

Cellular Injury Causes

1. Critically evaluate the major causes of cell injury; provide suitable examples from recent literature to illustrate your answer.

Which type is most common? Which has the most severe effect? Is genetic cell injury worse as it cannot be altered by behaviours? Are there treatments for the genetic disorders underway?

What are the major causes of cell injury? Give examples.

Discuss and describe etiology of cell injury with examples.

There are three main causes of cellular injury; **congenital, acquired and genetic**.

Acquired injury

- Result of the environment. This can include physical or chemical agents, infections, immunological responses poor nutrition, hypoxia and ischemia.
- **Ischemia:** limited blood flow > hypoxia > lack of oxygen being supplied to the tissue > Oxygen needed for oxidative metabolism, without it cells may become injured or die completely
- Reduces ATP production by the oxidative phosphorylation system in mitochondria > Lack of energy > cells stop functioning
- Myocardial infarction: No longer energy to contract.
- No oxygen > creatinine kinase anaerobically metabolises creatine phosphate > glycogen depletion > lactic acid + inorganic phosphates.
- No energy > membrane pumps fail > sodium + water enters > cell oedema.
- REVERSIBLE: Cell oedema + increased acid (acidosis) > clumping of nuclear chromatin > bulges in plasma membrane (blebs) > mitochondrial swelling
- IRREVERSIBLE: increased calcium > pyknosis of nuclei > disruption of plasma membranes + lysosomes breaking open releasing their enzymes.
- Cytosolic calcium increase > released from intracellular stores + influx across the membrane > activates enzymes
- Phospholipases: disrupt cell membrane.
- Proteases: break down membrane and cytoskeletal proteins.
- Endonucleases: DNA and chromatin fragmentation.
- ATPases increasing ATP depletion. (Study depleting extracellular calcium found delayed cell death after hypoxia)
- Ischemia reperfusion. Restoration of blood flow after ischemia > mitochondrial damage incomplete oxygen reduction > increase of reactive oxygen species (ROS).
- One study found that thrombolytic therapy lead to an increase in transient focal cerebral ischemia (stroke). The following reperfusion had a strong association with blood brain barrier permeability. This was found to be associated with nitric oxide synthases, therefore inhibitors of this NOSs could help to prevent infarction and haemorrhage.
 - <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3966853/>
- Myocardial infarction: when treating patients who have suffered from ischemic myocardial infarction are treated by timely reperfusion using thrombolytic therapy or primary percutaneous coronary intervention (PPCI). This can lead to further myocardial reperfusion injury