after some forms of cell injury, especially DNA damage

Types of necrosis

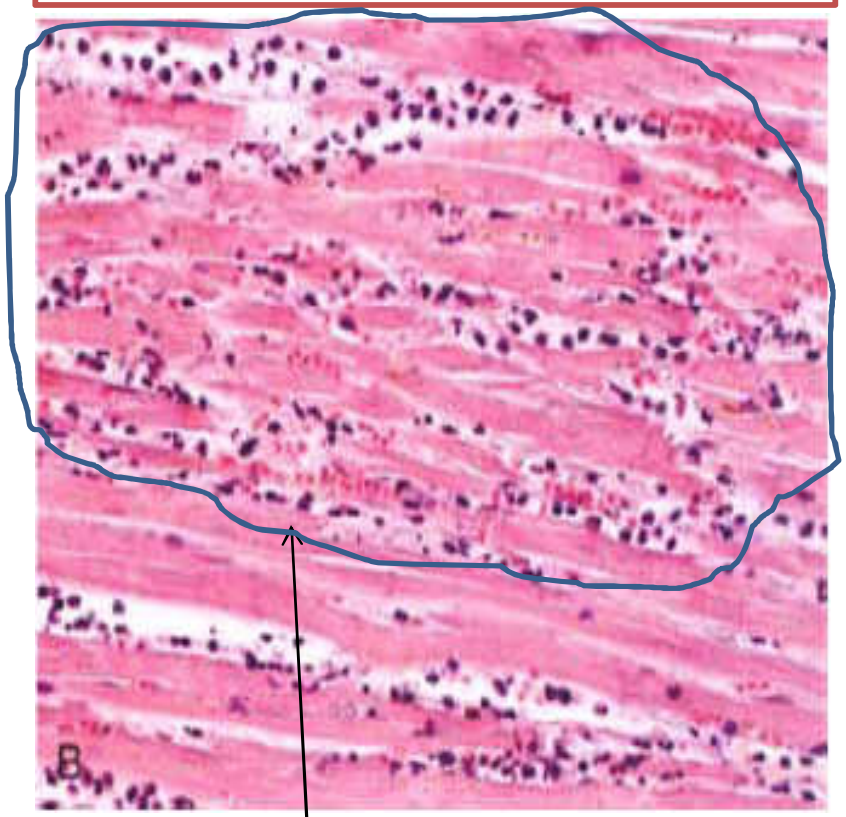
Types	Mechanism	Pathological Changes
Coagulative necrosis	Results from Ischaemia Seen in organs with end arteries (e.g. heart, kidneys)	General architecture preserved. Nuclear changes, increased cytoplasmic binding of acidophylic dyes
Liquefactive necrosis	Enzymatic liquefaction of necrotic tissue. Often in CNS. Hypoxia/ischaemia common cause. Seen in areas of bacterial infection	Necrotic tissue soft & liquefied
Caseous necrosis	Shares features of coagulation & liquefactive necrosis. TB good example.	Architecture not preserved. Soft cheesy. Histology – amorphous with increased affinity of acidophilic dyes
Grangrenous necrosis	Ischaemic to lower limb or bowel	Dry or wet gangrene depending on tissue involved
Fibrinoid necrosis	Deposition of fibrin-like proteinaceous material in walls of arteries. Often seen in immune mediated vasculitis.	Smudgy pinky appearance in vascular walls. Actual necrosis may or may not be present
Fat necrosis	Autodigestion of pancreatic parenchyma from pancreatic enzymes. Trauma to fat cells	Necrotic fat cells. Acute inflammation, haemorrhage, Ca soap formation, clusterin of lipid-laden macrophages (in pancreas)

Coagulative Necrosis

Normal myocardial fibers

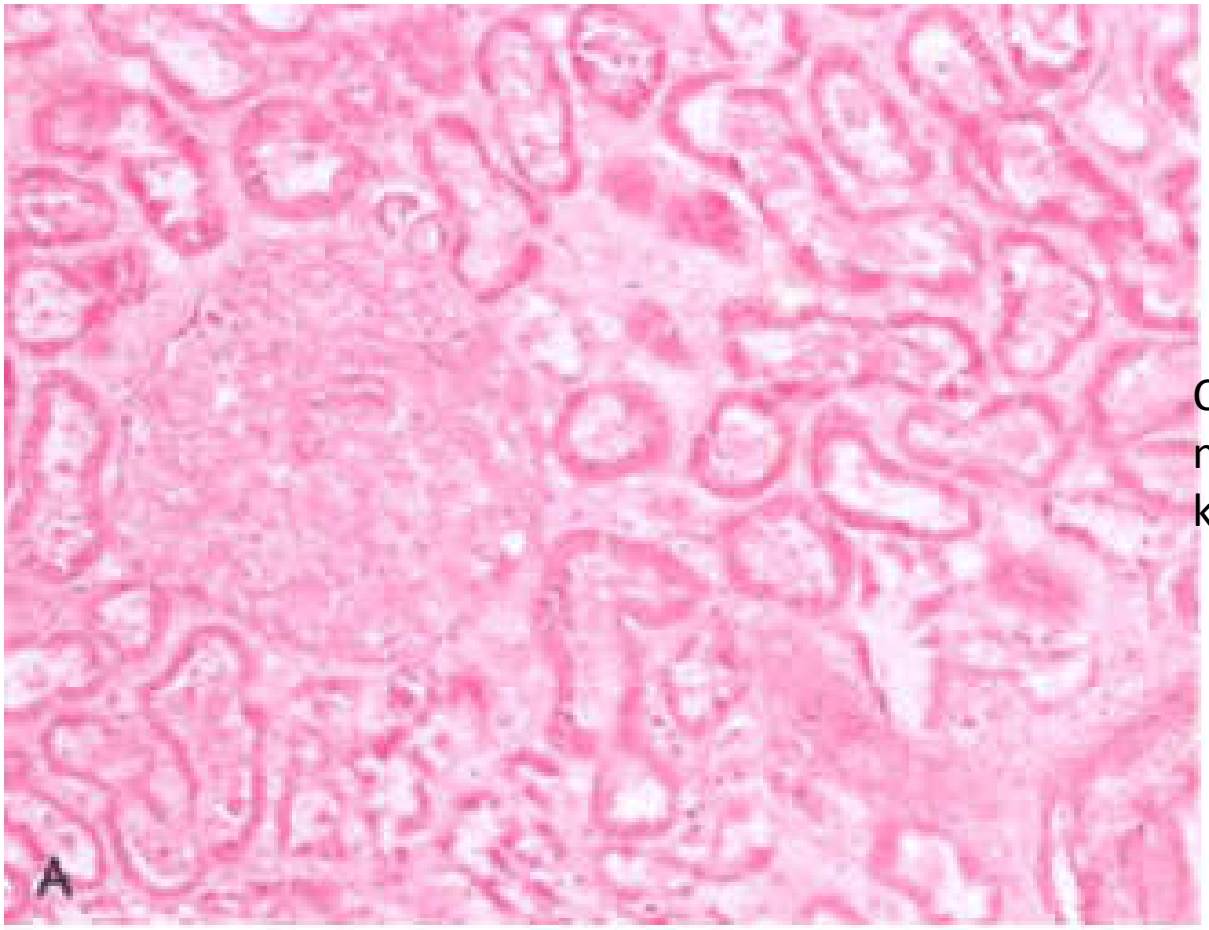


Coagulative necrosis of myocardial fibers



Upper 2/3 shows: strongly eosinophilic anucleate myocardial fibres. Leucocytes in in interstium (early rxn to necrotic material).

Coagulative Necrosis



Coagulative necrosis in kidney

Loss of nuclei, clumping of cytoplasm. Basic outline of glomerular & tubular architecture preserved.

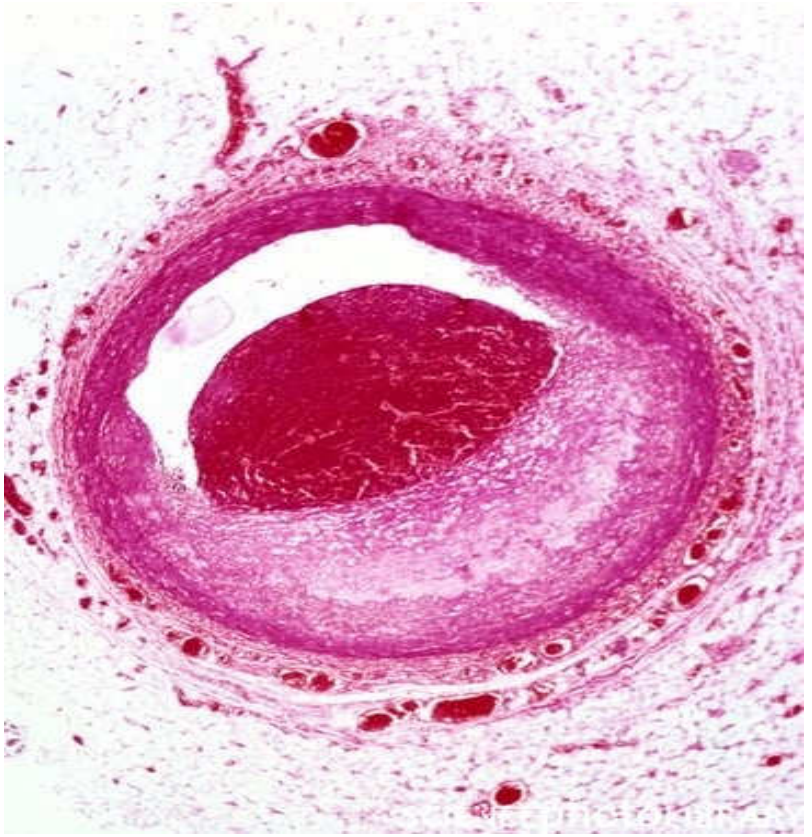
Cerebral Infarct

- 4 major causes hypoxic injury to brain.
- **Thrombosis** – involves cerebral arteries from atherosclerosis.
- **Embolism** – middle cerebral artery is more prone. Embolus from cardiac mural thrombi, vegetations (infective endocarditis), tumor cells, air bubbles or fat droplets (from fractures).
- **Hypotension** – involves "watershed" areas & deep layers of the cortex. *What are "watershed" areas?*
- **Hypertension** – lacunae (small pits) infarcts common (multiple cystic infarcts, prominent in basal ganglia). Due to arteriolar occlusion in hypertensive patients.

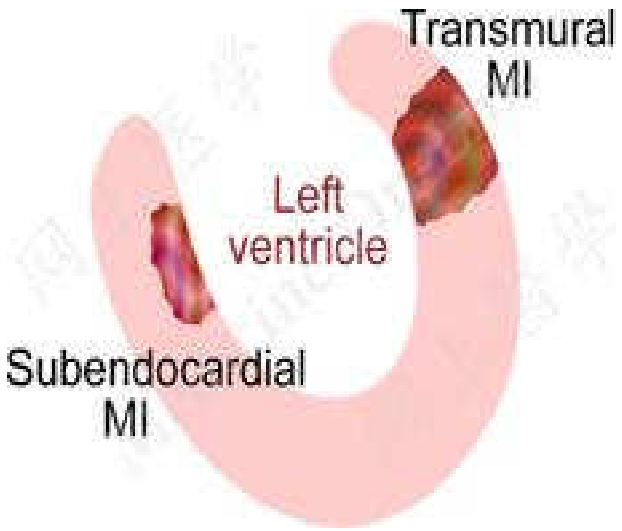
Myocardial Infarct

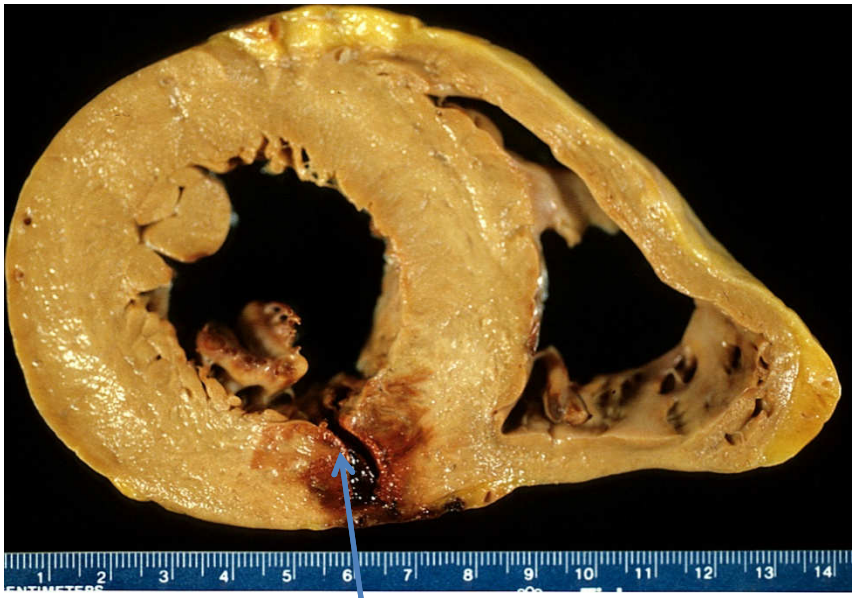
General Considerations

- Results from partial or complete interruption of arterial blood flow to the myocardium.
- Most occurs because of atherosclerotic plaque within one or more coronary arteries
- Ischaemia maybe clinically silent, manifest as angina pectoris or MI.

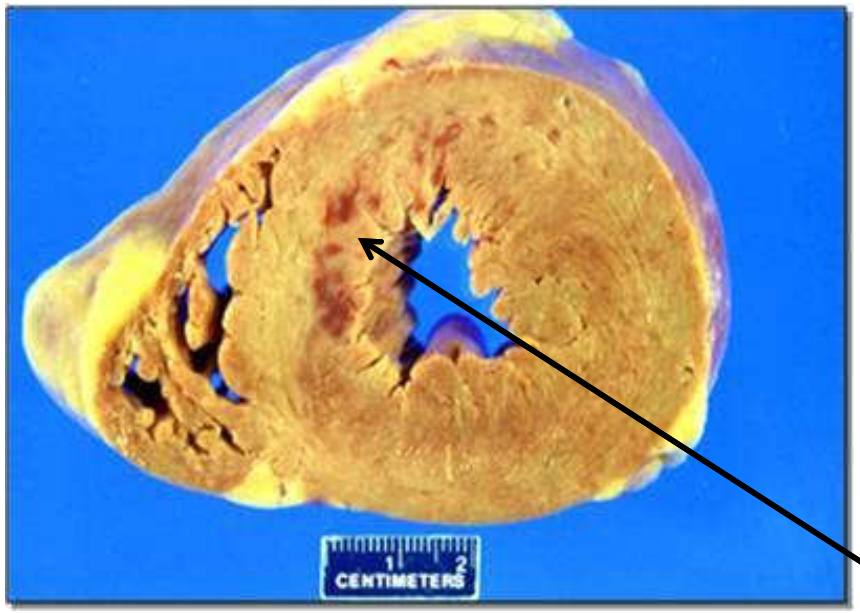


Types of MI

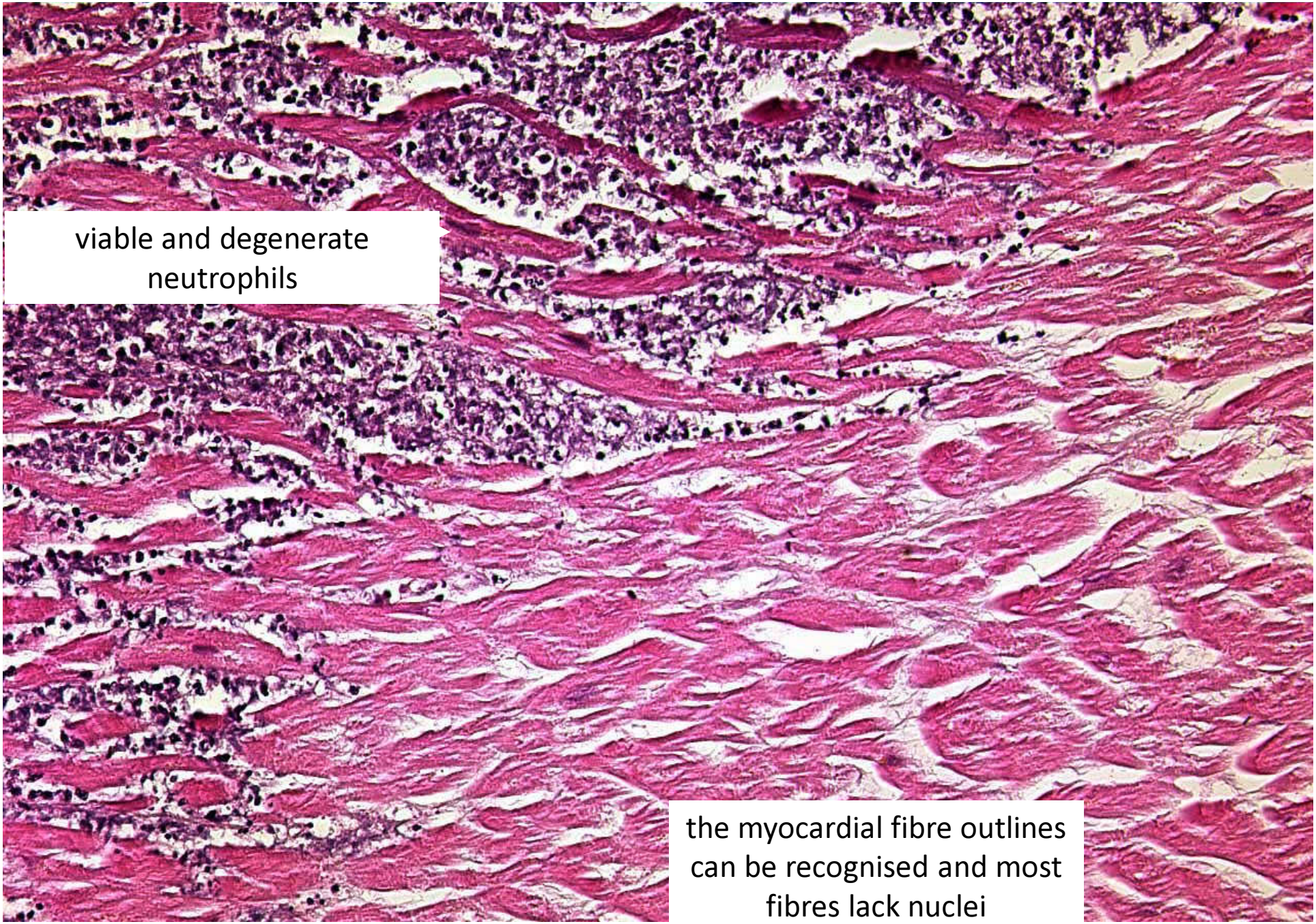




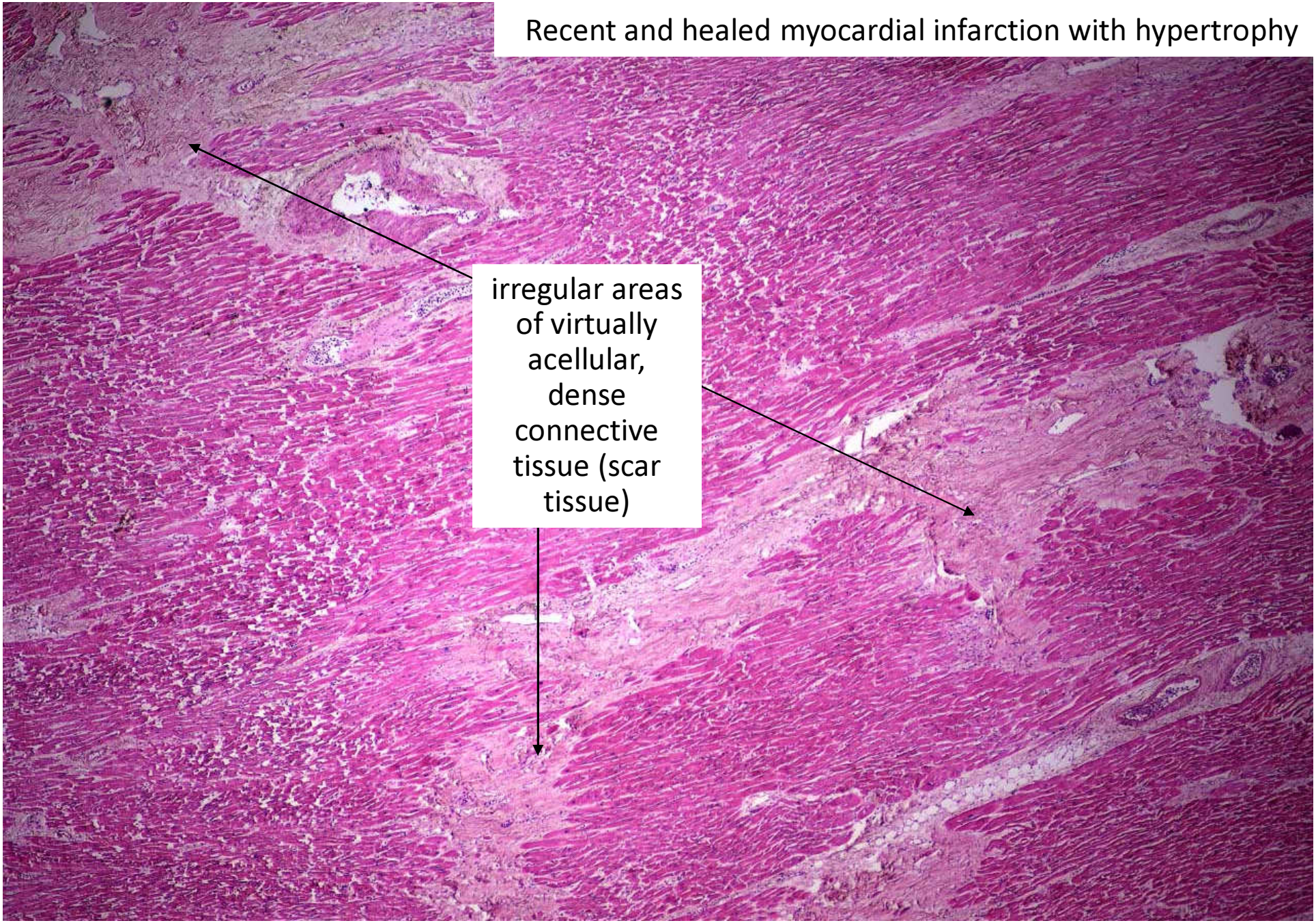
Transmural: infarct localised to anatomical area supplied by affected artery.



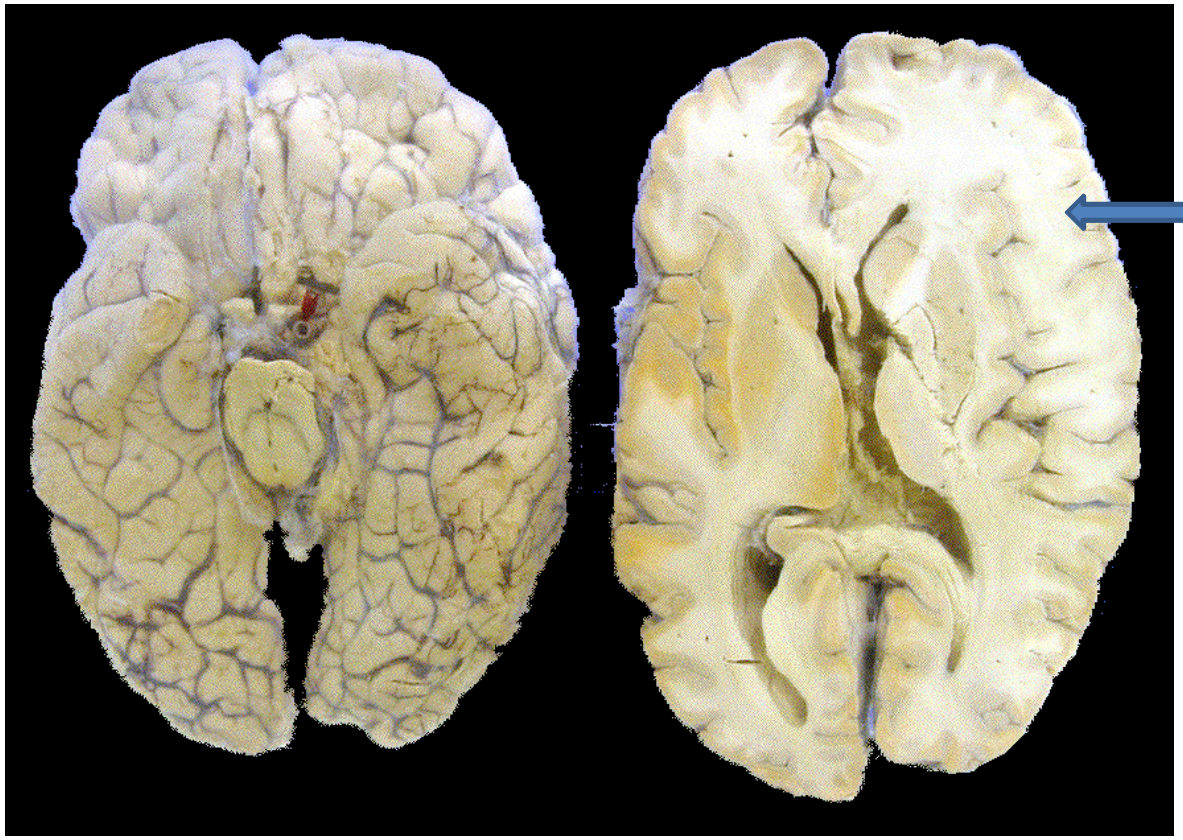
Subendocardial: necrosis of subendocardium


viable and degenerate neutrophils
the myocardial fibre outlines can be recognised and most fibres lack nuclei

Recent and healed myocardial infarction with hypertrophy



CNS



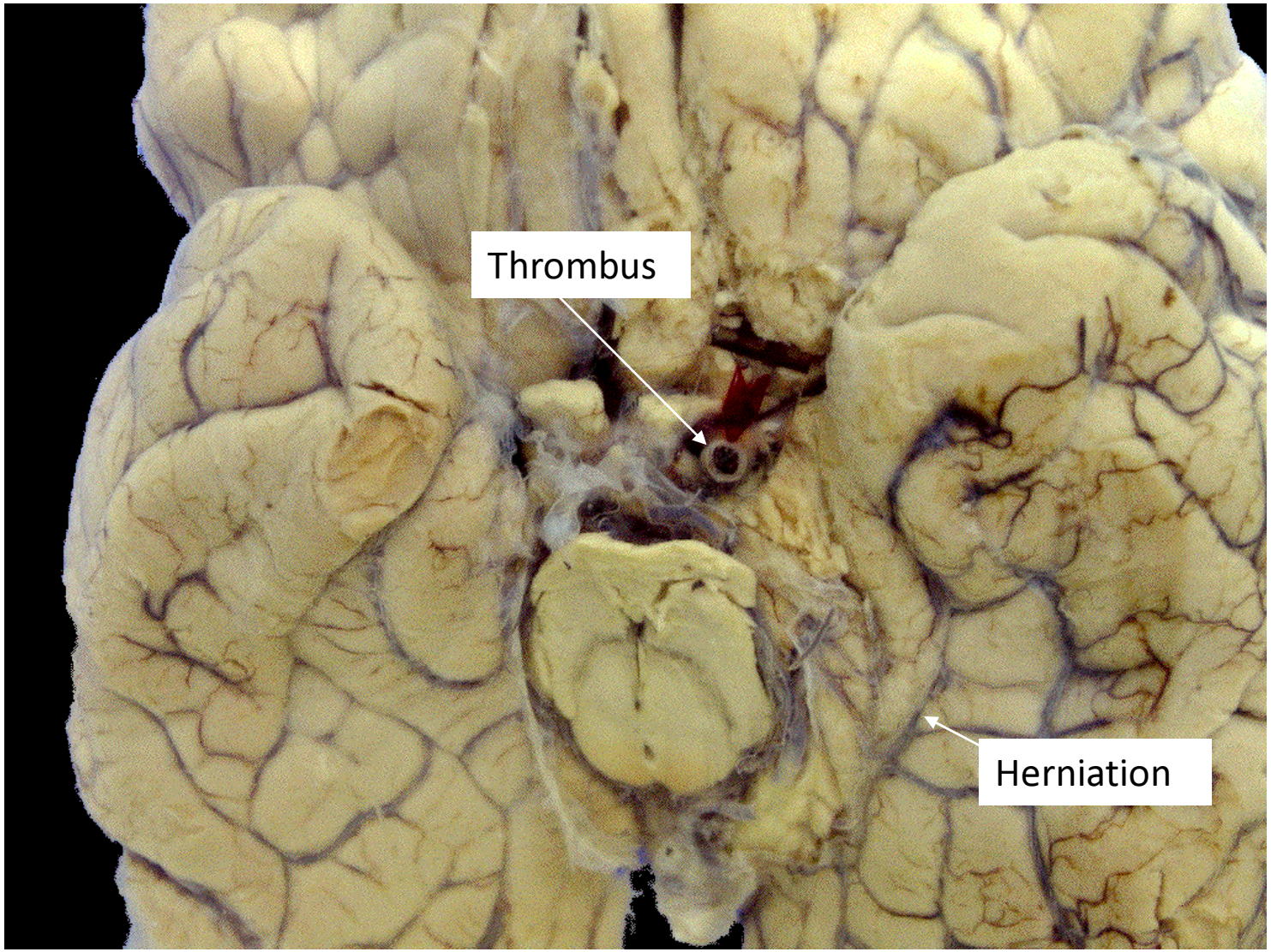
Gross Pathology

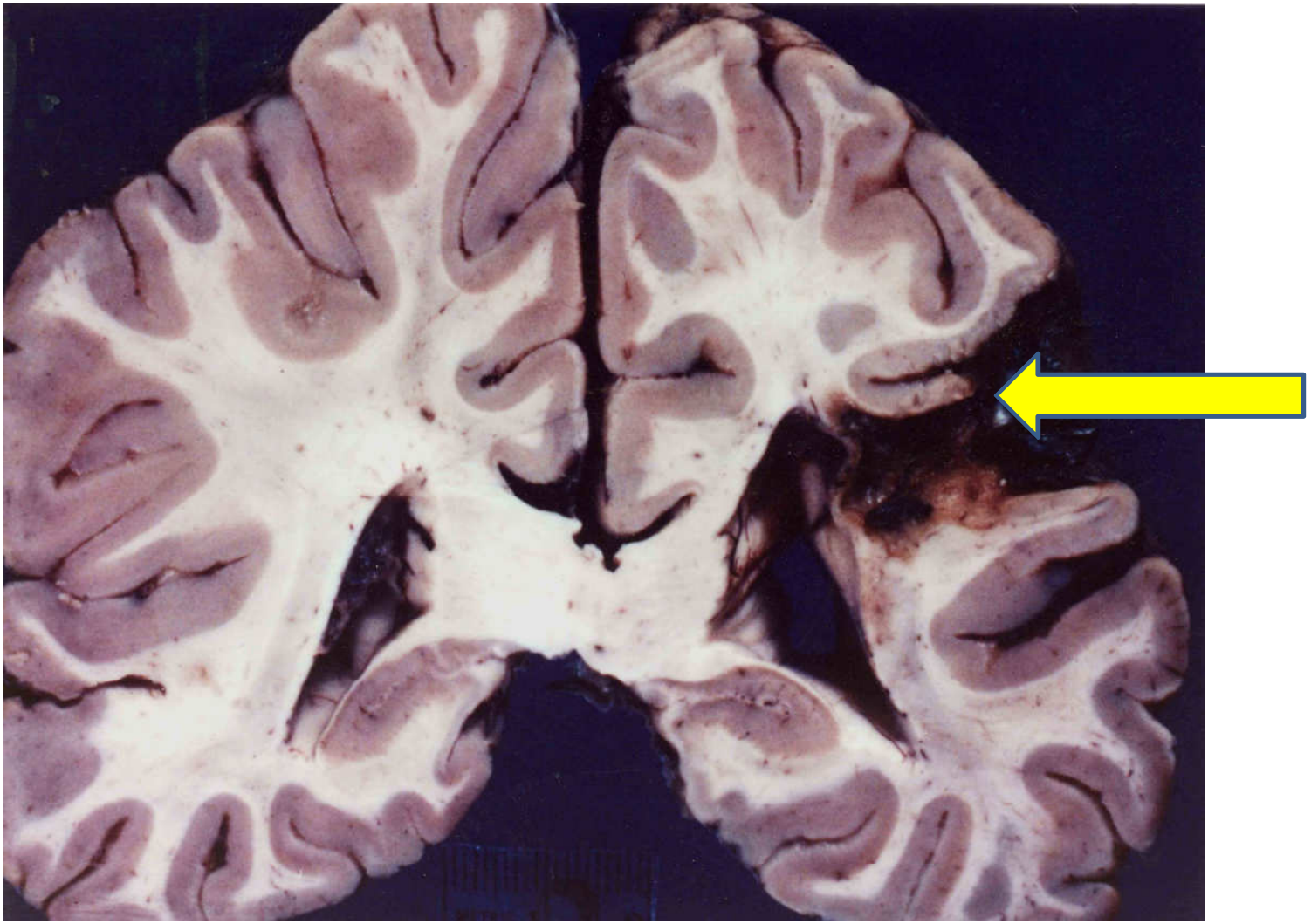
The mounted specimen of the brain shows marked swelling of the left cerebral hemisphere. Thrombus can be seen occluding the left internal carotid artery.

This appearance is consistent with that of an extremely recent (10 hours) cerebral infarct.

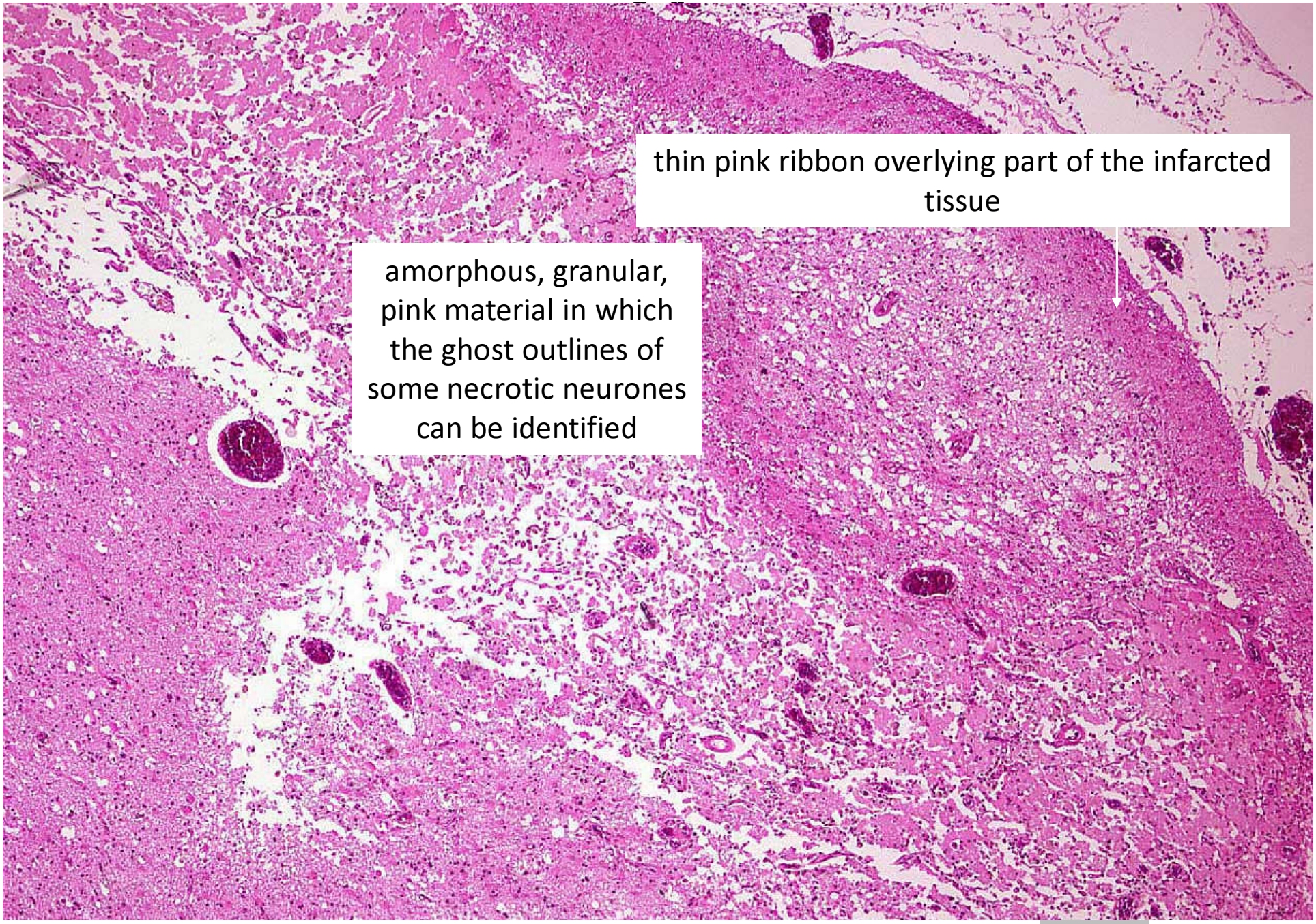
Ref: UTAS interactive Pathlogy CD

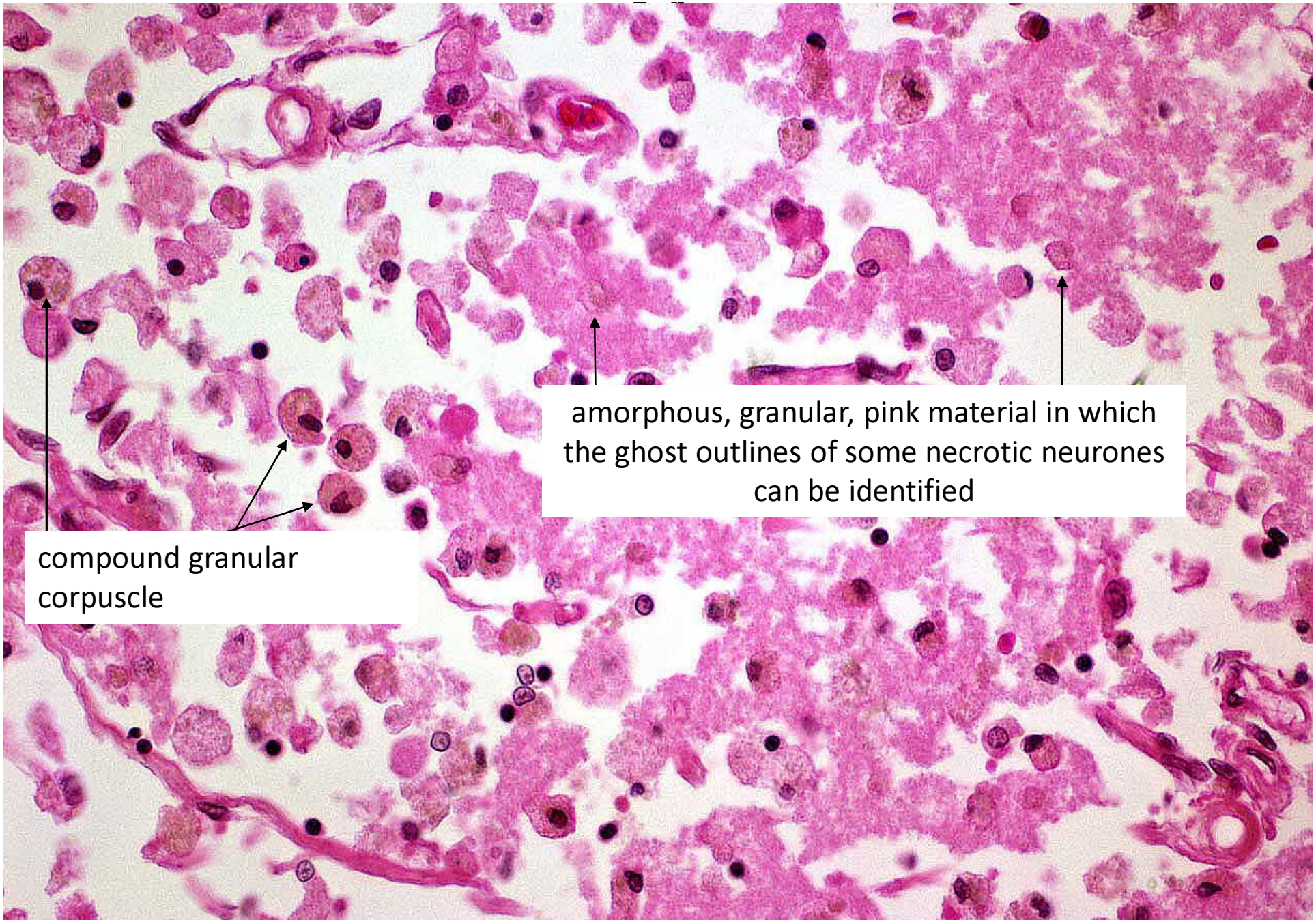
Gross pathology - magnified view of thrombus and uncal herniation



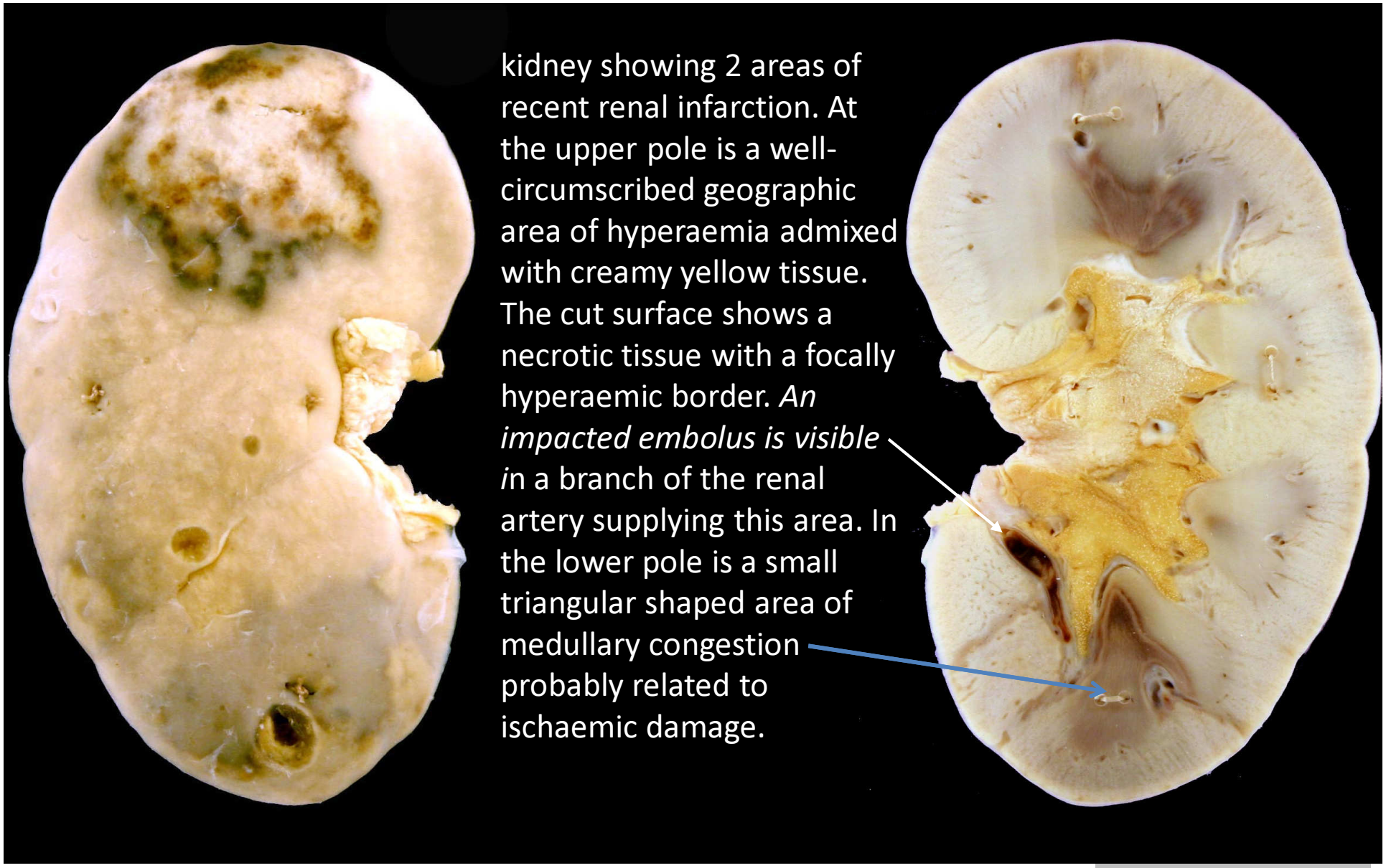


The photograph shows a coronal slice of brain. An old cerebral infarct is present in the territory of the left middle cerebral artery represented by a cystic space surrounded by gliosis


thin pink ribbon overlying part of the infarcted tissue
amorphous, granular, pink material in which the ghost outlines of some necrotic neurones can be identified

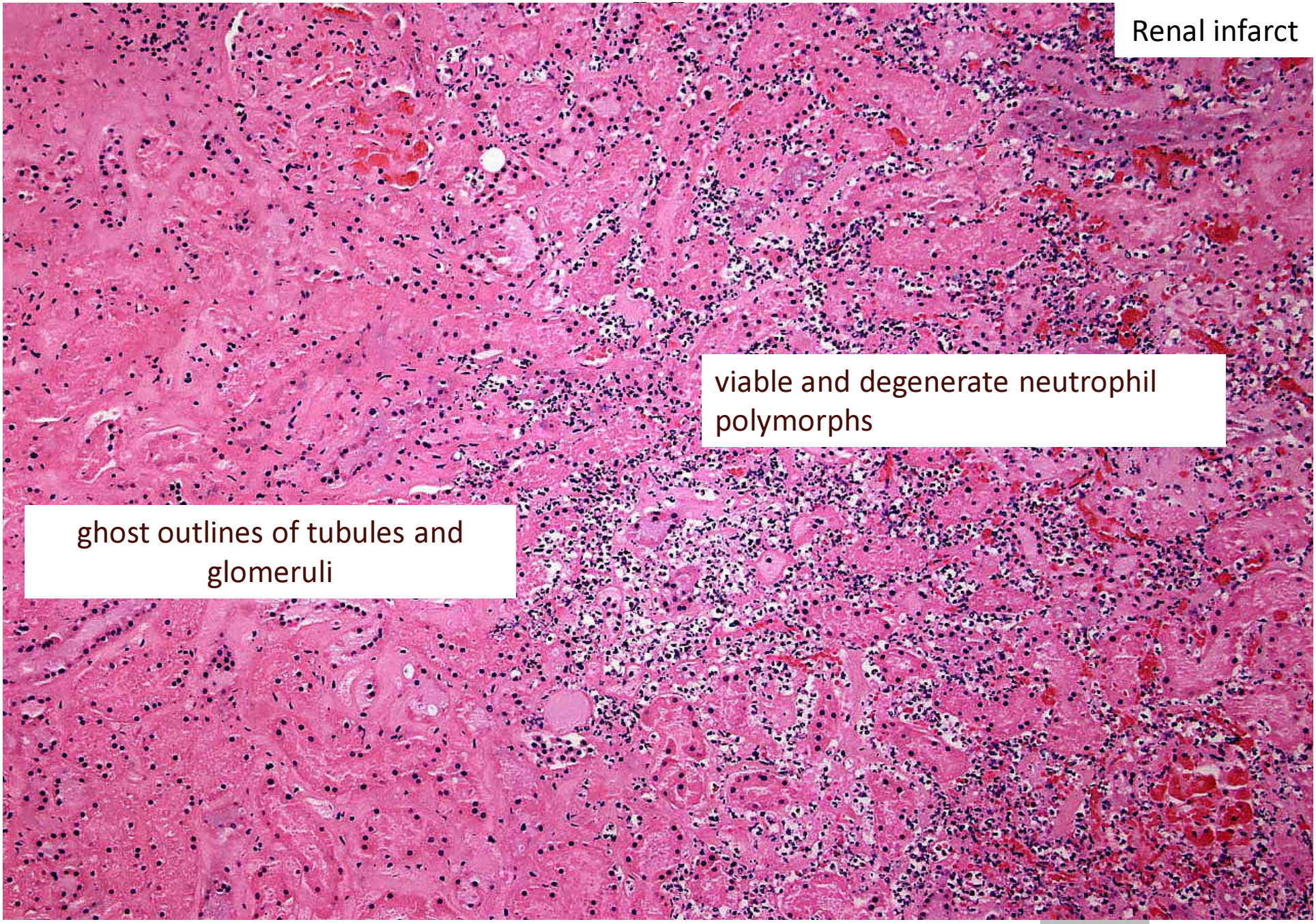

amorphous, granular, pink material in which the ghost outlines of some necrotic neurones can be identified
compound granular corpuscle

Kidney

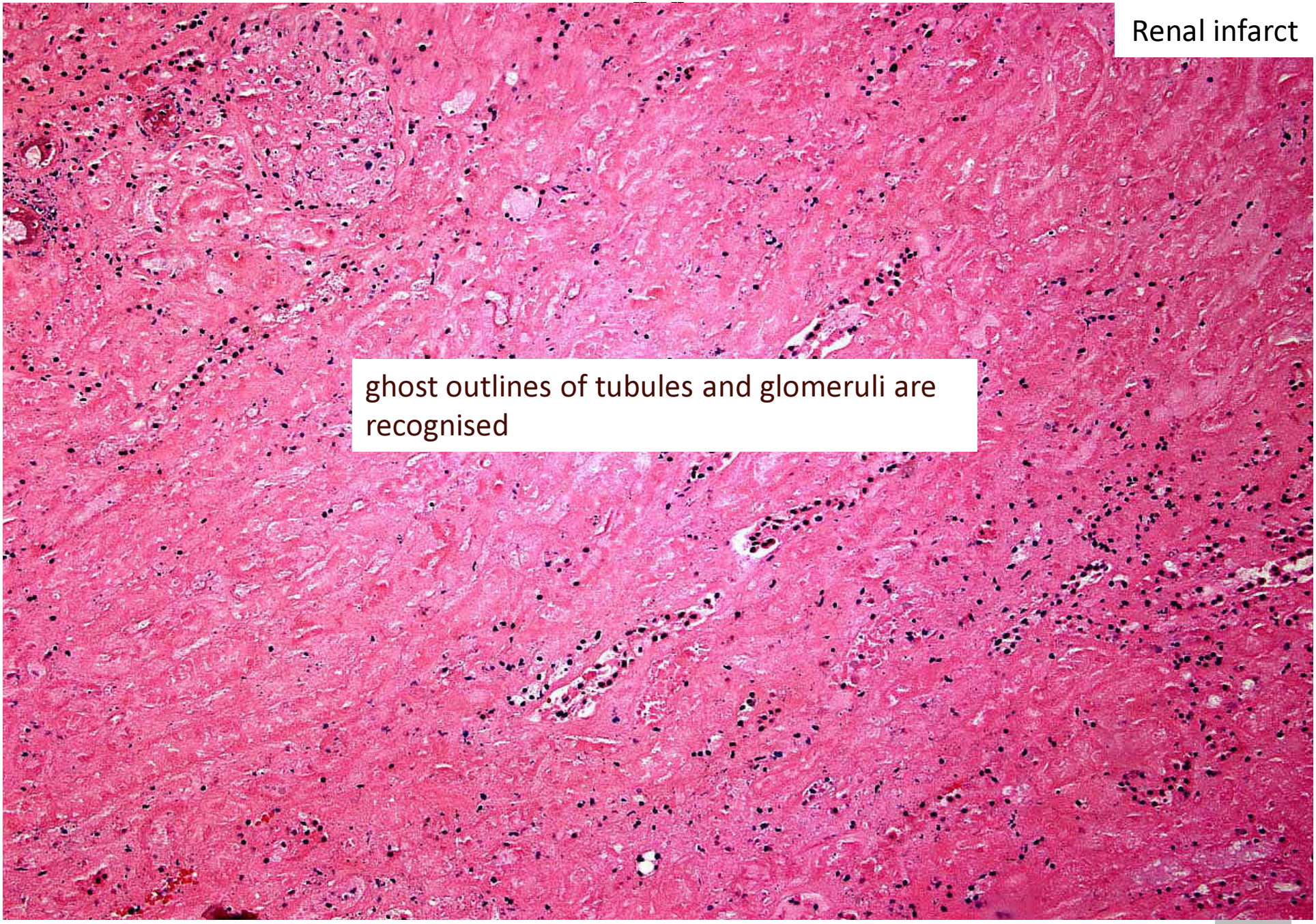


kidney showing 2 areas of recent renal infarction. At the upper pole is a well-circumscribed geographic area of hyperaemia admixed with creamy yellow tissue. The cut surface shows a necrotic tissue with a focally hyperaemic border. *An impacted embolus is visible i*n a branch of the renal artery supplying this area. In the lower pole is a small triangular shaped area of medullary congestion probably related to ischaemic damage.

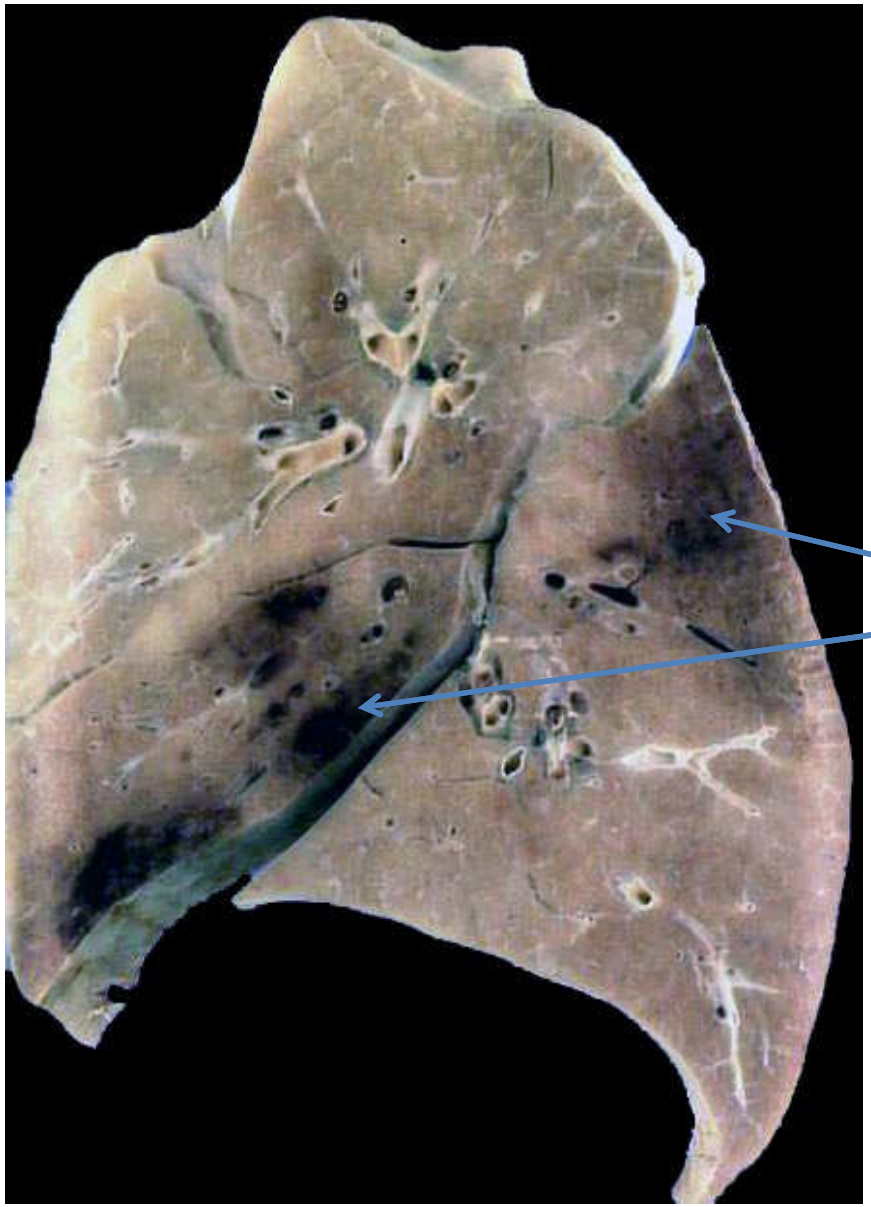
Renal infarct



Renal infarct

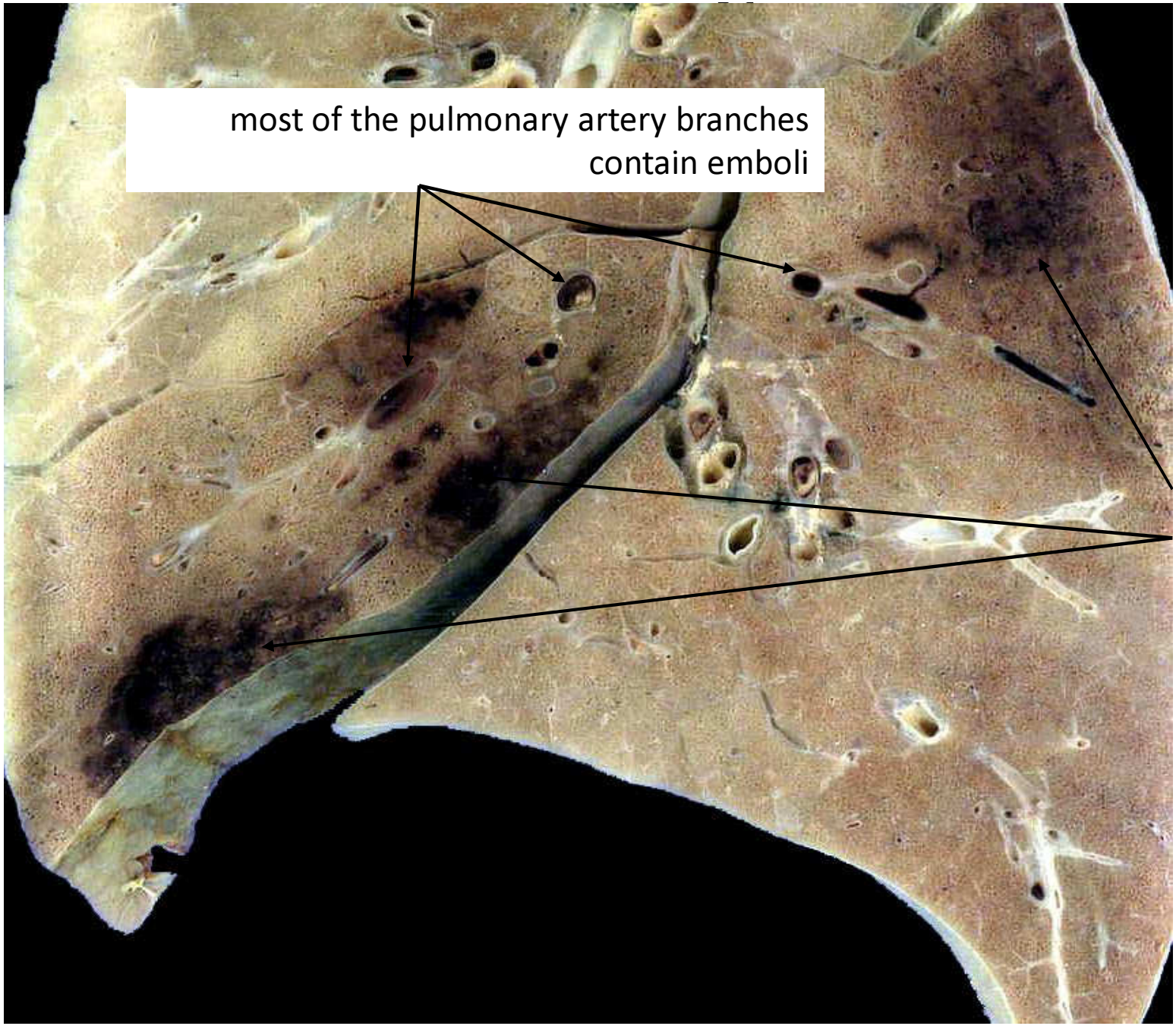


Lungs



Gross Pathology

Most of the pulmonary artery branches contain emboli. *The apical segment of the lower lobe and most of the middle lobe show evidence of pulmonary infarction*. These infarcts are haemorrhagic (dark brown to black in colour) and the surrounding pulmonary parenchyma is consolidated. Compare this parenchyma with that of the upper lobe which is normal.

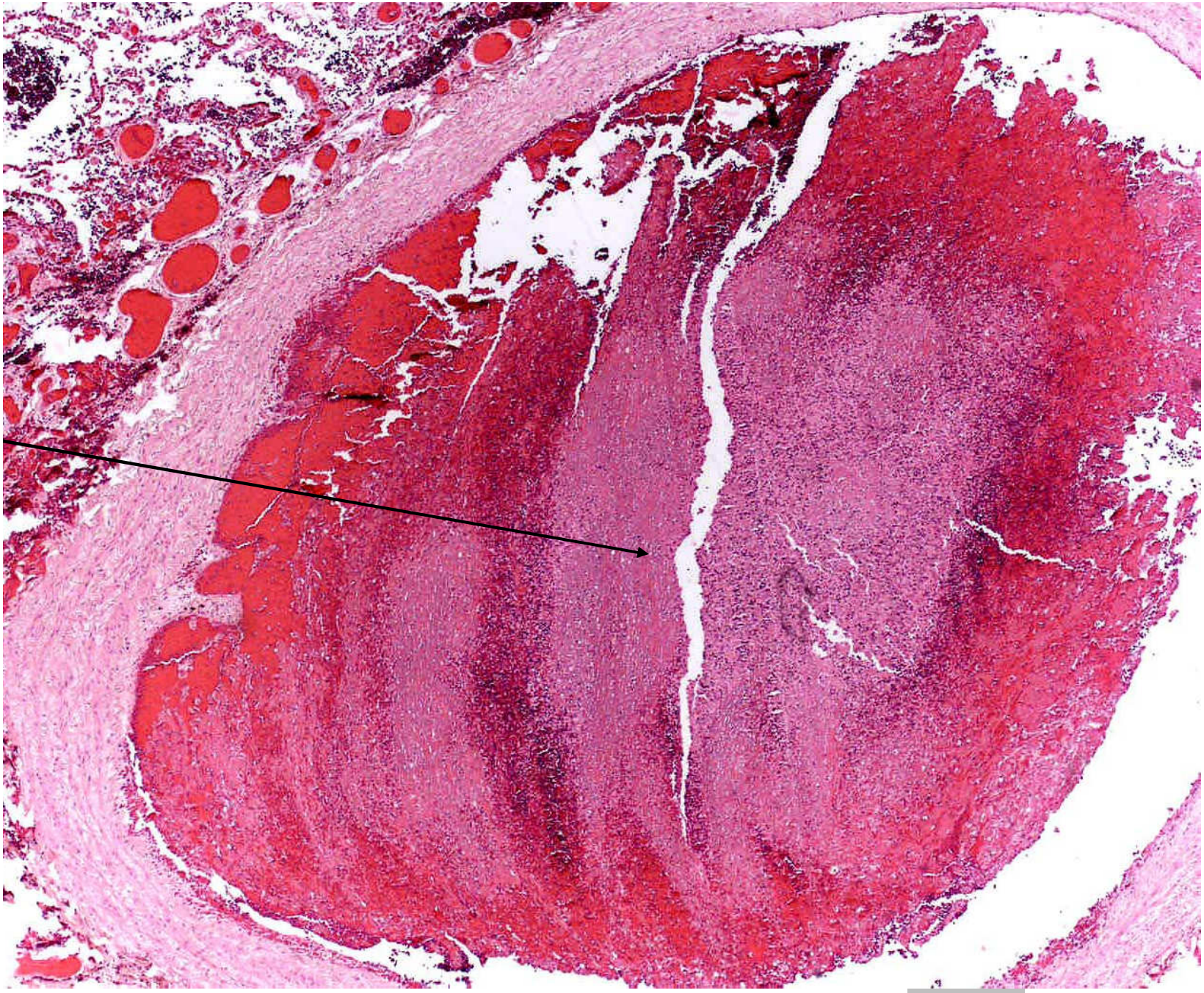


Pulmonary embolism and infarction

the apical segment of the lower lobe and most of the middle lobe show evidence of pulmonary infarction.

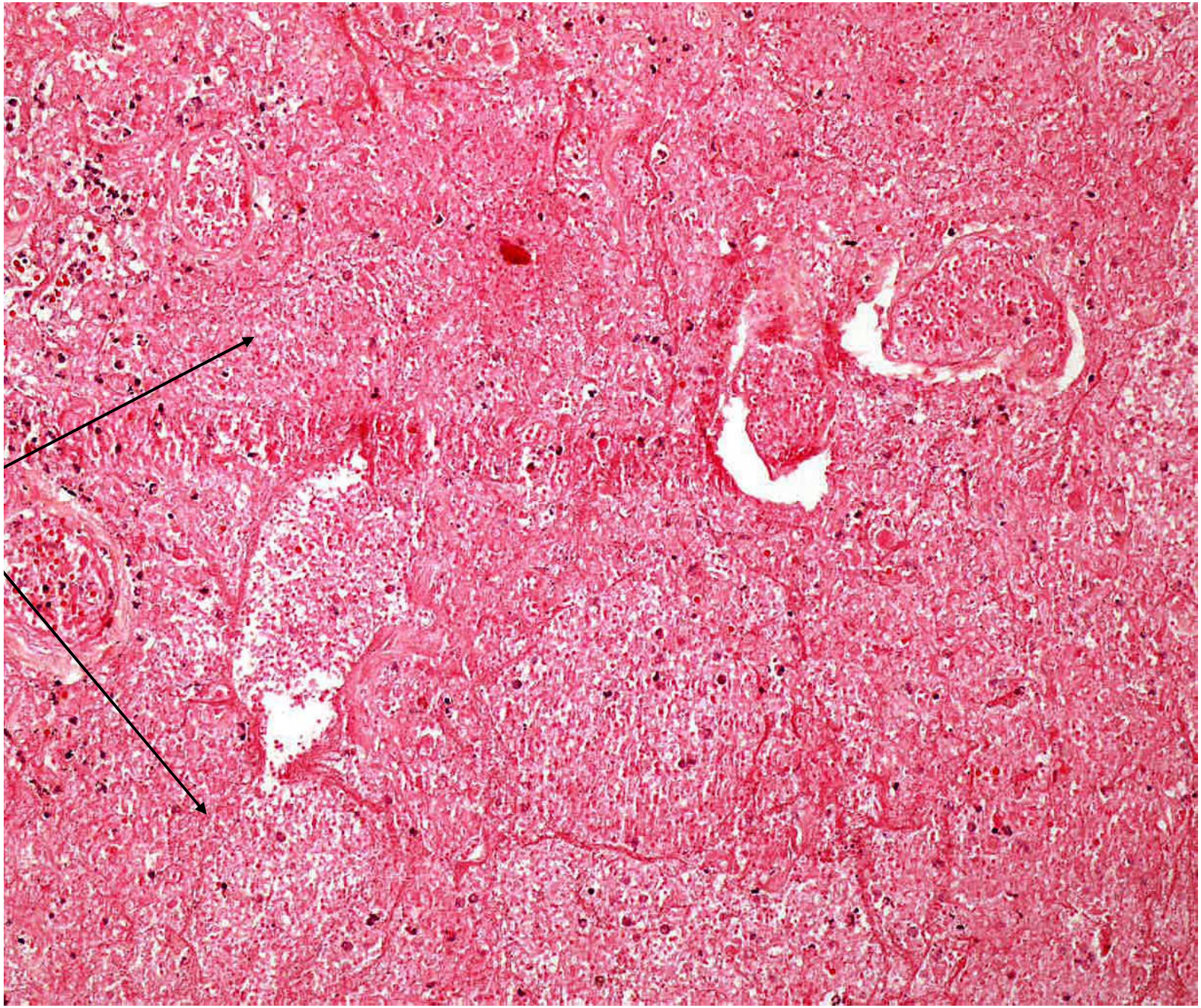
Pulmonary embolism and infarction

thromboembolus. It has the same internal structure as seen in recent thrombus.

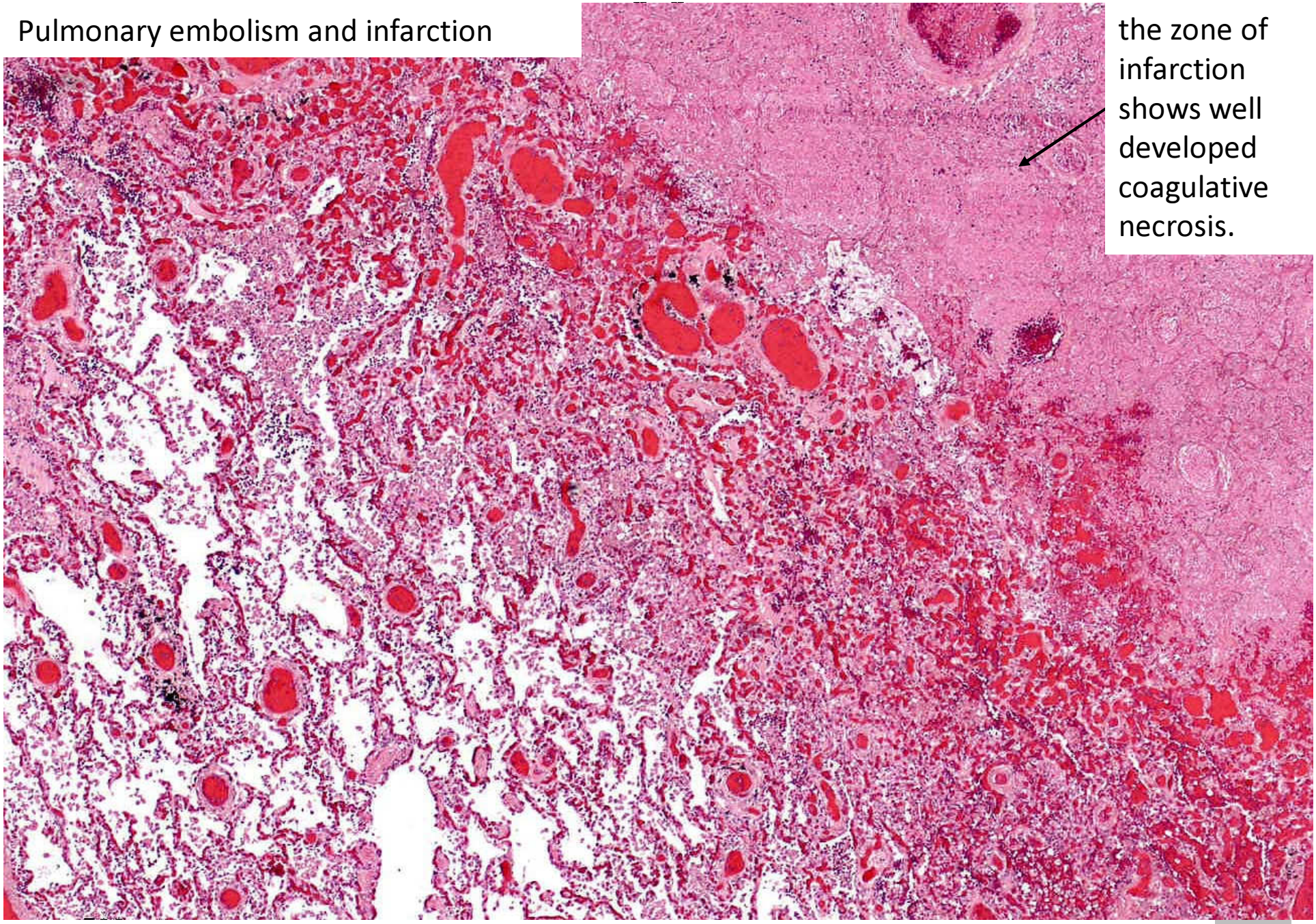


Pulmonary embolism and infarction

the pulmonary parenchyma is intensely congested with intra-alveolar oedema and haemorrhage



Pulmonary embolism and infarction



the zone of infarction shows well developed coagulative necrosis.

Laboratory Diagnosis

- Serum: Enzyme assays – e.g. AST, LDH, CK
- Serum: protein markers – e.g. Troponin I & T, myoglobin
- Tissue – biopsy (post mortem).
- CT scan – CVA
- CT angiogram – pulmonary embolism
- Ventilation-Perfusion scan – pulmonary angioram
- USS – kidneys.

Study Guides

- List the cellular adaptive mechanisms to environmental stress & give an example for each type.
- Agents of cellular injury are generally classified as: hypoxic injury, free radical injury & chemical injury. Describe the mechanism in each type using an example in each.
- Describe the light microscopic features of necrosis.
- Compare & contrast reversible & irreversible cellular injury, including microscopic features.
- Define the following: pyknosis, karyorrhexis & karyolysis in the setting of coagulative necrosis.

END

References
Robins Pathologic Basis of Disease 6th & 7th Ed
Images from: UTAS interactive Pathology CD

Download PDF copy of notes at:
www.pathologyatsmhs.wordpress.com