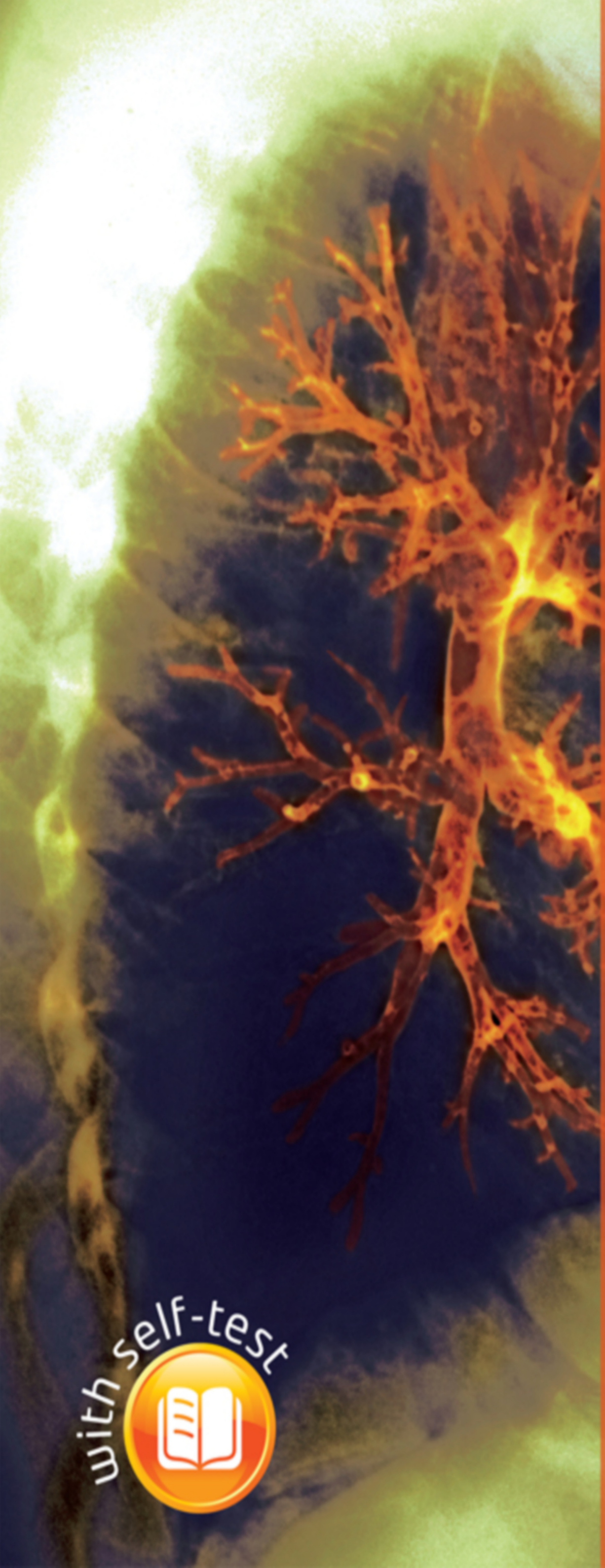

The Respiratory System at a Glance

Third Edition

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WILEY-BLACKWELL

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Preface to third edition

The medical curriculum has become increasingly vertically integrated, with a much greater use of clinical examples and cases to help in the understanding of the relevance of the underlying basic science, and conversely use of basic science concepts to help in the understanding of the pathophysiology and treatment of disease. *The Respiratory System at a Glance* has been written to take account of this trend, and to integrate core aspects of basic science, pathophysiology and treatment into a single, easy to use revision aid. As such, it should be useful to medical students throughout their training, and also to other healthcare professions, including nursing.

As with other volumes in the *At a Glance* series, it is based around a two-page spread for each main topic, with figure and text complementing each other to give an overview of a topic at a glance. Case studies based on some of the most commonly encountered conditions are also provided, and can be used for both basic science and clinical study. Although primarily designed for revision, the book covers all the core elements of the respiratory system and its major diseases, and as such could be used as a main text in the first couple of years of the course. It is advised, however, that additional reference to more detailed textbooks will aid deeper and wider understanding of the subject. This is particularly the case for the pathophysiological chapters, as a book of this length cannot hope to provide a complete guide to clinical practice.

The most notable change to this third edition is that the figure are now in colour, which should aid understanding. There are also new or expanded sections on topics such as public health and smoking, sarcoidosis and sleep-disordered breathing, additional case studies and self-assessment MCQs. Most of the other chapters and figure have been revised and updated. Hopefully, we have also corrected remaining errors found in the last edition. We have been greatly assisted in this by our many colleagues and students who have kindly advised us and commented on the contents, but any remaining errors and omissions are entirely our responsibility. We also thank all the staff at Wiley-Blackwell, without whom we would not have been able to produce this edition on time.

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Units and symbols

Units

The medical profession and scientifi community generally use SI (Système International) units.

Pressure conversion: SI unit of pressure: 1 pascal (Pa) = 1 $N \cdot m^{-2}$. As this is small, in medicine the kPa (=10^3 Pa) is more commonly used. Note that millimetres of mercury (mmHg) are still the most common unit for expressing arterial and venous blood pressures, and low pressures – e.g. central venous pressure and intrapleural pressure – are sometimes expressed as centimetres of H_2O (cmH_2O). Blood gas partial pressures are reported by some laboratories in kPa and by some in mmHg, so you need to be familiar with both systems.

1 kPa = 7.5 mmHg = 10.2 cmH_2O

1 mmHg = 1 torr = 0.133 kPa = 1.36 cmH_2O

1 cmH_2O = 0.098 kPa = 0.74 mmHg

1 standard atmosphere (≈1 bar) = 101.3 kPa = 760 mmHg = 1033 cmH_2O

Contents are still commonly expressed per 100 mL (dL^{-1}), and these need to be multiplied by 10 to give the more standard SI unit per litre. Contents are also increasingly being expressed as mmol $\cdot L^{-1}$.

For haemoglobin: 1 g $\cdot dL^{-1}$ = 10 g $\cdot L^{-1}$ = 0.062 mmol $\cdot L^{-1}$

For ideal gases (including oxygen and nitrogen): 1 mmol = 22.4 mL standard temperature and pressure dry (STPD; see Chapter 4)

For non-ideal gases, such as nitrous oxide and carbon dioxide: 1 mmol = 22.25 mL STPD

Standard symbols

Primary symbols

F = Fractional concentration of gas

C = Content of a gas in blood

V = Volume of a gas

P = Pressure of partial pressure

S = Saturation of haemoglobin with oxygen

Q = Volume of blood

A dot over a letter means a time derivative, e.g. $\dot{V}$ = ventilation (L/min); Q = blood fl w (L/min)

Secondary symbols

Gas: I = Inspired gas
E = Expired gas
A = Alveolar gas
D = Dead-space gas
T = Tidal
B = Barometric
ET = End-tidal

Blood: a = Arterial
v = Venous
c = Capillary
A dash means mixed or mean
e.g. $\bar{v}$ = Mixed venous
A′ after a symbol means end
e.g. c’ = End-capillary

Tertiary symbols

O_2 = Oxygen
CO_2 = Carbon dioxide
CO = Carbon monoxide

Examples

$\dot{V}O_2$ = Oxygen consumption
P_ACO_2 = Alveolar partial pressure of carbon dioxide

Typical values

Typical inspired, alveolar and blood gas values in healthy young adults are shown in the table below. Ranges are given for arterial blood gas values. Mean arterial PO_2 falls with age, and by 60 years is about 11 kPa/82 mmHg. Typical values for lung volumes and other lung function tests are given in the appropriate chapters. Ranges for many values are affected by age, sex and height, as well as by the method of measurement, and hence it is necessary to refer to appropriate nomograms.

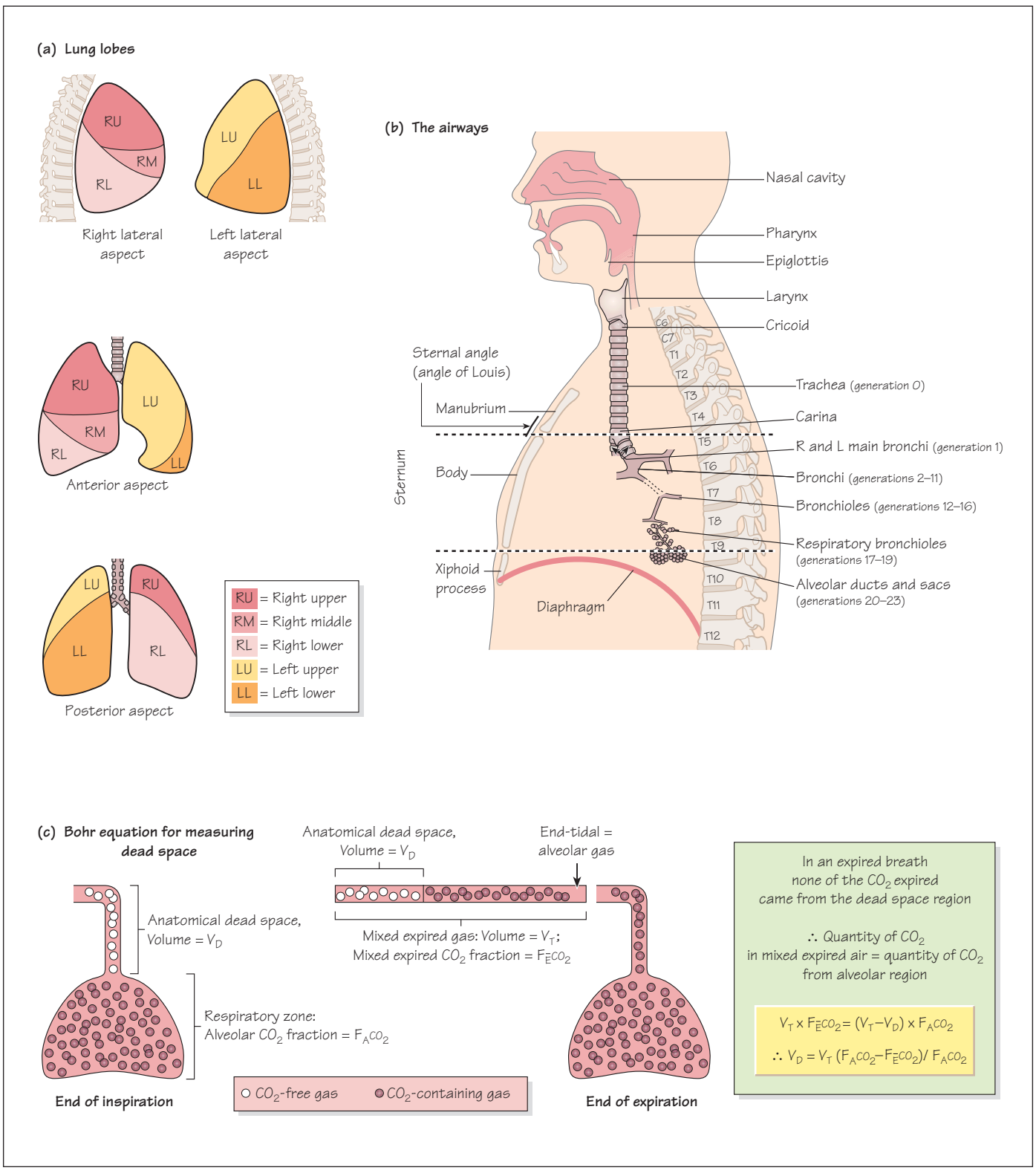
Inspired PO_2(dry, sea level)	21 kPa	159 mmHg
Alveolar PO_2	13.3 kPa	100 mmHg
Arterial PO_2	12.5 (11.2–13.9) kPa	94 (84–104) mmHg
A–a PO_2 gradient	<2 kPa	<15 mmHg (greater in elderly)
Arterial oxygen saturation	>97%	
Arterial oxygen content	200 mL $\cdot L^{-1}$	20 mL $\cdot dL^{-1}$
Inspired PCO_2	0.03 kPa	0.2 mmHg
Alveolar PCO_2	5.3 (4.7–6.1) kPa	40 (35–45) mmHg
Arterial PCO_2	5.3 (4.7–6.1) kPa	40 (35–45) mmHg
Arterial CO_2 content	480 mL $\cdot L^{-1}$	48 mL $\cdot dL^{-1}$
Arterial $[H^+]$/pH	36–44 nmol $\cdot L^{-1}$	7.44–7.36
Resting mixed venous PO_2	5.3 kPa	40 mmHg
Resting mixed venous O_2 content	150 mL $\cdot L^{-1}$	15 mL $\cdot dL^{-1}$
Resting mixed venous O_2 saturation	75%	
Resting mixed venous PCO_2	6.1 kPa	46 mmHg
Resting mixed venous CO_2 content	520 mL $\cdot L^{-1}$	52 mL $\cdot dL^{-1}$
Arterial $[HCO_3^-]$	24 (21–27) mM	

List of abbreviations

A–a gradient	(A–a P_{O_2}) gradient, the difference between ideal alveolar and arterial P_{O_2}
AAT	α_1-antitrypsin
AHI	apnoea plus hypopnoea index
AIDS	acquired immune deficien y syndrome
AIP	acute interstitial pneumonia/pneumonitis (Hamman–Rich syndrome)
ALI	acute lung injury
ANA	anti-nuclear antibody
ANCA	anti-neutrophil cytoplasmic antibody
AP	anterior–posterior
ARDS	acute (formerly adult) respiratory distress syndrome
ATPS	ambient temperature and pressure saturated
ATS	American Thoracic Society (guidelines)
BAL	bronchoalveolar lavage
BALT	bronchus-associated lymphoid tissue
BCG	bacille Calmette–Guérin
BiPAP	bilevel positive airway pressure, biphasic positive airway pressure
BP	blood pressure
BTPS	body temperature and pressure saturated
BTS	British Thoracic Society (guidelines)
CA	carbonic anhydrase
cAMP	cyclic adenosine monophosphate
CAP	community-acquired pneumonia
CCF	congestive cardiac failure
CF	cystic fibrosi
CFA	cryptogenic f brosing alveolitis
CFTR	cystic fibrosi transmembrane conductance regulator
C_L	lung compliance = $\Delta V/\Delta P$, where P = alveolar – intrapleural pressure
CMV	controlled mechanical ventilation
CMV	cytomegalovirus
CNS	central nervous system
COAD	chronic obstructive airway disease (synonymous with COPD, COLD)
COLD	chronic obstructive lung disease (synonymous with COAD, COPD)
COPD	chronic obstructive pulmonary disease (synonymous with COAD, COLD)
COX	cyclooxygenase
CPAP	continuous positive airway pressure
CREST	calcinosis, Raynaud's phenomenon, esophageal involvement, sclerodactyly and telangiectasia
CSA	central sleep apnoea
CSF	cerebrospinal f uid
CT	computed tomography
CTPA	computed tomography pulmonary angiogram
CWP	coal worker's pneumoconiosis
CXR	chest X-ray
DIP	desquamative interstitial pneumonia
$D_L$co	diffusing capacity of the lungs for carbon monoxide
D_Lg	diffusing capacity of the lungs for gas
D_LO_2	diffusing capacity of the lungs for oxygen
DRG	dorsal respiratory group
DVT	deep venous thrombosis
EBV	Epstein–Barr virus
ECG	electrocardiogram
ECMO	extracorporeal membrane oxygenation
ECP	eosinophil cationic protein
EEG	electroencephalogram
EGF	epidermal growth factor
ELISA	enzyme-linked immunoassay
EMG	electromyogram
EOG	electrooculogram
ERV	expiratory reserve volume
ESR	erythrocyte sedimentation rate
FDG	fluorodeoxyglucos
FDG PET	fluorodeoxyglucos positron emission tomography
FEF_{25-75}	mean forced expiratory fl w over middle 50% of forced vital capacity
FER	forced expiratory ratio
FEV_1	forced expiratory volume in 1 second
FEV_1/FVC	FEV_1 expressed as a fraction, or more usually a percentage of FVC (= FER)
FGF	fibroblas growth factor
FRC	functional residual capacity
FVC	forced vital capacity
GBM	glomerular basement membrane
GM-CSF	granulocyte macrophage colony-stimulating factor
GU	genitourinary
HAART	highly active antiretroviral therapy
HAP	hospital acquired pneumonia
HCAP	healthcare-associated pneumonia
HIV	human immunodeficien y virus
HR	heart rate
HRCT	high-resolution computed tomography
ICU	intensive care unit
IFN-γ	interferon-γ
Ig	immunoglobulin, e.g. IgA, IgE, IgG and IgM
IL	interleukin, e.g. IL-10
ILD	interstitial lung disease
INPV	intermittent negative pressure ventilation
IPF	idiopathic pulmonary fibrosi (synonymous with CFA)
IPPV	intermittent positive pressure breathing
IRV	inspiratory reserve volume
IVC	inferior vena cava
JVP	jugular venous pressure
***K*co**	D_LCO divided by alveolar volume or Krough coefficien
KS	Kaposi's sarcoma
LA	left atrium, left atrial
LDH	lactate dehydrogenase
LG	lymphomatoid granulomatosis
LIP	lymphocytic interstitial pneumonia
LMWH	low-molecular-weight heparin
LT	leukotriene, e.g. LTC_4
LV	left ventricle, left ventricular
MBP	major basic protein

MDR multidrug resistant
MI myocardial infarction
MIE meconium ileus equivalent
MMV mandatory minute ventilation
MOF multiorgan failure
MRSA methicillin-resistant *Staphylococcus aureus*
MVV maximal voluntary ventilation
NANC non-adrenergic, non-cholinergic (nerves)
NHL non-Hodgkin's lymphoma
NIPPV non-invasive positive pressure ventilation
NRDS neonatal respiratory distress syndrome
NREM non-rapid eye movement
NSAID non-steroidal anti-inflammator drug
NSC non-small cell
NSIP non-specifi interstitial pneumonia
OSA obstructive sleep apnoea
P_{50} partial pressure at which haemoglobin is 50% saturated with O_2
P_A alveolar pressure
PA posterior–anterior
PA pulmonary arterial
P_ACO partial pressure of carbon monoxide in the alveoli
P_aCO_2 arterial partial pressure of carbon dioxide
P_ACO_2 alveolar partial pressure of CO_2
PAF platelet-activating factor
PAH pulmonary arterial hypertension
P_aO_2 partial pressure of oxygen in the arterial blood
PCP *Pneumocystis carinii* pneumonia
$PD_{20}FEV_1$ provocative dose (e.g. of histamine or methacholine) that induces a 20% fall in FEV_1
PDGF platelet-derived growth factor
PE pulmonary embolus, pulmonary embolism
PEEP positive end-expiratory pressure
PEFR peak expiratory fl w rate
PET positron emission tomography
Pg prostaglandin, e.g. PgD_2
PH pulmonary hypertension
pHa arterial pH
pK_A log of dissociation constant K_A
PMF progressive massive fibrosi
PMI point of maximal impulse (also known as Apex beat)
PPD purifie protein derivative
PPHN persistent pulmonary hypertension of the newborn
PSP primary spontaneous pneumothorax
R respiratory gas exchange ratio
RAD right axis deviation (electrocardiography)
RANTES regulated on activation normal T cell expressed and secreted
RAW airway resistance (mouth–alveolar pressure/airfl w)
RBBB right bundle-branch block
RBC red blood cell
REM rapid eye movement
RV residual volume
RV right ventricle
RVD restrictive ventilatory defect
S_aO_2 oxygen saturation of arterial blood (%)
SC small cell
SCUBA self-contained underwater breathing apparatus
SIADH syndrome of inappropriate secretion of antidiuretic hormone
SIMV synchronized intermittent mandatory ventilation
SLE systemic lupus erythematosus
SO_2 oxygen saturation (oxygen content/oxygen capacity)
SP surfactant protein, e.g. SP-A
STPD standard temperature and pressure dry
SVC superior vena cava
TB tuberculosis
TGFβ transforming growth factor β
TLC total lung capacity
T_LCO carbon monoxide transfer factor (alternative name for D_LCO)
UFH unfractionated heparin
UIP usual interstitial pneumonia
VAP ventilator-associated pneumonia
V_A/Q ventilation–perfusion ratio (alveolar ventilation/blood fl w in a lung region)
VC vital capacity
VEGF vascular endothelial growth factor
VIP vasoactive intestinal peptide
$\dot{V}O_2max$ maximum oxygen consumption
VRG ventral respiratory groups
V_T tidal volume
WBC white blood cell
WCC white cell count
WG Wegener's granulomatosis

1 Structure of the respiratory system: lungs, airways and dead space



Lungs

The respiratory system consists of a pair of **lungs** within the **thoracic cage** (Chapter 2). Its main function is gas exchange, but other roles include speech, f ltration of microthrombi arriving from systemic veins and metabolic activities such as conversion of angiotensin I to angiotensin II and removal or deactivation of serotonin, bradykinin, norepinephrine, acetylcholine and drugs such as propranolol and chlorpromazine. The **right lung** is divided by **transverse** and **oblique fissures** into three lobes: upper, middle and lower. The **left lung** has an **oblique fissure** and two lobes (Fig. 1a). Vessels, nerves and lymphatics enter the lungs on their medial surfaces at the lung root or **hilum**. Each lobe is divided into a number of wedge-shaped **bronchopulmonary segments** with their apices at the hilum and bases at the lung surface. Each bronchopulmonary segment is supplied by its own segmental bronchus, artery and vein and can be removed surgically with little bleeding or air leakage from the remaining lung.

The **pulmonary nerve plexus** lies behind each hilum, receiving fibre from both **vagi** and the second to fourth thoracic **ganglia** of the **sympathetic trunk**. Each vagus contains sensory afferents from lungs and airways, parasympathetic bronchoconstrictor and secretomotor efferents, and non-cholinergic non-adrenergic nerves (NANC). Sympathetic noradrenergic fibre supplying airway smooth are sparse in humans, and the β_2-adrenergic receptors are stimulated by circulating catecholamines from the adrenal glands (Chapter 7).

Each lung is lined by a thin membrane, the **visceral pleura**, which is continuous with the **parietal pleura**, lining the chest wall, diaphragm, pericardium and mediastinum. The space between the parietal and visceral layers is tiny in health and lubricated with pleural f uid. The right and left pleural cavities are separate and each extends as the **costodiaphragmatic recess** below the lungs even during full inspiration. The parietal pleura is segmentally innervated by **intercostal nerves** and by the **phrenic nerve**, and so pain from pleural inflammatio (**pleurisy**) is often referred to the chest wall or shoulder-tip. The visceral pleura lacks sensory innervation.

Lymph channels are absent in alveolar walls, but accompany small blood vessels conveying lymph towards the hilar **bronchopulmonary nodes** and from there to **tracheobronchial nodes** at the tracheal bifurcation. Some lymph from the lower lobe drains to the **posterior mediastinal nodes**.

The **upper respiratory tract** consists of the nose, pharynx and larynx. The **lower respiratory tract** (Fig. 1b) starts with the trachea at the lower border of the **cricoid cartilage**, level with the sixth cervical vertebra (C6). It bifurcates into **right** and **left main bronchi** at the level of the **sternal angle** and T4/5 (lower when upright and in inspiration). The right main bronchus is wider, shorter and more vertical than the left, so inhaled foreign bodies enter it more easily.

Airways

The airways divide repeatedly, with each successive **generation** approximately doubling in number. The **trachea** and **main bronchi** have U-shaped cartilage, linked posteriorly by smooth muscle. Lobar bronchi supply the three right and two left lung lobes and divide to give **segmental bronchi** (generations 3 and 4). The total cross-sectional area of each generation is minimum here, after which it rises rapidly, as increased numbers more than make up for their reduced size. Generations 5–11 are small bronchi, the smallest being 1 mm in diameter. The lobar, segmental and small bronchi are supported by irregular plates of cartilage, with bronchial smooth muscle forming helical bands. **Bronchioles** start at about generation 12 and from this point onwards cartilage is absent. These airways are embedded in lung tissue, which holds them open like tent guy ropes. The **terminal bronchioles** (generation 16) lead to **respiratory bronchioles**, the firs generation to have alveoli (Chapter 5) in their walls. These lead to **alveolar ducts** and **alveolar sacs** (generation 23), whose walls are entirely composed of **alveoli**.

The bronchi and airways down to the terminal bronchioles receive nutrition from the **bronchial arteries** arising from the descending aorta. The respiratory bronchioles, alveolar ducts and sacs are supplied by the **pulmonary circulation** (Chapter 13).

The airways from trachea to respiratory bronchioles are lined with **ciliated columnar epithelial cells**. **Goblet cells** and **submucosal glands** secrete **mucus**. Synchronous beating of cilia moves the mucus and associated debris to the mouth (**mucociliary clearance**) (Chapters 18). Epithelial cells forming the walls of alveoli and alveolar ducts are unciliated, and largely very thin **type I alveolar pneumocytes** (alveolar cells, *squamous epithelium*). These form the gas exchange surface with the capillary endothelium (**alveolar–capillary membrane**). The **type II pneumocytes** make up only a small proportion of the alveolar surface area and are mostly found at the junction between alveoli. They are stem cells, which can divide following lung damage. They secrete **surfactant**, which reduces surface tension and has a role in lung immunity (Chapter 6 and 18). A similar substance is produced by the non-ciliated Clara cells found in the bronchiolar epithelium close to their junction with alveoli.

Dead space

The upper respiratory tract and airways as far as the terminal bronchioles do not take part in gas exchange. These **conducting airways** form the **anatomical dead space** whose volume (V_D) is normally about 150 mL. These airways have an air-conditioning function, warming, filterin and humidifying inspired air.

Alveoli that have lost their blood supply– for example because of a **pulmonary embolus** – no longer take part in gas exchange and form **alveolar dead space**. The sum of the anatomical and alveolar dead space is known as the **physiological dead space**, ventilation of which is wasted in terms of gas exchange. In health, all alveoli take part in gas exchange, so physiological dead space equals anatomical dead space.

The volume of a breath or **tidal volume** (V_T) is about 500 mL at rest. Resting **respiratory frequency** (f) is about 15 breaths/min, so the volume entering the lungs each minute, the **minute ventilation** ($\dot{V}$), is about 7500 mL/min ($= 500 \times 15$) at rest. **Alveolar ventilation** ($\dot{V}_A$) is the volume taking part in gas exchange each minute. At rest, with a dead-space volume of 150 mL, alveolar ventilation is about 5250 mL/min ($= (500 - 150) \times 15$).

The **Bohr method** for measuring anatomical dead space is based on the principle that the degree to which dead-space gas (0% CO_2) dilutes alveolar gas ($\sim$5% CO_2) to give mixed expired gas ($\sim$3.5%) depends on its volume (Fig. 1c). **Alveolar gas** can be sampled at the end of the breath as **end-tidal gas**. The Bohr equation can be modifie to measure physiological dead space by using arterial P_{CO_2} to estimate the CO_2 in the gas-exchanging or **ideal alveoli**.