Respiratory System
Module 1
Structure and Defense Mechanisms

Alfonso López
Atlantic Veterinary College
University of Prince Edward Island
Canada
lopez@upei.ca

©2018
If you find this tutorial useful, feel free to share it with fellow students. Also, if you have any questions, please let me know at lopez@upei.ca

QUIZ ALSO AVAILABLE

At the end of this module, there is a simple QUIZ to test your knowledge on this subject.

It is a QUIZ just for you, and nobody gets to see your answers.
The respiratory tract has 3 independent but continuous systems:

1.- **Conducting system** consists of the nasal cavity, sinuses, larynx, trachea, and bronchi, all lined by ciliated epithelium and goblet cells (mucociliary epithelium).

2.- **Transitional system** consists exclusively of the bronchioles lined by non-ciliated secretory cells, Club (Clara) cells, and only a few ciliated cells. Healthy bronchioles DO NOT have goblet (mucus) cells.

3. **Exchange system** consists of alveoli lined by epithelial type I (membranous) and type II pneumonocytes.

Each of 3 these systems has a particular susceptibility to injury and a distinct type of host response and repair.
In addition to oxygenation, the respiratory system also plays several other physiological functions

<table>
<thead>
<tr>
<th>Phonation</th>
<th>Temperature regulation</th>
<th>Blood Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olfaction</td>
<td>Acid-base</td>
<td>Detoxification</td>
</tr>
<tr>
<td>Metabolism</td>
<td>Hormones</td>
<td>Inflammatory Mediators</td>
</tr>
</tbody>
</table>
Like any mucosa in contact with the external environment, the mucosa of the proximal respiratory tract harbors a healthy population of bacteria known as the nasal flora or microbiota.

If a sterile swab is inserted into the nasal cavity of any healthy animal, and the swab is sent for microbiological culture, many species of bacteria will grow.

These organisms constitute the normal flora of the respiratory tract.
Mannheimia haemolytica and Bordetella bronchiseptica are normal nasal flora, yet both bacteria are also responsible for "Shipping Fever" in cattle and "Atrophic Rhinitis" in pigs.

Although most organisms of the nasal flora are harmless, others can potentially become pathogenic for the lung. For example:

Bacteria isolated from a dead animal is sometimes erroneously incriminated by veterinarians as the causative agents of disease.
The nasal flora only inhabits the most proximal regions of the conducting system; that is the nasal cavity, the nasopharynx, larynx, and trachea.

The bronchi, bronchioles, and alveoli are essentially sterile.
Bacteria from the nasal flora, including potentially pathogenic organisms, are continuously being carried into the lung by the inspired air. However, these organisms are rapidly destroyed and removed from the lungs.

In spite of this continuous bacterial bombardment, the bronchioles and alveoli remain sterile due to the efficient defense mechanisms of the lung.
Even the cleanest atmospheric air contains zillions of particles such as pollen, bacteria, viruses, yeasts, mites, silica, carbon and dust. The air also contains vapors and gasses.

Imagine how many air particles are present in a dusty barn or feedlot.

In the healthy lung remains microorganisms are destroyed, particles are removed and toxicants and neutralized.
Particle Deposition in the Respiratory Tract

- **> 10 microns**: Nasal Deposition
- **10-2 microns**: Bronchial Deposition
- **2 µm or less**: Alveolar Deposition
Defense Mechanisms

Non specific
- Air turbulence
- Particle trapping in mucus
- Mucociliary clearance
- Cough
- Sneeze

Specific
- Antibodies
- Secretions
- Cellular immunity
- Phagocytosis
- Inflammation
10 microns or larger particles are filtered out in the nasal cavity.

Note narrow spaces (arrows) between dorsal (D), ventral (V) and ethmoid (E) conchae.

These tight spaces are known as meatuses. LT = Lymphoid tissue.

Also, the coiled shape of the conchae (asterisks) create vortexes that result in the impaction of air particles on the nasal mucosa.
Histology: pollen particle trapped in the nasal meatus
Particles 2-10 microns collide on the mucus at the bronchial bifurcation due to the sudden change in the air direction (red oval circle)

The mucociliary blanket
- Inhaled particles

- 100-200 cilia/cell
- 1,000 ciliary beats /minute

Metachronous pulse of the cilia moves mucus out of the airways like a wave propels surfers to the beach.
Particles 2 microns or smaller reach the alveoli but are rapidly taken by the pulmonary alveolar macrophages. Bacteria and viruses are in this size range.

PAMs exit the lung via the mucociliary escalator.

Ciliary movement transport PAMs into the nasopharynx where they are swallowed.

Alveoli do not have cilia or mucus.
How effective are the pulmonary defense mechanisms?

To answer this question scientists developed an experimental model known as Pulmonary Bacterial Clearance in which animals receive an aerosol of bacteria, and the number of bacteria remaining in the lung is calculated over time.

When a healthy animal inhales *Mannheimia haemolytica*, the number of bacteria in the lung decreases exponentially. By 24 hours all bacteria disappear as shown in this graph.
**Question:** If bacteria are rapidly eliminated from the lung then why bacterial pneumonia is so prevalent in animals?

**Answer:** Viral infections suppress the defense mechanisms allowing bacteria to colonize the lung. See graphic

This experimental model demonstrates two facts:

1. Healthy lungs rapidly eliminate inhaled bacteria.
2. Viruses such as IBR, BRSV, PI-3, EVR, FHV, distemper inhibit the pulmonary defense mechanisms thus predisposing the lungs to secondary bacterial pneumonia.

Rapid elimination of inhaled bacteria in a healthy lung (---).

Bacteria multiply in the lung after a viral infection (----).
Besides viruses which other factors could also impair pulmonary bacterial clearance?

- Lung Edema
- Stress
- Immuno-deficiency
- Dehydration
- Uremia
- Ammonia
Because of the abundant vascularization, the nasal cavity is unusually prone to:

- Hyperemia
- Congestion
- Hemorrhage (epistaxis)
• **Epistaxis**: medical term that describes a nose bleed.
• **Hemoptysis**: coughing up blood or presence of blood in mouth, saliva or sputum.
Common Causes of Epistaxis

- Inflammation
- Neoplasia
- Foreign body
- Trauma
- Pulmonary hemorrhage
The color of blood in feces varies depending on the site of bleeding; dark in gastric bleeding (digested blood) and fresh blood in colonic or rectal bleeding.

In epistaxis, the blood always looks the same regardless if bleeding is in the nose or the lung. In other words, blood in epistaxis still looks fresh even if originates in the lungs.

http://www.patrickmahaney.com/
Nasal congestion and hemorrhage occur in bloat, toxemia, sepsis, irritant gases and inflammation.

Epistaxis is also a frequent indicator of nasal trauma or nasal neoplasia.

In cattle, epistaxis-hemoptysis often results from ruptured pulmonary vessels (aneurysm).

In horses, epistaxis occurs in “Exercise-induced pulmonary hemorrhage” and Ethmoid hematoma.

Careful examination of the respiratory tract is required to localize the source of bleeding.
The Ethmoid Hematoma is an equine disease of older horse clinically manifested by unilateral or less frequently bilateral nasal bleeding.

Grossly, an ethmoidal hematoma is a pedunculated (tumor-like) soft mass (arrows) arising from the ethmoid conchae, easily detected by endoscopy.

Microscopically, the mass is composed of a thinly encapsulated mass of connective tissue containing many blood vessels, red blood cells, a large number of siderophages (macrophages with iron pigment) and a few leukocytes.

Surgically removal is often recommended.
The nasal mucosa is well vascularized, and therefore vessels can easily engorge with blood during inflammation (hyperemia) or circulatory failure (congestion).

Nasal congestion and hemorrhage are commonly caused by irritant gases such as ammonia, hydrogen sulfide (H2S), nitrogen dioxide (NO2), etc.

Nasal congestion and hemorrhage also result from shock, bloat, and of course in rhinitis.
Before reviewing the inflammatory process in the nasal cavity (rhinitis), let’s first review how the nasal mucosa reacts to injury and how the damaged mucosa repairs. To illustrate the mechanisms of injury and repair let’s use the common cold as an example.

When you get a cold (rhinovirus) this is what happens:

1. The infected cells degenerate and detach from the basal lamina (necrosis).

2. After cellular detachment, there is a host response (inflammation) which causes pain, runny nose and eyes, and sometimes fever.

3. Finally, new epithelial cell replace necrotic cells (repair).

The entire process from necrosis to repair takes 10-14 days.
Injury, Necrosis and Repair of the Nasal Mucosa

(Summary)

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

- Degeneration
- Loss of attachment
- Necrosis
- Exfoliation

- Inflammation
- Repair
- Mitosis
- Cell differentiation

- Healed epithelium
- Normal function
The respiratory system consists of 3 independent but continuous compartments.

1- The conducting system extends from the nostrils to the bronchi;
2- The transitional system is composed by the bronchioles;
3- The exchange system is composed of millions of alveoli.

The conducting system is primarily lined by pseudostratified ciliated epithelium, and its primary defense mechanism is the trapping and removal of particles by mucociliary action.

The transitional system is lined with ciliated and non-ciliated (secretory) epithelium, and its primary defense mechanism is provided by locally produced secretions.

The alveoli are lined by alveolar type I (membranous), and II pneumocytes (pneumocytes) and the primary defense mechanism is the pulmonary alveolar macrophage (PAM). Also, the lung has defense mechanisms against toxins, circulating organisms and free radicals.

The nasopharyngeal mucosa harbors a vast population of organisms which constitute the nasal flora. The inspired air carries microorganisms of the nasal flora into the lung.

The healthy lungs rapidly destroy and remove bacteria from the lung.

Virus, stress, dehydration, lung edema, uremia, ammonia, and immunodeficiency reduce the pulmonary defense mechanisms and predispose the lung to secondary bacterial pneumonia.
The nasal mucosa is highly vascularized, and the blood vessels quickly engorge with blood often resulting in hyperemia or hemorrhage.

Nasal congestion and hyperemia are common in bloat, toxemia, sepsis, and rhinitis.

Nosebleed is also referred to as epistaxis, while blood in saliva or sputum is called hemoptysis.

In epistaxis and hemoptysis, the blood in the nostrils looks the same whether it originates in the nose, trachea or the lung.

Significant causes of epistaxis in horses are Ethmoid Hematoma and the Exercise-Induced Pulmonary Hemorrhage.

Nasal tumors and rhinitis are also sources of epistaxis.

The nasal mucosa has remarkable ability to repair. Injured cells degenerate, exfoliate and then become replaced by new cells within 14 days as long as the basement membrane remains intact.
I sincerely hope that you enjoyed this module, but most important, that you learned something about respiratory pathology.

If you have any critiques or found mistakes, please let me know at lopez@upei.ca

For a quick Quiz, please go to the next slide.
Click or “copy and paste” the link into your browser

http://people.upei.ca/lopez/respiratory/1_quiz_defense/1a_structure_defense%20-%20Presenter%20output/presentation.html
ACKNOWLEDGEMENTS

- Some images are from veterinary colleges of Canada, United States, and Mexico and the names of pathologists who contributed with some slides are unknown. Their valuable contribution is sincerely acknowledged.

- I would like to thank Dr. María Forzán, Atlantic Veterinary College, for critically reviewing these modules.