Tishk International University,

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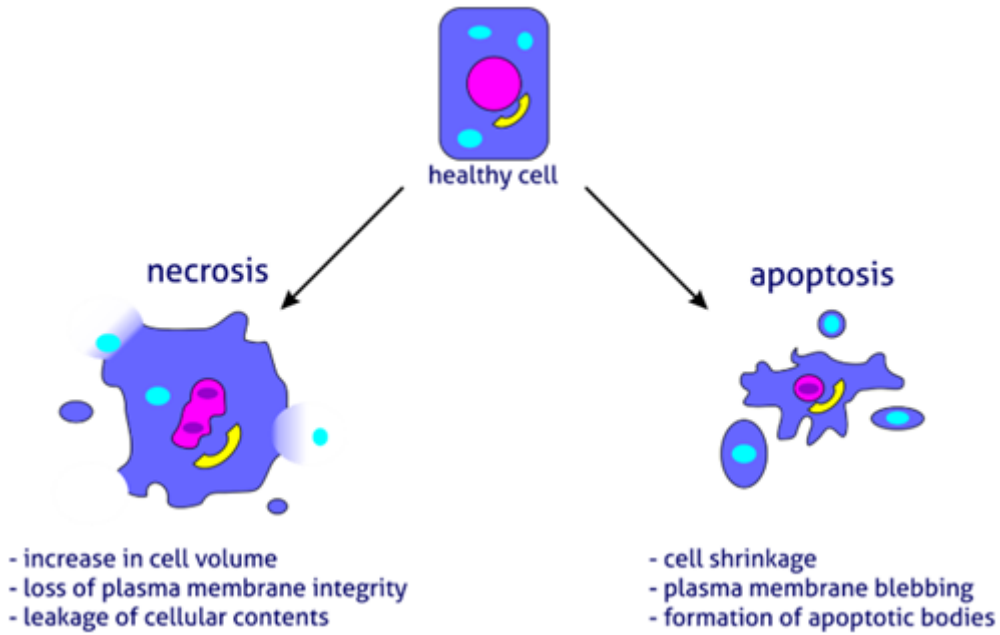
Cell Biology, 1st Semester/W9

Apoptosis vs. necrosis

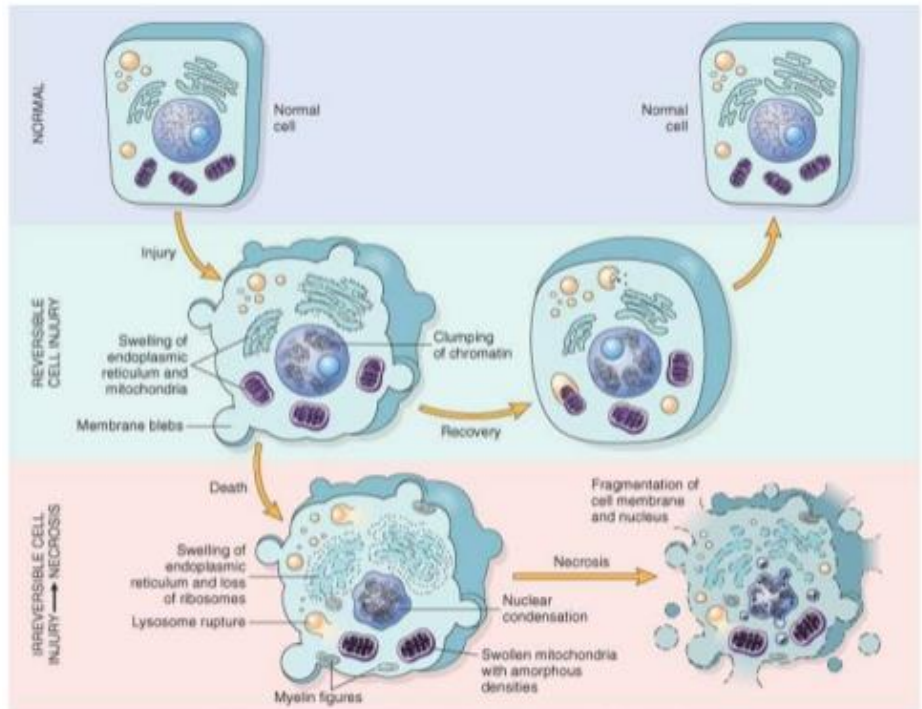
- Broadly speaking, there are two ways that cells die in a multicellular organism such as yourself:
- They are killed by things that harm them (such as toxic chemicals or physical injury), a process called **necrosis**.
- They are triggered to undergo programmed cell death. The best-understood form of programmed cell death is **apoptosis**.
- Necrosis and apoptosis occur under different circumstances and involve different steps. Simply put, necrosis is messy and causes an immune response of inflammation, while apoptosis is tidy and splits the cell into little parcels that can be taken up and recycled by other cells.

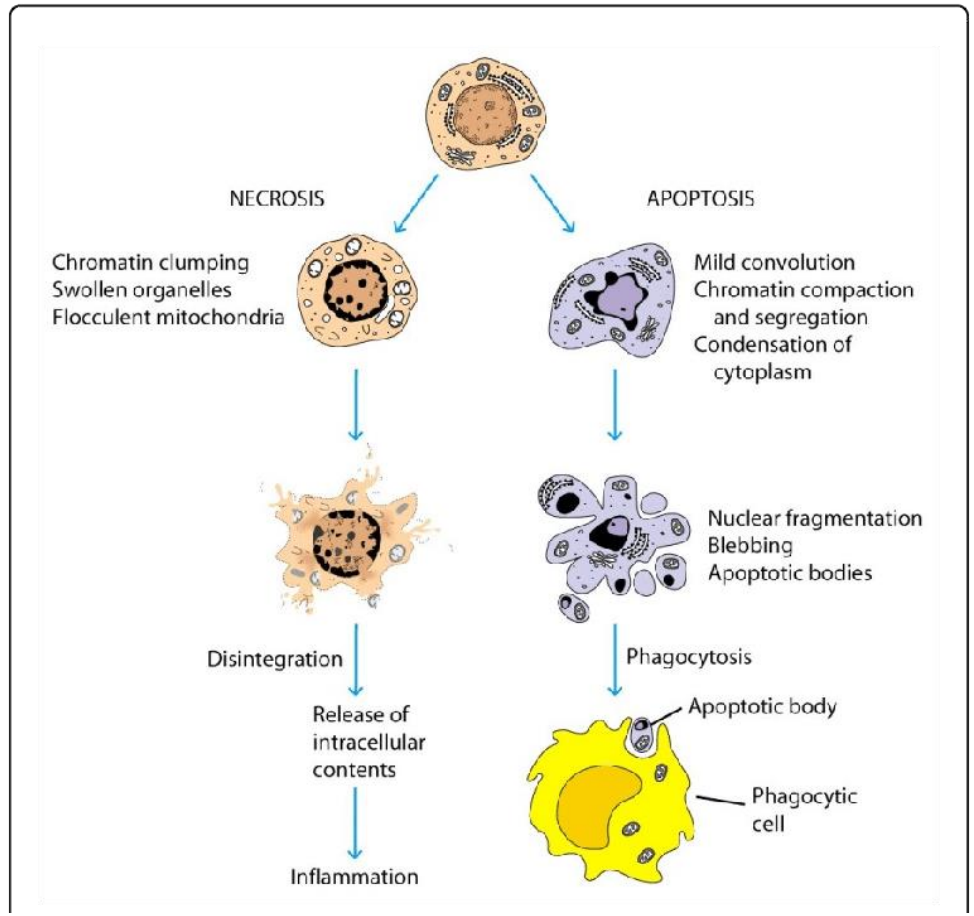

healthy cell
necrosis
apoptosis
- increase in cell volume
- loss of plasma membrane integrity
- leakage of cellular contents
- cell shrinkage
- plasma membrane blebbing
- formation of apoptotic bodies

Necrosis (the messy way)

- When cells are damaged by harmful factors (such as injury or toxic chemicals), they usually “spill their guts” as they die.
- Because the damaged cell’s plasma membrane can no longer control the passage of ions and water, the cell swells up, and its contents leak out through holes in the plasma membrane.
- This often causes inflammation in the tissue surrounding the dead cell.

Reversible and Irreversible Cell Injury



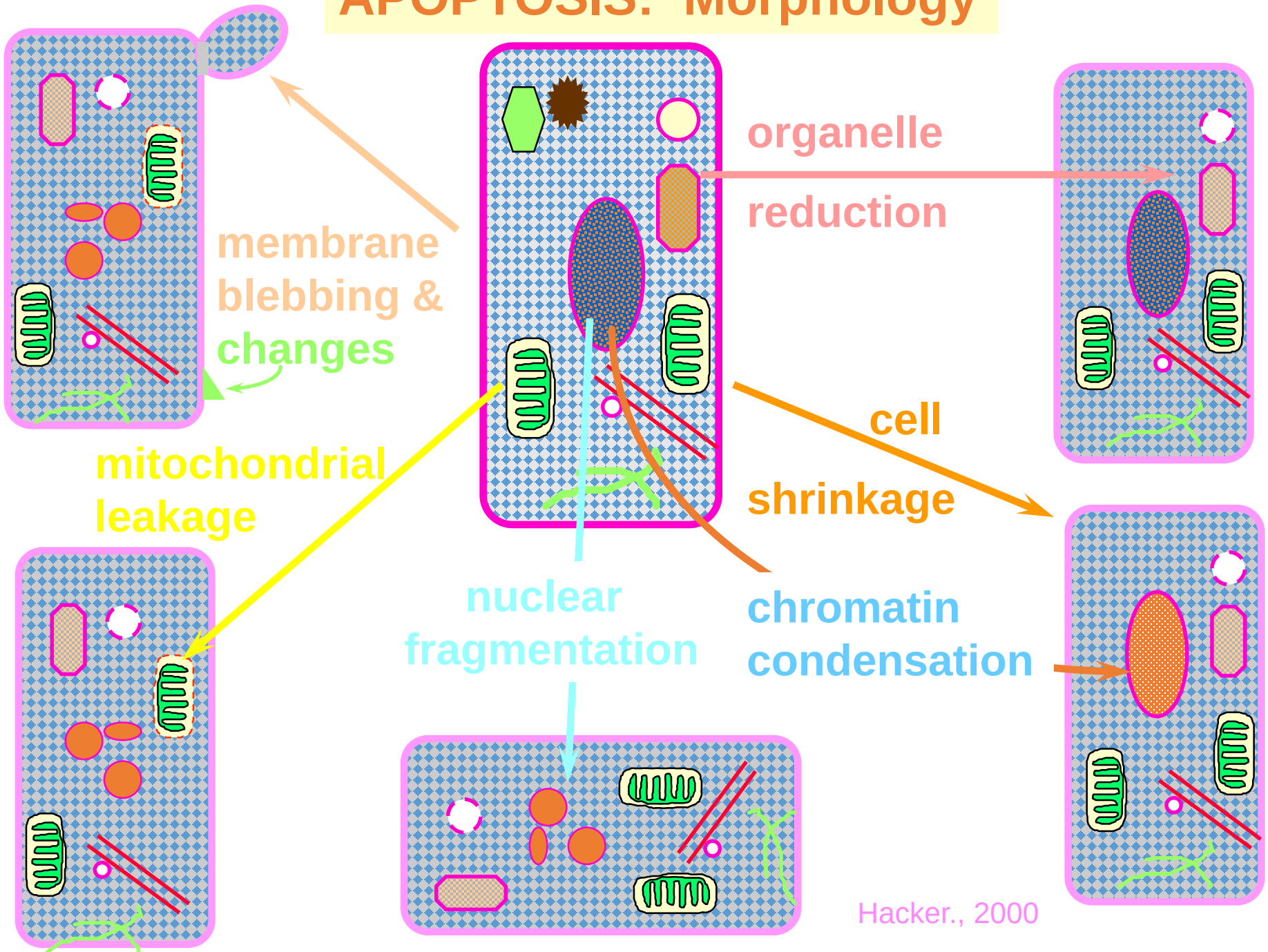

NECROSIS
APOPTOSIS
Chromatin clumping
Swollen organelles
Flocculent mitochondria
Mild convolution
Chromatin compaction
and segregation
Condensation of
cytoplasm
Nuclear fragmentation
Blebbing
Apoptotic bodies
Disintegration
Phagocytosis
Release of
intracellular
contents
Apoptotic body
Phagocytic
cell
Inflammation

Apoptosis (the tidy way)

- Cells that undergo apoptosis go through a different and much more orderly process. They shrink and develop bubble-like protrusions (technical name: “blebs”) on their surface.
- The DNA in the nucleus gets chopped up into small pieces, and some organelles of the cell, such as the endoplasmic reticulum, break down into fragments.
- In the end, the entire cell splits up into small chunks, each neatly enclosed in a package of membrane.

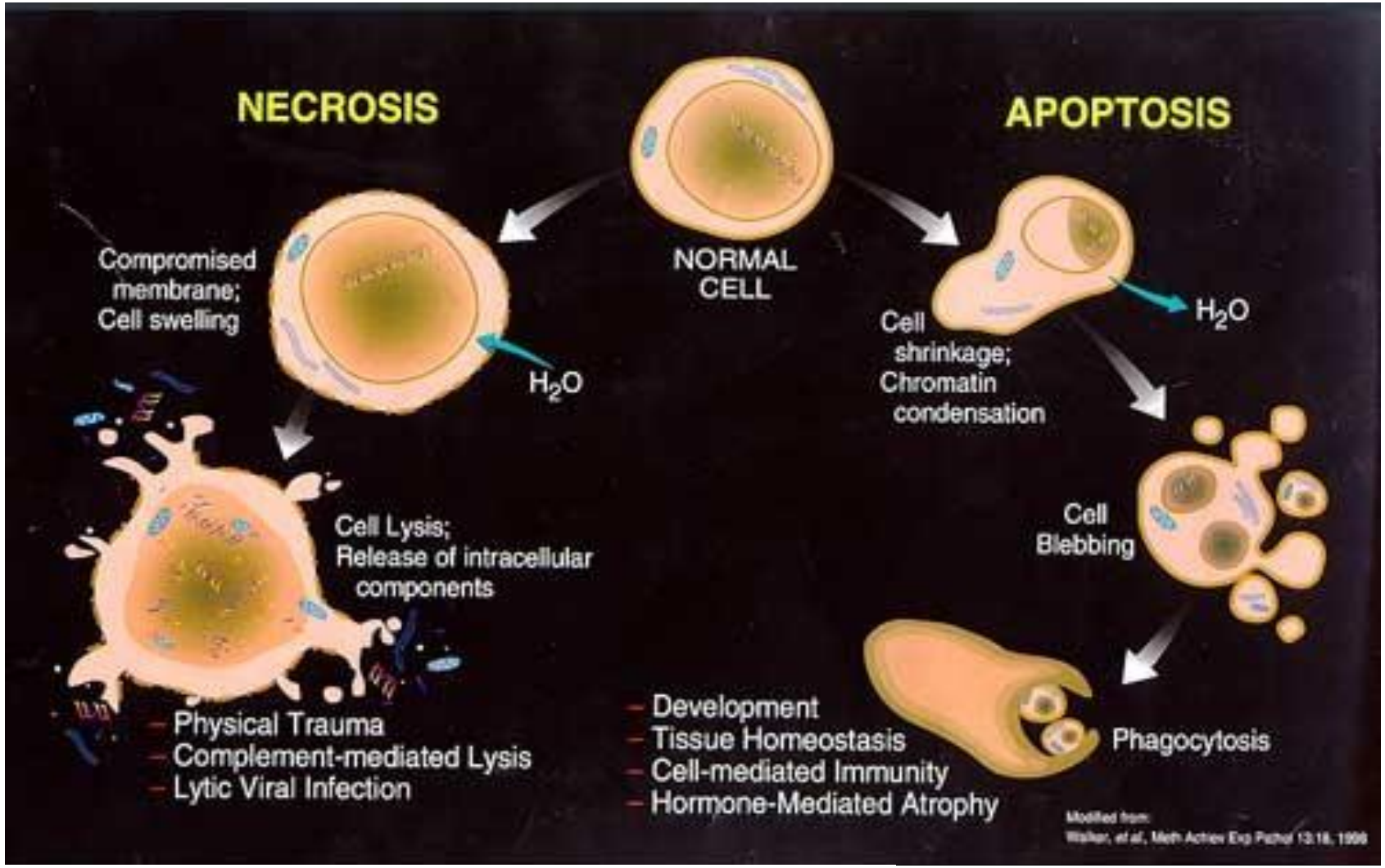
- What happens to the chunks? They release signals that attract debris-eating (phagocytic) immune cells, such as macrophages.
- Also, the fragments of the dying cell display a lipid molecule called **phosphatidylserine** on their surface.
- Phosphatidylserine is usually hidden on the inside of the membrane, and when it is on the outside, it lets the phagocytes bind and "eat" the cell fragments.

APOPTOSIS: Morphology



Hacker., 2000

NECROSIS Vs APOPTOSIS



Why do cells undergo apoptosis?

- Many cells in the human body have the built-in ability to undergo apoptosis (in the same way that they have the built-in ability to copy their DNA or break down fuels). Basically, apoptosis is a general and convenient way to remove cells that should no longer be part of the organism.
- Some cells need to be “deleted” during development – for instance, to whittle an intricate structure like a hand out of a larger block of tissue.
- Some cells are abnormal and could hurt the rest of the organism if they survive, such as cells with viral infections or DNA damage.
- Cells in an adult organism may be eliminated to maintain balance – to make way for new cells or remove cells needed only for temporary tasks.

Apoptosis is part of development

- In many organisms, programmed cell death is a normal part of development.
- Apoptosis also plays a key role in human development. For instance, your hand started out as a paddle-like block of tissue when you were an embryo. The block was “carved” into fingers by apoptosis of the cells in between the developing fingers.

- This process occurs in all sorts of vertebrate species that have finger- or toe-like digits, and less apoptosis results in more webbing between the digits. Sometimes, if a small mistake happens during finger or toe development, apoptosis may be incomplete (leading, for instance, to fused toes).
- Other examples of apoptosis during normal development include the loss of a tadpole's tail as it turns into a frog, and the removal of unneeded neurons in as neural circuits in the brain are "wired."

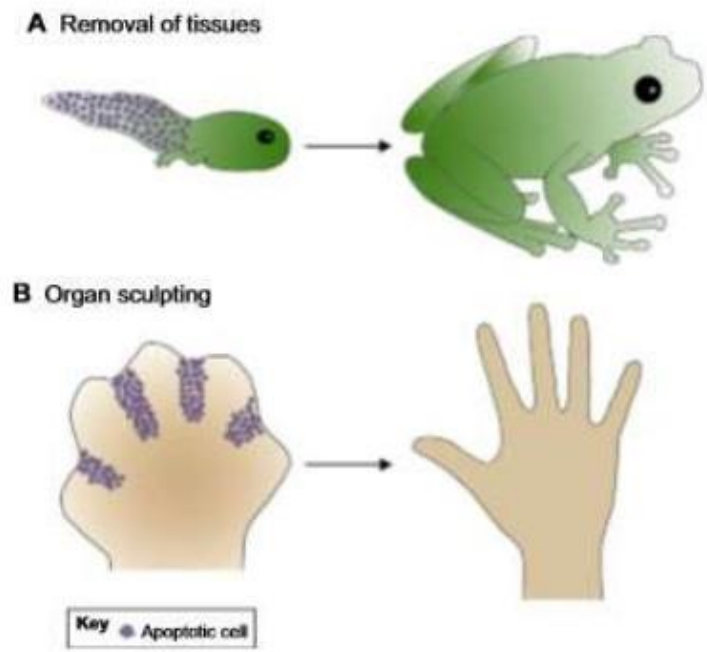
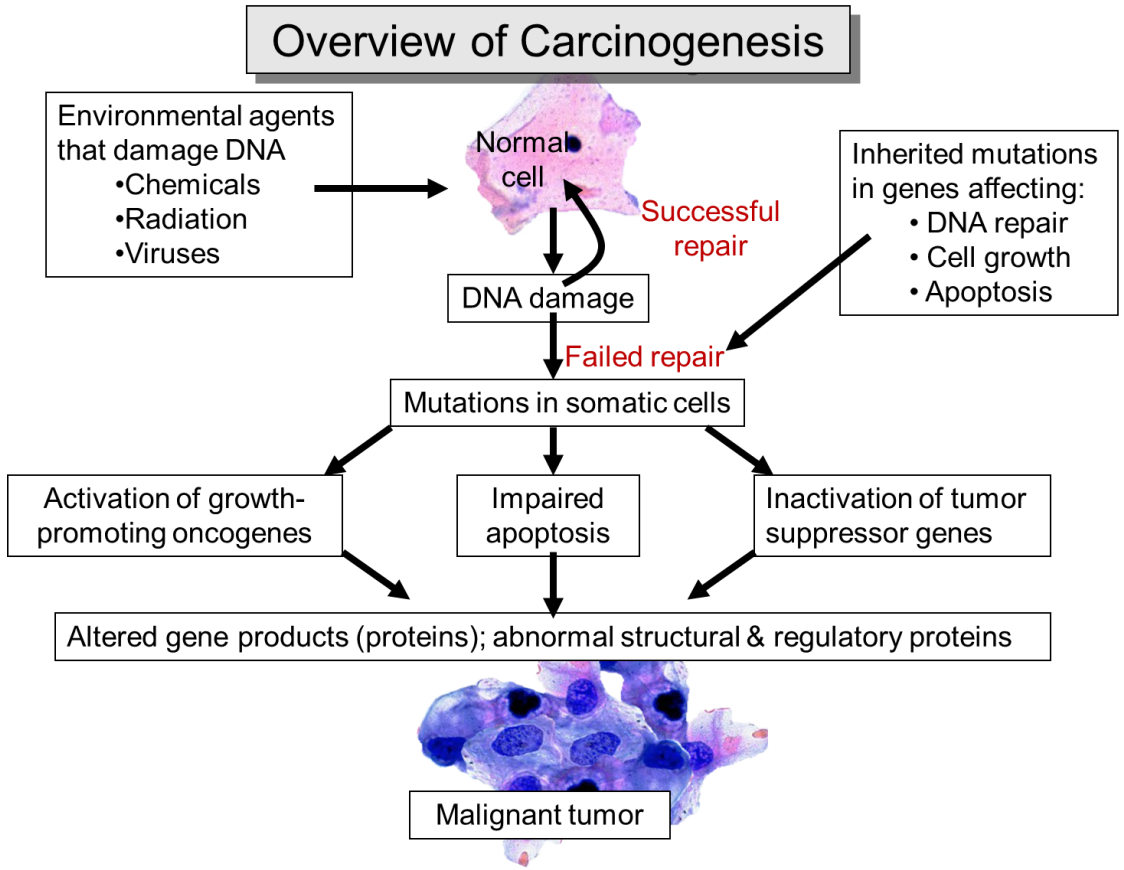


Fig. 1. Roles for apoptosis in tissue and organ sculpting. (A) Apoptosis is known to play a role in eliminating organs and tissues that are useful only during the embryonic or larval stages of development. For example, the tadpole tail is removed by apoptosis at the time of its metamorphosis into a frog. (B) The coordinated elimination of large populations of cells can provide a means to sculpt tissues without affecting neighboring cells, as shown here for the vertebrate limb.

Apoptosis can eliminate infected or cancerous cells

- In some cases, a cell can pose a threat to the rest of the body if it survives.
- For instance, this may be the case for cells with DNA damage, pre-cancerous cells, and cells infected by viruses.
- If these cells undergo apoptosis, the threat to the rest of the organism (such as cancer or spread of a viral infection) is removed.

Overview of Carcinogenesis



- When a cell’s DNA is damaged, it will typically detect the damage and try to repair it.
- If the damage is beyond repair, the cell will normally send itself into apoptosis, ensuring that it will not pass on its damaged DNA.
- When cells have DNA damage but fail to undergo apoptosis, they may be on the road to cancer.

- Sometimes, pre-cancerous cells that have avoided internal apoptosis cues are detected by immune cells, which try to trigger apoptosis through an external signaling pathway.
- Successful cancer cells, however, manage to duck both internal and external cues that would normally trigger apoptosis.
- This allows them to divide out of control and accumulate mutations (changes in their DNA).

Apoptosis is key to immune function

- Apoptosis also plays an essential role in the development and maintenance of a healthy immune system.
- When B and T cells (immune cells that bind specific molecules) are first produced, they're tested to see if they react against any of the body's own "self" components.
- Cells that do are eliminated right away by apoptosis. If this process fails, self-reactive cells may be released into the body, where they can attack tissues and cause autoimmune conditions.

- Apoptosis also plays an important role in allowing the immune system to turn off its response to a pathogen.
- When a pathogen is detected, the immune cells that recognize the pathogen divide extensively, undergoing a huge increase in numbers with the purpose of destroying the pathogen.
- Once the pathogen is cleared from the body, the large numbers of pathogen-specific immune cells are no longer needed and must be removed by apoptosis to maintain homeostasis (balance) in the immune system.

Summary

- Apoptosis is a form of programmed cell death, or “cellular suicide.” It is different from necrosis, in which cells die due to injury.
- Apoptosis is not the only form of programmed cell death, but it is the form we understand best.
- Apoptosis is an orderly process in which the cell’s contents break down and are packaged into small packets of membrane for “garbage collection” by immune cells.

- It contrasts with necrosis (death by injury), in which the dying cell's contents spill out and cause inflammation.
- Apoptosis removes cells during development. It also eliminates pre-cancerous and virus-infected cells, although "successful" cancer cells manage to escape apoptosis so they can continue dividing.
- Apoptosis maintains the balance of cells in the human body and is particularly important in the immune system.