PATHOLOGY

بسم الله الرحمن الرحيم

MID – Lecture 3

Mechanism of cell injury (pt.2)

﴿ وَإِن تَتَوَلَّوْا يَسْتَبْدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَالَكُم ﴾

اللهم استعملنا ولا تستبدلنا

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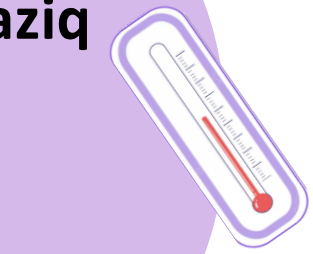

Common Events in Cell Injury From Diverse Causes

All mechanisms of cell injury mentioned in the last lecture end up with one of the 2 following damages :

- Mitochondrial Dysfunction
- Defects in Membrane Permeability — Whether the plasma membrane, mitochondrial or lysosomal membrane

Mitochondrial Dysfunction

- Energy factory
- Hypoxia, toxins, radiation.
- In necrosis and apoptosis.

All decrease the efficiency of the mitochondria → decrease ATP production leading to either apoptosis or necrosis

- **Consequences:**
- Failure of oxidative phosphorylation, ATP depletion.
- Abnormal oxidative phosphorylation, formation of ROS
- Mitochondrial permeability transition pores, loss of membrane potential.
- Release of cytochrome c >> apoptosis

Which leads to the leak of cytochrome c to the cytoplasm, activating caspases and initiating apoptosis

Mitochondrial Damage and Dysfunction

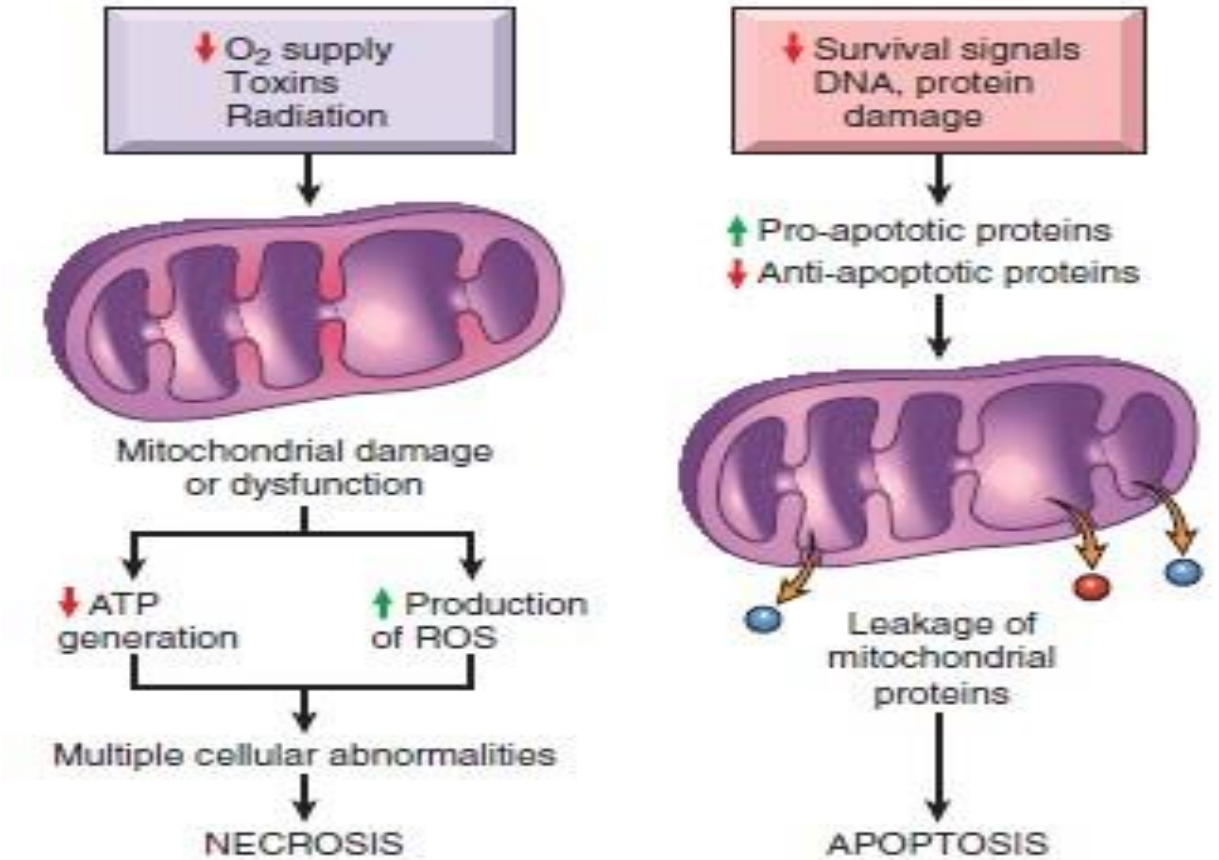

Figure 1–16 Role of mitochondria in cell injury and death. Mitochondria are affected by a variety of injurious stimuli and their abnormalities lead to necrosis or apoptosis. This pathway of apoptosis is described in more detail later. ATP, adenosine triphosphate; ROS, reactive oxygen species.

Depletion of ATP

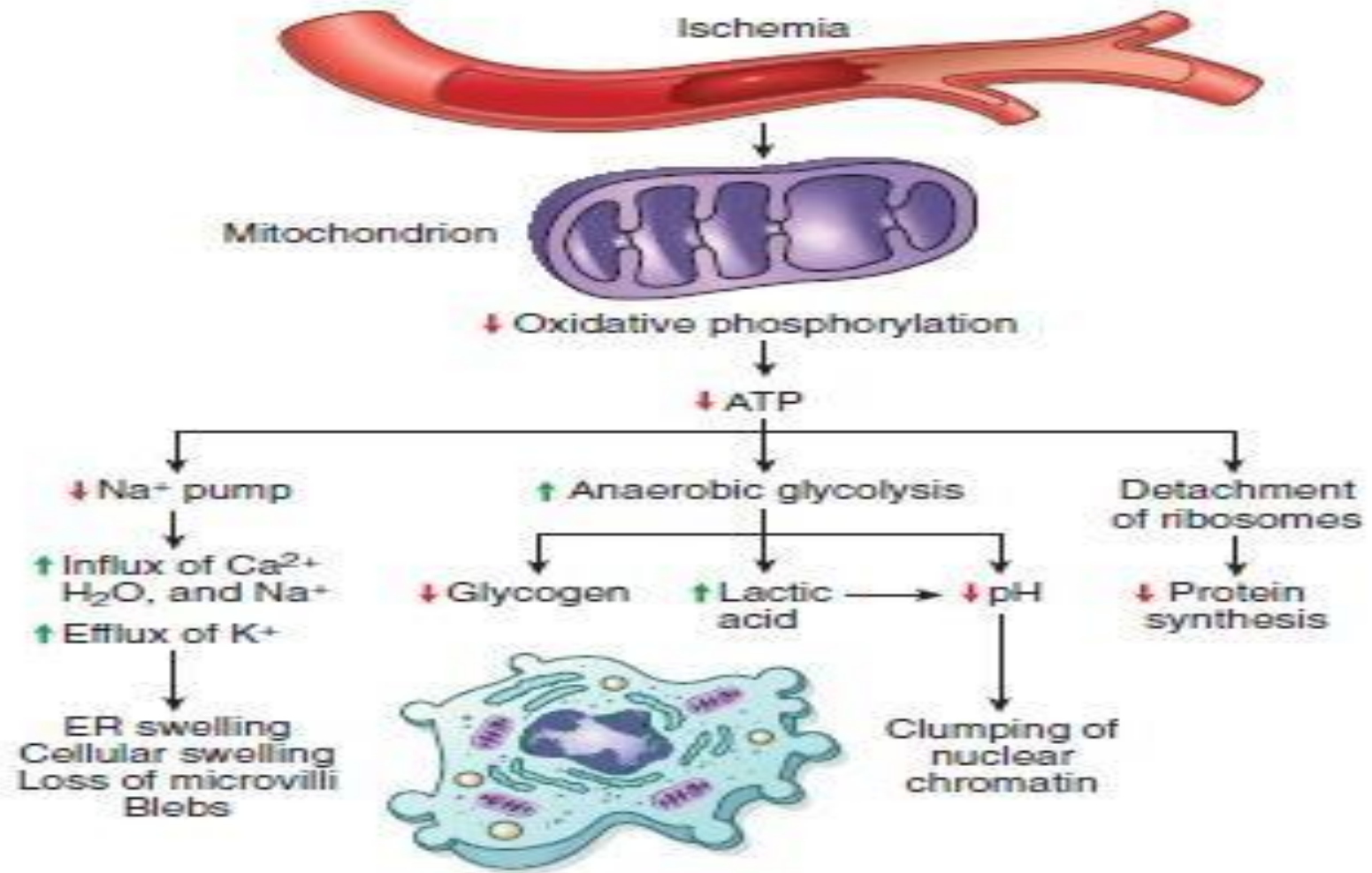

Figure I–15 The functional and morphologic consequences of depletion of intracellular adenosine triphosphate (ATP). ER, endoplasmic reticulum.

Defects in Membrane Permeability

- Mitochondrial membrane damage: decreased ATP

  In addition to the release of cytochrome c to the cytoplasm because of the increased permeability

- Plasma membrane damage: loss of osmotic balance, influx of fluids, leak of contents

- Lysosomal membranes: leakage of enzymes >> cellular digestion.

Just a quick revision! 

Answers are at the bottom right

- A 20 year old male is involved in a motor vehicle accident. The left femoral artery is lacerated resulting in extensive blood loss.He is hypotensive for hours during transport to the ER. Which of the following tissues is most likely to withstand the impact of these events with the least damage?

- A Intestinal epithelium
- B Skeletal muscle
- C Retina
- D Cerebral cortex
- E Renal tubules

Answer explanation :

Extensive blood loss → Hemorrhage → Ischemia

Skeletal muscle can withstand 3-4 hours of ischemia

B

Thrombolytic agents (fibrinolytics) are medications used to dissolve blood clots that obstruct blood vessels.
They are commonly used to treat conditions such as :
Acute myocardial infarction & ischemic stroke

- A 50 year old female suffers an acute myocardial infarction. Thrombolytic agents are used to restore coronary blood flow. In spite of this therapy, the degree of myocardial fiber injury may increase because of which of the following cellular abnormalities?

- AIncreased production of ATP
- B Decreased intracellular pH from anaerobic glycolysis
- C Increased free radical formation
- D Mitochondrial swelling
- E Decreased phospholipid peroxidation

Answer explanation :
What is the case ? It is ischemia-reperfusion injury!
which leads to increased production of ROS

C

- In an experiment, cells are subjected to oxidant stress. There are increased numbers of free radicals generated within the cells. Generation of which of the following enzymes within these cells is the most likely protective mechanism to reduce the number of free radicals?

- A. Phospholipase
- B . Endonuclease
- C . Glutathione peroxidase
- D . Myeloperoxidase
- E. Cytochrome p450.

Answer explanation :

GSH converts hydrogen peroxide into water preventing the formation of other harmful ROS

C

- A cellular mutation results in a protein that does not fold properly. The misfolded protein remains within the cell and is not excreted. Activation of which of the following cytoplasmic enzymes is most likely to occur?

- A NADPH oxidase
- B Glutathione peroxidase
- C Ribonuclease
- D Caspase
- E Telomerase

Answer explanation : The misfolded proteins that can't refold or degrade cause ER stress . Persistent ER stress activates signaling pathways that can result in apoptosis

D

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	2	All mechanisms of cell injury mentioned in the last lecture mainly occur as a result of 2 main causes	All mechanisms of cell injury mentioned in the last lecture end up with one of the 2 following damages
V1 → V2			

Additional Resources:

رسالة من الفريق العلمي:

{إنّ بَطشَ رَبّكَ لَشَديدٌ}
أي أنّ عقوبتهُ لأهلِ الجرائمِ والذّنوبِ قويّةٌ وهُو بالمِرصادِ للظالمِينَ |السّعديّ|
الظالمونَ والمجرمونَ سيُحاسِبهمُ اللهُ بِعدلِه ، والمظلومونَ والمقتولونَ الذين نحسبُهم من الشّهداءِ سيجزيهمُ الله من فضله وكرمهِ يومَ لا همٌّ ولا نصَبٌ ولا ألمٌ ولا تعَبٌ ...
ولكن ، ماذا عنك؟
قُم للهِ ، وانهض من غفلتكَ ، وقُل يارب أنا وَقفٌ لكَ ولِدينك
جاهد هواكَ وذنوبكَ ومعاصيكَ حتى إن مكّن اللهُ المسلمين كنت قادرًا على أن تجاهدَ حبّ الحياة
أوَتظُنُّ أنّ مَن جاهدَ بِروحهِ كان هذا أولُ الطّريقِ عِندَه؟!
لا واللهِ فالرُّوح غاليةٌ ولا تهونُ إلّا عند من عرفَ الله وكان منهُ قريبًا
فليكُن هذا مشروعك