DEGENERATIONS AND METABOLISM DISORDERS

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Degeneration

- In Latin, it means deterioration.
- **Degeneration** is called when cells and tissues remain less active in terms of function by preserving their viability and undergo various structural changes.
- With the disruption of metabolism, morphological changes characterized by disturbances and accumulations in cells and intercellular regions (intercellular-ground subject) are understood.
- It is made by bringing "osis" appendix to the end of the degenerated organ or tissue. E.g: Nephrosis, hepatosis, etc.
- Naming is also made according to its morphological type. Ex: parenchymatous degeneration, amyloidosis, lipidosis.

Classification

- With the disturbance of the water and electrolyte balance in the cell
- Disruption of protein metabolism
- Disruption of carbohydrate metabolism
- Disruption of lipid metabolism
- Disruption of pigment metabolism
- Disruption of the metabolism of mineral substances (especially calcium)

Degeneration

- The effects that disrupt the metabolism, functions and structure of cells and tissues are grouped under various headings.
  - Physical effects
  - Chemical and toxic effects
  - Nutritional disorders
  - Disorders due to metabolic substances
  - Immunological disorders
  - Gene and chromosome disorders
  - Biological agents
  - Aging

DEGENERATIONS RELATED TO WATER - ENERGY - ELECTROLYTE BALANCE DISORDERS IN CELLS

- Acute cell swelling
- Vacuolar degeneration
- Hydropic degeneration

Acute cell swelling

- Acute cell swelling is also defined as turbid, fuzzy degeneration. Because the nucleus is ambiguous, as if it were visible from behind the tulle curtain.
- It is called **parenchymatous degeneration** due to the determination of organs or tissues such as liver, kidney, testicle, heart muscle, skeletal muscle.

Acute cell swelling

- **Histologically**; Considering the granular appearance of the cytoplasm of the cell, it is called **"granular degeneration".** (Since mitochondria are bulging, they are seen in granular structure)
- Histochemically, it is suggested that such granular structures are in the protein structure and this degeneration is also called **"albuminous degeneration"** (albumin degeneration).
- It covers the changes that take shape at the onset of cell edema.
- **It is reversible.** However, it may turn into vacuolar-hydropic degeneration and become irreversible resulting in necrosis.

Acute cell swelling

- It is characterized by damage to the membranous organelles in the cell (mitochondria, endoplasmic reticulum, lysosome, golgi apparatus) and their inflow by taking on water.
- **The main change is in the mitochondria.**
- Since the mitochondria swell by taking in water, on light microscopic examination, the cell cytoplasm takes on a granular appearance.
- The granules in the cytoplasm cover the nucleus, and the nucleus has an unclear appearance, as if behind a tulle curtain, sometimes it has disappeared.

Etiology

- Hypoxia
- Infectious agents
- Toxic, chemical effects, Drugs, Intoxications
- Immunological effects
- Mechanical effects

Pathogenesis

- The above effects disrupt the cell membrane, the cell's electrolytes, water, and energy metabolism.
- **The cell whose osmotic balance is disturbed receives water.**
- The water that ultimately enters the cell, collects in the membrane organelles, especially in the mitochondria, swelling them.
- Due to this, the cell acquires a bulging, fuzzy appearance with granular, thin vesicles.
- The changes seen so far are **reversible, if the effect is mild.**

Pathogenesis

In hypoxia;

- The mechanisms that provide energy to the cell through the oxidative route (oxidation) are disrupted.
- ATP and creatine phosphate reserves are depleted.
- In the absence of oxygen, glycogen is broken down by anaerobic glycolysis.
- Lactic acid↑, pH ↓
- Since the energy metabolism is disturbed, the **Na-K** ion pump cannot perform its task.
- As Na increases inside the cell, the osmotic pressure↑

Pathogenesis

- If the **effect is severe** and lasts a long time, then **irreversible** events occur in the cell.
- Vacuolar, hydropic degeneration are formed.
- Eventually, the cell nectrotizes and dies.
- In this case: $Ca+^{2}$ and PO_4^{-}become free.
- The crystals of the mitochondria break down, the mitochondria turn into a vacuole structure and break down.
- Other membranous organelles, such as the endoplasmic reticulum, ribosomes, also swell by taking on excess water, become large vacuoles and break down.
- At this stage, vacuolar, hydropic degeneration is mentioned.

Pathogenesis

- At this time, changes occur in the nucleus.
- Nucleoproteins are denatured.
- In relation to this, the osmotic pressure increases even more.
- The nucleus swells, hyperchromasia is formed.
- Then, one of the pyknosis, karyorrhexis or karyolysis occurs.
- With the breakdown of lysosomes in the cytoplasm, proteolytic enzymes are released.
- As a result, the cell undergoes necrosis (coagulation necrosis) and dies.

Pathomorphological findings

Grossly

- The organ is swollen, the edges are blunted.
- Its color is lighter than usual, brown (gray) and cooked in appearance.
- In the presence of severe hyperemia, the organ is degraded red or brownish-red.
- Its consistency is crunchy or soft.

Histological findings

- The parenchymal cells of the organ swell, their cytoplasm loses its normal basophilic structure, is painted a darker red with eosin; The cytoplasm takes on a vaguely small granular and blurry, fuzzy appearance.

Histological findings

- When shaped in muscle cells (heart, skeletal muscle), the cells lose their stripes and take on the same appearance.
- The nucleus is faint, as if visible from behind the tulle curtain.
- Sometimes it is completely lost.
- In **irreversible events**, pyknosis and other changes occur in the nucleus.

Hydropic degeneration

- Swelling of cell organelles by taking excessive water, formation of vacuoles of different sizes in the cell; then they are changes characterized by the fact that the whole cell is filled with water and the nucleus is pushed to the edge.
- It is a more severe, more advanced form of acute cell swelling.
- If the effect is more severe, if it lasts a long time, it either follows it or is directly shaped by some effects.

Pathogenesis

- If the energy deficiency in the cell is excessive,
- If the osmotic balance between the cell and the environment in which the cells are located is too disturbed, the cells take in excess water.
- Morphological changes begin as in acute cell swelling (parenchymal degeneration). However, the incident is more severe.

Pathogenesis

- As a result of the swelling of the organelles (mainly the endoplasmic reticulum) by taking in excess water, IRREGULAR EDGES AND MULTIPLE VACUOLES OF DIFFERENT SIZES APPEAR IN THE LIGHT MICROSCOPIC EXAMINATION.
- In the later period, with the combination of these, larger vacuoles with uneven environments are shaped.
- If the first of these is seen, **vacuolar**, and if the second is seen, **hydropic degeneration** is mentioned.
- Hydropic degeneration is also called **ballooning degeneration** due to the fact that the cell is highly swollen.

Pathogenesis

- If, the cytoplasm between the highly growing vacuoles stands out in thin (narrow) strips, and when staining with Hematoxylin-eosin, these areas are stained pale pink with eosin; if the cytoplasm is seen in the network-like; Hydropic degeneration at this stage is also called **reticular degeneration** histologically.

Pathogenesis

- Sometimes, with the gradual growth of vacuoles, a single large vacuole is formed, which occupies a significant part or all of the cytoplasm. In this case, the nucleus of the cell is also flattened and pushed aside.
- Hydropic degeneration of such type falls under the definition of **cell edema or hydrops.**
- If the degeneration occurs in many cells of the tissue, the tissue takes on the appearance of a honeycomb.
- With the breakdown of the organelles, the cytoplasm of the cell is filled with water and the nucleus of the cell is pushed aside, and with the deterioration of the cell nucleus, the cell undergoes necrosis **(Colliquative necrosis).**

Etiology

- Although it is also seen in some parenchymatous organs such as the testicle, the cortex of the adrens, the liver epithelial cells (hepatocytes), the tubular epithelium of the kidney, it is more commonly encountered in the **mucous epithelium and skin (epidermis)**.
- In the urinary system in Distemper
- *Staphylococcus hyicus* infection in pigs, in the urinary tract
- In shock
- In severe diarrhea events that cause electrolyte disorders
- In some endocrine disorders
- In the decrease in potassium in the blood,

Etiology

- It occurs in the skin and mucous epithelium in poxvirus diseases, foot and mouth diseae
- In the skin under the influence of chemical irritants or in the mucous epithelium such as the mouth, upper respiratory tract,
- In the skin in events caused by physical effect such as burns
- In non-specific testicular degenerations
- In epithelial tumors
- In the tympany in cattle, in the rumen epithelium,
- Towards the end of pregnancy, in the fetal membranes.

Gross findings

- When shaped in the parenchymal organs, findings similar to parenchymal degeneration are encountered. There is no specific finding.
- It is DIFFERENT when it occurs on the mucous membranes and skin. **Vesicles** are formed.
- Fluid-filled sacs with raised skin or mucosa the size of a pinhead or larger are formed.
- In severe cases, these combine with each other to form larger vesicles (large sacs filled with fluid), which are called **bullas.**
- With the progression of the event, the vesicle or bullae are torn, erosion is formed in its place.
- Later they can be covered with **crust.**
- In FMD, for example, erosions heal with regeneration or ulcerate with secondary bacterial complications and are replaced by **scar tissue.**

Histological findings

- The cell is bulging.
- Initial findings are similar to parenchymal degeneration.
- With the gradual intake of water and considerable expansion of the cell organelles, especially the endoplasmic reticulum, the above-mentioned changes (large-small vacuoles with irregular edges, reticular structures, single large vacuole, hydrops, cell edema) that can be seen with a light microscope are formed and in advanced cases ultimately result in colliquative necrosis.

Histological findings

- When **the skin and cutaneous** are formed in the mucosa (in areas of the multilayered flat mucous epithelium, such as the mouth), the intercellular connections dissolve, the cells melt, separating from each other, forming **vesicles, bulla** in the region. They are replaced by erosion; then it heals with regeneration.
- If it becomes complicated, ulcerated, scarring develops in their place.
- On histopathological examination, vacuoles in hydropic degeneration may be confused with fat vacuoles.
- But the circumference of the fat vacuole is regular. Those in hydropic degeneration are irregular.

DEGENERATIONS RELATED TO THE DETERIORATION OF PROTEIN METABOLISM

- Amyloidosis
- Hyaline degeneration, hyaline accumulation
- Fibrinoid degeneration
- Mucoid degeneration

Amyloidosis

- It accumulates **extracellular**.
- It occurs during the course of a number of diseases.
- It is caused by the accumulation of pathological substances with different and complex structures between cells.
- In this way, it is not a disease in itself, but is shaped as a result of another disease.
- But when it accumulates, it interferes with the nutrition and function of cells and tissue. This time, apart from the first disease, it causes the occurence of new signs.
- For example, when it accumulates in the kidneys, it causes the dysfunction leading to uremia.

Amyloidosis

- The reason it is called amyloid is because it stains similarly to starch (amyloid = starch).
- If the tissues are stained with an **iodized dye such as lugol, then sulfuric acid is added, it will become blue like starch.**
- Other than that, it has no similarity with starch.
- In H&E slides, it is amorphous, homogeneous red.
- In this case, **it can be confused with hyaline, collagen and fibrin.**

Amyloidosis

- But it is distinguished by special staining methods.
- Another feature is that it shows **metachromasia.** In other words, it is not the color of the stain it is stained in, but another color. This feature is an important clue in diagnosis.
- When the tissues are stained by congo red and examined under a polarized microscope, the amyloid deposited areas are not red, but blue green; When stained by toluidine blue, it takes on a red color, not blue. It also gives fluorescence radiation when it is stained by thioflavin T and S and examined under a fluorescence microscope.
- The cause of metachromasia is due to the fraction (zigzag) arrangement of the bundles of fibrillar proteins in its structure; is because the incoming light hits such fibrils and reflects at a different angle, and the color is seen differently from the color in which it is stained.

Classification

- It is made taking into account various criteria.
- One of these criteria is the classification according to the organ, taking into account the etiology. **Primary and secondary** (Lubarsch 1929)
- **Histological** classification was also made according to its location in the tissue.
- According to its distribution, it is divided into **localized and generalized (systemic)** according to its presence in an organ or various organs.
- Glenner and Page (1976) preferred classification based on **clinical criteria.**

Classification

- Its current classification is made by taking into account its **distribution** and **localization** in the organs, but also by taking into account its main **immunohistochemical and chemical structure.**
- In this way**, AA and AL amyloid** are mainly mentioned.
- Immunohistochemical examination identified over 15 different substances in the structure of amyloid.
- This difference is due to the difference of the disorder.
- Therefore, such classification elucidates the etiology and pathogenesis of amyloid.

Systemic amyloidosis

AA amyloidosis (secondary, typical, reactive amyloidosis)

- It occurs in two stages, preamyloid and amyloid period.
- In the first stage, SAA (Serum A protein Amyloid) is encountered in the blood.
- In the second stage, amyloid precipitates into the tissues.
- It is caused by continuous antigenic stimulation in **long-lasting infections** or by the similar effect of tissue destruction products in **non-infectious chronic diseases such as rheumatoid arthritis.**
- For example, in **chronic purulent inflammations, chronic bone marrow inflammations (osteomyelitis), leishmaniosis; develops in cyclic neutropenia in dogs**.

Systemic amyloidosis

AA amyloidosis (secondary, typical, reactive amyloidosis)

- The classic example is **serum sickness of horses.**
- To produce antiserum; amyloid accumulates in organs such as spleen and liver of horses that are constantly stimulated with antigen and made hyper immune.
- After all, the spleen, liver swells and ruptures, and the animal dies from internal bleeding.
- Familial amyloidosis is a variant of AA.
- In the kidney in Abyssinian cats and Shar-Pei dogs; In Siamese cats, it is seen in the liver.

Systemic amyloidosis

AL amyloidosis (primary, atypical amyloid; paraamyloid)

- It is based on the dysfunction of the immune system.
- Neoplastic B lymphocytes, more precisely, are caused by plasma cells producing defective immunoglobulin G.
- This is the case in humans with **multiple myeloma** and is associated with monoclonal gammapathy.
- **Plasmacytoma in dogs** also shows similarity.

Systemic amyloidosis

AL amyloidosis (primary, atypical amyloid; paraamyloid)

- Its morphological appearance and the tissues in which it is located are almost like AA.
- Distinction, investigation of the disease; depends on immunological, biochemical and other analyzes. However, when the tissues are treated with potassium permangant and stained with congo red: if amyloid loses its ability to stain, AA; if it does not lose, AL is considered amyloid.

Localized amyloidosis

- A single organ or part of the body is affected.
- Its etiology, structure, and the tissues in which it is located are different from the system.
- For example, **horses have only the mucosa of the entrance to the nasal cavity (vestibulum nasi), diffuse or nodule style.**
- Although it is not certain, its cause is attributed to the local allergic reaction to insecticide poisons.

Miller MA, Zachary JF. Mechanisms and Morphology of Cellular Injury, Adaptation, and Death. Pathologic Basis of Veterinary Disease. 2017:2–43.e19

Localized amyloidosis

- Senile amyloidosis (amyloidosis of old age, β-amyloidosis) is formed by the accumulation of Aβ in the brain in older dogs; It has also been reported in the heart, digestive tract, lungs.
- It develops in **Alzheimer's disease** in humans.
- In the brain, **mad cow diseases** in cattle, **scrapie** in sheep;
- **Insulinoma** (a type of neoplasia that develops from Langerhans islets of the pancreas) and **type II diabetes mellitus** are also observed in the pancreas of cats.

Other types of amyloid

- **AE Amyloid (APUD-amyloid, E-amyloid, E = endocrine amyloid; APUD= endocrine cell system localized to various organs of the body):**
- This type of amyloid is mostly localized in areas where the C cells of the thyroid are located, in the islets of the pancreas and between enterochromaffin cells.
- Thyroid C-cell carcinoma and especially type II diabetes melllitus in older cats are observed in the islets of langerhans.

Other types of amyloid

AP (Amyloid P):

- It contains glycoprotein compounds formed by prealbumin in its structure.
- Genetically induced neuropathies are found in peripheral nerve tissue.

AF and AS (S and F) Amyloid:

- Structure has prealbumin-like substance.
- F amyloid has only been identified in humans.
- S amyloid is the (senile) amyloid that occurs in old age.
- It has been detected in the heart muscle, coronary vessels and brain vessels in older dogs as well as humans.

Gross findings

- Systemic amyloidosis most often involves organs such as the **liver, kidney, spleen, adren**.
- The organ is **increased in volume and pale**; the cut surface is **dry and like a wax.**

Histological findings (Spleen)

a) Local amyloidosis:

- It is collected in the lymph follicles.
- It first accumulates in the intima of the A. centralis in the central parts of the lymphoid follicles and then covers the entire follicle.
- In this case, since the appearance of the spleen resembles a date section, this appearance of the spleen is called **"sago spleen"** (sago = date=hurma).
- The lymph follicles stand out between the red pulp in a glassy shape.

b) Diffuse amyloidosis:

- The amyloid substance is distributed in all the sinuses of the spleen (red pulp) and collected in the red pulp between the cells of the reticulum.
- Since the section of the spleen resembles ham, it is also called **"ham spleen".**

Histological findings (Kidney)

- Amyloid substance accumulates in the intima of the vessels of the glomerulus capillaries, in the basement membranes of tubular epithelial cells and in the intima of the vessels in the interstitium.
- In cats, it can be observed among the peritubular connective tissue in the medulla.

Histological findings (Liver)

- It is collected under the cells lining the sinusoids with disse spaces.
- When the Remak cords are under pressure, they undergo necrosis or atrophy in the parenchymal cells (hepatocytes).
- It is the cause of dysfunction of the liver.

Histological findings

Adren

- In cortical sinuses,
- intima layer of capillaries,
- sometimes it accumulates extracellular in the pericapillary areas.

Intestine

- Villus,
- Localized among the smooth muscle and veins in the propria layer.

Hyaline, Hyalinization and Hyaline Degeneration

Hyaline

- It means "glass" in Greek.
- The reason why it is called hyaline is that during the light microscopic examination of tissues stained with HE and PAS (periodic acid schiff): located **intracellular and extracellular**; homogeneous pink color, amorphous, glassy areas, masses, droplets.
- It consists of protein whose basic structure is disrupted and has collapsed into or out of the cell.
- Its etiology is based on a disorder of protein metabolism.
- However, although the microscopic appearance of light is the same, its chemical composition, location in tissues and etiology are different.

Hyaline

- Not every hyaline is covered by degeneration.
  - If hyalinization occurs in muscle tissue, it is hyaline degeneration.
  - However, the presence of hyaline droplets in the epithelial tissue (for example, in the tubule epithelium) does not indicate hyaline degeneration.
- Not every hyaline is **pathological,** unless it reflects a fundamental disorder; it can also be **physiological.**
  - In order to be considered pathological, protein metabolism must be disrupted, either directly or indirectly.
  - **Hyalinization of connective tissue cells in the vessel wall in chronic inflammatory granulation tissue or arteriosclerosis** is pathological.
  - But the **hyalinization of corpus albicans**, which is formed in the ovary, is **physiologica**l; it is not covered by degeneration.

Hyaline

- It is intracellular in epithelial tissue; intracellular and extracellular in mesenchymal tissue. It is also collected in tissue spaces.
- It is important in terms of defining the tissue in which it develops.
- **The form that fits the definition of degeneration is the intracellular one in the muscles**. This is also called **Zenker degeneration.**
- The hyalinization of connective tissue is usually defined as **hyalinosis.**
- In such cases, the basis of the hyalinization encountered in the connective tissue due to nutrition deficiency.

Hyaline

- Capillaries decrease with increased and pressure of collagen strands in chronic granulation tissue; since the tissue cannot be nourished, it becomes hyalinized.
- Hyalinization begins in areas far from the vessels. Hyalinization in some connective tissue areas in the elderly is also related to the inability to nourishing.
- Physiologically, the hyalinization of the corpus luteum by becoming corpus albicans is based on the elimination of the tissue that does not need it by reducing its nutrition.

Classification

- Intracellular hyaline
- Extracellular hyaline
- Hyaline degeneration

Intracellular hyaline

- It is also normally found in the secretory form in the gland epithelium. **(Physiological)**
- It appears in the cell in the form of droplets or granules.
- It has proteoglycan and glycoprotein structure and is stained red by giving PAS (periodic acid schiff) reaction.
- **Pathological:**
  - - As a result of cell disruption
  - - Due to albumin ingested into the cell from the outside
  - - With chronic toxic or dietetic effects
  - - In protein secretion disorder

Intracellular hyaline

As a result of cell disruption

- In lead poisoning, hyaline droplets are found in the epithelium of the kidney tubular and mainly in the nucleus.
- It is related to the disorder of protein metabolism due to the disruption of cell organelles.

In the form of protein (albumin) accumulation in the cell

- In proteinuri, which occurs in nephritis and nephrosis, the protein (albumin) that cannot be retained in the glomeruli passes into the tubule lumen. In this case, it is resorbed by the tubule epithelium.
- It accumulates in the lysosomes of the tubule epithelium, heterophagolysosomes, appearing in the cytoplasm in the form of hyaline droplets.

Intracellular hyaline

With chronic toxic effect or in dietetic (nutritional) disorders and deficiencies;

- **Mallory (Mallory-Denk) bodies** are formed in the hepatocytes.
- It is in the form of homogeneous-glassy red bodies that give a PAS reaction.
- Toxic hepatosis in animals is characterized by cirrhosis of the liver,
- Especially chronic alcoholism in humans.

Intracellular hyaline

Related to protein secretion disorder in chronic inflammation;

- **Russell bodies** appear in plasma cells in the spleen and lymph nodes.
- On light microscopic examination, these bodies consist of blackberry-shaped hyaline droplets.
- Under the electron microscope, they are arranged like pearls in the ribosomal endoplasmic reticulum cavities.
- Their chemical structure is immunoglobulin.

https://www.webpathology.com/slides-13/slides
HemePath_MM_RussellBody1_resized.jpg

Extracellular hyaline

- This type of hyaline is usually described as hyalinization **"hyalinosis".**
- Most often it is evaluated outside of degeneration.
- The collagen strands of the mesenchymal tissue, the glands and the hyalinization of the basement membranes of the vessels are like this.
- The deterioration of the hyaline, collagen structure in the connective tissue is caused by the formation of poorer quality collagen.
- This situation occurs when the tissue cannot be nourished and the metabolism is disrupted.
- Hyaline in this shape is demonstrated by some special dyeing methods, such as **Van Gieson** staining.

Extracellular hyaline

a. Hyalinization of connective tissue

In old age

- Hyalinization of collagen, heart valves and ligaments in the connective tissue intervals develops in this way.
- It is caused by food intake and slowing down of metabolism.
- It loses its collagen structure and shows abnormal structure, becomes hyalinization.

On the serosa

- Hyalinization of subserous connective tissue
- Especially in the capsula of the spleen, porcelain white foci are encountered. That is why the spleen capsula is seen as "sugar coated spleen".

Extracellular hyaline

a. Hyalinization of connective tissue

In the old scar tissue

- It is formed in the form of hyaline of connective tissue collagen, especially in the serosal regions.
- In keloid and cirrhosis, connective tissue collagen is hyalinized. (Keloid: an area of irregular fibrous tissue formed at the site of a scar or injury.)

Stroma of tumors

- If the stroma is rich in connective tissue and the tumor is benign, the connective tissue in the stroma may become hyalinized.

Extracellular hyaline

b. Hyalinization of the basement membrane and blood vessels

- **In physiological cases**, there is an **age-related** thickening in the basement membranes of the glands, in the media of blood vessels.
- Normally, it is formed in the ovum and uterine veins (artery, arterioles) during ovulation and pregnancy.
- **Pathologically** in the glandular organs, in such cases as fibrosis and cirrhosis; The basement membranes of the glands can become hyalized.
- Especially in metabolic disorders such as **diabetes mellitus** or with **toxic effects** it is formed in the basement membranes of the vessels.

Extracellular hyaline

c. Hyaline in gland lumens and lung alveoli

Hyaline cylinders (casts)

- With regard to proteinuria, it is in the form of cylinders (limited round masses in tissue sections) stained homogeneously red color by hematoxylin eosin staining in the lumen of the kidney tubule.
- It is very common in distal tubules.

Extracellular hyaline

Corpora amylacea

- Loss of the liquid part of the milk secretion in the lumen of the mammary gland and condensation of the protein in it; It is characterized by the fact that pink becomes a mass resembling homogeneous hyaline.
- It is a normal **(physiological)** event.
- It is especially observed in cows that have gone to dry, weaned elderly.
- Also reported formations similar to corpora amylacea, which are caused by the condensation of the secretion of the gland in the prostate.

Extracellular hyaline

Hyaline membrane

- It is a pink, homogeneous mass that surrounds the inner surface of the lung alveoli and terminal bronchi in the form of a membrane.
- It has a mucopolysaccharide structure.
- The main reason is related to insufficient surfactant production and production.
- It is encountered in various congenital or acquired cases.

Extracellular hyaline

Hyaline membrane

- **Congenital;** It may be observed in "idiopathic respiratory distress syndrome" in newborn babies and capillary permeability disorder in newborn animals.
- **Acquired;**
  - Chemical toxic-physical effects (effect of gases), Fog Fever in cattle
  - Metabolic effects (endogenous effect such as uremia)
  - Infectious effects, lung parasites and especially interstitial pneumonias consisting of viral agents are seen as characteristic findings.

Hyaline Degeneration (Zenker Degeneration)

- It is formed in contractile fibrils within the muscle cell.
- It is also called Zenker degeneration, after the name of the definer.
- In some cases, Zenker's necrosis is followed by nothing more than coagulation necrosis.

- **Etiology;**
  - Trauma,
  - Chemical toxic (intramusvular infection),
  - Ischemia,
  - Infection (Foot and mouth disease),
  - Dietary (White muscle disease) effects

Hyaline Degeneration (Zenker Degeneration)

Grossly;

- The muscles initially have a light pink color and crunchy consistency.
- Later it turns into the yellowish brown in color; with air contact it takes on the appearance of fish or chicken meat.

Hyaline Degeneration (Zenker Degeneration)

Histologically;

- Muscle cells and nuclei are bulging.
- First, its contractile fibrils are coarse, eosinophilic and fragmentary in appearance.
- Then it is formed into Zenker's necrosis, when the sarcoplasma becomes a completely eosinophilic homogeneous mass and its nucleus is destroyed.
- Depending on the case-by-case, inflammatory reaction related to the cleaning of necrosis, repair of the area and reparation related to regeneration, dystrophic calcification and granulation tissue are also added.

Foot and Mouth Disease

- Picornaviridae-Rhinovirus-Aphtovirus
- It is mainly a disease of cattle (ruminants).
- **In adults**, the virus has **epitheliotropic** character.
- The findings are mostly located in the oral mucosa and its surroundings, breast skin and feet (interdigital region).
- **In young animal** (calves, lambs, capricorns), the virus acquires **myotropic** characteristics and locates in the heart (myocardium), leading to death.
- Myocarditis intersitisyalis nonpurulenta characterized by lympho-histiocytic cell infiltration in the heart muscle is observed.
- Hyaline degeneration and necrosis of myocardial cells are also formed.
- The heart muscle is seen like "tiger skin" (Tigroid)

White muscle disease

- It is especially frequent and important in lambs and goats. It is also seenin calf, foal, camel and ducklings and chicks.
- It is a **nutritional disease** characterized by dystrophic disorders in the heart and skeletal muscles (hyalin-zenker degeneration and zenker necrosis).
- It is a **deficiency of vitamin E** (d-tocopherol) and **selenium.**
- Selenium and vitamin E alone or together prevent the formation of peroxide from unsaturated fatty acids.

White muscle disease

- **Selenium is the essential factor.** Glutation reduces lipid peroxides to lactic acid by means of peroxidase. The harmful effect of these on the cell membrane is prevented.
- **Vitamin E is an antioxidant**. It prevents the formation of high concentrations of peroxide from fatty acids.
- Without selenium and vitamin E, **peroxide damages the cell membrane, hyaline degeneration and then necrosis develops**.
- Insufficiency of vitamins A, C and some amino acids in the formation of the disease is also considered.

White muscle disease

- It is mostly localized in certain muscle groups (lumbal, dorsal, extremity muscles, heart muscle, diaphragm, and sometimes pharyngeal muscles).
- It is characterized by **resorbtive-regenerative and reperative changes in animals that survive with hyaline degeneration (Zenker's degeneration), necrosis (Zenker's necrosis), dystrophic calcification.**

White muscle disease

- The muscle groups initially have a light pink color and a crunchy consistency.
- In advanced cases, the affected muscles are yellowish and brown in color.
- When in contact with air, it takes on the appearance of fish or chicken meat.
- Lesions can sometimes be in the middle of muscle groups or limited to several muscle groups.
- There are radial, yellowish brown lesions in the diaphragm.
- If localized in the muscles of the chest and larynx, due to difficulty swallowing, aspiration pneumonia (gangrenous pneumonia) occurs as a result of improper swallowing.

White muscle disease

- In the heart, it is most often localized in the interventricular septum, musculus papillaris, both ventricles.
- Lesions are close to the subendocardial and epicardial regions.
- The muscle changes in these areas are similar to those in skeletal muscles.
- It then undergoes dystrophic calcification; widespread calcification, especially under the endocardium, is encountered.
- As a result of these changes, hypertrophy in the heart, edema in the lung and passive hyperemia (congestion) occur.

Equine exertional rhabdomyolysis

- Tying-Up, Monday Morning Sickness/Disease, Azoturia myoglobinuria, sacral paralysis, Lumbago
- Signs may appear during or immediately after exercise, but only rarely is exertional rhabdomyolysis associated with exhaustive exercise.
- High grain feeding and lack of regular exercise.
- It is seen in the glycogen-rich lumbal, gluteal, scapular and upper limb muscles.
- As a result of the intake of carbohydrate-rich foods at rest, glucose accumulates in the muscles in the form of glycogen.

Fibrinoid Degeneration and Necrosis

Fibrinoid degeneration

- Fibrinoid is a substance that is formed by the degeneration of collagen in various organs and tissues.
- It occurs especially in the wall of blood vessels and connective tissue. In hematoxylin-eosin staining, it is bright, eosinophilic (red), homogeneous in light microscopy. The reason it is called fibrinoid is because it stains like fibrin.
- But although fibrin is sometimes present in its structure, it has nothing to do with fibrin.

Fibrinoid degeneration

- Collagen disorder is always occur extracellular.
- **Structure:** Degraded, fragmented collagen, proteoglycan or its residues (mucopolysaccharide acid [glycosaminoglycan, hyaluronic acid]), serum proteins from the blood (especially globulin), antigen antibody complexes, some fibrin and fibrin intermediates and fibrinogen.
- Since it is always seen in inflammatory, allergic, necrotic phenomena, in addition to these, there are also fragments of destroyed cells, residues, chromatin from the blood.

Etiology and pathogenesis

- Especially often develops in **hypersensitivity reactions (allergic reaction)**, on the vessel wall or in connective tissue-rich areas of various tissues.
- Most often, it is based on **immunological effects**, such as the collapse of antigen-antibody complexes on the walls of the vessels.
- In addition, **toxic effects and infectious effects that disrupt vascular permeability** are among the causes.
- **In nodules formed in rheumatism; It is seen in the wall of medium-sized arteries in Malignant catarrhal fever, in the wall of artery that develops in the stomach in uremia, in the equine viral arteritis and bovine Ephemeral fever in the vessel walls.**

Pathomorphology

- There are three following forms: **Fibrinoid bloating-fibrinoid precipitation and fibrinoid necrosis.**
- Collagen firstly swells; it is seen in the form of fiber under the light microscope. Then the substances that come out of the veins and are mentioned above locate between them. Then the collagen is broken down and a mass consisting of these substances and other destruction products of the tissue is formed. This is called **fibrinoid necrosis.**

Rheumatism

Rheumatoid granuloma

- In polyarthritis cases.
- It is histomorphologically defined as a subcutaneous palisading granuloma with central fibrinoid necrosis.

Aschoff Bodies

- They found in the hearts of individuals with rheumatic fever.
- They result from inflammation in the heart muscle and are characteristic of rheumatic heart disease.
- Anitschkow cells are enlarged macrophages found within granulomas (called Aschoff bodies) associated with the rheumatic heart diseases.

Equine viral arteritis

- ***Togoviridae-pestivirus-equine arteritis virus***
- It is characterized by high fever, leukopenia, edema and conjunctivitis of the eyelid, edema of the legs, pulmonary edema, hemorrhagic enteritis, colic or respiratory, catarrhal inflammation of the digestive systems.
- Vascular lesions occur with fibrinoid necrosis in the media of medium-sized vessels (arteries) in organs and tissues such as the intestinal wall, lymph nodes, adren.
- Since vascular endothelium is not disturbed, thrombosis does not occur.
- However, edema, lymphocytes and granulocytes are seen in vascular adventitia layer.

Coryza Gangrenosa Bovum

- The causative agent is herpes virus type 3.
- The disease occurs sporadically.
- In the clinic, there are such forms as acute form (high fever, death), acute intestinal form, head-eye form, abortive form (the form in which the signs of the disease are not pronounced).
- Clinical findings such as fever, keratoconjunctivitis, nasal discharge, corneal opasity, diarrhea, nervous findings are seen.

Coryza Gangrenosa Bovum

- **Grossly;** Necrosis and erosions of the lips-gums; nose, pharynx, larynx, trachea, bronchi pseudomembrane formation, petechial hemorrhages, nonpurulent meningoencephalitis, interstitial nonpurulent nephritis.
- **Fibrinoid necrotic vasculitis** in medium-sized vessels.
- Mononuclear cell infiltration occurs in the vascular adventitia layer.
- Since the vascular endothelium is also impaired, thrombosis also develops.
- These changes are **pathognomonic** for this disease.

Uremia

- **Chronic nephritis** in dogs, fibrinoid necrosis occurs in the uremia, especially in the arteries in the stomach.
- Grosslly; gray-yellowish discoloration and thickening on the vessels wall.
- Nodular swellings are seen.
- Histopathological examination reveals **fibrinoid necrosis** in the media and adventitia.
- In uremic gastritis, besides vascular changes, necrosis of the mucosa, edema and linear calcium deposits and neutrophil infiltration are seen between the glands
- **Uremia also causes gastric bleeding**.

Bovine Ephemeral Fever
(Three Day Sickness)

- Bovine ephemeral fever virus (BEFV) an arthropod-borne **rhabdovirus** which is classified as the type species of the genus ***Ephemerovirus*****.**
- It causes an acute febrile illness of cattle and water buffalo.
- It is characterized by **fibrinoid necrosis in the vessels.**

Mucus and Mucoid Degeneration (Mucoid connective tissue dystrophy)

Mucus

- It is a sticky, transparent, gelatinous substance.
- Structure: mucopolysaccharides, nucleoproteins.
- Related to the nucleoproteins, it stains blue in HE slides.
- As the amount of protein in its structure increases, its color becomes red.
- **Mucus** is a secretion of the mucous glands.
- Some secretion of mucus from the mucous glands is physiological.
- For example, rhinitis in which exudate is found cell debris, and inflammatory cells mixed with mucus, are called catarrhal inflammation.

Pseudomucin

- It is especially observed in degenerative changes and neoplasms of the gland epithelium.
- There are masses similar to mucus in adenocarcinoma of the bile ducts, cystadenoma of the ovary.
- But these masses are pseudomucin.
- Histologically, it is stained red instead of blue with HE due to other substances.

Mucoid degeneration

- **Mucoid** (mucus-like), macroscopically, it is similar to mucin.
- Its chemical composition is glycosaminoglycan (mucopolysaccharide).
- It is an **amorphous** substance. (Methylene blue, toluidine blue, alcian blue)
- It is formed by increasing the amorphous ground substance of the connective tissue or expanding it by taking in water.
- It is caused by collection of a substance similar to mucin in connective tissue; the degeneration and melting of the tissue parts in the region (especially elastin, collagen melting and breakdown).

Mucoid degeneration

Morphologically;

- Developed connective tissue resembling embryonal tissue again; it is characterized by acquiring a loose, gelatinous, jelly-like, appearance.
- Since it takes on a loose appearance, like embryonal connective tissue, it has also been called **myxomatous degeneration.**

Mucoid degeneration

- It is seen in collagen tissue diseases.
- In addition to fibrinoid degeneration, mucoid degeneration is also seen in rheumatism.
- Therefore, it is located in organs and tissues that have more connective tissue.
- Between the heart and skeletal muscle bundles or between the smooth muscle bundles in the arteries wall;
- It is observed in areas of loose connective tissue under seroza and other membranes.
- The seroses have a bulging, jelly-like appearance.
- It is in the form of a large, gelatinous-yellowish mass in the subserosal loose connective tissue.

Mucoid degeneration

- If it happens in adipose tissue, the fat cells that degenerate and draw water take on an aqueous appearance.
- It occurs especially in areas where the coronary vessels of the heart are located.
- Instead of mucoid degeneration, it is called mucoid fat atrophy or serous fat atrophy, "edema exvacua".
- The adipose tissue has a yellowish color, gelatinous, juicy appearance.
- In HE slides, it is stained red rather than blue.

Mucoid degeneration

- Toxic effects, the main reason is protein deficiency.
- Senile (old age) atrophy is related to nutritional deficiency (protein deficiency).
- Sometimes it can occur in the connective tissue and ligaments in the scar.
- In myxoma, the amorphous structure between them is mucoid.
- It occurs due to protein loss in cachexia.
- It occurs most often in myxomatosis, which is caused by pox viruses in rabbits.
- Dystrophic calcification and metaplastic ossification are seen in the duramater of M. spinalis in dogs.

LIPID METABOLISM DISORDERS

- Decrease and increase of fat in adipose tissues
- Increase and decrease in blood lipids
- Fat changes except adipose tissues
- Hereditary enzymopathies
- Disorder of cholesterine metabolism
- Fat necrosis (Steatonecrosis)
- Fatty degeneration

Decrease and increase of fat in adipose tissues

Obesity

Adipositas

Cachexia

Ketonemia

Blood lipids

- Lipids circulate in the blood bonded to protein.
- These are triglycerides, cholesterol and phospholipids.
- It is made in the liver and given to the blood.
- It decreases and increases in these situations; such as age, nutritional status, gender, hormones and stress.
- **VLDL, LDL, HDL**
- VLDL and LDL accumulate in the vessels and cause atherosclerosis.

Hyperlipidemia

Alimentary

- After digestion, it increases physiologically.

Non-alimentary

- Inadequate processing and transport of the lipids ingested; releasing from the fat stores; disruption of lipid synthesis in the liver.
- **Primary** (as a result of hereditary enzymopathies)
- **Secondary** (Starvation, diabetes mellitus, pancreatic necrosis, hyperthyroidism)

Fat changes except adipose tissues

- Physiological-Pathological
- Physiological accumulation of fat in cells;
  - **Especially after digestion in the liver**
  - Zona fasciculata cells in the adrenal cortex
  - Stomach gland epithelium
  - Skeletal muscles
  - Glands in the skin
  - Kidney tubular epithelium

Lipomatosis

- It is characterized by infiltration of non-neoplastic fat cells (lipocytes) into the interstitium of the parenchymal organs.
- It is formed in tissue parts close to the fat storage.
- **Lipomatosis cordis:** Adipose tissue around the heart, infiltration from the epicardium to the interstitium between the heart muscle
- Adipose tissue under the skin can also infiltrate between the muscles.

Extracellular lipid accumulation

- It is characterized by the presence of fat, not lypocytes, between cells.
- With the disruption of lipocytes or other lipid-containing cells; The fat (phospholipids and triglycerides) contained within these cells accumulate in tissue. It is phagocytosed by macrophages.
- Cholesterol crystals are dissolved out of the tissue specimen during histologic processing, leaving characteristic acicular (needle-shaped) clefts **(Cholesterol clefts)** in histologic sections.
- Fat is phagocyted by macrophages in such cases as the disruption of fatty tissues, necrosis, direct outflow of fat into tissue spaces, degeneration of fatty cells. These cells are called lipophagic cells **(foam cells). E.g.: Gitter cell, Xanthoma cells**

Fat necrosis (Steatonecrosis)

- Enzymatic necrosis of fat.
- It is seen mainly in peripancreatic adipose tissue, where it is attributed to release of lipases from necrotic pancreatic acinar cells
- In pancreatic diseases such as acute hemorrhagic pancreatitis, pancreatic necrosis

Fat necrosis

Grossly;

- Necrotic adipose tissue becomes firm and nodular with off-White chalky deposits, the result of saponification (soap formation).

Fat necrosis

Microscopically,

- Fat necrosis elicits inflammation that consists mainly of lipid-laden macrophages and variable number of neutrophils.

Necrosis of adipose tissues in other parts of the body

- The **pancreatic enzyme is not responsible**.
- It occurs from physical effects, chemical effects, and sometimes infectious causes.
- In **trauma**, subcutaneous fatty tissue is disrupted.
- Neutral fats accumulate extracellular. An inflammatory reaction to the accumulated fat occurs. (Lipophagic cells, foreign body giant cell-granulation tissue)
- It is most commonly observed in the subcutaneous fatty tissue in areas such as udder, abdomen, extremities.

Disorders of cholesterine metabolism

- Arteriosclerosis in humans
- Generalized or localized
- Familial Hypercholesterolemia
- Cholesterine is found in the artery wall, interstitial tissue and Kupffer cells.
- Cholesterin crystallizes and forms Xanthoma in the media and intima layer of the vessels, and in the tissue
- Xanthoma– light tan to yellow papules, plaques, or nodules

Lipidosis

- It is characterized by the accumulation of lipid and lipid metabolites in cell phagosomes as a result of genetic enzymopathy.
- **Mostly in nervous system**; rarely in the mononuclear phagocytosis system (MPS), skeletal muscle, skin and liver cells.
- Hereditary lipidosis is caused by the defect of enzymes involved in the metabolism of complex lipids, especially **ganglioside, cerebroside**, etc.
- For example, the cerebroside is found in the structure of the myelin. In its deficiency, myelin is disrupted and phagocytosed by macrophages.

Fatty degeneration

- Except for physiological fat, the fat in the cells is invisible by binding to other substances such as protein.
- This is called "masked fat".
- The fact that the masked fat in the cell becomes visible is called **"fat phenerosis".**
- In such cases, both invisible fat is seen in the form of fat vacuoles and other morphological changes occur in the cell.
- It is **most common in the liver.**
- **Main causes**; Excess fat coming from the intestines, excess fatty acids coming from fat deposits, Degradation of fat metabolism, Degradation of fat transport from the liver

Etiology

Hypoxia

- Anemia
- Carbonmonoxide poisoning
- Blockage of blood flow in V. centralis
- Passive hyperemia related to heart failure
- Centrilobular fatty liver- panlobular

Toxication

- Various toxins that come to the liver vi hematogenous
- Bacteria, fungal toxins
- Chloroform, phosphorus
- Peripheral of the liver lobes
    - Hepatitis
    - Ketosis
    - Diabetes

Gross findings

- The liver is swollen, yellow, the edges are blunted; its consistency is crispy and fragile.
- Trauma-rupture- Hemoabdomen-death
- The lobule structure cannot be easily distinguished.
- The liver is anemic when bulging lobes exposure pressure on the vessels.

Microscopical findings

- In acute cases; the fat vacuoles are small in the cell .
- In chronic cases; since the effect is continuous, these vaculoes merge and form large vacuoles.
- lipid vacuoles (sharply defined and unstained because the lipid is leached by the solvents of histologic processing)
- **Sudan III**, Oil Red O staining
- Nuclear morphological changes are important in diagnosis.
- Nucleus is swollen. Karyorrhexis and karyolysis are seen. If large vacuole occur in the cytoplasm, displace the nucleus to the periphery of the cell.

Fatty degeneration in kidney

- Hyperlipidemia, increasing of fat resorption, toxicity (CCl4), hypoxia, circulatory disturbance
- Tissue is pale and friable.
- Physiologic; in cats and rarely in dogs (lipid vacuole in kidney tubules)

Fatty degeneration in heart

- Toxication, hypoxia, circulatory disturbance
- **In Lipomatosis cordis**; when muscle cells remain under pressure, fatty degeneration is also seen.
  - Myocardium has tigroid appearance
  - Lipocytes in the myocardium
- Myocardium is pale.
- Lipid vaculoes and nuclear changes.

CARBOHYDRATE METABOLISM DISORDERS

- Mostly;
- Increase or decrease in glucose in the blood,
- Increase or decrease in glycogen in tissues with glycogen.
- Accumulation of glycogen in tissues without glycogen.
- These disorders are caused by the deficiency of necessary enzymes and hormones in glycogen metabolism, or dysfunction of glycogen metabolism.

Hypoglycemia

- Decrease in blood sugar.
- In the administration of iatrogenic insulin,
- In neoplasms, such as insulinoma (beta-cell tumor of the pancreas),
- Liver diseaes
- prevention of gluconeogenesis by the effect of insulin antagonists
- It occurs due to over-released insulin.
- The brain is most affected by glucose deficiency and convulsions occur.

Hyperglycemia

- Increase in glucose in the blood.
- Resorbtive glycemia after nutrition.
- Nervous and hormones in stress (such as adrenaline), a temporary hyperglycemia may occur in the blood.
- A persistent hyperglycemia is observed in diabetes mellitus.

Diabetes mellitus

I. Primary

- Type I-Diabetes mellitus
- Type II-Diabetes mellitus

II. Secondary

- Due to the reasons affecting the production of insulin
- Non-pancreatic form

Type I-Diabetes mellitus

- It is related to insulin deficiency.
- It is also defined as "juvenile diabetes mellitus" because it is mostly seen in children and adolescents.
- It is related to a disorder (deficiency, disorder, or absence) of beta cells of the pancreas.
- It occurs mainly in dogs.
- In the treatment, insulin hormone is given externally.

Type II-Diabetes mellitus

- It does not depend on the insulin.
- Beta cells and blood insulin levels may be normal, or even increased.
- However, insulin cannot act on target cells.
- Insulin receptors are few in hepatocytes, they show resistance to insulin.
- Autoantibodies against insulin are responsible.
- This type is not often observed in animals.
- Adult type diabetes is seen in humans.
- It cannot be treated by administering insulin.

Due to the reasons affecting the production of insulin

- Pancreatitis, which results in pancreatic necrosis and cirrhosis,
- Pancreatic neoplasms,
- Amyloidosis in Langerhans islets. (diabetes mellitus in cats 80%)

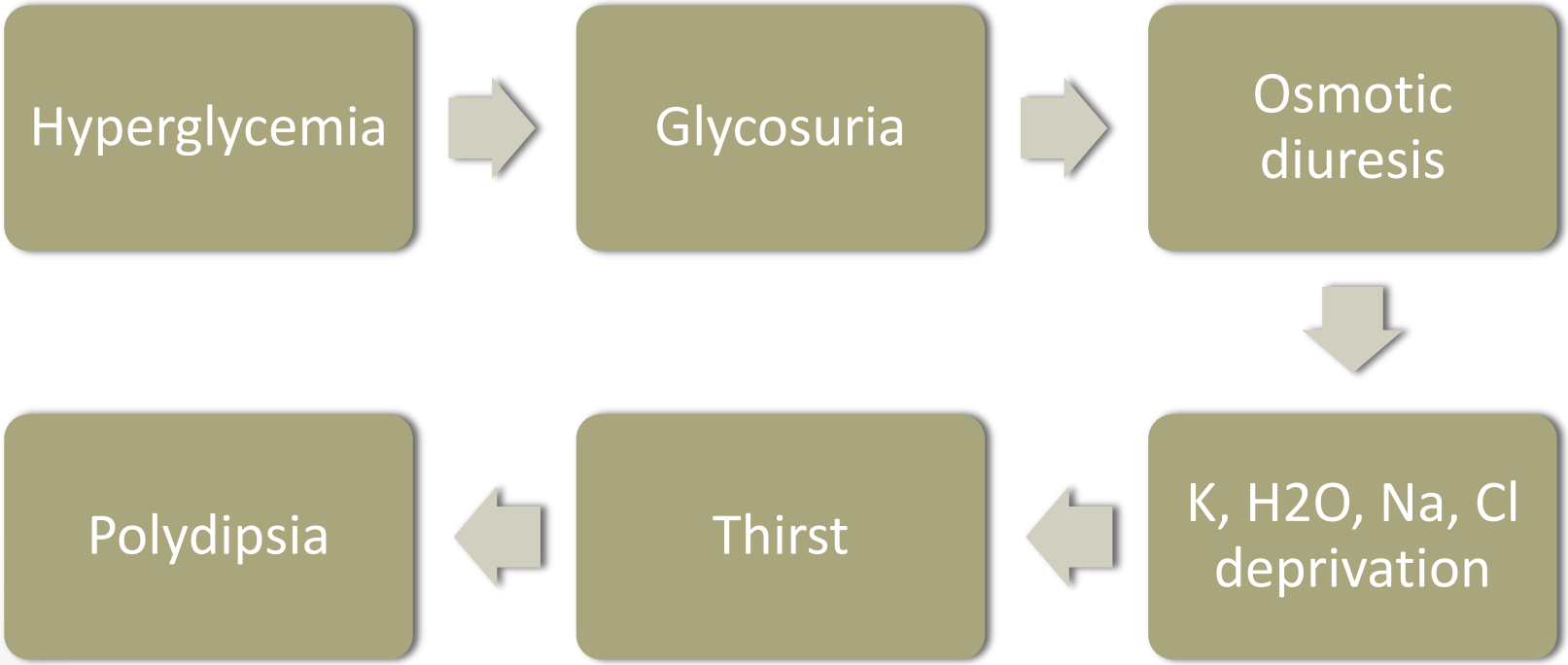
Non-pancreatic form

- It is seen in **Cushing's syndrome (disease)** in older dogs.
- Iatrogenic hyperadrenocorticism is the result of glucocorticoid therapy, which results in decreased ACTH secretion and adrenocortical atrophy.
- Spontaneous Cushing’s syndrome, in contrast, is usually the result of ACTH secretion by hyperplastic or neoplastic adenohypophyseal (anterior pituitary gland) corticotrophs, which causes adrenocortical hyperplasia.
- Functional adrenocortical adenomas or carcinomas are a less common cause of canine Cushing’s syndrome.
- Increased gluconeogenesis, lipogenesis, and protein catabolism explain many of the clinical signs and lesions.

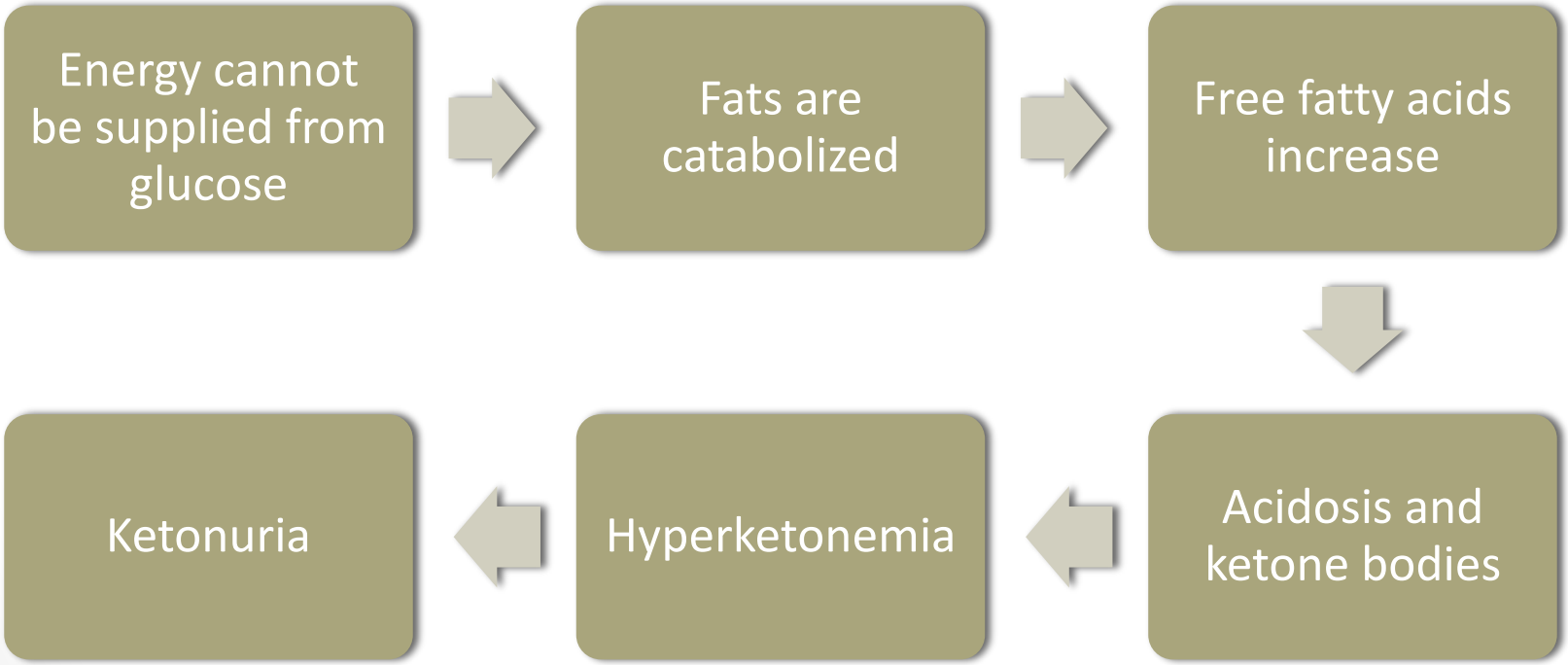
Non-pancreatic form

- Over-released glucocorticoids both occur adipocytosis and increase gluconeogenesis.
- It is seen that the beta cells in the islets of Langerhans destroy their structure as a result of continuous effects and undergo hydropic degeneration, and as a result, insulin decreases.
- Long-term cortisone administration in dogs for therapeutic purposes and growth hormones that prevent progesterone have a similar effect.

The end of diabetes mellitus



The end of diabetes mellitus



The end of diabetes mellitus

- Arteriosclerosis
- Angiopathy in small vessels.
  - Uremia as a result of glomerulosclerosis in kidney.
  - Hydrarthrosis
- Blindness
- Vascular disorders in the brain and heart
- Articular disorders are seen.

Glycogen accumulation and reduction in tissues

Glycogen and fixation

- Liver, skeletal muscles, cartilage and stratified squamous epithelium
- Tissue samples are fixed in dextrose saturated formalin solution, absolute alcohol, 70% alcohol.
- Frozen section (Cryostat)
- It is not stained with hematoxylin&Eosin (HE) and appears in the cytoplasm as light-colored areas or vacuoles. (irregular and amorphous)
- Sometimes vacuoles can also be found in nuclei.
- These features distinguish glycogen accumulation from lipidosis and hydropic degeneration.
- Glycogen is stained in bright pink color with **"Best's carmine".**
- The PAS staining method can also be used.

Glycogen Accumulation

- Glycogen is usually stored in the liver, kidney, heart and skeletal muscles; rarely in the spleen, lymph nodes, brain and smooth muscles.
- Hyperglycemia
- Chondroma-Chondrosarcoma
- Diabetes mellitus or canine hyperadrenocorticism
- Glycogen storage diseases.
- Nodular hyperplasia in the liver (in dogs over 10 years)
- Hyperglycemia and glycosuria develop in some intoxications and clostridial enterotoxemia.
- This condition is related to the excessive breakdown of glycogen in the liver (glycogenolysis)

Glycogen Accumulation

- **Physiologically,** increase in uterine secretion during pregnancy in humans, glycogen is collected in stromal cells in the uterine mucosa.
- These cells are called **decidual cells**.
- The increase of these cells is also called a **decidual reaction.**

Decrease in glycogen in tissues

- **Strychnine poisoning**--muscles
- **Starvation**--muscles and liver
- During the **lactation** period in cows
- **Ketosis and diabetes mellitus-**-liver

Glycogenosis type II (Pompe disease)

- It occurs in deficiency of the lysosomal enzyme **glucosidase (alpha 1,4 glucosidase = maltase).**
- It mostly occurs in liver, brain and muscle cells.
- Glycogen accumulates in the lysosomes of cells.
- Glycogenosomes (glycogen bodies), intracellular
- It has been found in cats, calves and quails.

Glycogenosis type III (Cori disease)

- is an autosomal recessive disease that results from deficiency of the glycogen debranching enzyme, **amylo-1,6-glucosidase.**
- It occurs mainly in German shepherd dogs.
- Glycogen is stored in the cytosol of hepatocytes.
- In addition, myocardium, skeletal and smooth muscle cells and nerve cells are also found to accumulate small amounts of glycogen.
- Hepatomegaly and hypoglycemia occur.

Glycogenosis type IV

- Inherited abnormality of glucose metabolism that is seen in Norwegian Forest cats.
- It occurs as a result of a deficiency of the **branching enzyme (amylose transglucosidase)** in the glycogen molecule.
- Glycogen accumulation is observed, especially in the heart and skeletal muscle.
- Stillbirth or death within a few hours of birth.
- Degeneration and atrophy in the heart and skeletal muscles are observed in cats.

Glycogenosis type VII (Tarui disease)

- Inherited metabolic disorder affecting English Springer Spaniels.
- It occurs as a result of deficiency of the **phosphofructokinase enzyme.**
- Intravascular hemolysis, hemoglobinuria, hemolytic anemia, reluctance to move, muscle weakness, cramp
- Histologically, muscles are pale and PAS positive material accumulation is seen under the sarcolemma.

Keratinization Disorders

Keratin

- It is found in the skin epithelium and other skin appendages such as hair, horns, nails that originate from the skin.
- It is the structural protein of epithelial tissue.
- It is not excreted from the cell, it matures until the death of the cell and is shed.
- Since keratin matures and multiplies to the surface in the skin epithelium, granules (keratohyaline) in the stratum granulosum layer; it is found in a common layer in str. lucidum and str. corneum.
- It stains red with HE.

Dyskeratosis

- It is called disorders such as an increase or decrease in keratin.
- It occurs in two ways:
  - **Hyperkeratosis:** Increased keratinization
  - **Hypokeratosis:** Decreased keratinization, keratin deficiency

Hyperkeratosis

- Cornification ≠ Carnification
- Orthokeratotic hyperkeratosis refers to the thickening of the keratin layer with preserved keratinocyte maturation, while parakeratotic hyperkeratosis shows retained nuclei
- Congenital (due to a genetic disorder) or acquired
- Generalized or localized

Generalized hyperkeratosis

- **Ichthyosis congenita**
  - Heterogeneous group of inherited skin disorders seen principally in cattle and dogs.
  - In severe forms of ichthyosis the skin is thickened by marked scaling and can crack into plates resembling fish scales.
  - Thus the disease is named “ichthys” from the Greek word meaning fish.
  - The skin is dry, usually hairless and thickened.
  - Most calves are stillborn or die within days of birth.

Hyperkeratosis

- **X-disease or Bovine hyperkeratosis**
- Lesions of **chlorinated naphthalene toxicity** are the result of the interference of the conversion of carotene to vitamin A and result in vitamin A deficiency.
- Vitamin A is necessary for normal differentiation of stratified squamous epithelium.
- Clinical lesions consist of alopecia and lichenified, fissured plaques of scale that spare only the legs.
- Histologic lesions consist of marked hyperkeratosis of the epidermis and follicles.
- Squamous metaplasia of the epithelial lining of the glands and ducts of the liver, pancreas, kidneys, and reproductive tract also develop.

Hyperkeratosis

- **Hypovitaminosis A in birds**
  - Oral mucosa and esophagus has the property of the cutaneous mucosa
  - The esophageal gland epithelium is single cubic layered.
  - These epithelium undergo metaplasia and first turn into a stratified squamous epithelium and then into a keratinized stratified squamous epithelium.
- **Leukoplakia:** White patches on a mucosal membrane
- **Colpokeratosis:** Keratinization of the mucous membrane of the vagina.

Local hyperkeratosis

- Local hyperkeratosis occurs on the skin that is under pressure continuously or intermittently. It is called **callus.**
- **Cornu cutaneum** (Cutaneous horn)
  - It is most common in cattle, sheep and poultry.
  - It is located more in the head, ears, mammary regions.
  - Horn-like protrusion is formed on the skin.
  - There is no pedicle and not attached to bone tissue.

Parakeratosis

- Retention of pyknotic nuclei in epidermal cells of the stratum corneum
- The skin is prone to crusting and dermatitis occurs as a result of secondary infections.

Parakeratosis in pigs

- The disease is caused by a relative deficiency of zinc and consumption of excessive calcium.
- **Differential diagnosis:** Exudative dermatitis, sarcoptic mange