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Lesson 1
Normal Structure and Function

The respiratory system is composed of a conducting portion and a gas-exchange portion.

IMPORTANT POINT: The air-conducting portions are quite different from the air-exchange portions and also have fairly different clinical syndromes associated with their dysfunctions.

FROM THE OUTSIDE IN….

External nares – this is the “nose.” Then it leads into the nasal cavity, where air is warmed and moistened.
Paranasal sinuses communicate directly or indirectly with the nasal cavity, usually through a fairly small channel. (Remember that – SMALL hole for drainage – this is why sinusitis can take such a long time to resolve.)

The nasopharynx is that portion of the pharynx located dorsal to the soft palate. The oropharynx, in contrast, is that part of the pharynx that is common to the respiratory and digestive systems.

The trachea runs from the larynx down to the bifurcation where it splits and turns into bronchi. Cartilaginous open rings hold the tube open.

Then, on to the BRONCHI –

It is called a tree because it has many BRANCHES. Bronchi branch and branch again and then become bronchioles. Bronchi – cartilage; bronchioles – no cartilage. Then bronchioles move into the respiratory and terminal bronchioles, and finally… ALVEOLI, which is where the air exchange takes place.

Alveolar epithelium consists of alveolar cells. Most are Type I, the workhorse of gas exchange, they have very thin cytoplasm. Type II cells, in contrast, are cuboidal – thicker cytoplasm and covers much less surface.

So, guess what happens when Type I cells get killed? All replacement cells are of the Type II variety, they eventually flatten into Type I, but in the meantime gas exchange suffers.
Lesson 2
Defense and Immune Responses in the Lung

AIR FLOW

It may seem obvious, but a pathogen will not cause pneumonia unless it reaches the lung. The body has a variety of defenses designed to prevent this from happening.

Harmful agents can be removed in the nasal passages and conducting airways OR they can be removed at the alveolar level. The two mechanisms are quite different.

FIRST ⇒ ⇒ ⇒

TAking Care of particles in the conducting airways:

Deposition and the mucociliary apparatus

Turbinates are designed so that anything coming into the nose has to twist and turn, so particles are likely to get caught here on the mucous surface.

Mucociliary escalator (sometimes also called the mucociliary apparatus)

The mucociliary blanket consists of ciliated cells that beat in a watery phase on top of which is a mucus phase. The particles land in the mucus, which is composed of water, immunoglobulins (especially IgA), and mucus. The mucus and adhered particles are constantly moved by the cilia towards the pharynx where they are swallowed (and inactivated by stomach acids).
Cilia are an important component of the mucociliary apparatus and may be adversely affected by pathogens. *Mycoplasma* spp. is the main organism that establishes residence in between the cilia. *Bordetella bronchiseptica* is another one. In humans the number one cause of ciliary damage is *cigarette smoke*, and this is the primary reason why smokers are predisposed to bronchitis and pneumonia.

SECOND ⇒ ⇒ ⇒

**TAKING CARE OF PARTICLES IN THE ALVEOLI:**

The primary means of defense at the alveolar level is phagocytosis by pulmonary alveolar macrophages (PAMs).

Neutrophils can be summoned into alveoli as well; however in the lung, they are regarded as a second line of defense, functioning only after the resident alveolar macrophages have attempted to contain the agent.

**BALT**

Bronchial-associated lymphoid tissue (BALT) is found throughout the bronchial tree as lymphoid aggregates within the submucosa.

**DEFENSE IMPAIRMENT**

There are some well known causes of pulmonary defense impairment that predispose to pneumonia:

- → **Viral infection.** As many as 40% of bacterial pneumonias in humans result from previous viral infections which alter pulmonary defense. Viral diseases in animals also predispose to bacterial pneumonias. How does this work?
  - Macrophages from animals with viral infections are dysfunctional. There is usually decreased chemotaxis, phagocytosis, phagosome formation, killing and degradation.
  - Viral-infected cells have impaired mucociliary function and thus clearance of anything decreases.

- → **Cardiac failure** is also a predisposing cause of pneumonia. When the heart is failing, there is increased hydrostatic pressure in the lung, with leakage of serum proteins into alveoli (pulmonary edema), which inhibits defenses and provides a hospitable environment for bacteria.

- → **Persistent antibiotic therapy** is a predisposing factor for fungal infections in the respiratory system, but not a major predisposing factor in bacterial pneumonias.
Lesson 3
Diseases of the Nares, Nasal Cavity and Nasal Sinuses

Developmental Anomalies

◆ Palatoschisis (cleft palate) is one of the most common and important defects in cattle and dogs. When the young animal nurses, it may aspirate milk into the nasal passage and cause aspiration pneumonia.

External Nares

- Epistaxis may be a sign related to several respiratory lesions (trauma, infection, neoplasia, etc.)
- A mucopurulent exudate at the nares may be secondary to a rhinitis.
- Lesions at the external nares normally do not affect respiration unless they cause occlusion of the nasal passages.

Rhinitis

Rhinitis is the word for inflammation of the nasal cavity. It can be caused by physical, chemical, viral, bacterial, or fungal agents. In addition, some cases of rhinitis are allergic.

Most cases of acute rhinitis begin with a serous exudate, which then progresses to catarrhal (mucus-y) as glandular secretions get increased. If bacteria are in there as well, accumulations of neutrophils will cause the exudates to become purulent.

| RHINITIS: | Serous → → → catarrhal → → →+ bacteria → → → purulent |

Specific diseases associated with rhinitis

- Infectious bovine rhinotracheitis (IBR)

Infectious bovine rhinotracheitis (IBR) is an acute contagious disease of cattle caused by bovine herpesvirus-1. Lesions develop in the upper respiratory tract, trachea, and conjunctiva. IBR occurs throughout the world, in all breeds of cattle. Pretty contagious.
One of the BIGGEST problems with IBR is that it predisposes to *Mannheimia* moving south (e.g., into the lung), creating a dire clinical situation due to shipping fever (more on that soon).

- **Strangles**

  “Help, my pus-laden lymph nodes are strangling me.....!”

  Caused by *Streptococcus equi*, this disease creates lots of pus and abscesses form in the lymph nodes of the neck. These swollen lymph nodes press on the trachea and esophagus, making the horse feel like it is choking, hence the name of the disease.

- **Glanders**

  Glanders is a disease of horses caused by *Burkholderia mallei*. The bacteria enter through the nasal cavity and cause big caseo-necrotizing tracts through the sinuses, within the subcutis, and in the lung. When the lesions occur in the subcutis of the skin, the disease is called “farcy.” Horses shed significant bacteria with their nasal secretions and contaminated feed and watering troughs are a good way to spread it around. Glanders will also infect (and kill) humans.

**Parasitic diseases of the nasal cavities**

*Nasal bots in sheep*

A common problem in sheep is infection with *Oestrus ovis* larvae. They can be found in the nasal passages, sinuses and pharynx of sheep and occasionally goats. The fly deposits the first stage larvae on the nares and these molt twice as they migrate through the nasal passages. After development, they come back out, but they are sometimes trapped in turbinates or sinuses because they grow rapidly and cannot pass back through the narrow orifices through which they migrated.

**Sinusitis**

Sinusitis is a more significant problem than rhinitis due to the close proximity of the sinus to the brain, the diminished chance of drainage and spontaneous resolution, and the more likely predisposition to epithelial atrophy and metaplasia, distortion of the facial bones, and osteomyelitis.
Frontal sinusitis in cattle may occur secondary to dehorning and subsequent wound infection.

Sinusitis is most significant in the horse, because this species has the largest and most complex sinus structure, coupled with the poorest drainage. In addition, in horses, periodontitis often extends into the sinuses.

**Guttural pouch of horses**

The guttural pouches of horses are ventral diverticula of the Eustachian tubes. They get involved in inflammation the same way as the paranasal sinuses do, that is, inflammation starts in the nasal cavity and spreads by extension into this area. However, the guttural pouches are contiguous with a number of critical structures, including cranial nerves (VII, IX, X, XI, XII), blood vessels, and the cranial sympathetic trunk.
Lesson 4
Diseases of the Pharynx, Larynx and Trachea

Laryngeal edema

Severe laryngeal edema will result in death by asphyxiation. What causes the larynx to fill with edema? Poking that endotracheal tube around too much, systemic anaphylaxis, horses with purpura hemorrhagica, allergic reactions in any species. Death by asphyxiation. Not good.

Laryngeal blockage

In any species, foreign bodies, including medication boluses can lodge in the larynx to cause problems.

Laryngitis and tracheitis

- Necrotic laryngitis due to *Fusobacterium necrophorum* is referred to as *calf diphtheria*. The bacteria localize in laryngeal “contact ulcers” (1 cm circular ulcers in the arytenoid cartilage). These contact ulcers are thought to be caused by mechanical forces acting on the laryngeal tissues. The mechanical forces result from increased rapid opening and closing of the larynx due to stress conditions (dust, coughing, swallowing, and increased vocalization or “bawling”).
Lesson 5

Diseases of the bronchi and bronchioles

The bronchi and bronchioles have a hybrid nature. Their function is conducting air. However, they are embedded within the lung parenchyma, which is predominantly focused on gaseous exchange.

Inflammation of the bronchi and bronchioles very easily extends into pneumonia.

**Bronchitis**

Morphologic manifestations of bronchitis include similar general descriptions as those described for more upper airways. That is, catarrhal bronchitis may precede purulent or ulcerative bronchitis.

**Bronchiectasis**

The definition of bronchiectasis is “permanent, abnormal dilation of bronchi”. How does it happen? Chronic inflammation alters the normal elasticity through the build-up of debris. Eventually fibroplasia holds the lumen in a permanently distended state.
Bronchiolitis

Bronchioles have the worst of both worlds. They are often involved along with the bronchi in inflammatory lesions targeting the conducting pathways. Also, because they are so close to the alveoli, they are usually affected by pneumonic processes as well. In addition, some viral and toxic insults will specifically target alveolar cells and bronchioles.

Bronchiolitis obliterans

The big problem with inflammation of bronchioles is that there is not much room for any exudate to accumulate. Consequently, they get plugged very easily. What happens next is that fibroblasts migrate into the exudates and tend to make the plug permanent. Bronchiolar epithelium grows over the fibroblastic mass. What is left is a permanent polypoid projection nearly obliterating the bronchiolar lumen. This lesion is referred to as bronchiolitis obliterans. These bronchioles never return to normal function.
Lesson 6
General disorders of the lung

Physical abnormalities

Torsion of a lung lobe can occur but is quite rare.

Atelectasis

Atelectasis is defined as incomplete expansion of the lung. Grossly, atelectasis appears as red-brown solid depressed areas without obvious inflammation.

- **Fetal atelectasis**

  Fetal lungs are supposed to be like this because they have yet to be expanded by air. When dealing with an aborted animal, one good way to tell if the animal ever took a breath is to take a piece of lung and drop it in water (or formalin). If it sinks, the animal was born dead. Remember that from last year?

- **Acquired atelectasis**

  After the lung is inflated at birth, then there are only two reasons that atelectasis can occur:

  ✓ Atelectasis can occur as a result of **airway obstruction**. No air can get in and the existing air within the alveolus leaks out through the walls, collapsing the alveolus.

  ✓ **Compression atelectasis** arises from pressure on the outside of the lung – could be hydrothorax, pneumothorax, chylothorax, hemothorax, or tumor.
Pulmonary Emphysema

Emphysema means tissue puffed up by air. Although pulmonary emphysema is a very common and important clinical entity in humans (largely thanks to the tobacco industry), it is not so problematic in animals. There are some specific examples.

- **“Heaves” in horses**

  Chronic bronchiolitis-emphysema complex in the horse is also known as “heaves” or “broken wind” or the more scholarly “chronic obstructive pulmonary disease.” As with many disease syndromes with multiple names, the causes and pathogenesis are poorly understood. Allergies to inhaled fungal antigens are incriminated most regularly.

  There is a chronic bronchiolitis with epithelial hyperplasia, intense goblet cell activity, and peribronchiolar fibrosis. Eosinophil numbers vary greatly from case to case. Alveoli tend to be hyperinflated because of air trapping. It is thought that recurrent bronchospasms occlude alveolar ducts.
Bovine pulmonary emphysema

Emphysema in cattle develops very easily with any kind of severe pulmonary problem. As cattle inhale and exhale vigorously, air spaces rupture, releasing gas into the interstitium. Consequently interlobular and interlobar septa can fill up with air. Sometimes it gets so severe that the air spills over into the mediastinum and, in some cases tracks right into the subcutis. Bubble wrap!!! However, emphysema is rarely the primary problem in cattle – rather it is a reflection of the very vigorous respiratory efforts made because of some other problem in the lung.

Any increased respiratory effort results in emphysema in cattle. It is usually the result of a pulmonary problem rather than the primary problem.
Lesson 7

Vascular disorders in the lung

PULMONARY THROMBOEMBOLISM is a very severe disorder that kills quickly. Think about a deep vein thrombosis (like maybe a big thrombus in the lower leg) - part of it dislodges and travels through progressively larger veins (without getting stopped because the vessels get bigger and bigger), and into the right heart - still no blockage. It gets through the right heart, and goes to the lungs. Now the vessels start to get smaller. Eventually it gets stopped, plugging the vessel, which in this case will be a pulmonary artery. If it is big, it will compromise the unoxygenated blood going to the lung that is supposed to pick up oxygen and take it around the body. So, there isn’t ischemia of the lung, but instead, there is HYPOXIA OF THE WHOLE BODY – that will kill you…..

Congestion

- *Pulmonary congestion* is seen in a variety of disease syndromes. The lung is incredibly vascular - it has 2,500 km of capillaries! So if there is anything in the systemic circulation, such as septicemia or toxicity, that will promote congestion, we will see it in the lung!

- *Hypostatic congestion* in the lung is seen in animals in lateral or dorsal recumbency for long periods of time. In these cases, gravitational pooling may occur. The significance is that there is decreased pulmonary clearance in these areas, predisposing to infection.

Edema

Some causes of pulmonary edema include:

1. **Increased hydrostatic pressure** – This will occur with cardiac failure, backup of blood, and consequently increased hydrostatic pressure in the alveoli, forcing fluid out between endothelial cells.

2. **Damage to endothelial cells** – The reason here is obvious – loss of integrity of the capillary retaining wall. This type of pulmonary edema occurs in specific viral infections – African horse sickness, bluetongue, epizootic hemorrhagic disease. Additional causes might include endotoxins or high levels of certain cytokines.

3. **Damage to alveolar cells** - These cells form an important part of the support structure for the endothelium. As alveolar cells are damaged, fluid is likely to leak out into the alveolus. Some causes include toxic gases and systemic toxins.

Grossly, edematous lungs are wet, heavy, and fail to collapse. Often pulmonary edema is accompanied by hydrothorax.
Hemorrhage

- Hemorrhage into the lung can occur with any *coagulopathy*. Warfarin poisoning in dogs tends to present as massive mediastinal hemorrhage, due to the thymus being affected preferentially.

Emboli

Emboli occurs frequently in the lung, in fact, the lung is a major site of embolization from the vascular system. **Deep vein thrombosis** (DVT), when there is a coagulopathy that predisposes to thrombosis and a big one forms in a deep vein, like maybe in the leg, often bits of the thrombus will break off and can travel to the lung with pretty bad results (also discussed above).

Lung is often a site of metastatic tumors, because of the possibility of tumor emboli getting stuck in the meshwork of small capillaries throughout the lung. Other types of emboli that may be found in lung include fat (usually as a result of a broken bone with release of fat from marrow), fragments of nucleus pulposus from intervertebral disks, or bits of epidermis and hair introduced at the time of injection.
Lesson 8

Diseases of the Pleura and Pleural Cavity

As a refresher, here is the anatomy:

Pneumothorax

Pneumothorax means presence of air or gas in the pleural cavities. Because inflation of the lungs requires negative thoracic pressure, the presence of air causes the lungs to collapse. Pneumothorax commonly results from a broken rib fracturing the pleural membrane, allowing air to escape from the pulmonary parenchyma.

Pleural effusions

Pleural effusion is a generic term meaning accumulation of any kind of fluid (without inflammation) in the thoracic cavity.

- Hydrothorax means there is too much edema fluid in the thoracic cavity.
- Hemothorax refers to the presence of blood in the pleural cavities. It usually happens as a result of traumatic rupture of blood vessels.

What are sequelae of pleural effusions? The fluid causes compression of the dependent lung resulting in atelectasis, and therefore pulmonary impairment. They can usually be resolved through resorption unless the quantity is too large.

Pleuritis

The term for inflammation of the pleura is pleuritis. Pleuritis often accompanies severe pneumonia, in which case the term pleuropneumonia should be used.

- Pyothorax means the pleural cavity is full of pus.
- Blackleg, caused by Clostridium chauvoei, will also create a pleuritis.

If enough fibrin exudes, it will progress to organizing fibrosis, leading to long-term adhesions which will continue to impair respiratory function for a very long time.
Lesson 9
Tumors of the Respiratory System

As a review, classification of tumors, from General Pathology:

<table>
<thead>
<tr>
<th>Origin</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>epithelial cells</td>
<td>polyp</td>
<td>carcinoma</td>
</tr>
<tr>
<td></td>
<td>papilloma</td>
<td>squamous cell carcinoma</td>
</tr>
<tr>
<td></td>
<td>adenoma</td>
<td>adenocarcinoma</td>
</tr>
<tr>
<td>mesenchymal cells</td>
<td>-oma</td>
<td>sarcoma</td>
</tr>
</tbody>
</table>

Tumors of the nasal cavity and sinuses:
Adenoma/adenocarcinoma
Fibroma/fibrosarcoma
Squamous cell carcinoma

Tumors of the lung:
Adenocarcinoma, or bronchogenic carcinoma – usually very malignant
Plus many tumors from other locations will metastasize to lung!

Tumors of the pleura and mediastinum:
⇒ Mesotheliomas may arise from the pleura but are rare.
⇒ Lymphosarcoma is the most common tumor in the mediastinum.
⇒ Thymomas also occur in the cranial mediastinum, as well as ectopic thyroid and parathyroid tumors and heart base tumors.
Lesson 10
Types of Pneumonia

Pneumonia means any inflammation of the lung. This term is preferred over “pneumonitis.”

Because this is a course about mechanisms of disease, we will begin with classifying pneumonias by their overall patterns. After this simple (maybe overly simple) system of classification, then we will use other terms to talk about specific types of pneumonia. So, here is our simple system:

<table>
<thead>
<tr>
<th>Type of pneumonia</th>
<th>Portal of entry</th>
<th>Lesion distribution</th>
<th>Kind of exudates</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Broncho-pneumonia</td>
<td>Aerogenous</td>
<td>Anteroventral</td>
<td>Suppurative or fibrinous, on surfaces (bronchi, pleura)</td>
<td>Enzootic pneumonia, shipping fever, Bordetella</td>
</tr>
<tr>
<td>Interstitial pneumonia</td>
<td>Aerogenous or hematogenous</td>
<td>Anteroventral or diffuse</td>
<td>Often can’t see them, they are within alveoli</td>
<td>Influenza, PRRS, toxins</td>
</tr>
<tr>
<td>Granulomatous pneumonia</td>
<td>Aerogenous or hematogenous</td>
<td>Multifocal</td>
<td>Granulomas, caseous nodules</td>
<td>TB, Blasto, Aspergillus</td>
</tr>
<tr>
<td>Embolic pneumonia</td>
<td>Hematogenous</td>
<td>Multifocal</td>
<td>Purulent foci</td>
<td>Septicemia, Actinobacillus equuli</td>
</tr>
</tbody>
</table>

So, here is what each might look like:

<table>
<thead>
<tr>
<th>Type of pneumonia</th>
<th>Appearance</th>
<th>Why?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal lung</td>
<td><img src="A" alt="Image" /></td>
<td>Pink, <strong>spongy, uniform</strong>, everything works fine.</td>
</tr>
<tr>
<td>Broncho-pneumonia</td>
<td><img src="B" alt="Image" /></td>
<td><strong>Anteroventral</strong> portion has the inflammation and the exudates, can be <strong>firm and reddened</strong> in this region</td>
</tr>
</tbody>
</table>
Interstitial pneumonia

The whole thing is swollen, so you see the rib imprints. Lung is affected **diffusely**, and will feel **rubbery**. Might be regular color, like this, or it might be red.

Granulomatous pneumonia

Big blobs, **distributed randomly**, varying sizes

Embolic pneumonia

Small foci, **uniformly distributed** throughout the lung, got there via the circulation

**BRONCHOPNEUMONIA**

The hallmark feature of bronchopneumonia is that the **inflammation originates in the bronchial tree**. As would be expected, the origin of bronchopneumonia is aerogenous – something nasty comes down the conducting tree.

**Grossly**, bronchopneumonias have irregular consolidation in anteroventral regions. What is consolidation? Basically it means that instead of air, that part of lung is solid and is filled with exudates or fibrin. If the bronchopneumonia is severe enough, it will involve the overlying pleura.

**What’s the time course?**

Within 2-3 days of bacteria becoming established at the bronchioloalveolar junction, there is red consolidation evident. Leukocytes migrating in in large numbers will change the color of the exudates to more of a gray appearance in 5-7 days. It may begin to resolve by 7-10 days, with slow turnover of type II alveolar cells back to the more efficient type I variety. The lung can return to normal by 3-4 weeks. Or, on the other hand, the whole lung can go to heck in a hand basket and the end result will be available for full viewing in the necropsy room within days, with all shades of red and gray, consolidation, and fibrin exudation.
However, many bronchopneumonias become chronic. This is seen most commonly in cattle and to a lesser extent in sheep. There is chronic suppuration with fibrosis. These animals will have poor growth.

**Gangrenous pneumonia, a special type of bronchopneumonia**

The usual cause of gangrenous pneumonia is entrance into the lung of material that shoulda stayed in the digestive tract. This includes ingesta that are vomited and inhaled OR intubating the trachea rather than the esophagus for delivery of material destined for the stomach. Oops. The definitive lesion of gangrenous pneumonia is death of tissue, big time. Death of the animal often occurs within 24 hours of aspiration. The characteristic lesion is liquefactive necrosis in a defined area. Putrefying bacteria help to enhance the odor. Gangrenous pneumonia is an especially nasty and acute form of bronchopneumonia. Animals usually die of septic shock and acute, severe alveolar damage.

**INTERSTITIAL PNEUMONIA**

Interstitial pneumonias are inflammatory conditions in which the predominant exudative and proliferative responses involve alveolar walls. Grossly, the lesions are distributed widely throughout the lungs. It is often caused by a blood-borne insult, but can also be aerogenous.

With interstitial pneumonia, we often don’t see exudates when we cut into the lungs. There is plenty of exudate, that is for sure, but since the damage is at the level of the alveolus, not a lot builds up in any one place to cause enough of an accumulation to actually see. Instead, the whole lung seems just bigger and firmer than normal, sometimes even rubbery. The lesions are really easy to see histologically though.

*The focus of damage is on and within the alveolar walls.*

There is a wide variety of causes of interstitial pneumonias. Inhalation of high concentrations of toxic gases or fumes will cause interstitial pneumonia. Many of the viruses that arrive at the lung, either from the blood stream, or from the air, settle at the bronchoalveolar junction, and from there quickly move to the alveoli, creating an interstitial pattern.

**GRANULOMATOUS PNEUMONIA**

This is a particular type of pneumonia where a pathogen, either inhaled or arriving at the lung via the bloodstream, settles out in the parenchyma to incite a typical chronic
granulomatous inflammation. Fungal diseases are most commonly the reason, but also some of the higher bacteria, such as mycobacteria or Rhodococcus equi, will do this as well. Distribution is multifocal, without regard for cranioventral or caudodorsal - they can settle out anywhere.

**EMBOLIC PNEUMONIA**

This term can be used to include pneumonias caused by any circulating particulates. Lungs are a biologic filter for circulating particulate matter. Causes of embolic pneumonia include those bacteria that tend to travel as septic aggregates – Histophilus somni and Actinobacillus equuli. Right-sided vegetative valvular endocarditis often causes an embolic pneumonia, as septic thrombi travel to and lodge in the lung.

The next 3 lessons will deal with pneumonia, based on ETIOLOGY. For each, keep in mind the classification method we just covered.
Lesson 11
Pneumonia – Viral

Many of the viral pathogens of lung replicate in airway and alveolar epithelial cells. Viruses use a specific receptor to ENTER a cell and many of these viral respiratory diseases of animal involve attachment to a receptor found on respiratory epithelium.

PARAMYXOVIRUSES

Parainfluenza-3
Parainfluenza type 3 virus induces acute respiratory disease in a wide variety of species including cattle, sheep and goats, and horses. It attacks cells of the conducting airways. It can cause pneumonia alone, but is more commonly part of the etiologic complex of enzootic pneumonia in calves or shipping fever in adults.

Bovine respiratory syncytial virus
Bovine respiratory syncytial virus occurs either alone in an outbreak form of pneumonia or in concert with other agents, especially bacteria, in the shipping fever syndrome. The virus attacks conducting airway epithelium, most severely that at the broncho-alveolar junction. Histologically there are frequently syncytial giant cells formed by fusing bronchiolar epithelial cells. Bronchiolitis obliterans is often seen in BRSV infections.

Canine distemper
Canine distemper remains endemic globally, with virus maintained in wild carnivores even if totally controlled in domestic dogs. So there is a continuing reservoir to spill over into unvaccinated dogs. Infection with canine distemper virus is pantropic, which means that a number of tissues and organs are targeted by the virus. The virus infects epithelium in multiple organs, so for the respiratory system, this would include nares, trachea, bronchi, bronchioles, and alveolar cells. Yikes. Also, a big problem with canine distemper is that it also affects the lymphoid system, there is usually immunosuppression and so secondary infections of lung are common. Two such secondary agents are Bordetella bronchiseptica and Toxoplasma gondii. Consequently, the pneumonia could look like a bronchopneumonia or an interstitial pneumonia. And, if the dog survives the pneumonia, the virus usually goes on the brain.

Peste des petits ruminants
This virus is closely related to rinderpest, and causes enteritis and pneumonia in sheep and goats. The disease is endemic in much of Africa and the Middle East, but is foreign to this hemisphere. Grossly and histologically, the lung lesions look just like canine distemper.
ORTHOMYXOVIRUSES

The Orthomyxoviridae include the influenza viruses, which infect several domestic species.

✓ Equine influenza
   Disease usually occurs in young animals that are stressed and/or grouped with older horses. It may occur in outbreak form, with high morbidity but low mortality. The primary importance of the disease is its economic impact, as horses with current influenza infections cannot race or train. The virus infects both ciliated and alveolar cells, so it can look like a bronchopneumonia or an interstitial pneumonia.

RETROVIRUSES

✓ Caprine arthritis-encephalitis
   This lentivirus usually attacks the joints of goats, causing festering and long term arthritic problems. However, occasionally it causes a distinct pneumonia in older goats – with extensive alveolar filling by dense, acidophilic, lipoproteinaceous material, with widespread alveolar type II cell hyperplasia. The pathogenesis of this pneumonia is unclear, but because it primarily affects alveoli, it is classified as an interstitial pneumonia.
Lesson 12

Bacterial pneumonias

BOVINE ENZOOTIC PNEUMONIA

Bovine enzootic pneumonia is composed of a number of etiologies, all of which can be interacting in synergy. It usually starts with a viral infection, maybe PI-3, or BHV-1, or a mycoplasmal infection, *Mycoplasma bovis* or *Ureaplasma*. After those are set up, then opportunists move in and set up camp - *Pasteurella multocida*, *Arcanobacterium pyogenes*, or *E. coli*. In some cases, *Mannheimia hemolytica* can move in and cause a full-fledged shipping pneumonia, which is covered further below.

The main features of bovine enzootic pneumonia are that it is ANTEROVENTRAL and that this part of the lung has evidence of consolidation - there is exudate in there, and the respiratory exchange in that part of the lung is impaired. With the organisms actively causing infection, there may be constant or recurrent fever, lack of sufficient growth, and some degree of respiratory compromise.

![Image of bovine enzootic pneumonia](image)

Sheep also get a chronic enzootic pneumonia with similar players, pathogenesis, and clinical picture.

PNEUMONIC PASTEURELLOSIS

The members of the *Pasteurella* genus are widely distributed among a variety of animal species. All are strict parasites of animals and survive poorly, if at all, in the environment. They are carried subclinically, usually in the upper respiratory tract, and migrate down the bronchial tree to cause disease when the opportunity presents itself.

époque CATTLE

In cattle, the *Pasteurella* that causes severe lung damage is now reclassified as *Mannheimia*, so this disease should be rightly called “pneumonic mannheimiosis”. *Mannheimia haemolytica*, formerly known as *Pasteurella haemolytica*, biotype A, causes a fibrinous or fibrinonecrotic bronchopneumonia, often with significant hemorrhage. It has a bronchopneumonia pattern but often spreads quickly and extensively to many parts of the lung. This disease occurs so regularly after a period of transport that it is commonly referred to as “shipping fever.”
Infecting animals with *Mannheima hemolytica* alone doesn’t cause disease! It can ONLY gain a foothold to cause disease after the respiratory defenses have been compromised.

Grossly, the lungs have extensive red-black consolidation in cranioventral regions, with generous coverings of the pleura by fibrin. Histologically, the necrotic regions are multifocal but may be coalescing and very extensive.

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Endotoxin and leukotoxin, both elaborated by the bacteria, figure importantly in the pathogenesis.
- Endotoxin facilitates thrombosis, leading to ischemic necrosis.
- Leukotoxin incapacitates the white blood cells recruited to the scene.

It should be noted that *Pasteurella multocida* may also cause severe fibrinohemorrhagic pneumonia but usually disease due to *P. multocida* is less severe than that due to *Mannheimia haemolytica*. Also, *P. multocida* is often associated with enzootic bovine pneumonia.

**SHEEP**

*Pneumonic pasteurellosis* in sheep is usually caused by *Mannheimia* (previously *Pasteurella*) *haemolytica*. Lambs are especially prone to develop disease, and, as with pneumonic pasteurellosis in cattle, there is almost always an intercurrent stress or viral infection.

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*Histophilus somni* (formerly known as *Haemophilus somnus*) is the cause of a number of disease syndromes in cattle, all related to the ability to produce septic emboli. The organism survives within phagocytic cells, can bind immunoglobulin, making for big clusters of protected pathogens that can circulate. When they lodge in the brain, the disease is known as thrombotic meningoencephalitis (TME), but it can also cause arthritis, ophthalmitis, and abortion. In the lungs, the bacteria can engender a severe fibrinohemorrhagic embolic pneumonia.

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*Tuberculosis*

Bovine tuberculosis, caused by *Mycobacterium bovis*, is the principal respiratory tuberculous disease seen in animals. *M. bovis* will also infect some other species, including humans. The usual route of infection is respiratory. The tuberculous pulmonary process starts at the bronchiolo-alveolar junction and develops into a tuberculous granuloma, or tubercle. This tubercle is the result of an ongoing battle between the tubercle bacilli and the cell mediated immune response. Macrophages are unable to overwhelm this facultative intracellular parasite and so inflammatory cells are
continually recruited. Formation of giant cells is typical as macrophages continue to battle the agent unsuccessfully.

Tuberculosis is a chronic disease caused by bacteria of the genus Mycobacteria. Human tuberculosis is an ancient disease and of great historical as well as current importance. Mycobacterium tuberculosis infects one of every three humans in the world and continues to cause extensive mortality.

Rhodococcus equi

This is an important cause of pneumonia in foals. Rhodococcus equi lives in soil and the intestinal tract of a number of species. Disease is usually seen in foals <6 months of age. Mortality with this disease is commonly 40-80%.

Grossly, there are multiple firm nodules of various sizes. The nodules are poorly encapsulated and consist of slimy to friable material. Rhodococcus pneumonia is often accompanied by a pyogranulomatous lymphadenitis. Pleuritis is rare; this is a disease of the pulmonary parenchyma.

Mycoplasma diseases

Most species of animals have their own mycoplasma species responsible for a chronic lymphoproliferative pneumonia, with relatively few clinical signs other than decreased growth rate. However, there are two mycoplasmal diseases which are extremely different from all the others –but of great importance globally – contagious bovine pleuropneumonia and contagious caprine pleuropneumonia. Contagious bovine pleuropneumonia is restricted to Africa and won’t be covered.
ENDEMIC MYCOPLASMAS

☞ CATTLE

Respiratory mycoplasmosis of calves - Mycoplasma bovis is the most common Mycoplasma in calves. It can occur alone or be part of the enzootic pneumonia complex. The organisms live among the cilia in the bronchi and so cause a chronic bronchitis and predispose to bacterial secondary infections. The organisms also incite great proliferation of the bronchial-associated lymphoid tissue (BALT). Many airways become surrounded by prominent lymphofollicular sheaths, leading to the term “cuffing pneumonia” for this disease.

☞ SHEEP

Respiratory mycoplasmosis of sheep – M. ovipneumoniae is one of the etiologic factors that combine to cause enzootic pneumonia of sheep. Lesions are identical to that seen in respiratory mycoplasmosis of calves.

★ Contagious caprine pleuropneumonia

The causative agent is Mycoplasma capricolum subsp. capripneumoniae. It gets in and causes a terrible, necrotizing, usually unilateral disease that KILLS. Mostly in goats but occasionally a sheep that is with goats may get it.

⇒ ⇒ ⇒ NONSPECIFIC BACTERIAL PNEUMONIAS

Lots of bacteria can cause inflammation when they get down into the deeper airways and pulmonary clearance mechanisms are impaired.

In particular, all of the pyogenic organisms are associated with suppurative bronchopneumonia – these include streptococci, staphylococci, Actinomyces pyogenes, Pseudomonas aeruginosa, and Klebsiella pneumoniae.

Young animals with septicemias can have bacteria localizing in lungs and engendering a severe interstitial pneumonia. These include streptococci, E. coli, Actinobacillus equuli in foals, and Salmonella sp.
Lesions due to parasites in the lung come in two categories. There are those parasites who live specifically in lung, then there are others who merely do damage as they migrate through to somewhere else. Each one in the text below is marked accordingly:

- \( \text{µ} \) = lives in lung
- \( \text{η} \) = just passes through

The life cycle of each parasite is in a box like this – you are not responsible for all the details but you should be aware of the pertinent features of each.

**SHEEP AND GOATS**

_ Muellerius capillaris_

This is the most common of the lungworms. The adults live in the alveolar parenchyma rather than the bronchi and bronchioles. Also known as the nodular worm, this parasite is noted for its ability to cause multiple granulomatous nodules in the lung, especially the dorsocaudal areas.

Adults lay eggs in the nodules; first stage larvae get on the mucociliary escalator and are pooped out. Slugs and snails are the intermediate host; sheep and goats swallow these; larvae are liberated in the digestive tract and pass through the lymphatics to the lung.

**Dictyocaulus filaria**

_D. filaria_ lives in the small bronchi. Adult worms can cause chronic catarrhal and eosinophilic bronchitis and bronchiolitis. Excess mucus production is present. There may be atelectasis because of bronchiolar plugging.

The life cycle of ALL the _Dictyocaulus_ is direct. Embryonated eggs hatch in the lung or in the digestive tract after their ride on the escalator. Then larvae are either coughed out or pooped out. Development to an infective stage requires moist ground and low temperatures and takes at least a week.
COW

Dictyocaulus viviparus
The adults live in the large bronchi and cause obstruction through inflammation and also through large numbers of parasites. As a result air can flow into the alveoli, but the plug of exudate and parasites prevents complete expulsion of air on expiration. The alveolar lumens become distended with air and emphysema results.  
Life cycle is direct.

HORSE

Dictyocaulus arnfieldi
The donkey is considered the natural host for Dictyocaulus arnfieldi. Donkeys can tolerate large numbers of D. arnfieldi without ill effects, but horses cannot. These parasites accumulate in the small bronchi, inciting a chronic catarrhal bronchitis. Air becomes trapped in alveoli distal to the accumulation, resulting in a gross picture of scattered foci of hyperinflated pulmonary parenchyma. D. arnfieldi is usually not patent in horses – thus examination of fecal samples may not be helpful.  
Life cycle is direct.

Parascaris equorum
This is probably the most common nematode that migrates through equine lung. Large numbers of migrating larvae may cause coughing, anorexia and weight loss. An interstitial interstitial pneumonia may result.