CELL AGING

- Senescence or ageing is a progressive deterioration of the structural properties and functional efficiencies of cells
- gradual loss of their reparative and restorative powers
- Reproductive phase gradually merges into senescence phase
- Loss in structure and function result from changes due to wear and tear

CHARACTERISTICS OF AGEING(SENILE SYMPTOMS)

- Inefficiency of vital organs
- Fall in metabolic efficiency
- Loss of reparative and restorative regenerating powers
- Low adaptability fitness and survival potential
- High vulnerability to diseases and environmental stresses

Changes associated with ageing

- Morphological changes
- Physiological and anatomical changes
- Cellular changes
- Extracellular changes

Morphological changes

- Observable changes in the form and appearance
- Shrivelled and stooping body
- Sagged and wrinkled skin
- Grey hairs
- Fragile and brittle bones
- Weak and flabby muscles

ANATOMICAL AND PHYSIOLOGICAL CHANGES

- Changes in the structure and functions of internal organs
- Low heart rate cardiac output
- Reduced blood supply to brain and kidneys
- Low cellular uptake of oxygen
- Reduced production of RBC
- Large scale death of brain cells
- Lack of functional coordination between body parts
- Low metabolic rate
- Loss of immune powers
- High vulnerability to diseases

CELLULAR CHANGES

- Abnormal changes taking place within the cells
- Chromatin condensation (heteropycnosis) and nuclear shrinkage (pycnosis)
- Abnormal shortening and thickening of chromosomes leading to death of the cell
- degeneration of cytoplasmic organelles

- degeneration of mitochondria –decrease in energy supply

- degeneration of endoplasmic reticulum- impairs cellular transport and synthetic process

- Chromosomal and gene mutations

- abnormally affect DNA replication and genetic transcription and translation

-irreversible changes in genetic code cell structure cell function

- Decrease in rate of cell division

-shift in balance between the creation of new cells and loss of old ones

-results in loss of weight

- -hayflick limit-Leonard Hayflick
- The fixed number of divisions a cell may undergo is referred to as Hayflick limit

1. a somatic cell can divide only a fixed number of times
2. Immortal cells are cancerous cells in which cell division has gone out of control

- Hayflicks limit appears to be a potential barrier to the immortalisation of cells

- Changes in collagen
- Component of the connective tissue containing fibrils made of monomers
- In young animals collagen is flexible soluble and permeable to molecules
- As the age advances it becomes less flexible and less soluble
- This prevents the free passage of food nitrogenous waste and gases through it
- Results in the decline of metabolic activities of ageing cells and the animal as a whole
- Leads to geriatric symptoms

- Accumulation of ageing substance
- Lipofuscin and keratin accumulated
- These are called age pigments
- Adversely affect the normal cellular functions

- Changes in hormone levels

1. Fall in the blood levels of thyroid, gonadal and adrenal hormones
2. rise in FSH and LH
3. Increase in the sensitivity of some tissues to insulin

THEORIES OF AGING

- Somatic mutation theory
- Gene regulation theory
- Wear and Tear theory
- Error catastrophe theory
- Free radical reaction theory

Somatic mutation theory

- Ageing is due to random mutations
- Mutations result in non production of functional proteins
- Such products accumulate with age and inactivate the cells
- The number of functional cells falls low with aging
- Leads to malfunction of vital organs and ultimate death of the organism

GENE REGULATION THEORY

- Gene clock hypothesis
- Basic cause of aging lies at the level of the gene
- Genes undergo structural changes resulting in the synthesis of wrong or inactive enzymes or proteins
- The degree of expression of genes may change with age causing alterations in the levels of enzymes
- Harmful genes get expressed
- Leads to malfunctioning
- Example-adult progeria andWerner syndrome-premature aging
- Exhibit symptoms of decelerated growth and premature ageing in adolescence
- Werner syndrome- similar to project but its manifestations appear in later years

- Early graying and loss of hairs
- Short stature
- Juvenile cataract
- High incidence of malignancy

ERROR CATASTROPHE THEORY

- Leslie Orget
- Errors in the transcriptional and translational processes of information transfer cost the synthesis of abnormal defective or harmful proteins
- Transcriptional errors result in the production of defective mRNA
- TRANSLATIONAL ERRORS RESULT IN DEFECTIVE PROTEINS
- Results in the alteration of triplet codon and incorporation of amino acids
- Initially errors maybe lo but they accumulate exponentially with the passage of
- This lead to an error catastrophe resulting in the death of the cell

Wear and tear hypothesis

- Cells and tissues are subjected to continuous wear and tear due to constant internal and external stresses
- DNA and protein synthetic apparatus lose the power off repair
- Results in functional deterioration leading to aging

Free radical reaction theory

- Free radical reactions are involved in aging
- Free radicals interact with enzymes and inactivate them
- Countered by antioxidants- Vitamin E

APOPTOSIS

- Programmed cell death
- Supplements cell cycle regulation
- Establishes cellular homeostasis
- Maintain dynamic balance between production and loss of cells
- Initiated by the cell itself in response to extrinsic and intrinsic stimuli
- Often regarded as cell suicide
- Important role in the formation and maintenance of normal tissues during development
- Inhibition can lead to cancer development

Cellular changes during apoptosis

- Condensation and peripheralization of chromatin
- Degradation and fragmentation of chromosomal DNA
- Shrinkage and fragmentation of nucleus
- Loss of cytoplasm and compaction of cell organelles
- Breakdown of mitochondria and degradation of energy system
- Fusion of ER with plasma membrane
- Cell detaches from neighbours and undergoes fragmentation in to numerous apoptotic bodies

REGULATION

- At membrane level
  - Death signal receptotrs
  - Secretion of death ligands
  - Sends apoptotic signals interior
  - Also induce death of neighbouring cells

- At cytoplasmic level
  - Regulatory role of cytoplasmic proteins
  - Inhibitors/activators
  - Promote/inhibit release of cytochrome c from mitochondria
  - Create ionic imbalance apoptosis

- At nuclear level
  - Involves synthesis of tumour suppressor protein p53 through transcription and translation of respective gene
  - P53 can induce apoptosis in response to extensive DNA damage which cell cannot repair
  - 2 main roles
    - Inhibition of cell cycle
    - Induction of apoptosis

APOPTOSIS IN DISEASES AND CANCER

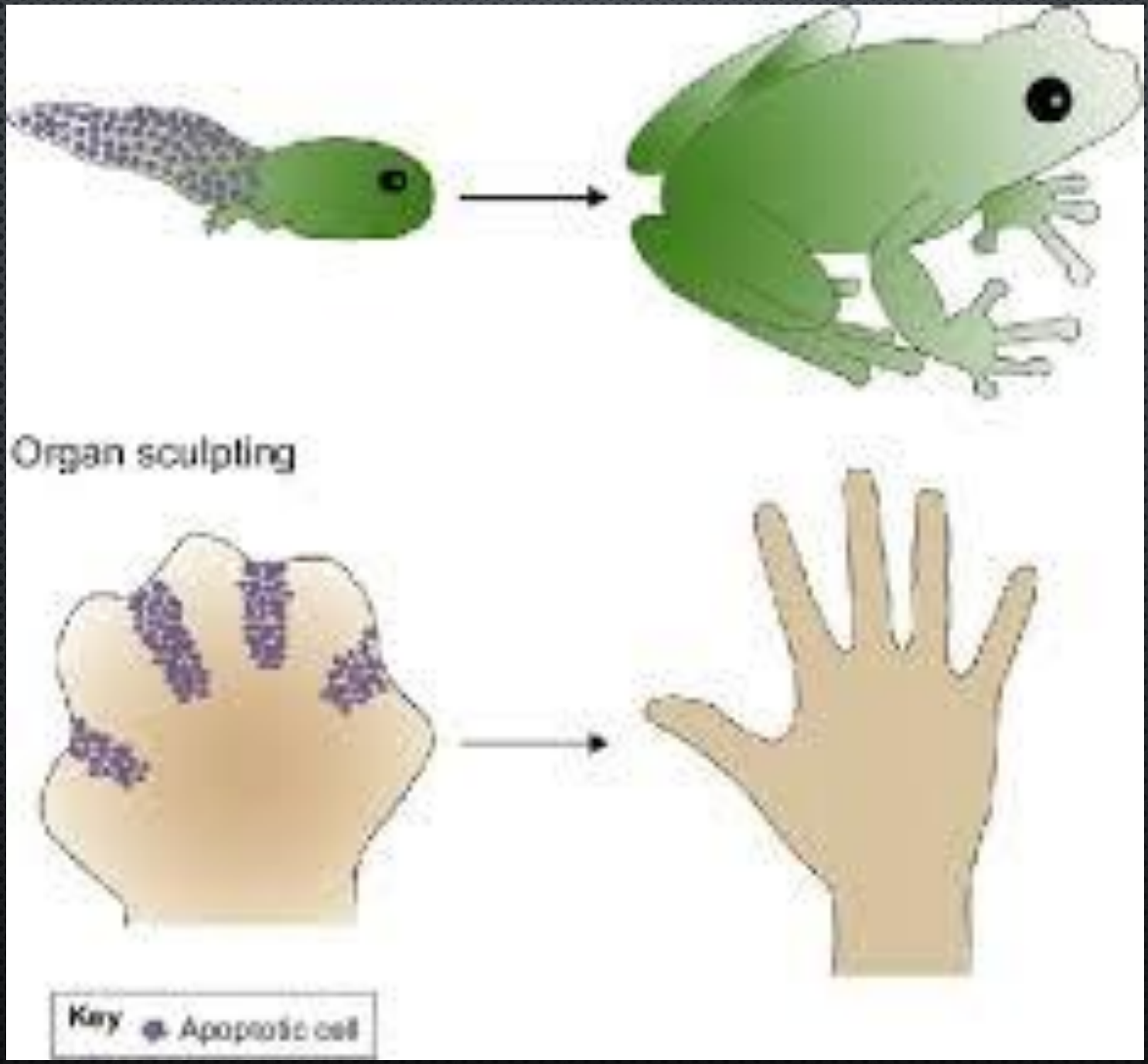
- Defective control of apoptosis-neurodegeneration, immunodeficiency, cell death following heart attack, stroke
- Important role in Cancer

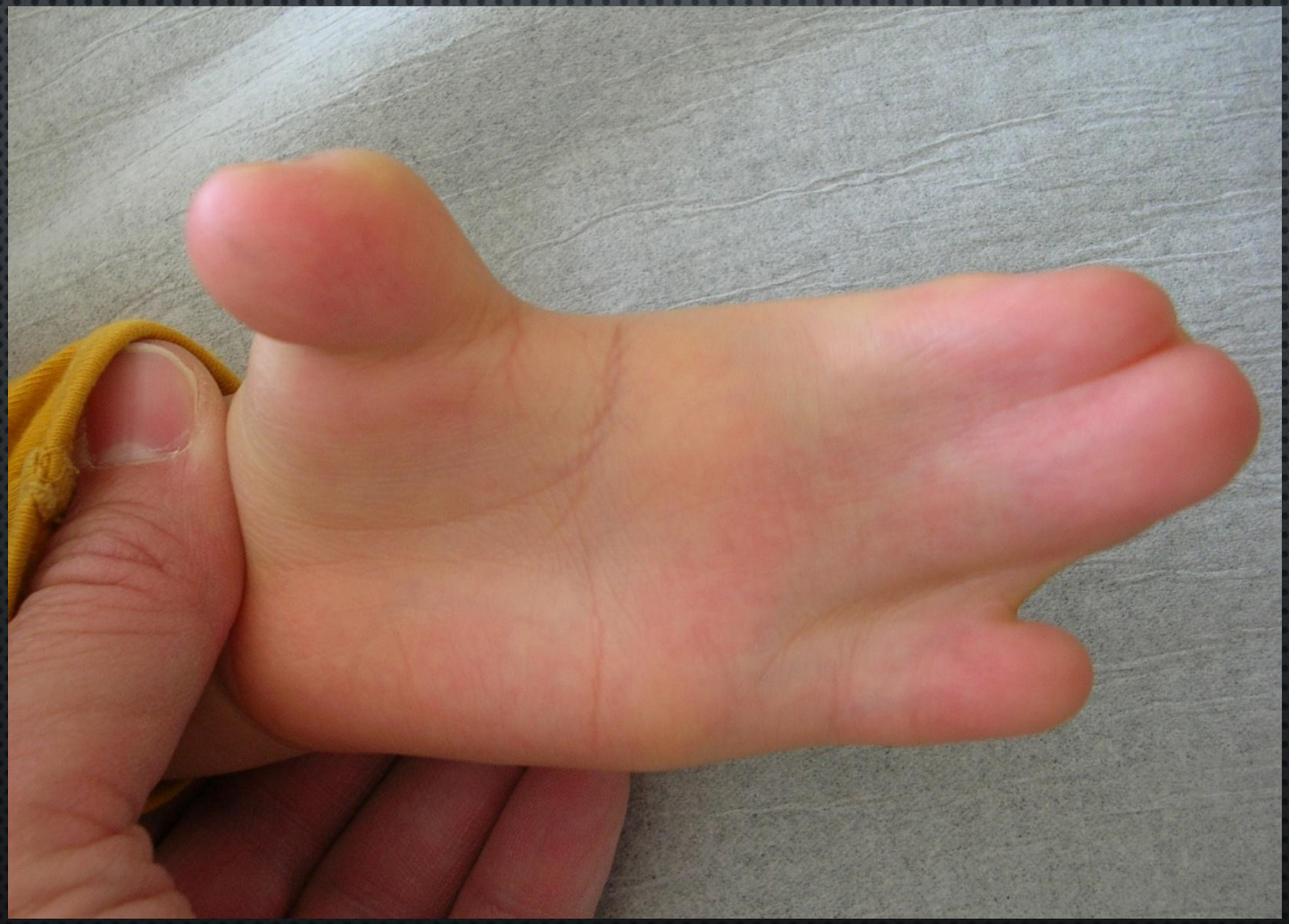
SIGNIFICANCE OF APOPTOSIS

- Important role in the formation maintenance and moulding of normal tissues during development
- Specialised mechanism for the disposal of unwanted cells
- Avoids autoimmunity by eliminating self reactive t cells
- Elimination of virus infected cells
- Defence against infections and harmful chemicals
- Prevents tumour formation
- Balance between cell division and apoptosis- maintaining a constant number of cells in the body

EXAMPLES OF APOPTOSIS

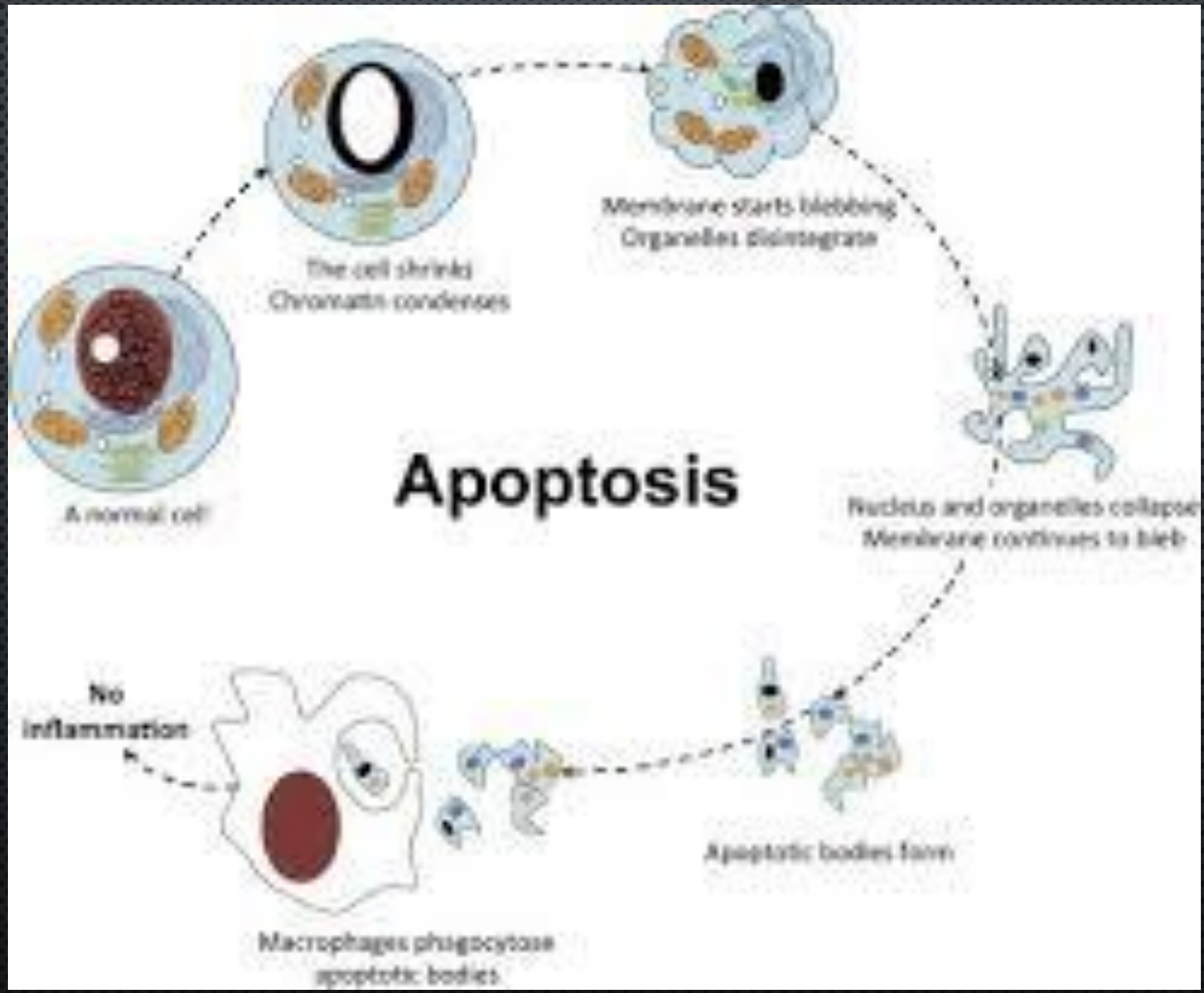
- Formation of gaps between human fingers and toes which would otherwise be webbed
- loss of larval cells during metamorphosis-loss of the tail of amphibian tadpole during metamorphosis
- Destruction of 90% of the t cells in thymus
- Destruction of cells with DNA damage
- Disintegration of the endometrium of primates during menstruation
- Elimination of the surplus cells during the formation of neuronal synapses in the brain


Organ sculpting
Key
Apoptotic cell



Mechanism of apoptosis

- Cells shrink
- Mitochondrial breakdown
- Develop bubble like blebs on their surface
- Chromatin degradation
- Break into small membrane wrapped fragments
- Phospholipid ,phosphatidylserine gets exposed on the surface
- Gets bound by receptors on phagocytic cells like macrophages
- Phagocytic cells secrete cytokines that inhibit inflammation


Apoptosis
A normal cell
The cell shrinks
Chromatin condenses
Membrane starts blebbing
Organelles disintegrate
Nucleus and organelles collapse
Membrane continues to bleb
Apoptotic bodies form
No inflammation
Macrophages phagocytose apoptotic bodies