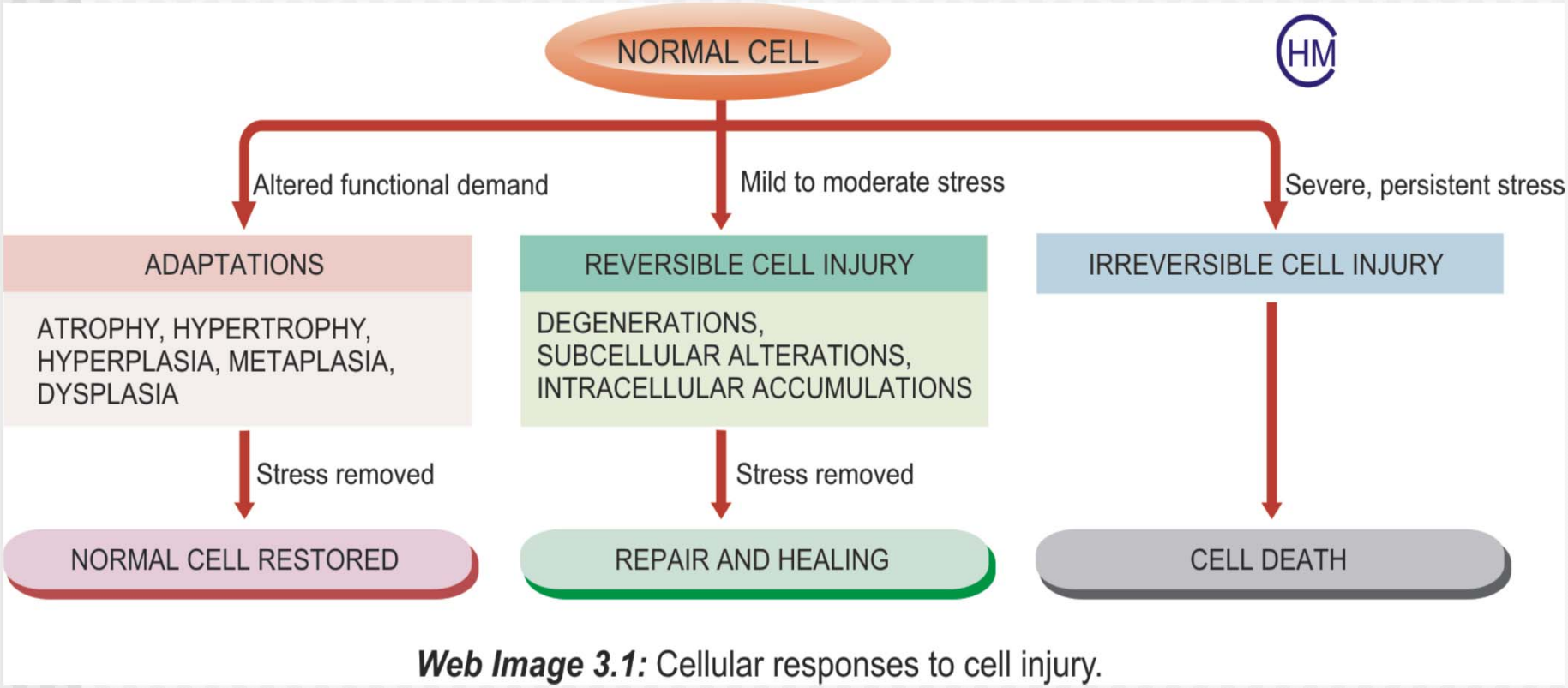
HM/CH-1/L-2,3

CELL INJURY & CELLULAR ADAPTATIONS

CELL INJURY

- DEFINITION
- VARIABLES FOR CELL RESPONSE:
- Type of cell and tissue involved
- Extent and type of cell injury

CELLULAR RESPOSES



Web Image 3.1: Cellular responses to cell injury.

ETIOLOGY OF CELL INJURY

- GENETIC CAUSES
- ACQUIRED CAUSES

1. Hypoxia and ischaemia
2. Physical agents
3. Chemical agents and drugs
4. Microbial agents
5. Immunologic agents
6. Nutritional derangements
7. Ageing
8. Psychologic Diseases
9. Iatrogenic causes
10. Idiopathic diseases

PATHOGENESIS OF CELL INJURY

Basic underlying principles:

1. Type, duration and severity of injurious agent
2. Type, status and adaptability of target cell
3. Underlying intracellular phenomena:

   -Mitochondrial dysfunction

   -Membrane damage

   -Release of toxic free radicals
4. Morphologic consequences

PATHOGENESIS OF ISCHAEMIC AND HYPOXIC CELL INJURY

- REVERSIBLE CELL INJURY
- IRREVERSIBLE CELL INJURY

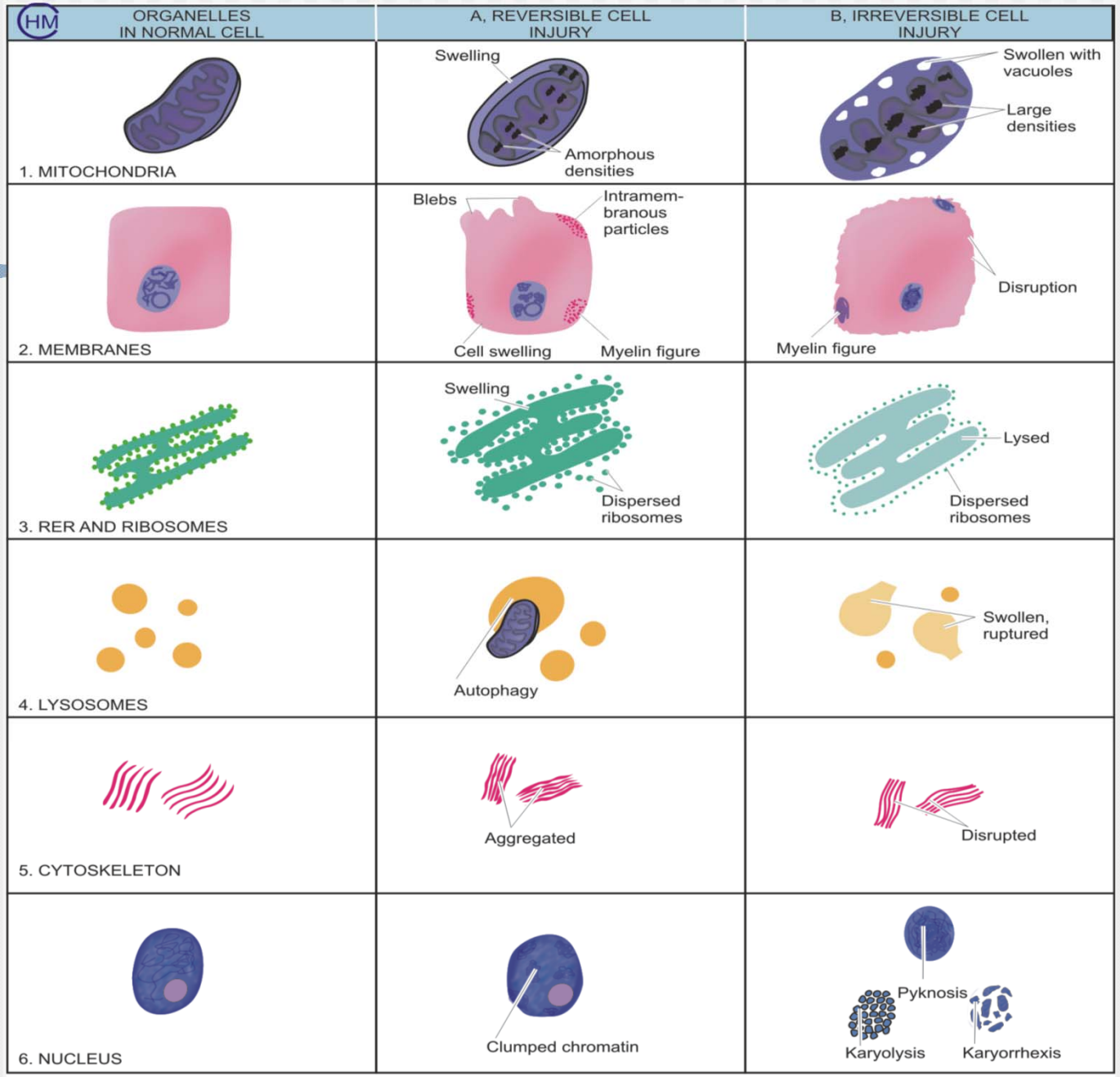
REVERSIBLE CELL INJURY

MECHANISM

1. Decreased generation of cellular ATP
2. Intracellular lactic acidosis
3. Damage to plasma membrane pumps (Na-K, Ca)
4. Reduced protein synthesis

EFFECT

1. Damage by ischaemia *versus* hypoxia from other causes
2. Nuclear clumping
3. Hydropic swelling and other membrane changes
4. Dispersed ribosomes



Web Image 3.7: Ultrastructural changes during cell injury due to hypoxia-ischaemia.

IRREVERSIBLE CELL INJURY

Key events in “point of no return”:

- Inability to reverse mitochondrial dysfunction
- Disturbed membrane function
- Continued reduction of ATP, depletion of proteins, reduced intracellular pH, leakage of lysosomal enzymes

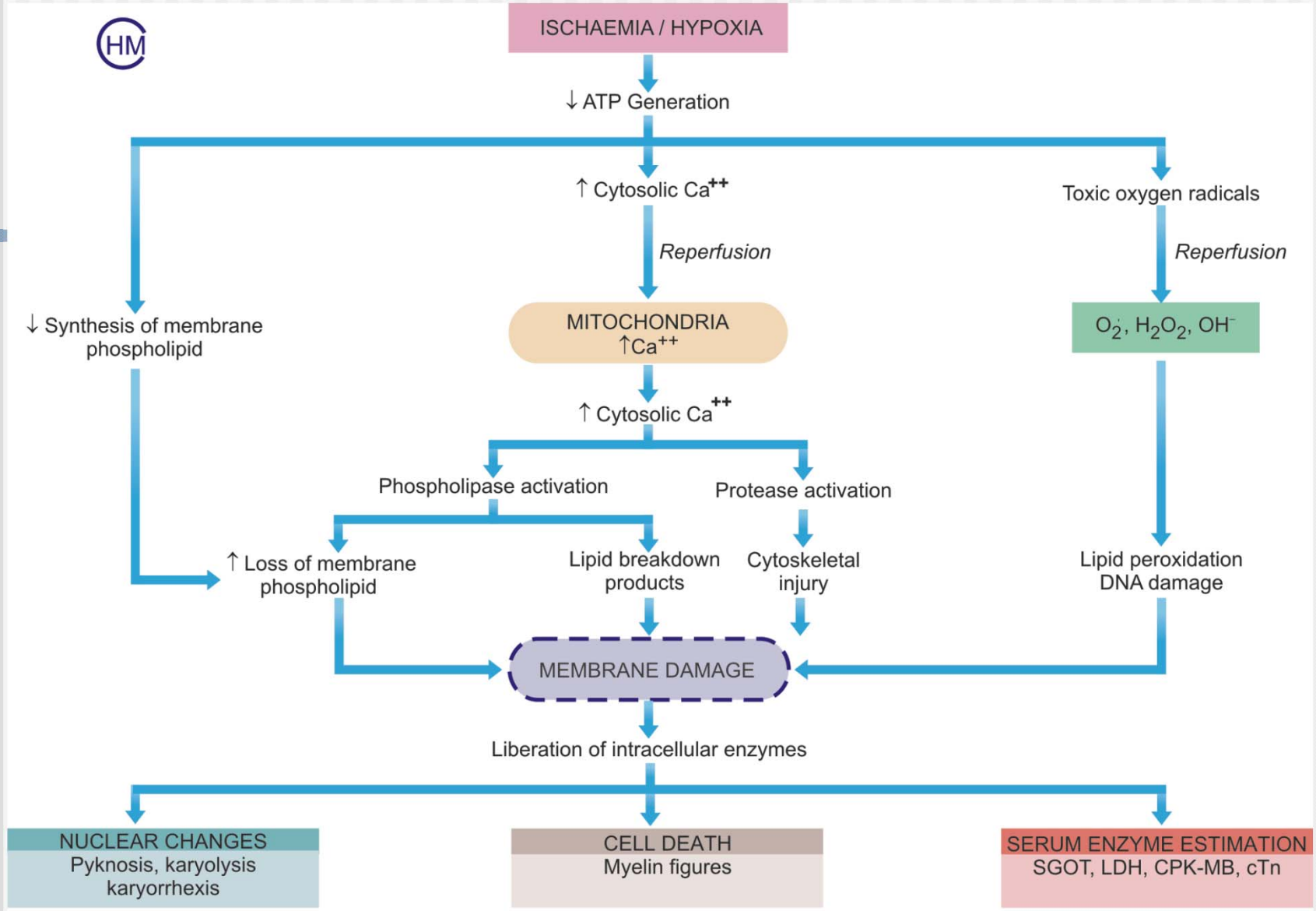
IRREVERSIBLE CELL INJURY

MECHANISM

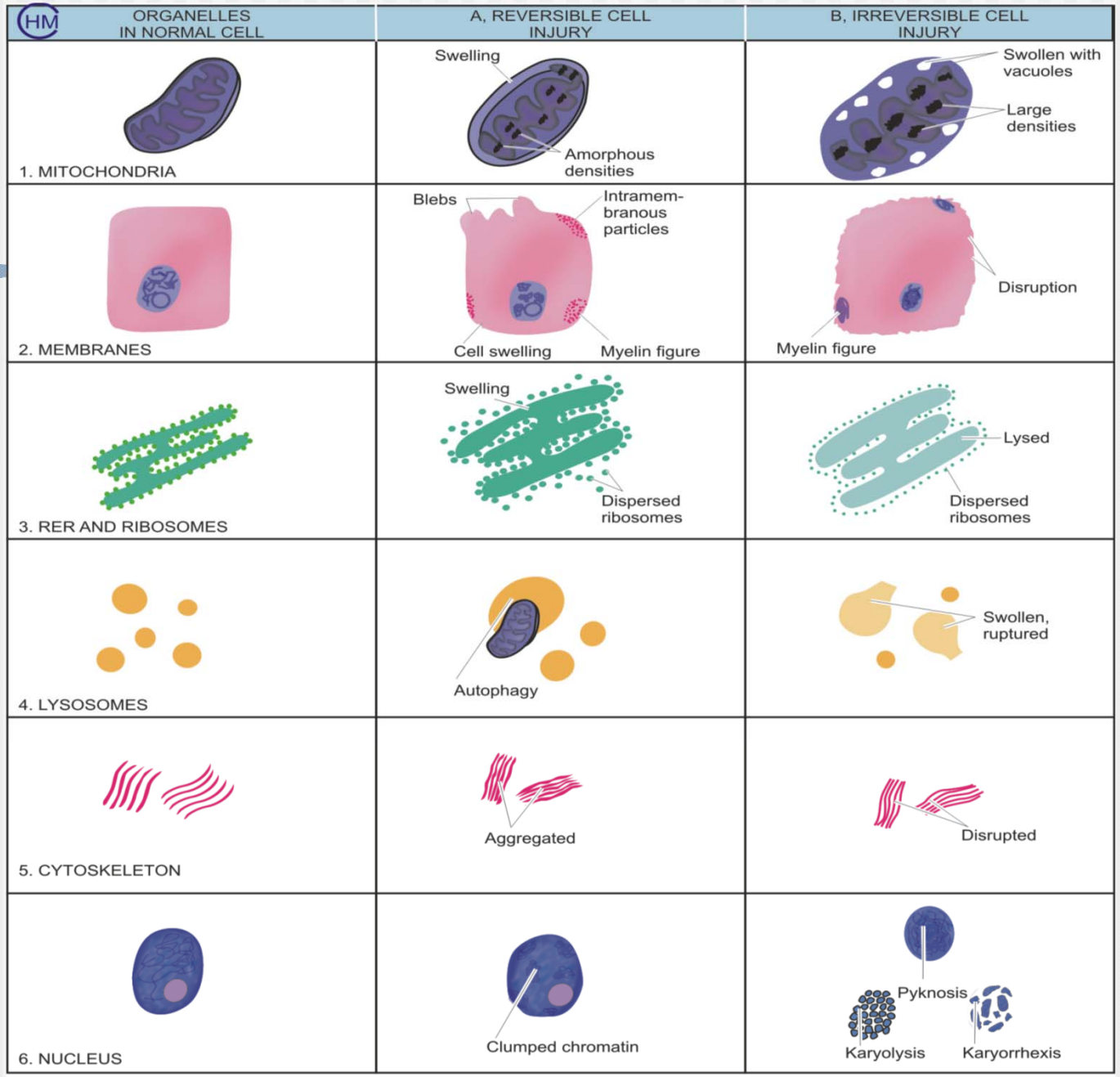
1. Calcium influx
2. Activated phospholipases
3. Intracellular proteases
4. Activated endonucleases
5. Lysosomal hydrolytic enzymes

EFFECT

1. Mitochondrial damage
2. Membrane damage
3. Cytoskeletal damage
4. Nuclear damage
5. Lysosomal damage, cell death, phagocytosis



Web Image 3.6: Sequence of events in the pathogenesis of reversible and irreversible cell injury caused by hypoxia/ischaemia.



Web Image 3.7: Ultrastructural changes during cell injury due to hypoxia-ischaemia.

Web Table 3.1: Common Enzyme Markers of Cell Death. HM

Enzyme	Disease
1. *Aspartate aminotransferase (AST, SGOT)*	Diffuse liver cell necrosis e.g. viral hepatitis, alcoholic liver disease Acute myocardial infarction
2. *Alanine aminotransferase (ALT, SGPT)*	More specific for diffuse liver cell damage than AST e.g. viral hepatitis
3. *Creatine kinase-MB (CK-MB)*	Acute myocardial infarction, myocarditis Skeletal muscle injury
4. *Lipase*	More specific for acute pancreatitis
5. *Amylase*	Acute pancreatitis Sialadenitis
6. *Lactic dehydrogenase (LDH)*	Acute myocardial infarction Myocarditis Skeletal muscle injury
7. *Cardiac troponin (CTn)*	Specific for acute myocardial infarction

Attempts at restoration of blood supply

- Cell injury due to oxygen deprivation: depends upon duration of ischaemia and blood restoration
- Cell injury accentuated by restoration of perfusion (ischaemia-reperfusion injury) and subsequent events (liberation of toxic free radicals)

3 different consequences:

- Ishaemia to reversible cell injury
- Ischaemia to reperfusion injury
- Ischaemia to irreversible injury