

# TLALELETSO

## Chronic Lung Disease

This issue is focused on chronic lung disease. We discuss diagnosis, management and prevention, focusing on the importance of smoking cessation!

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is an important, yet often unrecognized cause of morbidity and mortality in Botswana.

In this issue of Tlaleletso we review the epidemiology of COPD in Africa, as well as discuss the best way of managing COPD in Botswana

### Definitions

**Chronic bronchitis** is defined clinically as the presence of a chronic productive cough for 3 months during each of 2 consecutive years (other causes of cough being excluded).

**Emphysema** is defined pathologically as an abnormal, permanent enlargement of the air spaces distal to the terminal bronchioles, accompanied by destruction of their walls and without obvious fibrosis.

## Notes from the Editor.....

Tlaleletso is a monthly publication produced by the Botswana UPenn Partnership, in response to your expressed need for accessible, digestible clinical information.

In this issue we focus on chronic lung disease, a frequently unrecognized problem in Southern Africa.

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## Epidemiology

COPD results in high mortality and morbidity worldwide. WHO states that COPD is the fifth and sixth cause of death in high income and low income countries, respectively. Mortality increases with decreasing lung function, acute cardiac events and infective exacerbations.

Worldwide estimates of COPD prevalence vary from 7-19%. The Burden of Obstructive Lung Disease (BOLD) study found a global prevalence of 10.1%<sup>1</sup>. Men were found to have a pooled prevalence of 11.8% and women 8.5%. Unfortunately, there is very limited published literature on COPD in Africa, despite substantial epidemiological evidence from populations with similar exposures, indicating that COPD may be a problem in the region. Cape Town, South Africa has the highest prevalence in the world, with COPD affecting 22.2% of men and 16.7% of women<sup>2</sup>.

## Smoking Cessation

Smoking cessation continues to be the most important therapeutic intervention for COPD. Most patients with COPD have a history of smoking or are currently smoking tobacco products. A smoking cessation plan is an essential part of a comprehensive management plan.

However, the success rates for cessation programs are low because of the addictive power of nicotine. These rates can also be negatively impacted by such factors as conditioned responses to smoking-associated stimuli, poor education, forceful promotional campaigns by the tobacco industry, and psychological problems, including depression.

Simple strategies: Setting a quit date may be helpful. Physicians and other health care providers should participate in setting the target date and follow-up with respect to maintenance.



### Simple Strategies:

- A target date to quit
- Follow-up support
- Relapse prevention
- Advice for healthy lifestyle changes
- Social support systems
- Adjuncts to treatment (ie, pharmacologic agents)

**See page 6 more details**

## Risk factors

Causality between tobacco smoke and COPD is well established and it remains the primary risk factor for COPD. Smoking levels have increased worldwide, except in Europe and the Americas which may also effect COPD prevalence.

As well as the dose-dependent risk of COPD from tobacco smoke, it is increasingly recognized that occupational, household and environmental exposures are important risk factors<sup>1</sup>. An estimated 50% of all households worldwide use solid fuels for cooking and heating. The use of biomass fuels for heating is a well documented risk factor for COPD. Women are at increased risk of developing COPD secondary to biomass fuel exposure.

**Infections**, particularly in childhood, have been regarded as risk factors for COPD. Post tuberculous obstructive airways disease has been a recognized cause of COPD for many years. A nationwide study in South Africa recently demonstrated that a history of previous TB was a strong predictor of chronic bronchitis. In addition several studies have confirmed airflow limitation as a consequence of tuberculous disease. Occupational exposure, for example silicosis exposure among miners, may also increase the risk of COPD<sup>3</sup>.

**HIV** – HIV infection is increasingly recognized as a cause of premature emphysema in southern Africa. Two recent reviews by Crothers<sup>4</sup> and Petrache<sup>5</sup> have highlighted current knowledge of this association. It would appear that emphysema occurs earlier, with fewer years of smoking, and may be associated with colonization by *P. jiroveci*.



In addition to the complex pathological pathways identified in HIV-negative smokers, HIV virus specific factors play a role. Unfortunately, the natural history of COPD in HIV is unclear. It is also not known if the use of anti-inflammatory or bronchodilator therapy is of any value or if antiretroviral therapy will halt the development or progression of the disease.

## Clinical Presentation

Patients typically present with a combination of signs and symptoms of chronic bronchitis, emphysema, and reactive airway disease. Symptoms include the following:

- Cough, usually worse in the mornings and productive of a small amount of colorless sputum
- Breathlessness: The most significant symptom, but usually does not occur until the sixth decade of life
- Wheezing: May occur in some patients, particularly during exertion and exacerbations

The sensitivity of physical examination in detecting mild to moderate COPD is relatively poor, but physical signs are quite specific and sensitive for severe disease. Findings in severe disease include the following:

- Tachypnea and respiratory distress with simple activities
- Use of accessory respiratory muscles and paradoxical indrawing of lower intercostal spaces
- Cyanosis
- Elevated jugular venous pulse (JVP)
- Peripheral edema

(continued)

## Clinical Presentation

Thoracic examination reveals the following:

- Hyperinflation (barrel chest)
- Wheezing – Frequently heard on forced and unforced expiration
- Diffusely decreased breath sounds
- Hyperresonance on percussion
- Prolonged expiration
- Coarse crackles beginning with inspiration in some cases

Certain characteristics allow differentiation between disease that is predominantly chronic bronchitis and that which is predominantly emphysema. Chronic bronchitis characteristics include the following:

- Patients may be obese
- Frequent cough and expectoration are typical
- Use of accessory muscles of respiration is common
- Coarse rhonchi and wheezing may be heard on auscultation
- Patients may have signs of right heart failure (ie, cor pulmonale), such as edema and cyanosis

Emphysema characteristics include the following:

- Patients may be very thin with a barrel chest
- Patients typically have little or no cough or expectoration
- Breathing may be assisted by pursed lips and use of accessory respiratory muscles; patients may adopt the tripod sitting position
- The chest may be hyperresonant, and wheezing may be heard
- Heart sounds are very distant

## Diagnosis

The defining feature of COPD is irreversible airflow limitation during forced expiration. This may result from a loss of elastic recoil due to lung tissue destruction or from an increase in the resistance of the conducting airways. The formal diagnosis of COPD is made with spirometry; when the ratio of forced expiratory volume in 1 second over forced vital capacity ( $FEV_1/FVC$ ) is less than 70% of that predicted for a matched control, it is diagnostic for a significant obstructive defect. Unfortunately, this test is not widely available in Botswana and instead clinicians must rely on clinical presentation to make the diagnosis.

Other studies, including laboratory studies and imaging, are particularly important during acute exacerbations of disease. No blood-based biomarkers are accepted in COPD. However, a study by Sin et al<sup>6</sup> investigated the use of serum pulmonary and activation-regulated chemokine (PARC/CCL-18) as a potential biomarker. The study determined that PARC/CCL-18 levels are elevated in COPD and track clinical outcomes. This blood test is still under investigation and is neither used in clinical practice in high-income settings nor available in Botswana yet.

## Treatment

No treatments aside from lung transplantation have been shown to significantly improve lung function or decrease mortality. However, once the diagnosis of COPD is established, it is important to educate patients about the disease and to encourage his or her active participation in therapy.

## Management

One approach to managing COPD is that adopted by the Global Initiative for Chronic Obstructive Lung Disease (GOLD). In the Botswana setting not all components of the GOLD guidelines are feasible, since not all recommended medications are available. A simple way of stratifying the severity of an individual's disease is in terms of the number of exacerbations in the previous 12 month period. A history of zero or one exacerbation in the past 12 months suggests a low future risk of exacerbations, while two or more exacerbations suggest a high future risk. An suggested approach is outlined below:

- **Stage I** (mild obstruction, 0 to 1 exacerbation per year): reduction of risk factors (influenza vaccine, smoking cessation); short-acting bronchodilator as needed
- **Stage II** (moderate obstruction, 0 to 1 exacerbation per year): reduction of risk factors (influenza vaccine); short-acting bronchodilator (salbutamol) as needed; cardiopulmonary rehabilitation
- **Stage III** (severe obstruction,  $\geq 2$  exacerbations per year): reduction of risk factors (influenza vaccine); short-acting bronchodilator as needed; inhaled glucocorticoids if repeated exacerbations
- **Stage IV** (very severe obstruction or moderate obstruction with evidence of chronic respiratory failure,  $\geq 2$  exacerbations per year): reduction of risk factors (influenza vaccine); short-acting bronchodilator as needed; inhaled glucocorticoids if repeated exacerbation; long-term oxygen therapy (if criteria met and oxygen available); consider surgical options such as LVRS and lung transplantation

## Medications

Oral and inhaled medications are used for patients with stable chronic obstructive pulmonary disease (COPD) to reduce dyspnea, improve exercise tolerance, and prevent complications. Most of the medications used in COPD treatment are directed at the following 4 potentially reversible mechanisms of airflow limitation:

- Bronchial smooth muscle contraction
- Bronchial mucosal congestion and edema
- Airway inflammation
- Increased airway secretion

**Beta<sub>2</sub>-agonists (e.g., salbutamol)** activate specific B<sub>2</sub>-adrenergic receptors on the surface of smooth muscle cells, which increases intracellular cyclic adenosine monophosphate (cAMP) and smooth muscle relaxation. Beta<sub>2</sub>-agonists produce less bronchodilatation in COPD than in asthma. Patients should use beta<sub>2</sub>-agonists primarily for relief of symptoms of COPD. In patients with mild, intermittent symptoms, short-acting beta<sub>2</sub>-agonists are recommended for symptomatic relief.

**Anticholinergic drugs (e.g. Atrovent)** compete with acetylcholine for postganglionic muscarinic receptors, thereby inhibiting cholinergically mediated bronchomotor tone, resulting in bronchodilatation. They block vagally mediated reflex arcs that cause bronchoconstriction. Clinical benefit is gained through a decrease in exercise-induced dynamic hyperinflation. These agents are poorly absorbed systemically and are relatively safe.

Reported adverse effects include dry mouth, metallic taste, and prostatic symptoms.



## Medications (cont.d)



**Inhaled corticosteroids (e.g. beclomethasone):** Inhaled corticosteroids provide a more direct route of administration to the airways and, similar to other inhaled agents, are only minimally absorbed. Inhaled steroids have fewer adverse effects than do oral agents, although they improve expiratory flows less effectively, even at high doses.

However, in the combination with Alluvia or other PIs even inhaled steroids can cause Cushing-like symptoms, this effect is the smallest with beclomethasone and largest with fluticasone.

**Oral corticosteroids (e.g. prednisolone):** The use of oral steroids in the treatment of acute exacerbations is widely accepted and recommended, given their high efficacy. Note that oral steroids are not as effective in treating COPD exacerbations as they are in treating bronchial asthma exacerbations.

**Xathines (e.g.) theophylline:** Relaxes the smooth muscles of the bronchi and pulmonary blood vessels. Theophylline is not recommended as a first line agent. It has a narrow therapeutic window with significant adverse effects, including anxiety, tremors, insomnia, nausea, cardiac arrhythmia (particularly multifocal atrial tachycardia), and seizures. Patients can develop arrhythmias and/or seizures without severe symptoms of toxicity. It is reserved for patients with hard-to-control COPD or for individuals who are not able to use inhaled agents effectively.



**Diet:** Inadequate nutritional status associated with low body weight in patients with COPD is associated with impaired pulmonary status, reduced diaphragmatic mass, lower exercise capacity, and higher mortality rates. Nutritional support is an important part of comprehensive care in patients with COPD.

## Advice for patients wanting to quit smoking:

1. Don't smoke any cigarettes. Each cigarette you smoke damages your lungs, your blood vessels, and cells throughout your body. Even occasional smoking is harmful.

2. Discuss why you want to quit. Do you want to:

- Feel in control of your life?
- Have better health?
- Set a good example for your children?
- Protect your family from breathing other people's smoke?

Really wanting to quit smoking is very important to how much success you will have in quitting.

3. Know that it will take commitment and effort to quit smoking. Nearly all smokers have some feelings of nicotine withdrawal when they try to quit. Nicotine is addictive.<sup>a</sup> Knowing this will help you deal with withdrawal symptoms that can occur, such as bad moods and really wanting to smoke.

4. Concerned about weight gain? It's a common concern, but not everyone gains weight when they stop smoking.

5. Remember this good news! More than half of all adult smokers have quit, and you can, too. Millions of people have learned to face life without a cigarette. Quitting smoking is the single most important step you can take to protect your health and the health of your family.

TIPS: courtesy of CDC  
([http://www.cdc.gov/tobacco/quit\\_smoking/how\\_to\\_quit/quit\\_tips/index.htm](http://www.cdc.gov/tobacco/quit_smoking/how_to_quit/quit_tips/index.htm))

## CONCLUSION

Chronic obstructive lung disease is increasing in prevalence in southern Africa. It is the cause of considerable morbidity and mortality, especially among people living with HIV. Clinicians should identify it promptly and take steps to address the factors that accelerate its pathogenesis. Educating patients about the importance of smoking cessation is essential!

## REFERENCES

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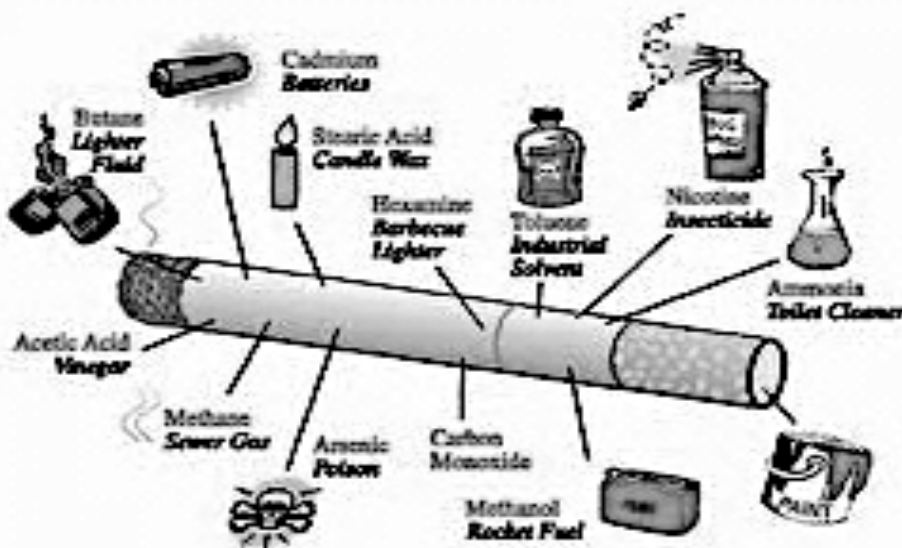
<sup>2</sup> Buist AS, McBurnie MA, Vollmer WM et al. (2007) International variation in the prevalence of COPD (the BOLD study): a population-based prevalence study. *Lancet* 370, 741–750.

<sup>3</sup> Kiraz K, Kart L, DemirRet al. (2003) Chronic pulmonary disease in rural women exposed to biomass fumes. *Clinical and Investigative Medicine. Medecine Clinique et Experimentale* 26, 243–248.

<sup>4</sup> [Rev Environ Health](#). 2007 Oct-Dec;22(4):255-72. Chronic obstructive pulmonary disease and occupational exposure to silica.

<sup>5</sup> Crothers K. Chronic obstructive pulmonary disease in patients who have HIV infection. *Clin Chest Med* 2007; 28: 575–587.

<sup>6</sup> Petrache I, Diab K, Knox KS, et al. HIV associated pulmonary emphysema: a review of the literature and inquiry into its mechanism. *Thorax* 2008; 63: 463–469.



## Upcoming Lectures

**June**

Chronic lung disease

**July**

Updates in PMTC

**August**

Updates in Anemia

Got a clinical question about a complicated medical patient or a patient with HIV?

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