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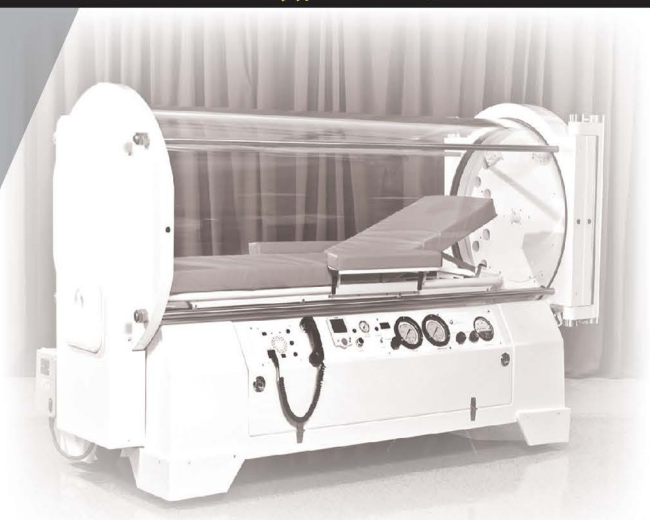

A Practical Guide to Oxygen Therapy

Previously known as Oxygen Therapy

3rd Edition

SK Jindal
Ritesh Agarwal

Foreword
Randeep Guleria

JAYPEE

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Chapter 3

Respiratory Physiology of Gas Exchange

Uma Maheswari K

INTRODUCTION

The respiratory system is intricately designed to serve the purpose of gas transfer and transport. During breathing, oxygen is transferred from atmospheric air to blood for participating in the vital process of cellular respiration while carbon dioxide, the main byproduct of cellular respiration, egresses from the lung into the atmosphere.

Gas transfer can be conceptualized as a four part process consisting of:

1. Ventilation—physical movement of air in and out of the lungs.
2. Diffusion of gases across the alveolocapillary membrane.
3. Gas transport in blood in their dissolved and protein-bound forms
4. Diffusion across the cell membrane during cellular respiration.

In this chapter, design features of the lung and processes facilitating gas exchange will be discussed.

Section 1: Design of the Human Lung for Gas Exchange

The respiratory system consists of air passages, alveoli, interstitium and pulmonary vasculature housed within the thoracic cavity. During ventilation, atmospheric air is transported from the airway opening to alveoli across a pressure gradient created by expansion of the thorax. Thereafter, gas diffuses through the gas-liquid interface in the alveoli and alveolo-capillary membrane to blood in the pulmonary capillaries. The design features of the airways, parenchyma and vasculature that facilitate efficient gas transfer will be discussed.

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ORGANIZATION OF THE AIRWAYS

The bronchial tree consists of about 23 generations of branching tubes ending in roughly 8 million alveolar sacs. Hypotheses about airway branching have evolved from the pure dichotomous branching theory (Weibel) to the widely accepted irregular dichotomous branching theory according to which airway branching shows considerable variability, with a dichotomous pattern predominating till the conducting airways and trifurcation or irregular branching patterns occurring thereafter.

Airway branches have a variable diameter and structure corresponding to the functions they subserve- gas conduction by convection or gas transfer by diffusion. Classification of airways and their anatomical features are depicted in **Tables 3.1 and 3.2**.

Two aspects are important in the understanding of gas transfer. Firstly, airway diameter decreases with each successive generation and the resultant increase in resistance to airflow is offset by increase in total cross-sectional area **(Fig. 3.1)**. Secondly, pattern of airflow changes from turbulent in the larger airways to laminar in the smaller airways to facilitate diffusion.

To put this into numerical perspective, cross-sectional area of the trachea is about 2.5 cm^2, that of the 10th generation airways is 13 cm^2 and acinar airways 300 cm^2. As the same volume of air flows through the bronchial tree, mean flow velocity falls 100-fold from 1 m/s in the trachea to <1 cm/s in the first-order respiratory bronchioles.

Airway structure is also adapted to facilitate gas transfer, from the nearly non-collapsible conducting airways with a cartilaginous-muscular envelope which transitions to a thin muscular layer in the smaller airways. While patency of cartilage containing airways is

Table 3.1: Classification of airways.

Generation 0	Trachea
Generations 1 to 4	Main, lobar and segmental bronchi
Generations 5 to 11	Small bronchi
Generations 12 to 14	Terminal bronchioles
Generations 15 to 18	Respiratory bronchioles
Generations 19 to 22	Alveolar ducts
Generation 23	Alveolar sacs

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Table 3.2: Structural characteristics of air passages.

Airway	*Name and generation*	*Number*	*Cartilage*	*Muscle*
Trachea	Conducting airways (generation 1–14)	1	U shaped	Links open end of cartilage
Main bronchi		2		
Lobar bronchi		4 ↓ 8	Irregular shape	Helical bands
Segmental bronchi		16		
Small bronchi		32 ↓ 2000		
Terminal bronchioles		4000 ↓ 16,000	Absent	Strong helical muscle bands
Respiratory bronchioles	Acinar airways (generation 15–23)	32,000 ↓ 260,000		Muscle bands between alveoli
Alveolar ducts		520,000 ↓ 4,000,000		Thin bands in alveolar septa
Alveoli	Gas exchanging area	8,000,000		

Source: Nunn's Applied Respiratory Physiology, 8th edn. P8.

influenced by atmospheric and intra-thoracic pressures, terminal and respiratory bronchioles, which traverse the pulmonary parenchyma are influenced by lung volume and kept open by the fiber scaffold of the lung.

THE PULMONARY ACINUS (FIG. 3.2)

A pulmonary acinus the region of lung supplied by a first-order respiratory bronchiole and includes respiratory bronchioles, alveolar ducts, and alveolar sacs distal to a terminal bronchiole. An acinus represents generations 15 to 23 of the airway but can have between 6 and 12 divisions beyond the terminal bronchiole depending on its location. There are about 30,000 acini, each of which contains more than 10,000 alveoli.

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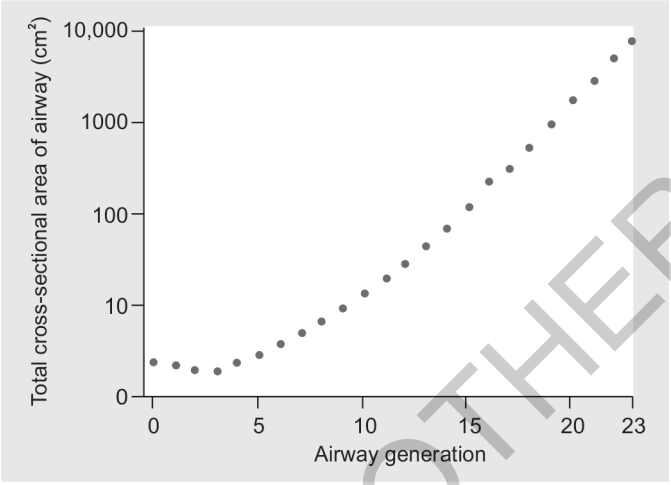

Fig. 3.1: Total cross-sectional area (CSA) of the air passages at different airway generations with minimum CSA at generation 3.

Source: Nunn's Applied Respiratory Physiology, 8th edn. P7.

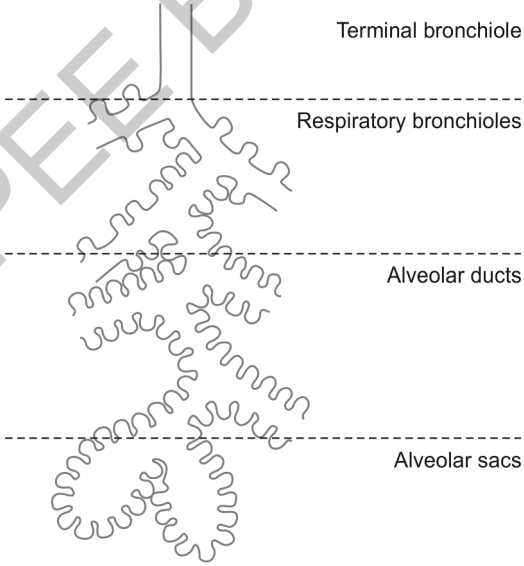

Fig. 3.2: Diagram of a pulmonary acinus.

Source: Nunn's Applied Respiratory Physiology, 8th edn. P7.

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ALVEOLI AND ALVEOLAR SEPTA (FIG. 3.3)

Alveoli

Average number of alveoli in the human lung is about 400 million. Alveolar size depends on lung volume with the largest alveolar sizes in the upper lung. Differential ventilation and capability to recruit alveoli ensures optimal gas transfer during diverse physiological and pathological conditions.

Alveolar Septa

Alveolar septa are made of collagen and elastin fibers and are usually stretched out due to tension created by these fibers and surface tension at the air-fluid interface. They are perforated by the pores of Kohn which facilitate collateral ventilation between alveoli.

On the 'active' gas exchanging side of the alveolar wall, which is only 0.3 μm thick, the capillary endothelium and alveolar epithelium are closely apposed with almost no interstitial space and the capillary bulges into the alveolar wall. However, the opposite wall of the capillary, the 'service' side, is thicker (1–2 μm) and has considerable

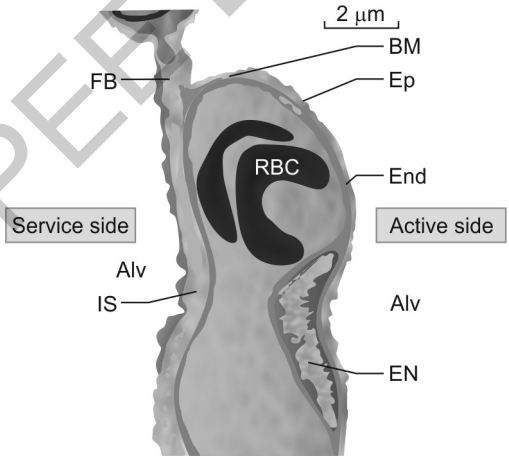

Fig. 3.3: The alveolo-capillary membrane.

(Alv: alveolus; BM: basement membrane; EN: endothelial nucleus; End: endothelium; Ep: epithelium; FB: fibroblast process; IS: interstitial space; RBC: red blood cell)

Source: Nunn's Applied Respiratory Physiology, 8th edn. P11.

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interstitial space. Thus, the active side is protected from interstitial edema and can efficiently transfer gases even in pathological conditions.

INTERSTITIAL FIBER SYSTEM

There are three types of fibers criss-crossing the interstitium, these include:

1. **Axial spiral fibers:** Running from the hilum along airways.
2. **Peripheral fibers:** From visceral pleura extending inwards into the lung.
3. **Septal fibers:** Interweaving 'basket-like structures' in the alveolar septa, through which the pulmonary capillary network passes.

All these fibers are constantly in tension; this 'tensegrity structure' confers support to the interstitium and maintains alveolar and small airway patency. These fibers also aid in alveolar recruitment as lung volume increases from residual volume to total lung capacity.

PULMONARY VASCULATURE

The pulmonary vasculature is a low resistance, high compliance system and accommodates the same volume of blood as the systemic circulation. Pulmonary arterial pressure and vascular resistance are normally only 1/6th of the systemic circulation. This is achieved by the thinner arterial media (half as thick as systemic vessels). Besides, media of pulmonary arterioles is devoid of smooth muscle and has elastic tissue making them very distensible. Arterioles give rise to the extensive pulmonary capillary network which weaves through the fiber system and lies very close to the alveolar walls. One capillary network traverses multiple alveolar septa, increasing the efficiency of gas exchange.

Section 2: Physiology of Gas Transfer

VENTILATION

Ventilation is the physical process of air moving in and out of the lungs. Ventilation is facilitated by respiratory muscles and mechanical properties of the conducting airways and lung parenchyma. Mechanical properties may be 'static' (at zero airflow and constant volume) or 'dynamic' (when airflow is present).

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Respiratory Muscles (Fig. 3.4)

From a functional standpoint, respiratory muscles can be classified as muscles of the upper airway and those of the trunk and abdomen. While upper airway muscles play an important role in maintaining upper airway patency, the latter are the 'muscles of respiration' and play an important role in the process of breathing.

The main inspiratory muscle is the diaphragm and is assisted by the external intercostals and scalenii during quiet breathing and by accessory muscles (sternomastoids, vertebral column extensors, pectoralis minor, trapezii and serratii) when ventilatory demand increases during exercise and disease. Inspiratory muscle contraction expands the ribcage antero-posteriorly, laterally, and upwards generating a negative intrathoracic pressure which creates a pressure gradient for air to flow into the respiratory tract.

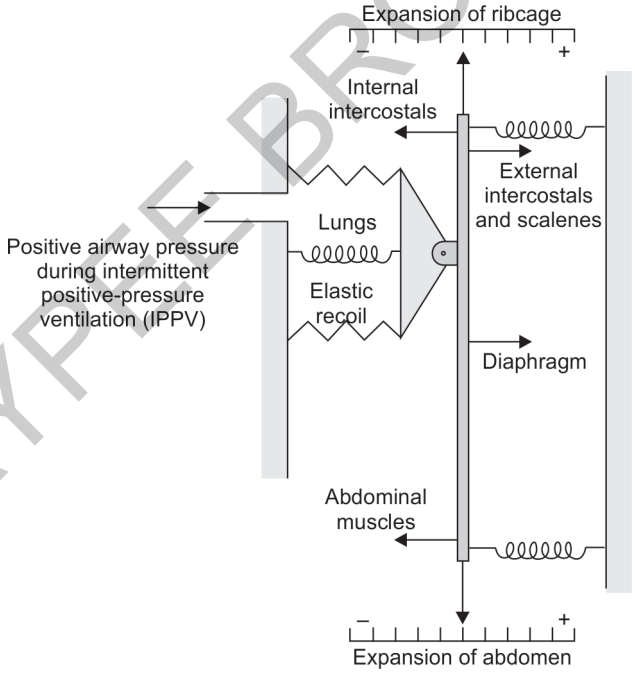

Fig. 3.4: Role of respiratory muscles in ventilation.

Source: Nunn's Applied Respiratory Physiology, 8th edn. P78.

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Expiration is usually a passive process aided by elastic recoil of the lung; however, it becomes active during talking, singing, coughing/sneezing and in flow limitation caused by airway disease. Main expiratory muscles are the rectus abdominis, external and internal obliques and transversalis abdominis.

Mechanical Properties of the Respiratory System

Ventilation is influenced by three mechanical properties of the lung-resistance, compliance and inertance. Resistance is mainly offered by the airways and influences airflow, compliance is determined by distensibility of the lung and inertance contributes to acceleration of airflow. The role of each of these factors in ventilation are discussed below.

RESISTANCE

The 80% of the airflow resistance is offered by conducting airways **(airway resistance)**; the remaining 20% is offered by tissue **(elastic resistance)**. While airway resistance is an important factor influencing ventilation and gas transfer, elastic resistance is only operational in conditions of zero airflow and is contributed by lung tissue, chest wall and surface tension at the gas-liquid interface. The role of airway resistance in regulating ventilation will be discussed.

As mentioned earlier, airflow decreases progressively down the bronchial tree, and it is almost zero in the terminal bronchioles. As flow velocity decreases, the driving pressure and resistance fall and airflow switches from turbulent to laminar. Thereafter, Brownian motion of air molecules in the respiratory bronchioles facilitates diffusion across the alveolocapillary membrane. Characteristics of turbulent and laminar flow and respiratory gas transport are depicted in **Figures 3.5 and 3.6**.

Turbulent flow occurs with high gas flow rates through unbranched/irregular tubes, with formation of local eddies. Turbulent flow has a square advancing front and the volume of gas entering the tube is equal to the volume of the tube. Driving pressure is proportional to the square of the gas flow rate and density of gas, inversely proportional to the fifth power of the tubing's radius but independent of viscosity **(Fanning's equation)**.

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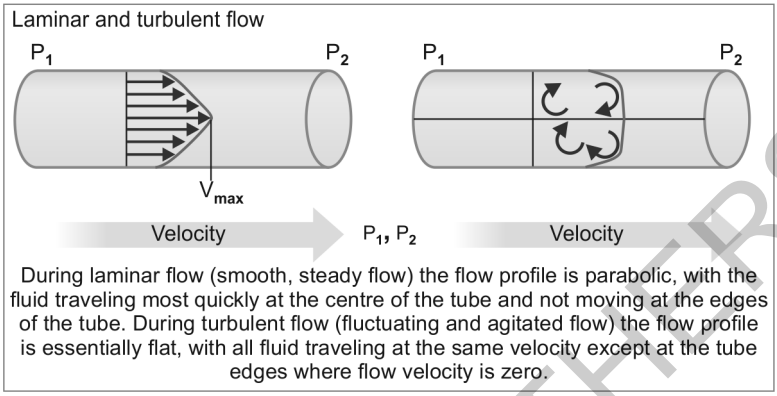

Fig. 3.5: Laminar and turbulent flow.

Source: Reference 3.

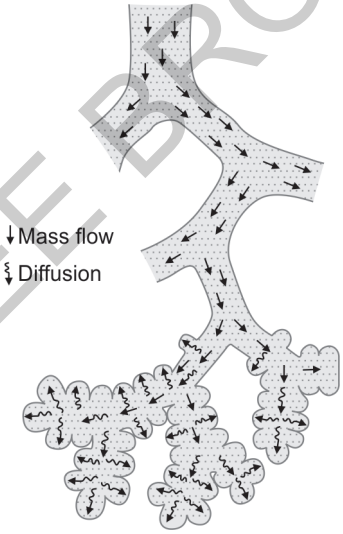

Fig. 3.6: Gas transport within the respiratory tract.

Source: Fishman's Pulmonary Diseases and Disorders, 5th edn. P158.

In laminar flow, gas flows along a straight unbranched tube as a series of concentric cylinders sliding over one another, with stationary peripheral cylinder and an advancing conical central cylinder. This implies that some gas will reach the end of the tube even if volume of

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gas entering the tube is less than the volume of the tube. In a straight unbranched tube, the **Hagen-Poiseuille equation** quantifies gas flow as follows:

$$\text{Flow rate} = \frac{\Delta P \times \pi \times (\text{radius})^4}{8 \times \text{length} \times \text{viscosity}}$$

(where ΔP = flow rate × resistance)

$$\text{Resistance} = \frac{8 \times \text{length} \times \text{viscosity}}{\pi \times (\text{radius})^4}$$

Thus, resistance is inversely related to the fourth power of radius in laminar flow. If tube dimensions are constant, viscosity is the only property of gas that is relevant during laminar flow.

Transition from turbulent to laminar flow is determined by the Reynolds' number (N_R). Flow is laminar with $N_R < 2000$ and becomes turbulent at $N_R > 4000$. If NR is 2000–4000, both types of flow coexist; a critical length of tubing is necessary before laminar flow is established. Thus for gases with low N_R, resistance will be less during turbulent flow and laminar flow will occur faster after airway narrowing.

COMPLIANCE

Pulmonary compliance is defined as the change in volume of lung per unit change in transpulmonary pressure. Compliance is expressed in Litres/kiloPascal (l/kPa) or mL/cmH_2O with a normal value of 1.5 L/kPa.

Compliance may be static or dynamic depending on the conditions of measurement. Static compliance is measured after the lungs have been held at a fixed volume for as long as practicable, whereas dynamic compliance is measured during normal breathing. Elastance is the reciprocal of compliance and is expressed in kilopascals per liter. Elastic recoil of the lung tends to collapse the lung even at residual volume. Thus, the lungs would collapse to an almost airless state if removed from the thoracic cage.

The pressure-volume graph obtained during compliance measurement is curvilinear **(Fig. 3.7)** and exhibits 'hysteresis' due to which pressure-volume curve is slightly greater during deflation than inflation. Hysteresis is influenced by elasticity of the lung parenchyma and surface tension in alveolar spaces.

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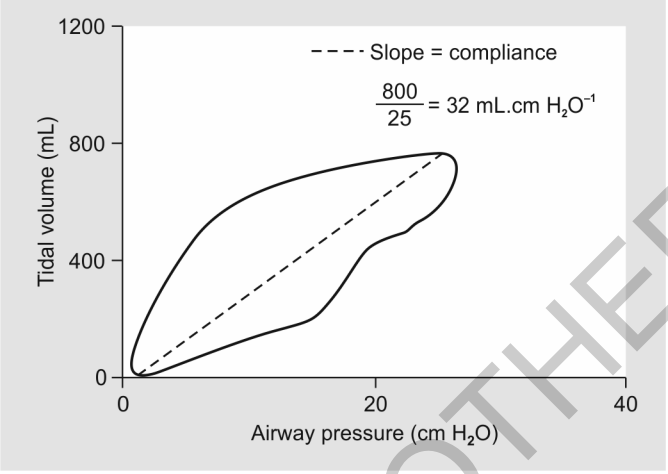

Fig. 3.7: Pressure volume graph during dynamic compliance measurement.
Source: Nunn's Applied Respiratory Physiology, 8th edn. P30.

FACTORS AFFECTING LUNG COMPLIANCE

- **Recruitment:** At low lung volumes, some small airways remain closed lowering compliance. However, they sequentially open-up as transpulmonary pressure rises, a phenomenon called recruitment. Recruitment in the initial phase of inspiration increases compliance and contributes to hysteresis.
- **Surface tension:** Surface tension present at the air-fluid interface is considerably reduced by surfactant produced by type II alveolar cells. At low lung volumes, as diameter of the alveoli decreases, pressure within them increases in accordance with Laplace's Law (Pressure = 2 × surface tension/radius), increasing propensity for alveolar collapse. This is prevented by surfactant which decreases surface tension despite decreasing alveolar radius and allows gas flow from larger to smaller alveoli and helps maintain stability of alveoli at lower lung volumes.
- **Physical characteristics of lung tissues:** Elastic properties of lung are due to elastic fibers in the interstitium. Lung expansion occurs due to unfolding and geometric re-arrangement of elastic fibers. Ageing alters elastin and collagen fibers in the lungs and increases lung compliance.

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INERTANCE

As respired gases, lungs and chest wall have mass and therefore inertia, they offer impedance to change in direction of gas flow. This component called inertance, is difficult to measure but offers resistance to airflow that increases with respiratory frequency. For practical purposes, inertance is negligible and gas flow depends primarily on compliance and resistance.

Components and Distribution of Ventilation

Total and Alveolar Ventilation

Inhaled air gets distributed in the lungs depending on resistance and compliance of regional lung units. While a major portion of inhaled air reaches the alveoli and participates in gas exchange (alveolar ventilation, V_A), another portion called dead space volume (V_D) never reaches the alveoli. Total ventilation is the sum of dead space ventilation and alveolar ventilation **(Fig. 3.8)**.

Dead space comprises 2 components, the **anatomical dead space**, which is fixed and comprises the air in the conducting airways (~ 150 mL or 1/3rd of tidal volume) and **physiological dead space**,

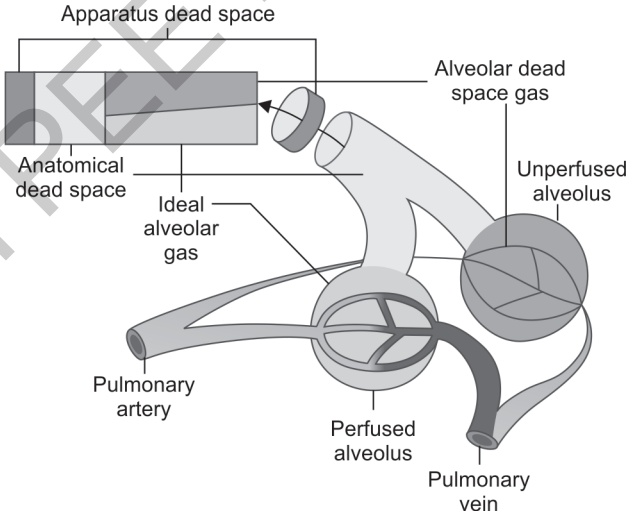

Fig. 3.8: Components of dead space.

Source: Nunn's Applied Respiratory Physiology, 8th edn. P120.

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A Practical Guide to Oxygen Therapy

Salient Features

- Presents a concise and practical guide to various aspects of oxygen therapy by different subject-experts to help practitioners of all medical and surgical specialties in their day-to-day practice
- In a simple language, it tends to cover the basic physiology, clinical indications, methods of oxygen delivery, storage and supply
- Also provides glimpses into need of oxygen for special situations such as the intensive care units, high altitude, air-travel, and deep-sea diving
- Issues related to children and neonates have been separately covered.
- Overall, it serves as an excellent feast for students and clinicians of all hues.

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