RESPIRATORY DISEASES

JOHN CROFTON
ANDREW DOUGLAS

SECOND EDITION

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BLACKWELL SCIENTIFIC PUBLICATIONS

OXFORD LONDON EDINBURGH MELBOURNE

Preface to the Second Edition

We were naturally gratified by the reception of the first edition of this book. Subsequently the literature has continued to pour out in a logarithmic flood. We have pursued it breathlessly and, of course, very incompletely. Nevertheless we have had to make alterations or additions on almost every page. In response to suggestions from readers we have added a chapter on Immunology of Respiratory Diseases and we have also thought it useful to include a new chapter on Pulmonary Hypertension. The chapter in the first edition on Glanders and Melioidosis, which was added more or less as an afterthought when the book was far advanced, has now been incorporated in the chapter on Pneumonia. A section on the physiological and pathological effects of high altitude on the respiratory system has been added. The few reproductions of x-rays which were included in the first edition have been omitted; we decided that the small number contributed very little and inclusion of a really wide range of x-ray plates would have made the book very bulky and expensive.

We are most grateful to Drs. Barry Kay and Angus Stuart for reading a draft of the immunological chapter and making many constructive suggestions. Any residual errors are our own. . .

The additions have, we regret, made the book somewhat larger. This was inevitable if it was to remain a reference book, however modest. We hope that the increased bulk will not too greatly interfere with digestion.

Preface

This book is designed principally for postgraduates wishing to learn something of chest disease and as a modest reference book for general physicians or others. It is not primarily an undergraduate book but we hope the occasional enthusiastic undergraduate may dip into it in search of more detail on a particular theme.

We are well aware that no one, certainly not ourselves, can know all about respiratory disease. The book is founded on our own clinical practice, on many years' experience of teaching undergraduates and postgraduates and on an inevitably limited study of the literature. As the book purports to be in English we have mainly confined ourselves to references in that language. On the more important themes we have given only a few key foreign references, if any at all, but we have been a little more ecumenical in the case of some of the more exotic diseases.

In order to enable us to deal with certain important subjects more fully, and yet to keep the book within a reasonable compass and within a reasonable price, we have severely curtailed the number of x-rays included, though in places we have thought it useful to elaborate the text with diagrams or drawings. The reader in search of illustrative x-rays is recommended to consult radiological textbooks, such as Le Roux B. T. and Dodds T. C. (1964) *A Portfolio of Chest Radiographs*, Edinburgh: Livingstone; Le Roux B. T. and Dodds T. C. (1968) *A Second Portfolio of Chest Radiographs*, Edinburgh: Livingstone; Simon G. (1962) *The Principles of Chest X-ray Diagnosis*, 2nd Edition, London: Butterworth or Shanks S. C. and Kerley P. eds (1962) *A Textbook of X-ray Diagnosis by British Authors*, vol. 2, 3rd Edition, London: Lewis.

A number of colleagues have been kind enough to read individual chapters. Their constructive criticism has been of great value to us, although of course we alone are responsible for any residual errors. For this help our sincere thanks are due to Professor A. L. Cochrane, Dr. Charles Fletcher, Dr. Wallace Fox, Professor L. P. Garrod, Dr. I. W. B. Grant, Dr. N. W. Horne, Mr. R. J. M. McCormack, Dr. G. J. R. McHardy, Dr. A. T. Wallace and Dr. F. J. Wright. We are most grateful to Dr. Eileen Crofton for providing much epidemiological information and for reading the proofs, and to both our wives for tolerating the distortions of family life implicit in authorship. We would also like to thank our junior colleagues not only for all they have taught us but also for inevitably taking an increased share of the routine work while we have been engaged in writing the book.

We cannot too greatly praise Miss May Corkey and Miss Margaret Ballantine for their skill in typing, for their disciplined marshalling of our disordered references into orderly ranks, for their brilliant interpretation of scribbled drafts which must sometimes have been as challenging as Etruscan, and for facing all these exacting tasks with unfailing intelligence and good humour.

We would also like to thank Mr. Per Saugman, Managing Director of Blackwell Scientific Publications, who cajoled us into writing this book in the first place and Mr. Nigel Palmer, Manager of their Edinburgh office, for patiently nursing a pair of tyros through the vicissitudes of publication.

Some Symbols used in Respiratory Physiology

PRIMARY SYMBOLS

V	Volume of gas
$\dot{V}$	Volume of gas per unit time
Q	Volume of blood
$\dot{Q}$	Volume of blood per unit time
P	Pressure
S	Saturation
RQ	Respiratory quotient
R	Respiratory exchange ratio (under steady state conditions = RQ)
D	Diffusing capacity
T	Transfer factor

SUFFIXES

E	Expired gas
A	Alveolar gas
T	Tidal gas
D	Deadspace
a	Arterial blood
v	Venous blood
c	Capillary blood
L	Lung

Examples of use of symbols and suffixes

Pa, O_2	Partial pressure of oxygen in arterial blood
P_A, O_2	Partial pressure of oxygen in alveolar gas
$\dot{V}_A$	Alveolar ventilation per unit time
V_D	Volume of deadspace gas
V_T	Tidal volume
D_L	Diffusing capacity of the lung
T_{CO}	Transfer factor for carbon monoxide

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CHAPTER 1

The Structure and Function of the Respiratory Tract

The respiratory system brings air into contact with the mixed venous blood, so that appropriate gas exchange ensures an adequate content of oxygen in the systemic circulation to the tissues and the gaseous product of metabolism, carbon dioxide, is eliminated. In land animals the lungs not only provide an enormous interface for oxygen and carbon dioxide transfer between blood and environment but have the secondary function of an air pump. Atmospheric air undergoes purification, warming and humidification within the upper respiratory tract before onward transmission through the conducting passages (bronchi and bronchioles) to the alveoli where it comes into intimate contact with the mixed venous blood. The structure of each part of the respiratory system reflects its function.

The respiratory tract is arbitrarily divided at the level of the lower border of the cricoid cartilage into upper and lower parts. Whereas the lower respiratory tract is primarily concerned with conduction of air to and from the alveoli, the upper respiratory tract has several physiological functions in addition to air conduction. Among these are swallowing, conditioning of air before its passage into the trachea, smell and speech.

THE UPPER RESPIRATORY TRACT

THE NOSE

The nose has four important respiratory functions.

Air conduction

Unless there is obstruction, e.g. nasal polypi or mucosal congestion, the adult breathes through the nose. In normal subjects the resistance to air flow is 50% greater with nose breathing than with mouth breathing.

Defence mechanism

The hairs in the anterior part of the nose, the vascular mucous membrane, the ciliated epithelium, the watery secretions with their bactericidal properties and the extensive lymph drainage all combine to provide an important defence against noxious elements in the inspired air.

Warming and humidification of inspired air

These are probably the most important functions of the nose. Inspired air is heated to approximately body temperature (37°C) by the highly vascular mucous membrane of the nose, and the relative humidity of the inspired air is raised to the 95% which the bronchi and alveoli require for adequate function. The moisture is obtained from transudation through the mucosal epithelium, to a less extent from the secretions of mucous glands and goblet cells and also from the inspired air. 10,000 l of air pass through the nose every 24 hours and require about 0·75 l of nasal secretion for appropriate humidification. The vascularity of the nasal mucous membrane and the activity of the numerous mucous glands is under control of the autonomic nervous system.

When inspired air bypasses the nose, e.g. after endotracheal intubation or tracheostomy, the

lower respiratory mucosa becomes dry and cessation of ciliary activity rapidly follows, predisposing to infection. It is important, therefore, to ensure that inspired air is adequately humidified. Even the nasal inhalation of dry gas can be harmful if prolonged. The importance of the warming and humidifying function is readily appreciated after strenuous exercise in a cold atmosphere when rapid mouth breathing leads to drying of the tracheal mucous membrane and retrosternal soreness.

There is no doubt, however, that the tracheobronchial mucosa can adapt itself to those situations in which the warming and humidifying functions of the nose are no longer effective. Patients with total laryngectomy breathe directly in and out of the trachea and, although there is initially a period of adjustment, there appears to be little final inconvenience from excluding the nose from the airways [54, 105 & 184].

THE PARANASAL SINUSES

There is no general agreement regarding the functions of the accessory air sinuses but among those more frequently mentioned are temperature insulation, voice resonance and protection combined with lightness. They are lined by ciliated columnar epithelium and communicate with the nasal cavity by narrow openings which may become occluded if the sinuses are infected. Impaired drainage results in infection persisting chronically in the sinuses, providing a potential source for aspiration of infected material into the lower respiratory tract.

THE EUSTACHIAN TUBE

At rest the walls are normally in apposition, acting as a valve, but during yawning, eating and swallowing they separate through the action of the tensor veli palatini [221]. Blowing against the closed lips and nose can raise the pressure in the nasopharynx sufficiently to open the tube. Pressures of 25–35 mm Hg are required for this [66, 186, 187 & 237]. Mucosal oedema, tenacious secretions and excessive adenoid tissue may occlude the tube so that a negative pressure develops in the middle ear and mastoid air cells, drawing the tympanic membrane inwards.

THE PHARYNX

The pharynx is divided by the soft palate into an upper nasopharyngeal portion and a lower oropharyngeal portion. The nasopharyngeal part has numerous lymph glands including the nasopharyngeal tonsil (or adenoids) and the Eustachian, lingual and palatine tonsils which are arranged in a circular fashion around the nasopharynx. Swelling of the lymphoid tissue can result in partial obstruction of the airway. Infection of lymph glands in the posterior wall of the pharynx may result in a retropharyngeal abscess, most commonly associated with extension of infection from a peritonsillar abscess but sometimes from sepsis of cervical vertebrae. A large retropharyngeal abscess presents difficulties for the anaesthetist if nasal intubation is necessary.

In the unconscious patient the tongue tends to fall back and obstruct the laryngeal opening. This may be prevented by bringing the lower jaw forwards and upwards so that the lower incisors lie in front of the upper teeth, and by hyperextending the head so that the tongue is carried upwards and forwards. If there are no contraindications the unconscious patient, e.g. after anaesthesia, should be nursed on his side for in this position the tongue falls away from the posterior pharyngeal wall and aspiration into the larynx is less likely.

THE LARYNX

The larynx comprises a number of articulated cartilages, the vocal cords and the various laryngeal muscles and ligaments. The nerve supply of the mucous membrane is from both the superior and the recurrent laryngeal nerves. The principal motor nerve to the larynx is the recurrent laryngeal. The only other motor nerve is the external branch of the *superior laryngeal nerve*. This supplies the cricothyroid muscle, which is the principal tensor of the vocal cords. Paralysis of this nerve results in reduction in the anteroposterior diameter of the glottis and laxity of the vocal cords. Local anaesthesia of the throat and larynx as well as blocking the sensory nerve endings of the superior and recurrent laryngeal nerves may block the external branch of the superior laryngeal nerve and result in alteration of the shape of the glottis and the vocal cords (fig. 1.1.). It is important to remember this when local anaesthesia is employed for diagnostic laryngoscopy (p. 91). The superior laryngeal nerve may be injured at thyroidectomy. The functional effect of injury to the superior laryn-

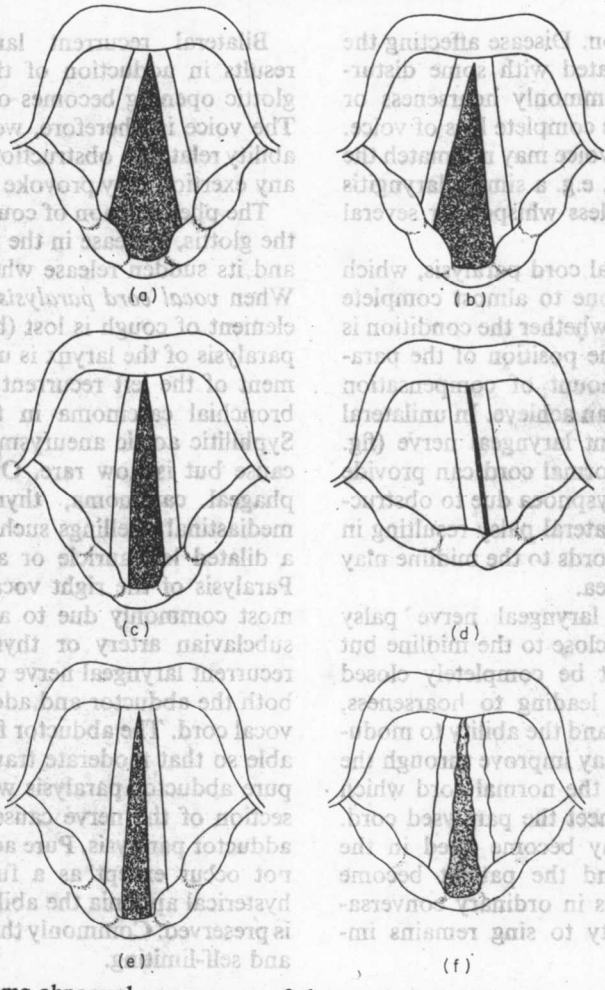

FIG. 1.1. Normal and some abnormal appearances of the vocal cords; all drawn as seen in the mirror, i.e. patient's left to observer's right. (a) Normal larynx during inspiration. (b) Left recurrent laryngeal nerve paralysis during inspiration. (c) Uncompensated left recurrent laryngeal nerve paralysis during phonation. (d) Compensated left recurrent laryngeal nerve paralysis during phonation. (e) Bilateral recurrent laryngeal nerve paralysis during inspiration. (f) Superior laryngeal nerve paralysis resulting in foreshortened larynx and lax vocal cords.

geal nerve is that the voice is weak, rough and easily fatigued, and the pitch is lower so that the singing voice is lost.

The left *recurrent laryngeal nerve* leaves the vagus at the level of the aortic arch and after hooking round the arch runs upward through the mediastinum, between the trachea and the oesophagus and then deep to the thyroid to reach the larynx beneath the lower edge of the inferior constrictor muscle. The course of the right recurrent laryngeal nerve differs in the lower part, the origin being at the level of the subclavian artery, which it hooks round before passing upwards into the neck. Apart from the sensory fibres to the mucous membrane of the larynx below the level of the vocal cords, the recurrent laryngeal nerve supplies all the muscles of the larynx with the exception of the cricothyroid muscle.

As well as being the site of some of the most important protective mechanisms in the respiratory tract, e.g. cough reflex, the larynx is also the

organ of voice production. Disease affecting the larynx is usually associated with some disturbance of phonation, commonly hoarseness or huskiness and sometimes complete loss of voice. The extent of the loss of voice may not match the seriousness of the lesion, e.g. a simple laryngitis may permit only a toneless whisper for several days.

The symptoms of vocal cord paralysis, which vary from practically none to almost complete loss of voice, depend on whether the condition is unilateral or bilateral, the position of the paralysed cord and the amount of compensation which the normal cord can achieve. In unilateral paralysis of the recurrent laryngeal nerve (fig. 1.1), abduction of the normal cord can provide an adequate airway so dyspnoea due to obstruction is not a feature. Bilateral palsy resulting in approximation of both cords to the midline may cause distressing dyspnoea.

Unilateral recurrent laryngeal nerve palsy leaves the affected cord close to the midline but since the glottis cannot be completely closed phonation is imperfect leading to hoarseness, loss of the singing voice and the ability to modulate. In time the voice may improve through the compensatory action of the normal cord which crosses the midline to meet the paralysed cord. The paralysed cord may become fixed in the paramedian position and the patient become unaware of the paralysis in ordinary conversation although the ability to sing remains impaired.

Bilateral recurrent laryngeal nerve palsy results in adduction of the cords so that the glottic opening becomes only a 2–3 mm chink. The voice is, therefore, weak but the main disability relates to obstruction of the airway so that any exertion may provoke dyspnoea and stridor.

The phenomenon of cough requires closure of the glottis, increase in the intrathoracic pressure and its sudden release when the glottis relaxes. When *vocal cord paralysis* occurs the explosive element of cough is lost (bovine cough). Motor paralysis of the larynx is usually due to involvement of the left recurrent laryngeal nerve by a bronchial carcinoma in the left hilar region. Syphilitic aortic aneurysm was once a frequent cause but is now rare. Other causes are oesophageal carcinoma, thyroid carcinoma and mediastinal swellings such as malignant glands, a dilated left auricle or a pericardial effusion. Paralysis of the right vocal cord is rare and is most commonly due to aneurysm of the right subclavian artery or thyroid carcinoma. The recurrent laryngeal nerve carries motor fibres to both the abductor and adductor muscles of the vocal cord. The abductor fibres are more vulnerable so that moderate trauma usually results in pure abductor paralysis while severe trauma or section of the nerve causes both abductor and adductor paralysis. Pure adductor paralysis does not occur except as a functional disorder. In hysterical aphonia the ability to cough normally is preserved. Commonly the condition is transient and self-limiting.

THE LOWER RESPIRATORY TRACT

CONDUCTING AIRWAYS

GROSS ANATOMY

THE TRACHEA [101]

The trachea extends from the larynx to the bifurcation in the mediastinum. It is fixed above to the larynx and so to the skull. Below it is anchored to the mediastinum by means of the main bronchi and oblique connective tissue fibres running to the dorsal surface of the pericardium. The bifurcation is normally displaced slightly to the right, possibly because of the greater elastic pull of the right lung. As both ends can move independently the length is variable, averaging 10–12 cm. The transverse diameter is approximately 25% greater than the sagittal. About half the trachea lies in the cervical region and half is intrathoracic. The calibre of the intrathoracic portion is affected by intrathoracic pressure changes, while that of the cervical portion is not (p. 12). *Position and movements of the body* affect the position and length of the trachea. With flexion of the head the cricoid cartilage at the upper end of the trachea may be only 1 cm above the manubrium, whereas with full extension it may be 7 cm higher. There is up to 3 cm movement of the upper trachea with swallowing, while the bifurcation may move 1 cm. In the supine position and in expiration the bifurcation lies at the cranial end

of the 5th thoracic vertebra, separated from it only by the oesophagus. In the prone position it moves forward about 2 cm. On inspiration the bifurcation moves caudally by about 1 vertebral level and away from the vertebrae by about 3 cm. The angle of bifurcation narrows on deep inspiration but the amount probably varies with the relation between diaphragmatic and costal breathing.

THE BRONCHI

The trachea divides into the right and left main bronchi, the left running somewhat more horizontally than the right. The angle between the bronchi varies from 50° to 100°. The right main bronchus gives rise to 3 *lobar bronchi*, the left to 2. The *right main bronchus* is only 1–2·5 cm in length before it gives off the *right upper bronchus* (fig. 1.2). The intermediate bronchus then passes down to divide into the *middle* and *lower lobe bronchi*. The *left main bronchus* is approximately 5 cm in length before it divides into the *left upper lobe* and *lower lobe bronchi*. Each lobar bronchus divides in turn into *segmental divisions* which are shown in fig. 1.2. These are important clinically as pathological processes are often confined to segments. The precise anatomy of divisions below segmental are in general not important to the clinician, with the exception of the axillary subdivisions of the anterior and posterior segmental bronchi of the right upper lobe. As individuals often lie on their side in sleep, aspirated material from the upper respiratory tract may gravitate into these divisions and give rise to pneumonia or lung abscess. It may also be noted that the apical bronchus of the right lower lobe usually comes off the lower lobe bronchus almost opposite the origin of the middle lobe bronchus. A lower subapical bronchus is not uncommon. Another relatively frequent variation is that the anterior segmental bronchus of the left upper lobe comes directly off the left upper lobe bronchus, thus forming a trifurcation with the apicoposterior and lingular bronchi. Very occasionally a separate bronchus comes directly off the trachea to the apex of the right upper lobe. Variations in bronchial segmental anatomy are common and are given in detail by Boyden [19].

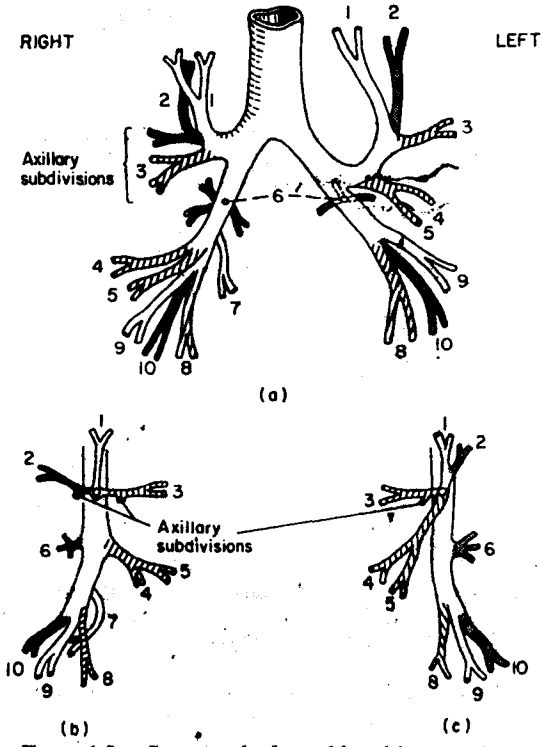

FIG. 1.2. Segmental bronchi; (a) anterior, (b) right lateral and (c) left lateral. Upper lobes: 1 apical, 2 posterior, 3 anterior; 4 and 5 superior and inferior lingular branches (left only). Middle lobe: 4 lateral, and 5 medial, branches. Lower lobes: 6 apical lower, 7 medial (right only), 8 anterior, 9 lateral, and 10 posterior, branches. After Brock [23] and Foster-Carter [85].

Number of divisions in the bronchial tree. The lower airways are known as bronchi down to the smallest divisions containing cartilage, however sparse, in their walls. Thereafter they become *bronchioles*, which remain purely conducting airways. The final branch of this type of airway is known as the *terminal bronchiole* which gives off the *respiratory bronchioles*, so named because alveoli occur in their walls. From the tracheal bifurcation the smallest bronchi are reached after some 8–13 divisions, depending on the area of lung supplied [101]. There is a good deal of variation according to the size and shape of the segments. For instance, in the apical lower segment, where the bronchi run a relatively short course, the terminal bronchioles may be reached after some 15 generations from the origin of the segmental bronchus, whereas in the lingula it may be 25. There tend to be fewer generations in lateral branches than in axial [198].

From the smallest bronchi, which are about