Lung General, Circulatory and Inflation Disturbances

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Parasitic Bronchitis and Bronchiolitis

Some nematodes parasitize the bronchi and bronchioles causing chronic bronchitis and bronchiolitis. As a result of prolonged parasitic injury, the bronchial mucosa becomes hyperplastic and the bronchiolar mucosa becomes metaplastic with proliferation of mucus producing goblet cells.

Affected animals develop obstructive pulmonary disease caused by bronchial plugs of mucus mixed with parasites. These parasitic diseases are often referred to as verminous pneumonia or verminous bronchitis.
Few respiratory diseases in domestic animals affect exclusively the transitional system (bronchioles). Bronchioles are typically affected as part of a generalized lung disease such as it is the case with bronchopneumonias, viral infection, etc.

Asthma in cats and heaves in horses are the most important veterinary diseases in which lesions are exclusively centered in the bronchioles.

There histological features of bronchioles are shown in the next slide.
Transitional System (Bronchioles)

- Unlike bronchi, bronchioles do not have cartilage.
- Bronchioles have thin walls and are lined by a very specialized epithelium.
- Normal bronchioles DO NOT have mucus (goblet) cells.
- Bronchioles have few ciliated cells.
- Bronchioles contain large numbers of highly metabolic cells known as Clara cells. These cells are involved in metabolism and detoxification.
- Not surprisingly, bronchioles of smokers have considerable more Clara cells to try to detoxify the hundreds of toxicants present in inhaled tobacco smoke.
Microscopic view of a equine lung with **Heaves** stained with Alcian blue to demonstrate the mucus. Note the bronchioles lined by goblets cells (arrows) discharging mucus into the bronchiolar lumen. The lumen is filled with mucus causing obstruction (asterisk). There are also inflammatory cells in the bronchiolar walls (red circle).
"Heaves" (COPD), Recurrent Airway Obstruction (RAO).

This is a common and important equine disease. Airflow impairment eventually leads to alveolar emphysema (discussed under inflation disturbances of the lung).

As a result of what appears to be an allergic response, bronchiolar epithelium undergoes inflammation and goblet cell metaplasia. Remember that there are no goblet cells in the healthy bronchiole, hence the term metaplasia rather than hyperplasia.

Abnormal respiration in affected horses results in hypertrophy of the abdominal muscles which is clinically referred to as "heave line."

Gross lesions in the lung are not remarkable except perhaps for some degree of emphysema in the most severely affected horses.

Microscopic view of lung from a horse with clinical history of Heaves. Note again the bronchioles obstructed with a dense plug of mucus (blue material).
Canine and Feline Asthma are relatively rare. As it occurs in equine heaves, there is mild bronchial and bronchiolar inflammation but severe goblet cell hyperplasia and metaplasia. The airways are plugged with mucus hence the severe clinical signs. However, there is very little to observe on gross examination of the lungs.
What is this? Any idea?

Cast of mucus coughed-up by a patient with chronic obstructive pulmonary disease. Look at the size (see ruler).
There are marked anatomical differences in the lungs of domestic animals. For example, in horses, pulmonary lobes are not well-defined as in pigs, cows, dogs and cats.

Besides differences in lobation (lobes), there are also differences in the lobulation (lobules) of lungs. Pigs and cattle have defined lobules while dog and cats have poorly defined lobules.
Normal lungs collapse when the thorax is opened (loss of negative pressure) i.e., lungs are smaller than thoracic cavity (arrows).

Note the uniform normal pink appearance of lung parenchyma.
Note the color difference between these two normal lungs.

The lung on the top belongs to a calf that was exsanguinated prior to post-mortem examination.

The equine lung on the bottom is also normal but there was no exsanguination.
Lung / Plastic embedded section 1µ thickness.

A terminal bronchiole appears as a small round structure lined by cuboidal epithelial cells (Br). Some of the cells lining bronchioles are Clara cells which are highly metabolically active cells involved in detoxification of substances in the lung.

Most of the alveolar surface facing the air (A) is lined by thin cells known as membranous or type 1 pneumonocytes (not seen by light microscopy). There are also a few plump surfactant-producer cells called pneumocytes type 2 (P-2) and some pulmonary alveolar macrophages (PAM).

The alveolar walls are notably thin (arrows).

The three-layer endothelium/basement membrane/type 1 pneumocytes constitute the blood-air barrier. The dark cells within capillaries (C) are erythrocytes (rbc) and some of them were artificially displaced into the alveolar lumen during processing.
Blood-Air Barrier / Diagram

Air blood barrier:
- Capillary endothelium
- Basal lamina
- Pneumonocyte type 1
Note numerous black dots on the lungs of this dog. The most common exogenous lung pigmentation in domestic animals (pneumoconiosis) is anthracosis which literally means deposition of inhaled carbon.

Anthracosis is seen in animals living in an environment contaminated with carbon such as in big polluted cities, mines or even in houses with fireplaces or smokers.

If you are a heavy smoker, your lungs will accumulate monumental amounts of carbon which could make this canine lung appear as clean as Snow White’s wedding dress.
Pulmonary Hyperaemia / Pneumonia / Ovine.

Note the distinct deep red color of the cranioventral lung with acute inflammation (pneumonia). In contrast, the caudal lung (C) appears essentially normal.

As in any other tissue, inflammation results in active vasodilation with increased blood in the organ (hyperaemia).

Hyperemia should be differentiated from passive stagnation of blood referred to as congestion (see next slide).
Pulmonary Congestion / Congestive Heart Failure / Dog.

Note red-patchy discoloration of congested lung parenchyma in contrast to the normal, more pale parts of the lungs.

Pulmonary congestion in this dog was due to heart failure from a congenital heart defect. The asterisk shows an abnormal communication between the left and right ventricle (ventricular septal defect or VSD).

In pulmonary congestion, fluid and erythrocytes escape into the alveolar space causing edema and intra-alveolar hemorrhages.

"Heart failure cells" are alveolar macrophages filled with hemosiderin from RBCs.

Macrophages with brown pigment known as "heart failure cells" in alveoli are seen histologically. Irons stain (Prussian-blue) confirm the presence of iron in these macrophages.
Ruptured Pulmonary Aneurism

- Massive fatal epistaxis from a ruptured pulmonary aneurism.
- This condition often develops when a pulmonary abscess erodes a major pulmonary vessel.
Fatal Pulmonary Hemorrhage

Holstein cow found dead in a pool of blood. Postmortem examination revealed a large abscess in the lung that cause the rupture of a major pulmonary blood vessel.

Bronchial tree filled with clotted blood
Fatal intrapulmonary hemorrhage and epistaxis occur occasionally in cattle when a pulmonary abscess erodes the wall of a major vessel (aneurism).

The diagram shows how an abscess (brown) erodes a blood vessel (red) with heavy intrapulmonary hemorrhage into the airways (blue).

Affected animals cough large amounts of blood (hemoptysis and epistaxis). Bleeding is often massive, causing rapid death due to hemorrhagic anemia. The bronchi and trachea are filled with blood (asterisks).

The is the lung of a cow that died acutely with epistaxis. Note massive amounts of blood in bronchi.

Animals affected with this condition suddenly expel considerable amounts of blood through nostrils and mouth. Death occurs within minutes.
Pulmonary Hemorrhage

Common causes include:

- Congestive heart failure
- Trauma (rib fractures, pulmonary contusion)
- Coagulopathies (anticoagulants, Immune-mediated thrombocytopenia)
- Disseminated Intravascular Coagulation (DIC)
- Lung embolisms
- Rupture of blood vessels due to abscesses, aneurisms, parasites, etc.

Lungs of dog poisoned with warfarine
Jugular Thrombosis and Pulmonary Infarcts / Bovine.

Jugular vein (jv) with large thrombus (t) attached to the surface. Black arrows point to the valves in vein.

**Lung** (right photo) shows a large embolus lodged in the pulmonary artery (**white arrow**). Sterile thrombi, unless extremely large in size, are rapidly dissolved and removed by fibrinolysis causing little, if any ill effect.

Large of lung shows several pulmonary infarcts (**white asterisks**) that appear as small dark-red foci in generally found in the margin of the lung. In contrast to other organs such as kidney, brain, heart, pulmonary infarct are rarely clinical significant because of double circulation of the lung.
Pulmonary Thrombosis

Histological view of an early thrombus (T) in a medium size pulmonary artery adjacent to a bronchiole.

Histological view of a thrombus (T) in a medium size pulmonary artery of a cat that died of cardiomyopathy. There are few “heart failure cells” in the alveoli.
PULMONARY EDEMA

- Pulmonary edema is often the terminal cause of death in many diseases.

- Pulmonary edema is characterized by accumulation of fluid in interstitium and alveoli.

The most common forms of lung edema are caused by:

- Increased vascular permeability (injury to alveoli, inflammation)
- Increase hydrostatic pressure (heart failure)
- Lymphatic obstruction (tumor metastasis)
Foam in the nostrils and mouth is often seen in animals dying of severe pulmonary edema

Note foam coming out through the nostrils in an steer that died of severe pulmonary edema. Foam is formed when the protein-containing fluid in airways is mixed with inspired air following vigorous inspiratory movements.

Clinically, pulmonary edema is subdivided in two main types:

• **Cardiogenic edema** where fluid accumulates in the lungs due to cardiac failure. There is increased hydrostatic pressure with leakage of fluid first to the interstitium and then to the alveoli.

• **Non-cardiogenic edema** that generally results from altered vascular permeability. Injury to the blood-air barrier (endothelium or pneumocytes) allows fluid to pass from capillaries to alveoli. Obstruction of lymphatic drainage is also considered a non-cardiogenic edema.
Pulmonary Edema

Pulmonary edema / Froth in the trachea.

A good indicator of a pulmonary edema at postmortem is the presence of froth in major airways.

Remember that froth is formed when fluids in the bronchoalveolar space mixes with air during respiration.

Since considerable edematous amounts of fluid in the lungs are required to kill an animal, it is necessary to see this froth to incriminate pulmonary edema as actual cause of death.
• Remember that the lungs normally produce fluid that is absorbed at the same rate by the pulmonary lymphatic vessels. Lymphatic drainage has considerable reserve capacity and edema only develops when this drainage has been overwhelmed.

• How effective is the removal of fluids from the lungs by normal lymphatic drainage? Experiments have shown that several gallons of fluid can be infused into the lung of horses without causing edema as long as the infusion is done slowly.

• Edema develops rapidly in animals when leakage of fluid exceeds the lymphatic removal or when there is lymphatic obstruction by inflammation or lymphatic metastasis.
Gross Examination

Lung edema. Pleural surface

• Interlobular septa appears distended (arrows).
• Interlobular distention occurs when overactive lymphatic vessels become distended with fluid.

Lung Edema cut surface.

• The lungs appear wet
• Note also the edematous distention of the interlobular septae (arrows).
• Edema often appear as gelatinous fluid.
**Pulmonary Edema**

**Gross**

*Cut Surface.* Note considerable amounts of fluid coming out of airways. Remember, no foam in airways, no postmortem diagnosis of an edema.

Always make sure you check the trachea and bronchi for foamy fluids before you diagnose or rule out the edema in non-deflated lungs.

**Histology.** The alveoli are filled with edematous fluid. Edematous fluid, particularly in permeability edema, is rich in protein and therefore appears pink (eosinophilic) in tissue sections. Very few alveoli in this section contain air (see asterisks)

It is important to emphasize that moderate amounts of fluid produced in the lungs of normal animals are removed through normal lymphatic drainage.
Lungs: Histopathology H&E. Normal and Pulmonary Edema

On one left side there is a normal lung in which the airspaces are filled with air (empty alveoli).

The lung on the right side is notably edematous and the alveolar spaces are filled with fluid. The eosinophilic (pink) appearance of the fluid is due to the plasma protein leaked out from the blood vessels. The animal died, foaming from the nostrils.

In general terms, cardiogenic pulmonary edema has less protein than non-cardiogenic, since injury to air-blood barrier in the latter results in leakage of plasma protein into alveoli.

Remember that lung edema in non-fatal cases impairs pulmonary defense mechanisms and therefore may predispose animals to secondary bacterial pneumonia. It also explains why human patients with lung edema are generally put on antibiotics.
There is another interesting type of lung edema in which the pathogenesis involves severe brain injury. It is generally referred to as “Neurogenic pulmonary edema.

Respiratory failure in the neurological patient: the diagnosis of neurogenic pulmonary edema.

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Neurogenic pulmonary edema (NPE) is a potential complication of a central nervous system (CNS) insult such as intracranial hemorrhage, uncontrolled generalized seizures, head trauma, tumors, and neurosurgical procedures. The proposed etiology is massive sympathetic discharge following a CNS event. The pathogenesis is not completely understood. However, there are two theories on how NPE occurs: the blast theory and the permeability defect theory. There is evidence for both theories, and NPE is probably the result of a combination of the two. The treatment is mainly supportive with the use of mechanical ventilation and oligoanuric hemodialysis.
Atelectasis

Fetal lungs do not contain air and therefore are in a state of atelectasis. Inflation of alveoli occurs immediately at birth following inspiration.

Congenital atelectasis occurs when lungs fail to inflate after birth due to deficient production of pulmonary surfactant, a tensoactive substance produced by type II pneumocytes and is required for keeping the alveoli un-collapsed. Congenital atelectasis can also occur when meconium is aspirated into the lungs during birth. Meconium lodged in the airways does not allow for normal inflation.

**Acquired atelectasis** occurs when previously inflated alveoli are deflated due to pressure or obstructed with exudate or aspirated material.

This diagram illustrates the appearance of a normally distended alveolus (n) and an atelectatic alveolus (a). Atelectasis means atele= incomplete; ectasia= dilation; therefore atelectasis could be simply defined as incomplete distention of alveoli.

**Pathogenesis:**
**Neonatal:**
- Meconium aspiration
- Lack of surfactant
**Acquired:**
- Compressive
- Obstructive
Fetal lung / Porcine.

Lung inflation occurs with the first breath at the time of birth. In this slide, the fetal lungs appeared "meaty" due to lack of distention (aeration) of airspaces and "wet" due to presence of fetal lung fluid. This fluid is normally present in the fetal lung and it is rapidly reabsorbed by the lymphatic system soon after birth.

**Congenital atelectasis** is rarely diagnosed in animals as compared with humans. It is associated to airway obstruction (mucus or meconium), or with the defective production of surfactant by type II pneumocytes. These surfactant problems are seen in babies born to diabetic or alcoholic mothers. Biochemical analysis of amniotic fluid (amniocentesis) in “high risk mothers” allows the physician to be prepared for the delivery of babies with impending "neonatal distress syndrome.” Most important, this permits treatment by intratracheal administration of synthetic surfactant. A few days later, the type II pneumocytes of affected babies are already producing normal surfactant and treatment is no longer required.
**Congenital Atelectasis**

Lack of alveolar aeration results from airway obstruction caused by aspiration of amniotic fluid containing pieces of meconium (fetal intestinal contents 1-4).

**Meconium Aspiration Syndrome** used to be a common problem in newborn babies. However, it is rarely seen nowadays since current obstetric procedures routinely prevent the occurrence of this syndrome. At the time of birth and before the first breath of air is taken, the nasopharynx is aspirated to remove any meconium present in the airways. The relevance of Meconium Aspiration Syndrome in Veterinary Medicine is not completely understood.

Note a mosaic pattern in the lung of this calf born with meconium aspiration syndrome. The patchy appearance of the lung results from the presence of normally aerated (pale) lobules next to non-aerated (dark) lobules.
Focally extensive atelectasis / Bovine.

Note large circumscribed area of dark discoloration (meaty appearance) in an intermediate lobe of the lung (asterisk).

Atelectasis in this calf resulted from chronic lung inflammation, likely a bronchopneumonia. Plugs of exudate mixed with mucus obstructed the airflow.

It is important to emphasize that atelectasis and pneumonia have a rather similar gross appearance. Close observation reveals that atelectasis lung is depressed in relation to the adjacent normal parenchyma. In contrast, the pulmonary parenchyma of a consolidated pneumonic lung appears raised in relation to the normal tissue. The problem is that atelectasis and bronchopneumonia often coexists.
**Traumatic Reticulopericarditis / Cow.**

Note dark appearance of lungs. In this case, atelectasis resulted from the compressive effect of a massively enlarged pericardial sac due to traumatic reticulo-pericarditis (hardware disease). The pericardial sac is thickened and contains large amounts of organized fibrin ("bread and butter").

**Click her to see open pericardium**

**Hydrothorax / Dog.**

Note dark appearance of lungs (arrows). In this case, atelectasis resulted from the compressive effect of fluid in the thorax (hydrothorax). The primary problem is this dog was congestive heart failure due to valvular endocarditis.
Atelectasis / Histology H&E

Note collapsed alveoli (double-arrow) in one affected lobule. There is a complete loss of airspaces.

Normal / Histology H&E

Note expanded alveoli (a) in a normal lobule. There is normal expansion of airspaces.

Cattle and pigs have well lobulated lungs, so it is possible to have a normal lobule contiguous to an atelectatic one.
Emphysema is an abnormal, permanent enlargement of alveoli with destruction of walls. Reversible enlargement without destruction of alveolar walls is called "hyperinflation."

Emphysema is a common lesion seen in both animals and humans.

In animals, primary emphysema is rare. It generally develops in association to other pulmonary obstructive or inflammatory lesions.

Agonal emphysema is common in animals dying with exaggerated inspiratory movements, particularly in cattle.

There are three main types of emphysema in animals:

- Alveolar emphysema
- Interstitial emphysema
- Bullous emphysema
Alveolar Emphysema

Normal

Emphysema
permanent enlargement
of alveoli with
destruction of alveolar
cells.
**Alveolar Emphysema**

**Pulmonary emphysema / Bovine.**

Note many variable size pockets of air involving all areas of the lung.

As you may expect from the appearance of this lesion, the lung texture would be crepitous due to the excessive presence of gas.

Alveolar emphysema is difficult to evaluate in mild cases. It may require to insert a plug in the trachea during the necropsy and rapidly perfuse the lungs with fixative.

Equine Heaves is an important disease causing alveolar emphysema in horses (See Pathology of the Transitional System)

In animals with well-developed interlobular septa such as cattle and pigs, air gains access to the interlobular septum causing interstitial emphysema. In these cases the interlobular interstitium becomes markedly distended as shown in the next slide.
Interstitial Emphysema

Bovine.

Note that the interstitial septum is distended with air (arrows), and some areas of emphysema have become confluent giving origin to emphysematous bullae. Emphysematous bullae are large pockets of air (>1 cm diameter).

Also note in this slide some pulmonary lobules with atelectasis appear darker in color (as tersks). Atelectasis here is likely due to the compressive effect of emphysema.

Since distention of one part may produce compression of another part of the lung, it is not surprising that emphysema and atelectasis often are present together in the same lung.

For a close-up of a bullous emphysema click here.
Emphysematous Bullae

Canine, Lung Dysplasia. Note large pockets of air in the lungs.

The texture of affected lung would be crepitous.
Pulmonary Emphysema; Equine; History of colic. Aspiration of mineral oil 48 hours prior to death. Note small pockets of air in the pulmonary parenchyma. Texture would be crepitous.
For many years it was thought to be the result of chronic obstruction of airways. Numerous investigations have revealed that alveolar emphysema in human beings results from the effects of elastases and other proteolytic enzymes released by phagocytic cells in the lung. The release of proteolytic enzymes in the lung is notably enhanced by tobacco smoke since there is an increase influx of macrophages and neutrophils into the lung.
Besides lung cancer and cardiovascular diseases,...
--there is also unequivocal scientific association between cigarette smoking and pulmonary emphysema (COPD)