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CPD feature

Smoking-related chronic obstructive pulmonary disease (COPD)

Salim Khan PhD
Senior Academic (Neurophysiology), Faculty of Health, Birmingham City University, UK

Patricia Fell PhD
Senior Academic (Physiology), Faculty of Health, Birmingham City University, UK

Pat James PhD
Senior Academic (Physiology), Faculty of Health, Birmingham City University, UK

What is COPD?

Chronic obstructive pulmonary disease (COPD) is a growing problem worldwide and a major cause of disability, hospital admission and premature death (Pauwels and Rabe, 2004). It is projected to become the third most common cause of death by the year 2020 (Murray and Lopez, 1996). From the patient's perspective, it is also a disease that has a profound effect on quality of life (Rennard *et al*, 2002).

COPD is an umbrella term used to describe a number of lung conditions that obstruct airflow and make breathing difficult. COPD is multifactorial (stemming from a number of different causes or influences) and multigenic (genes may also play a significant role in why some people who smoke develop COPD). It is a progressive disease process which becomes more severe with time although signs and symptoms vary greatly between individuals. It is characterised by an abnormal inflammatory response which leads to irreversible structural and functional changes within the lungs and airways resulting in chronically poor airflow.

Key point: Chronic bronchitis and emphysema are common types of COPD. Asthma, which results in chronic airway obstruction, is traditionally recognised as a distinct disease from COPD although there are shared overlapping features.

A brief summary of chronic bronchitis

There are several key events which lead to a productive cough, a symptom characteristic of the disease.

- Recurrent injury to the airways caused by inhaled irritants causes inflammation and narrowing of the bronchi, tubes carrying air to and from the lungs.
- Membranes lining the bronchial airways become inflamed. These membranes are responsible for secreting a sticky substance called mucus, essential for trapping foreign particles and bacteria entering the lungs.
- Impairment of cilia, small hair-like waving projections in the upper airways. Cilia are responsible for removing the sticky mucus in the airways. Poor removal of the mucus can lead to subsequent lung infections caused by bacteria such as *Streptococcus pneumonia* and *Haemophilus influenzae*.

A brief summary of emphysema

This disease is characterised by a gradual loss of elasticity of lung tissue often caused by exposure to toxic chemicals or long-term exposure to tobacco smoke. Destruction of the elastic fibres in the alveoli leads to their collapse when breathing out. Consequently, air becomes trapped in the lungs. As the disease worsens, alveoli walls become permanently damaged. This reduces the surface area of the lungs and, in turn, the amount of oxygen that reaches the bloodstream.

Key points: Some individuals may have a heightened susceptibility to emphysema due to inherited genetic factors. Bronchitis is frequently a complication in emphysema.

How does COPD affect respiratory function?

COPD is characterised by physiological changes which develop in a particular order over the course of the disease. These changes include excessive mucus production, impairment of cilia, reduction in airflow, and gas exchange abnormalities (Blackler *et al*, 2007). These physiological changes can be categorised into three separate, often interconnected, disease processes:

- thickening and narrowing of airways (airflow obstruction)
- mucus hypersecretion (chronic phlegm and cough production)
- emphysema (dilation of distal airspaces with destruction of alveolar walls).

Key point: The obstruction to airflow does not revert either in response to bronchodilators, anti-inflammatory treatment, or spontaneously (GOLD, 2013).

These disease processes result in airway obstruction (narrowing) and reduced lung compliance (elasticity) which requires an increased effort to exhale and empty the lungs. Consequently, more air will be retained within the lungs, impacting on the rate of respiratory gas exchange. Blood oxygen levels can fall, depriving cells and tissues of this essential gas required for energy (ATP) production. In addition, as the disease progresses, levels of carbon dioxide, an acidic gas, may build up within the body leading to hypercapnia.

Smoking as a risk factor of COPD

Whilst there is overwhelming evidence that tobacco smoking is the major cause of COPD, it is also clear that only a fraction of smokers develop the disease, suggesting that inherited genetic variation modulates susceptibility to the development of COPD. Although tobacco smoking is the primary cause of this inhalation injury, repeated exposure to passive smoking (Eisner *et al*, 2005), and many other environmental pollutants and occupational exposures (e.g. grain, flour, coal) contribute to the pathology of COPD (GOLD, 2013).

Key point: Risk for COPD is related to an interaction between genetic factors and many different environmental exposures, which could also be affected by comorbid disease. Some individuals may have a heightened susceptibility to COPD due to inherited genetic factors (Higgins *et al*, 1984).

Tobacco smoke contains in excess of 4000 chemicals in each puff and greater than 70 cancer-causing chemicals or carcinogens (Table 1) (Pryor, 1997). Aside from nicotine, heavy metals, and carcinogens, tobacco smoke exposes cells and tissues to high concentrations of damaging oxidants and free radicals (forms of oxygen that damage our health) which are present in both the gas and tar phase of cigarette smoke (Jones *et al*, 1980). Oxidants, including reactive oxygen species and reactive nitrogen species, result in oxidative stress, an imbalance in the damaging oxygen species and protective antioxidant defences. This oxidative stress can induce the inflammatory process in the airways and lung tissue (Saetta, 1999), and lead to subsequent tissue damage and cell death (Eiserich *et al*, 1995).

All cigarette smokers have some inflammation in their lungs and airways. However, smokers who develop COPD have an enhanced or abnormal response to inhaling toxic agents. Our bodies, under normal circumstances, are able to recover well from injury by initiating an in-built healing process known as the inflammatory response. This is important for tissue-repair and remodelling. Irritants entering the airway cause body defence cells such as neutrophils, macrophages and T lymphocytes (CD8/CD4) to accumulate in the airway. Here, they initiate the inflammatory response resulting in the arrival of inflammatory mediators at the site which destroy and remove the inhaled irritant (foreign debris). The inflammatory response will switch off once the foreign body has been removed.

In COPD however, the airways are continuously bombarded and exposed to the vast array of noxious substances in cigarette smoke. This results in a continuous and amplified cycle of inflammation that increases mucus production (chronic bronchitis); tissue destruction (emphysema); and disruption of normal repair and defence mechanisms. Excessive mucus production and the inability of the airway cilia to remove it, due to ciliary dysfunction caused by tobacco smoke, result in the chronic cough and wheezing characteristic of COPD. In addition, the mucus provides a warm, moist, and nurturing medium for bacterial growth leading to the exacerbations common in progressive COPD (Tetley, 2005). It is therefore unsurprising that COPD originates in the epithelial lining of the airway which is exposed to the initial brunt of inhaled cigarette smoke and its cocktail of damaging chemicals (Yoshida and Kaper, 2006).

Key point: It is this continued inflammatory response that results in the progressive structural changes to the lungs and associated airways even after smoking cessation.

Table 1 Cancer-causing chemicals in tobacco smoke

Carcinogen	Effect
Tar	A mixture of dangerous chemicals
Benzene	Known carcinogen particularly associated with leukaemia
Cadmium	Known carcinogen that can damage the kidneys and linings of arteries
Arsenic	Known carcinogen that can also damage the heart and its blood vessels
Chromium	Known carcinogen associated with lung cancer. It allows other carcinogens (e.g. polycyclic aromatic hydrocarbons) to adhere strongly to DNA and damage it
Formaldehyde	Known carcinogen and one of the substances in tobacco smoke most likely to cause diseases in lungs and airways
Polonium-210	A radioactive element which can be deposited inside airways and deliver radiation directly to surrounding cells
1,3-Butandiene	A carcinogen found in large amounts in tobacco smoke. May present greatest overall cancer risk
Polycyclic aromatic hydrocarbons	Group of powerful carcinogens which damage DNA and promotes tumour formation e.g. benzo(a)pyrene directly damages p53, a gene that normally protects our bodies against cancer
Nitrosamine	Powerful carcinogens that directly damage DNA
Acrolein	Abundant in cigarette smoke and can cause DNA damage. Suggested to be a major cause of lung cancer
Other poisons in tobacco smoke	**Effect**
Hydrogen Cyanide	A poisonous gas causing much damage to the heart and blood vessels. It increases the risk of other chemicals causing cancer by damaging cilia lining the airways
Carbon monoxide	CO attached to red blood cells in place of oxygen lowering the blood's ability to transport oxygen to tissues and organs. It kills cilia in the airways and increases the risk of other chemicals causing cancer
Nitrogen oxide	Large amounts directly damage lung tissue and cause inflammation in the lungs
Ammonia	Kills airway cilia reducing the lungs' ability to clear away toxins

Pathogenesis of COPD caused by tobacco smoke – a summary

The effect of tobacco smoke on COPD pathogenesis, that is, the production and development of the disease can be summarised as:

- Induces a continuous and abnormal inflammatory response (Weathington *et al*, 2006)
- Leads to the generation of tissue-damaging oxidants and subsequent oxidative stress (Seimetz *et al*, 2011)
- Reduces levels of protective antioxidants (Tsuchiya *et al*, 2002)
- Reduces other important protective molecules (e.g. antiproteinases) in the cells increasing susceptibility to alveolar cell death and development of emphysema (Rangasamy *et al*, 2004)
- Induces cell death (apoptosis) (Shoshani *et al*, 2002).

WANT TO KNOW MORE?

British Lung Foundation website: www.blf.org.uk/Conditions/Detail/COPD

Education for Health website: www.educationforhealth.org

Devereux G (2006) ABC of chronic obstructive pulmonary disease. Definition, epidemiology, and risk factors *BMJ* 332(7550):1142–4.

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NICE guideline CG101 on diagnosing, managing and treating COPD. www.nice.org.uk/nicemedia/live/13029/49397/49397.pdf

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ADDRESS FOR CORRESPONDENCE

Dr Salim Khan, Faculty of Health, Birmingham City University, City South Campus, Westbourne Road, Edgbaston, Birmingham B15 3TN, UK. Phone: +44 121 331 6023. Email: salim.khan@bcu.ac.uk

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We note that there has been remarkably little published in this journal on respiratory illness and/or tobacco control but that the following may be of some relevance to the issue:

Lam KBH, Kurmi OP, Ayres JG (2010) Indoor air pollution: a poorly recognised hazard *Diversity in Health and Care* 7(1):5–7.

Poureslami I, Nimmon L, Doyle-Waters MMR, FitzGerald JM (2011) Using community-based participatory research (CBPR) with ethno-cultural groups as a tool to develop culturally and linguistically appropriate asthma educational material. *Diversity in Health and Care* 8(4):203–15.

Shum J, Poureslami I, Cheng N, FitzGerald JM (2014) Responsibility for COPD self-management in ethno-cultural communities: the role of patient, family member, care provider, and the system. *Diversity and Equality in Health and Care* 11(3–4):201–13.