STRUCTURE AND FUNCTION OF THE RESPIRATORY TRACT

The respiratory tract is arbitrarily divided into three continuous systems:

- **Conducting system**: The conducting system includes the nasal cavity, sinuses, larynx, trachea and bronchi.
- **Transitional system**: The transitional system is formed by the bronchioles.
- **Exchange system**: This system is composed of the alveoli where gas exchange occurs.

<table>
<thead>
<tr>
<th>Respiratory tract functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gas Exchange</td>
</tr>
<tr>
<td>Phonation</td>
</tr>
<tr>
<td>Temperature regulation</td>
</tr>
<tr>
<td>Blood pressure regulation</td>
</tr>
<tr>
<td>Olfaction</td>
</tr>
<tr>
<td>Acid-base balance</td>
</tr>
<tr>
<td>Detoxification</td>
</tr>
<tr>
<td>Enzyme synthesis</td>
</tr>
<tr>
<td>Hormone synthesis</td>
</tr>
<tr>
<td>Inflammatory mediators</td>
</tr>
</tbody>
</table>

One or more of these functions can be affected as a result of respiratory disease.

NORMAL FLORA OF THE RESPIRATORY TRACT (FYI)

Like any other body system that is in contact with the external environment, the respiratory tract has normal bacterial flora. Various species of bacteria will be grown if a sterile swab is passed deep into the nasal cavity of any healthy animal and is sent for microbiological culture. This flora is restricted to the most proximal region of the conducting system (nasal cavity, the pharynx, larynx and trachea). The distal portions of the respiratory tract, i.e. the bronchioles and alveoli, are normally sterile.

The types of bacteria present in the nasal flora vary considerably among species. Some bacteria in the nasal flora are the same pathogens associated with respiratory infections. For instance, *Mannheimia hemolytica* is part of the bovine nasal flora, yet this bacterium causes a devastating disease in cattle known as Shipping Fever.
Experimental studies have demonstrated that microorganisms from the nasal flora are continuously carried into the lungs via the tracheal air. In spite of this constant bombardment from contaminated air (bacteria, viruses, gases, particles, pollen, antigenic substances, etc), the normal lung remains sterile due to its remarkably effective defence mechanisms.

<table>
<thead>
<tr>
<th>The respiratory tract is continuously exposed by inhaled air to:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microorganisms (virus, bacteria, fungi)</td>
</tr>
<tr>
<td>Gases (SO₂, NO₂, H₂S, ozone)</td>
</tr>
</tbody>
</table>

Under normal conditions, toxicants are detoxified; toxins are neutralized; particles are trapped and removed; and microorganisms are trapped, destroyed and removed from the respiratory tract.

**Defence mechanisms**

The most important defence mechanisms against inhaled particles and microbes are:

- **Air Filtration** (conchae, bronchial bifurcation, turbulences, attachment to mucus, coughing and sneezing)
- **Mucociliary clearance** for the conducting system (nasal, tracheal and bronchial mucosa)
- **Phagocytosis** (pulmonary alveolar macrophages for the exchange system alveoli and intravascular macrophages for the pulmonary capillaries)
- **Innate and acquired immunity** (antibodies and cell-mediated immunity)
- **Detoxification of gases** (soluble gases are mixed and expelled in mucus)

Defence mechanisms are rather effective at destroying most inhaled bacteria. If these defence mechanisms fail, inhaled bacteria can colonize the lung and cause bacterial pneumonia. There are many factors known to impair defence mechanisms. The most common are viral infections, immunodeficiency, stress, dehydration, pulmonary edema, uremia, ammonia, etc. Note in this graph the rapid elimination of inhaled bacteria given by aerosol to a normal animal (dotted line). In contrast, note that in viral infected animals (squared line) that the number of inhaled bacteria increases with time.
**POSTMORTEM EXAMINATION OF THE RESPIRATORY TRACT (FYI)**

**Nasal Cavity:** Make transverse or longitudinal sections of the nasal cavity. Check conchae, meatuses and sinuses and investigate for the presence of exudate, parasites, ulcers, hemorrhage, foam, nodules, or tumors.

**Thoracic Cavity:** Check negative pressure by puncturing the diaphragm and observing for retraction. Failure to retract suggests pneumothorax, pulmonary inflammation, edema or emphysema. Check for fluid or exudate as well as for fractured ribs.

**Larynx, Trachea and Bronchi:** After removing the pluck, open all these structures with scissors and check the mucosa. Investigate for the presence of exudate, ulcers, parasites, foam, nodules or tumors.

**Lungs:** Check if the lungs collapse when the thorax is opened. An uncollapsed lung in a fresh animal suggests inflammation or emphysema. Check for rib imprints on the pleural surface. Palpate the lungs for texture (normal vs. firm, hard, elastic or nodular). Also examine the lungs on cut surface and compress the parenchyma looking for exudate or parasites. Record the severity and extension of lung involvement expressed as percentage of total lung volume.

**Special considerations - Guttural Pouches** (horses) and **Air sacs** (avian)

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**THE CONDUCTING SYSTEM**

**Anatomy of the Nasal Cavity**

- **Turbinates** (=conchae) are curled shelves of bone covered by mucosa
  - Nasal turbinate (dorsal)
  - Maxillary turbinate (ventral)
  - Ethmoidal turbinate

- **Meatuses** are the narrow spaces between turbinates where air circulates.

**Histology of Nasal cavity**

- Squamous epithelium (nasal planum, mucocutaneous junction)
- Pseudostratified ciliated epithelium with abundant goblet cells
- Olfactory epithelium (ethmoidal conchae)

**Anatomy of the trachea and bronchi**

- The trachea and bronchi are formed by cartilage and lined with a mucosal membrane.

**Histology of the trachea and bronchi**

- Pseudostratified ciliated epithelium with abundant goblet cells
  - The mucus and the cilia constitute the mucociliary escalator.
- Tracheal and bronchial mucosa have numerous bronchial glands which become enlarged in chronic irritation.
CIRCULATORY DISTURBANCES OF THE CONDUCTING SYSTEM

Congestion and Hyperemia:
- The submucosa is highly vascularized; therefore, congestion and hyperemia are common. Hyperemia is most frequently seen with inhalation of irritant gases, acute inflammation and trauma. Congestion occurs nonspecifically as an agonal change (due to circulatory failure) and in bloated ruminants.

Nasal hemorrhage (Epistaxis and Hemoptysis)*:
- Epistaxis (nose bleeding) and hemoptysis (blood in mouth, saliva or sputum) are common findings in all species. Unlike the intestine, the color of the blood does not change between proximal (nasal) and distal (lung) hemorrhage. Epistaxis or hemoptysis don’t necessarily imply that hemorrhage has occurred in the nasal or oral mucosa, since both conditions can also be caused by pulmonary hemorrhage.
- Epistaxis is a common problem in all animal species. It can be the result of trauma, foreign body, nasal neoplasia or pulmonary hemorrhage (aneurysm).

Epistaxis is commonly seen in horses with:
- Exercise induced pulmonary hemorrhage (to be discussed later)
- Guttural pouch mycosis (to be discussed later)
- Progressive ethmoidal hematoma*: Pedunculated mass typically arising from the ethmoidal turbinate that looks grossly like a tumor but is simply composed of encapsulated and hemorrhagic fibrovascular tissue. Since it is thinly encapsulated the mass frequently cause hemorrhage into the nasal cavity. The etiology is unknown.
- Nasal cysts

INJURY AND REPAIR OF THE CONDUCTING SYSTEM

The nasal mucosa has a remarkable capacity to repair following injury and necrosis. The type of injury and repair in the nasal cavity, trachea and bronchi are all morphologically similar. The lesions and stages of repair are similar in viral infections and toxic or traumatic injury.

<table>
<thead>
<tr>
<th>Stages of injury and repair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus (toxin) in air or saliva → virus replication in epithelial cells (or toxic damage) → cell degeneration → loss of cellular attachment → cell exfoliation → ulceration → exudation (fluid and cellular) → cell mitosis → repair.</td>
</tr>
<tr>
<td>Complete repair occurs in approximately 10 - 14 days.</td>
</tr>
</tbody>
</table>

Chronic injury to the nasal (also tracheal and bronchial) epithelium results in goblet cell hyperplasia with abundant production of mucus, or squamous metaplasia where ciliary epithelium is replaced by squamous epithelium. Chronic changes also cause fibrosis and extensive loss of ciliary function.
INFLAMMATION OF THE CONDUCTING SYSTEM
(RHINITIS, SINUSITIS, LARYNGITIS, TRACHEITIS, BRONCHITIS)*

According to exudate these inflammatory lesions can be classified as:

- **Serous**: Mild irritants, eg. low levels of ammonia or chlorine
- **Catarrhal (Mucoid)**: Mucus, eg. viral infections
- **Purulent (suppurative)**: Pyogenic bacteria, eg. *Streptococcus equi*
- **Fibrinonecrotizing (fibrinous)**: Bacterial + potent bacterial toxins
- **Granulomatous**: Foreign body, allergic response, fungi, parasites

Rhinitis and Sinusitis are clinically characterized by nasal discharge.

Laryngitis, Tracheitis and Bronchitis result in coughing +/- dyspnea.

Viral infections of the upper respiratory tract (URT) are common in animals but infections are generally self-limiting unless complicated with bacteria or mycoplasmas. Gross lesions in viral infections are often minimal with only noticeable hyperemia of mucosa unless complicated with a bacterial infection. For diagnosing viral infections, you will want to collect swabs (nasal/tracheal samples) or fresh/frozen tissues for PCR or FAT testing. Less often viral isolation is performed. Bacterial culture is typically indicated.

### Examples of viral URT infections in domestic animals:

<table>
<thead>
<tr>
<th>Viral Infection</th>
<th>Clinical Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bovine Rhinotracheitis ((BoHV-1)</td>
<td>Hyperemia and multifocal necrosis of nasal, pharyngeal, laryngeal, tracheal, and sometimes bronchial mucosa. With secondary bacterial infections, causes fibrinous (fibrinonecrotizing) rhinitis and tracheitis. Bronchopneumonia is an important sequel and may result from aspiration of exudate or depression of pulmonary defences.</td>
</tr>
<tr>
<td>Parainfluenza (PIV)</td>
<td></td>
</tr>
<tr>
<td>Equine Viral Rhinopneumonitis (EHV-1 &amp; 4)</td>
<td></td>
</tr>
<tr>
<td>Feline Rhinotracheitis (FeHV-1) and Feline Calicivirus</td>
<td>Exuberant plaques of fibrinonecrotic exudate on top of deep ulcers in the laryngeal mucosa. Sequelae: exudate can occlude the airway causing asphyxiation or be</td>
</tr>
<tr>
<td>Canine Distemper (Morbillivirus)</td>
<td></td>
</tr>
<tr>
<td>Inclusion Body Rhinitis piglets (Cytomegalovirus)</td>
<td></td>
</tr>
</tbody>
</table>

### Examples of Upper Respiratory Infections in Domestic Animals

**Cattle**

**Infectious Bovine Rhinotracheitis (IBR)**

- **Etiology**: Bovine herpesvirus 1 (BoHV-1).
- **Clinical signs**: transient fever, nasal discharge, conjunctivitis, salivation, coughing, and rarely inspiratory dyspnea
- **Lesions**: Hyperemia and multifocal necrosis of nasal, pharyngeal, laryngeal, tracheal, and sometimes bronchial mucosa. With secondary bacterial infections, causes fibrinous (fibrinonecrotizing) rhinitis and tracheitis. Bronchopneumonia is an important sequel and may result from aspiration of exudate or depression of pulmonary defences.

**Necrotic Laryngitis (Calf diphtheria)**

- **Etiology**: *Fusobacterium necrophorum*
- **Important secondary bacterial infection that typically occurs following trauma (balling gun, coarse feed, vocalization) or viral infection (eg BoHV1). Mostly affects feedlot calves.**
- **Clinical signs**: fever, anorexia, depression, halitosis, moist painful cough, dysphagia, and inspiratory dyspnea
- **Lesions**: Exuberant plaques of fibrinonecrotic exudate on top of deep ulcers in the laryngeal mucosa. Sequelae: exudate can occlude the airway causing asphyxiation or be
aspirated and cause aspiration pneumonia. Severe cases may cause sepsis/death.

**Horses**

**URT viral infections in horses include the following:**

<table>
<thead>
<tr>
<th>Disease name</th>
<th>Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equine Viral Rhinopneumonitis (EVR)</td>
<td>Equine herpesvirus 1 (EHV-1)</td>
</tr>
<tr>
<td></td>
<td>Equine herpesvirus 4 (EHV-4)</td>
</tr>
<tr>
<td>Equine Influenza</td>
<td>Equine Influenza virus</td>
</tr>
</tbody>
</table>

These viruses typically cause transient mild rhinitis but can predispose to bacterial infections.

**Strangles**:  
- **Etiology:** *Streptococcus equi subsp. equi.*  
- Important bacterial disease that often occurs as an outbreak with high morbidity (~90%), but low mortality (~5% but higher in foals). Infection occurs when horses come into contact with feed, exudate or air droplets containing the bacterium.  
- **Clinical signs:** Purulent nasal discharge, submandibular swelling

**Lesions:** Typically suppurative rhinitis and regional lymphadenitis with formation of abscesses. Some horses develop purpura hemorrhagica (vasculitis). Bacterial spread to internal organs such as spleen and liver occurs sporadically (and is called bastard strangles). Involvement of retropharyngeal lymph nodes can compress laryngeal nerves and cause secondary laryngeal hemiplegia. Strangles is a notifiable disease in Canada.

**Pigs**

**Inclusion Body Rhinitis**
- **Etiology:** *Suid herpesvirus 2* (Cytomegalovirus).
- Occurs in piglets less than 5 weeks old.
- **Clinical signs:** Infection is usually mild with serous discharge, sneezing and epiphora (overflow of tears).

**Lesions:** Grossly, only nasal hyperemia. Microscopically there is epithelial necrosis, inflammation and most remarkable, enlargement of epithelial cells (megalocytosis) with large intranuclear inclusion bodies.

**Atrophic Rhinitis**
- **Etiology (somewhat controversial):** *Pasteurella multocida & Bordetella bronchiseptica* (toxigenic strains)
- Clinical signs: Sneezing, coughing, facial deformation, minimal nasal discharge
- The effect on growth rate and pneumonia is controversial.

**Lesions:** Postmortem examination is best achieved by making a transverse cross section of the snout between the 1st and 2nd premolar teeth. Various degrees facial deformity and conchal atrophy (progressive) resulting in widening of the nasal meatuses. Exudate is generally absent but, in advance cases, facial deformity (deviation of the snout) is evident.

**Dogs**

**The following viruses cause upper respiratory tract (URT) infections in dogs:**

<table>
<thead>
<tr>
<th>Virus</th>
<th>Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canine distemper virus (CDV)</td>
<td>Canine herpesvirus 1 (CaHV-1)</td>
</tr>
<tr>
<td>Canine adenovirus 2 (CAV-2)</td>
<td>Canine Influenza virus (CIV)</td>
</tr>
<tr>
<td>Canine parainfluenza virus (CPIV)</td>
<td>Canine respiratory coronavirus (CRCoV)</td>
</tr>
</tbody>
</table>

Generally cause acute and transient upper respiratory infections. CDV is more important as a cause of encephalitis. Influenza virus can cause acute and severe respiratory signs. Viral rhinitis can also predispose dogs to secondary bacterial rhinitis (*Bordetella*...
bronchiseptica, Pasteurella multocida, Escherichia coli, Streptococcus spp
Staphylococcus spp) which is often mucopurulent.

**Canine Infectious Respiratory Disease (CIRD) (= Canine Tracheobronchitis, Kennel Cough)**
- **Etiology:** Complex!
  - Most commonly implicated viruses: canine adenovirus-2 (CAV-2)*, canine parainfluenza virus 2 (CPIV-2)*.
  - Most commonly implicated bacteria: *Bordetella bronchiseptica*
  - Less commonly implicated: reovirus type I, Canine adenovirus-1 (CAV-1), CaHV-1, CRCoV, Mycoplasma spp., Escherichia coli, and Streptococcus spp
- **Clinical signs:** Dry hacking cough, nasal discharge, and sneezing
- **Lesions:** Usually acute, self-limiting rhinitis and tracheobronchitis with just hyperemia. If secondary bacterial involvement, fibrinosuppurative or fibrinonecrotizing tracheitis may occur.

**Canine Verminous Nodular Bronchitis**
- **Etiology:** *Oslerus osleri.*
- **Parasitic disease of Canidae**
- **Lesions:** Typically large nodules (1 cm) on the mucosal surface of distal trachea and/or proximal bronchi contain adult worms. There is mild inflammatory reaction around the parasite (histology) and minimal (cough) or no clinical signs.

**Fungal rhinitis**
- **Etiology:** *Aspergillus* spp, *Penicillium*, less often, with *Cryptococcus neoformans* or *Blastomyces dermatitides*
- **Lesions:** Fibrinonecrotizing or granulomatous lesions are typical for fungal infections.

**Cats**
As in other species, respiratory viral infections in cats are generally acute and transient, but can also predispose to secondary bacterial rhinitis (*Bordetella bronchiseptica, Pasteurella multocida* and *Streptococcus*).

**Feline Rhinotracheitis**
- **Etiology:** *Felid herpesvirus 1* (FeHV-1)
- **Lesions:** Mucopurulent rhinitis, conjunctivitis and chronic sinusitis. Kittens may develop corneal ulcers.

**Feline Calicivirus**
- **Etiology:** *Feline Calicivirus*
- **Lesions:** Mucopurulent rhinitis, conjunctivitis and chronic sinusitis. Kittens may develop oral ulcers or transient arthritis (“limping kitten syndrome”). Rare virulent forms cause pneumonia or virulent systemic feline calicivirus (vasculitis, edema and hemorrhage), occasionally as outbreaks.

Chlamydial infections (*Chlamydia felis*) have also been associated with rhinitis and conjunctivitis in cats.

**Cryptococcosis**
- **Etiology:** *Cryptococcus neoformans* and *Cryptococcus gatti*
These dimorphic fungi are acquired through environmental exposure to fungal spores. The spores are associated with pigeon feces and certain tree species – respectively, and are inhaled. Many species are susceptible but this disease is most common in cats.

Infections may cause sneezing nasal discharge, snorting and occasionally mass-like lesions in the nasal cavity and nasal skin. Lesions: Granulomatous rhinitis (+/- pneumonia and systemic infection) with intralesional yeasts. Cytology and/or histology should be performed prior to requesting culture (due to potential risk of infection to humans).

<table>
<thead>
<tr>
<th>Possible Sequelae of Infectious Rhinitis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinusitis</td>
</tr>
<tr>
<td>Guttural pouch empyema (horses)</td>
</tr>
<tr>
<td>Pharyngitis</td>
</tr>
</tbody>
</table>

**SINUSES**

The types of injury and host response in the paranasal sinuses are similar to those in the nasal cavity. According to exudate, sinusitis is most commonly serous, catarrhal (mucoid), purulent, or granulomatous.

Unlike the nasal cavity, paranasal sinuses have poor drainage and exudate tends to accumulate and cause "sinus mucocele" or "sinus empyema."

In sheep, parasitic rhinitis/sinusitis is commonly caused by *Oestrus ovis*.

**Allergic Rhinitis-Sinusitis** is sporadically seen in dogs, cats, cattle and horses.

**GUTTURAL POUCHES**

**Guttural pouches:** Ventral diverticula of the eustachian (auditory) tubes in horses.

**Guttural Pouch Tympary:** Accumulation of gas in the guttural pouches in young foals. The pouches are distended with gas. Non-painful swelling and may resolve on its own.

**Guttural Pouch Empyema:** An accumulation of pus in the guttural pouches.
- Etiology: *pyogenic bacteria* - *Streptococcus equi* for example
- It is a common and important disease.
- Clinical signs include purulent nasal discharge, painful swelling of the parotid region, dysphagia and respiratory distress.
  Lesions: Accumulation of purulent exudate in guttural pouches.

**Guttural pouch mycosis:**
- Etiology *Aspergillus spp.*
- An important and occasionally fatal disease of horses. The fungus reaches the guttural pouches presumably through inhalation of spores from moldy hay.
- Sequelae include erosion of internal carotid artery, massive (fatal) nasal bleeding, cranial nerve deficits (Horner’s syndrome, dysphagia, etc), and cerebral infarcts (rare).
  Lesions: Grossly, the guttural pouch mucosa are covered by focal, rounded, raised
plaques of fibrinonecrotic exudate (fibrinonecrotizing eustachitis). Fungi can be seen microscopically and may be cultured from the lesion.

**TUMORS OF NASAL CAVITY AND SINUSES**

**Epidemiology:** There is a low incidence in domestic animals, but it is most commonly seen in dogs, cats and to a lesser extent, horses. The concept that long-nose breeds are most frequently affected has been recently challenged. In sheep, nasal carcinoma may be enzootic in some geographical areas.

**Pathology:** Nasal tumors can arise from epithelial or mesenchymal cells. Epithelial tumors of the nasal passages include adenomas (benign and rare) and carcinomas (malignant and common). Tumors of stromal origin include fibrosarcoma, osteosarcoma and chondrosarcoma. Lymphoma is the most common round cell tumor at this site. In general, 80% of nasal tumors are malignant. Malignant tumors are often locally invasive and can metastasize.

**Clinical Signs:** Nasal tumors often bleed causing epistaxis or become infected causing a nasal discharge (exudate) that may be mistaken for a simple bacterial or mycotic rhinitis. Some locally invasive tumors may cause severe damage to nerves and brain and cause a variety of neurological signs or facial deformities of exophthalmia. Metastasis to brain may also cause nervous signs.

**Diagnosis:** Biopsy or necropsy are required for confirmation of nasal tumors.

**Enzootic Nasal Tumor (Enzootic Ethmoidal Carcinoma)** *is a retroviral-induced neoplasia of sheep and goats that has high incidence in some endemic regions.

**Etiology:** **Enzootic nasal tumor virus (ENTV 1 & 2).** Causes development of an invasive tumor on the ethmoidal turbinate; metastases do not occur. Clinical signs are nonspecific and include severe respiratory distress because of air-flow obstruction, hemorrhage and in some cases the tumor becomes infected by bacteria causing mucopurulent discharge.

Non-neoplastic exophytic masses, such as **nasopharyngeal polyps**, that resemble neoplasms are commonly found in cats and horses, and, occur less often in other species. These polyps may cause sneezing, nasal discharge, gagging, changes in phonation, noisy breathing and dyspnea.

**TRANSITIONAL SYSTEM (BRONCHIOLES)**

**BRONCHIOLES (Transitional System)**

Unlike bronchi, the walls of the bronchioles do NOT contain cartilage and the mucosa does not normally have goblet cells. The pseudo-stratified epithelium in the bronchi gradually flattens and loses its cilia in the bronchioles and the mucosa contains special secretory cells called club cells.

While viral infections often extend to involve the bronchioles, primary diseases of the bronchioles are rare in domestic animals except for recurrent airway obstruction of horses and some parasitic diseases (lungworms) that cause chronic bronchiolitis.

**Recurrent Airway Obstruction (RAO)** *- also referred to as "Heaves" or Chronic Obstructive Pulmonary Disease (COPD) and is an important equine disease where*
the pulmonary lesions are centered in the bronchioles. Mild injury and recurrent inflammation induces goblet cell metaplasia in the bronchioles. There are no goblet cells in the healthy bronchiole, hence the term metaplasia rather than hyperplasia. This causes accumulation of mucus in the bronchioles that cannot be cleared by mucociliary movement. Airflow in bronchioles plugged with mucus is impaired causing increased expiratory effort and eventually leads to alveolar emphysema (discussed under inflation disturbances of the lung). Abnormal respiration in affected horses causes hypertrophy of the abdominal muscles which is clinically referred to as a "heave line." Lesions: Gross pulmonary lesions are not remarkable except for some degree of emphysema. However, microscopically, there is bronchiolar goblet cell metaplasia and extensive mucus obstruction of small airways (bronchioles), +/- smooth muscle hypertrophy and peribronchiolar fibrosis. A similar, milder, clinical condition, called Inflammatory Airway Disease (IAD), may affect horses of all ages resulting in poor racing performance.

**Feline Asthma** is a common respiratory ailment of cats characterized by reversible bronchial and bronchiolar inflammation with obstruction of the airways. There is smooth muscle hyper-reactivity with contraction causing wheezing, coughing and dyspnea. Also present are chronic eosinophilic bronchitis and bronchiolar mucus goblet cell metaplasia. It is, presumably, of allergic origin and responds well to steroidal and anti-inflammatory drugs.

EXCHANGE SYSTEM: LUNGS (ALVEOLI)

**General Structure of the Lungs**

- The lungs are salmon pink with a dry sponge-like texture normally.
- There are notable differences in lung morphology among animal species: E.g. horses have poorly defined pulmonary lobes compared to the other species.
- Pulmonary lobes are classified into: cranial lobes, middle lobe (right side only) and caudal lobes.
- Pulmonary lobes are subdivided into lobules by interlobular septa.
  - Lobules are prominent in bovines and pigs; poorly defined in horses and humans and absent in dogs and cats.

Histologically, the alveoli are covered by thin **type I pneumocytes**; interposed occasionally with **type II pneumocytes** which help produce pulmonary surfactant. This surfactant prevents alveolar collapse during respiration. **Type I (membranous) pneumocytes** are notably slender and particularly susceptible to injury. Necrotic type I pneumocytes are replaced by type II pneumocytes: these will eventually differentiate into type I pneumocytes.

**Lymphatic vessels** are abundant in the lung and constantly remove fluid.

**Bronchial associated lymphoid tissue (BALT)** is involved in lung defences, particularly in local immunity of the lung.

**The Blood-Air Barrier** – has three components*

<table>
<thead>
<tr>
<th>1. Vascular endothelium</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Basement membrane</td>
</tr>
<tr>
<td>3. Type I pneumocytes</td>
</tr>
</tbody>
</table>
DISORDERS OF THE LUNG

Congenital lung anomalies are relatively rare in animals. Most common ones are: lung or bronchial hypoplasia and pulmonary hamartoma.

Abnormal Pigmentation of the Lung *(For your information only)*

- **Pulmonary melanosis** is a common incidental pleural finding, particularly in sheep. There is **NO** change in lung texture.
- **Pneumoconiosis** is a general term used to describe pulmonary diseases characterized by deposition of inhaled particles in the lung. Such particles may include carbon (anthracosis), silica (silicosis) or asbestos (asbestosis).
  - **Anthracosis** is seen sporadically in animals, particularly dogs, exposed to carbon particles suspended in the air. Lungs have focal to confluent areas of black discoloration. It is considered an incidental finding.

CIRCULATORY DISTURBANCES OF THE LUNG

Hyperemia (active) is usually seen in acute pulmonary inflammation when the release of inflammatory mediators causes vasodilation and exudation. Hyperemic lungs are heavy with a deep red color. Blood oozes on cut surface.

Congestion (passive accumulation of blood)* is commonly associated with **congestive heart failure** (left sided). It can progress to lung edema and intra-alveolar hemorrhage with erythrophagocytosis by macrophages resulting in siderophages ("heart failure cells"). "Wet and heavy lungs" have red patchy discoloration. Please note: In animals euthanized with barbiturate, the lungs will be edematous and congested (no heart failure cells will be present).

**Pulmonary hemorrhages*** are commonly seen in postmortem specimens. The most common causes of pulmonary hemorrhages are:
  - **Trauma**: puncture of the lungs by fractured rib/penetrating wound
  - **Coagulopathies**: anticoagulant toxicity, thrombocytopenia, DIC
  - **Rupture of vessels**: erosion of vascular wall by abscesses; pulmonary aneurysm etc.
  - **Exercise Induced Pulmonary Hemorrhages (EIPH)** in horses.

**Gross:** Depending on magnitude, pulmonary hemorrhages vary from petechia to patchy or locally extensive areas of red discoloration.

**Microscopically:** Erythrocytes occur within the alveolar spaces and larger airways. With time, siderophages (macrophages filled with hemosiderin) appear.

"Exercise Induced Pulmonary Hemorrhage" (EIPH)* has been well described in race horses. Clinically, affected horses have nose bleeding following exercise. Some horses have a reduced athletic performance. Only exceptional cases result in acute death. Postmortem findings are minimal and characterized by dark-yellow (hemosiderin pigment) discoloration of the dorsocaudal aspects of the lung. Pathogenesis of EIPH is unclear but mechanical stress with rupture of alveolar walls has been proposed. **Histopathology:** Hemorrhage, siderophages, and moderate fibrosis.
PULMONARY THROMBOSIS AND INFARCTION*

Pulmonary thromboembolism (PTE)* is occasionally seen in domestic animals and is of variable clinical significance. If emboli are small and sterile they can be rapidly degraded and cause no clinical signs. If larger, they can cause small airway constriction, reduced surfactant production, pulmonary edema, and atelectasis resulting in hypoxemia, hyperventilation, and dyspnea. They may also cause pulmonary infarction.

Common causes/sources of pulmonary thromboembolism in animals*:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocarditis (right heart)</td>
<td>Dirofilaria immitis</td>
</tr>
<tr>
<td>Glomerular disease</td>
<td>Jugular vein thrombosis (IV injection/catheter)</td>
</tr>
<tr>
<td>Vena cava thrombosis in cattle (hepatic abscesses)</td>
<td>Endogenous / Exogenous steroids</td>
</tr>
</tbody>
</table>

Pulmonary infarcts: Pulmonary infarcts are rarely seen due to the dual circulation of the lungs (pulmonary and bronchial). Generally lung infarcts are non-fatal but can evolve into embolic pneumonia.

Lesions: Focal (multifocal) red discoloration/hemorrhage at the margins of the lung.

Other pulmonary emboli: Rarely, material other than thrombi can embolize to the lungs. Examples include: bone marrow, hepatocytes, foreign material (hair), etc.

PULMONARY EDEMA*

Pulmonary edema is a very common and sometimes important pulmonary lesion characterized by accumulation of fluid in the interstitium and alveoli. Generally a nonspecific lesion seen in many pulmonary, cardiac and neurological diseases and it is the terminal cause of death for many illnesses. Clinical signs of pulmonary edema include dry cough, dyspnea, tachypnea, and crackling noises during breathing.

Pathogenesis of pulmonary edema*

Normal lung produces fluid that is rapidly removed by the lymphatic system. When fluid production exceeds lymphatic removal, pulmonary edema may rapidly follow.

Causes of pulmonary edema include:

- **Increased hydrostatic pressure (= cardiogenic edema)** is commonly seen in animals with left heart failure or with fluid overload (iatrogenic). Left heart failure also causes pulmonary congestion and then intra-alveolar hemorrhage that results in the formation of "heart failure cells" in the lung. The edematous fluid in a cardiogenic pulmonary edema usually has low protein content.

- **Increase vascular permeability (= permeability lung edema)** is common and is seen when there is injury to the air-blood barrier via toxic gases, inflammation, allergies etc. The edematous fluid in permeability edema usually has high protein content.

- **Other causes** are less common and include hypoproteinemia (usually edema is more pronounced in other tissues) and obstruction of lymphatic drainage (obstructive lung edema), due to neoplasia involving the thoracic lymph nodes or vessels. Pulmonary edema also develops after severe brain injury which is referred to as “neurogenic lung edema.” Edematous fluid in these cases usually has low protein content.
**Gross lesions:** Foamy fluid (froth) in the conducting system. If there is no froth it is not possible to diagnose pulmonary edema as the terminal cause of death. The lungs appear wet, heavy and fail to collapse when the thorax is opened. Clear fluid distends the interlobular septa causing accentuation of the lobular pattern, particularly in cattle and pigs (these species have well developed pulmonary interlobular septa).

**CAUTION:** Acute pulmonary edema may grossly resemble pneumonia.

**Histopathology of lung edema:**
- Alveoli are flooded with fluid. In permeability edema the fluid is generally rich in protein (eosinophilic) while in cardiogenic edema the fluid is pale and difficult to see microscopically.
- Distention of the interlobular septa.
- Lymphatic vessels are notably distended which reflects attempts by the lung to clear the excess fluid.
- Often congestion accompanies edema

**ACUTE RESPIRATORY DISTRESS SYNDROME**

**Acute Respiratory Distress Syndrome (ARDS)** is a clinical condition characterized the acute onset of bilateral pulmonary disease with hypoxemia resulting from diffuse alveolar damage (DAD). The resulting marked permeability edema often results in death. The pathogenesis is obscure but is thought to involve activation of “hyper-reactive” macrophages causing a massive cytokine release that activates neutrophils. The neutrophils release cytotoxic enzymes and free radicals which damage the alveolar walls. Possible initiating causes are numerous and include pulmonary infections, sepsis, severe trauma/burns, smoke inhalation, strangulation, aspiration of gastric acid, pancreatitis to name a few. Clinical signs include dyspnea, cough, nasal discharge, fever, and signs referable to the underlying cause. The prognosis is poor.

**Gross lesions:** Uncollapsed, wet, heavy, congested lungs

**Histopathology:** Pulmonary edema, congestion and hyaline membranes (linear deposits of fibrin, protein and cell debris) in the acute exudative phase; type II pneumocyte hyperplasia in the subacute proliferative phase; and interstitial fibrosis in the chronic fibrosing stage. This is an interstitial lung pattern (discussed later in pneumonia).

**INFLATION DISTURBANCES (ATELECTASIS AND EMPHYSEMA)**

**Fetal Lungs:** Fetal lungs contain fetal fluid (and no air) and therefore sink when placed in formalin. At birth, fetal fluid is quickly reabsorbed and replaced by inspired air.

**ATELECTASIS** refers to an incomplete expansion of the lung or portion of a lung.

**Gross lesions:** Collapsed lungs, dark, firmer texture (resembles pneumonia)

**Histologically:** Collapsed alveoli and loss of alveolar spaces.

**Congenital (Neonatal) Atelectasis**
- **Airway obstruction at birth.**
  - Aspiration of meconium due to the so-called "valve effect" in which the meconium plug allows air to exit, but not to enter, the lung.
- **Lack of pulmonary surfactant.** (Humans > foals and piglets > other species).
**Acquired Atelectasis**

A) Normal alveolus
B) Obstructive atelectasis: Caused by airway obstruction by exudate, parasites, food particles, etc.
C) Compressive atelectasis: Large intra-thoracic masses (abscesses, tumors, pericarditis, etc) or external trauma compresses the lung.

**EMPHYSEMA**

**Definition:** Emphysema is an abnormal and permanent enlargement of air spaces distal to terminal bronchioles with destruction of their alveolar walls.

**Causes of Pulmonary Emphysema:**
Primary lung emphysema is rare in animals but extremely important in human beings. Emphysema in animals commonly occurs secondary to pneumonia due to obstruction of airflow by exudate within airways (acting as a valve, allowing more air in than out). Other underlying causes include heaves (horse) and fog fever in cattle. Be aware that pulmonary emphysema commonly develops in agonal states (violent gasping air), particularly in cattle.

Emphysema may be classified according to the site of accumulation of gas:

- **Alveolar emphysema:** Alveolar emphysema can occur in all species. It may be difficult to appreciate in mild cases. Equine heaves (RAO) is an important disease causing alveolar emphysema in horses.
- **Interstitial emphysema:** Interstitial emphysema is common in cattle and is characterized by distention of interlobular septa and pleura with gas. It is presumably caused by violent respiratory movements.
- **Bullous emphysema:** Bullous emphysema is a large focal accumulation, or pocket, of air (bulla) in the lung. Large bullae form when there is rupture of pulmonary tissue. Can arise in either alveolar or interstitial emphysema.

**PNEUMONIA**

**General:** There is no universal classification of pneumonia in veterinary medicine.

**There are numerous classifications such as:**
- **Etiological:** viral pneumonia, mannehimiosis, pneumatic histopilosis, distemper pneumonia, allergic pneumonia
- **Epidemiological:** enzootic pneumonia, contagious bovine pleuropneumonia
- **Exudate:** Suppurative, fibrinous, granulomatous pneumonia
- **Topographical (distribution):** diffuse, interstitial, focal, multifocal
- **Miscellaneous:** Progressive pneumonia, proliferative pneumonia, atypical pneumonia, pneumonitis
Confusion in veterinary medicine is rampant. For example: viral pneumonia of pigs, enzootic pneumonia of pigs, mycoplasma pneumonia of pigs, and chronic bronchopneumonia all refer to one disease caused by *Mycoplasma hyopneumoniae.*

### CLASSIFICATION ACCORDING TO TEXTURE, DISTRIBUTION AND TYPE OF EXUDATE*

#### 1. **Suppurative Bronchopneumonia**

- **Distribution:** Cranioventral consolidation of lungs.
- **Lung texture:** Firm.
- **Port of entry:** Aerogenous.
- **Etiology:** Generally caused by *bacteria or mycoplasmas* which produce **mild to moderate injury** to the lung (*i.e.* *Pasteurella multocida, Trueperella pyogenes, Bordetella bronchiseptica*).
- **Death** due to bronchopneumonia occurs when there is more than 60% of lung involvement in uncomplicated cases.
- **Gross lesions:** Affected lung is consolidated and the lobular pattern is accentuated. Color varies from red (acute, hyperemia) to grey (chronic inflammation, atelectasis, fibrosis). Typically, purulent exudate (pus) can be expressed from airways. Exudate in chronic bronchopneumonia takes a mucoid appearance.
- **Histopathology:** Large number of neutrophils in the bronchi/bronchioles and alveolar spaces in acute cases and a mixture of neutrophils, macrophages, and mucus (goblet cell hyperplasia) in more chronic cases.
- **Examples of Diseases:** Enzootic pneumonia of pigs, calves and lambs.
- **Common sequelae:**
  - Abscesses (in the cranioventral lobes)
  - Bronchiectasis (in the cranioventral lobes)
  - Fibrosis and fibrous pleural adhesions (in the cranioventral lobes)

#### 2. **Fibrinous Bronchopneumonia (Fibrinous pleuropneumonia)**

- **Distribution:** Cranioventral consolidation (except Porcine Pleuropneumonia).
- **Lung texture:** Firm to Hard.
- **Port of entry:** Aerogenous.
- **Etiology:** Caused by agents that produce **severe injury to the lung** (*i.e., Mannheimia haemolytica, Actinobacillus pleuropneumonia*, etc). There is severe toxemia due to bacterial toxins and tissue necrosis. Also occurs with aspiration of harsh material.
- **Death** may occur with less than 30% of lung involvement because of sepsis.
- **Gross Lesions:** Affected lung (cranioventral) is consolidated and varies in colour from dark red > yellow > grey. Yellow fibrin covers the pleura. On cut surface the interlobular septa are expanded by tan-yellow material (fibrin and edema) and there is coagulation necrosis of the tissue imparting a marbled appearance.
- **Histopathology:** Notable dilation and thrombosis of lymphatic vessels, massive exudation of fibrin and neutrophils into the bronchoalveolar space and pleural space and areas of coagulative necrosis.
Examples of diseases that cause fibrinous bronchopneumonia: Shipping fever, Porcine Pleuroneumonia, Contagious Bovine Pleuroneumonia.

Common sequelae: Survivors can develop large pulmonary sequestra (= large pieces of necrotic lung surrounded by connective tissue), pleural adhesions, and fibrosis.

3. Interstitial Pneumonia

- Distribution: Diffuse; lungs fail to collapse.
- Lung texture: Elastic (rubbery) texture with rib imprints. The cut surface has a meaty and often edematous appearance.
- Port of Entry: Aerogenous or hematogenous.
- Etiology: Viremia, airborne-viruses, septicemia, blood-borne toxins, systemic toxicants, allergy and inhaled gases. Injury to alveolar walls.
- Gross lesions: The lungs fail to collapse when the thorax is opened; occasional costal imprints are visible on the pleural surface. The color depends on blood:tissue ratio and type of exudate or fibrous scarring. Changes are often subtle and difficult to diagnose grossly - generally requiring histopathologic confirmation. Interstitial pneumonia may coexist with edema, emphysema or bronchopneumonia (Broncho-interstitial pneumonia).
- Histopathology: The primary lesion is centered in the alveolar wall. Thickening of alveolar walls by interstitial exudation or proliferation of type II pneumocytes. In chronic interstitial pneumonia there is alveolar fibrosis.
- Common sequelae: Pulmonary fibrosis and interstitial emphysema.

4. Embolic Pneumonia

- Distribution: Multifocal. Multiple foci or small nodules randomly distributed in all pulmonary lobes.
- Lung texture: Nodular - Variably sized nodules on cut surface.
- Port of entry: Hematogenous.
- Etiology: Bacterial showering resulting from endocarditis, ruptured hepatic abscess (vena cava thrombosis in cattle), omphalophlebitis, etc.
- Gross lesions: Variable number of nodules / foci, often with a white center and red hemorrhagic margins. Color varies depending on the amount of connective tissue and blood vessels.
- Histopathology: Septic emboli associated with pulmonary capillaries, pulmonary edema, microabscesses.
- Common sequelae: Abscesses in all pulmonary lobes.

5. Granulomatous Pneumonia

- Distribution: Typically multifocal. Multiple foci or small nodules randomly distributed in all pulmonary lobes.
- Port of entry: Aerogenous or hematogenous.
- Etiology: Tuberculosis, fungi and some parasites. Usually caused by microorganisms, parasites (ova, larvae) or foreign materials (inhaled food
particles) that are difficult to eliminate by phagocytosis.

- **Gross lesions**: White nodular lesions often with caseous necrosis at the center (granulomas) in the lung +/- other organs. Be aware that granulomatous pneumonia can resemble neoplasia and requires histopathology.

- **Histopathology**: Variable size nodules with a necrotic center infiltrated by macrophages and giant cells and surrounded by connective tissue mixed with lymphocytes and plasma cells (ie granulomatous inflammation).

- **Common sequela**: Cachexia (wasting) in chronic cases.

### EXAMPLES OF BRONCHOPNEUMONIAS IN DOMESTIC ANIMALS

#### Cattle

**Enzootic Pneumonia of Calves**. Multifactorial disease complex of young calves (Calf pneumonia). Etiology includes a combination of environmental factors (temperature, humidity, poor air circulation, crowding, stress), immune status, viral infections (BPIV-3, BRBV), bacterial infection (*Pasteurella multocida*, *Histophilus somni*, *Trueperella pyogenes*), *Mycoplasma* infection (*M. bovis*, *M. dispar*, etc). It has high morbidity, low mortality and a multifactorial pathogenesis.

Gross lesions: Chronic suppurative bronchopneumonia > bronchointerstitial pneumonia with prominent hyperplasia of BALT and mucopurulent exudate in airways.

**Shipping fever (Bovine Pneumonic Mannheimiosis)** is the number one cause of feedlot mortality in North America. It is caused by *Mannheimia haemolytica* which is not considered a true primary pathogen since it is often present as normal flora and is effectively destroyed and cleared by the normal bovine lung. When the defence mechanisms are compromised by viral infections (BPIV-3, BoHV-1, BRBV) or stress, inhaled *M. haemolytica* colonizes the lung and causes a severe fibrinous bronchopneumonia and toxemia. A powerful cytotoxin for ruminant leukocytes (leukotoxin) is produced by *M. haemolytica* which further compromises pulmonary defence mechanisms. Clinical signs include fever, anorexia, coughing, nasal exudate.

Gross lesions: Fibrinous bronchopneumonia, fibrin on pleura, pleural effusions. On cut surface, there are typical irregular areas of coagulation necrosis and expanded interlobular septa.

Histopathology: Distended interlobular septa with thrombosis of lymphatic vessels, irregular areas of coagulative necrosis which are surrounded by abnormal leukocytes (oat-shaped cells), abundant fibrin and PMN in bronchioles and alveoli.

Bacteriology: Consolidated lung typically yields pure culture of *M. haemolytica*. Determining the predisposing factors is required (virus, stress, management) to reduce the incidence of this disease. *Mannheimia* vaccines are of questionable value in field conditions. Viral vaccines and management practices reducing stress have a beneficial effect in the incidence of shipping fever.

Shipping fever should not be confused with Hemorrhagic Septicemia caused by *Pasteurella multocida* (Serotypes B and E) which is an important acute septicemia in Asia and Africa but not seen in the American continent. *Mycoplasma mycoides* ssp. *Mycoplasma mycoides*, small colony type causes Contagious Bovine Pleuropneumonia, a reportable disease. The lung lesions in these two diseases are similar to those seen in Shipping Fever (fibrinous bronchopneumonia).

**Histophilus somni / Histophilosis Complex**: *Histophilus somni* is an important bovine pathogen but it can also be found as normal vaginal flora. This "Complex" includes several forms:
- Thrombotic meningoencephalitis (TME)
- Reproductive (infertility, endometritis and abortion)
- Myocardial (myocarditis)
- Otitis (otitis)
- Respiratory: Respiratory Histophilosis* can result either in fibrinous bronchopneumonia identical to shipping fever, or chronic suppurative bronchopneumonia identical to enzootic pneumonia.

*Mycoplasma bovis* has been incriminated with increased frequency as a cause of bronchopneumonia in young cattle. It causes a necrosuppurative bronchopneumonia with large caseated or non-caseated nodules in the cranioventral lung. Bosselation of the lung surface occurs as a result of bronchiectasis. Isolation of *M. bovis* using special techniques or immunohistochemistry / PCR is needed to confirm the diagnosis. *M bovis* may also cause arthritis and otitis media/interna in calves.

**Sheep**

Ovine Chronic Enzootic Pneumonia: Multifactorial Disease of lambs (<1 year old) caused by environmental stressors, viral infections (PIV-3, Adenovirus, RSV, etc), bacterial infections (*M. haemolytica* and *Mycoplasma ovipneumoniae, P. multocida, H. somni*). High morbidity, low mortality. Gross lesions: Chronic suppurative bronchopneumonia/bronchointerstitial pneumonia with mucopurulent exudate in airways.

Ovine Mannheimiosis occurs in two distinct types*:

- **Pneumonic Mannheimiosis** – Etiology: *Mannheimia haemolytica**: Lesions and pathogenesis are similar to shipping fever of cattle: acute fibrinous bronchopneumonia. Predisposed by stress, viral infections (PIV-3, RSV, adenovirus) and chlamydial infections. *M. haemolytica* is present in the tonsils of 95% of normal sheep.

- **Septicemia** – Etiology: *Bibersteinia trehalosi* (formerly classified as *Pasteurella* and *Mannheimia*) in stressed sheep. Characterized by a fulminating septicemia with DIC, petechial hemorrhages, lung edema, (sometime necrotizing pharyngitis, esophagitis, glossitis).

**Horses**

Adult horses most commonly acquire bronchopneumonia (or pleuropneumonia) as a secondary or opportunistic bacterial infection. The most common isolate is *Streptococcus equi* subsp zooepidemicus. Other possible isolates include *Pasteurella* spp, *Actinbacillus* spp, *E coli*, *Klebsiella*, *Streptococcus* spp, etc.

**Pigs**

Porcine Enzootic Pneumonia* Generally nonfatal, highly contagious disease of young pigs. Etiology: *Mycoplasma hyopneumoniae*. Predisposing factors include temperature fluctuations, humidity, ammonia, crowding and stress. It has high morbidity but low mortality. Secondary infections with *Pasteurella multocida, Bordetella bronchiseptica, Trueperella pyogenes, and Mycoplasma hyorhinis* are common and may result in death.
Clinically, coughing is noted when the pigs are roused. **Gross lesions:** Chronic suppurative bronchopneumonia = mucopurulent exudate in airways and BALT hyperplasia. *Mycoplasma hyopneumoniae* is a fastidious organism to grow. Immunohistochemistry or PCR are more often used for a diagnosis.

**Porcine Pasteurellosis** (secondary infection by *Pasteurella multocida*): **Lesions:** *P. multocida* is isolated from the lungs of most pigs with chronic suppurative bronchopneumonia. Sometimes produces a fulminating fibrinous bronchopneumonia.

**Porcine Pleuropneumonia**: Etiology: *Actinobacillus pleuropneumonia*. A primary pathogen. Highly contagious aerogenous infection with a high mortality rate in naïve herds. Can occur as an acute disease with sudden death and blood stained froth around the nares. Subacute disease presents with coughing, dyspnea and signs of sepsis (fever, anorexia, lethargy). Bacteria produce toxins (Apx) that result in vascular leakage and thrombosis. **Gross lesions:** Often dorsocaudal (and unilateral) or cranioventral. Swollen areas of consolidation covered with fibrin. On cut surface, areas of coagulative necrosis similar to pneumonic mannheimiosis. Survivors can develop large pulmonary sequestra.

**Streptococcus suis type II**: Important zoonosis. Various presentations: neonatal septicemia, meningitis, arthritis, polyserositis, myocardial necrosis, endocarditis, abortion and bronchopneumonia. **Gross and histological lesions:** Nonspecific (often combined with other pathogens): Can cause suppurative bronchopneumonia. Fibrinous pleuritis is more common.

**Dogs and Cats**

Bronchopneumonia in cats and dogs is often secondary to viral infection or impairment of pulmonary defence mechanisms. Common isolates include *Pasteurella multocida*, *Streptococcus* spp, *Escherichia coli*, *Klebsiella pneumonias* and *Bordetella bronchiseptica*. *Bordetella bronchiseptica* occasionally causes outbreaks of pneumonia in shelter cats. *Streptococcus equi* subsp. *zooepidemicus* can cause acute and fatal hemorrhagic pleuropneumonia with hemorrhagic pleural effusion in dogs.

**All species:**

**Aspiration pneumonia** is caused by the aspiration of gastric contents following vomiting or due to neurological signs that impair swallowing. In cattle, aspiration pneumonia often occurs secondary to recumbency or weakness. It may also occur with improper intubation or inappropriate oral administration of medicines (iatrogenic).

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**EXAMPLES OF INTERSTITIAL PNEUMONIAS IN DOMESTIC ANIMALS**

**Cattle**

**Viral Pneumonias**: *Bovine Parainfluenza virus-3* (BPIV-3) and *Bovine Respiratory Syncytial Virus* (BRSV): cause transient rhinitis, tracheitis and bronchointerstitial pneumonia with intracytoplasmic inclusions and formation of syncytial (epithelial) cells. **Infectious Bovine Rhinotracheitis (IBR)**: Etiology: Bovine Herpesvirus-1 (causes respiratory disease, genital lesions and abortion). The respiratory form is generally an acute and transient rhinotracheitis. All these bovine respiratory viruses can cause severe impairment of defence mechanisms and predispose animals to secondary bacterial pneumonia.
**Atypical Interstitial Pneumonia:** This term should be abandoned, as what was once atypical is now typical. The so-called "atypical interstitial pneumonia" of cattle includes several distinct conditions characterized grossly by diffuse interstitial pneumonia:

- **Bovine Pulmonary Edema and Emphysema (BPEE or fog fever).**
  
  **Pathogenesis:** Ingestion of pasture (foggage) containing large amounts of L-tryptophan which is metabolized to 3-methylindole (3-MI) in the rumen → blood → lungs → metabolized by club cells into a pneumotoxicant → toxic injury to type 1 pneumocytes → interstitial pneumonia with severe edema and emphysema. BPEE is most commonly seen in grazing cattle.

- **Extrinsic allergic alveolitis** (also known as hypersensitivity pneumonitis or farmer's lung). Caused by inhalation of bacterial spores of *Saccharopolyspora rectivirgula* from moldy hay → induces an antibody response → deposition of antigen/antibody complexes in the blood air barrier (= type III hypersensitivity) → complement / polymorphonuclear cell mediated injury to type-I pneumocytes → interstitial pneumonia. Extrinsic allergic alveolitis is most commonly seen in cattle fed silage.

- **Reinfection syndrome.** Presumed hypersensitivity reaction to re-infection with larvae of *Dictyocaulus viviparous* or re-infection with Bovine Respiratory Syncytial Virus. Hypersensitivity reactions may cause diffuse alveolar damage and edema.

- **Other respiratory syndromes with interstitial pneumonia.** Pit (manure) gases (H₂S); "silo filler disease/silage" (NO₂), smoke inhalation, etc.

**Sheep and goats**

**Ovine/Caprine viral pneumonias**

**Ovine Progressive Pneumonia (Maedi or Lymphoid Interstitial Pneumonia - LIP).**

**Etiology:** Retrovirus (Visna/maedi virus - VMV). In Iceland, "Maedi" means shortness of breath. It is a lifelong infection but clinical disease only occurs in sheep older than 2 years of age. Clinical signs include weight loss, progressive dyspnea, +/- coughing.

**Gross lesions:** Lungs fail to collapse, heavy, elastic texture and prominent rib imprints typical of a severe interstitial pneumonia. Histopathology: Interstitial lymphocytic infiltrates with notable hyperplasia of bronchial associated lymphoid tissue (BALT) and smooth muscle.

**Caprine Arthritis and Encephalitis (CAE).** Also caused by a Retrovirus (CAE virus; closely related to VMV). Gross lesions: Interstitial pneumonia with grey-pink colouration and numerous 1-2 mm grey foci on section. Clinically characterized by progressive dyspnea. Histopathology: Lesions are similar to ovine progressive pneumonia except that the alveoli are filled with proteinaceous material and type II pneumocyte hyperplasia is prominent. Arthritis (adults) and encephalitis (kids) are more common manifestations.

**Horses (Equine Viral pneumonias)**

- Equine Viral Rhinopneumonitis (Equine herpesvirus 1 and 4 [EHV-1 and 4])
- Equine Influenza
- Equine Viral Arteritis (EVA)
- Equine Adenovirus
- Hendra virus
• Equine multinodular pulmonary fibrosis (EHV-5)

Lesions: Typically minimal; transient tracheitis or bronchointerstitial pneumonia. Viral impairment of lung defences causes secondary bacterial pneumonia (P. multocida, Streptococcus spp; E. coli; Rhodococcus equi). Fatal adenovirus infection is commonly seen in Arabian foals with combined immunodeficiency (CID). Equine herpesvirus-5 causes equine multinodular pulmonary fibrosis, a condition characterized by the development of well demarcated fibrotic nodules within the lung (resembles neoplasia).

Pigs (Porcine Viral Pneumonias)

• Swine Influenza*: Etiology: Swine influenza virus (SIV). Highly contagious and causes transient tracheitis and bronchointerstitial pneumonia. Affects all age groups and can cause fever, nasal discharge, dyspnea, weakness and coughing. This viral infection predisposes pigs to secondary bacteria invasion. Lesions: May be minimal with mild hyperemia of the tracheobronchial mucosa. Occasionally atelectasis of the cranioventral lung lobes occurs due to plugging of the airways with exudate – this looks very similar to enzootic pneumonia grossly. However, interstitial pneumonia characterized by bronchial/bronchiolar epithelial necrosis is seen histologically. Secondary bacterial infection leading to bronchopneumonia is commonly seen.

• Porcine Reproductive and Respiratory Syndrome (PRRS)*: Etiology: PRRS virus (family Arteriviridae). This syndrome has also been associated with abortion and reproductive failure in sows. In piglets and young pigs you can see sneezing, fever, anorexia, dyspnea, coughing. This virus targets pulmonary alveolar and intravascular macrophages and induces immunosuppression. This viral infection predisposes pigs to secondary bacteria invasion (bacterial pneumonia and sepsis are common). Lesions: Interstitial pneumonia and lymphadenopathy.

• Porcine Circovirus-Associated Disease*: Etiology: Porcine Circovirus-2. While many healthy pigs carry this virus, it also has been associated with several disease syndromes in pigs including PCV-2 associated pneumonia, systemic PCV-2 infection (Postweaning Multisystemic Wasting Syndrome or PMWS), PCV-2-associated enteritis, porcine dermatopathy and nephropathy syndrome (PDNS), PCV-2-associated reproductive failure and PCV-2-associated cerebellar vasculitis. Lesions: PCV-2 associated pneumonia is characterized by interstitial pneumonia +/- generalized lymphadenopathy (granulomatous lymphadenitis) and emaciation. Histologically botryoid intracytoplasmic inclusion bodies may be seen in macrophages and epithelial cells.

Laboratory tests (PCR, FAT, IHC) are required for the diagnosis and differentiation of viral pneumonias!

• Other causes of interstitial pneumonia in pigs include bacterial sepsis (especially Salmonella spp) and migration of nematode larvae (Ascaris suum). Pseudorabies (suid herpesvirus 1) causes neurological and respiratory disease with interstitial pneumonia. Nipah virus (belonging to the group Henipavirus) is emerging zoonotic disease affecting pigs and humans.
Dogs (Canine Viral pneumonias)
- Canine Distemper
- Canine Adenovirus-2
- Canine Parainfluenza virus
- Canid herpesvirus-1
- Canine Influenza virus: This disease was recently reported in the United States and appears to be caused by an equine strain of influenza virus. It has high morbidity and clinical signs similar to kennel cough. The mortality is low.

Lesions: Transient tracheobronchitis, bronchointerstitial pneumonia. Viral impairment of lung defences causes secondary bacterial pneumonia (Bordetella bronchiseptica; E. coli, Streptococcus spp).

Cats (Feline Viral Pneumonias)
- Feline Viral Rhinotracheitis (Feline herpesvirus 1)
- Feline Calicivirus

Lesions: Infections are more common in the upper respiratory tract and ocular conjunctiva (rhinitis and conjunctivitis). Generally see minimal, hyperemia of nasal and tracheobronchial mucosa. Can cause bronchointerstitial pneumonia. Secondary bacterial infections by P. multocida, B. bronchiseptica and Streptococcus spp. can result in bronchopneumonia. Virulent strains of feline calicivirus can cause a febrile systemic hemorrhagic syndrome in cats.

EXAMPLES OF GRANULOMATOUS PNEUMONIAS IN DOMESTIC ANIMALS

Tuberculosis*: Etiology: Mycobacterium spp (M bovis and M tuberculosis are important as both cause disease in humans and cattle). Important disease of human beings, ruminants, pigs, poultry and horses. Dogs and cats are relatively resistant. Lesions may be found in any organ or tissue. Infection often spreads via aerosol and the lungs may be the primary site or one of many organs involved with disseminated infection. Lymph nodes are frequently involved.

Gross lesions: Multiple, random, white firm nodules with caseous centers in the lung and lymph nodes (granulomatous pneumonia and lymphadenitis). Histopathology: Granulomas (necrotic center, macrophages and giant cells surrounded by connective tissue and lymphocytes) containing acid fast bacilli. These organisms are difficult to cultivate and require special media and/or PCR for species identification.

Rhodococcosis*: Etiology: Rhodococcus equi. Disease of horses of worldwide importance. Infection in foals has two major forms: respiratory and intestinal. The intestinal form causes ulcerative enterocolitis and the respiratory form is characterized by chronic cough and weight loss. The two forms often occur together. Bacteriologic culture is required for a diagnosis. This disease is occasionally seen in other species. Gross lesions: Bronchopneumonia, abscesses and pyogranulomas with necrotic centers are seen with the respiratory form.

Histopathology: Pyogranulomas formed by macrophages, neutrophils, giant cells and fibrous tissue.

Systemic Mycoses
- Blastomyces dermatitides
- Coccidiodes immitis
- Cryptococcus neoformans/gatti
- **Histoplasma capsulatum**
  These non-contagious fungal infections are typically acquired from the environment via inhalation. Many species are susceptible to infection (including humans).
  Gross lesions: Granulomatous pneumonia.
  Histopathology: Granulomas and fungal organisms. Typically, there is involvement of the lymph node and other organs.

**Feline Infectious Peritonitis (FIP):** Etiology: Mutated form of Feline enteric coronavirus (FECV). For details on the pathogenesis of FIP in cats see the section of digestive system. In the respiratory system, FIP virus causes pyogranulomatous pleuritis / pneumonia.

**Verminous Pneumonia:** Lung worms may induce granulomatous reaction in the lungs. The adults often live in the larger airways (bronchi and bronchioles) where they often cause mild bronchitis occasionally resulting in airway obstruction and atelectasis. The larvae and/or eggs are often released into the alveoli where may induce multifocal granulomas. The granulomas contain dead larvae, parasitic eggs and many eosinophils. These infections are often asymptomatic. In some cases larvae can cause interstitial pneumonia (as a hypersensitivity response).

- Cattle – *Dictyocaulus viviparus*
- Sheep/goats – lungworms: *Dictyocaulus filariae, Protostrongylus rufescens* and *Muellerius capillaris*
- Horses – *Dictyocaulus amnfieldi*
- Pigs – *Metastrongylus apri, Metastrongylus salmi,* and *Metastrongylus pudendotectus*
- Dogs – *Crenasoma vulpis, Filaroides spp, Eucoleus aerophila*
- Cats – *Aleurostronglus abstrusus, Eucoleus aerophila*

### NEOPLASTIC DISEASES OF THE LUNG

**Primary lung tumors**
Tumors arising from the lung are very common in human beings but are relatively rare in animals (seen more frequently in dogs and cats than other domestic species). Tumors may originate from any cell line of the lung and may be epithelial, mesenchymal or round cell in origin (epithelial tumors are most common). They are generally seen as a single nodule or mass in animals with signs of respiratory disease (cough, anorexia, lethargy, dyspnea). Signs could also be related to distant metastasis.

**Primary epithelial lung tumors**:  
- Adenoma, papilloma (benign)
- Adenocarcinoma, Bronchial gland carcinoma, squamous cell carcinoma (malignant).
  - Metastases occur most often to lungs, the regional lymph nodes, and the pleura.
  - Interestingly: primary pulmonary adenocarcinomas in cats often metastasize to the digits*

**Ovine Pulmonary adenocarcinoma (pulmonary adenomatosis or jaagsiekte)**: 
Etiology: *Jaagsiekte sheep retrovirus (JSRV).* Transmissible retrovirus-induced neoplasia of sheep. Most commonly reported from Scotland and South Africa but also occurs in North America. Causes chronic respiratory signs, weight loss and copious nasal discharge.
Gross lesions: Lungs fail to collapse, heavy, wet, with consolidation and nodules in cranioventral regions (looks like bronchopneumonia). In more chronic cases the lesions extends to all pulmonary lobes. Histopathology: Nodules are formed by papillary growth of epithelial cells. Metastasis to lymph nodes occurs in some cases.

Primary mesenchymal lung tumors:
- Hemangioma or hemangiosarcoma
- Fibroma or fibrosarcoma, etc.

Secondary (Metastatic) tumors in the lung

Secondary (metastatic) tumors in the lungs are more common than primary lung tumors. Lungs are highly vulnerable to metastasis because of circulation and density of capillaries. Metastatic tumors are seen as multiple nodules or masses with random distribution. Differential diagnosis requires clinical, radiographic and histopathological examination. Tumors in the thorax (space occupying lesions) are known to predispose to Hypertrophic pulmonary osteoarthropathy.

Table 1. Tumors that commonly metastasize to the lung

<table>
<thead>
<tr>
<th>Osteosarcoma</th>
<th>Chondrosarcoma</th>
<th>Fibrosarcoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemangiosarcoma</td>
<td>Lymphoma</td>
<td>Malignant Melanoma</td>
</tr>
<tr>
<td>Mammary carcinoma</td>
<td>Uterine carcinoma</td>
<td>Adrenal carcinoma</td>
</tr>
</tbody>
</table>

THORACIC CAVITY

The thoracic (pleural cavity) is lined by the parietal pleura (covers the ribs, diaphragm and mediastinum) and the visceral pleura (covers the lungs). There is negative pressure in the thoracic cavity and the lungs collapse when the negative pressure is lost by opening the thorax. Under normal conditions once the cavity has been opened, the lungs appear smaller in comparison to the rest of the cavity.

Pneumothorax*

Pneumothorax is the presence of air in the thoracic cavity (loss of negative pressure). It is caused by trauma, rupture of emphysematous bulla, rupture of the esophagus or iatrogenic (i.e. biopsy). You may also see gas in the mediastinum (pneumomediastinum) Gross lesions: Failure of the diaphragm to retract when punctured, atelectasis. Also may see evidence of trauma, bullae etc.

Pleural Effusions*:

Hydrothorax*

Hydrothorax is the accumulation of abnormal quantities of transudate (serous fluid) in thoracic cavity. Transudate is clear fluid with a low cellularity and low protein content. Common causes of hydrothorax include congestive heart failure, hypoproteinemia (liver, renal, intestinal disease, starvation) and lymphatic obstruction. Lesions: Clear fluid in thoracic cavity. Transudation must be differentiated from exudation via thoracocentesis and fluid cytology. Chronic transudation of fluid causes irritation and may result in mild pleural inflammation (modified transudate) and fibrosis.

Hemothorax*

Hemothorax is the presence of free blood in thoracic cavity. It is caused by severe
trauma or penetrating wound into the lungs, rupture of major blood vessels (aneurysm), coagulopathies, warfarin poisoning, etc.

**Lesions:** Blood in the thorax. You may see evidence of trauma, aneurysms, etc. depending on the underlying cause.

### Chylothorax*
Chylothorax is the presence of free lymph (chyle) in the thorax and it is caused by rupture of a major lymphatic duct. Possible causes include thoracic trauma, iatrogenic (surgery) and neoplasia. There is also an idopathic form of chylothorax in dogs.

**Lesions:** Milky fluid in the thoracic cavity. For diagnosis in live animals, submit fluid to clinical pathology – chyle is high in triglycerides and lymphocytes.

### Pleuritis*
Pleuritis is inflammation of the pleura and it can occur alone or in combination with pneumonia (i.e. fibrinous pneumonia/pleuropneumonia). The exudate in the thorax will be turbid with a high cellularity and high protein content. Depending on the exudate, pleuritis could be purulent (pyothorax), fibrinous, granulomatous, etc. Chronic pleuritis results in fibrous adhesions between visceral and parietal pleura. Etiologic diagnosis requires microbiology.

### Suppurative pleuritis = Pyothorax*
Pyothorax (pleural empyema) is the accumulation of purulent exudate (pus) in the thoracic cavity. Possible routes of entry include penetrating thoracic trauma with implantation of bacteria (e.g. bite wounds), rupture of a pulmonary abscess, rupture of the esophagus, and hematogenous spread (sepsis).

In cats, the most common isolate is *Pasteurella multocida* often resulting from bite wounds. In both dogs and cats, “tomato soup” pyothorax is caused by *Nocardia asteroides, Actinomyces* sp, or Bacteroides sp.

Differentials for fibrinous or fibrinosuppurative pleuritis in cattle include *Mannheimia haemolytica* and *Histophilus somni* and differentials in pigs include *Haemophilus parasuis, Streptococcus suis, Pasteurella multocida* and *Actinobacillus pleuropneumoniae*. The most common causes of suppurative (fibrinosuppurative) pleuritis in horses are *Streptococcus* or *Mycoplasma*

**Pyogranulomatous pleuritis** occurs in cats with FIP and affected cats often have increased fluid in the thorax.

### NEOPLASTIC DISEASES OF THE PLEURA

#### Primary pleural tumors

**Mesothelioma** is a rare tumor of serosal membranes (mesothelium) which readily disseminates by implantation.

**Lesions:** multiple growths involving most of the serosal surface. Histopathology or cytology required for confirmation. In humans there is strong correlation between exposure to asbestos and mesothelioma.

THE END