USMLE Step 1 Session

Pathology 1

22.10.2014, Klub A. Trýba

FB: USMLE @ Masaryk

Marek Čierny
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Q1

A 43-year-old man presents with a scaly, erythematous lesion on the dorsal surface of his left hand. A skin biopsy reveals atypical keratinocytes filling the entire thickness of the epidermis (shown in the image). The arrows point to apoptotic bodies. Which of the following proteins plays the most important role in mediating programmed cell death in this patient's skin cancer?

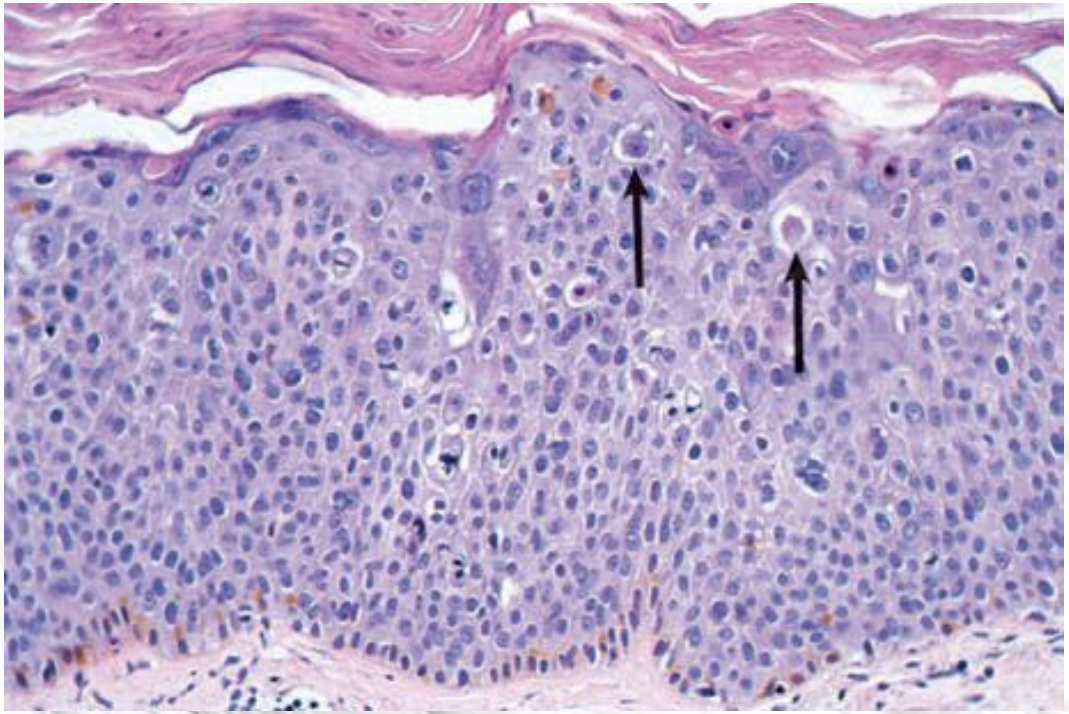
(A) Catalase

(B) Cytochrome c

(C) Cytokeratins

(D) Myeloperoxidase

(E) Superoxide dismutase



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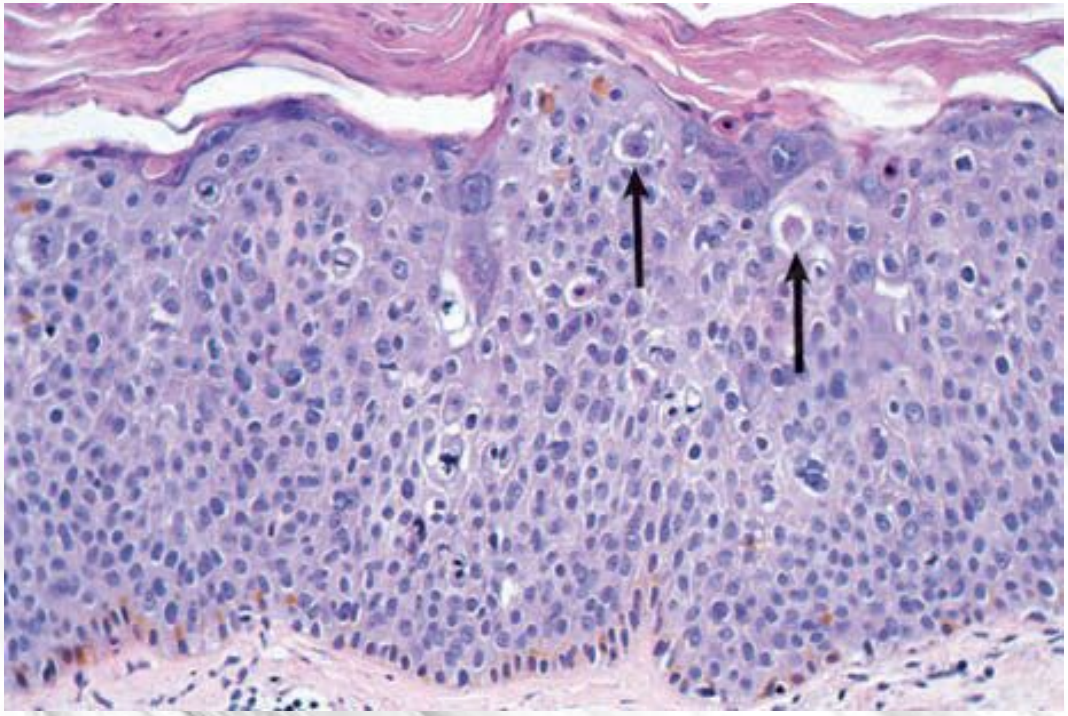

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A1: what is apoptosis?

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A1: what is apoptosis?

TABLE 2-4 Cell Necrosis Compared with Apoptosis

FEATURE	CELL NECROSIS	APOPTOSIS
General	Death of groups of cells usually accompanied by an inflammatory infiltrate	Programmed, enzyme-mediated individual cell death *without* a prominent inflammatory infiltrate
Size of cell	Intracellular swelling due to sodium-containing water entering the cell (dysfunctional Na^+/K^+ ATPase pump)	Shrunken cell due to loss of cytoplasm from cytoplasmic buds that pinch off and become apoptotic bodies
Enzymes involved	Phospholipase, protease, endonuclease	Initiator caspases, executioner caspases (protease, endonuclease)
Genes involved	None	*BCL*-2 (anti-apoptosis), *BAX* (proapoptotic), *BAK* (proapoptotic)
Role	Usually associated with a pathologic process	Physiologic functions (e.g., embryology, thymus involution); pathologic function (e.g., removal misfolded proteins, removal of neutrophils in acute inflammation)

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A1: what is apoptosis?

Apoptosis

Programmed cell death; ATP required. Intrinsic or extrinsic pathway; both pathways → activation of cytosolic caspases that mediate cellular breakdown.

No significant inflammation (unlike necrosis).

Characterized by deeply eosinophilic cytoplasm, cell shrinkage, nuclear shrinkage (pyknosis) and basophilia, membrane blebbing, nuclear fragmentation (karyorrhexis), and formation of apoptotic bodies, which are then phagocytosed.

DNA laddering is a sensitive indicator of apoptosis; during karyorrhexis, endonucleases cleave at internucleosomal regions, yielding 180-bp fragments. Radiation therapy causes apoptosis of tumors and surrounding tissue via free radical formation and dsDNA breakage. Rapidly dividing cells (e.g., skin, GI mucosa) are very susceptible to radiation therapy-induced apoptosis.

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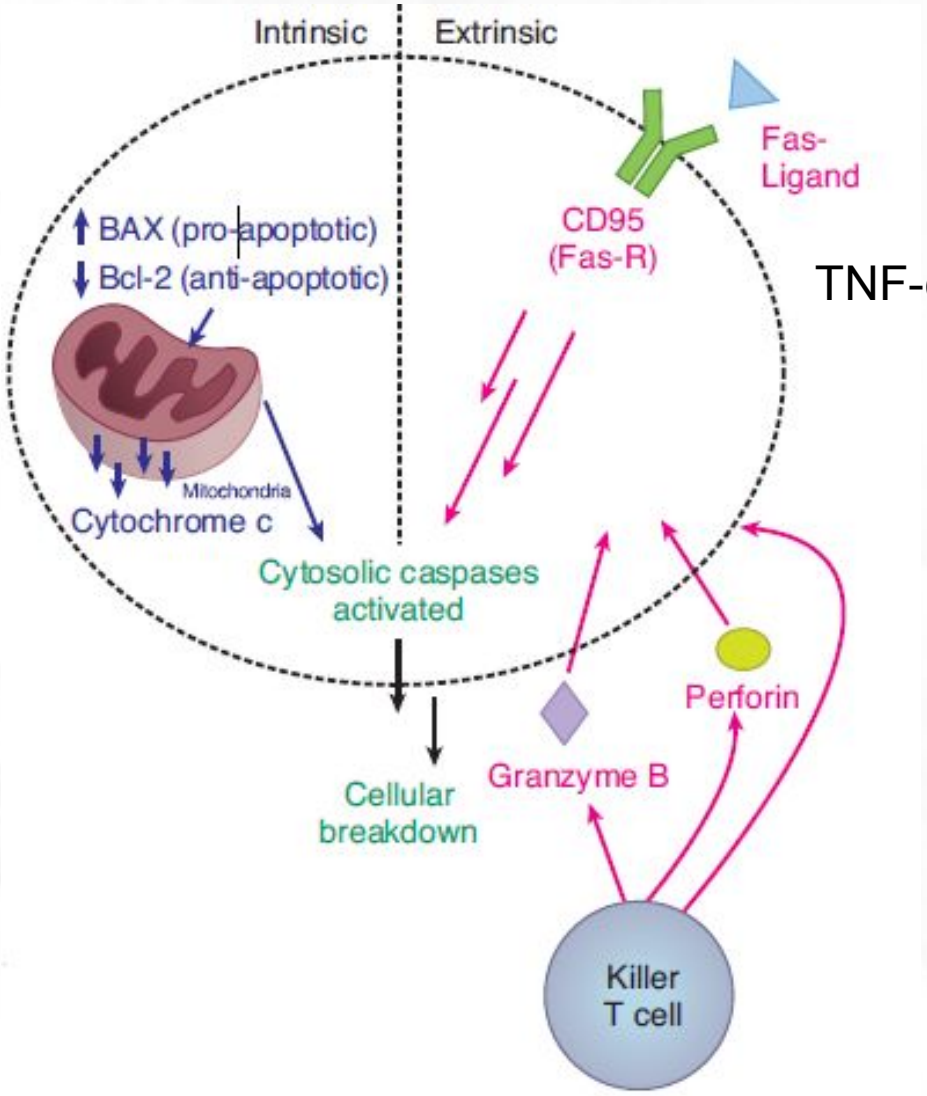
A1: how is it mediated?



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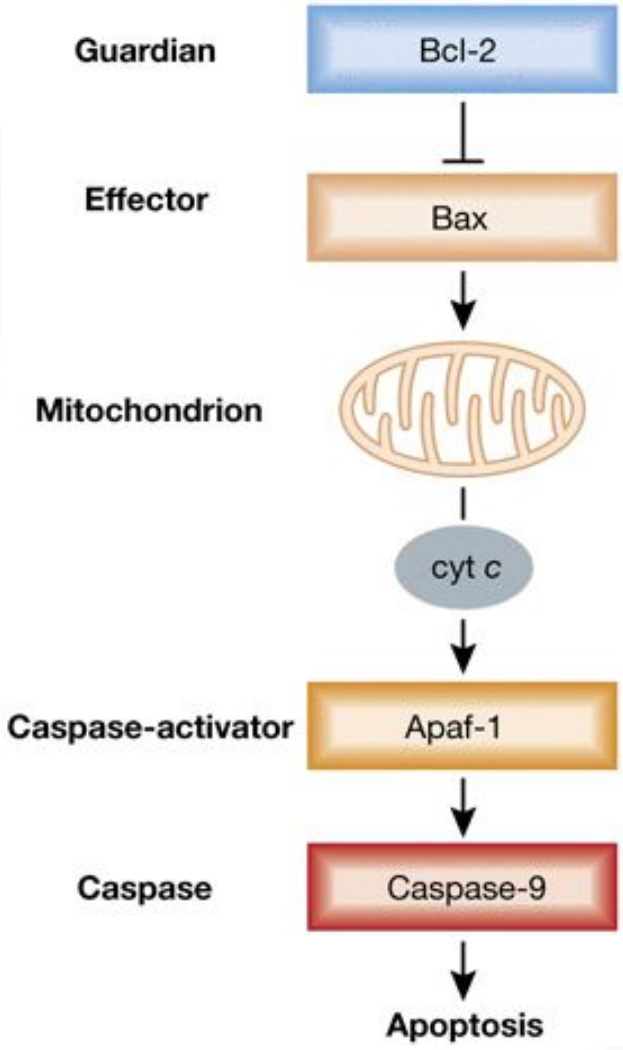

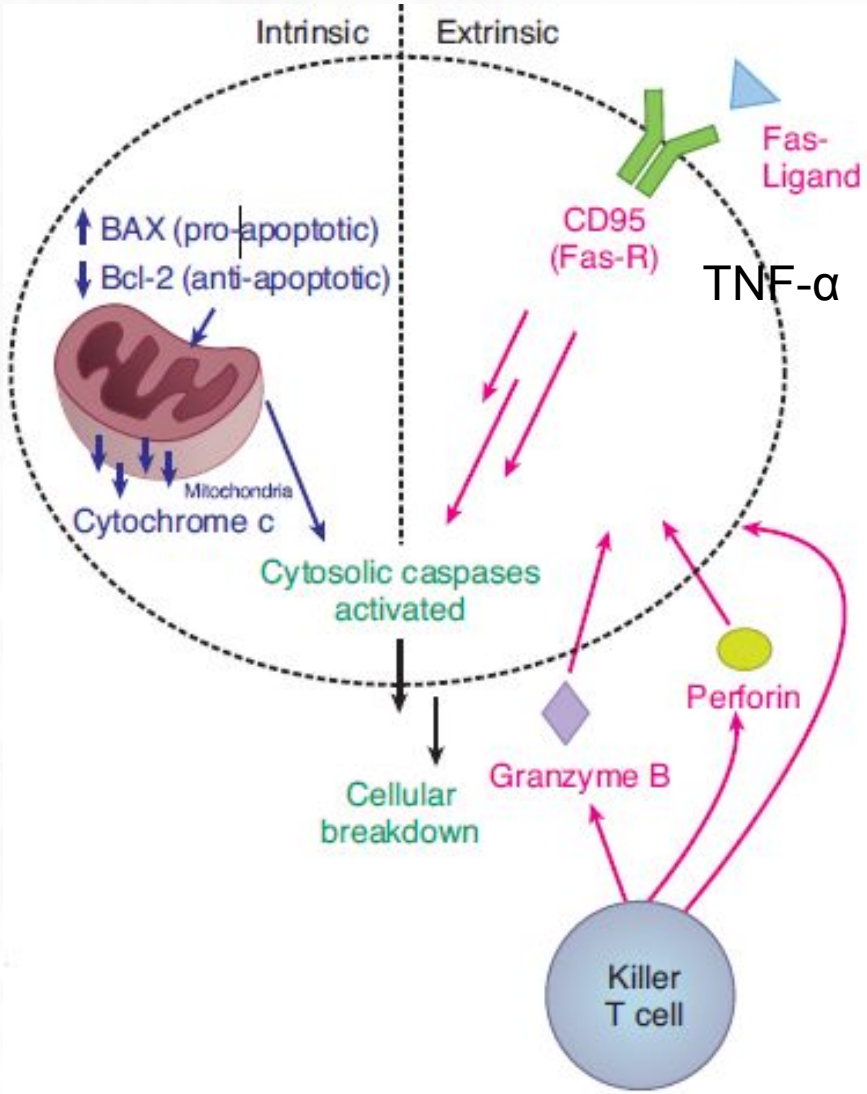

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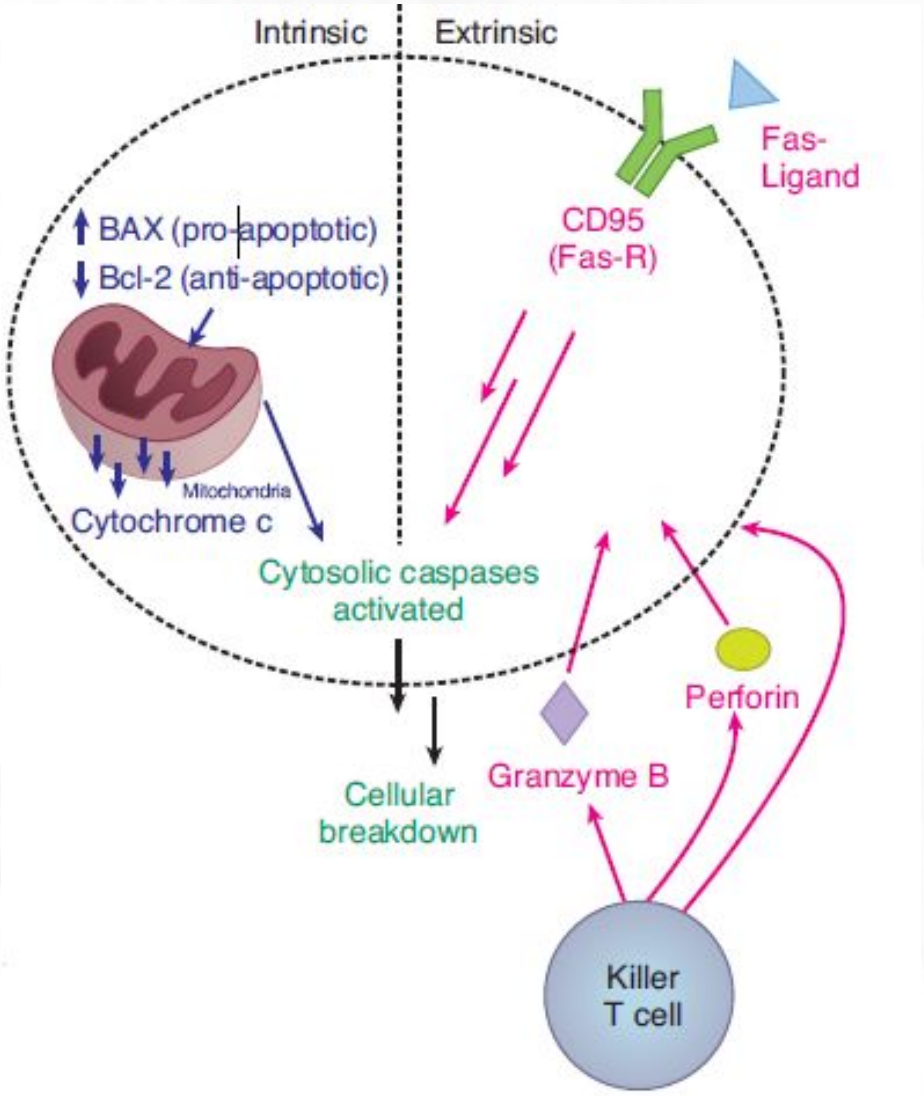
Strasser: *Deciphering the rules of programmed cell death to improve therapy of cancer and other diseases*, DOI: 10.1038/emboj.2011.307

A1: when is apoptosis initiated?



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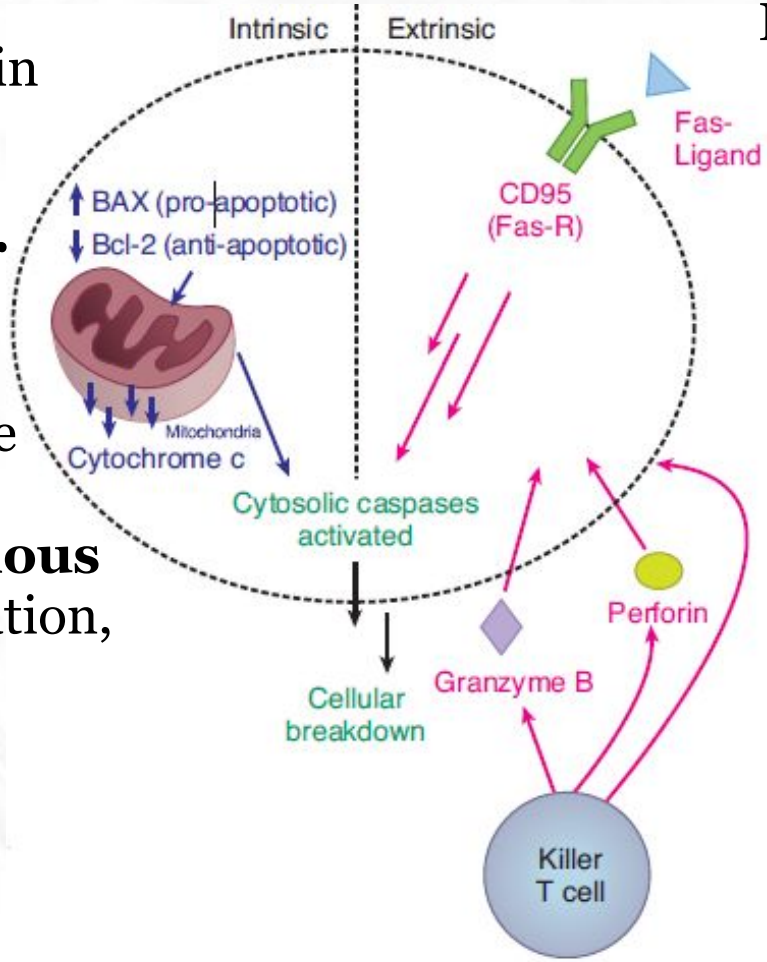
A1: when is apoptosis initiated?

Intrinsic:

- tissue remodeling in **embryogenesis**
- withdrawal of a stimulating **factor** (e.g. IL2, ACTH, estrogen & progesterone in the menstrual cycle)
- exposure to **injurious stimuli** (e.g. radiation, toxins, hypoxia).



Extrinsic:

- FasR-FasL interaction is necessary in **thymic** medullary **negative selection**
- TNF-α is involved in systemic inflammation and wasting (cachexia) in cancer
- **Cytotoxic CD8+ T** cells induce death of **tumor** cells and **virus infected** cells by forming pores (perforin) and release of granules containing Granzyme B

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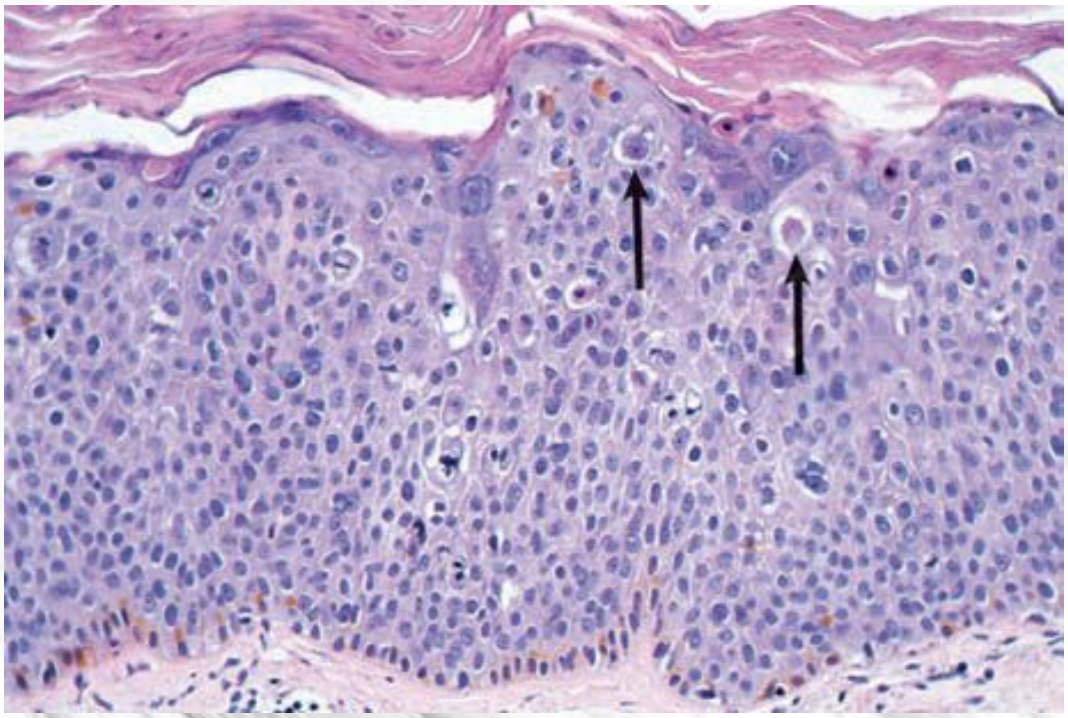

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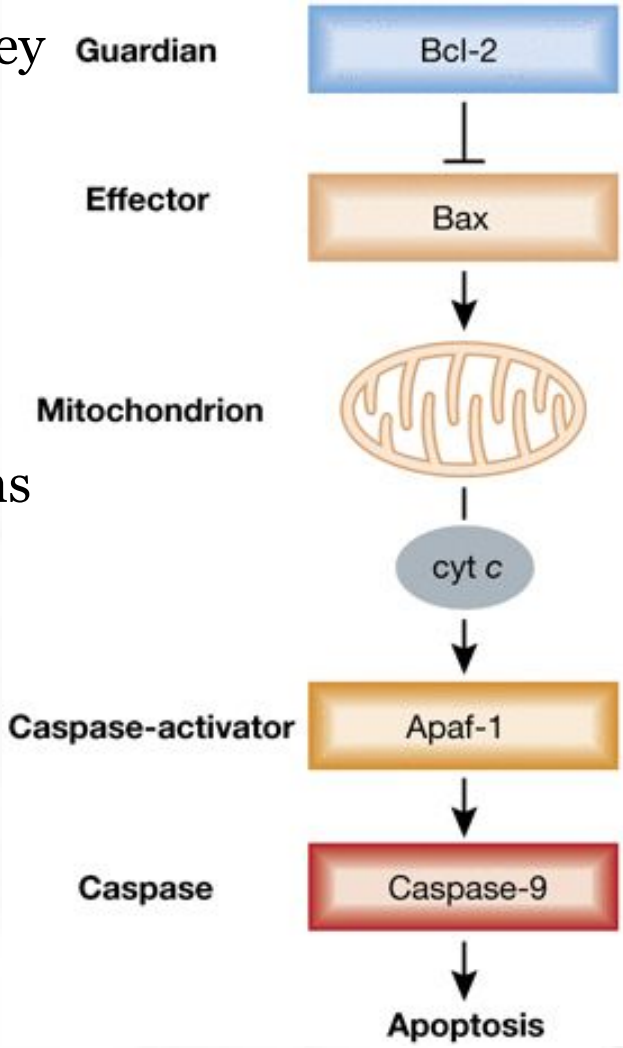
A1

B: Cytochrome c. The mitochondrial membrane is a key regulator of apoptosis. When mitochondrial pores open, cytochrome c leaks out and activates Apaf-1, which converts procaspase-9 to caspase-9, resulting in the activation of downstream caspases (cysteine proteases). These effector caspases cleave target proteins, including endonucleases nuclear proteins, and cytoskeletal proteins to mediate the varied morphological and biochemical changes that accompany apoptosis.

Reactive oxygen species (related to choices A, D, and E) are triggers of apoptosis, but they do not mediate programmed cell death.

Diagnosis: Apoptosis, squamous cell carcinoma of skin



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Q2

A 28-year-old man with a history of radiation/bone marrow transplantation for leukemia presents with severe diarrhea. He subsequently develops septic shock and expires. Microscopic examination of the colon epithelium at autopsy reveals numerous acidophilic bodies and small cells with pyknotic nuclei. Which of the following proteins most likely played a key role in triggering radiation-induced cell death in this patient's colonic mucosa?

(A) Cytochrome P450

(B) β-Catenin

(C) E-Cadherin

(D) P-Selectin

(E) p53

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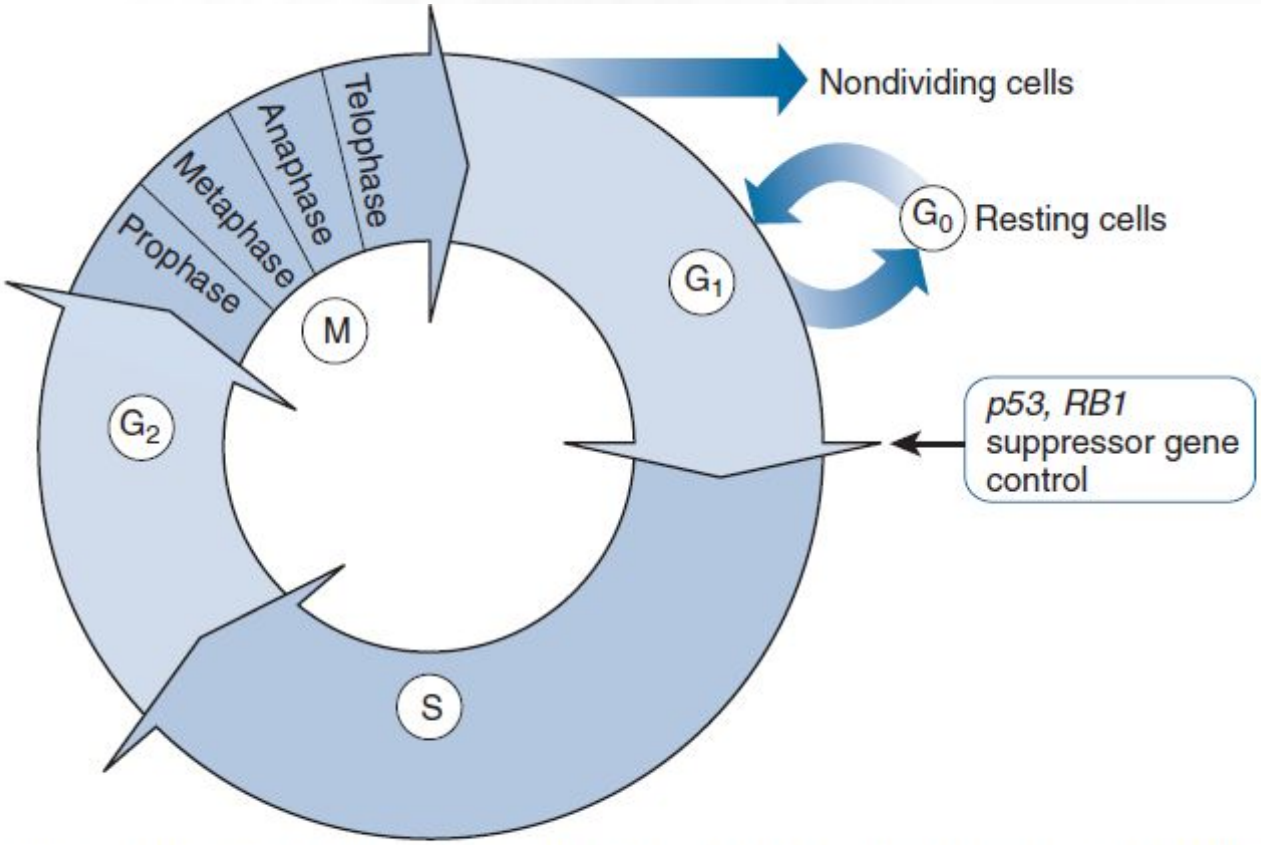
A2



3-11: Cell cycle. The G_1 to S phase is the most critical phase of the cell cycle and is controlled by the *p53* and *RB1* suppressor genes. Refer to a more detailed discussion in the text. *(Modified from Burns E, Cave D: Rapid Review: Histology and Cell Biology, Philadelphia, Mosby, 2004, p 36, Fig. 3-5.)*

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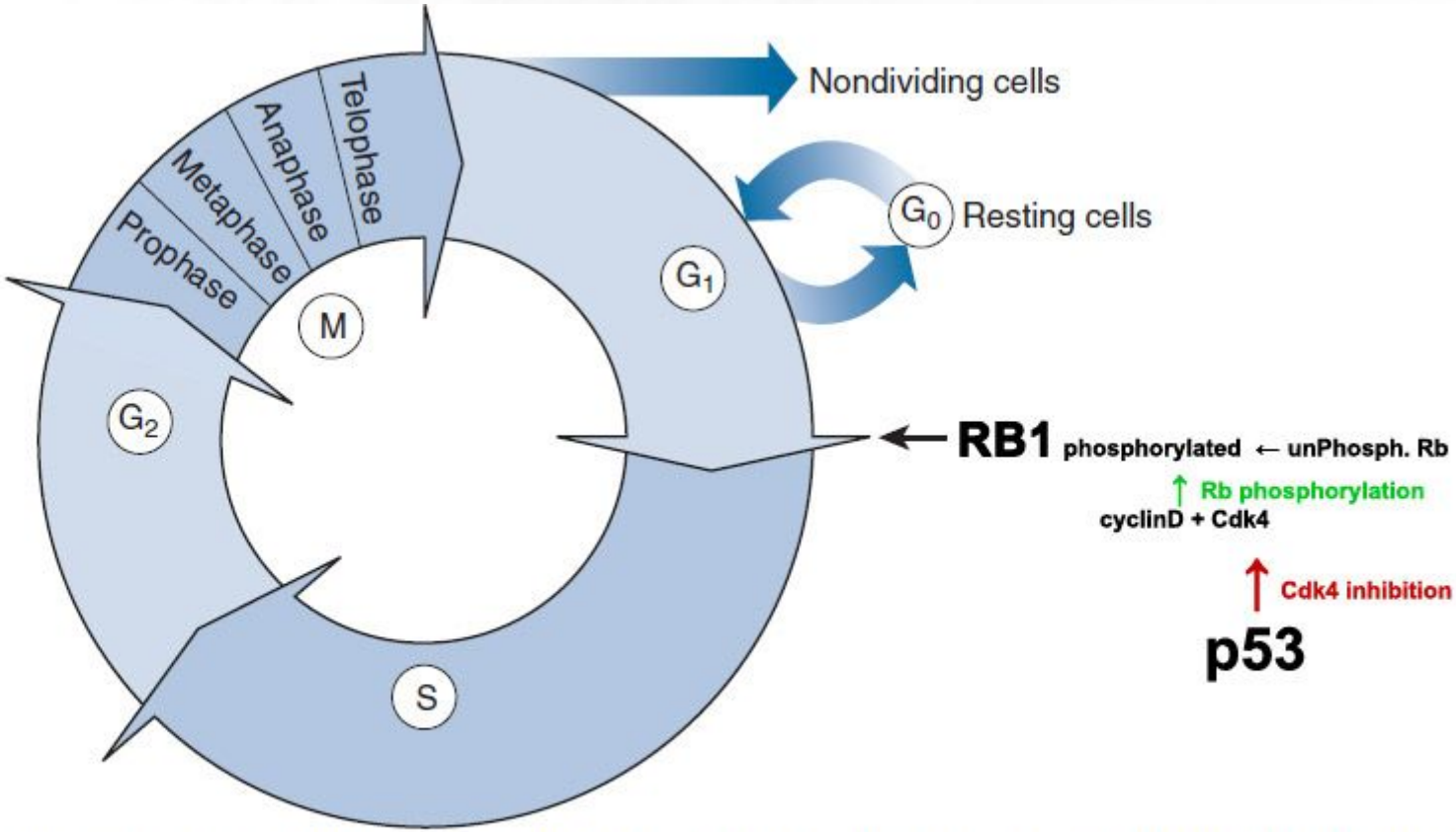
A2



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A2

The answer is **E: p53** protein arrests the cell in G1 phase by inhibiting Cdk4. Inhibition of Cdk4, prevents RB1 protein phosphorylation, which provides time for repair of damaged DNA in the cell.

In the event that there is **excessive DNA damage**, the p53 suppressor gene produces protein products that:

• Inhibit the translation of the BCL-2 antiapoptosis genes, which leads to **apoptosis** of the cell, or

• Inhibit the translation of growth-promoting genes (e.g., MYC proto-oncogene, leading to growth arrest.

Diagnosis: Apoptosis

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Q3

A 22-year-old construction worker sticks himself with a sharp, rusty nail. Within 24 hours, the wound has enlarged to become a 1-cm sore that drains thick, purulent material. This skin wound illustrates which of the following morphologic types of necrosis?

(A) Caseous necrosis

(B) Coagulative necrosis

(C) Fat necrosis

(D) Fibrinoid necrosis

(E) Liquefactive necrosis

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A3

E: Liquefactive necrosis. Polymorphonuclear leukocytes (segmented neutrophils) rapidly accumulate at sites of injury. They are loaded with acid hydrolases and are capable of digesting dead cells. A localized collection of these inflammatory cells may create an abscess with central liquefaction (pus). Liquefactive necrosis is also commonly seen in the brain.

Caseous necrosis (choice A) is seen in necrotizing granulomas.

Fat necrosis (choice C) is typically encountered in patients with acute pancreatitis.

Fibrinoid necrosis (choice D) is seen in patients with necrotizing vasculitis.

Diagnosis: Abscess, acute inflammation

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A3: types of necrosis

Necrosis	Enzymatic degradation and protein denaturation of a cell resulting from exogenous injury. Intracellular components leak; inflammatory process (unlike apoptosis).
Types	**Characteristics**
Coagulative	Heart, liver, kidney; occurs in tissues supplied by end-arteries; ↑ cytoplasmic binding of acidophilic dye. Proteins denature first, followed by enzymatic degradation.
Liquefactive	Brain, bacterial abscess; occurs in CNS due to high fat content. In contrast to coagulative necrosis, enzymatic degradation due to the release of lysosomal enzymes occurs first.
Caseous	TB, systemic fungi, *Nocardia*.
Fatty	Enzymatic (pancreatitis [saponification]) and nonenzymatic (e.g., breast trauma); calcium deposits appear dark blue on staining.
Fibrinoid	Vasculitides (e.g., Henoch-Schönlein purpura, Churg-Strauss syndrome), malignant hypertension; amorphous and pink on H&E.
Gangrenous	Dry (ischemic coagulative) and wet (infection); common in limbs and GI tract.

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Q4

A 58-year-old man presents with symptoms of acute renal failure. His blood pressure is 220/130 mm Hg . While in the emergency room, the patient suffers a stroke and expires. Microscopic examination of the kidney at autopsy is shown in the image. Which of the following morphologic changes accounts for the red material in the wall of the artery?

(A) Apoptosis

(B) Caseous necrosis

(C) Fat necrosis

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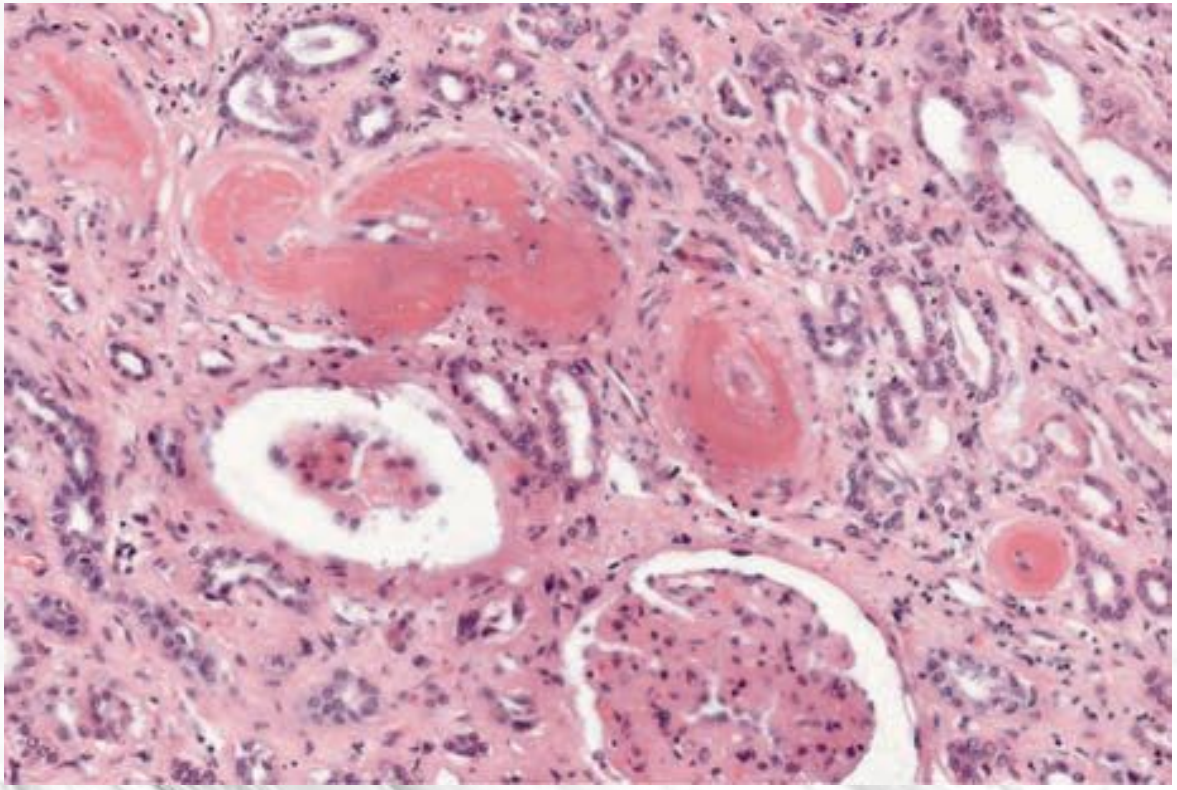

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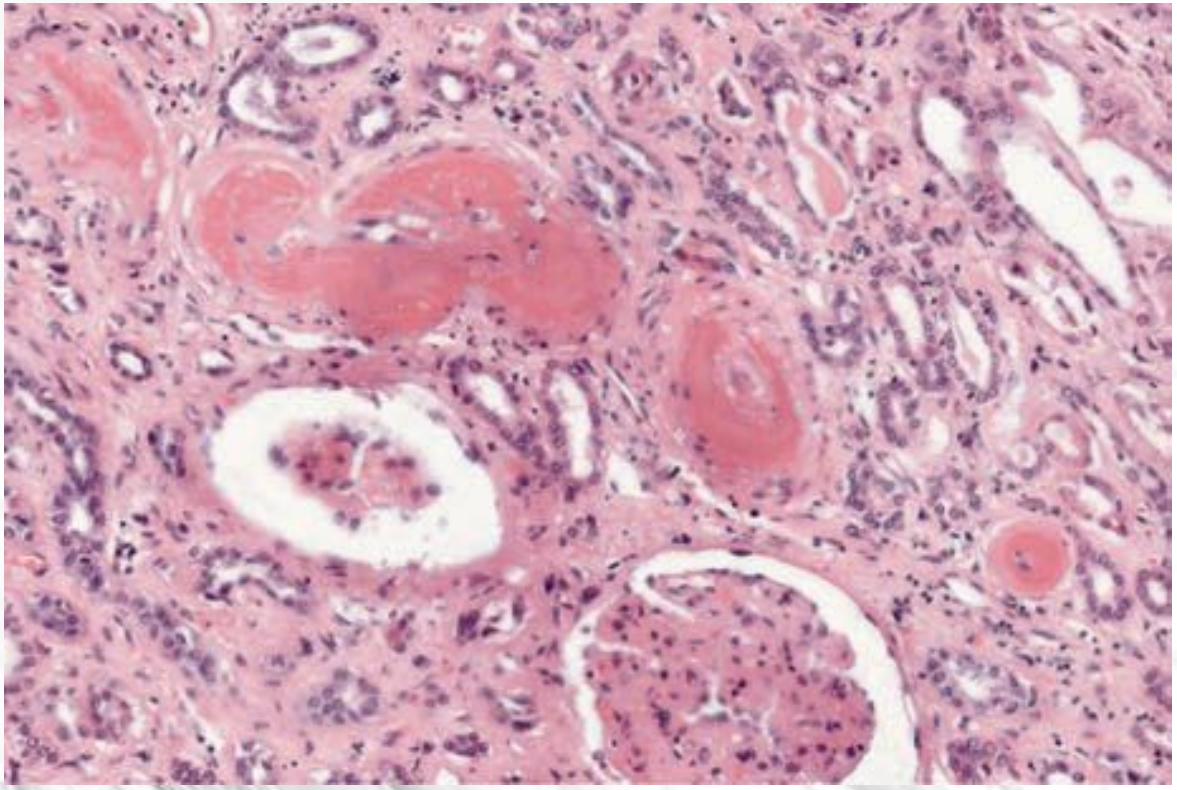

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A4

D: Fibrinoid necrosis. Fibrinoid necrosis is an alteration of injured blood vessels, in which the insudation and accumulation of plasma proteins cause the wall to stain intensely with eosin. The other choices are not typically associated directly with vascular injury.

Diagnosis: Malignant hypertension, fibrinoid necrosis

Necrosis	Enzymatic degradation and protein denaturation of a cell resulting from exogenous injury. Intracellular components leak; inflammatory process (unlike apoptosis).
Types	**Characteristics**
Coagulative	Heart, liver, kidney; occurs in tissues supplied by end-arteries; ↑ cytoplasmic binding of acidophilic dye. Proteins denature first, followed by enzymatic degradation.
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Q5

A 70-year-old man is hospitalized after suffering a mild stroke. While in the hospital, he suddenly develops crushing substernal chest pain. Analysis of serum proteins and ECG confirm a diagnosis of acute myocardial infarction. The patient subsequently develops an arrhythmia and expires. A cross section of the left ventricle at autopsy is shown in the image. Which of the following histologic features would provide definitive evidence of necrosis in the myocardium?

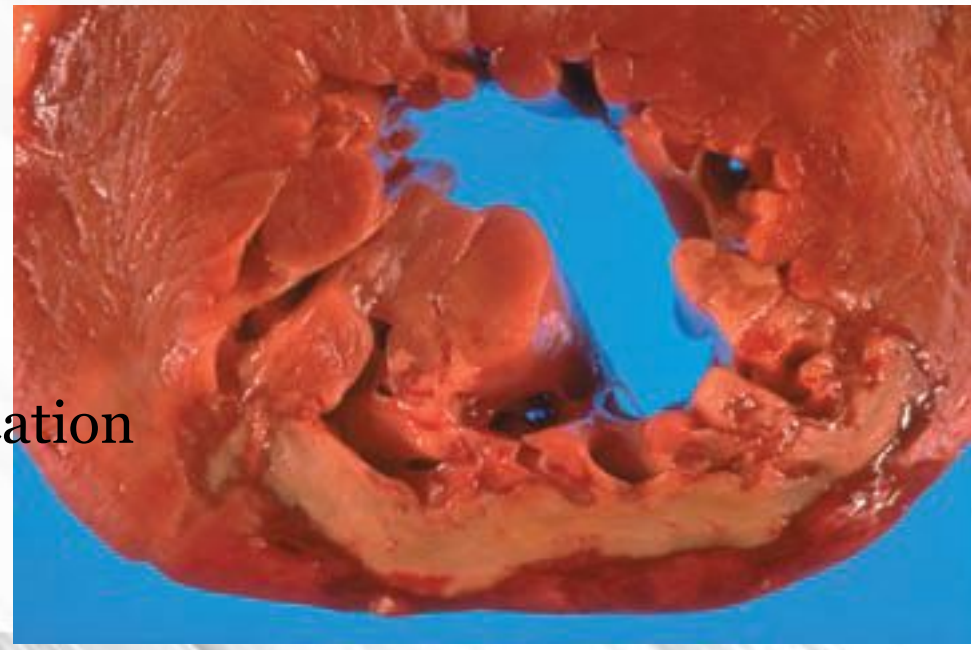
(A) Disaggregation of polyribosomes

(B) Increased intracellular volume

(C) Influx of lymphocytes

(D) Mitochondrial swelling and calcification

(E) Nuclear fragmentation



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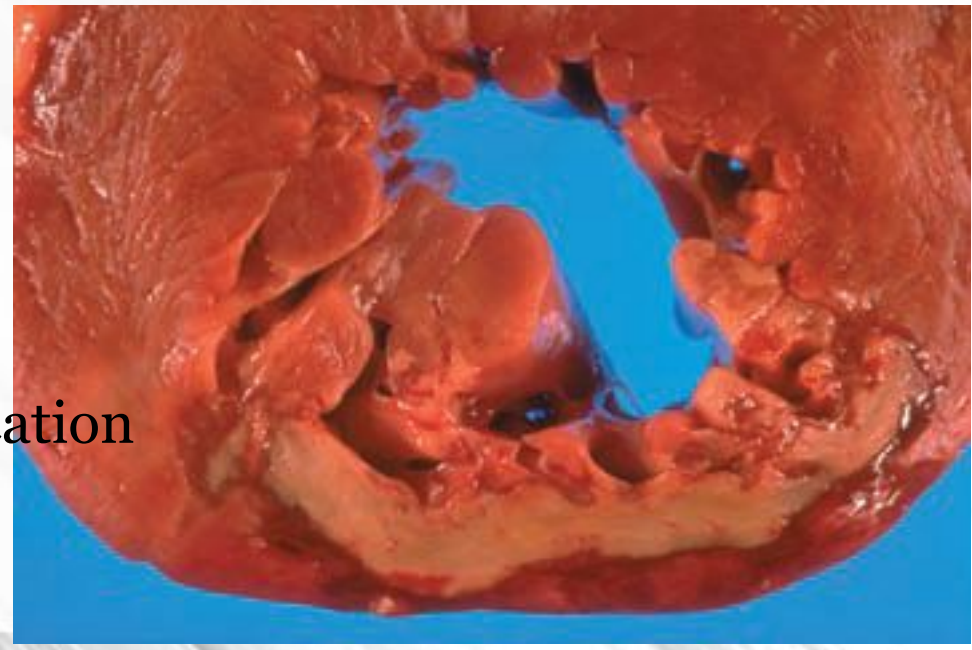

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A5 b

E: Nuclear fragmentation. Nuclear fragmentation (karyorrhexis and karyolysis) is a hallmark of coagulative necrosis.

Cell injury

REVERSIBLE WITH O_2	IRREVERSIBLE
ATP depletion	Nuclear pyknosis, karyorrhexis, karyolysis
Cellular/mitochondrial swelling (↓ ATP → ↓ activity of Na^+/K^+ pumps)	Plasma membrane damage (degradation of membrane phospholipid)
Nuclear chromatin clumping	Lysosomal rupture
↓ glycogen	Mitochondrial permeability/vacuolization; phospholipid-containing amorphous densities within mitochondria (swelling alone is reversible)
Fatty change	
Ribosomal/polysomal detachment (↓ protein synthesis)	
Membrane blebbing	

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Q6

A 64-year-old man with long-standing angina pectoris and arterial hypertension dies of spontaneous intracerebral hemorrhage. At autopsy, the heart appears globoid. The left ventricle measures 2.8 cm on cross section (shown in the image). This adaptation to chronic injury was mediated primarily by changes in the intracellular concentration of which of the following components?

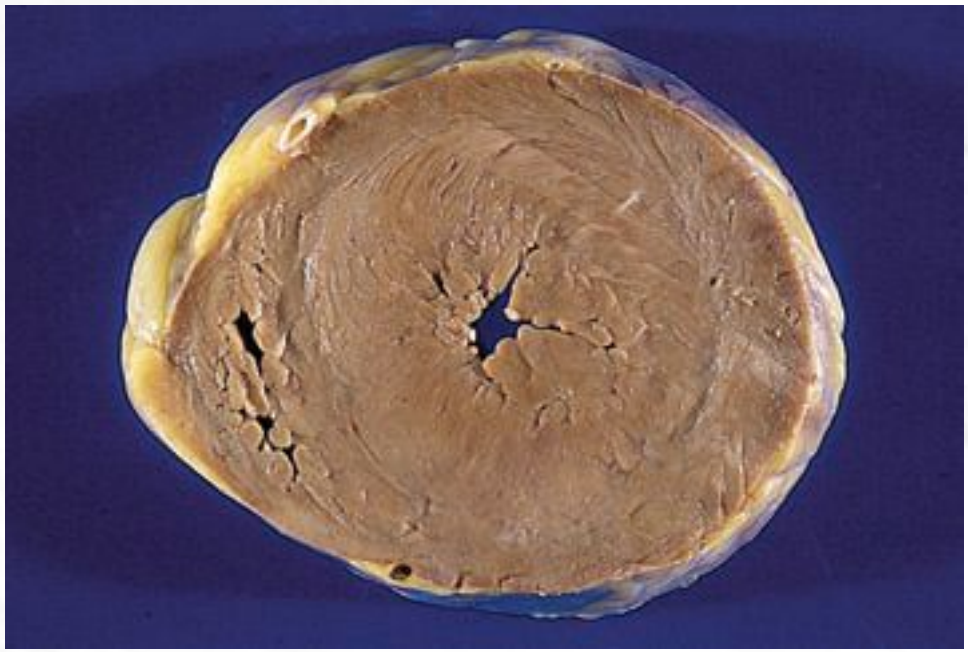
(A) DNA

(B) Glycogen

(C) Lipid

(D) mRNA

(E) Water



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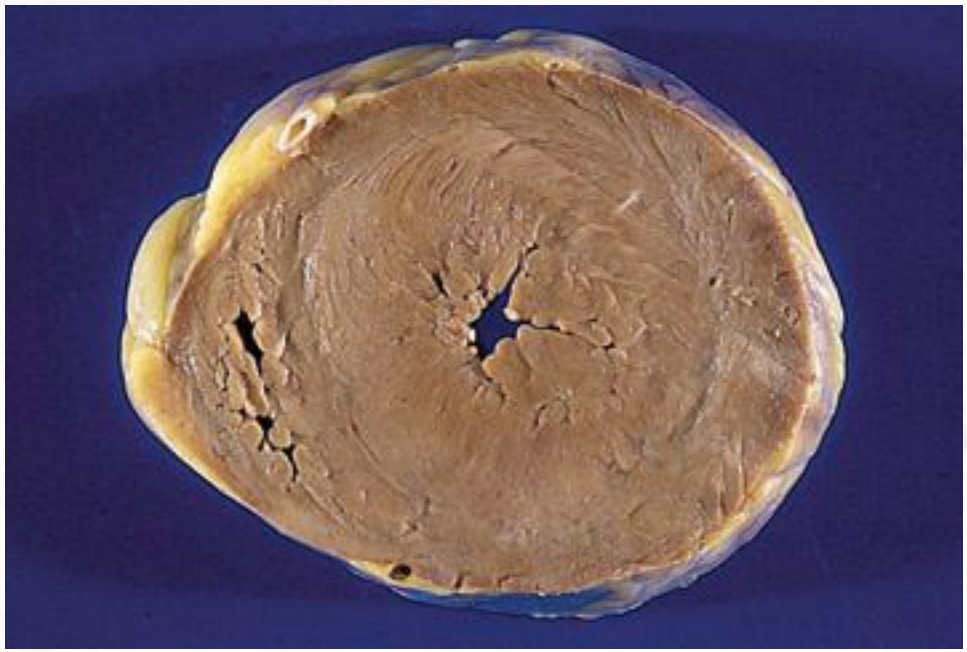

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A6

What is the inderlying mechanism of **concentric thickening of the ventricular wall**?

Proliferation?

Hypertrophy?

Deposition of a molecule?

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A6

D: mRNA. Hypertrophic cardiac myocytes have more cytoplasm and larger nuclei than normal cells. The final steps of pathogenesis include increases in mRNA, rRNA, and protein. Hypertrophy results from transcriptional regulation.

Aneuploidy (choice A) is not a feature of myofiber hypertrophy. Water influx (choice E), which is typical of hydropic swelling in acute injury, is not a common feature of hypertrophy.

Diagnosis: Hypertrophic heart disease, hypertrophy

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A6

II. Ventricular Hypertrophy

A. Definition

- Ventricular hypertrophy is a compensatory change related to alterations in pressure and/or volume imposed on the wall of the ventricle.

B. Pathogenesis of left and right ventricular hypertrophy

1. Sustained pressure in the ventricles increases wall stress.
2. Changes in wall stress alter gene expression in the muscle.
3. Changes in gene expression lead to duplication of sarcomeres.
   - Definition—contractile element of muscle
4. Changes occur in wall stress when there is an increase in afterload.
   a. Definition—resistance the ventricle contracts against to eject blood in systole
   b. Increased afterload produces concentric thickening of the ventricular wall (Fig. 11-1A).
      - Sarcomeres duplicate parallel to the long axis of the cells causing the individual muscle fibers to be thicker.
   c. Causes of concentric left ventricular hypertrophy (LVH) due to increased afterload include:
      (1) Essential hypertension (HTN; most common).
      (2) Aortic valve (AV) stenosis
      (3) Hypertrophic cardiomyopathy
   d. Causes of concentric right ventricular hypertrophy (RVH) due to increased afterload include:
      (1) Pulmonary hypertension (PH; see Fig. 17-9)
      (2) Pulmonary valve (PV) stenosis

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Q7

A 24-year-old woman contracts toxoplasmosis during her pregnancy and delivers a neonate at 37 weeks of gestation with a severe malformation of the central nervous system. MRI studies of the neonate reveal porencephaly and hydrocephalus. An X-ray film of the head shows irregular densities in the basal ganglia. These X-ray findings are best explained by which of the following mechanisms of disease?

(A) Amniotic fluid embolism

(B) Dystrophic calcification

(C) Granulomatous inflammation

(D) Metastatic calcification

(E) Organ immaturity

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Q7

A 24-year-old woman contracts toxoplasmosis during her pregnancy and delivers a neonate at 37 weeks of gestation with a severe malformation of the central nervous system. MRI studies of the neonate reveal porencephaly and hydrocephalus. An X-ray film of the head shows irregular densities in the basal ganglia. These X-ray findings are best explained by which of the following mechanisms of disease?

(A) Amniotic fluid embolism

(B) Dystrophic calcification

(C) Granulomatous inflammation

(D) Metastatic calcification

(E) Organ immaturity

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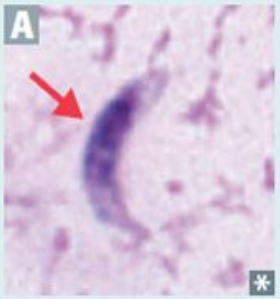
A7

Toxoplasma gondii

Protozoa–CNS infections

ORGANISM	DISEASE	TRANSMISSION	DIAGNOSIS	TREATMENT
Toxoplasma gondii 	Brain abscess in HIV (seen as ring-enhancing brain lesions on CT/MRI); congenital toxoplasmosis = "classic triad" of chorioretinitis, hydrocephalus, and intracranial calcifications	Cysts in meat or oocysts in cat feces; crosses placenta (pregnant women should avoid cats)	Serology, biopsy (tachyzoite) A	Sulfadiazine + pyrimethamine

AGENT	MODE OF TRANSMISSION	MATERNAL MANIFESTATIONS	NEONATAL MANIFESTIONS
Toxoplasma gondii	Cat feces or ingestion of undercooked meat	Usually asymptomatic; lymphadenopathy (rarely)	Classic triad: chorioretinitis, hydrocephalus, and intracranial calcifications

Tao Le, Vikas Bhushan: *First Aid for the USMLE Step 1 2014*, McGraw Hill Professional, 2014, ISBN 0071831436.

A7

B: Dystrophic calcification. Dystrophic calcification reflects underlying cell injury. Serum levels of calcium are normal, and the calcium deposits are located in previously damaged tissue. Intrauterine Toxoplasma infection affects approximately 0.1% of all pregnancies. Acute encephalitis in the fetus afflicted with TORCH syndrome may be associated with foci of necrosis that become calcified. Microcephaly, hydrocephalus, and microgyria are frequent complications of these intrauterine infections.

Metastatic calcification (choice D) reflects an underlying disorder in calcium metabolism. Example?

Diagnosis: Dystrophic calcification

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Q8

A 62-year-old man is brought to the emergency room in a disoriented state. Physical examination reveals jaundice, splenomegaly, and ascites. Serum levels of ALT, AST, alkaline phosphatase, and bilirubin are all elevated. A liver biopsy demonstrates alcoholic hepatitis with Mallory bodies. These cytoplasmic structures are composed of interwoven bundles of which of the following proteins?

(A) α1-Antitrypsin

(B) β-Amyloid (Aβ)

(C) Intermediate filaments

(D) Prion protein (PrP)

(E) α-Synuclein

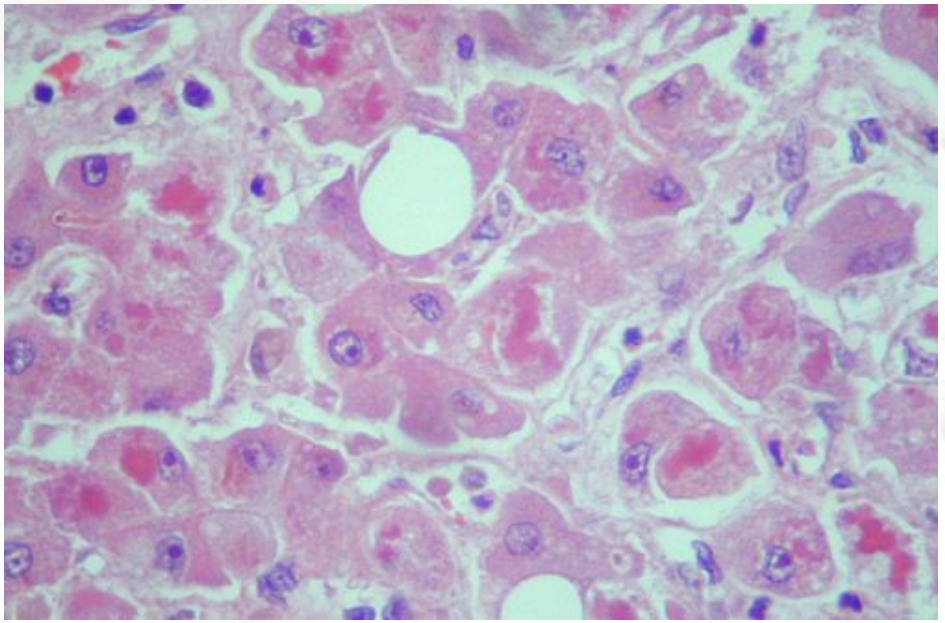

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Image: http://library.med.utah.edu/WebPath/CINJHTML/CINJ033.html

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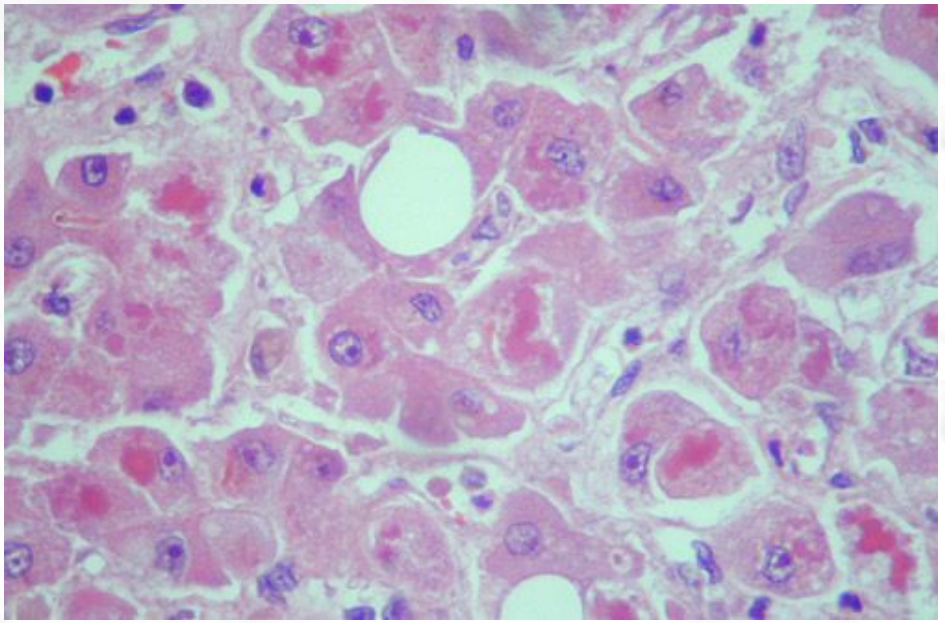

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A8: alcoholic liver disease

C: Intermediate filaments. Hyaline is a term that refers to any material that exhibits a reddish, homogeneous appearance when stained with hematoxylin and eosin (H&E). Standard terminology includes hyaline arteriolosclerosis, alcoholic hyaline in the liver (Mallory bodies), hyaline membranes in the lung, and hyaline droplets in various cells. Alcoholic (Mallory) hyaline is composed of cytoskeletal intermediate filaments (cytokeratins), whereas pulmonary hyaline membranes consist of plasma proteins deposited in alveoli.

Structurally abnormal α1-antitrypsin molecules (choice A) accumulate in the liver of patients with α1-antitrypsin deficiency.

α-Synuclein (choice E) accumulates in neurons in the substantia nigra of patients with Parkinson disease.

GOLJAN, Edward F. *Rapid review pathology*. Fourth edition. Philadelphia, PA: Elsevier/Saunders, 2014. ISBN 03-230-8787-6.

A8: alcoholic hepatitis

b. Alcoholic hepatitis
  (1) Pathogenesis
    (a) Genetic predisposition is likely.
    (b) Due to acetaldehyde damage to hepatocytes
    (c) Stimulation of collagen synthesis around the central venules
      • Perivenular fibrosis
  (2) Microscopic findings
    (a) Fatty change with neutrophil infiltration
    (b) Mallory bodies
      • Damaged cytokeratin intermediate filaments in hepatocytes (see Fig. 2-11)
    (c) Perivenular fibrosis
  (3) Clinical findings
    (a) Painful hepatomegaly
    (b) Fever, neutrophilic leukocytosis, ascites, hepatic encephalopathy
    (c) May progress to alcoholic cirrhosis
  (4) Laboratory findings
    (a) Absolute neutrophilic leukocytosis
    (b) Serum AST > ALT
    (c) Increased serum ALP and GGT
      • Serum GGT is disproportionately increased when compared to ALP (see Table 19-2)
    (d) Thrombocytopenia in some cases
    (e) Hypoglycemia in some cases
  (5) Treatment
    (a) Mandatory to stop drinking
    (b) Corticosteroids helpful in some cases

Alcoholic hepatitis: acetaldehyde damages hepatocytes

Alcoholic hepatitis: fatty change, neutrophil infiltration, Mallory bodies

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Q9

A 90-year-old woman with mild diabetes and Alzheimer disease dies in her sleep. At autopsy, hepatocytes are noted to contain golden cytoplasmic granules that do not stain with Prussian blue. Which of the following best accounts for pigment accumulation in the liver of this patient?

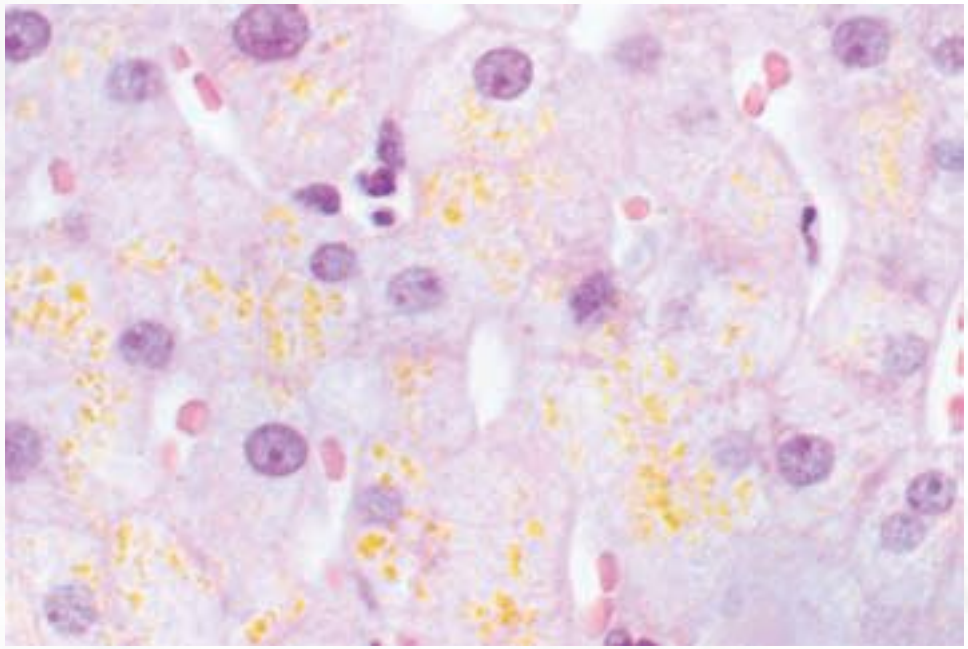
(A) Advanced age

(B) Alzheimer disease

(C) Congestive heart failure

(D) Diabetic ketoacidosis

(E) Hereditary hemochromatosis



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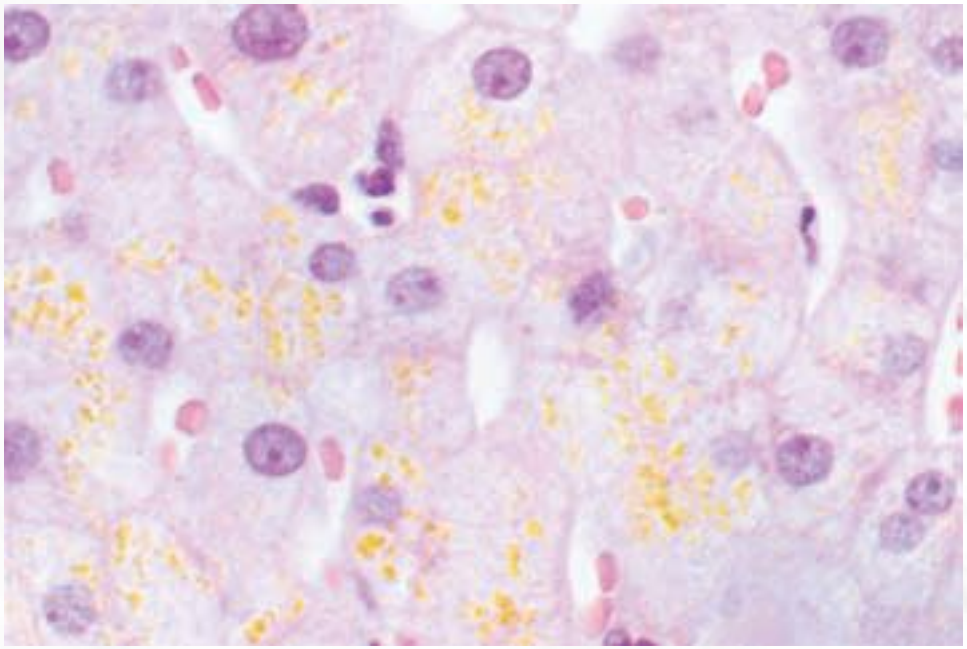

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A9

A: Advanced age. Substances that cannot be metabolized accumulate in cells. Examples include

- (1) endogenous substrates that are not processed because a key enzyme is missing (lysosomal storage diseases),
- (2) insoluble endogenous pigments (lipofuscin and melanin), and
- (3) exogenous particulates (silica and carbon). Lipofuscin is a "wear and tear" pigment of aging that accumulates in organs such as the brain, heart, and liver.

Accumulation of β-Amyloid in the brain is a hallmark of Alzeimer disease.

CHF and hemochromatosis could lead to accumulation of iron in the liver. This would be positive on Prussian blue stain.

Diagnosis: Aging, lipofuscin

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Q9 b

A 90-year-old woman with mild diabetes and Alzheimer disease dies in her sleep. At autopsy, hepatocytes are noted to contain golden cytoplasmic granules that do not stain with Prussian blue. Which of the following mechanisms of disease best describes the pathogenesis of pigment accumulation in hepatocytes in this patient?

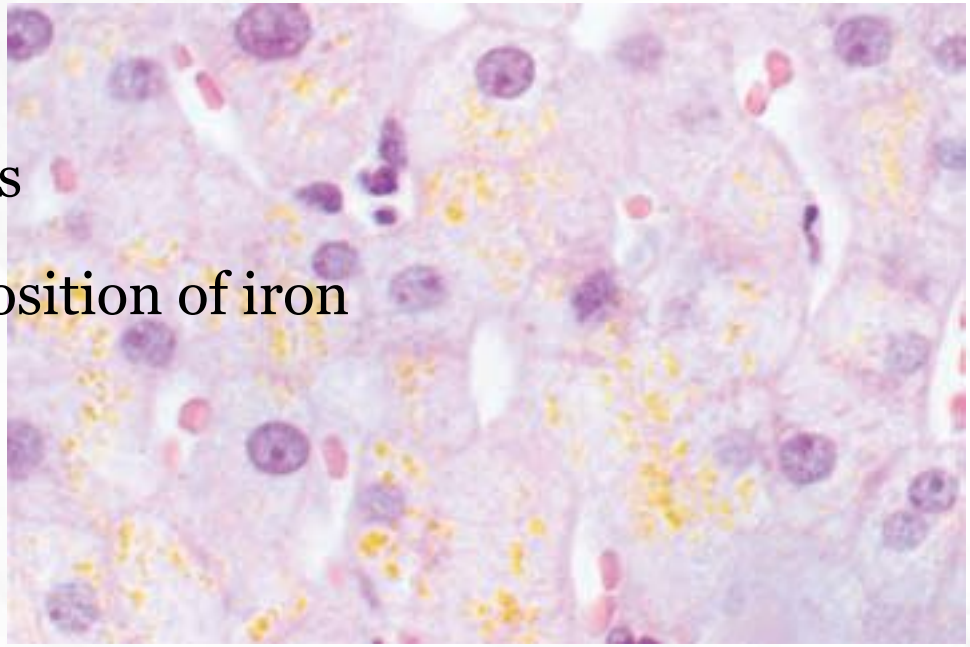
(A) Degradation of melanin pigments

(B) Inhibition of glycogen biosynthesis

(C) Malabsorption and enhanced deposition of iron

(D) Peroxidation of membrane lipids

(E) Progressive oxidation of bilirubin



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A9 b

D: Peroxidation of membrane lipids. Lipofuscin is found in lysosomes and contains peroxidation products of unsaturated fatty acids. The presence of this pigment is thought to reflect continuing lipid peroxidation of cellular membranes as a result of inadequate defenses against activated oxygen radicals.

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Q10

A 60-year-old man is rushed to the hospital with acute liver failure. He undergoes successful orthotopic liver transplantation; however, the transplanted liver does not produce much bile for the first 3 days. Poor graft function in this patient is thought to be the result of "reperfusion injury." Which of the following substances was the most likely cause of reperfusion injury in this patient's transplanted liver?

(A) Cationic proteins

(B) Free ferric iron

(C) Hydrochlorous acid

(D) Lysosomal acid hydrolases

(E) Reactive oxygen species

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A10

E: Reactive oxygen species. Ischemia/reperfusion (I/R) injury is a common clinical problem that arises in the setting of occlusive cardiovascular disease, infection, transplantation, shock, and many other circumstances. The genesis of I/R injury relates to the interplay between transient ischemia and the re-establishment of blood flow (reperfusion). Initially, ischemia produces a type of cellular damage that leads to the generation of free radical species. Subsequently, reperfusion provides abundant molecular oxygen (O2) to combine with free radicals to form **reactive oxygen species**. Oxygen radicals are formed inside cells through the xanthine oxidase pathway and released from activated neutrophils.

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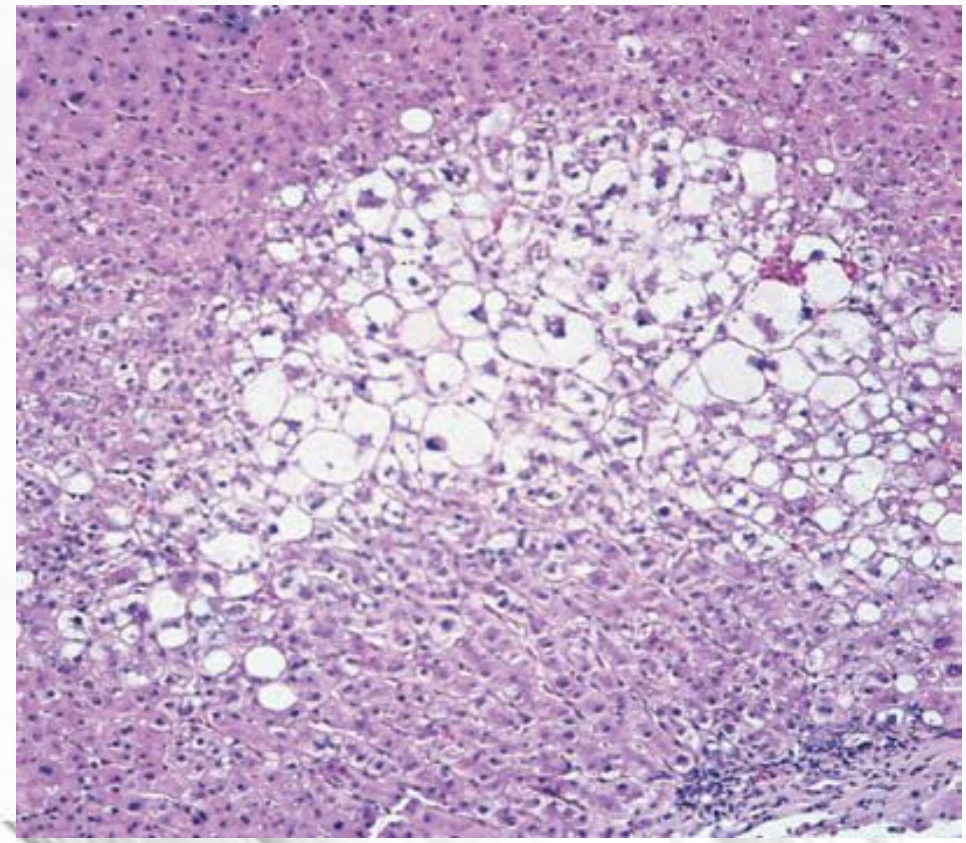
Q11

A 16-year-old girl with a history of suicidal depression swallows a commercial solvent. A liver biopsy is performed to assess the degree of damage to the hepatic parenchyma. Histologic examination demonstrates severe swelling of the centrilobular hepatocytes (shown in the image). Which of the following mechanisms of disease best accounts for the reversible changes noted in this liver biopsy?



(A) Decreased stores of intracellular ATP
(B) Increased storage of triglycerides and free fatty acids
(C) Intracytoplasmic rupture of lysosomes
(D) Mitochondrial membrane permeability transition
(E) Protein aggregation due to increased cytosolic pH

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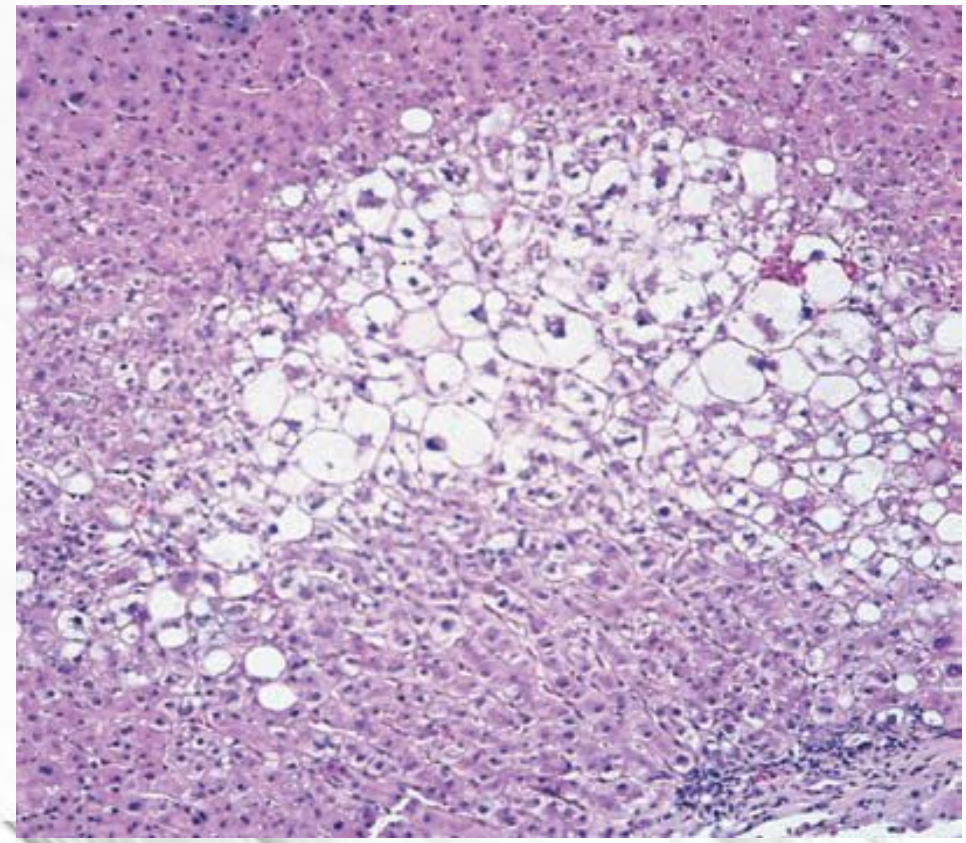

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A11

A: Decreased stores of intracellular ATP. Hydropic swelling may result from many causes, including chemical and biologic toxins, infections, and ischemia. Injurious agents cause hydropic swelling by

(1) increasing the permeability of the plasma membrane to sodium;

(2) damaging the membrane sodium-potassium ATPase (pump); or

(3) interfering with the synthesis of ATP, thereby depriving the pump of its fuel.

Diagnosis: Hydropic swelling, hepatotoxicity

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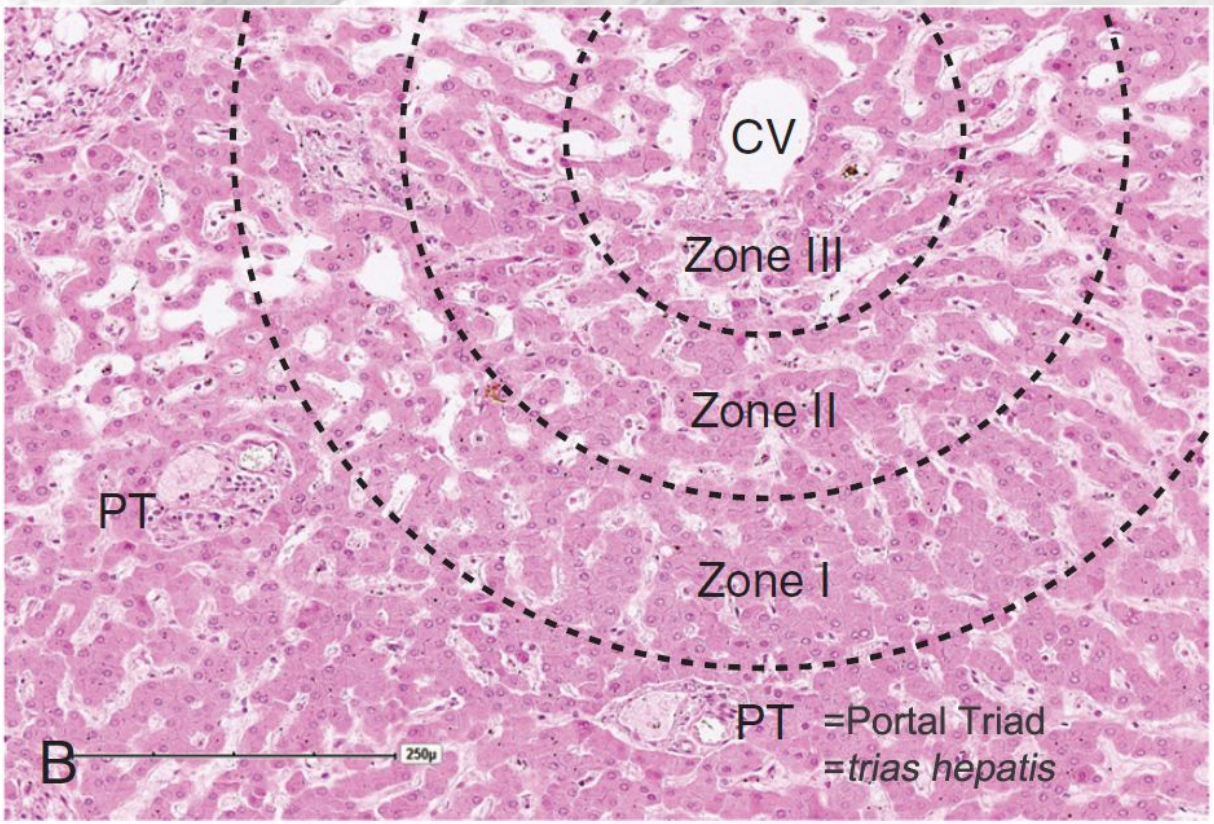
A11



Hepatocytes around the **central venules** (zone III) receive less O2 and nutrients and therefore are most susceptible to damage by

- Production of free radicals from drugs (e.g., acetaminophen), as GSH is used up in the portal triad
- tissue hypoxia (e.g., shock, CO poisoning), and
- alcohol-related fatty change of the liver

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Q12

A 32-year-old woman with poorly controlled diabetes mellitus delivers a healthy boy at 38 weeks of gestation. As a result of maternal hyperglycemia during pregnancy, pancreatic islets in the neonate would be expected to show which of the following morphologic responses to injury?

(A) Atrophy

(B) Dysplasia

(C) Hyperplasia

(D) Metaplasia

(E) Necrosis

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A12

C: Hyperplasia. Infants of diabetic mothers show a 5% to 10% incidence of major developmental abnormalities, including anomalies of the heart and great vessels and neural tube defects. The frequency of these lesions relates to the control of maternal diabetes during early gestation. During fetal development, the islet cells of the pancreas have proliferative capacity and respond to increased demand for insulin by undergoing physiologic hyperplasia. Fetuses exposed to hyperglycemia in utero may develop hyperplasia of the pancreatic β cells, which may secrete insulin autonomously and cause hypoglycemia at birth.

Diagnosis: Diabetes mellitus

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Q12 bonus

A 32-year-old woman with poorly controlled diabetes mellitus delivers a healthy boy at 38 weeks of gestation. After delivery, the mother is restarted on metformin. What is the mechanism of action of this drug?

(A) decreased conversion of glycerophosphate to dihydroxyacetone phosphate in mitochondria, leading to increased NADH/NAD ratio and decreased gluconeogenesis

(B) enhanced release of glucagon-like peptide 1

(C) augmented lactate production by enterocytes

(D) activation of AMP-activated protein kinase in hepatocytes

(E) delayed intestinal glucose absorption

(F) inhibition of glucagon signaling

(G) increased transcription of gluconeogenic enzymes

Ferrannini: *The Target of Metformin in Type 2 Diabetes.* N Engl J Med 2014; 371:1547-1548October 16, 2014DOI: 10.1056/NEJMcibr1409796

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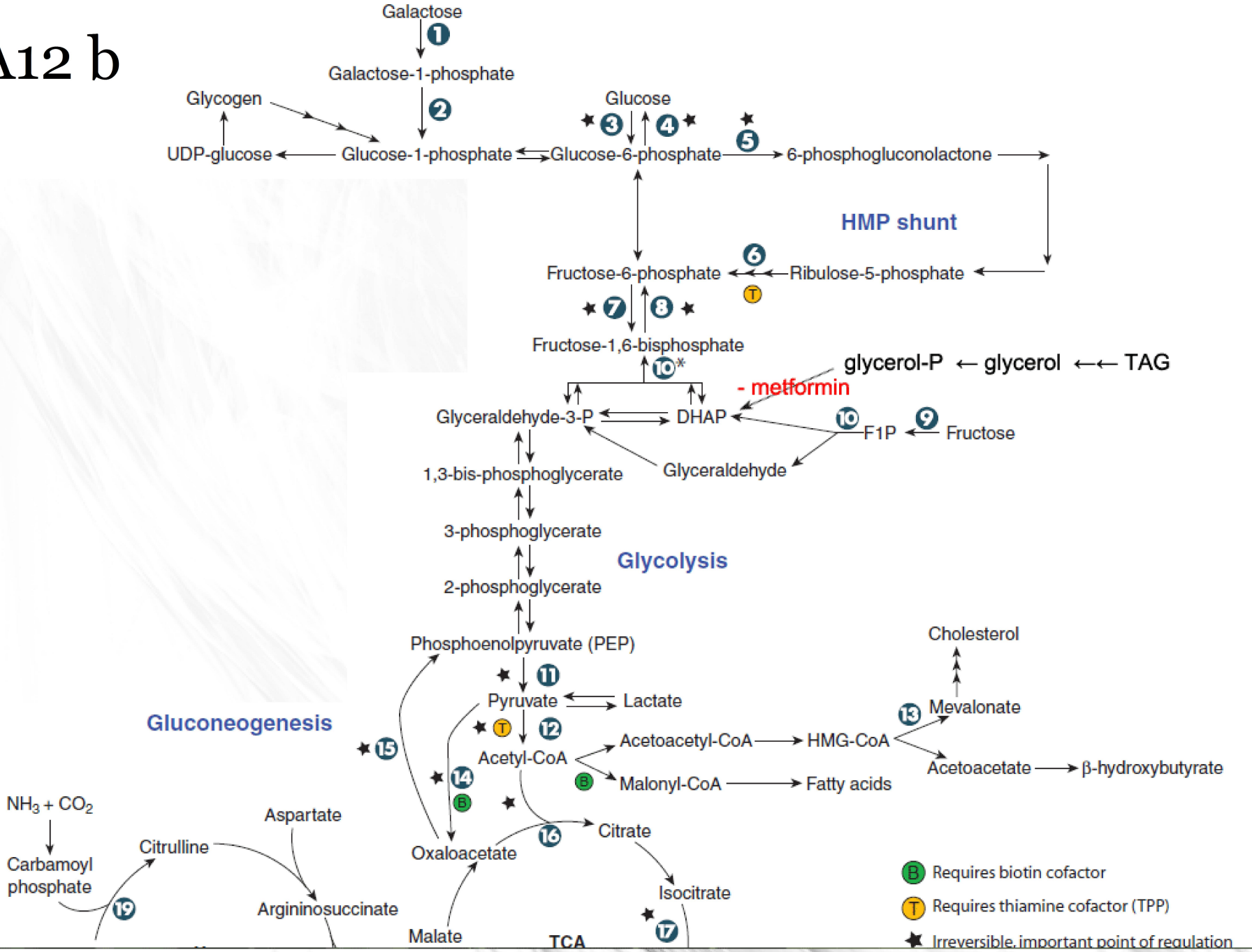
A12 b



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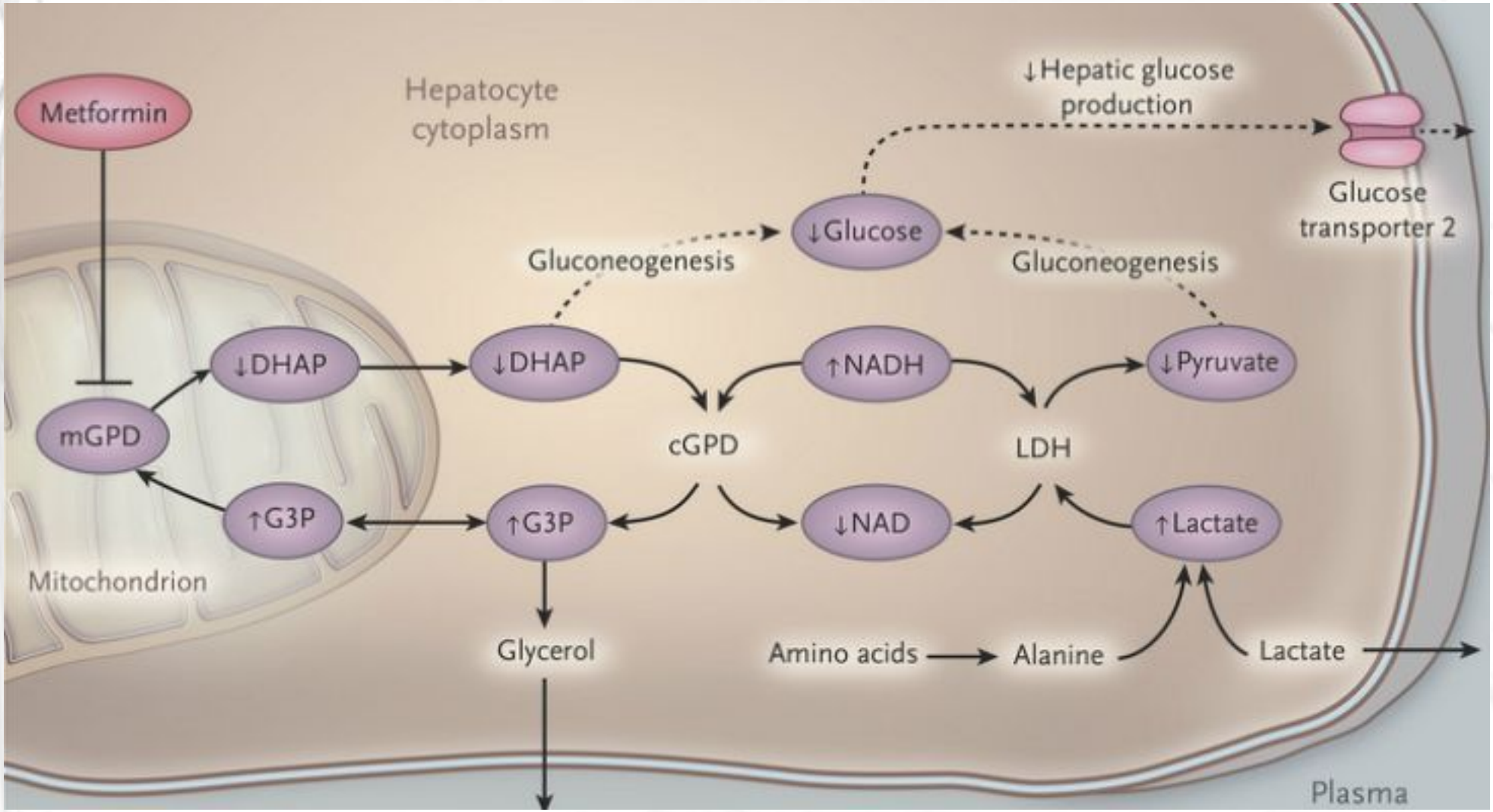
A12 b



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A12 b

Metformin acutely reduces endogenous glucose production and plasma glucose levels and raise plasma lactate and glycerol levels, without changing hepatic gluconeogenic gene expression or cellular energy charge.

Metformin selectively inhibits the mitochondrial isoform of glycerophosphate dehydrogenase, an enzyme that catalyzes the conversion of glycerophosphate to dihydroxyacetone phosphate (DHAP), thereby transferring a pair of electrons to the electron transport chain. The result is a reduction in cytosolic DHAP and a rise in the cytosolic NADH–NAD ratio, which restrains the conversion of lactate to pyruvate; the use of glycerol and lactate as gluconeogenic precursors therefore drops, and glycerol and lactate levels build up in the plasma.

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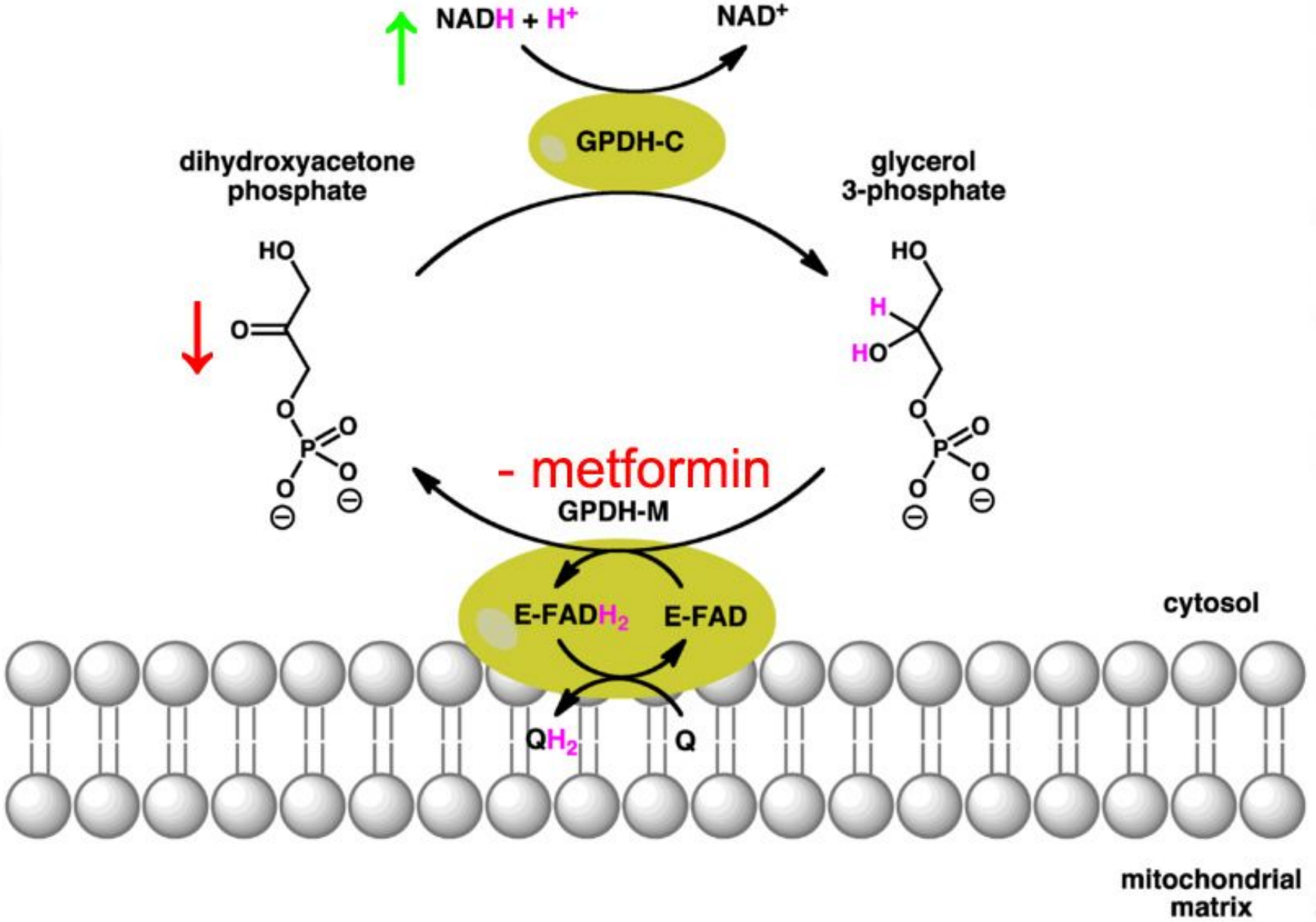
A12 b: G3P dehydrogenase shuttle



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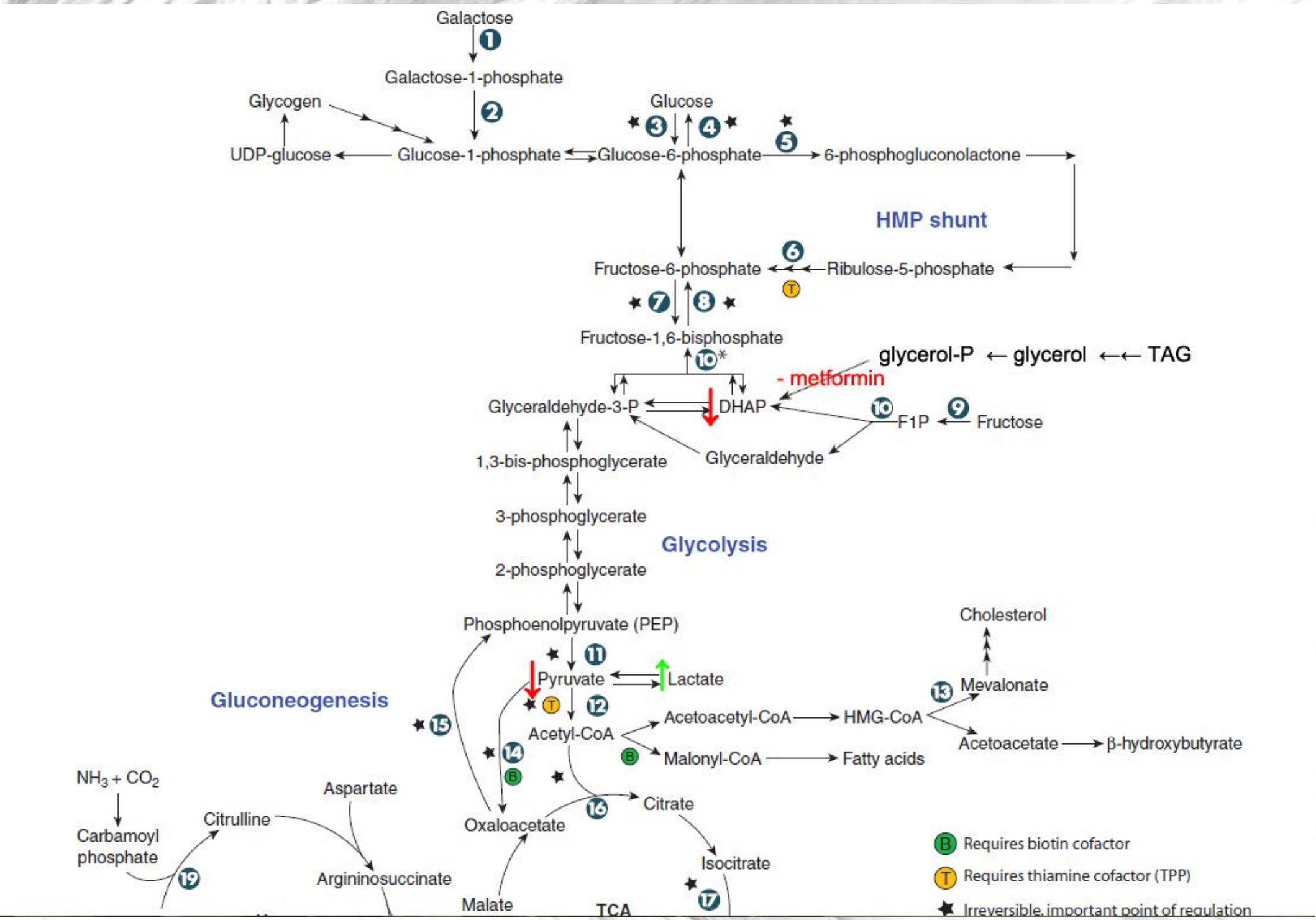

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Děkuji
za pozornost a diskusi

FB: USMLE @ Masaryk

Marek Čierny
(324602 at mail.muni.cz)

Q5

A 70-year-old man is hospitalized after suffering a mild stroke. While in the hospital, he suddenly develops crushing substernal chest pain. Analysis of serum proteins and ECG confirm a diagnosis of acute myocardial infarction. The patient subsequently develops an arrhythmia and expires. A cross section of the left ventricle at autopsy is shown in the image. Histologic examination of the affected heart muscle would demonstrate which of the following morphologic changes?

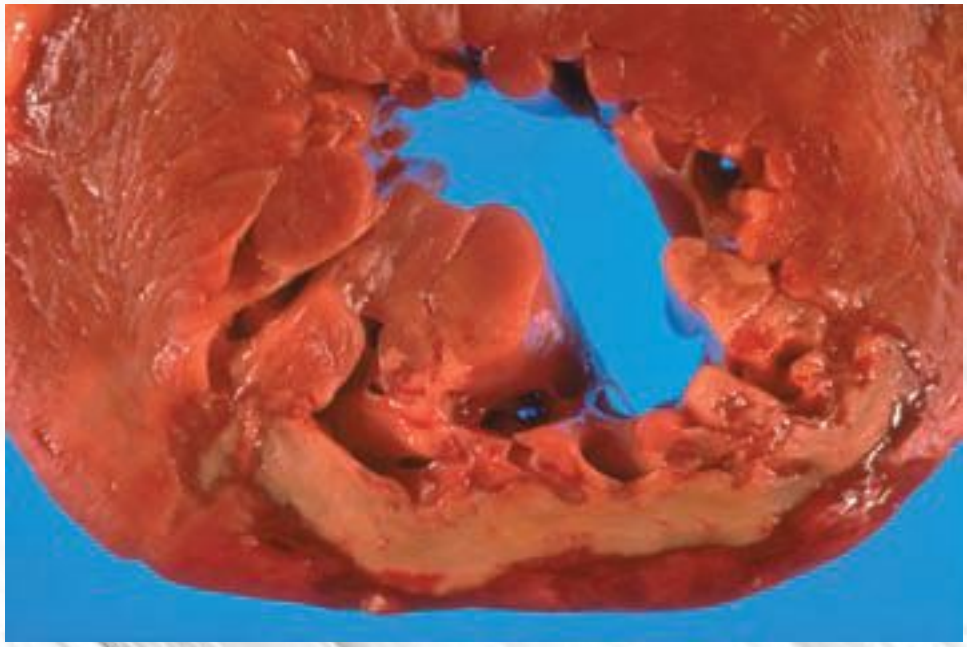
(A) Caseous necrosis

(B) Coagulative necrosis

(C) Fat necrosis

(D) Fibrinoid necrosis

(E) Liquefactive necrosis



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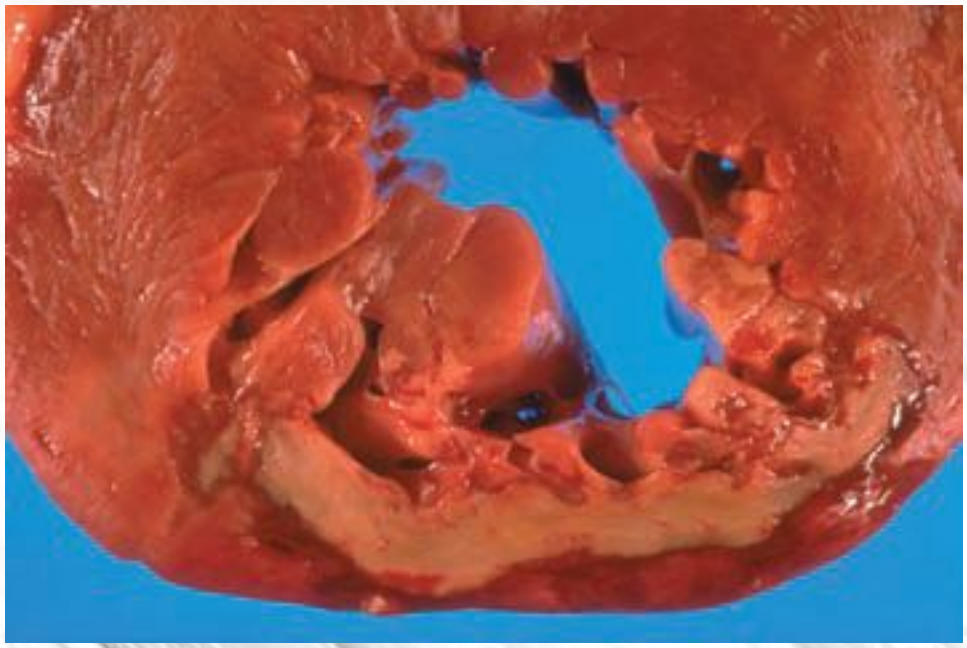

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A5

B: Coagulative necrosis. The interruption of blood supply to the heart decreases the delivery of O2 and glucose. Lack of O2 impairs mitochondrial electron transport, thereby decreasing ATP synthesis and facilitating the production of reactive oxygen species. Mitochondrial damage promotes the release of cytochrome c to the cytosol, and the cell dies. The morphologic appearance of the necrotic cell has traditionally been termed coagulative necrosis because of its similarity to the coagulation of proteins that occurs upon heating.

Necrosis	Enzymatic degradation and protein denaturation of a cell resulting from exogenous injury. Intracellular components leak; inflammatory process (unlike apoptosis).

Types	**Characteristics**
Coagulative	Heart, liver, kidney; occurs in tissues supplied by end-arteries; ↑ cytoplasmic binding of acidophilic dye. Proteins denature first, followed by enzymatic degradation.
Liquefactive	Brain, bacterial abscess; occurs in CNS due to high fat content. In contrast to coagulative necrosis, enzymatic degradation due to the release of lysosomal enzymes occurs first.
Caseous	TB, systemic fungi, *Nocardia*.
Fatty	Enzymatic (pancreatitis [saponification]) and nonenzymatic (e.g., breast trauma); calcium deposits appear dark blue on staining.
Fibrinoid	Vasculitides (e.g., Henoch-Schönlein purpura, Churg-Strauss syndrome), malignant hypertension; amorphous and pink on H&E.
Gangrenous	Dry (ischemic coagulative) and wet (infection); common in limbs and GI tract.

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