Pathophysiology

Cell injury & Tissue response

Terms and Definitions:

- **Physiology :** the function or mechanics of the body (The study of how living organisms function, including such processes as nutrition, movement, and reproduction).
- **Pathology:** the study of the diseases especially the structural and functional changes produced by them.
- **Pathophysiology :** the physiology of abnormal states , *specifically***:** the functional changes that accompany a particular syndrome or disease.
- **Pathogenesis :** the origin and development of disease (the mechanism whereby something causes a Disease).

Etiology: cause of a disease.

- **Pathogen**: agents of disease (ex. Bacteria , virus)
- **Multifactorial:** many factors) ex. Hypertension: multifactorial " family Hx , Genetic , Eating stess

- **Iatrogenic:** caused by treatment (disease caused by human intervention) (adverse reaction to medication)

- **Idiopathic**: no known cause.

- **Symptoms:** feelings (describes by the patient) (functional manifestations or evidences of a disease process). Described by the patient) the patient's history)

- **Signs:** objective findings as perceived by an examiner or physician (seen and measured by the doctor). Health provider's findings---(the physical examination)

- **Occurrence** of disease defined by 2 factors:

Incidence= new cases per unit of time.

Prevalence= new & old cases within a specific population per unit of time.

- **Congenital diseases** = diseases occurring at birth (related to genes and inheritance)0
- **Biopsy** = excision of small amounts of living tissue (for further evaluation and investigation.)
- **Autopsy** = examination after death.
- **Predisposing factors** = tendencies that promote development of disease, can include age, gender inherited factors, diet.
- **Exacerbating :** irritating / increasing symptoms (making worse).
- **Prevention** = vaccines, dietary of lifestyle changes, removal of harmful materials or stopping harmful activities like smoking.

Disease Terminology

- **Pathogenesis** = How disease begins and progresses.
- **Onset, can be:**
- Acute-sudden and obvious.
- Insidious–gradual, vague and very mild symptoms.
- **Acute disease** = short term illness, develops quickly (asthma, burn, heart attach….etc).
- **Chronic disease** = disease develops gradually and long terms causing more damage (Diabetes, hypertension, also asthma…. Etc.).
- Subclinical = pathologic changes occur, but no symptoms for a long time (diabetes, thyroid dysfunction, rheumatoid arthritis…etc).
- Latent stage = no clinical signs (*incubation period* of disease/ no symptoms) (HIV, CMV…etc)
- Prodromal period = early in disease, only general non-specific symptoms (flu, psychological disorders.. Etc).

- **Remission**: symptom free period (cancer, hepatits).
- **-Asymptomatic**: no noticeable symptoms (cancer, hepatitis, HIV, DM).
- -**Diagnosis**: identifying label for a disease.
- **-Prognosis**: Outcome (guessing).
- **-Morbidity**: disease rate / within a population.
- **-Mortality**: death rate / within a population.
- -**Infectious** : are caused by pathogenic microorganisms.
- -**Communicable**: are transmitted by agents, fomites , vector or carrier.

Cell injury

Introduction

- **Homeostasis:** cells maintain normal structure and function in response to physiological demands.
- **Cellular adaptation :**
- As cells encounter stresses they undergo functional or structural adaptations to maintain viability / homeostasis.
- Respond to some stimuli by increasing or decreasing specific organelle content.
- ~~**Adaptive processes**~~ **: atrophy , hypertrophy , hyperplasia , metaplasia .**
- **Cell injury :** is a sequence of events that occur if the **limits of adaptive capability are exceeded or no adaptive response is possible.**

Overview of cellular changes

Changes in Size of individual cell

- Atrophy = decrease in cell size.
- Hypertrophy = increase in cell size.

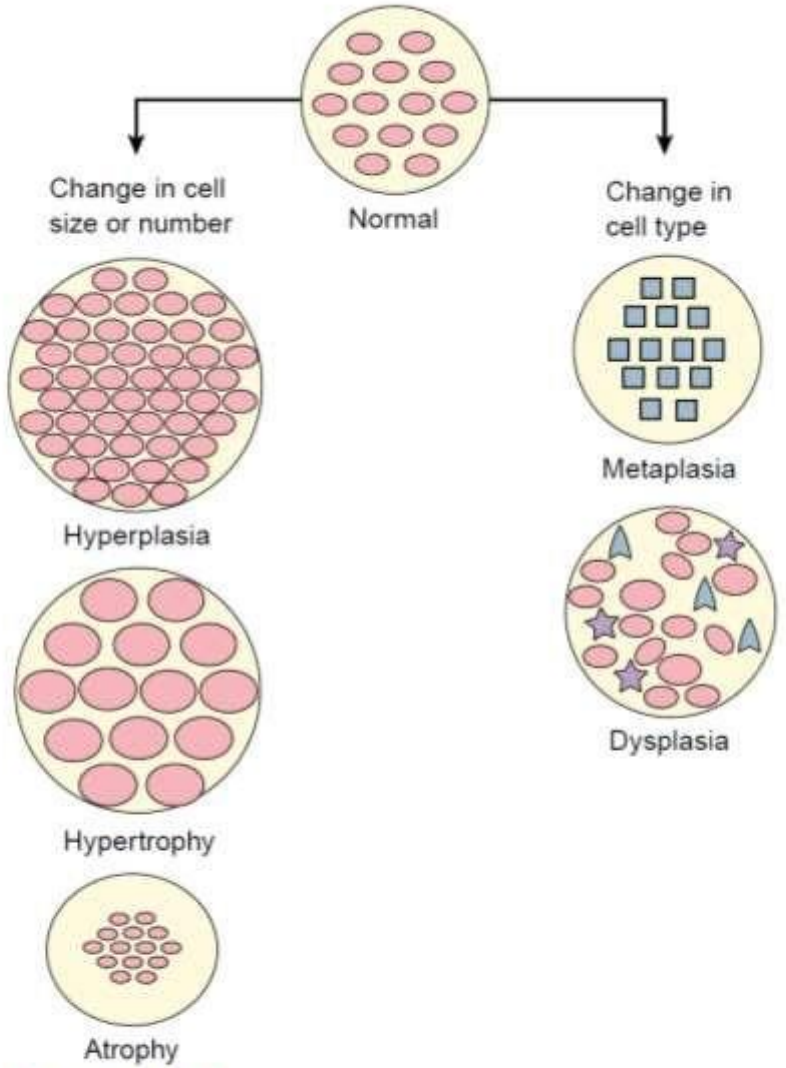
Changes in actual Number of cells

- Hyperplasia = increase in number of normal cells
- Dysplasia = increase in number of atypical cells
- Anaplasia = increase in rate of reproduction or increase number of frankly abnormal cells (cancer)

Change in Type of Cell

Change of one type into another type

Metaplasia =change one type of mature cell type to different mature cell type.



■ FIGURE 2-1 ■ Adaptive tissue cell responses (large circles) involving a change in number (hyperplasia), cell size (hypertrophy and atrophy), cell type (metaplasia), or size, shape, and organization (dysplasia).

Atrophy

- Defined as decrease in cell size. If enough cells in an organ undergo atrophy the entire organ will decrease in size. Atrophy could be due to:

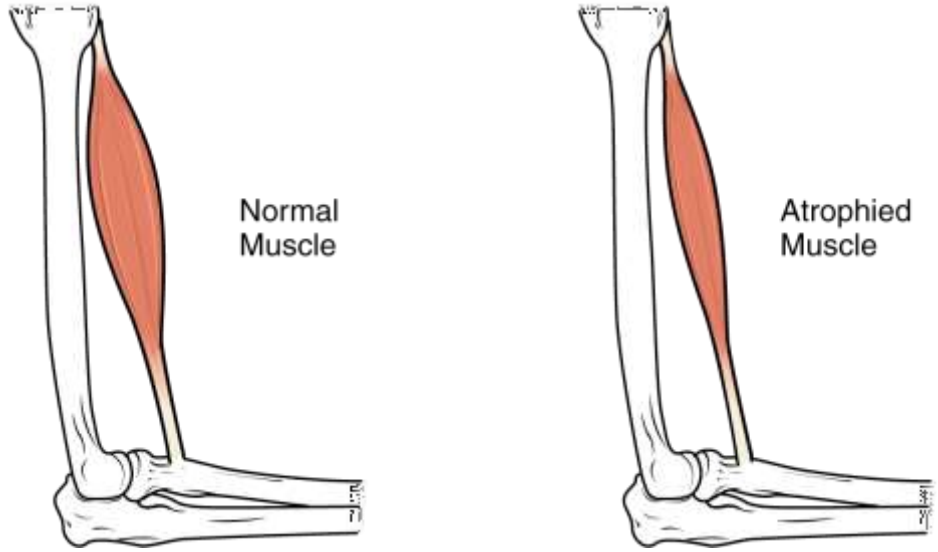
✓ **decreased use.**

✓ **decreased blood supply.**

✓ **decreased nutrition**.
ex.Thymus atrophy during early childhood is example of Physiological atrophy

- Skeletal muscle atrophy is a common **pathologic adaptation** to skeletal muscle disuse (commonly called "disuse atrophy"), it is called **pathological atrophy.**

- Tissue and organs especially susceptible to atrophy include **skeletal muscle, cardiac muscle and the brain.**

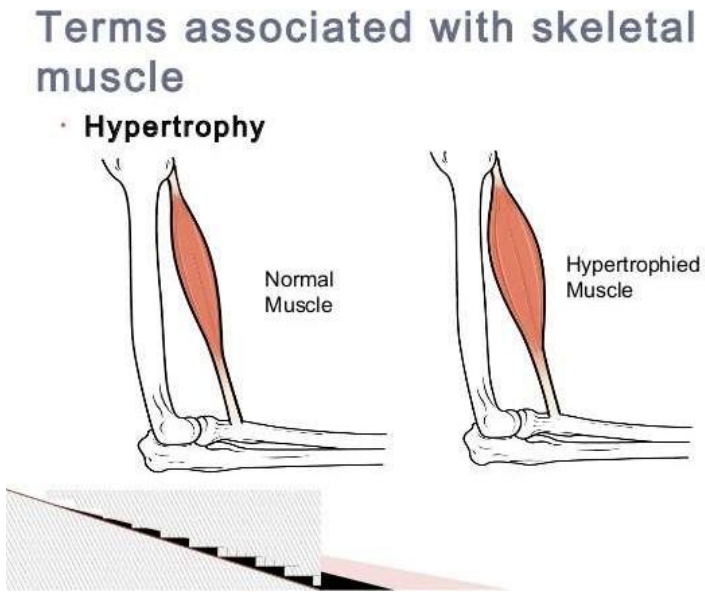


Hypertrophy

- is an **increase** in cell size and volume. If enough cells of an organ hypertrophy the whole organ will increase in size.
- For example, adipocytes (fat cells) may expand in size by depositing more lipid within cytoplasmic vesicles. Thus in human adults, increases in body fat tissue occurs mostly by increases in the size of adipocytes, not by increases in the number of adipocytes.

✓ An example of **physiologic hypertrophy** is in skeletal muscle with sustained weight bearing exercise.

✓ An example of **pathologic hypertrophy** is in cardiac muscle as a result of hypertension.

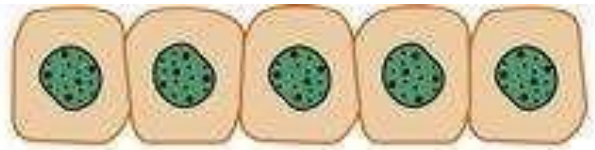


Hyperplasia

- is an increase in **the number** of cells. It is the result of increased cell mitosis or division (also referred to as cell proliferation).
- The two types of **physiologic hyperplasia**:

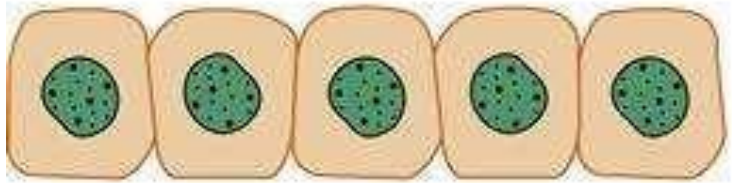
Compensatory and H**ormonal**.

- **Compensatory hyperplasia** permits tissue and organ regeneration. It is common in **epithelial** cells of the epidermis and intestine**, liver hepatocytes**, **bone marrow** cells, and **fibroblasts.**
- **Hormonal hyperplasia** occurs mainly in organs that depend on estrogen. For example, the estrogen-dependent uterine cells undergo hyperplasia and hypertrophy following pregnancy.
- **Pathologic hyperplasia** is an abnormal increase in cell division. A common pathologic hyperplasia in women occurs in the endometrium and is called endometriosis.

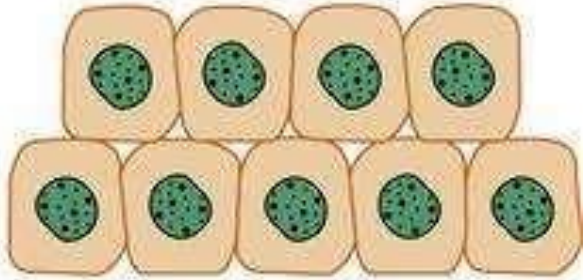


Normal

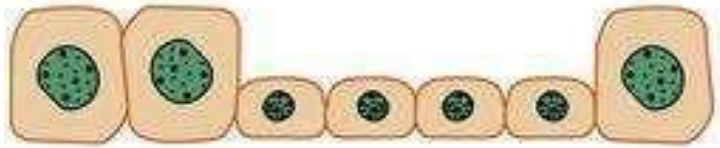
Atrophy
(decreased cell size)



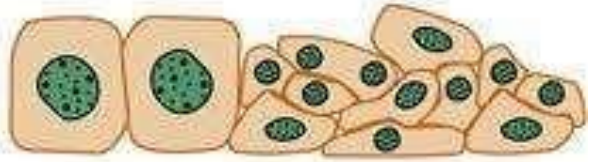
Hypertrophy
(increased cell size)



Hyperplasia
(increased cell number)



Metaplasia
(conversion of one cell
type to another)



Dysplasia
(disorderly growth)

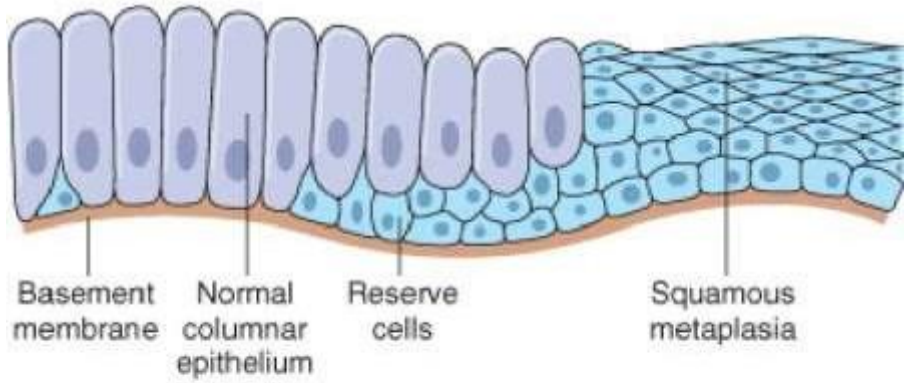
Metaplasia

- Metaplasia occurs when a cell of a certain type is replaced by another cell type, which may be less differentiated.
- It is a **reversible** process thought to be caused by **stem cell reprogramming**.
- A prominent example of metaplasia involves the changes associated with the *respiratory tract* in response to inhalation of irritants, such as smoke:

✓ The bronchial cells convert from mucus-secreting, ciliated, columnar epithelium to non-ciliated, squamous epithelium incapable of secreting mucus.

✓ These transformed cells may become **dysplastic or cancerous** if the stimulus (e.g., cigarette smoking) is not removed.

- The most common example of metaplasia is Barrett's esophagus, when the non-keratinizing squamous epithelium of the esophagus undergoes metaplasia to become mucinous columnar cells, ultimately protecting the esophagus from acid reflux originating in the stomach.
- **If stress persists, metaplasia can progress to dysplasia and eventually carcinoma; Barrett's esophagus, for example, can eventually progress to adenocarcinoma.**



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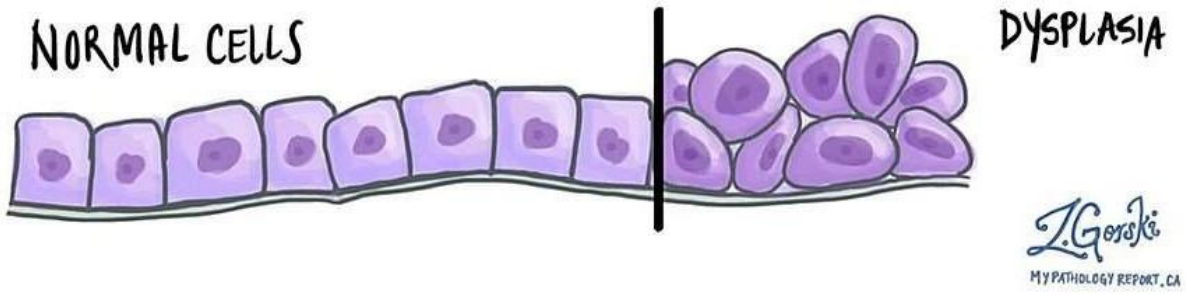
A, Schematic diagram of columnar to squamous metaplasia. *B*,

Dysplasia

- Dysplasia refers to abnormal changes in cellular shape, size, and/or organization. Dysplasia is not considered a true adaptation; rather, it is thought to be related to hyperplasia and is sometimes called "**atypical hyperplasia".**
- Tissues prone to dysplasia include **cervical** and **respiratory** epithelium, where it is strongly associated with the development of cancer. Although dysplasia is reversible, if stress persists, then dysplasia progresses to **anaplasia** and **irreversible carcinoma.**



Causes of cell injury

1. Hypoxia: (Oxygen deficiency) Mainly due to:
   - ischemia (impaired blood supply) most common
   - inadequate oxygenation of blood (cardio-respiratory failure)
   - loss of oxygen carrying capacity (anaemia)
   - Carbon monoxide poisoning
2. Physical Agents
   - Trauma, radiation, extremes of temperatures, electric shock
3. Chemicals and Drugs
   - Wide variety
4. Microbiologic Agents
   - Viruses, worms, bacteria .....
5. Immunologic Reactions
   - Allergic reactions, autoimmune diseases
6. Genetic Defects
   - Obvious congenital malformations (Down syndrome)
   - Subtle single amino acid substitution (hemoglobin S of sickle cell anemia)
7. Nutritional Imbalances
   - Deficiency of nutrients/ or excess
8. Aging

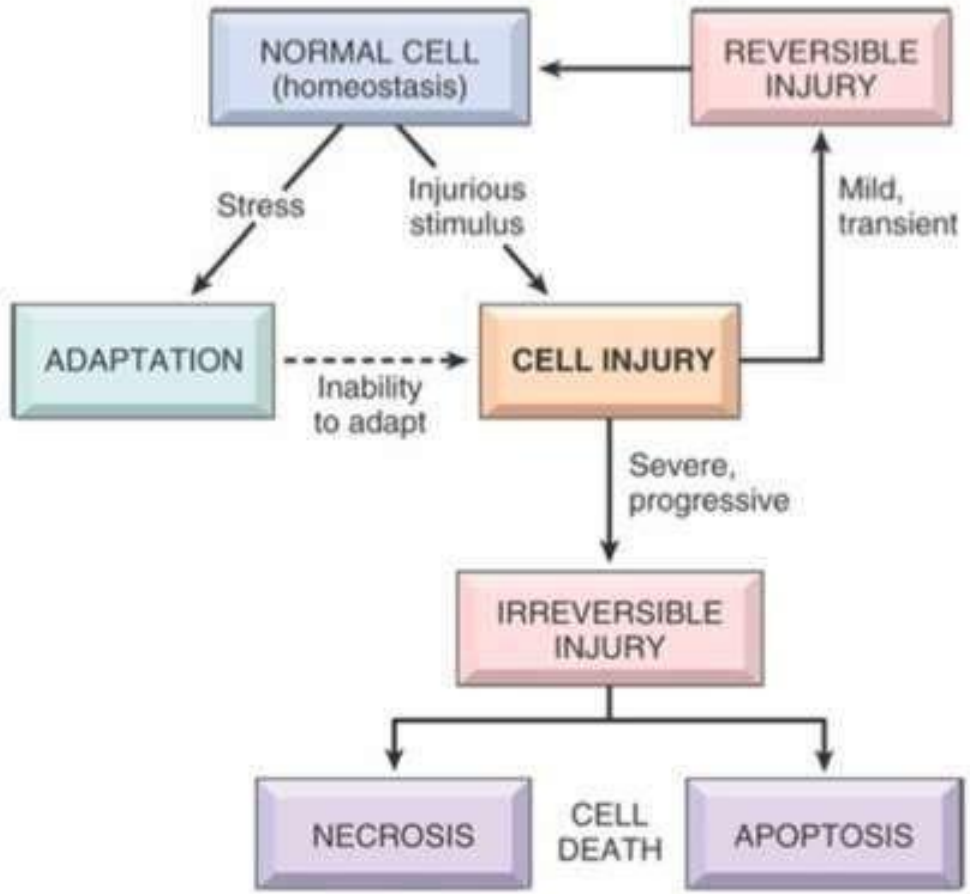
Cell injury and death

- When the cell is exposed to an injurious agent or stress, a sequence of events follows that is loosely termed cell injury.
- Cell injury is **reversible up to a certain point**.
- If the stimulus persists or is severe enough from the beginning, the cell reaches a point of no return and suffers **irreversible cell injury and ultimately cell death**.
- Cell death, is the ultimate result of cell injury .
- **Patterns Of Cell Death**
- There are two principal patterns of cell death:

1 **Apoptosis**

2 **Necrosis**

Cell Injury



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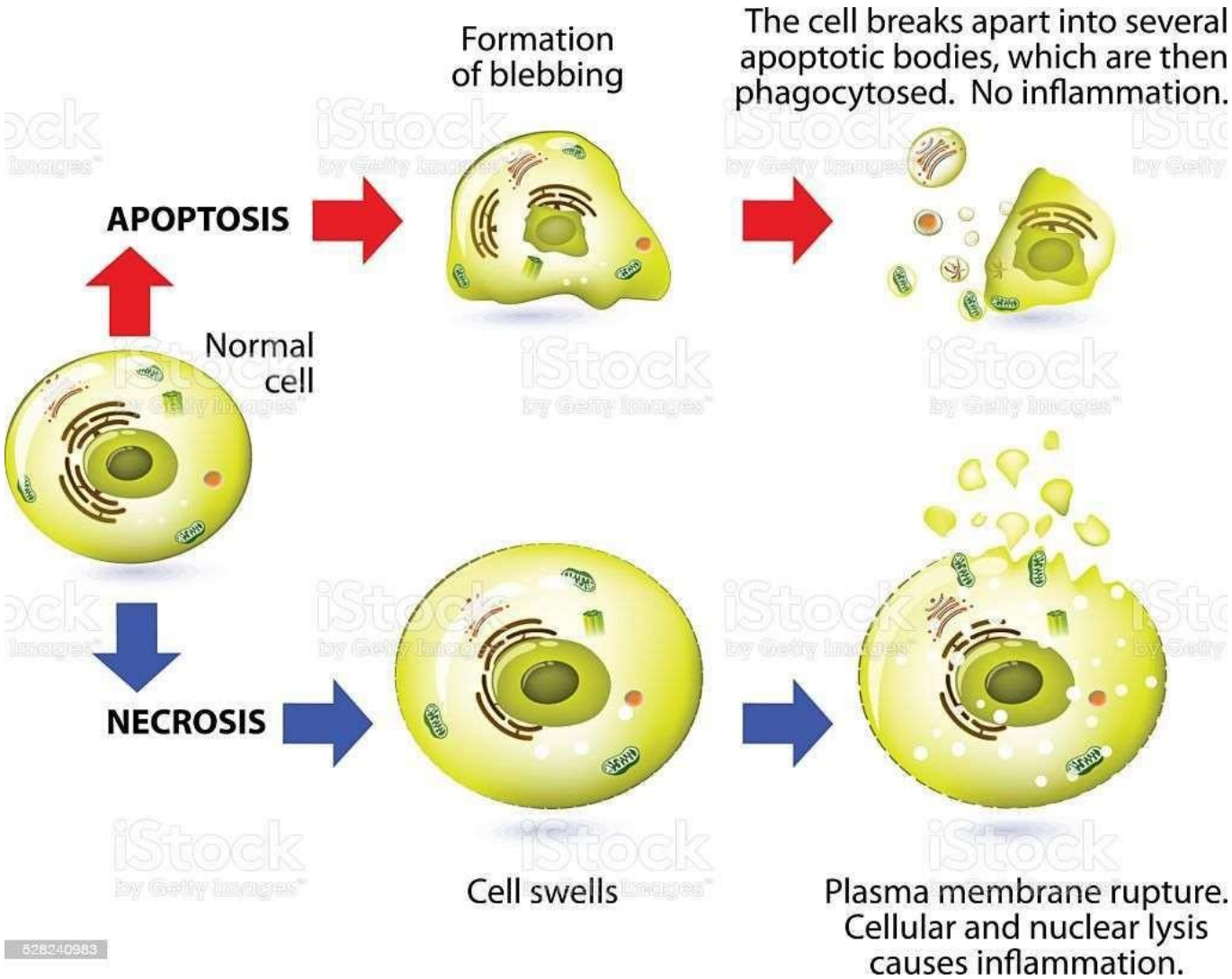
Apoptosis

- Apoptosis occurs when a cell dies through activation of an internally controlled suicide program. **(programmed cell death)**
- Apoptosis is designed to eliminate unwanted cells when cell development is abnormal, cell numbers are excessive, or cells are injured or aged.

Necrosis

- Necrosis is the type of cell death that occurs after ischemia and chemical injury.
- Necrosis is **always pathologic.**


Formation
of blebbing
The cell breaks apart into several
apoptotic bodies, which are then
phagocytosed. No inflammation.
APOPTOSIS
Normal
cell
NECROSIS
Cell swells
Plasma membrane rupture.
Cellular and nuclear lysis
causes inflammation.

NECROSIS	APOPTOSIS
Always pathological	May be **physiological** or **pathological**
Affects adjacent group of cells	Affect single cells
Cell size is increased	Cell size is **shrunken**
Passive	**Active**
Causes inflammatory reaction	**No inflammatory** reaction
Plasma membrane is disrupted	Plasma membrane is **intact**

THANK YOU