CHAPTER 2: RESPIRATORY PATHOPHYSIOLOGY

I. OBJECTIVES

Upon completion of this chapter, the student will be able to:

- Understanding the normal functioning of the respiratory system
- Identify and analyze the mechanisms of common lung diseases
- Explain how diseases affect the body's normal balance (acid-base balance or hypoxemia)
- Learning to assess the risks associated with these diseases, for example in the context of anesthesia, and to manage acute respiratory complications

II. INTRODUCTION

The energy animals need to carry out their normal activities comes primarily from the oxidative breakdown of food, especially carbohydrates and fats. During this process, called **respiration internally or cellularly**, mitochondria oxidize carbohydrates and fatty acids to generate ATP.

The oxygen required for this energy metabolism is taken up from the atmosphere by the process of **external respiration**, which also serves to eliminate the carbon dioxide produced by the cells. The key process of external respiration is the exchange of gases between the lungs and the blood that perfuses them.

In addition to their role in gas exchange, the lungs have various non-respiratory functions, such as their role in trapping particles carried by the blood (e.g., small fragments of blood clots) and the metabolism of various vasoactive substances.

III. ANATOMICAL REMINDERS

The airways consist of the nasopharynx, larynx, trachea, bronchi, and bronchioles, and are lined with mucociliary epithelium. The trachea and bronchi are kept open by rings or plates of cartilage. The bronchioles lack cartilage, and their walls are primarily composed of smooth muscle.

From the trachea, the airways divide dichotomously (by bifurcation) to reach the alveoli.

The alveoli are the main site of gas exchange. Their walls consist of a very thin epithelium beneath which lies a dense network of pulmonary capillaries. The alveolar walls also contain connective tissue.

The thoracic wall is formed by the rib cage, the intercostal muscles, and the diaphragm. It is lined by the pleural membranes and forms a large, airtight compartment containing the lungs.

The thoracic wall is therefore an integral part of the respiratory system. The respiratory muscles receive their motor innervation from the phrenic and intercostal nerves.

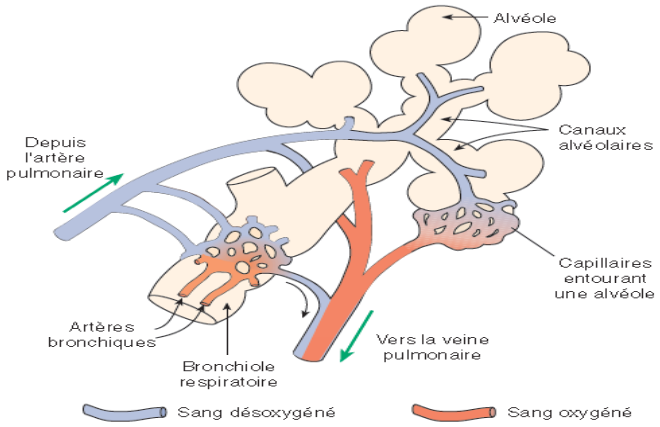

Figure 1: Diagram showing the arrangement of the pulmonary and bronchial circulations in relation to the alveoli (Pocock et al, 2019)

-Note that bronchial circulation does not supply the alveoli but empties into the pulmonary veins after bypassing the alveoli-

IV. PHYSIOLOGICAL REMINDERS

The functions of pulmonary respiration are, on the one hand, the supply of oxygen to the blood and, on the other hand, the regulation of acid-base balance through the concentration of carbon dioxide in the blood.

Respiratory mechanics allow the **ventilation of** the alveoli, through whose walls O2 can **diffuse** into the blood and CO2 from the blood into the alveoli.

The transport of respiratory gases in the blood occurs mostly in bound form; the amount transported depends, among other things, on the concentration in the blood and the pulmonary flow rate (**perfusion**).

The purpose of respiratory regulation is to adapt ventilation to needs.

V. PATHOPHYSIOLOGY OF RESPIRATORY DISEASES

A range of **disorders** can impair breathing to such an extent that sufficient O2 supply and satisfactory CO2 elimination are ultimately no longer guaranteed.

Respiratory problems are very common in domestic animals and often difficult to detect in living animals until they become complicated.

The pathophysiology of respiratory diseases involves **imbalances between the nervous control and the mechanical/cellular response of the respiratory system**, leading to **alterations in lung mechanics, gas exchange, and inflammation**. These imbalances manifest as **airway**

obstruction, lung parenchymal damage, or **respiratory muscle weakness**, resulting in symptoms such as dyspnea, cough, and hypoxemia (oxygen deficiency).

These disorders can be divided into those in which the **airways are obstructed (obstructive)** , and those in which **lung expansion is restricted (restrictive)** and those in which **the respiratory muscles are weakened** and unable to fully expand the thorax. This chapter discusses the pathophysiological processes underlying certain common respiratory disorders (figure 2). These include:

- Restrictive lung diseases
- Obstructive lung diseases
- Respiratory disorders
- Perfusion disorders
- Respiratory failure
- Hypoxemic syndromes

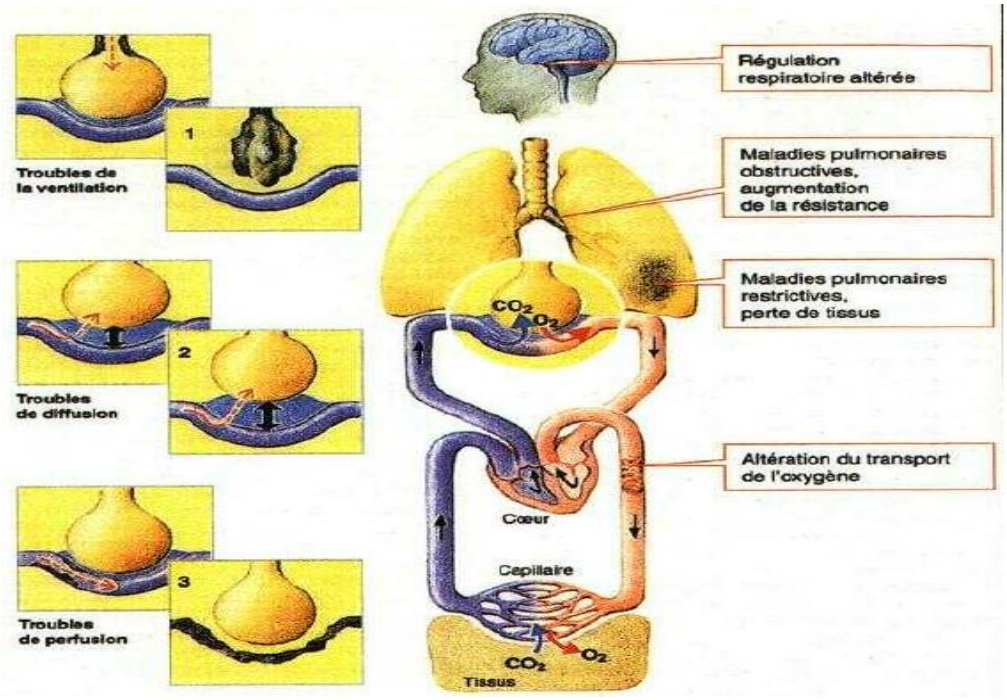

Figure 2: Pathophysiology of respiration (Silbemagi et al, 2000)

VI. OBSTRUCTIVE AND RESTRICTIVE PULMONARY DISEASES

VI.1 DEFINITION

Restrictive lung diseases are characterized by an anatomical or functional loss of the air-exchange surface area, observed after resection of lung tissue (lung destruction, surgery) or

occupation of this tissue (carcinoma, atelectasis, fibrosis, edema). This limits the amount of air entering with each breath due to a decrease in lung elasticity.

In cases of respiratory disorders, there is a problem with exchange between the alveoli and the lungs; CO_2 has difficulty leaving the lungs or O_2 has difficulty entering the alveoli (case of pneumonia or pulmonary edema).

VI.2 ETIOLOGY AND PHYSIOPATHOLOGICAL CONSEQUENCES

A functional limitation of the surface area for gas exchange occurs during exudation of plasma fluid into the alveoli, such as during **pulmonary edema** or during inflammation (increased vascular permeability, e.g., during pneumonia **)** .

In **pulmonary fibrosis**, activated and proliferating connective tissue invades the intact lung parenchyma (decreasing the diffusion surface area), infiltrates between the capillaries and alveoli (increasing the diffusion distance) and prevents normal lung unfolding (limiting alveolar ventilation).

A local or generalized blockage of lung retraction can also be caused by a **deformation of the thorax, paralysis of the diaphragm**, as well as an association of the two walls of the pleura (following inflammation) or during **pneumothorax**.

***The consequences of a restrictive lung disease are a decrease in lung compliance or elasticity, diffusion capacity and therefore hypoxemia.

The reduction of the vascular bed due to lung tissue loss or blood vessel congestion increases vascular resistance. Therefore, to pump cardiac output through the pulmonary circulation, higher pressure is required, which must be maintained by the right side of the heart, resulting in **right heart overload** (cor pulmonale).

VII. OBSTRUCTIVE PULMONARY DISEASES

VII.1. Asthma

Asthma is a chronic inflammation of the airways, defined by bronchial obstruction of varying severity. It is a condition in which the patient experiences difficulty breathing, particularly during exhalation.

Asthma attacks are characterized by the sudden onset of dyspnea. This is the result of bronchospasm, which usually occurs in response to an allergen present in the environment, although it can also occur in response to other factors such as exercise or stress.

The initial phase is likely triggered by an interaction between an allergen and IgE antibodies present on mast cells in the pulmonary interstitium. Once activated, mast cells secrete several

inflammatory mediators, including histamine and leukotrienes. These cause spasm of bronchial smooth muscle and increased mucus secretion into the airways, significantly narrowing the airways. During an asthma attack, functional residual capacity (FRC) and respiratory volume (RV) are elevated, although vital capacity remains normal.

FEV1 and peak flow are significantly reduced – in severe cases, by more than half. This limits ventilatory capacity and leads to dyspnea.

The bronchospasm that occurs in the initial phase of an asthma attack is relatively short-lived. For this reason, airway obstruction in asthma is considered reversible, even though bronchial inflammation persists long after the acute attack has ended. In chronic asthma, the bronchial epithelium is destroyed, and both the functional residual capacity (FRC) and the respiratory rate (RV) remain permanently elevated. If asthma is left untreated, chronic lung inflammation can lead to permanent airway obstruction due to irreversible thickening of the bronchial wall.

Asthma can be controlled and treated effectively, but not cured. Asthma is a pathological consequence of atopy (a genetic predisposition to develop an allergy to a certain allergen, leading to the production of specific IgE antibodies).

The **diagnosis** is made primarily by spirometry, and the **treatment** consists of corticosteroids and bronchodilators (sympathomimetics or anticholinergics).

Acute treatment for an asthma attack involves inhaled bronchodilators. Optimal treatment is achieved when symptoms are absent and the patient experiences no impairment of physical activity or exacerbations.

VII.2. Emphysema

Emphysema is a condition in which the size of the alveoli increases due to the destruction of the lung parenchyma.

Due to the reduced surface area, gas exchange will be less efficient. Air will remain trapped in the alveoli at the end of exhalation. This air trapping causes hyperexpansion of the rib cage, which reduces the mechanical properties of the respiratory muscles.

The pathophysiology of the disease is not entirely clear. Bronchial lavage shows that the air spaces in the lungs of affected individuals are invaded by neutrophils. It is now thought that these cells secrete proteolytic enzymes such as elastase, which damage the lung parenchyma.

Thus, the irritant effect of certain substances (smoking) is the likely cause of increased mucus secretion in the large airways. These effects combine to increase the risk of infection, leading to chronic inflammation of the bronchiolar epithelium.

Consequently, the diameter of the airways is reduced, and, as in asthma, exhalation becomes difficult, leading to air trapping in the lungs. Due to the loss of parenchymal tissue, traction on the airways decreases, and as they narrow, their resistance increases. This mechanism already limits ventilation, but the problem is compounded by the destruction of the alveoli. This results in a significant reduction in pulmonary diffusing capacity. Furthermore, because the destruction of the alveoli is not uniform, the ratios are altered in different parts of the lung, and the physiological dead space increases. This results in inadequate gas exchange, hypoxemia (poor blood oxygenation), and chronic dyspnea.

As the disease progresses, the patient may exhale with pursed lips, which produces a back pressure (positive end-expiratory pressure) that helps keep the airways open and prevents their collapse.

VII.3 Chronic obstructive bronchopneumopathy

Chronic obstructive pulmonary disease (COPD) is one of the most common respiratory diseases and a leading cause of death. It is characterized by chronic obstruction of the small bronchi and bronchioles due to inflammation (narrowing of the bronchial lumen), bronchoconstriction (bronchospasm) and secretory disturbances (hypersecretion of mucus due to dysfunction of the mucociliary escalator).

COPD includes various progressive lung diseases such as emphysema, chronic bronchitis (inflammation of the bronchi), chronic asthma, and certain forms of bronchiectasis.

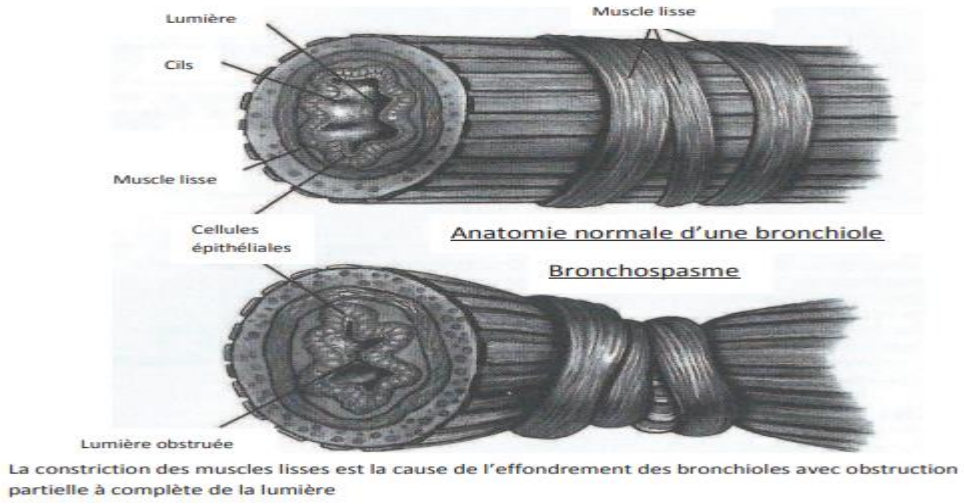

Figure 3 : Anatomy of a normal bronchiole (top) and bronchospasm (bottom) (Riegel, 2002)

Patients with COPD have a reduced peak flow rate and increased mucus production. As in asthma, FEV1 is significantly lower than normal (i.e., less than 70% of vital capacity).

This chronic disease is observed in horses. The condition is similar to human asthma. The

disease manifests acutely as "heaves." The frequency of these "heaves" varies from one horse to another. There is also a seasonal component to the disease: winter promotes heaves because horses remain stabled and therefore inhale more hay dust. Furthermore, exposure to cold, dry air causes inflammation of the respiratory tract, which is even more pronounced during exercise.

The main objectives of treatment are to prevent infections and to relieve bronchoconstriction and mucus buildup in the airways by inhaling a bronchodilator such as ipratropium.

VII. PERFUSIONAL PULMONARY DISEASES

In this type of problem, blood does not reach the exchange surface (alveolar capillary) due to a blood clot blocking the pulmonary artery and therefore the capillary. This is the case of a **pulmonary embolism**.

During a pulmonary embolism, a thrombus is sent into the vascular tree of the pulmonary trunk, obstructing pulmonary circulation and causing *a* dead space and then a pathological shunt. This is a multifactorial disease whose main risk factors are recent surgery, lower limb trauma, recent hospitalization, cancer with chemotherapy, oral contraception, hormone replacement therapy, recent pregnancy/postpartum, a history of thromboembolism, and congestive heart failure. Obstruction of the pulmonary arterial circuit by the thrombus causes an increase in pulmonary arterial pressure and right ventricular afterload. The obstruction causes a dead space effect, while the shunt effect is caused by the release of bronchodilators. The heart will try to compensate with tachycardia and an increased workload of the right ventricle. This situation leads to excessive oxygen consumption by the right ventricle, which will impede left ventricular contraction.

Obstructive shock is the pathophysiological outcome of pulmonary embolism. The dead space and shunt effect will initially cause hypoxemia, since oxygen cannot reach the left side of the heart, followed by tachypnea (the body attempts to compensate for the hypoxemia by breathing faster), and then hypocapnia. Symptoms include dyspnea and hemoptysis.

Pulmonary embolism is diagnosed using an algorithm based on clinical risk. Diagnostic methods include D-dimer testing, a fibrin degradation product (especially in individuals at low clinical risk), as well as CT angiography, Doppler ultrasound of the lower limbs, and ventilation-perfusion scintigraphy.

Treatment will be with anticoagulants (unfractionated heparin followed by vitamin K antagonists).

VIII. RESPIRATORY FAILURE AND HYPOXEMIC SYNDROME

VIII.1 Definition

Respiratory failure is defined as the inability of the respiratory system to perform its function, namely to ensure normal gas exchange (the transformation of venous blood rich in CO2 into arterial blood rich in O_2). It occurs when the respiratory system fails to maintain normal arterial PO_2 and PO_2 levels. It can be chronic (developing slowly) or acute (having a sudden onset).

If the oxygen content of the blood is reduced, there may be insufficient oxygen to support the aerobic metabolism of tissues. This condition is called **hypoxia**.

VIII.2 Etiologies

Respiratory failure can be caused by insufficient ventilation (restrictive, obstructive, or mixed) or alterations of the alveolar membrane or capillary wall hindering exchanges between air in the alveoli and blood in the capillaries: this is **post-ventilatory respiratory failure.**

Hypoxia (reduction of PO_2) can have several causes: poor ventilation, anemia, poor blood circulation, and metabolic poisoning.

VIII.3 Physiopathology

Disruptive mechanism considered, we always observe the same results :

- ✓ Hypoxia or hypercapnia
- ✓ Respiratory syncope

III.3.1 Hypoxia

We can distinguish four main types of hypoxia: hypoxemic (poor ventilation), due to stasis (poor blood circulation), and anemic (anemia) and histotoxic (metabolic poisoning).

Among these, hypoxic hypoxia and hypoxia of circulatory origin are the most frequent in clinical practice.

A. Hypoxemic hypoxia

In this type of hypoxia, oxygen does not reach the blood in the pulmonary capillaries in sufficient quantity: these hypoxias are characterized by a decrease in the partial pressure of O_2 in arterial blood, and these hypoxias have multiple origins:

- ➢ **Due to a decrease in inspired oxygen:** everything functions normally but there is not enough O_2 in the air breathed, there is a decrease in the partial pressure of alveolar oxygen and therefore a decrease in the partial pressure of oxygen in arterial blood .

- **By reduction of ventilation (hypoventilation): or we can distinguish two types of** global and localized alveolar hypoventilation.
  - **global alveolar hypoventilation**

  This is a decrease in ventilation that no longer allows alveolar gas to be maintained at a normal level; this results in an increase in $PaCO_2$ (hypercapnia) and a decrease in PaO_2 (hypoxemia). It is linked to:
    - ✓ Damage to the respiratory centers during trauma or depression of these centers by the action of barbiturates or toxins
    - ✓ Injury to the thoracic bellows during rib fractures , intercostal tears
    - ✓ Pleural or abdominal effusion
    - ✓ Paralysis of the respiratory muscles
  - **Localized alveolar hypoventilation: Shunt**

  A shunt effect occurs when blood comes into contact with alveolar gas, but because the alveolar region is normally perfused but poorly ventilated, alveolar gas exchange is impaired. Venous blood entering these areas undergoes poor oxygenation and contaminates the normally arterialized blood in the rest of the lung. This is linked to pneumonia, atelectasis, or bronchial obstruction by mucus (e.g., bronchitis).
- **Due to lack of distribution**

  This is the lengthening of the diffusion pathway across the alveolo-capillary membrane : Alveolo - capillary block ; this occurs when:
  - ✓ The alveolar wall is thickened.
  - ✓ The capillary membrane is thickened.
  - ✓ Or the two membranes are separated by interstitial edema fluid or by an exudate which may be replaced by fibrous tissue
- **Through contamination of arterial blood by venous blood**

  Everything functions normally but there is an anatomical shunt resulting in a mixing of oxygenated blood and carboxylated blood (Case of congenital heart disease).

B. Hypoxia due to stasis or insufficient blood supply

These stagnant hypoxias have been described in cardiac patients who present with peripheral stasis and a slowing of blood flow. These are patients whose deficient heart is unable to adequately irrigate the tissues (causes: edematous heart failure, cases of collapse).

C. Anemic hypoxia

There is a reduction in the amount of functional hemoglobin (Hb) leading to tissue hypoxia following:

- ✓ decrease in total hemoglobin
- ✓ decrease in red blood cells
- ✓ transformation of hemoglobin into methemoglobin incapable of binding O2 (intoxication).

C. Histotoxic hypoxias

In this case, the arterial blood has a normal O_2 content , but the cells are unable to use this O_2, the venous blood returns to the heart very rich in O_2 , there is a blockage of cellular use of oxygen, this hypoxia occurs during cyanide poisoning (by blocking cytochromes).

III.3.2 Respiratory syncope

Terminal stage of respiratory failure, can be paralytic, dyspneic, asphyxic, tachypneic

- ➢ The paralytic form: observed in poisonings by respiratory center depressants
- ➢ The dyspneic form: observed in acute or edematous heart failure.
- ➢ The asphyxial form: occurs in cases of pneumonia, pulmonary edema and obstructions of the upper airways.
- ➢ The tachypneic form: observed in hyperthermia