a. Serous inflammation

1. EXUDATIVE INFLAMMATION

- Accumulation of fluid relatively rich in protein on body surfaces, especially serous surface, represents serous inflammation.
- Etiological factors:

- Hypersensitivity reactions
- Bacterial and viral tissue injury
- Physical and chemical tissue injury

- Pus in the exudate → seropurulent inflammation

  Mucus in the exudate → seromucous inflammation

  Fibrin in the exudate → serofibrinous inflammation

b. Catarrhal inflammation

- Exudative inflammation occurring on the mucous membranes of the respiratory and gastrointestinal tracts and producing a watery exudate of serum and **mucus.**

- Etiological factors:

- Bacteria and viruses
- Chemical substances like phenol and cresol

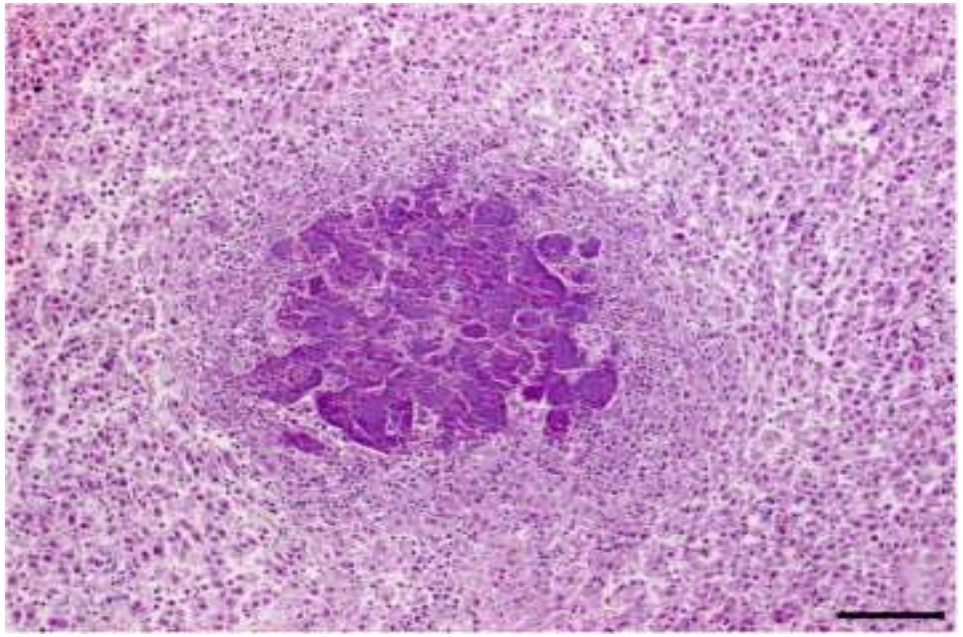
- *Grossly* the surface appears reddened and swollen and may be covered with or contain, a clear to slightly opaque, thick fluid.
- *Microscopically,* the vessels of the Lamina propria and the submucosa are hyperemic and desquamated epithelial cells and neutrophils can be seen.

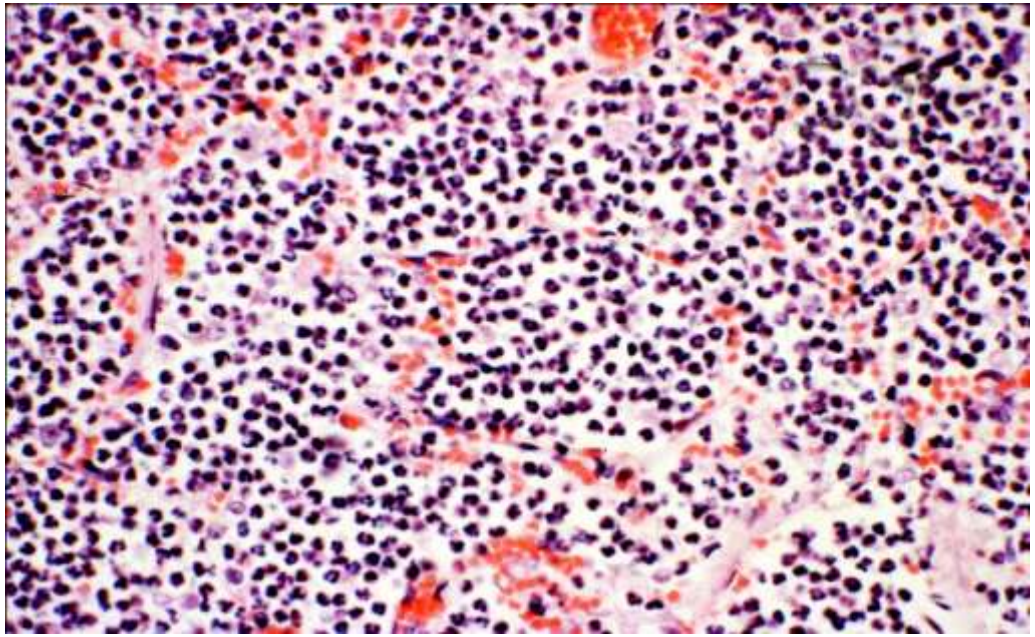
c. Purulent inflammation

- Purulent inflammation is characterized by the production of pus.
- Pus is an exudate consisting of neutrophils, the liquefied debris of necrotic cells, and edema fluid.
- The predominant feature of the exudate is the formation of pus, a creamy liquid.

- Etiological factors:

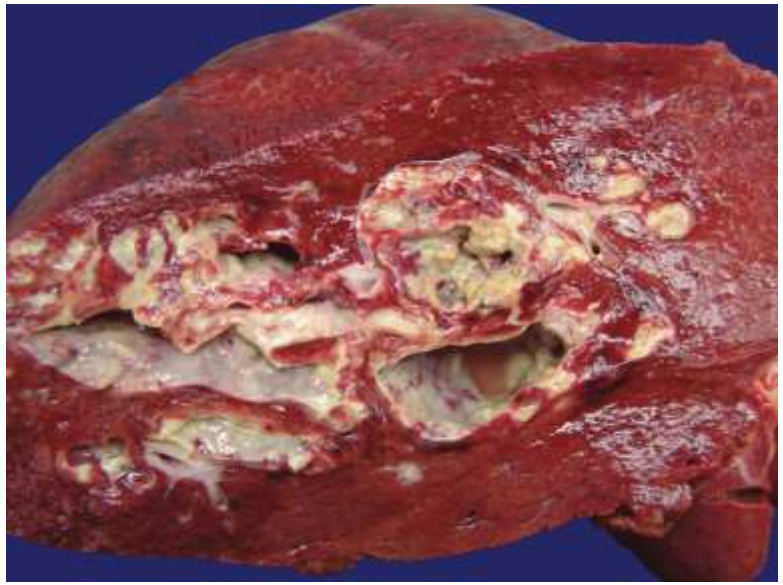
- Pyogenic bacteria: *Staphylococcus spp., Streptococcus spp., Escherichia coli, Listeria monocytogenes, ….*

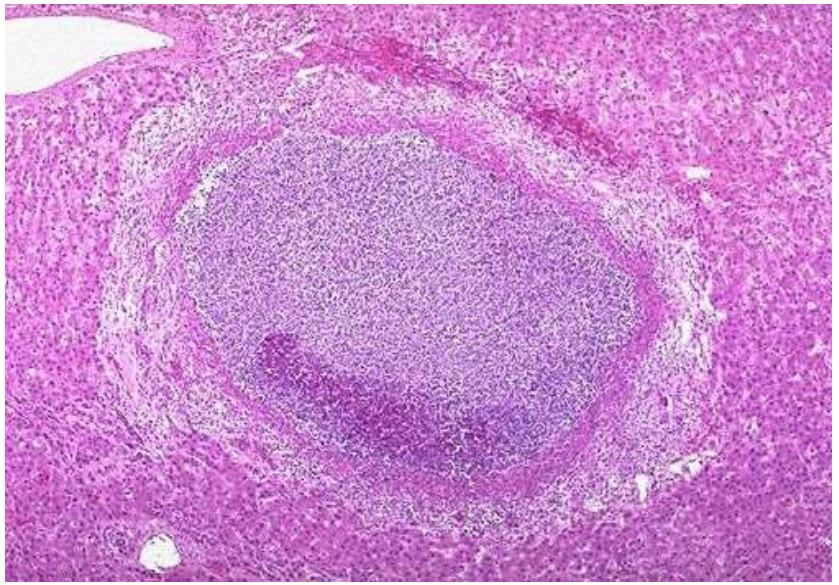




- **Pustule :** A small inflamed elevation of the skin that is filled with pus. Pustules are organized accumulations of neutrophils with or without serum within the stratum corneum.
- **Fistula:** opening through the skin

- **Abscess:** a circumscribed collection of pus.
- **Pyogenic membrane:** the inner lining of an organising abscess, (in contact with the offending agent) **"produces pus"**.
- **Pyemia:** Septicemia caused by pyogenic microorganisms in the blood, often resulting in the formation of multiple abscesses.
- **Metastatic abscess:** a secondary abscess formed, at a distance from the primary focus, as a result of the transportation of pyogenic bacteria by the lymph or bloodstream.





- **Folliculitis:** The purulent inflammation of the hair follicles of the skin.
- **Furuncle:** The purulent inflammation of the hair follicles and the sebaceous glands of the skin.
- **Acne:** Inflammation of the hair follicles and accompanying sebaceous glands of the skin and subcutaneous connective tissue.
- **Carbuncle:** Carbuncles are clusters of furuncles connected subcutaneously.

- **Phlegmon:** Diffuse suppurative inflammation that spreads primarily in loose fibrous connective tissue without sharp demarcation.
- **Cellulitis:** Bacterial infection involving the inner layers of the skin. It specifically affects the dermis and subcutaneous fat.

Pyorrhea: (periodontitis) The purulent inflammation of the tissues surrounding the teeth.

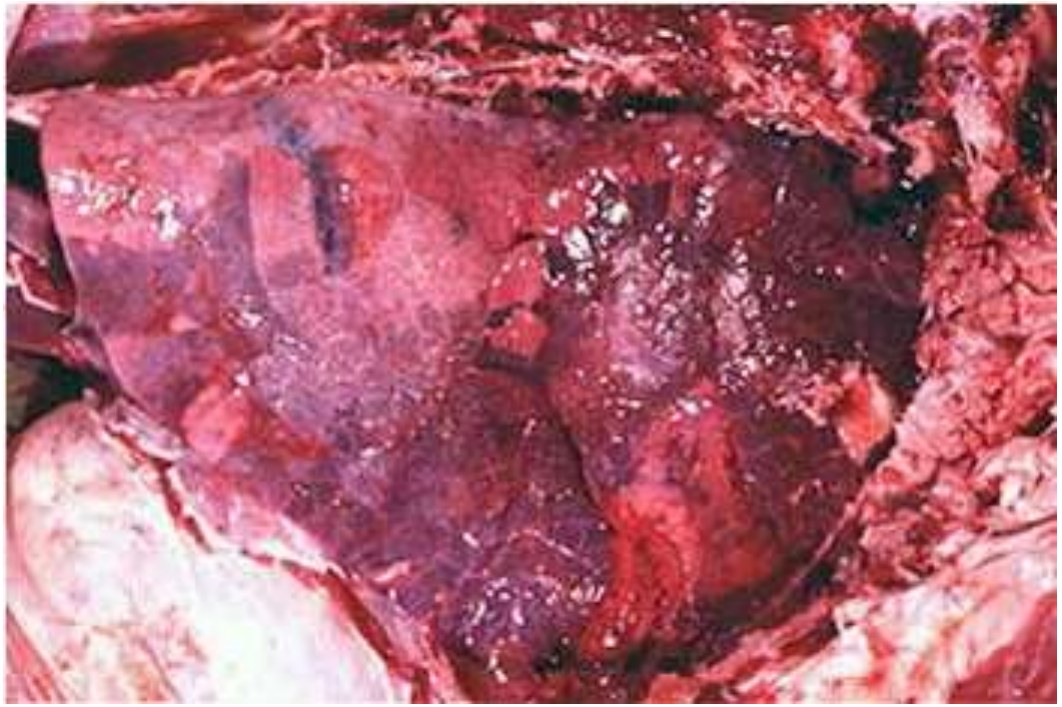
Empyema: Empyema is a condition in which pus from infected tissue collects in a body cavity. Empyema is most often used to refer to collections of pus in the space around the lungs (pleural cavity), but sometimes refers to similar collections in the gall bladder or the pelvic cavity.

D. HAEMORRHAGİC İNFLAMMATİON

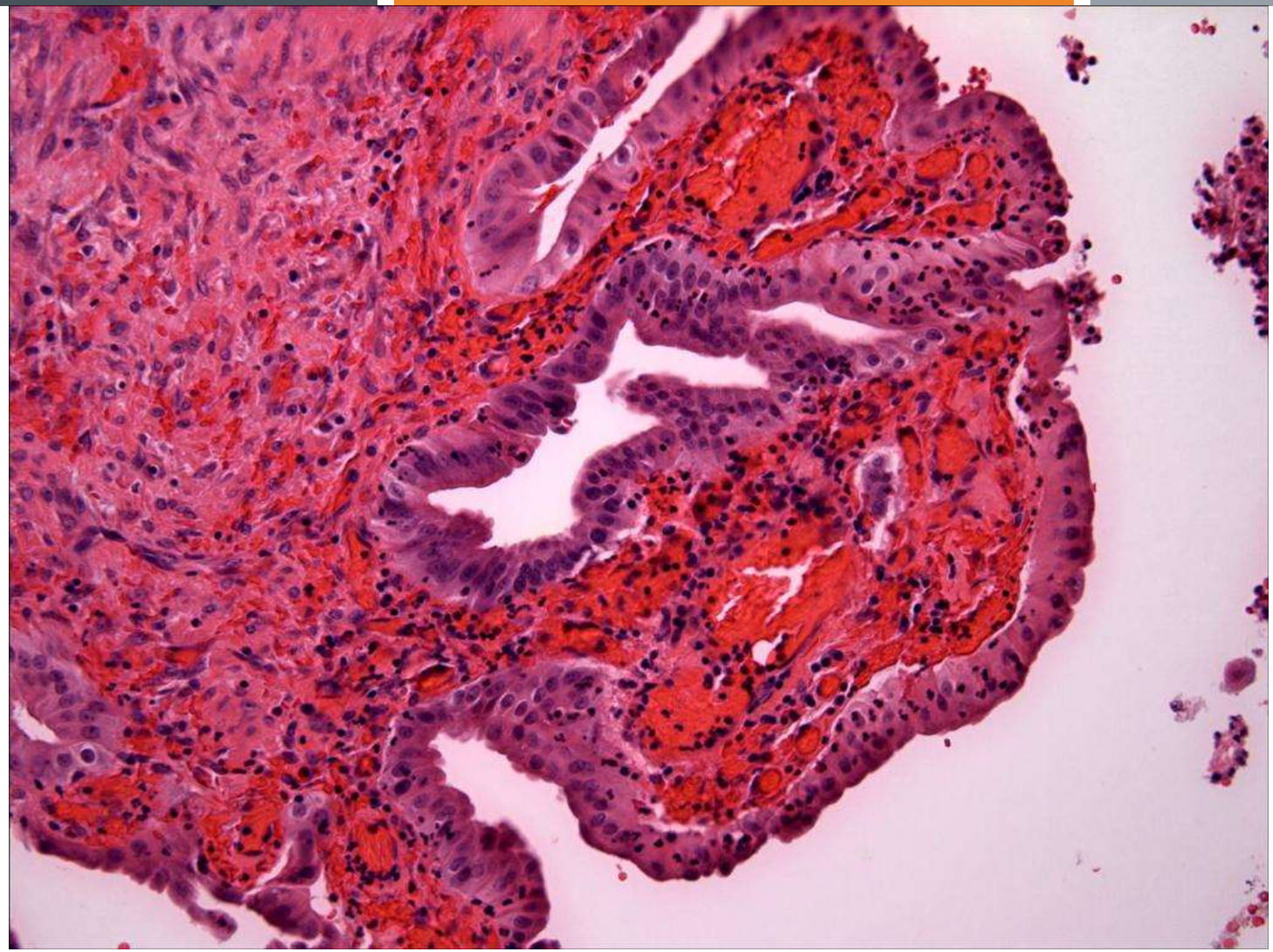
- Hemorrhagic inflammation is characterized by large numbers of erythrocytes in the exudate.

- Etiologic factors:
  - Microorganisms like *Bacillus anthracis*, hemolytic streptococci, clostridium species etc.
  - Viruses like **Infectious canine hepatitis** and **Infectious laryngotracheitis (ILT)**
  - Pathogenic *Leptospira interrogans* serovars
  - Some chemical substances that cause acute poisoning like phenol, arsenic and phosphorus, etc.
  - Some protozoa

- This type of inflammation arises quickly and is often fatal. There is massive damage to endothelium.
- The inflamed area is usually necrotic and filled with blood.

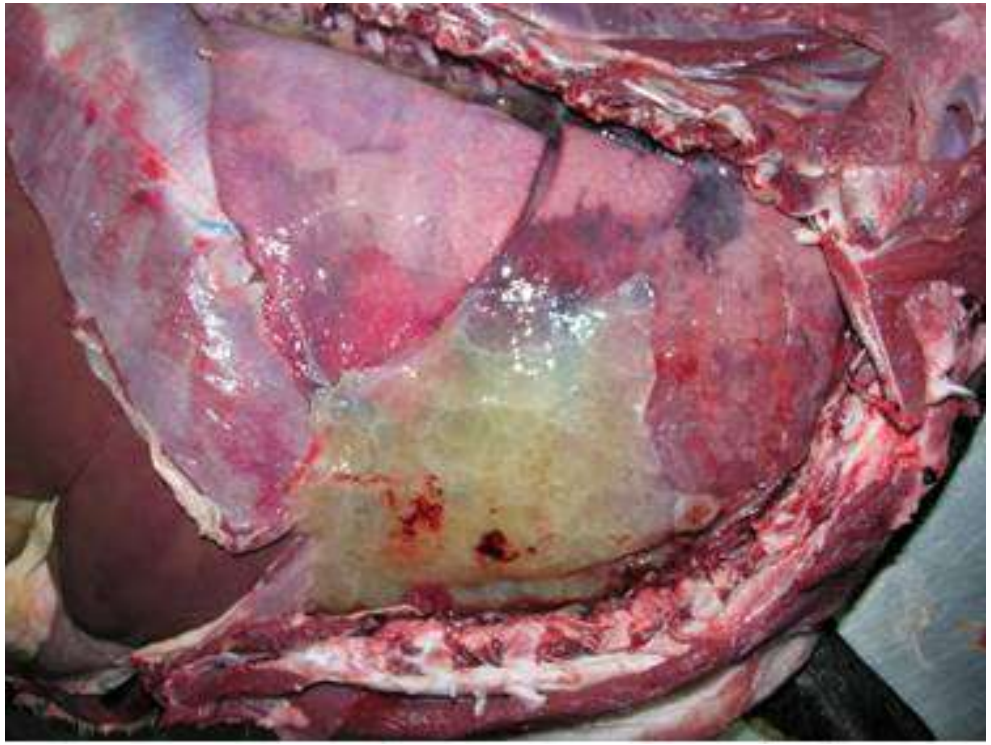


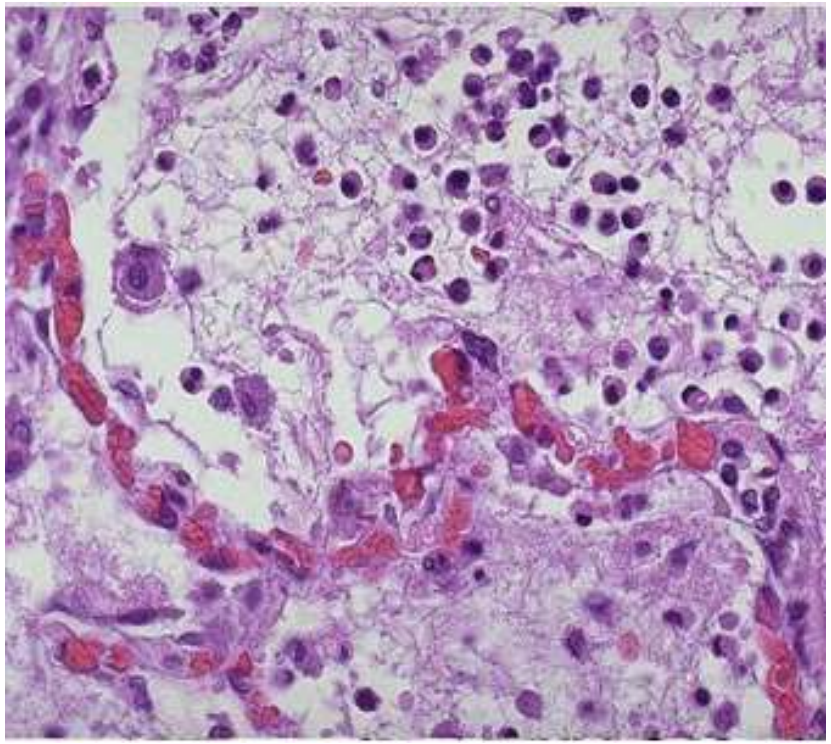
Hemorrhagic pneumonia



E. FİBRİNOUS İNFLAMMATİON

- Exudative inflammation with exudation of fibrinogen containing serum that **polymerizes to fibrin** outside the blood vessels.
- Fibrinous inflammation **occurs in more severe conditions.**
- A fibrinous exudate is characteristic of inflammation in the lining of body cavities, such as the meninges, pericardium, and pleura.





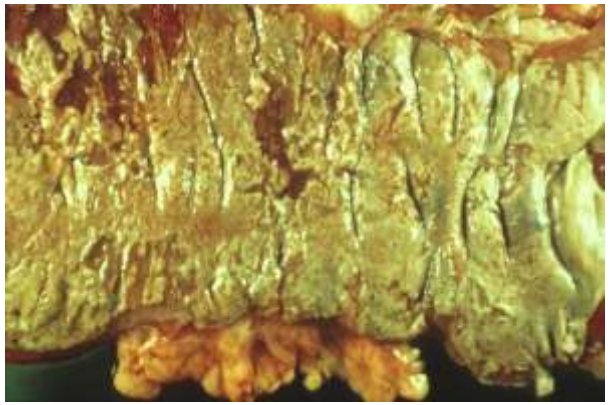
Fibrinous pleuropneumonia

Pseudomembranous inflammation

- In this type of inflammation, a membrane consisting of fibrin, neutrophil leucocytes and dead material forms especially in the oral mucosa, larynx, trachea and intestines.
- This membrane is called **pseudomembrane** and inflammation is called **pseudomembranous inflammation.**

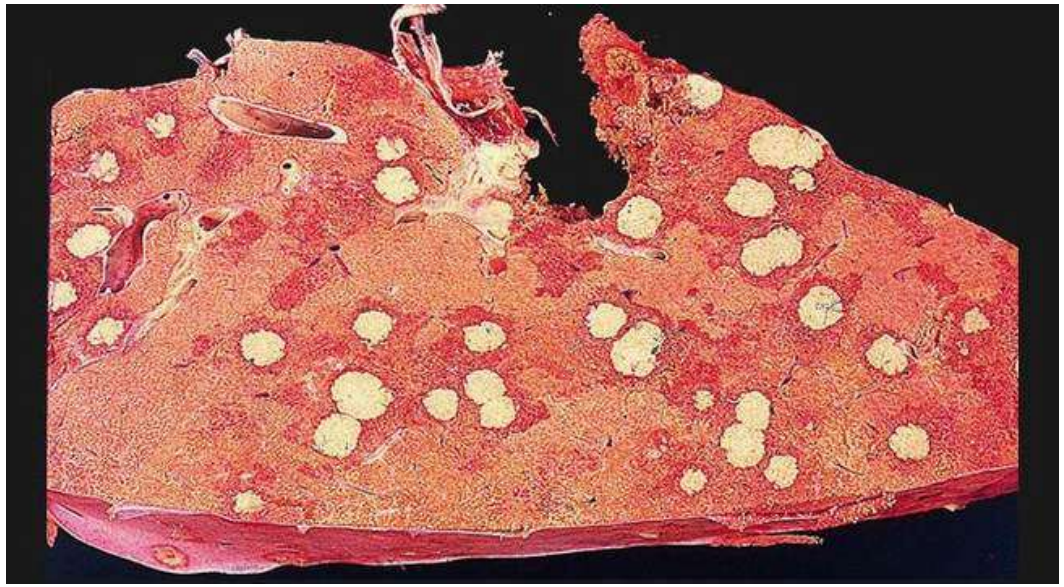
Diphtheroid inflammation

- If there is extensive necrosis of underlying areas so that the fibrin is tightly adhered to the tissue and ***is harder to peel away***, it is called a ***diphtheritic membrane***.
- This term diphtheritic membrane came from human diphtheria, caused by *Corynebacterium diphtheria*.



2. ALTERATİVE İNFLAMMATİON

- Characterized largely by necrosis and degeneration.
- Inflammations characterized by tissue loss (alteration= tissue loss) are examined into two groups:
  - **Necrotic inflammation of epithelial surfaces:** (such as the trachea, intestine, nasal passages). Examples: necrobacillosis in cattle, Rinderpest, ecthyma disease
  - **Necrotic inflammation of organs:** characterized by the formation of necrosis in organs and, in some cases, the formation of caverns resulting of necrosis melting. Examples: necrobacillosis, pulmonary tuberculosis, Campylobacteriosis in sheep, etc.



3. PROLİFERATİVE İNFLAMMATİON

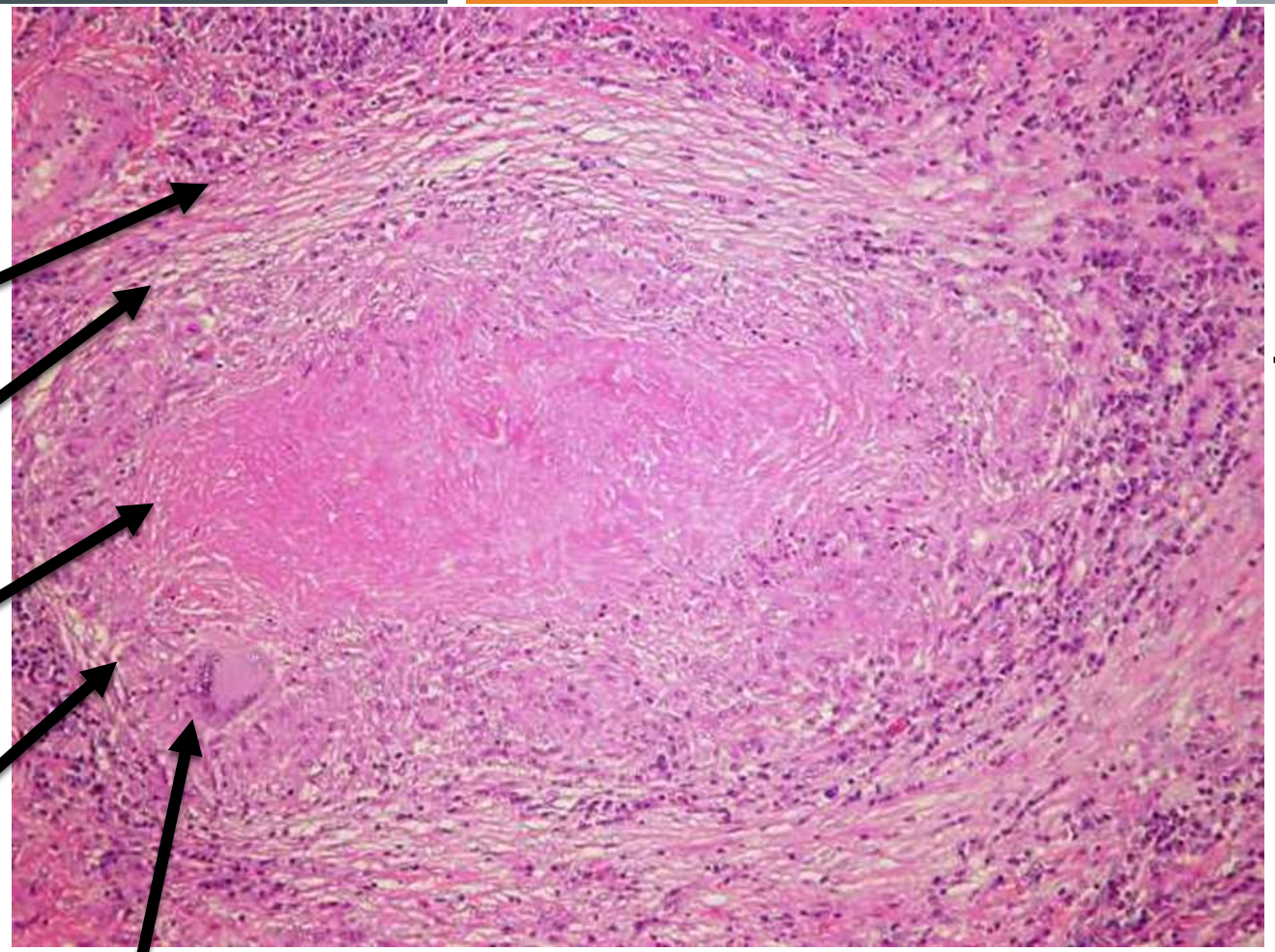
- An inflammatory reaction in which the distinguishing feature is an actual increase in the number of cells.
- This is characterized by the formation of granulation tissue. In the inflammation area; capillaries, connective tissue cells, leukocytes, lymphocytes, plasma cells, histiocytes and giant cells are seen.
- It occurs in the last period of acute inflammation or it occurs when the pathogenicity of the disease agent is low. For example; liver cirrhosis etc.

GRANULOMATOUS (PRODUCTIVE) INFLAMMATION

- Granulomatous inflammation is a distinct type of proliferative inflammation.
- It is marked by the formation of granulomas, which are small collections of modified macrophages called epithelioid cells and are usually surrounded by lymphocytes. Granulomas often contain giant, or Langhans, cells that form from the coalescence of epithelioid cells.

- Granulomas are seen in a wide variety of diseases, both infectious and non-infectious.
- Examples of infections characterized by granulomas include tuberculosis, paratuberculosis, glanders, brucellosis,...
- Examples of non-infectious agents causing granulomas formation are cholesterine crystals, uric acid crystals, splinters of wood or iron, operation residues.

Tubercle


Connective tissue
Collar of lymphocytes
Central caseous necrosis
Epithelioid cells
Langhans type giant cell

The nomenclature of inflammatory reactions

- Inflammation is expressed by using a prefix that refers to the organ and the **'-itis'** suffix.

For example; if the kidney is inflamed, the prefix "nephro-"is combined with the suffix "itis" to form the word "**nephritis**".

"nephro-" // "itis" ---------"**nephritis**

Exceptions : typhlitis, proctitis, etc…

Table 3-6 The Nomenclature of a Morphologic Diagnosis

Degree	Duration	Distribution	Exudate	Modifier	Tissue
Minimal	Acute	Focal	Serous	Necrotizing	Nephritis
Mild	Subacute	Multifocal	Catarrhal	Bronchointerstitial	Cystitis
Moderate	Chronic	Locally extensive	Fibrinous	Hemorrhagic	Enteritis
Marked (severe)	Chronic-active	Diffuse (interstitial)	Suppurative	Embolic	Pneumonia
		Cranioventral†	Granulomatous		Hepatitis

Pathologic Basis of Veterinary Disease, 6th Ed., Ed.: Zachary JF, (2017) Elsevier, St. Louis, Missouri.

Classification of inflammation

according to the duration

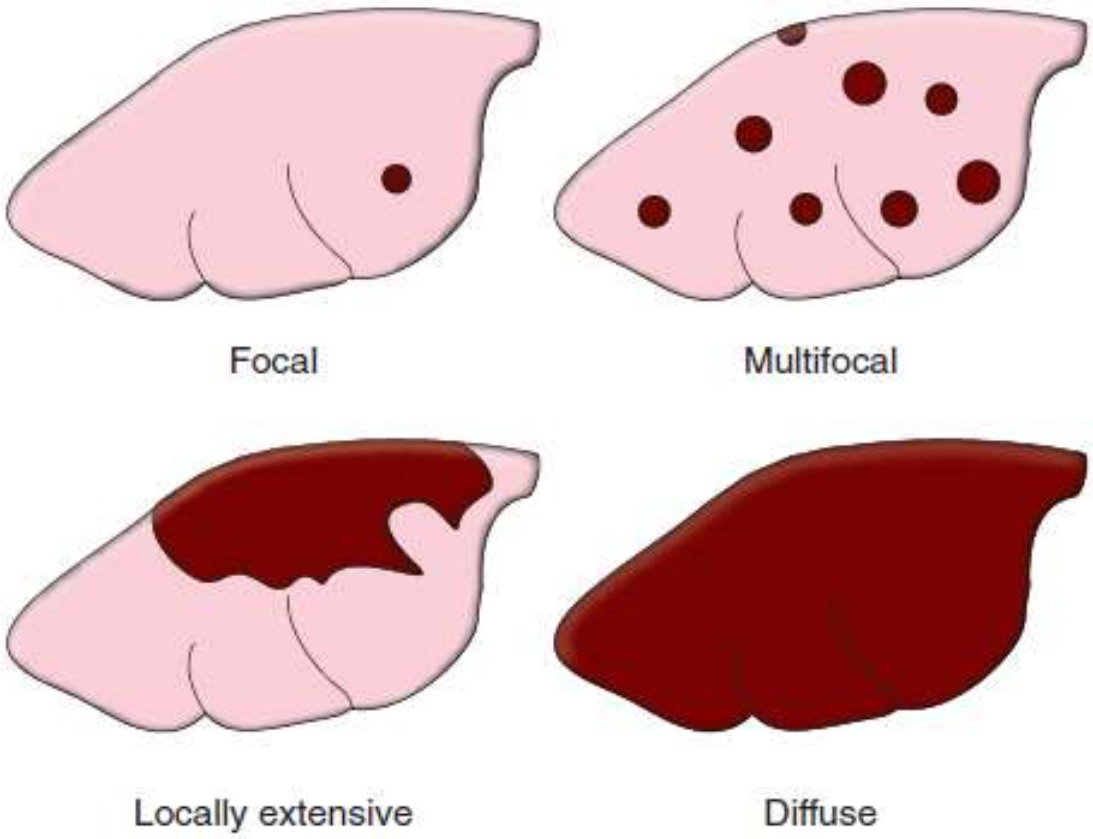
- **Acute inflammation** – has a short duration, ranging from a few hours to a few days.
  Vascular and exudative processes predominate.
  Marked clinically by the signs of heat, redness, swelling, pain, and loss of function.
  Neutrophils are often predominant, lymphocytes may be present.

- **Chronic inflammation** –inflammation of prolonged duration, usually weeks to months and even years.

The response is **characterized predominantly by lymphocytes and macrophages, tissue necrosis, and accompanied by tissue repair, such as healing, fibrosis, and granulation tissue** formation, all of which may occur simultaneously.

- **Subacute inflammation** – a condition intermediate between chronic and acute inflammation.

Distribution of inflammatory lesions



Pathologic Basis of Veterinary Disease, 6th Ed., Ed.: Zachary JF, (2017) Elsevier, St. Louis, Missouri.

SPREADİNG OF INFLAMMATİON

1. Local inflammation: limited in one region.
2. Metastatic inflammation: Spread to other tissues.
   - Intracanalicular path; Bronchitis,..
   - Hematogenous route
   - Lymphogen way
   - Neurogen; rabies,..
3. Inflammation following immunological reaction: Antigen-antibody complexes, immune complex glomerulonephritis, ..

Classification of inflammation according to the result

If hyperplasia occurs; ***hyperplastic*** inflammation

If hypertrophy occurs; ***hypertrophic*** inflammation

If fibrous connective tissue is produced; ***fibrous*** inflammation

If atrophy occurs; ***atrophic*** inflammation

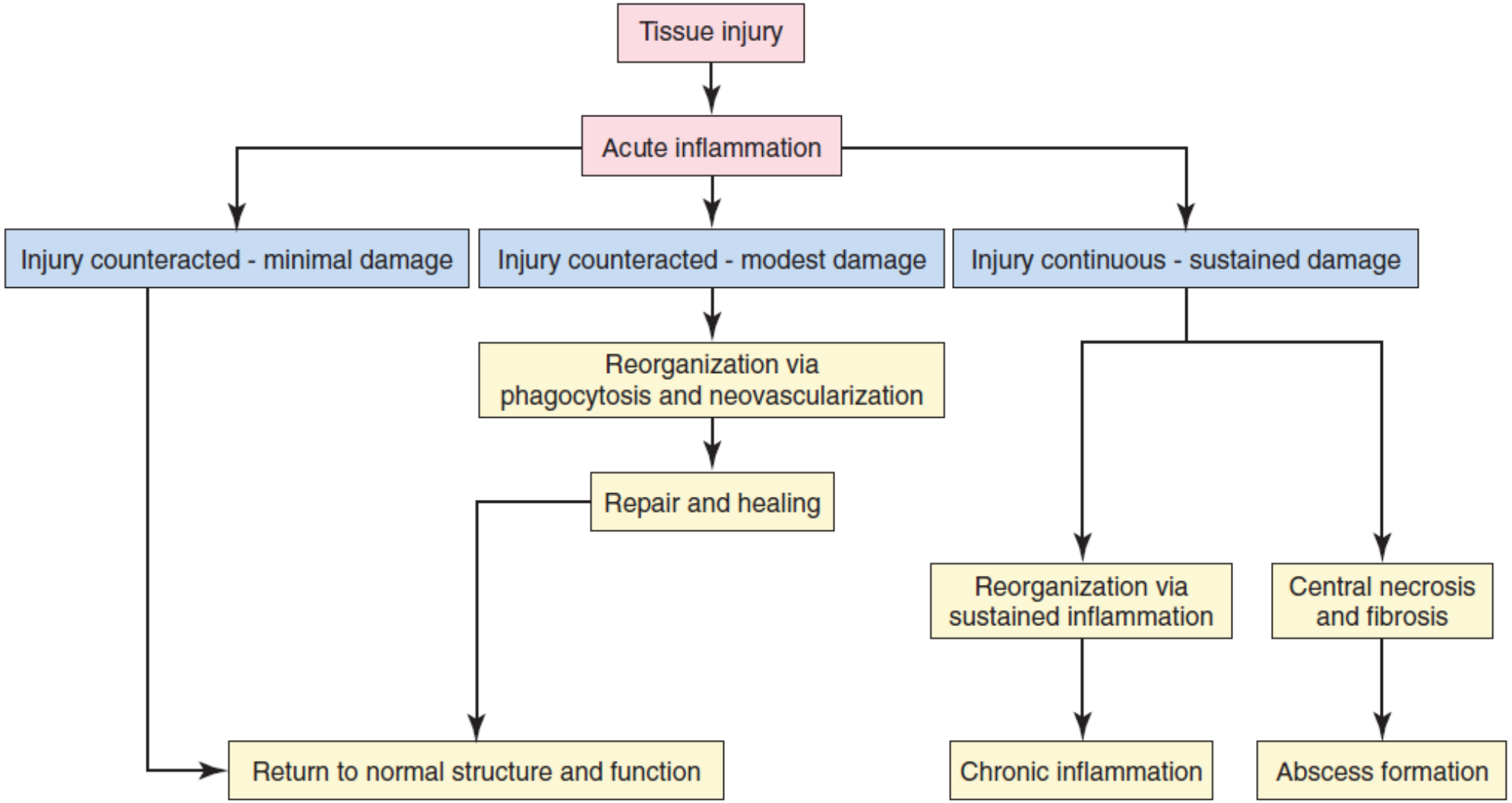
If the lumen is obstructed; ***obliterative*** inflammation

If adhesion occurs; ***adhesive*** inflammation

Outcomes of the Acute Inflammatory Response

The four main outcomes of acute inflammation are as follows:

- ✓Resolution (the return to normal structure and function)
- ✓Healing by fibrosis and regeneration
- ✓Abscess formation
- ✓Spread of inflammation
- ✓Progression to chronic inflammation
- ✓Death



Pathologic basis of veterinary disease, 6th Edition.

HEALİNG OF İNJURED TİSSUES

The “healing” responses of affected tissues include

1) Healing by **regeneration**
2) Healing by **fibrosis** (reparation)
3) Healing by **sequestration** (organization)

HEALİNG BY REGENERATİON

- Healing by regeneration is in the replacement of dead or damaged cells by new, healthy cells of the same functiomorphological andnal characteristics.
- Regeneration requires :

1. An intact connective tissue framework
2. Enough cells to regenerate
3. Labile or stable parenchymal cellular elements

There are three cell types based on ability to regenerate:

Permanent cells: (almost never divide). Cells in which regenerative attempts are generally absent or limited. Example; neuron and cardiac muscle cells.

Stable cells : (will divide if stimulated). Cells with a capacity for rapid division and cell proliferation in response to stimuli or insults. Example; fibroblasts, osteoblasts, parenchyma of liver, kidney, ….

Labile cells : (multiply through life). Cells that under normal physiological conditions continually multiply at a rapid rate. Example; epithelial cells of surfaces or linings of ducts, lymphoid and hematopoietic cells .

REGENERATİON OF EPİTHELİAL TİSSUE

- ✓ Surface epithelia, such as the stratified squamous surfaces of the skin, oral cavity, vagina, and cervix;
- ✓ Cuboidal epithelia of the ducts draining exocrine organs (e.g., salivary glands, pancreas, biliary tract);
- ✓ Columnar epithelium of the gastrointestinal tract, uterus, and fallopian tubes
- ✓ Transitional epithelium of the urinary tract.
- Liver: If basal membrane of hepatocytes and nutrient vessels are intact, regeneration occurs.

REGENERATİON OF CONNECTİVE TİSSUE

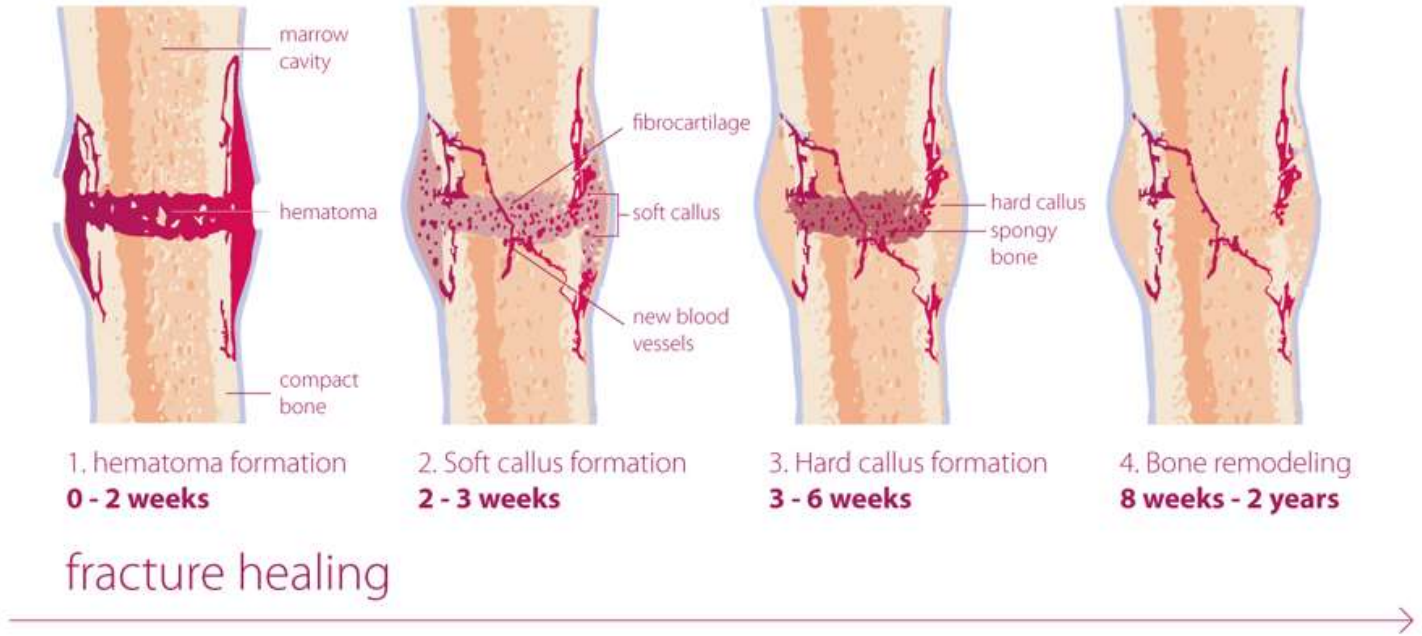
- The highest tissue in regenerating ability.
- Fibrosis

REGENERATİON OF CARTİLAGE TİSSUE

- Cartilage tissue regenerates if perichondrium is intact.
- Chondroblasts and hyalinous material form the encapsulated cartilage cells from the perichondriumum.

REGENERATİON OF BONE TİSSUE

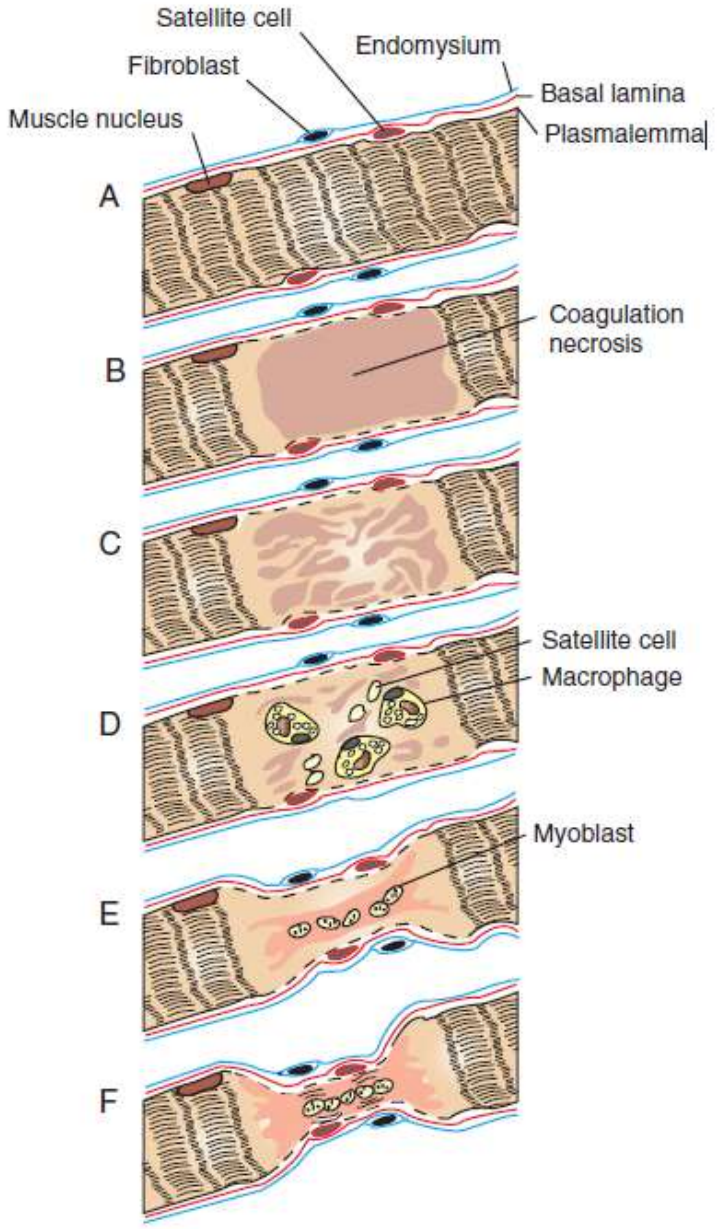
- The regeneration ability is high.



REGERATİON OF MUSCLE TİSSUE

- Cardiac muscle cells **X**
- Satellite cells → regenerative capacity for skeletal muscle tissue.

Skeletal muscle regeneration



- The regeneration ability is high in hematopoietic organs, blood and lymph vessels.

REGENERATİON OF NERVOUS SYSTEM

- **Central Nervous System:**
- Neurons do not have regeneration ability.
- The neurons are replaced by glia cells with a very high ability to proliferate and finally, a neuroglial tissue takes place.
- Astrocytes play a role as fibroblasts.

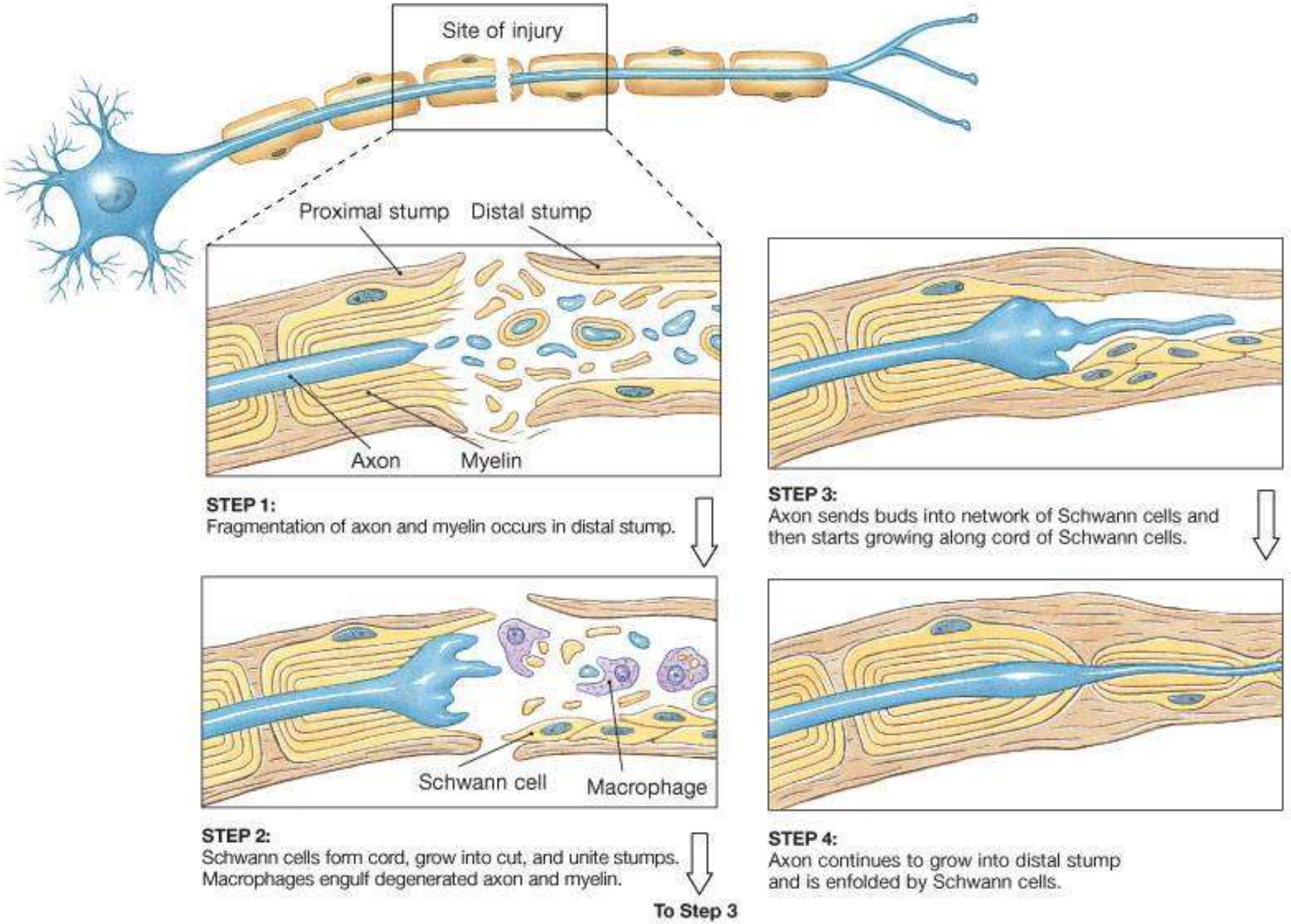
REGENERATİON OF NERVOUS SYSTEM

- **Peripheral nervous system:**
- If the distance of injury ends are close to each other, regeneration can occur.
- After mechanical injury in a peripheral nerve, the axon and myelin of the distal ends begins to degenerate along its length.
- Wallerian degeneration denotes the changes that follow acute focal injury to a myelinated axon.

WALLERIAN DEGENERATION

- First, Focal eosinophilic swellings occur, often containing accumulations of degenerate organelles, and then fragmentation happens.
- The myelin itself condenses into aggregates and fragments and, together with remaining axonal debris, becomes the target of invading macrophages.
- Some of the myelin debris is phagocytosed by Schwann cells themselves, and they begin to proliferate. As the debris is cleared away, proliferating Schwann cells form bands along the myelinated axons.

- Similar Wallerian changes occur at the opposite end of injured axon. If conditions are favorable at the site of injury, sprouts from the axonal stump will reach to their correct destinations along the Schwann cell bands .
- Finally, a new axon arise and is remyelinated by Schwann cells.



- If the injury ends are not close to each other, WHAT HAPPENS?
- Axonal regeneration do not occur;
- Schwann cell bands persist, and endoneurial fibrosis usually develops. Abortive regeneration can lead to a tangled clump of neurites, Schwann cells, and fibrocytes at the injury site.
- It is called Amputation neuroma or Traumatic neuroma.

HEALING BY FIBROSIS

- Parenchyma cells of injured tissue are **replaced** by stromal elements (**connective tissue cells**)
- Necrotic tissue and the acute inflammatory exudate are **removed** by **macrophages** (phagocytosis by cells of the monocyte-macrophage system), and the space is filled with **fibrovascular tissue.**
- Endothelial cells give rise to **new blood vessels**.

These blood vessels establish blood circulation in the healing area, and fibroblasts produce collagen that imparts mechanical strength to the growing tissue.

Eventually a scar consisting of densely packed collagen is formed.

WOUND HEALING

- ✓ Clot
- Bleeding from the edges of the wound
- ✓ Acute inflammation
- Exudation, fibrin and leukocyte increase. Drying of exudate and crust formation.
- ✓ Granulation tissue formation
- Surrounding fibroblast and capillary vessel increase and granulation tissue formation.
- ✓ Epithelial regeneration
- Epithelial proliferation from the edges of the wound and covering the surface.
- ✓ Scar formation
- Reduction of the veins and cells in the granulation tissue and the increase of collagen fibers (scar tissue)

HEALING BY **SEQUESTRATION** (ORGANIZATION)

- If chronic inflammation is unable to remove the inciting agent/substance, then the affected tissue attempts to "heal" itself by using defensive mechanisms that act to isolate and sequester the lesion and limit the spread of additional tissue damage.
- These outcomes are not healing but instead serve as compensatory defensive mechanisms to protect the animal against the cause.
- Defensive sequestration healing includes;
- (1) healing by abscess or granuloma formation with fibrosis and
- (2) healing by granulomatous inflammation with or without fibrosis.

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TRANSPLANTATION

- Transplantation is the transfer (engraftment) of cells, tissues or organs from a donor to a recipient with the aim of restoring function(s) in the body.
- **Autotransplantation (Autograft)**
- **Allotransplantation (Allograft)**
- **Syngenic transplantation (Isograft)**
- **Xenotransplantation (Xenograft)**

AUTOTRANSPLANTATION

- **Autotransplantation** is the transplantation of organs, tissues, or even particular proteins from one part of the body to another **in the same person.**

ALLOTRANSPLANTATİON

- **Allotransplantation** is the transplantation between **individuals of the same species**. Example; human to human or animal to animal.

SYNGENEİC TRANSPLANTATİON

- **Syngeneic transplantation** is the transplantation between two **genetically identical individuals of the same species**.
- Example; monozygotic or identical twins.

XENOTRANSPLANTATION

- **Xenotransplantation** is the transplantation of living cells, tissues or organs from **one species to another.**
- Example; from human to animal (chimpanzee-to-human kidney transplantations,…)

DISTURBANCES OF GROWTH AND DIFFERENTIATION OF TISSUES

Prof. Dr. Sevil Atalay Vural

APLASIA (AGENESIS)

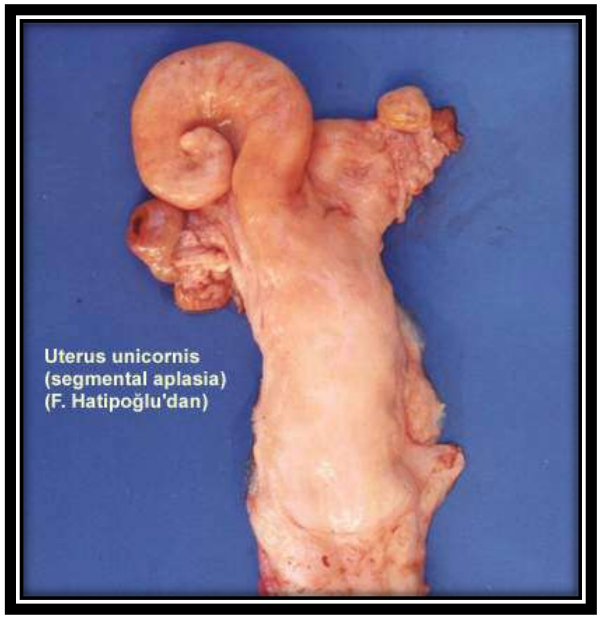
- Agenesis : congenital disturbance in which the tissue or organ did not develop and there is complete absence of growth of the organ.
- Aplasia: congenital disturbance in which there exists only primitive and usually small structures representative of the organ.

✓ Aplasia is commonly seen in paired organs such as the kidneys, gonads and adrenals.

✓ If the organ is a single vital organ, the fetus dies.

✓ Segmental aplasia is the aplasia of a segment of an organ.

✓ e.g. Uterus



APLASIA (AGENESIS)

- Hereditary defects
- Accidental death of a cell at some critical point in the development of the individual
- Diseases like viruses or poisoning during intrauterine life like *Veratrum Californicum*

HYPOPLASIA

- Incomplete development of a tissue or an organ. The organ is congenitally small.
- The major causes of hypoplasia are **genetic defects**, **infectious agents** and certain **poisonous agents** which induce congenital abnormalities in intrauterine life.
- Observed in all organs (vital and paired organs)
- Hypoplasia of the cerebellum is frequently observed in kittens, lambs and calves due to intrauterine viral infections during gestation. e.g.(blue tongue, Panleukopenia,..)

ATROPHY

- Atrophy is the decrease in the mass of a tissue or organ due to decreased size and/or number of cells after it has reached its normal size.

- Decrease in cell size = volumetric atrophy

Decrease in cell number = Numeric atrophy

Decrease in cell size and number = atrophy

- Atrophy can be physiologic and pathologic, systemic and local.

- Physiological atrophy is a function of the *growth changes* of an organism.

ATROPHY

- ✓ Atrophic organs are smaller than normal. Because the cells are smaller, the microscopic field may appear to be more cellular.
- ✓ Atrophic parenchymal cells, particularly in the heart and liver, may progressively accumulate a yellow, granular, lipid containing pigment (lipofuscin). Lipofuscin is derived from progressive oxidation of lipids. It is found within the cytoplasm of cells.
- ✓ In atrophic organs parenchymal elements may be partially replaced by connective tissue.
- ✓ Microscopically vessels may appear prominent and increased in number but it is actually due to the parenchyma decrease.

PHYSIOLOGICAL ATROPHY

Local physiological atrophy

- Atrophy of the thymus during puberty
- Atrophy of uterus after parturition takes place.

Systemic physiological atrophy

Senile atrophy

- Atrophy of the sex glands, skin, and bones in old people

PATHOLOGICAL ATROPHY

Local pathologic atrophy

- Can be caused by:

✓ Decreased workload (disuse atrophy)

✓ Insufficient supply of blood (e.g., atrophy of the brain cortex during atherosclerosis of the blood vessels of the brain)

✓ Loss of hormonal stimulation (e.g. atrophy of the adrenals due to destruction of pituitary glands)

✓ Denervation (especially in skeletal muscles),

✓ Compression (e.g., neoplasms, or distended body cavities).

✓ Exhaustion (prolonged overwork of an organ may be followed by atrophy)

Systemic pathologic atrophy

- Appears in cases of:
- ✓ Insufficient nutrition,
- ✓ Chronic infection or intoxication
- ✓ Disorders of the endocrine glands or of the central nervous system

Atrophy results

1. **Fibrosis** ; when parenchymal elements are replaced with connective tissue
2. **Pseudotrophy:** when parenchymal elements are replaced with adipose tissue. The organ may look bigger than normal.
3. **Serous atrophy:** fat cells are atrophic and replaced by proteinaceous fluid which converts the fat depots to gelatinous masses.
4. **Brown atrophy**: atrophic parenchymal cells, particularly in the heart and liver, accumulate lipofuscin pigment.

HYPERTROPHY AND HYPERPLASIA

Hypertrophy

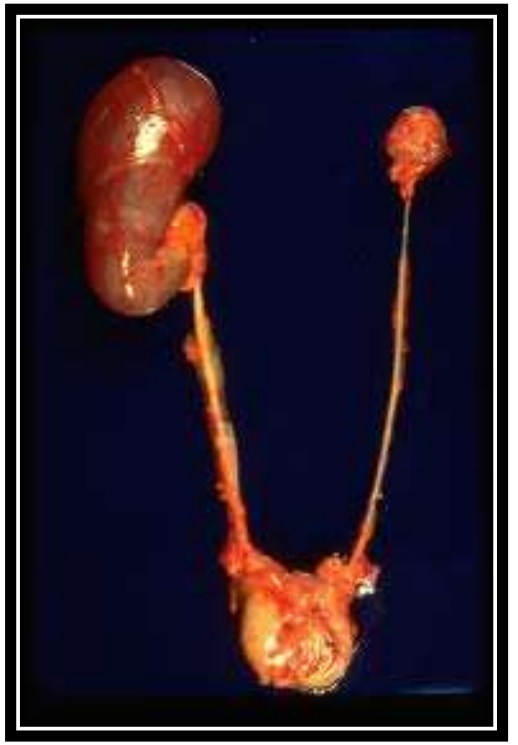
- Increase in the size of a tissue or organ by enlargement of the existing cells.

Hyperplasia

- Increase in the size of a tissue or organ as a result of an abnormal increase in the number of cells.

ETIOLOGY OF HYPERTROPHY

- Hormonal hypertrophy (e.g. Hypertrophy of the muscles due to the effect of testosterone)
- Compensatory hypertrophy
  (Increase in the size of an organ or volume of a tissue following loss or malfunction of the paired organ.



ETIOLOGY OF HYPERPLASIA

- Physiologic hyperplasia
  - Hormonal hyperplasia; e.g. estrogen-dependent uterine cells undergo hyperplasia and hypertrophy following pregnancy.
  - Compensatory hyperplasia; e.g. liver mass restoration after being resected

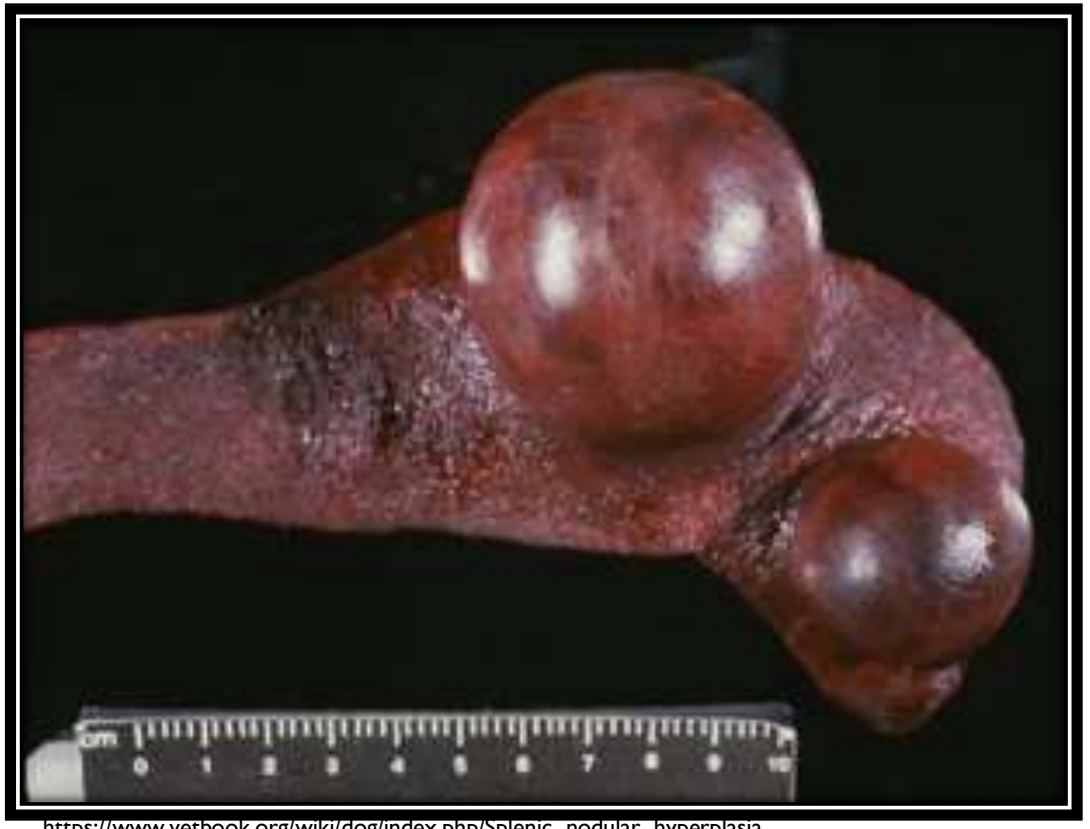
- Pathologic hyperplasia
  - Hormonal imbalances; e.g. estrogen-progesterone imbalance leading to endometrial hyperplasia in female dog.
  - Chronic irritation (e.g. Cutaneous hyperplasia, hyperplasia of the bile ducts in coccidiosis of the rabbit.
  - Chronic infections

ETIOLOGY OF HYPERPLASIA

Nodular hyperplasia

Encountered commonly in certain organs (e.g., liver, pancreas, or spleen).

Especially in older dogs.



https://www.vetbook.org/wiki/dog/index.php/Splenic_nodular_hyperplasia

METAPLASIA

- The transformation of **fully differentiated** normal adult tissue into another related type of differentiated adult tissue.
- The change occurs only to cell types from the **same germ layers** and is an alteration from a **less specialized** cell type to **more specialized** cell types.
- Metaplasia occurs in **epithelial** and **connective** tissue.

METAPLASIA

Metaplasia in epithelial tissue

Tissue	Normal	Metaplasia
Airways	Pseudostratified columnar epithelium	Squamous epithelium
Esophagus	Columnar epithelium	Squamous epithelium
Urinary bladder	Transitional epithelium	Squamous epithelium
Cervix	Glandular epithelium	Squamous epithelium

METAPLASIA

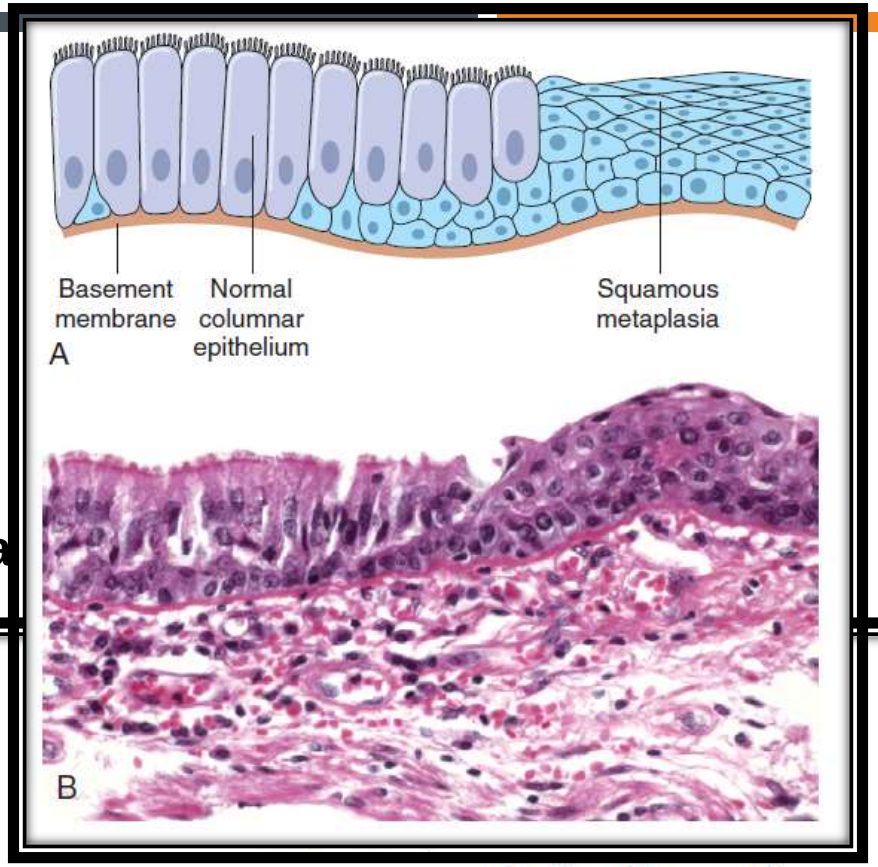
Metaplasia in connective tissue

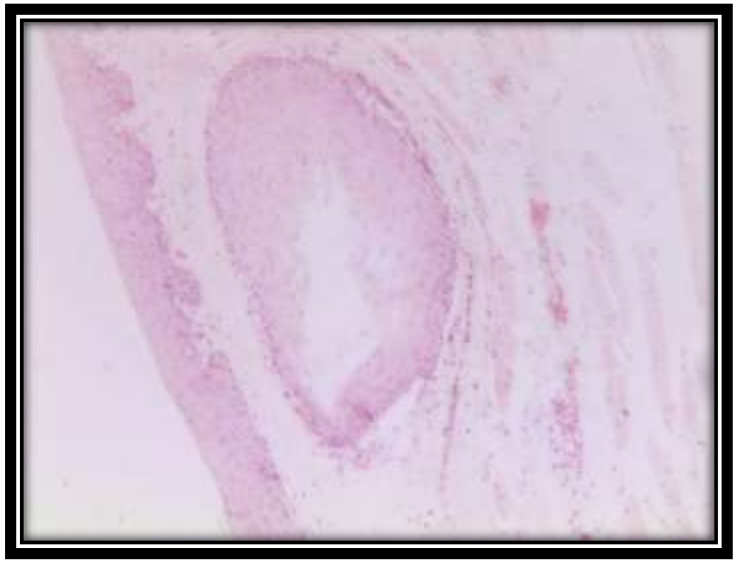
These changes are specially seen in mixed tumours, mammary gland tumours of bitches, tendinitis, etc.

CAUSES OF METAPLASIA

- Vitamin A deficiency (Vitamin A is *necessary for normal differentiation of stratified squamous epithelium*, deficiency or absence of Vit A leads to Squamous metaplasia of the epithelial lining of the glands and ducts)
- Chronic irritations (e.g. the respiratory epithelium lining the trachea, bronchi and bronchioles replaced by stratified squamous epithelium)
- Chronic infections (Metaplasia can occur under the influence of toxins secreted by microorganisms)
- Hormonal imbalance (e.g. estrogen-induced squamous metaplasia in the prostate gland)
- Chronic inflammation (e.g. mammary ducts in chronic mastitis)
- Function changes (Cells are replaced by more resistant ones. e.g. ossification of cartilage and tendons)

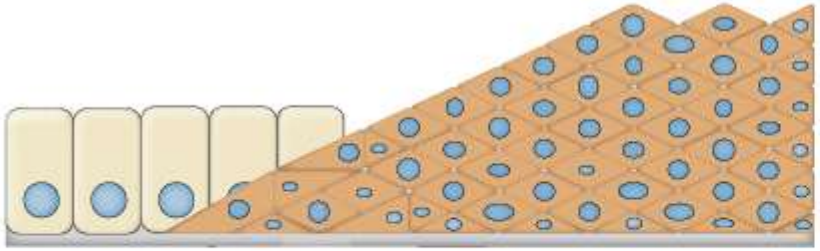
Metaplasia of normal columnar to squamous epithelium in a bronchus

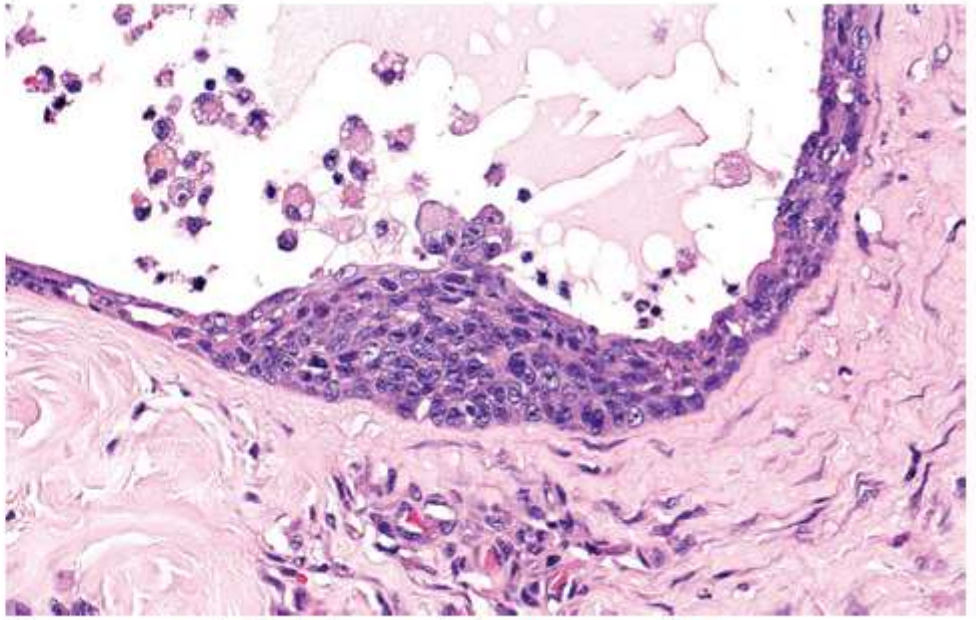




Hypovitaminosis A, oesophagus, chicken

Healing after mastitis
(low columnar → squamous)





Squamous metaplasia in an ectatic mammary duct

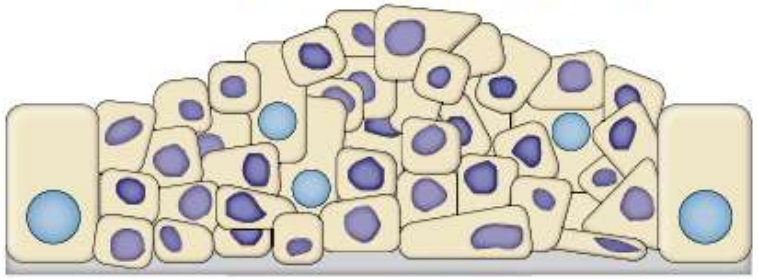
Pathologic Basis of Veterinary Disease, 6th Ed., Ed.: Zachary JF, (2017) Elsevier St. Louis, Missouri.

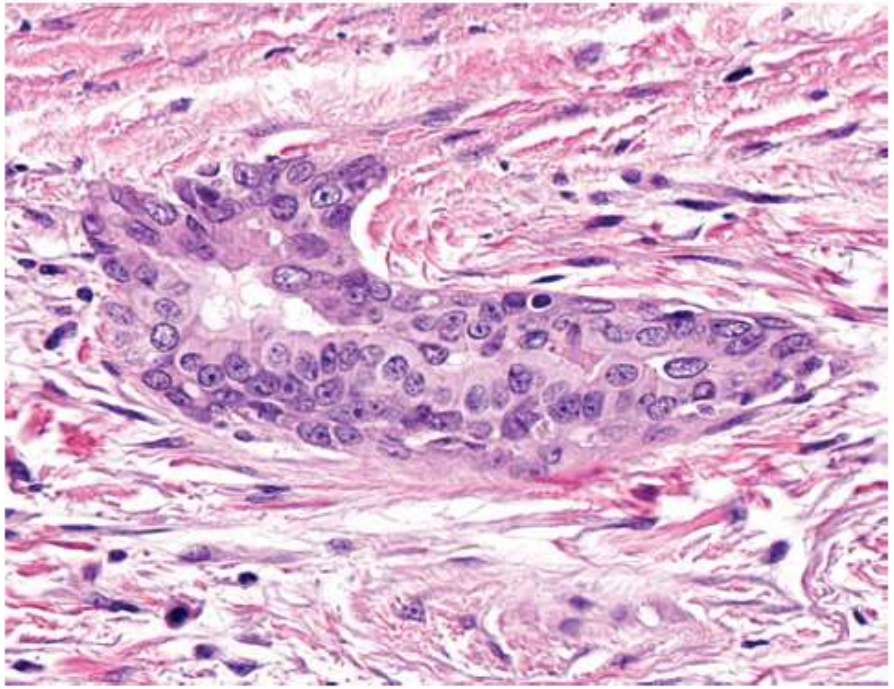
DYSPLASIA

- Dysplasia implies an abnormality in formation of a tissue. For example, *renal dysplasia* is the abnormal formation of the kidney.
- Refers to a loss of architectural orientation of cells or *loss in uniformity* of individual cells or both.
- Microscopically, dysplastic epithelial cells have atypical features, such as abnormal variation in size (anisocytosis) and shape (poikilocytosis), hyperchromatic nuclei, increased nuclear size (karyomegaly), and increased number of mitotic figures.
- Dysplasia is associated with chronic irritation and inflammation but may be due to nutritional disorders.

DYSPLASIA

Dysplasia (abnormal pattern of tissue growth, disorderly arrangement of cells within epithelium)





Dysplasia (atypical ductal hyperplasia)

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