# Respiratory system pathology

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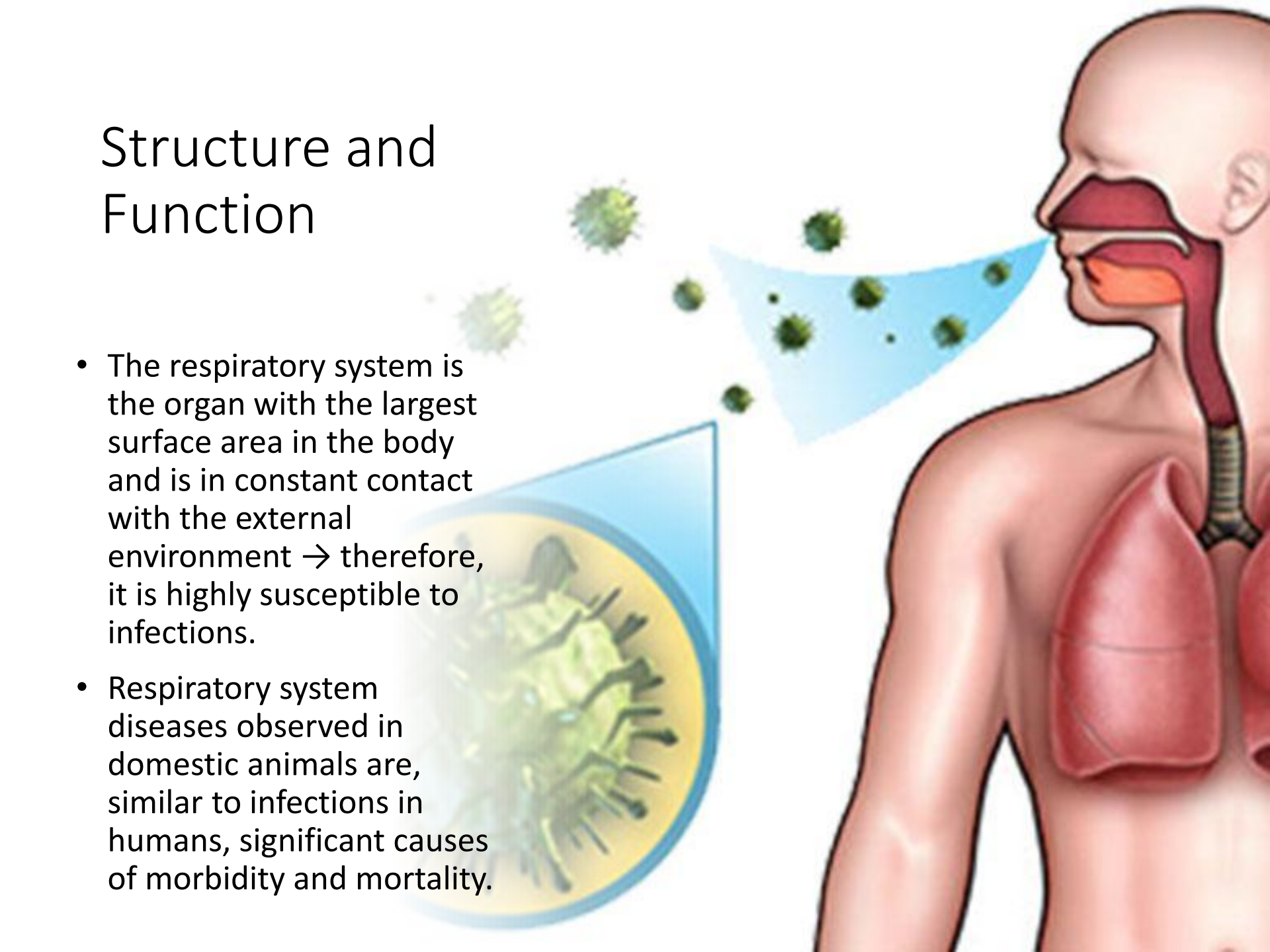
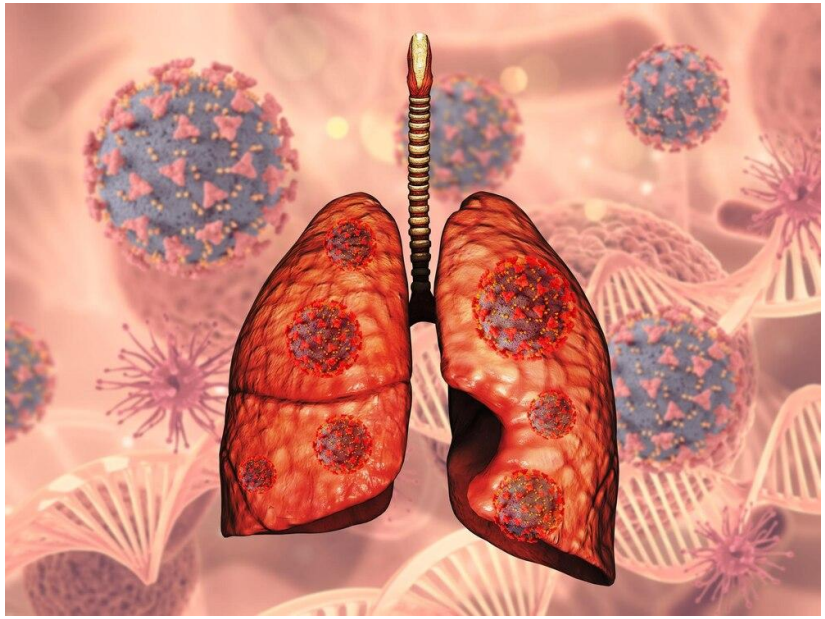
# Structure and Function

- The respiratory system is the organ with the largest surface area in the body and is in constant contact with the external environment → therefore, it is highly susceptible to infections.
- Respiratory system diseases observed in domestic animals are, similar to infections in humans, significant causes of morbidity and mortality.

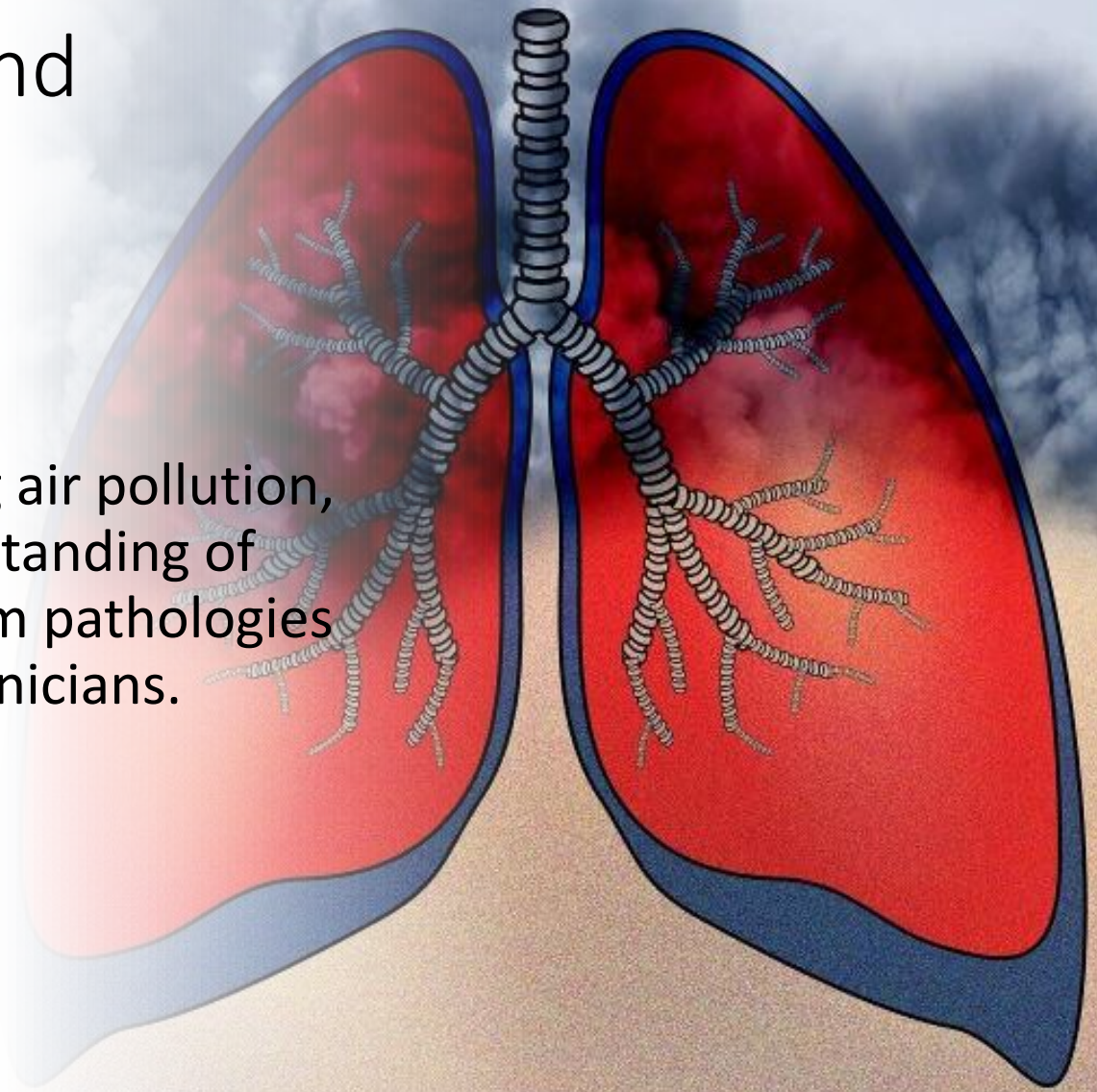


# Structure and Function

- The respiratory system cannot be directly visualized or palpated; therefore, the diagnosis of infections is generally estimated through the examination of tissues.
- Since the organism responds to inhaled microorganisms and toxins with limited mechanisms, making a diagnosis based on pathomorphological changes is often challenging.



# Structure and Function



- Due to increasing air pollution, a detailed understanding of respiratory system pathologies is essential for clinicians.

# Structure and Function

- The respiratory and cardiovascular systems are closely interconnected; examining them separately carries a risk of diagnostic error.

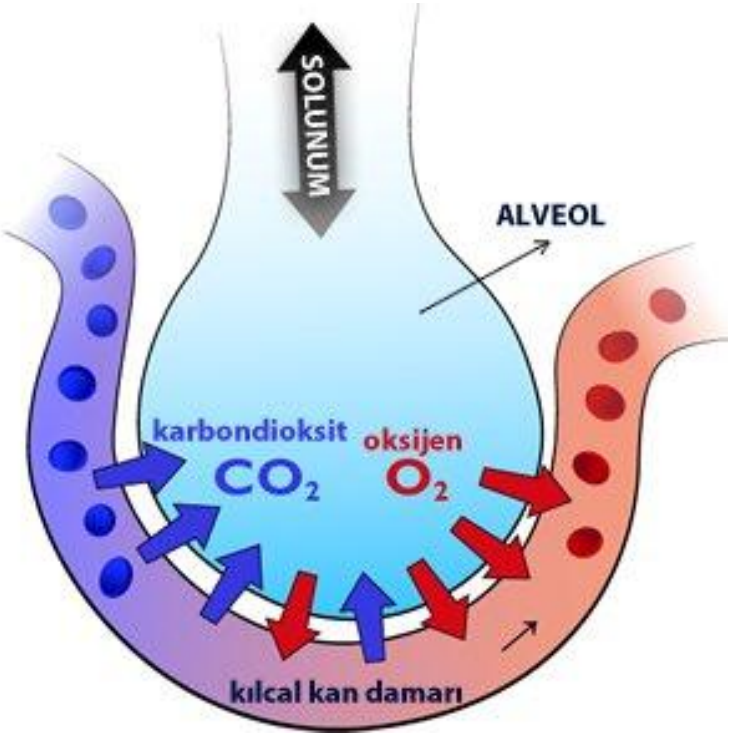
# Structure and Function

- The respiratory system is responsible not only for gas exchange but also for immunological and metabolic functions.

- Immunosuppressive drugs or viral infections (AIDS, BVD/MD, distemper) facilitate the development of pneumonia.

# Structure and Function

- The pulmonary capillary beds have a large surface area of approximately 70 $m^2$, and this area is important not only for gas exchange but also for metabolic and immunological functions.



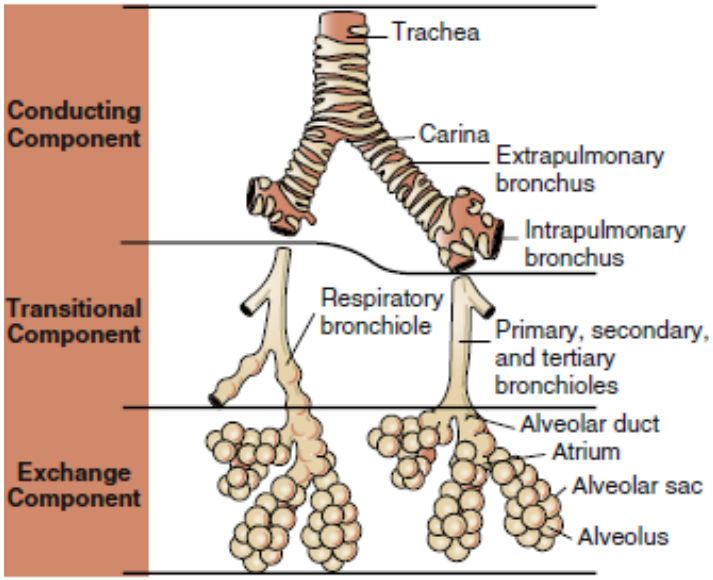
# Structure and Function

- Gas exchange
- Olfaction
- Sound production
- Regulation of air temperature, humidity, and acid-base balance
- Phagocytosis of foreign particles
- Activation of the defense system
- Blood reservoir
- Adjusts the composition of blood going to the heart and circulation or metabolizes other bioactive material.

# Components of the Respiratory System

## 1- Conducting component

- Nostrils
- Nasal cavity
- Paranasal sinuses
- Nasopharynx
- Trachea
- Extrapulmonary bronchi
- Intrapulmonary bronchi
- These structures are mostly lined by pseudostratified ciliated columnar epithelium and contain varying proportions of goblet (mucus) cells and serous cells.

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# Components of the Respiratory System

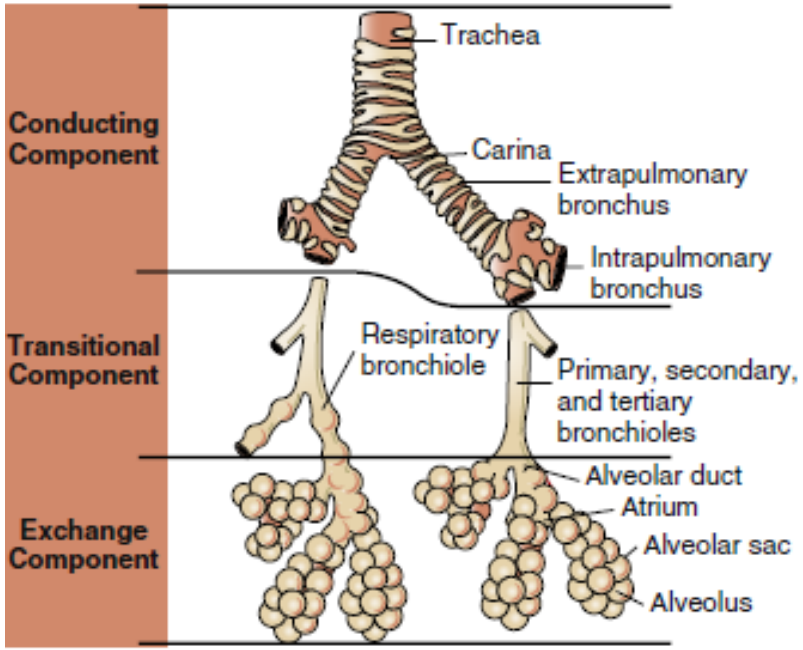
## 2. Transitional Component

- Bronchioles
  (Provides transition between the conducting system and the gas exchange region)
- **Cilia**: Decrease proximally and disappear completely distally.
- **Goblet cells are absent** → instead, **Club (Clara) cells** and **neuroendocrine cells** are present.
- **Club cells**:
- Detoxification of xenobiotics (similar to hepatocytes)
- Serve as stem cells in the repair of bronchioles and lungs
- Contribute to innate immunity (secretion of collectin, surfactant)
- **Respiratory bronchioles**: Especially seen in carnivores and primates; lined by cuboidal epithelium + alveolar capillaries and segment the terminal bronchioles into respiratory bronchioles.

# Components of the Respiratory System

## 3. Air Exchange Component

**In all mammals, the gas exchange region of the respiratory system consists of alveolar ducts and millions of alveoli.The alveolar surface is lined by two distinct types of epithelial cells: Type I (membranous) pneumocytes and Type II (granular) pneumocytes.**

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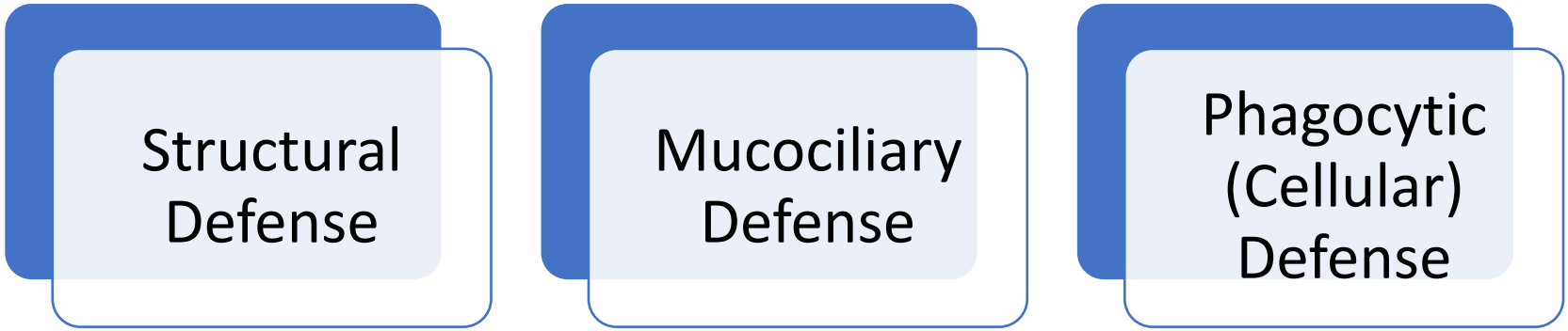
# Components of the Respiratory System

**Type II alveolar epithelial cells**
(granular/secretory pneumocytes) make up approximately 40% of alveolar cells but cover only a small portion of the surface.
They are the source of Type I cells and provide regeneration in case of injury.
Alveolar **epithelialization, fetalization**, and **hyperplasia** are associated with these cells.

Type II cells secrete **pulmonary surfactant** to prevent alveolar collapse.
Surfactant deficiency (especially in premature individuals) can lead to respiratory failure and death.

The function of Type III (brush) cells, which are present in some species, is unknown.

# Defense Mechanisms/Barrier Systems



# Structural Defense

- The upper respiratory tract traps large particles; the cough reflex and bronchoconstriction also contribute to this defense.

# Mucociliary Defense

- Mucociliary clearance enables the removal of particles and gases from the respiratory tract.
It is the primary defense mechanism of the nose, trachea, and bronchi.
- Mucus is a complex fluid produced by goblet cells, serous cells, and submucosal glands.

# Phagocytic (Cellular) Defense

- There are no ciliated or mucus-producing cells in the alveoli; therefore, the clearance of particles is slow.
- The primary defense is provided by **alveolar macrophages**, which phagocytose inhaled particles.

# Phagocytic (Cellular) Defense

- **Alveolar macrophages** originate from monocytes that migrate to the lungs and mature within the interstitial space.
- They can also be generated through local macrophage proliferation.
- They are adapted to function in an aerobic environment.
- During inflammation, they differentiate from monocytes and rapidly phagocytose bacteria and particles in the alveoli.
- The number of macrophages is closely related to the particle load reaching the lungs.

# Disruption of Respiratory System Mechanisms

- **Alterations in mucociliary clearance**
- Dysfunction of alveolar macrophages
- **Toxic gases**
- **Hypoxia, pulmonary edema, dehydration, anesthesia, peritonitis**
- **Acidosis, uremia, starvation, hypothermia, endotoxemia, stress, and age**
- **Viral infections**
- **Immunodeficiency**

# Nasal Cavity and Sinuses

# Responses to Functional Impairments and Injuries of the Respiratory System

- Most of the nasal cavity mucosa is lined by pseudostratified ciliated epithelium, the ethmoidal conchae are lined by olfactory epithelium, and the nasal vestibule is lined by stratified squamous epithelium.
- Injury, inflammation, and host response (wound healing) are characteristic for each of the three epithelial types.

# Responses to Functional Impairments and Injuries of the Respiratory System

- Pseudostratified ciliated epithelial cells are highly sensitive to injury.
- **When these cells are injured due to various causes:**
  - ✓ Ciliated cells swell and typically lose their attachment to the underlying basement membrane.
  - ✓ These cells are then rapidly shed.
  - ✓ A temporary and small amount of exudative fluid, plasma proteins, and neutrophilic leukocytes cover the area of injury.
  - ✓ In the absence of complications and secondary infection, basal cells normally present in the mucosa or a specific type of progenitor cell known as non-ciliated secretory cells (preciliated cells) migrate to cover the exposed basement membrane, undergo mitosis, and eventually differentiate into new ciliated epithelial cells.

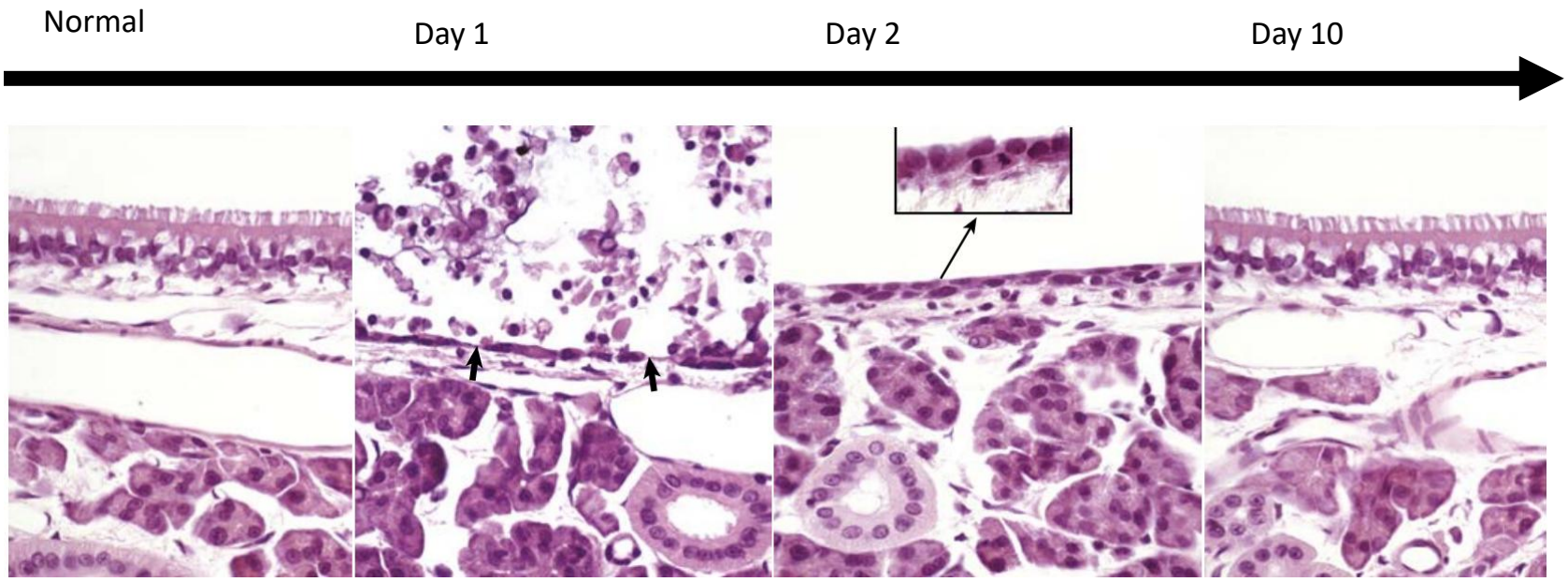
# Responses to Functional Impairments and Injuries of the Respiratory System

The ciliated epithelium has a high capacity for self-repair. **For example, in an uncomplicated ulcer of the tracheal mucosa, epithelial healing can be completed within just 10 days.**

**Examples of such transient infections include:**

- ✓ Common cold in humans (rhinovirus)
- ✓ Infectious bovine rhinotracheitis (IBR) (bovine herpesvirus-1)
- ✓ Feline rhinotracheitis (feline herpesvirus-1)
- ✓ Canine adenovirus 2 (CAdV-2) infection
- ✓ Canine parainfluenza virus 2 (CPIV-2)

**Nasal epithelium and normal epithelium damaged following inhalation of air containing an irritant gas (Hydrogen Sulfide),Nasal concha, Rat**




- Ciliated epithelium
- ~250 cilia/cell
- Highly vascularized
- Abundant glands

- Degeneration
- Loss of attachment
- Necrosis
- Exfoliation

- Repair
- Preciliated cells
- Mitosis
- Cell differentiation

- Healed epithelium
- Normal function

✓ On the first day, detached and shed ciliated cells leave the basement membrane exposed (arrows).This type of lesion is also observed in viral and mechanical injuries.

✓ Two days after inhalation of the irritant gas, the basement membrane is lined with **preciliated cells**, some of which exhibit mitotic activity (inset) and rapidly divide.

✓ Ten days after the injury, the nasal epithelium is **completely repaired.**

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**Schematic illustration of injury and repair processes in the upper respiratory tract mucosa.**

**Blue cells** represent **ciliated mucosal epithelial cells**

**Pink cells** represent **goblet cells**

**Red cells** represent **neutrophilic leukocytes**

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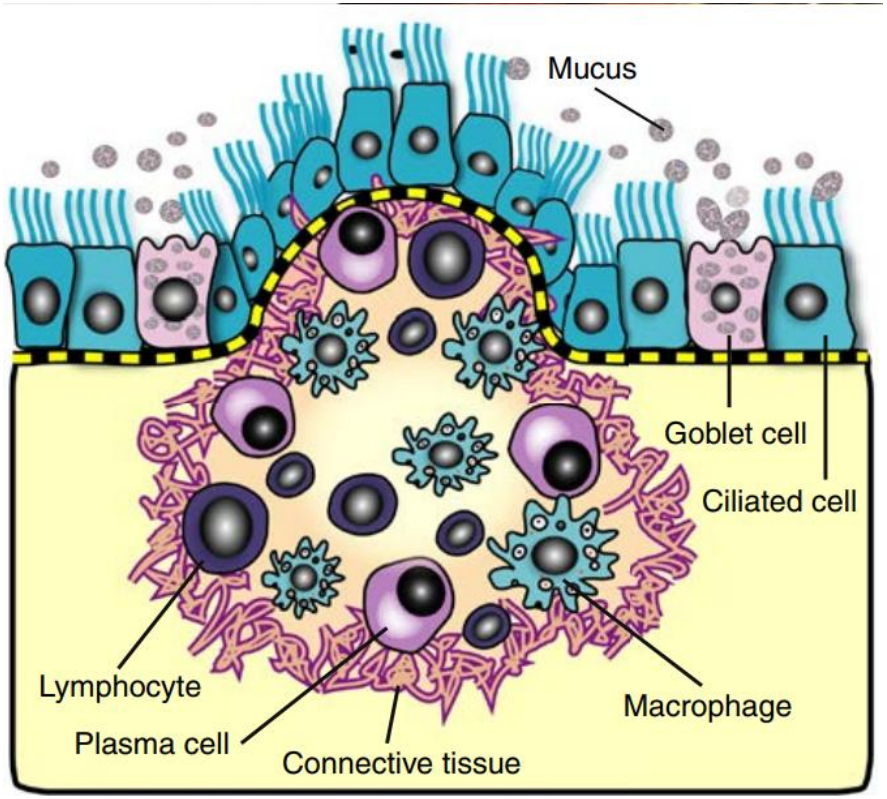
# Responses to Functional Impairments and Injuries of the Respiratory System

**In cases where damage to the mucociliary covering becomes chronic:**

- ✓ Hyperplasia occurs in goblet cells.
- ✓ As a result, excessive mucus production (hypersecretion) develops.
- ✓ This leads to reduced mucociliary clearance, and repair occurs through fibrosis and granulation tissue (scarring).
- ✓ In more severe cases, squamous metaplasia develops along with scarring, leading to airway obstruction and impaired mucociliary clearance.




- **Granulomatous Rhinitis**

➢ The outer wall of the granuloma, composed of connective tissue and surrounding a focus infiltrated by lymphocytes, plasma cells, and macrophages, is observed.

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# Responses to Functional Impairments and Injuries of the Respiratory System

- In the olfactory epithelium (responsible for the sense of smell), which is located particularly in the ethmoidal conchae and part of the nasal mucosa, the response to injury is similar to that of ciliated epithelium.
- However, its regenerative capacity is limited.When damage is extensive, the ulcerated areas of the olfactory mucosa are replaced by squamous epithelial cells or fibrous tissue.
- As a result, a reduction in the sense of smell **(hyposmia)** or complete loss **(anosmia)** may occur.

# Rhinitis ve Sinusitis

- **Inflammation of the nasal mucosa**: *rhinitis*
- **Inflammation of the sinuses**: *sinusitis*
- These two conditions often **occur together**; however, **mild cases of sinusitis** may often go unnoticed.

# Nasopharyngeal Flora and Its Protective Role

- **Normal microbial flora** is present on the nasopharyngeal mucous membrane.
- These bacteria, **adhering to the epithelial surface** of the nasal and pharyngeal mucosa:
  - Prevent the colonization of virulent microorganisms **(especially Gram-negative bacteria),**
  - Provide protection to the host through **competitive inhibition.**
  - Potential pathogens either **fail to establish themselves** or **are maintained at a low enough number to remain harmless.**

# Development of Rhinitis

- For infectious rhinitis to develop, **the normal microbial balance of the nasopharyngeal mucosa must be disrupted.**
- Damage to the mucosal surface **may cause some members of the normal flora to acquire pathogenic properties.** More importantly, **this damage affects the attachment sites of pathogenic microorganisms,** thereby **facilitating their colonization and establishment** in the mucosa.

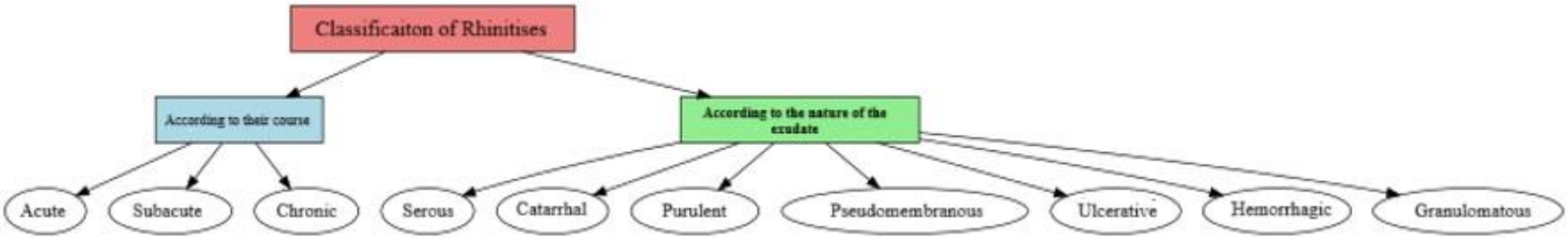
**Disruption of the Protective Barrier**

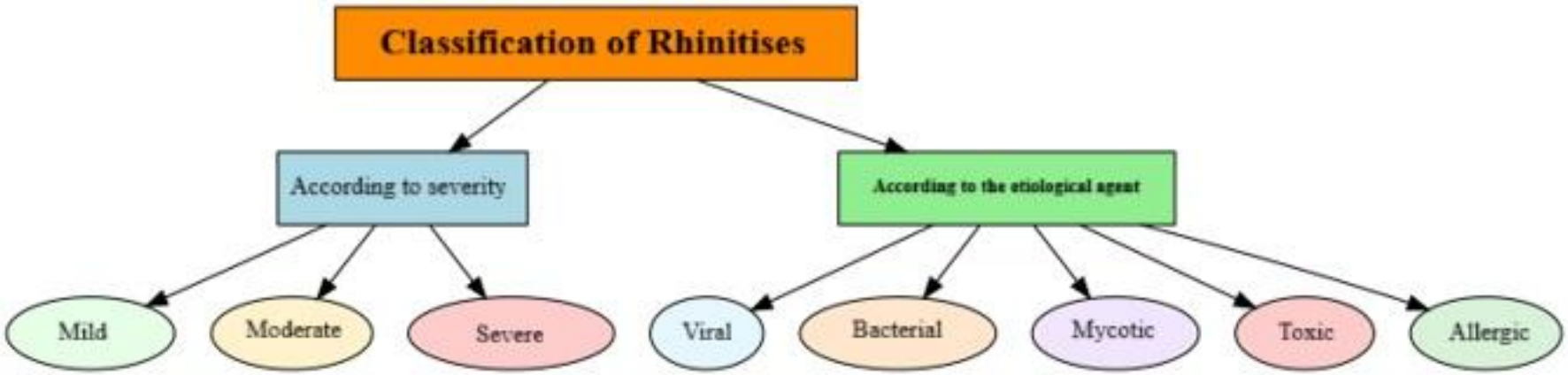
Normally, this barrier keeps most pathogens at bay. However, under certain conditions, it loses its function:

**Cytopathic viral infections,**

- Less commonly, **pathogenic bacterial infections**,
- **Irritant volatile gases** and **environmental changes**,
- **Allergens**,
- **Systemic immunodeficiencies**,
- **Stress following surgical interventions**,
- **Local traumas**,
- **Prolonged antibiotic treatments**,
- **Low-humidity environments**.

- **Importance of Allergens**
- The role of allergens is particularly significant in cattle, though it is also of lesser importance in dogs and cats.


Classificaiton of Rhinitises
According to their course
According to the nature of the exudate
Acute
Subacute
Chronic
Serous
Catarrhal
Purulent
Pseudomembranous
Ulcerative
Hemorrhagic
Granulomatous


Classification of Rhinitises
According to severity
According to the etiological agent
Mild
Moderate
Severe
Viral
Bacterial
Mycotic
Toxic
Allergic

- **Acute rhinitides** typically begin with *serous exudation*.
- As the disease progresses, the exudate becomes **catarrhal** and subsequently **purulent**.
- **Pseudomembranous, ulcerative, and hemorrhagic rhinitides** indicate **severe tissue damage**.
- In many cases, multiple types of inflammation coexist.
- For example, the exudate may be **fibrinopurulent** or **hemorrhagic-ulcerative** in character.
- Therefore, describing the lesions in combination contributes to a more accurate assessment of the pathological condition.

- When marked mucosal **thickening** and **polypoid proliferations** are observed, the condition is referred to as **rhinitis hypertrophicans**.
  In contrast, cases in which the mucosa appears thinned, pale, and **atrophic** are described as **rhinitis atrophicans**.

- **Chronic rhinitides** are mostly characterized by **proliferative changes.** However, in some cases particularly in **large breed dogs** and often in the region of the **basal conchae** atrophic rhinitis may develop. This form can be progressive, accompanied by mucosal thinning and loss of function.

# Serous Rhinitis

- The mildest form of rhinitis is characterized by **hyperemia** of the nasal mucosa along with a **clear and watery discharge secreted by the serous glands** in the submucosa.
  This condition typically reflects a superficial irritation of the mucosa and a mild inflammatory response.
- The clinical appearance closely resembles the early stage observed in humans following exposure to cold weather, **during which the initial nasal discharge is seen.**

# Serous Rhinitis

- **Causes**
- Mild irritant substances
- Cold air
- Often the early onset stage of viral infections
- **Clinical Significance**
  Serous rhinitis is particularly noteworthy in terms of respiratory function.
  Swelling of the mucous membrane leads to **respiratory discomfort.**

# Serous Rhinitis

**Gross Findings**

- Mukozada şişkinlik
- Belirgin hiperemi
- Hipereminin derecesine göre gri-kırmızı renk değişiklikleri

**Histological Findings**

- **Hydropic degeneration** and **loss of cilia** in epithelial cells
- Hyperactivity **in goblet cells** and **submucosal glands**
- The secretion is thin and **seromucinous** in character, containing a few **leukocytes** and **epithelial cells**
- The **lamina propria** is edematous, with only a small number of inflammatory cells observed

# Catarrhal Rhinitis
(*Rhinitis catarrhalis*)

- It is a more advanced form of inflammation than serous rhinitis.
- It usually develops within a few hours or **days following serous rhinitis**.
- It often emerges as a consequence of **bacterial infections**.
- In addition to serous secretion, there is abundant **mucus production** due to increased activity of **goblet cells** and **mucous glands.**

# Catarrhal Rhinitis (*Rhinitis catarrhalis*)

**Gross Findings**

- Marked **hyperemia**in the mucosa
- **Edema** resulting in mucosal thickening
- The mucous exudate is thick and opaque; due to the presence of **leukocytes** and **desquamated epithelial cells**, it appears semi-translucent
- Sometimes **fibrin strands** and **blood** may also be present within the exudate
- **Histological Findings**
- Severe hyperemia
- Pronounced edema
- Exudate contains leukocytes, desquamated epithelial cells, occasional fibrin strands, and blood
- **Regenerative hyperplasia** in surviving epithelium
- **Marked goblet cell hyperplasia** in chronic cases

# Purulent (Suppurative) Rhinitis
(*Rhinitis purulenta, suppurativa*)

- **Gross Findings**
- A thick, opaque layer of **exudate** is present on the surface of the mucosa.
- The color of the exudate may vary from **white to green or brown,** depending on the type of bacteria and the cellular components it contains.
- In severe cases, the nasal passages may be completely filled with exudate.
- **Ulcerations** frequently accompany the condition.

# Purulent (Suppurative) Rhinitis
(*Rhinitis purulenta, suppurativa*)

**Histological Findings**

- Varying degrees of **necrosis** are observed in the epithelial cells.
- **Regenerative** attempts may be seen in the remaining viable epithelial cells.
- There is intense neutrophilic infiltration in the **submucosa and mucosa,** along with **exudate plaques** on the mucosal surface.
- **Migration** of neutrophils between epithelial cells is notable.
- The components of this type of exudate may occasionally lead to **abscess formation**. In such cases, the condition is referred to as **suppurative rhinitis with abscesses** (*rhinitis apostematosa*).

# Pseudomembranous Rhinitis (*Rhinitis pseudomembranecea*)

- Fibrinonecrotic rhinitides occur in domestic animals during severe **bacterial infections.**
- They are also observed in injuries that cause **disturbances in vascular permeability.**
- Types of inflammation:
- **Fibrinous** (*croupous / pseudodiphtheritic*)
- **Fibrinonecrotic** (*diphtheritic*)

- Excessive exudation of plasma fibrinogen → coagulates into fibrin
- Fibrin accumulates on the surface → forming a **pseudomembrane**
- Upon removal of the exudate:
  - If the underlying mucosa is partially preserved → **fibrinous rhinitis**
  - If there is severe necrosis and an ulcerated surface remains after detachment → **fibrinonecrotic rhinitis**

- The term “diphtheritic” originates from human medicine and refers to the severe necrotizing inflammation caused by *Corynebacterium diphtheriae* in the respiratory mucosa.
- In domestic animals, a similar condition may occur due to different causative agents

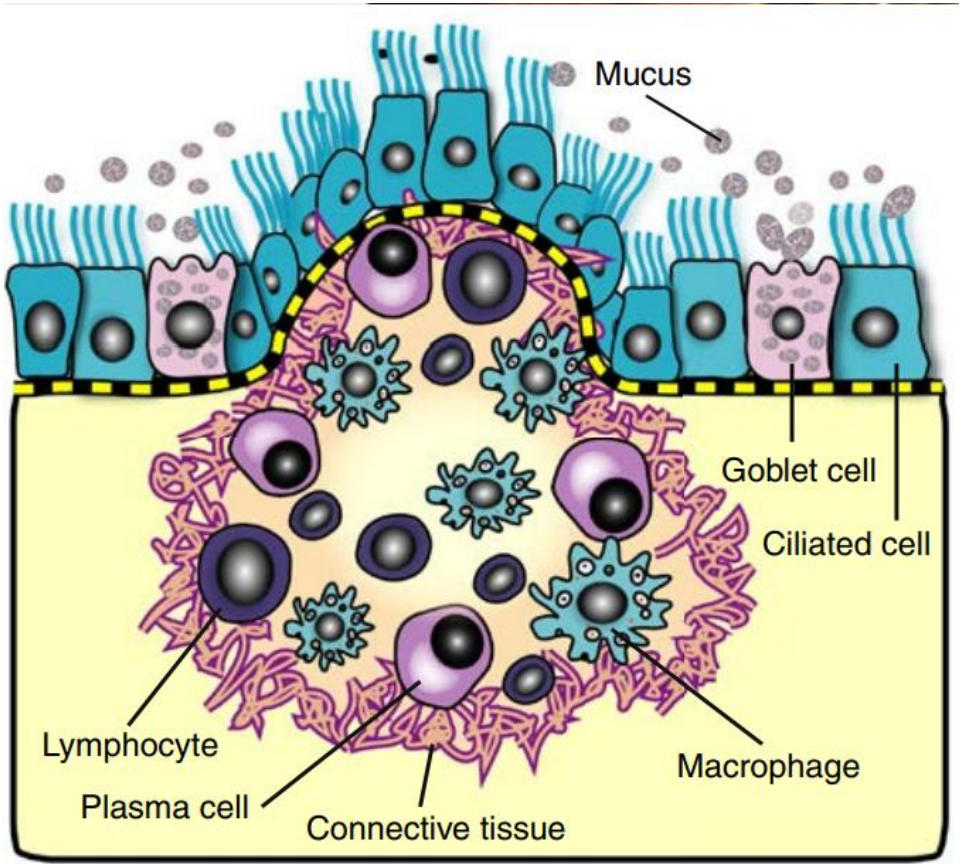
**Perivascular edema** and fibrin
**Neutrophilic infiltration** in the mucosa
**Epithelial necrosis** and remnants of necrotic cells
Exudate plaque composed of: leukocytes + fibrin strands + necrotic cells
Example: In *Fusobacterium necrophorum* infection, a **dry yellowish membrane forms.**

In some cases:

- **Hemorrhagic rhinitis** (*Rhinitis haemorrhagica*)
- **Ulcerative rhinitis** (*Rhinitis ulcerativa*)

# Granulomatous Rhinitis (*Rhinitis granulomatosa*)

- Characterized by **infiltration of macrophages**, **lymphocytes**, and **plasma cells** in the mucosa and submucosa.
- In some cases, **polypoid nodules** develop.
- In severe cases, these nodules may obstruct the **nasal passages.**
- Small nodules are typically **firm**, whereas larger ones tend to be **friable or gelatinous** in texture.




Histopathological structures are **specific to the disease.**
They usually develop in response to specific agents, such as:

- Systemic mycoses
- Tuberculosis
- Foreign bodies

In some cases, however, **the exact etiology cannot be determined**.

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# Chronic Nonspecific Rhinitis

**Pathogenesis:**

- It has not been fully elucidated.
- Initially, an injury occurs in the mucosa, but this lesion may later disappear.
- Due to localized defects in defense mechanisms, damage to the mucosa and a self-sustaining inflammation may develop under the influence of normal flora or new infections.

# Chronic Nonspecific Rhinitis

**Grossly:**

- Chronic, unilateral or bilateral mucopurulent–hemorrhagic discharge
- Inflammatory infiltration leading to diffuse or polypoid thickening of the nasal mucosa
- Obstruction in the nasal passages

# Chronic Nonspecific Rhinitis

**Histopatologically**

- Marked hyperplasia of glands
- Ulceration, hyperplasia, and squamous metaplasia in the mucosal epithelium
- Presence of edema
- Dense infiltration of lymphocytes and plasma cells within the fibrous stroma

# Outcomes of Rhinitis

- **Except for granulomatous rhinitides**, inflammatory processes in the nasal cavity generally have the potential to heal completely.
- The duration of healing varies depending on the severity of the condition.
- **In some cases:**
  - **Bronchopneumonia** may develop due to aspiration of exudate.
  - In advanced stages, **pulmonary abscesses** may form.
- **With local spread of the inflammation:**
  - **Sinusitis**
  - **Facial osteomyelitis**
  - **Meningitis** may occur.

# Nasal Polyps

- Nasal polyps form through diffuse or localized polypoid thickening of the mucosa in subacute and chronic rhinitides.
- They are initially **sessile** in structure and become **pedunculated** as they grow.
- The lamina propria is initially edematous and swollen.
- **Due to the pressure they exert on the basal region**, venous and lymphatic drainage is impaired; this leads to further enlargement of the polyps, causing them to protrude into the nasal passages.
- They are more commonly observed in horses and cats, and less frequently in other species.

# Nasal Polyps

- Polyps are soft**, pink-gray in color**, and irregularly nodular in appearance.
- Their centers display a chronically inflamed, edematous, myxoma-like structure.
- They are covered by **hyperplastic, metaplastic, or ulcerated epithelium.**
- Over time, older polyps acquire a more **fibrous** structure.

# Nasal Polyps

**Specific Types of Polyps**

- 🔶 **Hemorrhagic Nasal Polyp**
- It is particularly observed in the ethmoidal region of horses.
- Presents as unilateral, hemorrhagic masses.
- Tends to recur after surgical removal.
- Microscopically, it has a hemorrhagic structure with varying degrees of organization.
- Severe hemosiderosis and calcification in connective tissue fibers may be observed.
- 🔶 **Nasopharyngeal Polyp (in Cats)**
- It is a specific type of polyp seen in cats.
- It originates from the middle ear and the Eustachian tube.

# Sinusitis

- It is the inflammation of the sinuses.
- Most commonly seen in horses, and less frequently in other domestic animals.
- It may lead to facial deformity or the formation of fistulas on the skin.
- Often develops in conjunction with rhinitis or as a result of septic wounds.
    - For example:
    - In cattle, improper dehorning → **frontal sinusitis**
    - In horses and dogs, dental infections → **maxillary sinusitis**
    - In sheep, **Oestrus ovis larvae** → **parasitic sinusitis**

# Sinusitis

- Drainage in the paranasal sinuses is poor, and the openings (orifices) are easily obstructed.
- This can lead to various complications:
  - **Mucocele**: Accumulation of mucus
  - **Empyema**: Accumulation of pus
  - Spread of chronic sinusitis → **osteomyelitis**
  - Developing osteomyelitis may pose a risk of spreading to the brain, potentially leading to **meningitis**.