Harvard-MIT Division of Health Sciences and Technology
HST.035: Principle and Practice of Human Pathology
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Ischemia and Infarction

HST.035

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In the US:

~50% of deaths are due to ischemic heart disease (including myocardial infarction)

~15% of deaths are due to ischemic brain damage (including stroke)

Ischemia

- Greek *ischein* “to restrain” + *haima* “blood”
- Ischemia occurs when the blood supply to a tissue is inadequate to meet the tissue’s metabolic demands
- Ischemia has 3 principal biochemical components:
  - Hypoxia (including anoxia)
  - Insufficiency of metabolic substrates
  - Accumulation of metabolic waste
- Therefore, ischemia is a greater insult to the cells and tissues than hypoxia alone

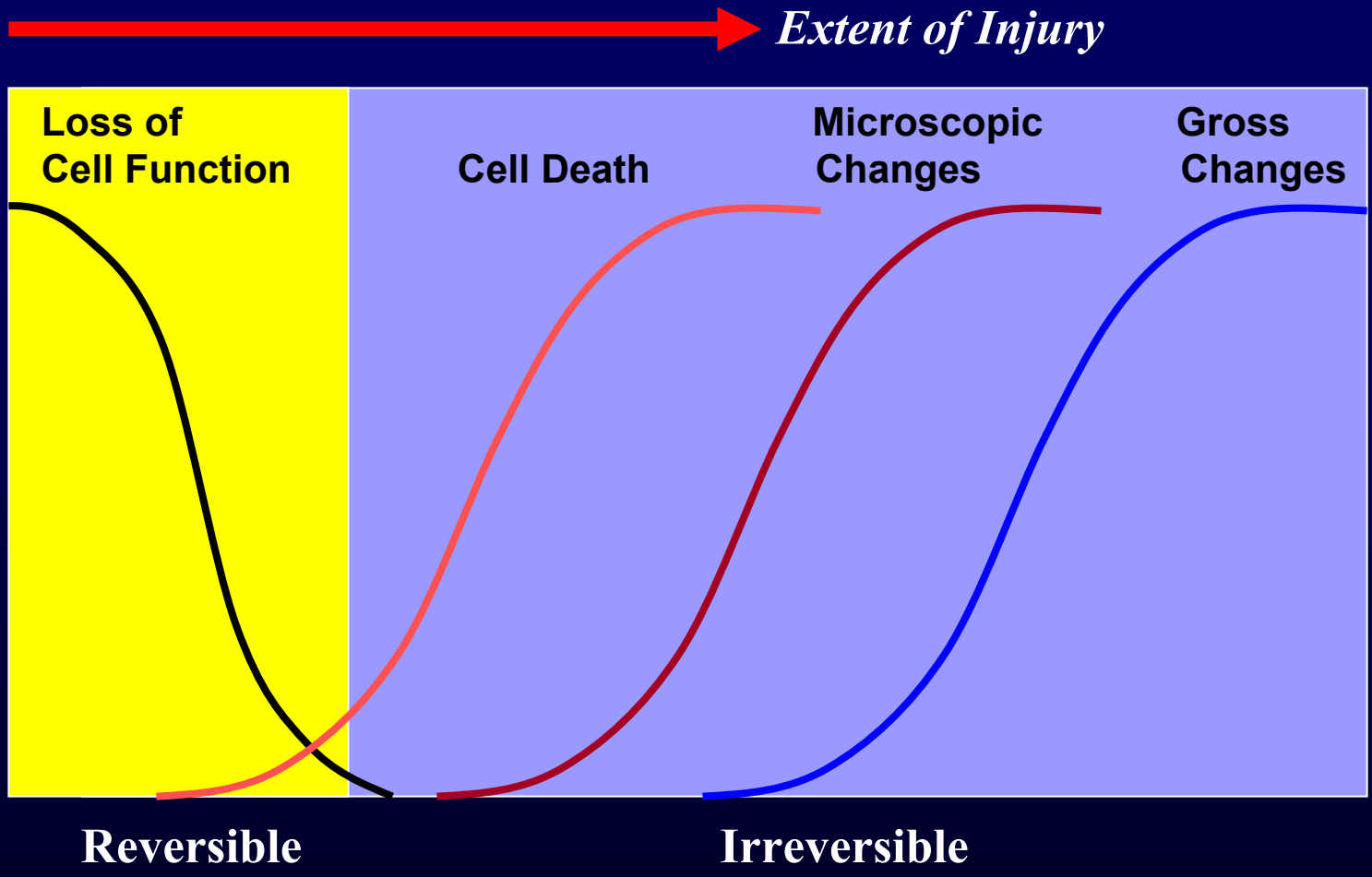
Causes of Ischemia: Decreased Supply

- Vascular insufficiency:
  - Atherosclerosis
  - Thrombosis
  - Embolism
  - Torsion
  - Compression
- Hypotension:
  - Shock
  - Hemorrhage

Causes of Ischemia: Increased Demand

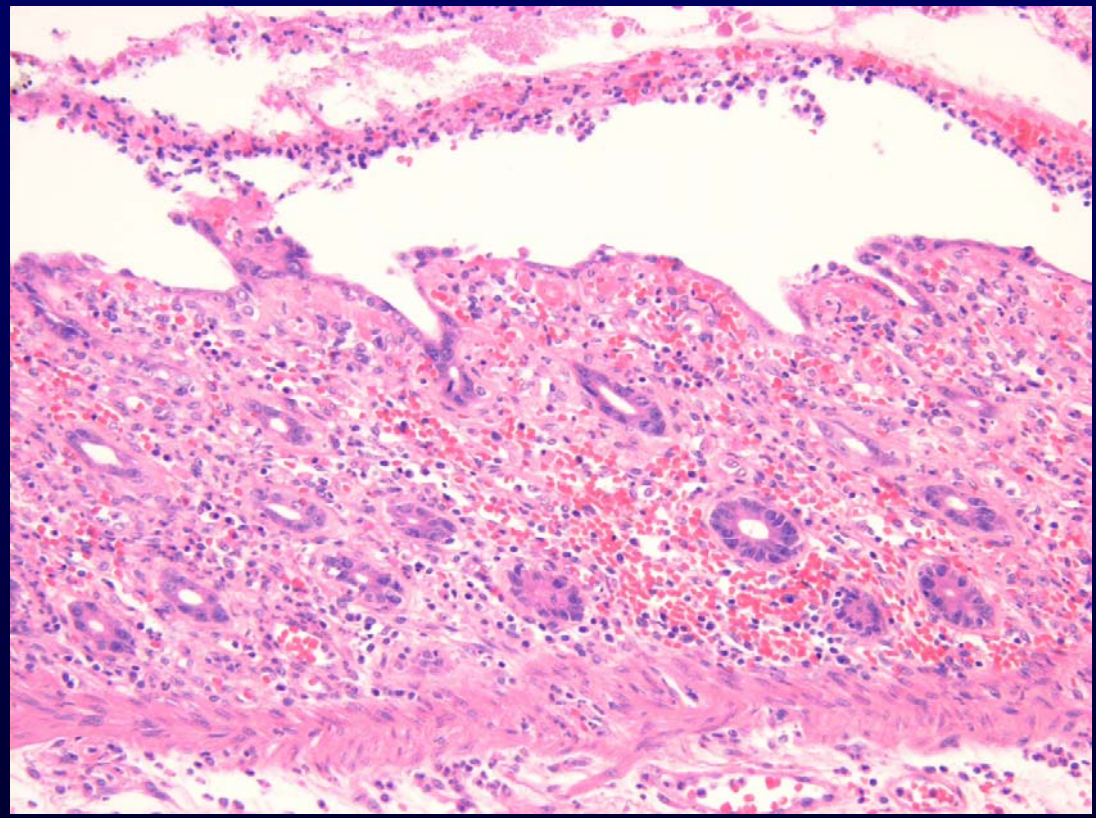
- Increased tissue mass (hypertrophy)
- Increased workload (tachycardia, exercise)
- Increased tissue “stress” (cardiac dilatation)

Effect of Ischemia Depends on Severity and Duration of Injury



Concept from Robbins Basic Patholgy, WB Saunders, 2003.

Effect of Ischemia Depends on Cell Type



Effect of Ischemia Depends on Cell Type

- "Parenchymal" cells are more susceptible than "stromal" cells
- Different parenchymal cells have different thresholds for ischemia:
  - Neurons: 3-4 min
  - Cardiac muscle, hepatocytes, renal tubular cells, gastrointestinal epithelium: 20-80 min
  - Fibroblasts, epidermis, skeletal muscle: hours

Effect of Ischemia Depends on Microvascular Anatomy

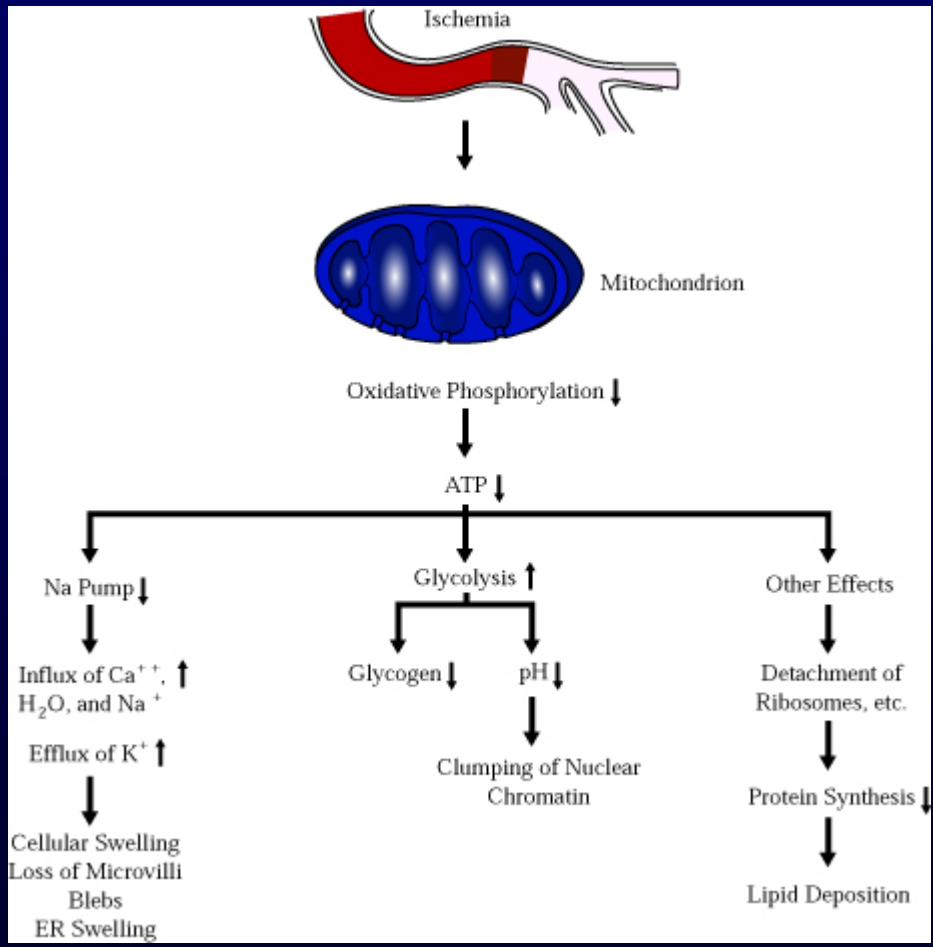
- Subendocardial hypoxia in the heart
- Watershed infarcts in the brain
- Ischemia due to countercurrent exchange in the intestinal villi
- Resistance in dual perfusion organs

Brain “Watershed” Infarct

Please see figure 4-4B of Kumar et al. *Robbins Basic Pathology*. 7th edition. WB Saunders 2003. ISBN: 0721692745.

Mechanisms of Damage

Reversible Ischemic Injury



Irreversible Ischemic Damage (Ischemic Cell Death)

Please see figure 1-6, pg. 9 of Cotran et al. *Robbins Pathological Basis of Disease*. 6th edition. WB Saunders 1999. ISBN: 072167335X.

Ischemic Damage $\stackrel{?}{=}$ Membrane Damage

Please see figure 1-8, pg. 11 of Cotran et al. *Robbins Pathological Basis of Disease*. 6th edition. WB Saunders 1999. ISBN: 072167335X.

Infarction

- Latin *infarctus*, pp. of *infarcire* “to stuff”
- An infarct is an area of tissue/organ necrosis caused by ischemia
- Infarctions often result from sudden reduction of arterial (or occasionally venous) flow by thrombosis or embolism
- Infarctions can also result from progressive atherosclerosis, spasms, torsions, or extrinsic compression of the vessels

Morphology of Infarcts

- Infarcts can be anemic (white) or hemorrhagic (red)
- White infarcts occur with arterial occlusion of solid organs
- Red infarcts occur with venous occlusion or with arterial occlusions in organs with double or collateral circulation
- White infarcts can become hemorrhagic with reperfusion

Splenic “White” Infarct

Please see figure 4-17b of Kumar et al. *Robbins Basic Pathology*. 7th edition. WB Saunders 2003. ISBN: 0721692745.

Pulmonary “Red” Infarct

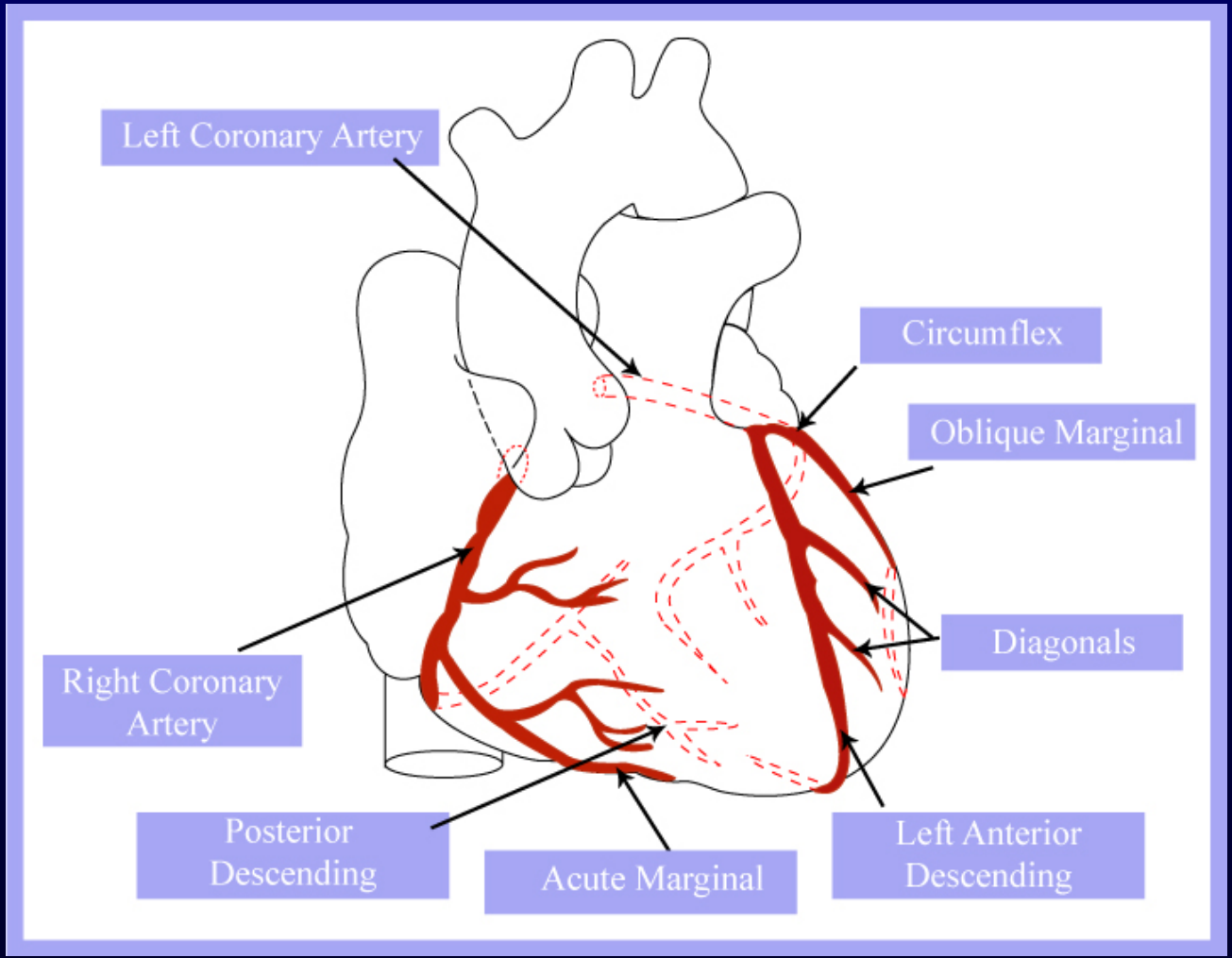
Please see Kumar et al. *Robbins Basic Pathology*. 7th edition. WB Saunders 2003. ISBN: 0721692745.

Clinically Significant Ischemic Lesions

Ischemic Heart Disease (IHD)

- Angina pectoris, myocardial infarction, sudden cardiac death, chronic IHD with congestive heart failure
- IHD is the leading cause of death in the US and developed countries
- Every year in the US, ~1.5 million have an MI and ~600,000 die from ischemic heart disease
- Atherosclerosis of the major coronary arteries is responsible for the vast majority of the cases of ischemic heart disease

Major Coronary Arteries



Atherosclerotic Coronary Artery Disease

Angina Pectoris

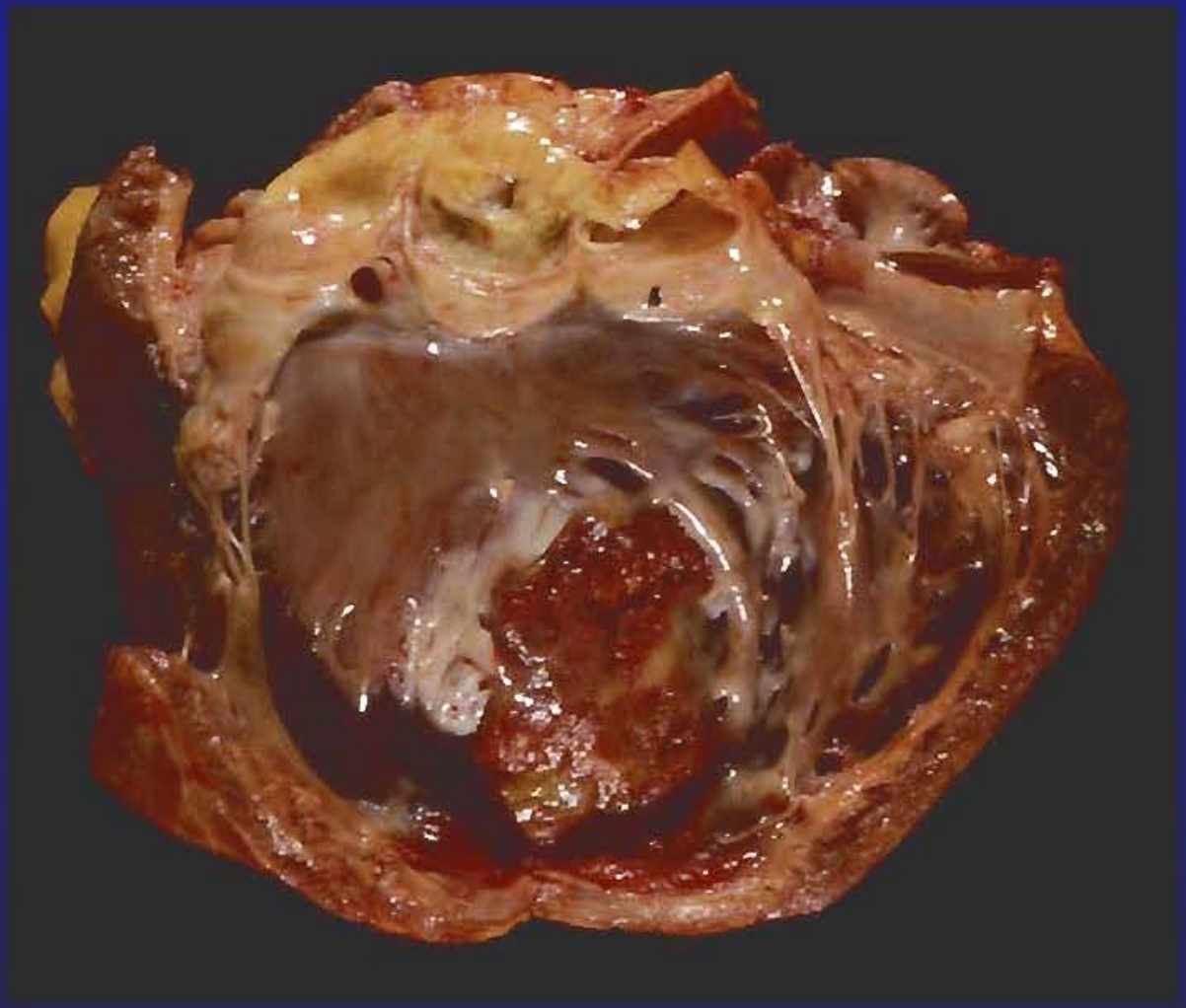
- Typical or stable angina is an episodic chest pain with exertion or stress, usually associated with fixed atherosclerotic narrowing of the coronary arteries
- Prinzmetal or variant angina occurs at rest, and is usually associated with coronary artery spasms in normal or atherosclerotic coronaries
- Unstable angina is characterized by increasing frequency of pain with less and less exertion, and is usually the harbinger of an MI

Acute Myocardial Infarction (MI)

- MI indicates the development of an area of myocardial necrosis
- MI's are typically precipitated by an acute plaque change followed by thrombosis at the site of plaque change
- Acute plaque changes include fissuring, hemorrhage into the plaque, and overt plaque rupture with distal embolism
- Most unstable plaques are eccentric lesions rich in T cells and macrophages, and have a large, soft core of necrotic debris and lipid covered by a thin fibrous cap

Cerebral Ischemic Injury

- The brain receives 15% of the cardiac output and accounts for 20% of the total oxygen consumption
- Neurons are the most vulnerable cells in the body
- Two common types of acute injury are recognized:
  - Cerebral infarction (stroke) is a regional ischemic lesion usually due to local vascular occlusion (thrombotic or embolic)
  - Ischemic (hypoxic) encephalopathy is a diffuse lesion characterized by selective loss of neurons due to global ischemia, usually as a result of hypotension



Pulmonary Emboli (PE) and Infarction

- PE's are large blood clots that often arise within the deep, large veins of the lower legs
- Proximal PE's can cause clinically significant and potentially life-threatening lung infarcts
- PE's cause respiratory and circulatory compromise due to non-perfused but ventilated segments, and increased resistance to pulmonary blood flow
- PE's are the most common preventable cause of death in hospitalized patients

VQ Scan in PE

Ischemic Bowel Disease