COPD exacerbation

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Learning objectives

At the end of this lecture students will be able to:

1) Critically assess patients for COPD and design a management plan.
2) Develop a step-wise approach to the diagnosis and treatment of COPD exacerbations including interpretation of clinical and objective data.

COPD

- The Global Initiative for Chronic Obstructive Lung Disease (**GOLD**) defines COPD as: *common preventable and treatable a disease characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities caused by significant exposure to noxious particles or gases.*

- Chronic inflammation→ **large airway inflammation** (chronic bronchitis) + **narrowing of small airways** (obstructive bronchiolitis) with decreased elastic recoil of the lung (d/t proteases) + enlargement of airspaces w/ **loss of diffusing surface area** (emphysema)→ air trapping (dynamic hyperinflation)+ static hyperinflation→ progressive airflow limitation with impaired gas exchange

- **Risk factors** include: **tobacco smoking**, environmental exposure (burning of biomass fuels), genetic factors (ex. alpha-1 antitrypsin deficiency)

COPD Subtypes

Subtypes include:

- Emphysema
- Chronic bronchitis
- Chronic obstructive asthma (reversible airway disease)

Most patients have a combination of emphysema (parenchymal destruction) and obstructive bronchiolitis (small airway disease): the contribution of each varies from person to person

Chronic bronchitis

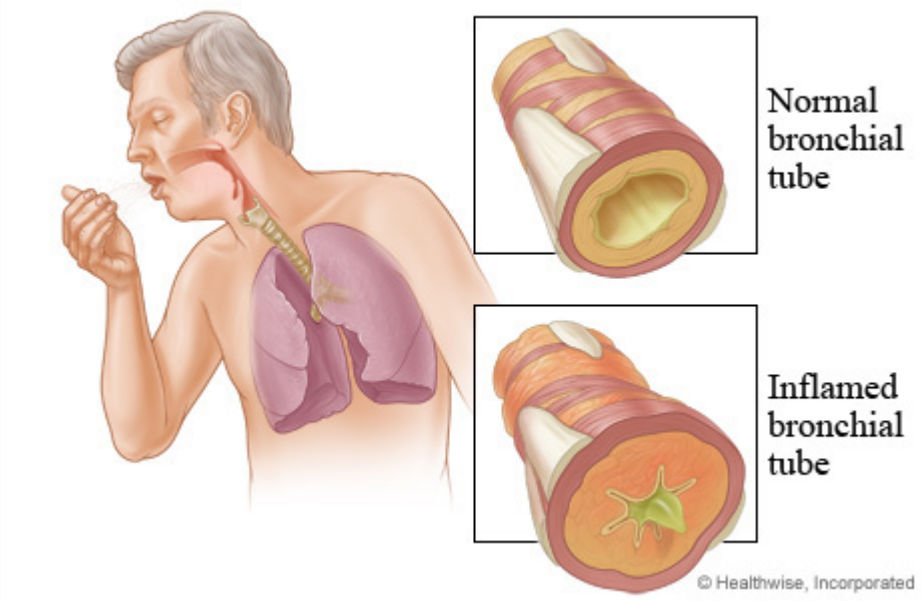


Image source: https://www.webmd.com/lung/chronic-bronchitis

Definition: Chronic productive cough x 3 months in 2 successive years in a patient in whom other causes have been ruled out

Emphysema

Pathological term referring to the structural changes sometimes seen in COPD patients= enlargement of airspaces distal to the terminal bronchioles and alveolar destruction

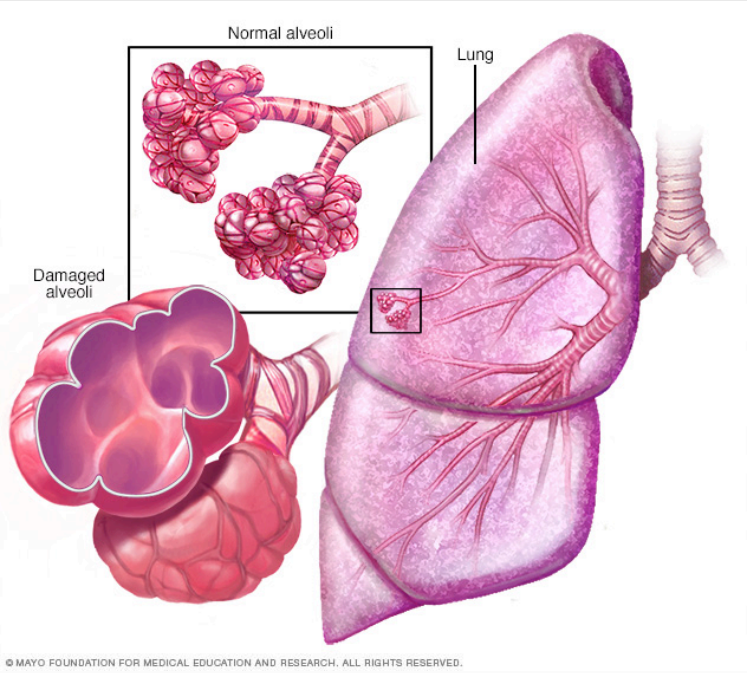


Image source: https://www.mayoclinic.org/diseases-conditions/emphysema/symptoms-causes/syc-20355555

COPD-Asthma overlap syndrome

Characterized by persistent airflow limitation with several features associated with asthma and several features associated with COPD (GOLD and GINA issued definition)

Great review article by NEJM on COPD-Asthma Overlap syndrome published in 2015: http://www.nejm.org/doi/full/10.1056/NEJMra1411863

Symptoms of COPD

- 3 features of COPD:
  - Dyspnea
  - Chronic cough
  - Sputum production
- Patient may initially present with respiratory complaints including a chronic cough (may be productive of mucous) and dyspnea with exertion which is progressive. Patient often state that the morning time is the worst.

Physical exam

- Early in the disease the physical exam may be normal but as the disease progresses:
  - Increased resonance to percussion (due to hyperinflation)
  - Decreased breath sounds
  - Wheezing and crackles at lung bases
  - “Barrel-shaped” chest (severe disease)
- Patients with end-stage COPD may be seen sitting leaning forward with arms outstretched (tripoding) with use of accessory muscles, expiration through pursed lips, or signs of cyanosis

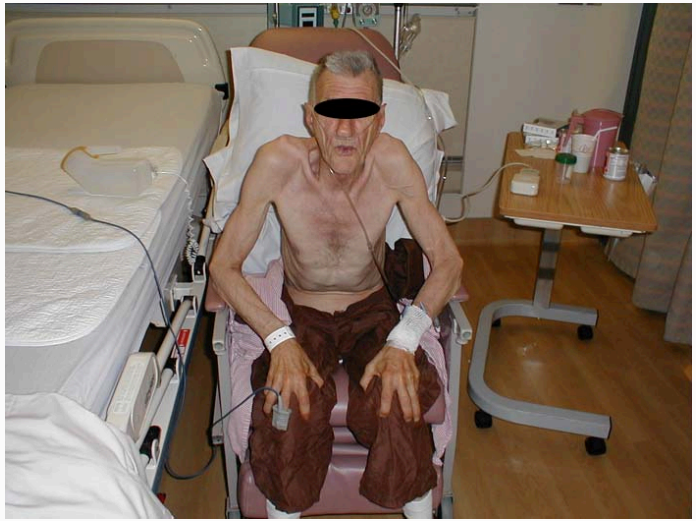


Image source: https://meded.ucsd.edu/clinicalimg/thorax_tripod.htm

Evaluation

- Patients reporting **dyspnea, a chronic cough, chronic sputum production** or a gradual decrease in exertional activity +/- history of exposure to smoke (tobacco, factories, etc) should be screened.
- All patients should be evaluated by **spirometry** and some patients should also have imaging and lab testing (which may include: CBC, BNP, alpha-1 antitrypsin)
    - Suspect AAT deficiency in young patient (<45 y/o) with emphysema, emphysema in a non-smoker or minimal smoker, emphysema with mostly basilar changes on CXR, or family history of emphysema

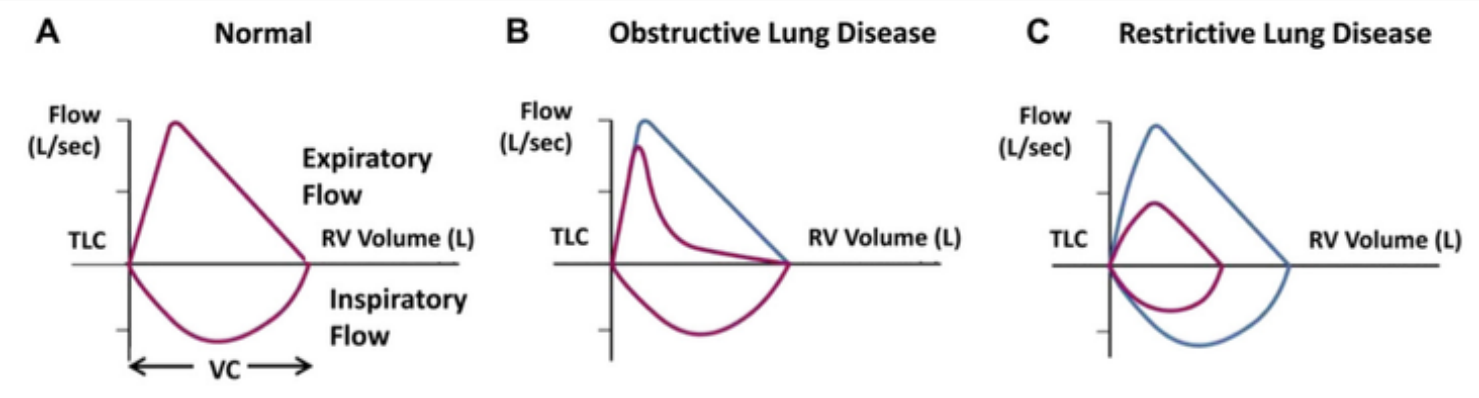
Assessment

Based on 3 parameters:

1. Severity of obstruction on **spirometry** testing
2. Patient **symptoms** rated on either the CAT (COPD Assessment Test) or the mMRC (modified Medical Research Council Dyspnea scale)
3. Frequency of **exacerbation**
4. Presence of **comorbidities**

Spirometry

- Essential test to confirm the diagnosis and stage COPD
- Perform *bronchodilator challenge* with albuterol 400mcg: if the airflow obstruction is only partially reversed or not reversed at all then it is suggestive of COPD rather than asthma
- Post-bronchodilator **FEV1/FVC ratio < 0.7** or < LLN is used to establish the presence of airflow limitation



https://www.memorangapp.com/flashcards/128836/Pulmonary+Function+Test/

GOLD Severity scale (spirometry)

In the presence of FEV1/FVC evidence of airflow limitation (FEV1/FVC<0.7):

- GOLD 1: Mild (FEV1 80% or greater predicted)
- GOLD 2: Moderate (FEV1 50- 79% predicted)
- GOLD 3: Severe (FEV1 30-49% predicted)
- GOLD 4: Very severe (FEV 1 < 30% predicted)

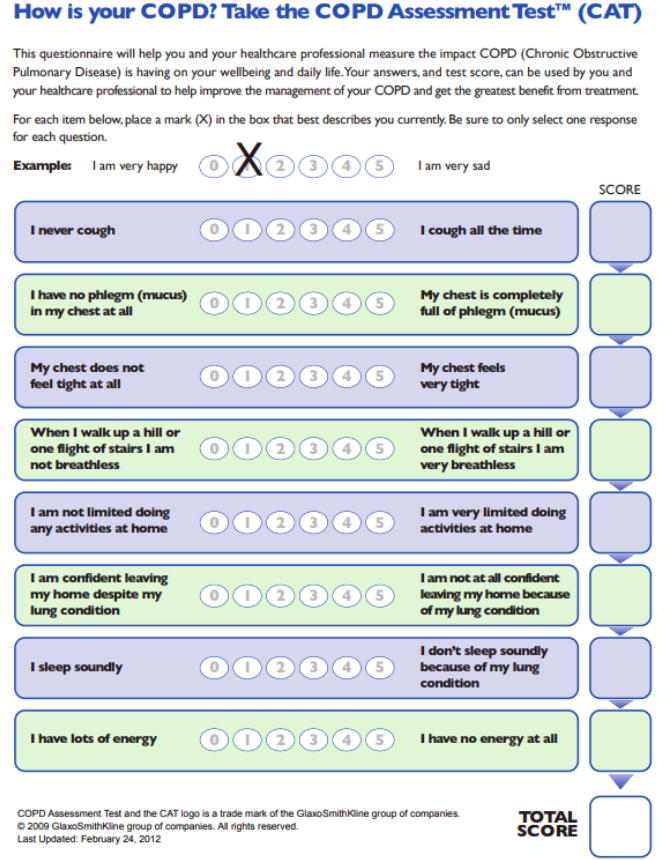
Patient symptoms: CAT, mMRC scales

Modified Medical Research Council (MMRC) dyspnea scale

Grade	Description of breathlessness
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing

mMRC dyspnea scale: 0-4 scale, score of 4 indicating highest degree of exercise intolerance

CAT scale: 0-40 scale with score >10 indicating COPD symptoms that limit quality of life



How is your COPD? Take the COPD Assessment Test™ (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I am very happy 0 X 2 3 4 5 I am very sad

SCORE

I never cough	0 1 2 3 4 5	I cough all the time
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition
I have lots of energy	0 1 2 3 4 5	I have no energy at all

Last Updated: February 24, 2012

TOTAL SCORE

Image source: http://www.catestonline.org/images/pdfs/CATest.pdf

Frequency of exacerbation

- 2011 GOLD guideline combined spirometry findings and likelihood of exacerbations into 4 groups (Group A, B, C, D)
- However, studies showed that the ABCD assessment was no better in predicting mortality or health outcomes than spirometric grades.
- So in 2017 the GOLD guidelines separated the spirometry testing from symptom evaluation.
    - Now patients undergo spirometry testing followed by assessment with either the CAT or mMRC tool and history of exacerbations to form a revised ABCD assessment tool

The Refined ABCD Assessment Tool

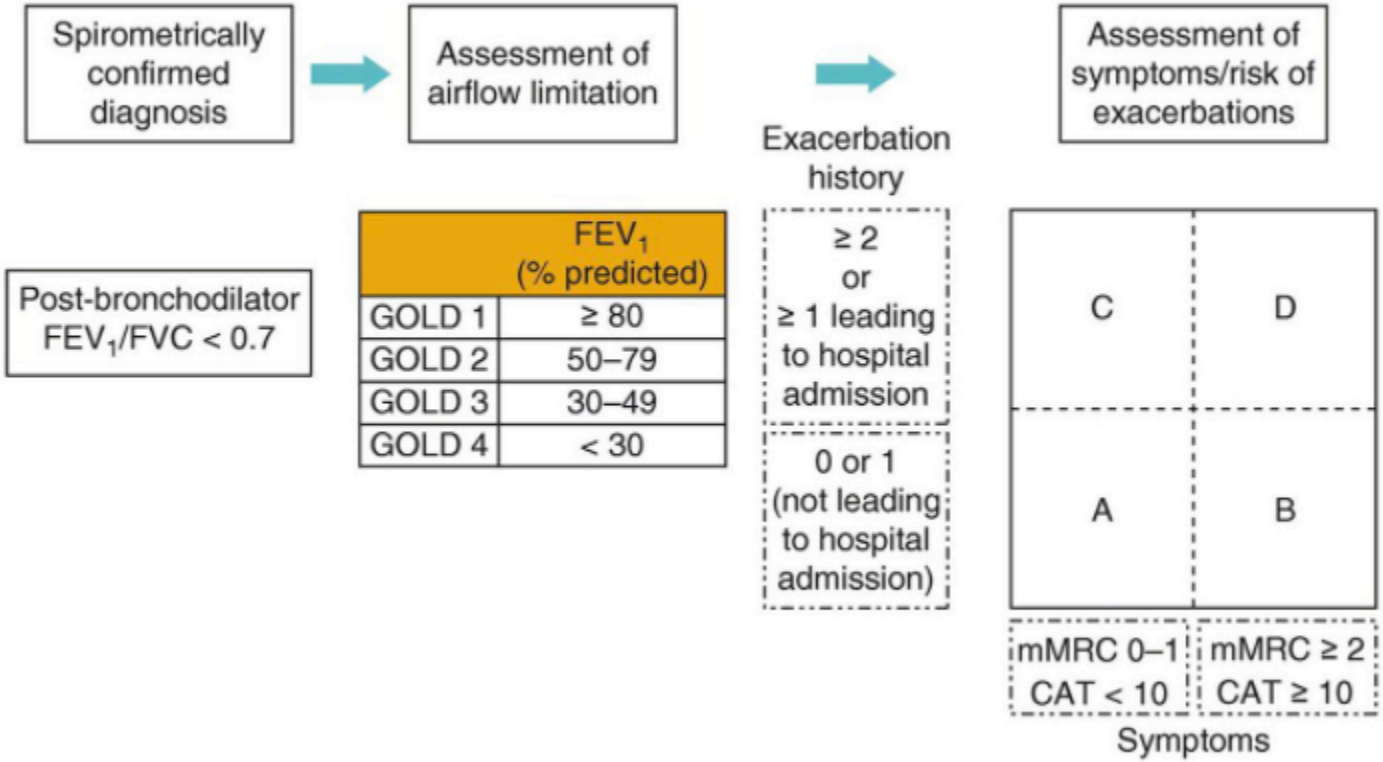


Image source: http://goldcopd.com

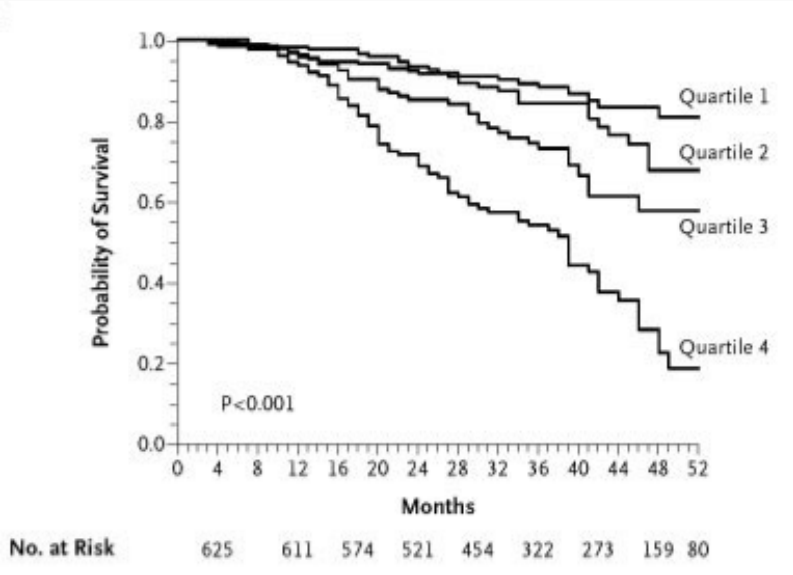
Presence of comorbidities

The presence of other conditions (cardiovascular, musculoskeletal, etc) needs to be documented in patients with COPD

BODE index (BMI, airflow Obstruction, Dyspnea, Exercise): multidimensional grading system that can be used to predict the risk of death from any cause and from a respiratory cause in patients with COPD

Table 2. Variables and Point Values Used for the Computation of the Body-Mass Index, Degree of Airflow Obstruction and Dyspnea, and Exercise Capacity (BODE) Index.*

Variable	Points on BODE Index			
	0	1	2	3
FEV_1 (% of predicted)†	≥65	50–64	36–49	≤35
Distance walked in 6 min (m)	≥350	250–349	150–249	≤149
MMRC dyspnea scale‡	0–1	2	3	4
Body-mass index§	>21	≤21		



Kaplan–Meier Survival Curves for the Four Quartiles of the Body-Mass Index, Degree of Airflow Obstruction and Dyspnea, and Exercise Capacity Index (Panel A). Quartile 1: BODE score 0-2, Quartile 2: BODE score 3-4, Quartile 3: BODE score 5-6, Quartile 4: BODE score 7-10

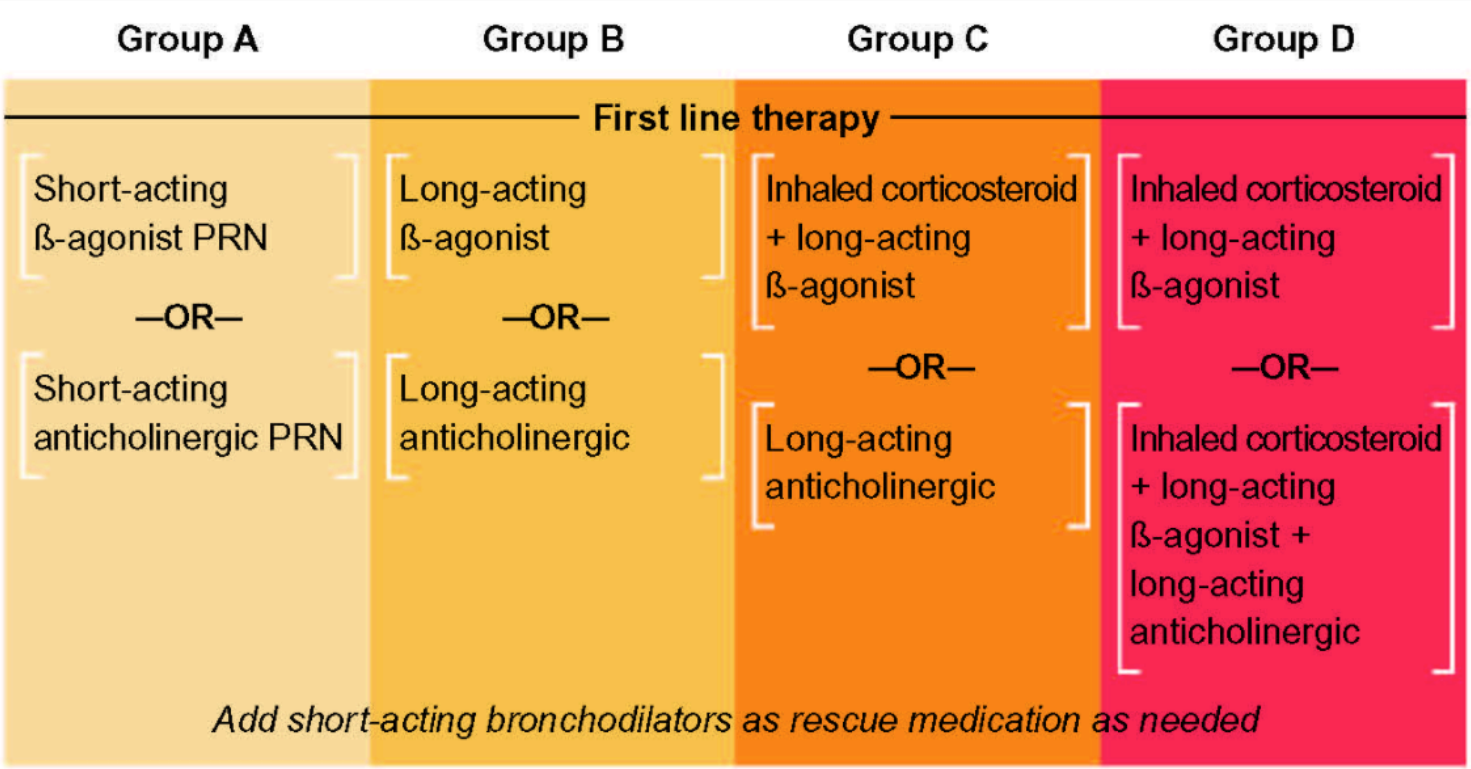
http://www.nejm.org/doi/full/10.1056/NEJMoa021322

Nonpharmacological management

- **Smoking cessation**
- Reduce environmental risk factors
- Vaccination
  - PPSV23 (pneumovax) for patients < 65 yo; PCV13 (prevnar) + PPSV23 for patients 65 yo+
  - Annual influenza vaccine
- Oxygen therapy
  - If PaO2 of 55mmHg or less or SaO2 88% or less on RA
  - If patient has cor pulmonale, PaO2 of 59mmHg or less or SaO2 of 89% or less
  - Continuous O2 therapy increases lifespan if used for the above criteria
- Pulmonary rehab
  - Improves symptoms and quality of life and decreases number of hospitalizations
- Lung volume reduction surgery

Pharmacologic therapy, GOLD criteria

- For all patients with COPD, the use of short-acting bronchodilators PRN
- For **category A** patients:
  - SABA PRN. A combination SABA-SAMA may be used if a single agent is not enough. (SABA ex. Albuterol, SAMA ex. Atrovent, Ipratropium)
- For **category B** patients:
  - regular treatment with LABA or LAMA. SABA PRN. (ex. LABA salmeterol, LAMA spiriva, tiotropium)
- For **category C** patients:
  - regular treatment with LAMA or LABA + ICS. SABA PRN.
  - Roflumilast can be used in patients with chronic bronchitis
- For **category D** patients:
  - regular treatment with LABA +/- LAMA + ICS. SABA PRN.
  - Roflumilast can also be used if chronic bronchitis present



Optional alternative therapies:

Group A: **[**Short-acting ß-agonist + short-acting anticholinergic**]** **or** **[**long-acting ß-agonist**]** **or** **[**long-acting anticholinergic**]**
Group B: **[**Long-acting ß-agonist + long-acting anticholinergic**]**
Group C: **[**Inhaled corticosteroid + long-acting anticholinergic**]** **or** **[**long-acting ß-agonist + long-acting anticholinergic**]** **or** **[**long-acting ß-agonist/long-acting anticholinergic + PDE4 inhibitor for chronic bronchitis**]**
Group D: **[**PDE4 Inhibitor added to first line therapy for chronic bronchitis**]**

Image source: https://resident360.nejm.org/pages/home?resource_collection_id=pulmonology&subtopic=copd&subgroup=fast-facts

Features of COPD exacerbation

- Diffuse wheezing, distant breath sounds, barrel-shaped chest, tachypnea, tachycardia
- Features of severe respiratory decline:
  - Use of accessory muscles
  - Brief, fragmented speech
  - Inability to lie flat
  - Profound diaphoresis
  - Agitation
  - Failure to improve with initial emergency treatment

Triggers for COPD exacerbation

- **Infections** account for ~70% of COPD exacerbations
- Environmental pollution
- Pulmonary embolism
- Unknown etiology

Table 1. Microbial Pathogens in COPD.*

Microbe	Role in Exacerbations	Role in Stable Disease
Bacteria		
Haemophilus influenzae	20–30% of exacerbations	Major role
Streptococcus pneumoniae	10–15% of exacerbations	Minor role
Moraxella catarrhalis	10–15% of exacerbations	Minor role
Pseudomonas aeruginosa	5–10% of exacerbations, prevalent in advanced disease	Probably important in advanced disease
Enterobacteriaceae	Isolated in advanced disease, pathogenic significance undefined	Undefined
H. haemolyticus	Isolated frequently, unlikely cause	Unlikely
H. parainfluenzae	Isolated frequently, unlikely cause	Unlikely
Staphylococcus aureus	Isolated infrequently, unlikely cause	Unlikely
Viruses		
Rhinovirus	20–25% of exacerbations	Unlikely
Parainfluenza virus	5–10% of exacerbations	Unlikely
Influenza virus	5–10% of exacerbations	Unlikely
Respiratory syncytial virus	5–10% of exacerbations	Controversial
Coronavirus	5–10% of exacerbations	Unlikely
Adenovirus	3–5% of exacerbations	Latent infection seen, pathogenic significance undefined
Human metapneumovirus	3–5% of exacerbations	Unlikely
Atypical bacteria		
Chlamydophila pneumoniae	3–5% of exacerbations	Commonly detected, pathogenic significance undefined
Mycoplasma pneumoniae	1–2% of exacerbations	Unlikely
Fungi		
Pneumocystis jiroveci	Undefined	Commonly detected, pathogenic significance undefined

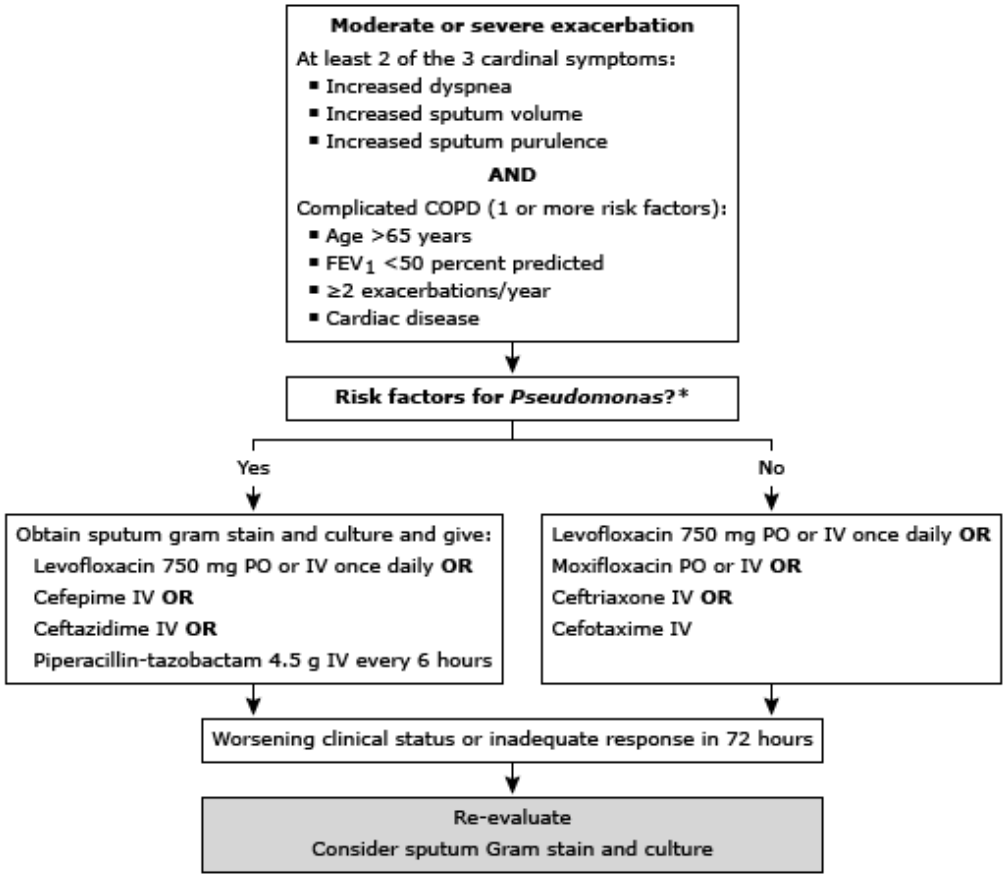
Image source: https://resident360.nejm.org/pages/home?resource_collection_id=pulmonology&subtopic=copd&subgroup=fast-facts

COPD exacerbation management

- Inhaled short-acting **bronchodilator** therapy
  - Short-acting beta adrenergic agonists (eg albuterol) are the mainstay of therapy +/- short-acting anticholinergic (eg ipratropium) (combination usually advised during severe exacerbations)
- Systemic **glucocorticoids** x 5 days (GOLD guidelines)
  - Patients not requiring ICU admission: Prednisone 40-60 mg PO daily
  - Patient requiring ICU admission: IV Methylprednisolone 60mg 1-4x/day
    - Study looking at mortality of patients receiving 240mg/day of IV methylprednisolone vs. <240mg/day showed no change in mortality but shorter hospital stay in ICU patients
- **Antibiotics** (next slide)

- Mucoactive agents, methylxanthines, and mechanical techniques to augment sputum clearance have not been shown to provide benefit in a COPD exacerbation

Antibiotic treatment of exacerbations of COPD in hospitalized patients



Supplemental oxygen

- Target oxygen saturation: 88 to 92%
- **BiPAP** improves clinical outcomes in patients having an acute exacerbation of COPD complicated by hypercapnic acidosis (do not start non-invasive ventilation in patients that do not have a respiratory acidosis)
- After starting NIV patient should have a decreased respiratory rate, increased tidal volume, and increased minute ventilation.
    - 8cm H20 inspiratory pressure, 3cm H20 expiratory pressure

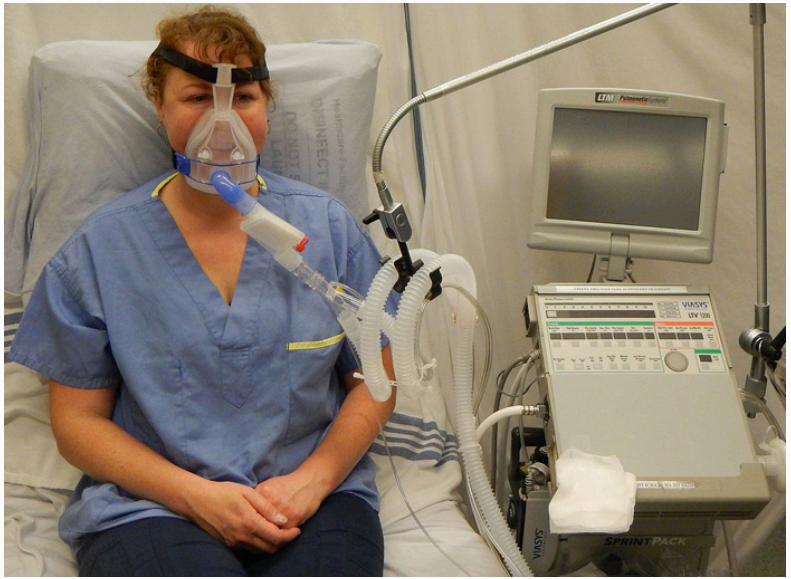
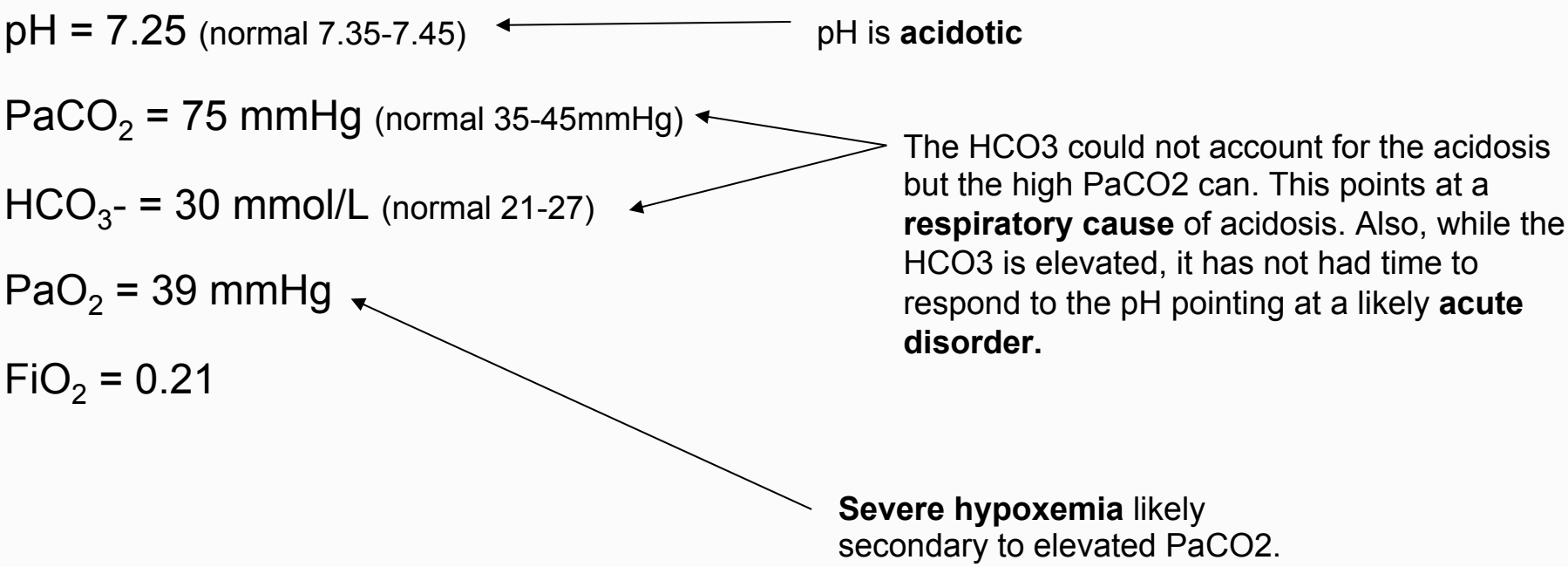


Image source: https://universityhealthnews.com/daily/sleep/what-is-a-bipap-machine/

Interpreting ABG in a COPD exacerbation



MKSAP Question 1

A 62-year-old woman is evaluated in the hospital after being admitted 4 days ago for an acute exacerbation of COPD. She has responded well to treatment and is ready to be discharged today. Her medical history is notable for moderate-severity COPD, heart failure, depression, osteoporosis, hypertension, and hyperlipidemia. Her discharge medications are lisinopril, carvedilol, simvastatin, sertraline, alendronate, vitamin D, calcium, tiotropium, levofloxacin, prednisone, and albuterol.

On physical examination, temperature is normal, blood pressure is 120/84 mm Hg, pulse rate is normal, and respiration rate is 18/min. Oxygen saturation is 93% breathing ambient air. No jugular venous distention is noted. Pulmonary examination reveals a few scattered wheezes and a few basal crackles. She is not using accessory muscles of breathing. Trace pedal edema is noted. She ambulates well without oxygen.

Which of the following factors increases this patient's risk for early hospital readmission for COPD?

A) Adequacy of discharge medications for COPD
B) Female gender
C) Length of hospitalization
D) Multiple comorbid conditions

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MKSAP Question 2

A 59-year-old woman is evaluated in follow-up in November after being diagnosed with moderate COPD 3 months ago. She has never received the influenza or pneumococcal vaccine. She has no allergies. Her medications are a long-acting inhaled anticholinergic agent and an as-needed short-acting β2-agonist inhaler.

On physical examination, vital signs and the remainder of the physical examination are normal.

Which of the following vaccinations are recommended for this patient?

A) Inactivated influenza vaccine and 13-valent pneumococcal conjugate vaccine (PCV13)
B) Inactivated influenza vaccine and 23-valent pneumococcal conjugate vaccine (PPSV23)
C) Inactivated influenza vaccine, PPSV23, and PCV13
D) Live attenuated influenza vaccine and PPSV13
E) Live attenuated influenza vaccine, PPSV23, and PCV13

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E) Live attenuated influenza vaccine, PPSV23, and PCV13

Patients with COPD should receive an annual inactivated influenza vaccine. Patients with COPD age 19 to 64 should receive PPSV23 with revaccination at age 65 or older if 5 years have elapsed since the previous pneumococcal vaccine. PCV13 should be given at age 65+ if 1 year has elapsed since the last PPSV23 immunization.

(If a patient with COPD received the PPSV23 vaccine at age 65+ they do not need revaccination)

MKSAP Question 3

A 67-year-old woman is evaluated in the emergency department for a 2-day history of fever, dyspnea, and increased cough with production of green sputum. She has severe COPD, which was diagnosed 2 years ago. She used albuterol several times yesterday with no relief of dyspnea, and she was unable to sleep last night. Her last spirometry, performed 6 months ago, showed an FEV1 of 48% of predicted. She is a current smoker with a 24-pack-year history. Medications are tiotropium and as-needed albuterol.

On physical examination, temperature is 38.9 °C (102.0 °F), blood pressure is 124/80 mm Hg, pulse rate is 118/min, and respiration rate is 30/min. Oxygen saturation is 82% breathing ambient air. Pulmonary examination reveals bilateral diffuse expiratory wheezing. After an albuterol nebulizer treatment and breathing 2 L of oxygen by nasal cannula, oxygen saturation is 91%. She remains tachypneic with bilateral expiratory wheezing.

Chest radiograph shows no infiltrate.

In addition to continuing this patient's supplemental oxygen and short-acting bronchodilator, which of the following is the most appropriate treatment?

A) Azithromycin and prednisone
B) Clarithromycin and fluticasone
C) Doxycycline and salmeterol/fluticasone
D) Erythromycin and roflumilast

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Antibiotics and systemic glucocorticoids (prednisone) are indicated for the treatment of COPD exacerbations along with short acting bronchodilators and oxygen as needed. Most COPD exacerbations are due to bacterial or viral infections—the most common bacterial pathogens are H. influenzae, H. parainfluenzae, Strep pneumoniae, and Moraxella catarrhalis. Common antibiotics includes: advanced macrolide, cephalosporin, or doxycycline. The prednisone course is typically 40mg/d x 5 days.

Questions

Resources

UpToDate
- Management of COPD
- Chronic obstructive pulmonary disease: Definition, clinical manifestations, diagnosis, and staging
- Management of exacerbations of COPD
- Management of stable COPD

NEJM Resident 360: “COPD”

NEJM review articles
- The Asthma-COPD Overlap syndrome
- The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in COPD

MKSAP 17
- COPD overview and questions

MedStudy Internal Medicine Review: Core curriculum
- COPD