THE NORTHERN HOSPITAL

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

LOUIS: *What in Heaven's name brought you to Casablanca?*

RICK: *My health. I came to Casablanca for the waters.*

LOUIS: *Waters? What waters? We are in the desert.*

RICK: *I was misinformed.*

"Casablanca", Warner Bros, 1942.

The "waters" were not the only thing Rick was misinformed about. He was also misinformed about the dangers of smoking. His health concerns (as well as Louis') would have been far better addressed had this information existed in 1942.

Humphrey Bogart would die of lung cancer in 1957. Universally seen as "sexy" in the 1940s virtually the entire cast of Casablanca can be seen smoking at some stage of the film. Fortunately today we are now well informed in this regard, however as time goes by it seems the fundamental things still apply; "sexiness" alas will all too commonly override "well-informed".

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Introduction

Chronic obstructive pulmonary disease (COPD) is a major public health problem on a global scale.

The diagnosis **COPD** typically includes a spectrum of disease that includes variable overlapping components of emphysema, chronic bronchitis and asthma, that has **partially irreversible airflow obstruction.**

Exacerbations of this disease is an extremely common cause of presentation to Emergency Departments.

The most important treatment modality of acute hypercapnic ventilatory failure presentations to the Emergency Department is **non-invasive ventilation** (**NIV)**. This is the current standard of care, but despite this, and surprisingly, this modality is still underutilized in many institutions. [1]

An important aspect of management in the ED will include the planning of, or indeed, the limitation of intubation and ventilation, should non-invasive ventilation be unsuccessful.

It is important that patients who present to the ED with frequent exacerbations be referred to specialist Chronic Lung Disease Units to allow for education, the development of care plans, and where appropriate, limitation of care plans.

Pathophysiology

Diagnosis:

Traditionally chronic bronchitis has been arbitrarily defined clinically as the presence of a persistent cough with sputum production on most days for greater than 3 months of the year for greater than 2 consecutive years.

Emphysema, although having characteristic clinical signs was strictly defined in histopathological terms as abnormal enlargement in the size of the air spaces distal to the terminal bronchioles and accompanied by destruction of their walls.

Today a formal diagnosis of COPD should be made in the first instance by a combination of formal lung function testing and clinical assessment by a respiratory physician.

Severity of **chronic** disease can be classified according to the **GOLD staging system, (see Appendix 2 below).**

Causes:

The predominant groups of causes include:

1. Smoking:
    - This is the cause in the vast majority of cases, the world over.
2. Occupational / Environmental exposure
    - Atmospheric pollutants
3. Congenital conditions:
    - Cystic fibrosis
    - Alpha 1 antitrypsin deficiency

Exacerbations:

Exacerbations of this disease is an extremely common cause of presentation to Emergency Departments.

An exacerbation is an event in the natural course of the disease characterised by a change in the patient's baseline dyspnoea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD (Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2006). [2]

Acute exacerbations of COPD often require hospital admission for treatment of respiratory failure.

The causes of exacerbation include:

1. Infection
2. Associated CCF
3. Associated ACS
4. Pulmonary embolism
5. Poor (or no) medication compliance
6. Refusal to cease smoking
7. Environment pollutants

Note that a significant number of cases will have **no obvious precipitating** cause, and may merely represent disease progression.

Infective exacerbations;

The following organisms commonly colonize the normally sterile lower airways, in patients with COPD: [2]

1. Streptococcus pneumoniae

2. Haemophilus influenzae

3. Moraella catarrhalis

As lung function deteriorates the following may also be seen:

4. Staphylococcus aureus

5. Pseudomonas aeruginosa, (multi-drug resistant species are associated with a 6 fold increase in the risk of death) [2]

While the *number* of organisms can increase in exacerbations of COPD, the precise role this plays in the exacerbation is unclear and somewhat controversial. [2]. General consensus however is that exacerbations *are* often infective in nature.

Clinical Assessment

The clinical assessment of acute presentations to the ED is done along similar lines to that of acute asthma except that in the case of COPD there will be a greater need for ABG analysis to assess the CO_2 status (and trend) of the patient.

Important points of history:

1. Patient's own rating of severity.

    - This should include as assessment of how well the patient is able to cope at home.

2. Previous history:

    - In particular the number of previous admissions, including any to ICU and the need for non-invasive ventilation or intubation.

3. Current and past treatment:

    - Especially if steroid or home oxygen dependent

    - The current treatment the patient is receiving, including their *compliance* with their regime.

4. Duration of the current episode.

5. Sputum production:

    - An increased amount above normal as well as a change in color from clear to yellow/green are commonly taken as evidence for an infective exacerbation.

6. The usual level of function of the patient with respect to normal daily activities.

7. The existence of any prior **limitation of medical treatment** or **advanced care plans**.

Important points of examination:

An assessment of the severity of the presentation can be made on the following parameters:

1. Ability to talk

2. Conscious state

3. Respiratory effort

4. Pulse rate

5. Breath sounds

6. Bedside lung function tests

    - PEFR, Spirometry readings FEV_1

7. Cyanosis (a *late* sign)

Note that the traditionally quoted *pulsus paradoxus* has been abandoned as a useful indicator of severity. It is seen in acute cases of **severe** asthma or COPD, but requires some skill to detect and in any case is redundant as severity is clear from other signs.

Bedside lung function tests are useful in the monitoring of cases of mild to moderate severity, but are academic point and inappropriate tests in the clearly acutely very unwell!

Episodes on history and examination may be assessed as MILD, MODERATE or SEVERE:

PRESENTATION	**MILD**	**MODERATE**	**SEVERE TO LIFE THREATENING**
Altered conscience State	No	No	Yes

Respiratory effort (physical exhaustion)	No	No	Yes (may include paradoxical chest wall movement).
Ability to talk	Sentences	Phrases	Words to none
Pulse	<100	100-120	>120 *(bradycardia can herald imminent respiratory arrest)*
Breath sounds	Moderate wheeze	Loud wheeze	Silent: Decreased air entry or pneumothorax.
PEFR (% predicted)	More than 75% predicted (or best if known)	50-75% predicted (or best if known)	Less than 40% predicted (or best if known) or less than 100 L per min *(if patient is able to perform this)*
FEV_1(% predicted)	More than 75% predicted	50-75% predicted	Less than 40% predicted or less than 1 Liter *
Cyanosis	No	No	Yes
Pulse Oximetry	>95%	92-95%	<92%
ABGs. **PaO_2** **$PaCO_2$**	Not needed	Perform if initial treatment response is poor (if $PaCO_2$ >40 mm Hg treat as severe attack)	$PaCO_2$ > 45 mmHg indicates respiratory failure. PaO_2 < 60 mmHg indicates respiratory failure.

** For patients with stable levels below these values (i.e. chronic severe COPD), the most important signs of a severe exacerbation will be worsening hypoxia, acute respiratory acidosis (with CO_2 retention), or both.* [2]

Investigations

Blood tests:

1. FBE

2. CRP

3. U&Es/ glucose

    - Note that hypokalemia can develop with prolonged used of nebulized salbutamol.

4. Baseline **arterial / venous blood gases**:

    Blood gas analysis is an important part of the assessment of ventilatory function in patients with respiratory distress.

    Traditionally, analysis of arterial blood has been used. Repeated arterial blood gas sampling however causes significant distress, to patients who are already significantly distressed from their dyspnea. More recently, there has been a move towards **venous** blood gas analysis for selected conditions.

    The **SpO_2 (pulse oximeter reading)** correlates **well** with the **PaO_2 (the partial pressure of oxygen in arterial blood)** as predicted by the standard oxygen–haemoglobin dissociation curve, at values of **> 85 %.**

    For adult patients undergoing NIV in the ED, arterio-venous agreement is as follows:

    - There is good agreement between venous and arterial pH.

    - There is good agreement between venous and arterial bicarbonate

    - The correlation between $PvCO_2$ and $PaCO_2$ is **good** when the $PvCO_2$ is **< 45 mmHg**

        However

        The correlation between $PvCO_2$ and $PaCO_2$ is **not good** when the $PvCO_2$ is **> 45 mmHg**

    The $PvCO_2$ however, is an accurate **screening test** for *significant* arterial hypercarbia

The *absolute* need for an **A**BG (or at least a baseline measurement) in the assessment of a COPD patient has been the subject of some debate.

If the $PvCO_2$ is **> 45 mmHg** and there is *insufficient data* from the vpH, $vHCO_3$ and clinical assessment to guide clinical decision making, then consider an **arterial blood gas** to accurately quantify the $PaCO_2$. (*Personal communication, Professor Anne-Maree Kelly, May 2017*).

5. Blood cultures

6. Cardiac enzymes

7. BNP

CXR:

Very unwell patients will require their x-rays to be done in the resuscitation cube.

Look especially for evidence of:

- Infection / consolidation
- Associated CCF
- Pneumothorax.

12 lead ECG:

As for any unwell patient.

Common arrhythmias in the setting of exacerbation of COPD include:

- MFAT
- Rapid AF

Sputum for micro and culture:

Consider if the patient is well enough to cooperate.

Management

For acute exacerbations:

1. Attention to any immediate ABC issues:

2. Establish monitoring:

- Pulse oximetry monitoring
- Continuous ECG monitoring.
- Blood pressure monitoring, (non-invasive in the first instance).
    - ♥ Arterial lines are not essential in the first instance, and can cause unnecessary distress in an already greatly distressed patient.

      Arterial lines may be useful once the patient has been stabilized in those who require ongoing blood pressure monitoring and repeat blood gas analysis.

3. **Oxygenation:**

This is vital and must always remain the first priority.

Oxygen must **never** be withheld from a patient who is hypoxic even if they are CO_2 retainers.

Hypoxia may be lethal within minutes; hypercarbia can be dealt with later, if necessary.

Aim in general to provide enough inspired oxygen concentration to achieve an SaO_2 of **> 90-92 %.**

In some cases of severe disease a level of **88%** may be acceptable.

Initially this may be achieved with a face mask delivery system:

- **Nasal Prong delivery:**
    - ♥ Give **2.0 liters of oxygen per minute** delivered via **nasal prongs** may be used. [2]
- **Hudson mask** with high flow oxygen (up to the maximum 15L/min if necessary

In less severe cases oxygen therapy should be restricted to the minimum concentration **that is able to achieve the desired oxygen saturation levels quoted above.** This can most accurately be achieved via a **venturi device**.

CO_2 retainers may suffer from rising CO_2 levels when unnecessarily excessive oxygen concentrations are administered. (*It is interesting to note that this effect actually has more to do with the Haldane effect of oxygen that results in off-loading of Hb bound CO_2, and not, as has been traditionally taught, because of any "removal of central hypoxic respiratory stimulus" by oxygen administration!*)

- **Venturi oxygen delivery:**

    - ♥ Generally a safe level of oxygen concentration is **28%** which can be accurately delivered via a **venturi device.** [2]

Failing the success of the above oxygenation measures a non-invasive ventilation technique will need to be considered.

4. **Humidification:**

- In the longer term a humidifying device should be used which will provide, warmed as well as humidified inspired O2 which will assist in cilia function and secretion clearance.

5. **High flow nasal oxygen:**

Nasal High Flow (NHF) oxygen delivery systems provide a novel form of respiratory support for patients in respiratory distress.

These devices can also deliver the important functions of warming and humidifying the delivered inspired oxygen for those who will require prolonged treatment with supplemental oxygen.

They may provide an important "step down" option between full NIV i.e. face mask CPAP and BIPAP (or NIPPV) and plain traditional Hudson/Venturi masks or nasal prong oxygen delivery systems.

They can provide higher oxygen delivery and a limited amount of CPAP support, but will be less effective for CO_2 retainers.

They are better tolerated than full non-invasive ventilation techniques and require much less intensive nursing support and so can be used in a general ward setting providing staff have been appropriately trained to use the device.

6. **Non-invasive ventilation: BIPAP/ CPAP**

This will provide up to 100% inspired oxygen and the positive pressure support, which will alleviate the work of breathing.

Non-invasive ventilation can decrease mortality and reduce the need for intubation.

In general BIPAP (or **NIPPV**) is desirable for patients with COPD and ventilatory failure (i.e. CO_2 retention), as this modality will more actively assist in patient ventilation, (compared to CPAP which relies more on the patient's own efforts to ventilate).

BIPAP may on the other hand increase risk of barotrauma, when compared to CPAP and so close monitoring will be essential.

This will be required when:

- Adequate oxygenation cannot be maintained
- There is a rising pCO_2
- Patient exhaustion.
- Altered conscious state, (a *relative* contraindication to BIPAP, but this needs to be judged on a case by case basis)

The duration required of non-invasive ventilation is likely to be relatively prolonged, (up to 24 hours) [3] when compared to cases of pure acute cardiogenic pulmonary edema.

For patients not responding to initial treatment, **NIV should be commenced *earlier* rather than later!**

7. **Salbutamol** (Ventolin):

- Salbutamol 5mg nebules should be given via a nebulizer at 6 liters per minute flow rates, as required.
- This can be given continuously in severe cases if necessary.
- Note that nebulized drugs can now be given via most NIV devices.

8. **Ipratropium** (Atrovent):

- Atrovent 500 micrograms via nebulizer as required, particularly if response to the beta 2 agonist is poor.
- In severe cases it can be given **20 minutely** (or even more frequently in life threatening situations) over the first hour, (i.e 3 doses over one hour). [1]

  Thereafter can be given 1 hourly if required.
- Atrovent can be given together with the nebulized salbutamol.

9. **Corticosteroids:**

A short course of systemic corticosteroids has been shown to shorten the duration of hospital admission and hasten return to previous lung function and stable symptom control. They should be used routinely for severe exacerbations of COPD. [3]

- IV dexamethasone 10 mg tds

Alternatively:

- Hydrocortisone 100 mg IV, 6-hourly

In those who are less severely compromised, oral prednisolone may be used:

- Prednisolone 30 to 50 mg orally, daily, (for up to 2 weeks) [3]

10. Antibiotics:

    For severe exacerbation IV antibiotics, should be given, (the majority of exacerbations will be infective in nature)

    Give:

    - Cefotaxime 1-2 gms daily.

    - Consider the addition of IV 500 mg azithromycin daily.

11. **Antivirals:**

    Viral exacerbations are frequent, and these may be due to influenza.

    In very **unwell patients**, and/or on **epidemiological grounds**, antiviral agents should also be considered.

    - **Oseltamivir** is the agent most commonly prescribed for influenza infection.

12. Aminophylline:

    - Although very popular in the past, this agent is **not** currently routinely recommended.

      It offers no significant advantages over salbutamol and has significant toxic effects.

13. Minimize the use of any sedating agents, such as morphine where possible:

    - Small titrated doses of morphine may be considered however in order to enable some patients to **tolerate non-invasive ventilation**.

14. **Intubation and mechanical ventilation:**

    If the patient deteriorates despite BIPAP, or is very unwell, intubation needs to be considered.

The decision to intubate a COPD patient will depend on a number of factors including:

- There is a definite diagnosis of COPD.
- The patient's quality of life.
- The presence of a reversible disease process eg infection or associated CCF
- Whether the patient is a known CO_2 retainer.
- The patient's own wishes, if previously documented.
- Discussion, where possible, with the patient's family/ GP/ treating medical unit.
- A previous (and current) limitation of medical treatment or advanced care plan.

If there is uncertainty regarding the suitability of a patient for intubation, the case should be discussed early with ICU.

The indications for intubation in patients will include:

- Patient exhaustion
- A declining level of consciousness or increasing confusion and agitation.
- A rising $PaCO_2$
- Failure to maintain an adequate oxygenation saturation (> 88 %) or PaO_2 > 60 mmHg.

Ventilator settings for Permissive Hypercarbia in asthma / COPD:

Patients with COPD have airflow obstruction and so require an **obstructive lung ventilation** strategy.

Therefore use:

- High inspired oxygen levels (100%) initially, then titrate FiO_2 to achieve an adequate SaO_2 (> 90 - 92 %)

Tidal volume:

- Do not use more than **6 mls/kg.**

- In severe cases it is necessary to reduce Vt by as much as 50 % to **3 - 4 mls /kg** ideal body weight. This will still provide sufficient oxygen to prevent hypoxia.

Frequency (f):

- In severe cases it is necessary to reduce by 50 % to **6-8 per minute**

- Monitor the $PaCO_2$ (and/or $ETCO_2$) but **do not treat hypercapnia (by increasing respiratory rate)**

  This strategy is safe to a pH > 7.1 - (the risk versus benefit at pH values < 7.1 are less clear).

  This technique is known as "**permissive hypercapnia**".

  Note that IV bicarbonate does **not** help. It will only increase the $PaCO_2$ further, lead to hypocalemia and will not improve the circulatory status.

  Increasing the RR to treat hypercapnia may cause pneumothorax or hypotension.

PEEP:

- Turn **off** all PEEP**.**

I:E ratio:

- Reducing the frequency will reduce the I:E ratio.

- In severe cases reduce inspiratory time ≤ 1 second.

- Sometimes an I:E ratio of 1:4 or even less will be required.

Note that most ventilators will register or alarm "low exhaled tidal volume" alarms because they are unable to measure volume when the expiratory flow rate is very low. So check chest rise/fall, capnometry, and SpO_2 to confirm sufficient ventilation is occurring.

Additional strategies:

Sufficient sedation is important:

- Long-acting muscle relaxants may be required to prevent any spontaneous breathing, until airflow obstruction is resolving, especially during inter-hospital transfers.

- Insert naso- (or oro-) gastric tube to decompress the stomach.

For hypotension:

- Disconnect the ventilator for 20-30 seconds to treat dynamic hyperinflation, then reconnect and reduce the respiratory rate (f) by 2 breaths.

- Check CXR to exclude pneumothorax or right main bronchus intubation.

Monitor but do not treat:

- High $ETCO_2$

- High $PaCO_2$

- High PIP:

    - ♥ It is safe to increase the PIP alarm (> 40 cm H_20) as long as **Plateau Pressure (Pplat)** remains < 30 cm H_2O.

      If Plateau pressure > 30 mmHg - reduce frequency by 2

Avoid:

- Normal or high frequency respiratory rates.

- Normal or High Vt

- High **Plateau pressures**

- Spontaneous breathing.

In summary:

Ventilation for obstructive lung disease:

- Low Vt

- Low frequency

- Low I:E ratio

- **No** PEEP

- High FiO_2

- Adequate sedation ± muscle relaxants.

Disposition

Patients with exacerbation of COPD will usually require admission. Generally these patients are not suitable for short stay unit admissions, but each case must be assessed on its individual merits.

Unwell patients will require early HDU / ICU consultation, particularly those with:

- Failure to respond to initial treatment in the ED
- A severe past history, requiring ICU admissions, non-invasive ventilation or intubation.
- Failure of weaning from non-invasive ventilation.

Patients who have prior limitation of medical treatment or advanced care plans or who have these implemented whilst in the ED and are not suitable for an ICU or HDU admission will be able to be admitted to a general ward.

Note that a limitation of medical treatment plan does not necessarily exclude a patient from a trial of NIV, as most of these plans refer more specifically to withholding CPR, intubation or inotropic support.

Depending on bed availability patients may undergo a "trial of NIV" whilst in the ED, or as an inpatient in a HDU.

If patients do not respond to NIV after a reasonable period of time, then a decision may need to be made regarding the withdrawal of this modality and palliating the patient. This kind of decision must be made in close consultation with other relevant specialties, such as the treating respiratory unit and/or the ICU, as well as family and where possible the patient themselves.

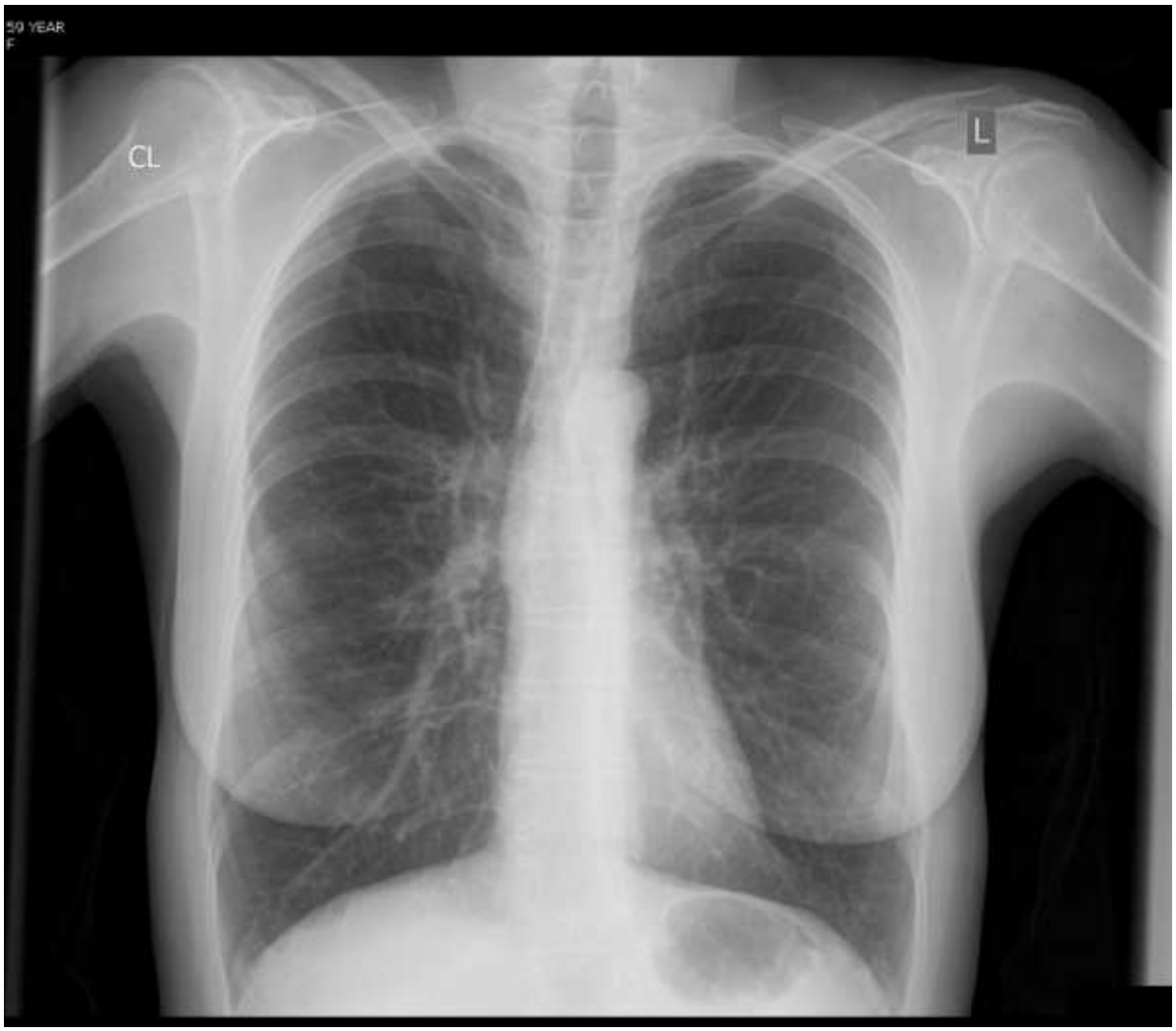
Follow-up

All patients with moderate to severe COPD, especially those with recurrent presentations to the ED should be considered for a referral to a specialized respiratory out-reach unit dealing in the longer term management of these patients.

These teams can assist in optimizing education, and home management of patients suffering from COPD and will help with reducing the need for ED presentations.

Early diagnosis and treatment of exacerbations will often assist in prevention the need for hospital admission and may help reduce progressive functional deterioration.[2]

Appendix 1



A-P CXR demonstrating the classical changes of COPD in a 59 year old woman with predominant emphysema.

There are signs of hyperinflation of the lungs, including flattening of diaphragms, (the origin of the 11th rib can be identified) and a long narrow heart shadow, rapid tapering vascular shadows and hyperlucency of the lung fields. Lateral films typically an show increased retrosternal air space. There is also some "peri-bronchial thickening" seen due to chronic inflammatory changes of the airways.

With complicating pulmonary hypertension, the hilar vascular shadows are prominent; with right ventricular enlargement, although this can be difficult to assess because of the hyperinflation.

Appendix 2

Staging of Chronic Disease: The Global Initiative on Chronic Obstructive Lung Disease (GOLD)

STAGE	FEV_1 / FVC	% of Predicted FEV_1	Symptoms
I	< 0.70	FEV_1 > 80 %	Patient is usually unaware of their abnormal lung function.
II	< 0.70	50 % > FEV_1 < 80 %	Patient seek medical attention for symptoms
III	< 0.70	30 % > FEV_1 < 50 %	Repeated exacerbations that significantly impact quality of life
IV	< 0.70	< 30 % *Or* < 50 % with evidence of chronic respiratory failure.	Severe reduction on quality of life / Life threatening exacerbations.

References:

1. J. Considine, M. Botti and S. Thomas. Emergency department management of exacerbation of chronic obstructive pulmonary disease: audit of compliance with evidence-based guidelines. doi:10.1111/j.1445-5994.2009.02065.x Internal Medicine Journal, June 2009.

2. David K McKenzie, Michael Abramson, Alan J Crockett, Nicholas Glasgow, Sue Jenkins, Christine McDonald, Richard Wood-Baker, Peter A Frith on behalf of The Australian Lung Foundation. The **COPD-X Plan:** Australian and New Zealand Guidelines for the Management of Chronic Obstructive Pulmonary Disease 2011

3. eTG - November 2015.

    - Respiratory Therapeutic Guidelines, 5th ed 2015.

4. J.Leung, M. Duffy, COPD in Cameron et al. Textbook of Adult Emergency Medicine, 4th ed Cameron et al, Churchill Livingston, 2015

5. Anne-Maree Kelly, Sharon Klim. Agreement between arterial and venous pH and pCO2 in patients undergoing non-invasive ventilation in the emergency department. Emergency Medicine Australasia (2013) 25, 203 - 206. doi: 10.1111/1742-6723.12066

Dr. J. Hayes

Acknowledgments:
Dr A. Casamento
Dr. G. Duke
Reviewed 7 May 2017