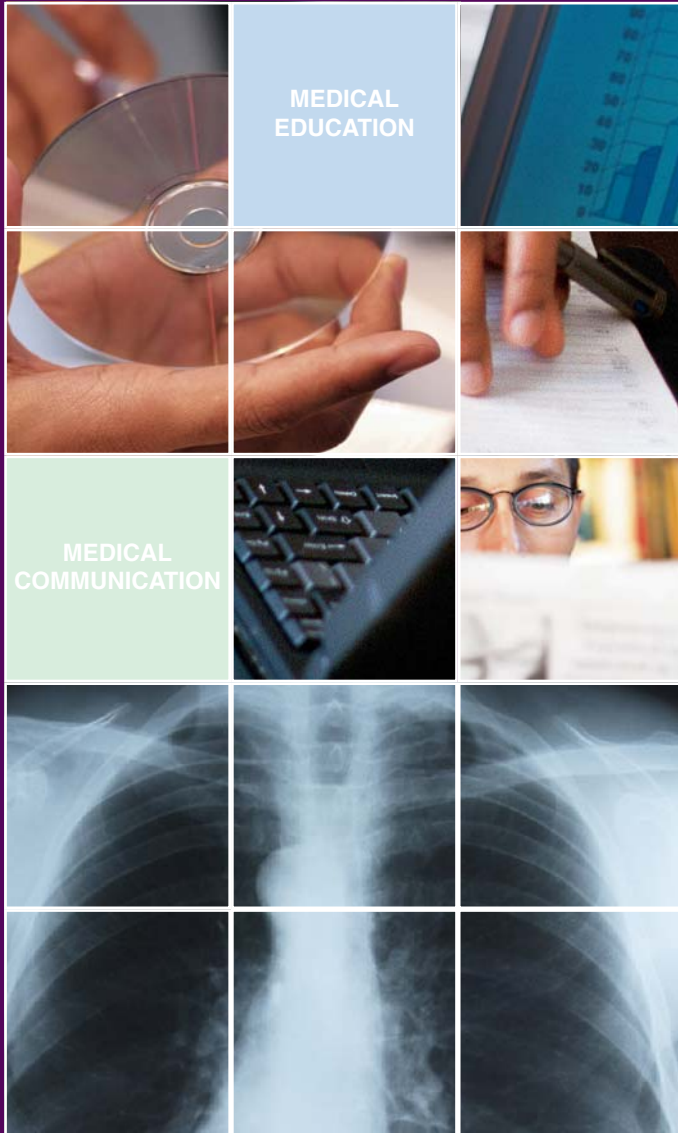




Healthcare Education Services



PharmaEssentials™
guide to **asthma & COPD**

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ISBN 1-905310-09-9

This edition published in Great Britain in September 2005 by

Bridgehead International Limited
Pera Innovation Park
Nottingham Road
Melton Mowbray
Leicestershire LE13 0PB, UK

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1 Introduction

1.1 Learning Objectives

On completing this section, the reader should be able to:

- understand the basic anatomy of the respiratory system
- list key organs and structures involved in respiration
- link key respiratory organs and structures to respiratory function
- understand the basics of the process of respiration
- understand the role of pulmonary circulation in respiration.

1.2 What are Asthma and COPD?

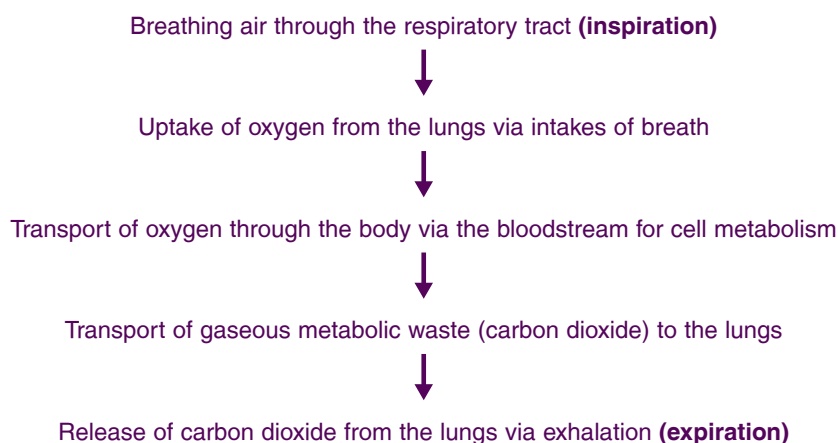
Asthma and Chronic Obstructive Pulmonary Disorder (COPD) are common diseases of the respiratory tract and are each characterised by chronic inflammation of the airways. Both diseases have major impact at the level of the individual and society as a whole. A patient's quality of life (QoL), general workplace efficiency and healthcare costs can all be affected by the presence of either disease.

Historically, asthma has a range of therapeutic options in contrast to COPD, which was underserved with therapeutics that provided only symptomatic relief. Recently, first-in-class medicines have become available for the treatment of COPD and there is ongoing research. Pharmaceutical companies continue to integrate developments in the understanding of the underlying disease pathology of both diseases into therapeutic advancements. Global clinical guidelines are also improving patient management and along with patient organisations raising the profile of both diseases.

To provide a basis for this introduction to asthma and COPD, the respiratory organs and structure, and associated function are first described.

1.3 The Respiratory Tract

Respiratory tract organs and structures facilitate pulmonary ventilation and tissue respiration, allowing gaseous exchange between ambient air and the blood circulating through the lungs. Respiration, the primary function of the respiratory tract, involves:



Each day the average person breathes nearly 25,000 times, inhaling more than 10,000 litres of air.

Respiration also provides warm air for the larynx and vocal cords, which is key to speech. The lungs are the main organ of respiration and the **pulmonary circulation** serves to facilitate gaseous exchange. Organs and structures of the respiratory tract are illustrated in Figure 1.1.

The respiratory tract, or respiratory system, consists of:

- the upper airways (upper respiratory tract)
- the lower airways (lower respiratory tract).

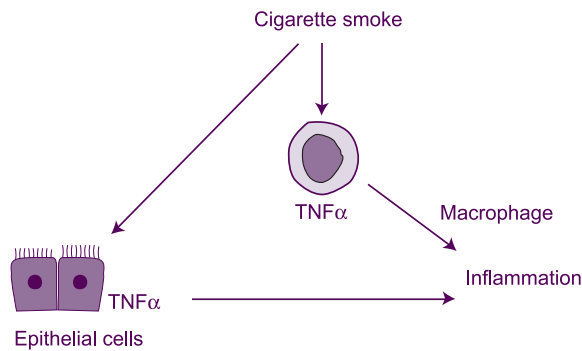


Figure 5.4 Pathogenesis of COPD

An additional cause of inflammation is oxidative stress, a factor instrumental in COPD pathogenesis. Oxidants can activate transcription factors that upregulate inflammatory genes. Inflammation is just one, of what appears to be, many ways that oxidative stress can initiate or exacerbate COPD. Common oxidants are hydrogen peroxide and nitric oxide, and both can be generated by cigarette smoke. The role of oxidative stress and other factors in COPD pathogenesis is further illustrated in Figure 5.4 and Figure 5.5.

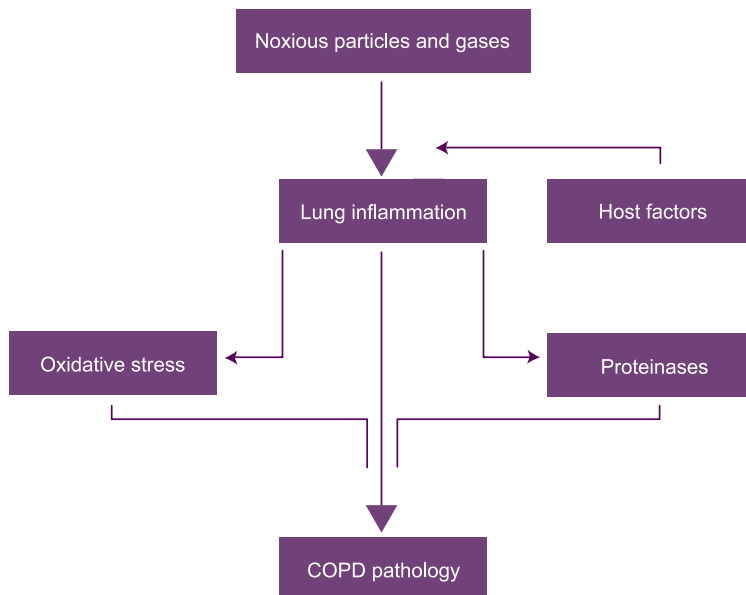


Figure 5.5 The effects of noxious particles and gases in COPD (Source: GOLD <http://www.goldcopd.com>)

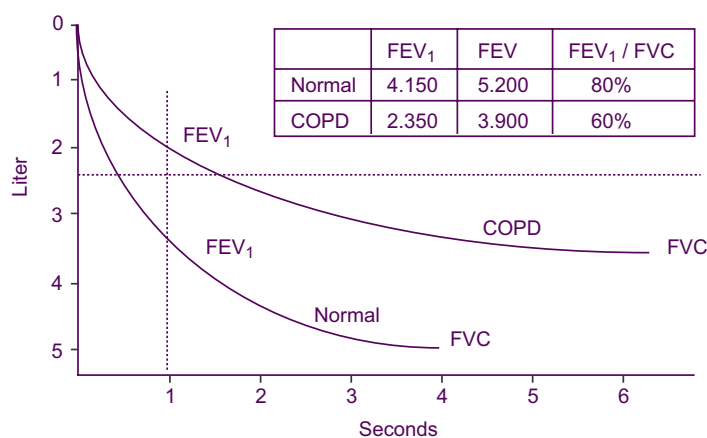


Figure 5.6 Spirometry and COPD (Source: GOLD <http://www.goldcopd.com>)

5.6.2 Pulse Oximetry

Pulse oximetry is used to measure the percentage of haemoglobin that is saturated with oxygen. Normal oxygen saturation (SaO₂) should be greater than 90% and this is greatly reduced in those with COPD. In COPD, pulse oximetry can be useful to assess the need for oxygen therapy.

Pulse oximetry measures the percentage of haemoglobin saturated with oxygen.

5.6.3 Chest X-ray

Chest X-rays are used to screen for factors other than COPD that may be causing symptoms, such as infections. Lung changes caused by COPD can sometimes be evident (for example, emphysema-related **bullae**).

5.6.4 Electrocardiogram

Electrocardiograms (ECG or EKG) are used to check heart function and rule out heart disease as a cause of shortness of breath.

5.6.5 Arterial Blood Gas Testing

Testing blood gases generally includes measuring the pH (acidity), oxygen and carbon dioxide content of the blood. This is mostly performed on arterial blood and is recommended in patients with severe COPD. The test is used to evaluate how well gaseous exchange is taking place in the lungs and can also be used to determine the effectiveness of oxygen therapy.

5.6.6 Exercise Testing

Exercise testing does not have a diagnostic value but may be useful in COPD management. It can be used to assess a patient's stamina and tolerance of physical activity. It can also be useful to measure oxygen levels in the blood during exercise (e.g. using pulse oximetry).

5.6.7 Assessing Breathlessness

Shortness of breath or dyspnoea can be measured on a defined scale known as the MRC Dyspnoea Scale (Table 5.1).

Grade	Degree of breathlessness related to activities
1	Not troubled by breathlessness except on strenuous exercise.
2	Short of breath when hurrying or walking up a slight hill.
3	Walks slower than contemporaries on the level because of breathlessness or has to stop for breath when walking at own pace.
4	Stops for breath after walking about 100m or after a few minutes on the level.
5	Too breathless to leave the house, or breathless when dressing or undressing.

Table 5.1 MRC Dyspnoea Scale

6 Management of Patients with COPD

6.1 Learning Objectives

On completing this section, the reader should:

- be aware of local and global COPD treatment guidelines
- appreciate goals for COPD treatment
- be aware of current COPD therapies
- understand general views on complementary therapy for COPD treatment
- be familiar with COPD therapeutics in pharmaceutical pipelines
- appreciate the economic impact of COPD.

6.4.2 Nutrition

For assessing the need for nutritional advice, the BMI (body mass index) calculation is recommended. If the BMI falls outside the normal range (20–25) then diet advice should be given. Nutritional supplements can be given when the BMI is lower than the normal range. Exercise is also recommended when dietary advice is given.

BMI measurement can be useful in assessing the level of nutritional advice.

6.5 Smoking Cessation

Prior to consideration of pharmacological therapies the most effective first line of treatment in COPD is smoking cessation. Smoking cessation is described as the only therapeutic intervention shown to reduce disease progression. Patients should be offered help with smoking cessation. This can include:

- nicotine replacement therapy
- behavioural therapy
- antidepressants (bupropion).

The most effective first line of treatment in COPD is smoking cessation.

The EFA recently reported that the Scottish Parliament is to implement legislation in 2006 that comprehensively bans smoking in public places. Increased support for smoking cessation in Scotland will also be given. Such initiatives are groundbreaking in improving public health and saving lives. The EFA is calling on the European Union and governments to consider COPD a public health priority. Additionally, the EFA wishes to convey the message to the public, and smokers in particular, that a cough or phlegm could be an early warning of COPD, and that early treatment and advice should be sought.

6.6 Current Pharmacological Therapies

For the most part, available pharmacological therapies offer symptomatic relief only to COPD sufferers. In disease management, patients follows a stepwise progression that is related to disease severity.

For the most part, available pharmacological therapies offer symptomatic relief only to COPD sufferers.

0	I	II	III	IV
At Risk	Mild	Moderate	Severe	Very Severe
Chronic symptoms	FEV ₁ /FVC < 70%	FEV ₁ /FVC < 70%	FEV ₁ /FVC < 70%	FEV ₁ /FVC < 70%
Risk factor exposure	FEV ₁ > 80%	50% ≤ FEV ₁ < 80%	30% ≤ FEV ₁ < 50%	FEV ₁ < 30% or FEV ₁ < 50%
Normal spirometry	With or without symptoms	With or without symptoms	With or without symptoms	predicted plus chronic respiratory failure
Avoidance of risk factors; influenza vaccine				
			Add short-acting bronchodilators, when needed	
		Add regular therapy with 1 or more long-acting bronchodilators		
		Add rehabilitation		
			Add inhaled corticosteroid if repeated exacerbations	
				Add long-term oxygen if chronic respiratory failure; consider surgical therapy

Figure 6.1 GOLD guidelines for management of each stage of COPD (Source: GOLD <http://www.goldcopd.com>)

7 Complications of Asthma and COPD

7.1 Learning Objectives

On completing this section, the reader should:

- be aware of the major complications of asthma and COPD
- recognise more minor complications of asthma and COPD
- know the most common side effects of drugs used in asthma and COPD treatment.

7.2 Heart Disease

Health complications can develop (particularly in COPD) as lung function declines and breathing ability is compromised. Some complications, such as respiratory distress and increased susceptibility to lung infection, are complications that may seem unsurprising in lung disease. Complications such as heart disease are indirect but no less serious.

7.2.1 Cor Pulmonale

As the lungs capacity for efficient gaseous exchange in COPD patients is compromised, the ability to transport oxygen decreases. This results in increasing strain on the heart. The end result is that the heart needs to work harder to pump blood. One complication that can occur as a result is cor pulmonale.

Cor pulmonale is characterised by right ventricular hypertrophy of the heart. Also known as pulmonary heart disease, cor pulmonale is caused by enlargement of the right ventricle. This is a result of high blood pressure in the blood vessels of the lungs (pulmonary hypertension), a factor linked to low oxygen levels. Pulmonary hypertension causes the right ventricle to dilate and bulge, eventually leading to its failure. COPD is the most common underlying respiratory cause of cor pulmonale and accounts for 80–90% of all cases.

Cor pulmonale is caused by enlargement of the right ventricle of the heart.

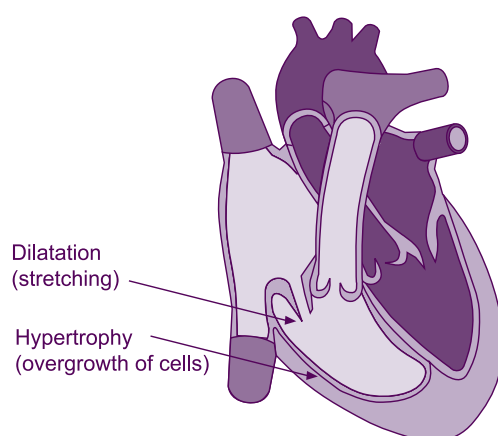


Figure 7.1. Illustration of Cor Pulmonale, otherwise known as right sided heart failure. The right side of the heart is enlarged due to high blood pressure in the lungs and normally the result of chronic lung disease

NICE COPD guidelines state that cor pulmonale should be considered in patients that have:

- peripheral oedema
- a raised venous pressure
- a systolic parasternal (located close to the sternum) heave
- a loud pulmonary second heart sound.

Some patients may need long-term oxygen therapy. Oedema can be treated with diuretic therapy.

8 Research and Clinical Studies

8.1 Learning Objectives

On completing this section, the reader should:

- be aware of current research needs in asthma and COPD
- be aware of current clinical needs in asthma and COPD
- be aware of current patient needs in asthma and COPD.

9 Appendices

9.1 Abbreviations

ALA	American Lung Association
BLF	British Lung Foundation
BTS	British Thoracic Society
cAMP	cyclic AMP
CFC	chlorofluorocarbons
COPD	chronic obstructive pulmonary disorder
DPI	dry powder inhalers
ECG	electrocardiogram
EFA	European Federation of Allergy and Airways Diseases Patients' Association
EKG	electrocardiogram
ERS	European Respiratory Society
FEV₁	forced expiratory volume
FRC	functional residual capacity
FVC	forced vital capacity
GINA	Global Initiative for Asthma
GOLD	Global Initiative for Chronic Obstructive Lung Disease
IgE	immunoglobulin E
iNOS	inducible nitric oxide synthase
IL	interleukin
kPa	kilo Pascals
MAPK	mitogen-activated protein kinase
MDI	metered dose Inhalers
mmHg	millimetres of mercury
NAEPP	National Asthma Education and Prevention Program
NFκB	nuclear factor kappa B
NHLBI	National Heart, Lung and Blood Institute
NICE	National Institute for Health and Clinical Excellence
PaCO₂	partial pressure of arterial carbon dioxide

PaO₂	partial pressure of arterial oxygen
PEF	peak expiratory flow
PDE	phosphodiesterase
RV	residual volume
SaO₂	saturation of oxygen
SIGN	Scottish Intercollegiate Guidelines Network
TLC	total lung capacity
TLCO	transfer lung factor for carbon monoxide
TNFα	tumour necrosis factor-alpha
VC	vital capacity
WHO	World Health Organization

9.2 Glossary

airflow limitation: bronchoconstriction that causes a narrowing of the airways and causes obstruction of airflow.

alpha-1 antitrypsin: a serine protease inhibitor.

airway hyperresponsiveness: the excessive narrowing of the airway lumen caused by stimuli that would cause little or no narrowing in the normal individual.

acetylcholine: a neurotransmitter that is particularly important in the stimulation of muscle tissue.

anteriorly: situated in the front or forward part of an organ, toward the head end of the body.

anticholinergics: agents that block acetylcholine from causing smooth muscle contractions and from producing excess mucus in the bronchi.

atopy: an inherited tendency to develop allergic reactions.

β_2 -agonists: agents that stimulate beta-adrenergic receptors to widen the airways.

basement membrane: a structure that supports an overlying epithelium or endothelium.

biomass fuel: crops grown specially for use as environmentally-friendly fuels.

body plethysmograph: the use of a chamber that surrounds the entire body to measure changes in the volume of organs or other body parts (e.g. lung volume).

bronchodilator: an agent that opens or expands the bronchi.

bronchospasms: the sudden, involuntary contraction of smooth muscle of the bronchi, as occurs in asthma.

bullae: enlarged air space, often associated with emphysema.

ciliary dysfunction: dysfunction of the hair-like structures on the cells lining the inner surface of the airways and lungs that act to remove mucus by constant sweeping motion.

chemokines: a family of structurally related glycoproteins capable of leukocyte activation and/or chemotactic activity.

cholinergic nerves: nerves that release acetylcholine are known as cholinergic nerves.

chronic bronchitis: characterised by a chronic cough and sputum production for more than three months of two consecutive years.

chronic obstructive bronchitis: characterised by cough, expectoration, and diminished airflow that does not improve significantly after bronchodilator inhalation.

collagen: a major structural protein, forming molecular cables that strengthen tendons skin and internal organs.

cyclic AMP: a key second messenger in signal transduction.

cytokines: soluble glycoproteins released by cells of the immune cells and regulators of immune responses.

cyanosis: a bluish tinge to the skin as a result of lack of oxygen.

deoxygenated: referring to a substance from which oxygen has been removed, e.g., deoxygenated blood.

dorsally: On, or toward, the dorsum, or back; on the dorsal side of.

dyspnoea: difficult or laboured respiration.

emphysema: the permanent destruction of the lung parenchyma by protease activity. Alveolar walls are destroyed and air spaces enlarge.

eosinophils: a white blood cell or mature granulocyte that responds to parasitic infections and allergic conditions.

expiration: release of carbon dioxide from the lungs via exhalation.

fibrosis: a proliferation of fibrous connective tissue.

functional residual capacity: the volume of air remaining in the lungs at the end of a quiet respiration.

glottis: the opening to the trachea.

glucocorticoids: a group of steroid like compounds, such as hydrocortisone, and have anti-inflammatory properties.

haemoptysis: the coughing up of blood from the respiratory tract.

helium dilution: the use of the inert gas helium to measure the total amount of gas in the lungs.

histamine: a hormone/chemical transmitter involved in immune responses and allergic reactions as a mediator of hypersensitivity.

hyperplasia: an abnormal increase in the number of cells in an organ or a tissue with consequent enlargement.

hypertrophy: enlargement of a tissue or organ of the body resulting from an increase in the size of its cells.

hypoxia: deficiency of oxygen in inspired gases or in arterial blood and/or in the tissues.

immunoglobulin E: the class of antibodies produced in the lungs, skin, and mucous membranes and responsible for allergic reactions.

inferior: Low or lower in order, degree.

inflammatory mediators: molecules released in an immune response.

inspiration: breathing in of air through the respiratory tract.

interleukins: glycoproteins secreted by a variety of leukocytes; they affect other leukocytes.

ischium faucium: an aperture between the pharynx and the mouth.

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