

# Current Therapy for Chronic Obstructive Pulmonary Disease

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# ➤ **Diagnosis and Overview**

➤ Therapeutic Options

➤ Manage Stable COPD

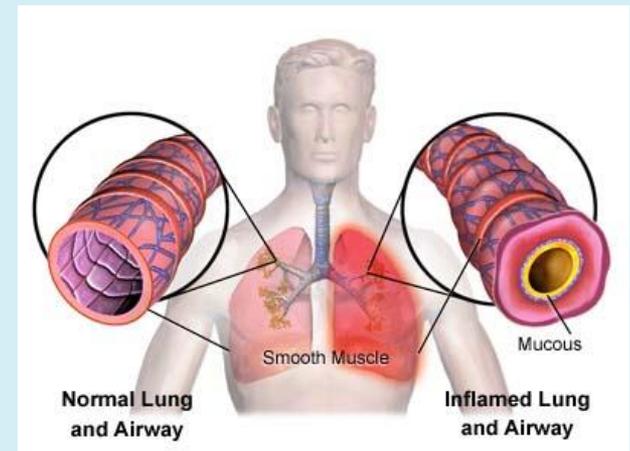
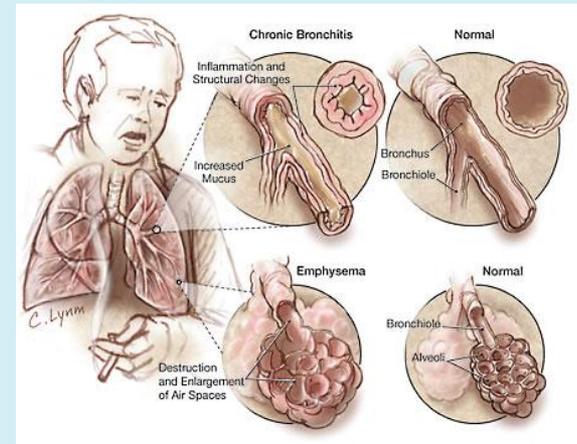
➤ Manage Exacerbations

# Chronic Obstructive Disease

- ▶ Airway and systemic inflammation
- ▶ Under-recognized / under-diagnosed
- ▶ Third leading cause of death in United States
- ▶ Expected to be third leading cause of death worldwide by 2020.
- ▶ Chronic Bronchitis
- ▶ Emphysema
  - Alpha 1 Anti-trypsin Deficiency
- ▶ Asthma
- ▶ Others closely related
  - Cystic Fibrosis
  - Bronchiolitis
  - Bronchiectasis

# DIAGNOSIS

- ▶ Consider COPD if
  - Dyspnea
  - Chronic Cough
  - Sputum production
  - Exposure to risk
- ▶ Spirometry is **REQUIRED** to make diagnosis



# SYMPTOMS



*COPD Assessment Test (CAT):* An 8-item measure of health status impairment in COPD (<http://catestonline.org>).

*Breathlessness Measurement using the Modified British Medical Research Council (mMRC) Questionnaire:* relates well to other measures of health status and predicts future mortality risk.

*Clinical COPD Questionnaire (CCQ):* Self-administered questionnaire developed to measure clinical control in patients with COPD (<http://www.ccq.nl>).

# SYMPTOMS

Use the COPD Assessment Test(CAT) OR mMRC Breathlessness scale OR Clinical COPD Questionnaire (CCQ)

PLEASE TICK IN THE BOX THAT APPLIES TO YOU  
(ONE BOX ONLY)

mMRC Grade 0. I only get breathless with strenuous exercise.

mMRC Grade 1. I get short of breath when hurrying on the level or walking up a slight hill.

mMRC Grade 2. I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.

mMRC Grade 3. I stop for breath after walking about 100 meters or after a few minutes on the level.

mMRC Grade 4. I am too breathless to leave the house or I am breathless when dressing or undressing.

# GOLD

## Spirometric Classification of COPD

### Stage

### Characteristics

I: Mild COPD

FEV1 /FVC <70 percent

FEV1  $\geq$ 80 percent predicted

II: Moderate COPD

FEV1 /FVC <70 percent

50 percent  $\leq$ FEV1 <80 percent predicted

III: Severe COPD

FEV1 /FVC <70 percent

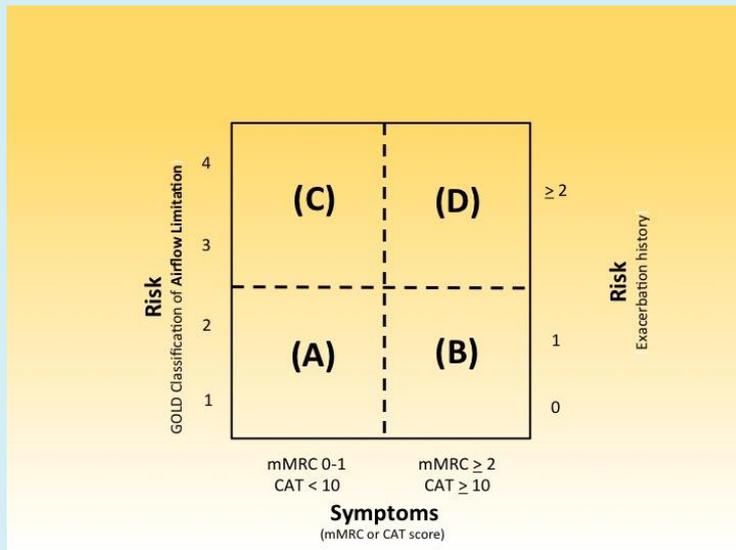
30 percent  $\leq$ FEV1 <50 percent predicted

IV: Very Severe COPD

FEV1 /FVC <70 percent

FEV1 <30 percent predicted or  
FEV1 <50 percent predicted plus  
chronic respiratory failure

# GOLD Classification of COPD



Patient is now in one of four categories:

- A: Less symptoms, low risk
- B: More symptoms, low risk
- C: Less symptoms, high risk
- D: More symptoms, high risk

Patient	Characteristic	Spirometric Classification	Exacerbations per year	mMRC	CAT
A	Low Risk Less Symptoms	GOLD 1-2	$\leq 1$	0-1	$< 10$
B	Low Risk More Symptoms	GOLD 1-2	$\leq 1$	$\geq 2$	$\geq 10$
C	High Risk Less Symptoms	GOLD 3-4	$\geq 2$	0-1	$< 10$
D	High Risk More Symptoms	GOLD 3-4	$\geq 2$	$\geq 2$	$\geq 10$

➤ Diagnosis and Overview

➤ **Therapeutic Options**

➤ Manage Stable COPD

➤ Manage Exacerbations

# PHARMACOTHERAPY GOALS

- ▶ Relieve Symptoms
- ▶ Improve exercise tolerance
- ▶ Improve health status

} Reduce symptoms

- ▶ Prevent disease progression
- ▶ Prevent and treat exacerbations
- ▶ Reduce mortality

} Reduce risk

- Diagnosis and Overview
- Therapeutic Options
- **Manage Stable COPD**
- Manage Exacerbations

# TREATMENT

- ▶ Inhaled Bronchodilators
- ▶ Beta2-agonists
  - Short acting
  - Long acting
- ▶ Anticholinergics
  - Short acting
  - Long acting
- ▶ Inhaled steroid
- ▶ Systemic steroid
- ▶ Combination therapy
  - SABA + anticholinergic
  - LABA + corticosteroids
- ▶ Oral
  - Bronchodilators
  - Glucocorticosteroids
- ▶ Phosphodiesterase-4 Inhibitor
- ▶ Methylxanthines

# BETA<sub>2</sub> AGONIST

## ▶ Short Acting

### ○ Albuterol

- Pro-Air<sup>®</sup> HFA – 90 mcg
- Ventolin<sup>®</sup> HFA – 90mcg
- Proventil<sup>®</sup> HFA – 90mcg
- AccuNeb<sup>®</sup> 1.25–5mg
- Alupent<sup>®</sup> MDI .65mg or  
4% and 6% neb

### ○ Levalbuterol

- Xopenex<sup>®</sup> HFA – 90mcg
- Xopenex<sup>®</sup> neb –  
.63mg –1.25mg

### ○ Pirbuterol

- Maxair<sup>®</sup> – 200mcg

# SHORT ACTING BETA<sub>2</sub>-AGONIST

## ▶ Dosing

- Inhaler 90mcg / metered inhalation dose
  - 2-4 puffs every 4 - 6 hours as needed
  - 2-3 puffs 3 to 4 times a day routinely
  - Alupent Inhaler .65mg 2-3 puffs 3-4 times per day routinely
- Nebulizer
  - Albuterol 2.5-5mg every 4 -8 hours as needed
  - Xopenex<sup>®</sup> 0.63-1.25mg three times daily (every 6-8 hours)
  - Alupent<sup>®</sup> 0.4%, 0.6% 3-4 times per day up to every 4 hours
- Oral
  - Albuterol 2-4 mg three to four times daily
  - Max 8mg four times per day

# SHORT ACTING BETA<sub>2</sub>-AGONIST

## ▶ Risks

- Overuse
- Tremor
- Reflex tachycardia
- Peripheral artery dilation
- Hypokalemia

## ▶ Benefits

- Improves lung function
- Short Acting
- Increased exercise capacity
- Decreases dyspnea
- Decreases cough

# SHORT ACTING ANTICHOLINERGIC

## ▶ Dosing

- HFA Inhaler 17mcg / metered inhalation dose
  - Ipratropium HFA 2 inhalations 4 times per day
  - Up to 8 puffs four times per day
- Nebulizer
  - Ipratropium Bromide Solution 500mcg/2.5ml three to four times daily

# ANTICHOLINERGIC

## ▶ Risks

- Anticholinergic effect
- Tachycardia

## ▶ Benefits

- Improves lung function
- Short Acting
- Increased exercise capacity
- Decreases dyspnea
- Decreases cough

# COMBINATION THERAPY

## ▶ Short Acting

- Short acting beta agonist and Anticholinergic
  - Combivent Respimat 20mcg/100mcg
    - One inhalation four times a day
  - Duonebs 0.5mg/2.5mg / 3ml
    - One vial 4–6 times per day

# SHORT ACTING COMBINATION THERAPY

## ▶ Risks

- Tremor
- Tachycardia
- Anxiety
- Headache
- Insomnia
- Anticholinergic effect

## ▶ Benefits

- Immediate relief

# LONG ACTING BETA<sub>2</sub>-AGONIST

## ▶ Dosing

- Salmeterol (Serevent Diskus<sup>®</sup>)
  - 50mcg – one inhalation twice daily
- Formoterol (Foradil<sup>®</sup> Aerolizer<sup>®</sup>, Perforomist<sup>™</sup>)
  - 12 mcg capsule inhaled every 12 hours via Aerolizer<sup>™</sup> device
- Arformoterol (Brovana<sup>®</sup>)
  - Nebulization – 15 mcg twice daily / maximum: 30 mcg/day
- Indacaterol<sup>®</sup> 75mcg one inhalation daily with neoinhaler

# LONG ACTING BETA<sub>2</sub>-AGONIST

## ▶ Risks

- Anxiety
- Tachycardia
- Increased risk of hospitalizations

## ▶ Benefits

- Decrease exacerbations
- Improves lung function
- Improves health-related quality of life
- Possibly decrease in mortality

# LONG ACTING ANTICHOLINERGIC

## ▶ Dosing

### ◦ Tiotropium

- Spiriva Handihaler<sup>®</sup> Dosing–1 capsule (18 mcg)
  - 2 inhalations of one capsule once daily using HandiHaler

### ◦ Aclidinium Bromide

- Turdoza Pressair<sup>®</sup> 400mcg one inhalation twice a day.

# LONG ACTING ANTICHOLINERGIC THERAPY

## ▶ Risks

- Anticholinergic effect
- DO NOT use if patient has narrow angle glaucoma
- Bronchospasms

## ▶ Benefits

- Improves lung function
- Decreases hyperinflation
- Decreases dyspnea
- Decreases exacerbations
- Slows decline in FEV1

# METHLYXANTHINE

## ▶ Theophylline

- Main purpose is in refractory COPD
- Least preferred
  - Toxicity
  - Not much benefit
  - Add on therapy

## ▶ Dosage

- 10 mg/kg per day
- Up to 300mg daily for initial dose
- Twice a day dosing

## ▶ Monitoring

- Peak serum levels
- 3–7 hours after morning dose
- Normal serum levels 8–12mcg / ml
- Once patient is within normal limits check every 6 months

# Inhaled Glucocorticoid

## SINGLE THERAPY

### ▶ Dosing

#### ▶ Fluticasone (Flovent<sup>®</sup> Diskus<sup>®</sup>; Flovent<sup>®</sup> HFA)

- Flovent HFA 44mcg 110mcg 220mcg
- Flovent Diskus 50mcg 100mcg 250mcg
  - one inhalation twice daily

#### ▶ Budesonide

- Pulmicort Flexihaler<sup>®</sup>
  - 90mcg or 180mcg two inhalations twice a day
- Pulmicort respules<sup>®</sup>
  - .25mg or .5mg or 1mg per nebulizer 1 vial once daily

# Inhaled Glucocorticoid COMBINATION THERAPY

- ▶ Dosing
- ▶ Mometasone / Formoterol HFA
  - Dulera 100/5mcg or 200/5mcg
    - Two inhalations twice a day
- ▶ Budesonide / Formoterol HFA
  - Symbicort 80/4.5mcg or 160/4.5 mcg
    - Two inhalation twice a day
- ▶ Fluticasone with Salmeterol HFA Discus
  - Advair Discus 100/50mcg, 250/50mcg,,500/50mcg one inhalation bid
  - Advair HFA 45/21mcg, 115/21mcg, 230/21mcg two inhalations bid
- ▶ Fluticasone with Vilanterol
  - Breo Ellipta 100/25mcg DPI
  - One inhalation once daily



# INHALED STEROIDS

## ▶ Risks

- Increase pneumonia
- Dysphonia
- Thrush
- Cough
- Throat irritation
- Reflex bronchoconstriction
- Systemic effects

## ▶ Benefits

- Reduce inflammation
- Decrease exacerbations
- Slows the progression of symptoms
- Minimal impact on lung function
- Minimal impact on mortality
- Never use as SOLE therapy

# SYSTEMIC STEROIDS

- ▶ Acute Use
  - Exacerbations
  -
- ▶ Chronic Use
  - Avoid
  - If used – start out at minimal amount 1 mg
  - Need objective measurement of improvement

Generic name	Brand name	How it is given	Dosage
<i>Methylprednisolone</i>	Medrol	Tablet	4–48 mg
<i>Prednisolone/prednisolon</i>	Prelone	Tablet	2.5–60 mg
<i>Prednisone</i>	Deltasone	Tablet	5–60 mg

# SYSTEMIC STEROIDS

## ▶ Risks

- Systemic effects
- Edema
- Weight gain
- Increased morbidity and mortality
- Quick withdrawal

## ▶ Benefits

- Reduce inflammation
- Less dyspnea
- Increases exercise capacity
- Quality vs quantity of life
- Improves lung function – short term use

# PHOSPHODIESTERASE-4 INHIBITORS

- ▶ Romflilast
  - Daliresp 500mcg one tablet daily

# PHOSPHODIESTERASE-4 INHIBITORS

## ▶ Risks

- No change in symptoms

## ▶ Benefits

- Reduces exacerbation risk
- Increased FEV1
- Improved quality of life

# TRIPLE INHALER THERAPY

- ▶ Long Acting Beta Agonist plus
  - ▶ Inhaled Glucocorticoid plus
  - ▶ Long Acting Anticholinergic
- 
- ▶ Improves lung function
  - ▶ Improves quality of life
  - ▶ Reduces hospitalizations

# MUCOACTIVE Agents

- ▶ Helps symptoms
  - Thick tenacious mucus
- ▶ Does Not help lung function
- ▶ Agents
  - Guaifenesin – expectorant
  - Acetylcysteine – mucolytic
  - Fluid intake – helpful or hindrance?

# Chronic ANTIBIOTIC therapy

- ▶ Azithromycin 250mg once daily
- ▶ Erythromycin 500mg bid
- ▶ Moxafloxacin 400mg daily
- ▶ If using antibiotic more than twice in 2 months if chest x-ray was done, get a CT

# OXYGEN

- ▶ Exercise oximetry
  - Six minute walk test
  - Qualifications
    - SpO<sub>2</sub> <88%
    - SpO<sub>2</sub> <90% with secondary condition i.e. Heart failure
- ▶ Start at liter flow that increases SpO<sub>2</sub> >90%
- ▶ Order portable tank
  - Take into consideration activity level, mobility

# SMOKING CESSATION

## MOST IMPORTANT

- ▶ Counseling
- ▶ Oral Agents
  - Bupropion
  - Chantix
- ▶ Patches
  - Nicotine tapering system
- ▶ Gum
- ▶ Visualization
- ▶ Meditation



# VACCINATIONS

- ▶ Influenza
  - H1N1
  
- ▶ Pneumonia

# REHABILITATION

- ▶ Physician ordered
- ▶ Benefits
  - Improves exercise capacity
  - Improves quality of life
  - Decreases dyspnea
  - Decreases health care utilization
  - May reduce mortality

# NUTRITION

- ▶ Protein calorie malnutrition
  - Increases mortality
  - Impairs respiratory function
  - Diminishes immune competence
  
- ▶ Replacement
  - High calorie dietary supplements
  - Megace Acetate

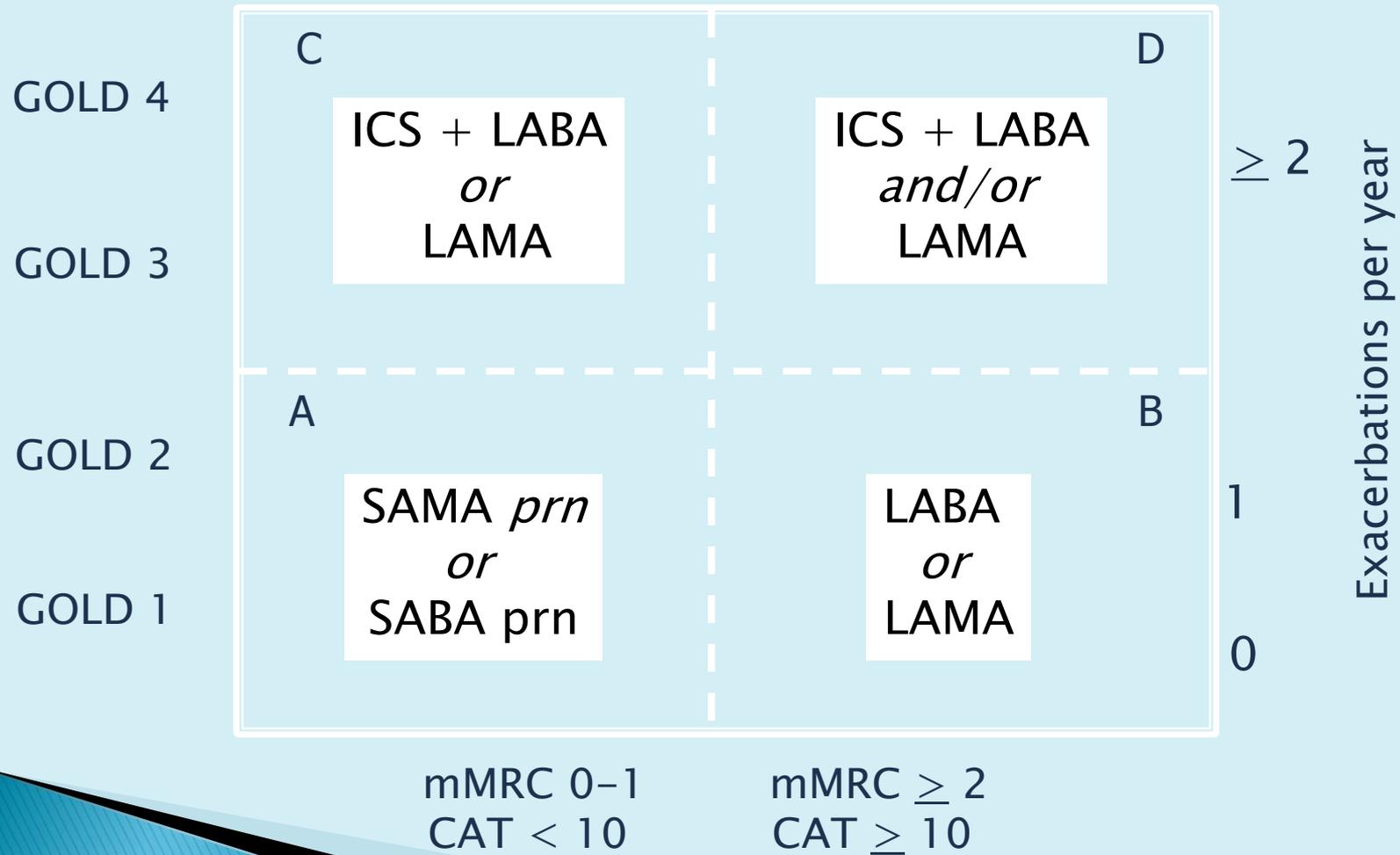
# OTHER TREATMENT

- ▶ Opiates
  - Severe dyspnea
- ▶ Anti-anxiety
  - Anxiety related to dyspnea in late stages of disease
- ▶ Psychoactive
  - Depression and anxiety related to disease process
- ▶ Surgery
  - Lung reduction
  - Transplant
- ▶ Alpha1 Antitrypsin treatment

# OTHER TREATMENT

- ▶ Palliative care
- ▶ End of Life
- ▶ Hospice care
  - *Communication* with advanced COPD patients about end-of-life care and advance care planning gives patients and their families the opportunity to make informed decisions.

# Manage Stable COPD: Pharmacologic Therapy RECOMMENDED FIRST CHOICE



# Manage Stable COPD: Pharmacologic Therapy

## ALTERNATIVE CHOICE

	C	D	
GOLD 4	LAMA and PDE4-inh <i>or</i> LABA and PDE4-inh	ICS + LABA and LAMA <i>or</i> ICS + LABA and PDE4-inh <i>or</i> LAMA and LABA <i>or</i> LAMA and PDE4-inh	$\geq 2$
GOLD 3			
GOLD 2	A	B	1
GOLD 1	LAMA <i>or</i> LABA <i>or</i> SABA and SAMA	LAMA <i>and</i> LABA	0
	mMRC 0-1 CAT < 10	mMRC $\geq 2$ CAT $\geq 10$	Exacerbations per year

# Manage Stable COPD: Pharmacologic Therapy

## OTHER CHOICES

	C	D	
GOLD 4	<i>SABA and/or SAMA</i>  <i>Theophylline</i>	<i>Carbocysteine</i>  <i>SABA and/or SAMA</i>  <i>Theophylline</i>	$\geq 2$
GOLD 3			
GOLD 2	A	B	1
GOLD 1	<i>Theophylline</i>	<i>SABA and/or SAMA</i>  <i>Theophylline</i>	0
	mMRC 0-1 CAT < 10	mMRC $\geq 2$ CAT $\geq 10$	Exacerbations per year

# COPD EXACERBATIONS

- Diagnosis and Overview
- Therapeutic Options
- Manage Stable COPD
- **Manage Exacerbations**
-

# ACUTE EXACERBATIONS

- ▶ Defined as an acute event characterized by worsening of symptoms beyond normal day-to-day variations.
  - Dyspnea
  - Cough
  - Sputum
  - Fever
  - Wheeze
- ▶ Assessment is key
- ▶ Most exacerbations from bacterial or viral infection. (50–60%)
- ▶ Some are related to serious medical conditions. (30%)
  - Congestive Heart Failure
  - Aspiration
  - Pulmonary Embolus (20%)
- ▶ Environmental Conditions (10%)

# ER TREATMENT 346\*

- ▶ Assess severity of symptoms blood gases, chest X-ray
- ▶ Administer controlled oxygen therapy and repeat arterial blood gas measurement after 30–60 minutes
- ▶ Bronchodilators:
  - Increase doses and/or frequency
  - Combine 2-agonists and anticholinergics
- ▶ Consider adding intravenous methylxanthines
- ▶ Add glucocorticosteroids
- ▶ Consider antibiotics when signs of bacterial infection
- ▶ Consider noninvasive mechanical ventilation

# PHARMACOLOGICAL THERAPY

## Treatment Goals

- Determine / eliminate cause
- Optimize lung function
- Improve oxygenation
- Secretion clearance
- Prevent complications

# Inhaled Bronchodilators

## BETA AGONIST

- ▶ Mainstay therapy is short-acting beta agonists
- ▶ Albuterol
  - Rapid onset
  - Bronchodilation
- ▶ Nebulizer
  - 1.25–5mg (diluted to 3ml with normal saline)
  - Use every 1–4 hours as needed
- ▶ Metered Dose Inhaler
  - 4–8 puffs (90mcg / puff) every 1–4 hours as needed

# Inhaled Bronchodilators

## ANTICHOLINERGIC

- ▶ Short-Acting anticholinergics used with Short-acting beta agonists
- ▶ Albuterol/Ipratropium
  - Increased bronchodilation when used together
- ▶ Nebulizer
  - 500 mcg every 4 hours as needed
- ▶ Metered Dose Inhaler
  - 2 puffs (18mcg / puff) every 4 hours as needed

# GLUCOCORTICOIDS

- ▶ Improves lung function
- ▶ Reduces hospital stay
- ▶ Treat for 7–10 days
- ▶ IV
  - Severe exacerbations
- ▶ ORAL
  - Rapid absorption
- ▶ INHALED
  - When IV steroid stopped transition to inhaled

# GLUCOCORTICOIDS

## ▶ IV

- Methylprednisolone 60mg -125mg two to four times per day
- Dexamethasone .75-9 mg per day in divided doses every 6-12 hours

## ▶ ORAL

- Prednisone 30mg-40mg daily tapering dose over 10-14 days

## ▶ INHALED

- One inhalation twice daily

# ANTIBIOTICS

- ▶ Three cardinal symptoms
  - Increased dyspnea
  - Increased sputum volume
  - Increased sputum purulence
  
- ▶ Mechanically ventilated patients.

# ANTIBIOTICS

- ▶ Use for 5–14 days
- ▶ Uncomplicated
  - Advanced Macrolide
    - Azithromycin, Clarithromycin
  - Cephalosporin
    - Cefuroxime, Cefpodoxime, Cefdinir
  - Doxycycline
  - Trimethoprim / Sulfamethoxazole
- ▶ Complicated
  - Fluoroquinolone
    - Moxifloxacin, Gemifloxacin, Levofloxacin
    - Amoxicillin / Clavulanate

If no better in 48 hours re-evaluate

# POTENTIAL MICROORGANISMS

Group	Definition	Microorganisms
Group A	Mild exacerbation: No risk factors for poor outcome	<i>H. Influenzae</i> <i>S. pneumoniae</i> <i>M. Catarrhalis</i> <i>Chlamydia Pneumoniae</i> Viruses
Group B	Moderate exacerbation with risk factor(s) for poor outcome	Group A plus, presence of resistant organisms (B-lactamase producing, penicillin-resistant <i>S. pneumoniae</i> ), Enterobacteriaceae ( <i>K.pneumoniae</i> , <i>E. coli</i> , <i>Proteus</i> , <i>Enterobacter</i> )
Group C	Severe exacerbation with risk factors for <i>P. aeruginosa</i> infection	Group B plus: <i>P. aeruginosa</i>

# ANTIBIOTIC TREATMENT

	Oral Treatment	Alternative Oral Treatment	Parenteral Treatment
<p>Group A</p> <p><i>Patients with only one cardinal symptom should not receive antibiotics</i></p>	<p>If indication then:</p> <p>B -lactam (Penicillin, Ampicillin/ Amoxicillind)</p> <p>Tetracycline</p> <p>Trimethoprim/ Sulfamethoxazole</p>	<p>B-lactam/ B- lactamase inhibitor (Co-amoxiclav)</p> <p>Macrolides (Azithromycin, Clarithromycin, Roxithromycine)</p> <p>Cephalosporins - 2nd or 3rd Generation</p> <p>Ketolides (Telithromycin)</p>	

# ANTIBIOTIC TREATMENT

	Oral Treatment	Alternative Oral Treatment	Parenteral Treatment
Group B	B-lactam/ B-lactamase inhibitor (Co-amoxiclav)	Fluoroquinolone (Gemifloxacin, Levofloxacin, Moxifloxacin)	B-lactam/ B-lactamase inhibitor (Co-amoxiclav, ampicillin/ sulbactam)  Cephalosporins – 2nd or 3rd generation  Fluoroquinolone (Levofloxacin, Moxifloxacin)

# ANTIBIOTIC TREATMENT

	Oral Treatment	Alternative Oral Treatment	Parenteral Treatment
Group C	<p>In patients at risk for <i>pseudomonas</i> infections:</p> <p>Fluoroquinolone (Ciprofloxacin, Levofloxacin – high dosef)</p>		<p>Fluoroquinolone (Ciprofloxacin, Levofloxacin – high dosef) or B-lactam with <i>P.aeruginosa</i> activity</p>

# FOLLOW UP OFFICE VISIT

- ▶ Assess at Follow-Up Visit 4–6 Weeks After Discharge from Hospital
  - ▶ Ability to cope in usual environment
  - ▶ Measurement of FEV1
  - ▶ Reassessment of inhaler technique
  - ▶ Understanding of recommended treatment regimen
  - ▶ Need for long-term oxygen therapy and/or home nebulizer

# PROGNOSIS

- ▶ Estimated 14% of patients admitted with an exacerbation will die within 3 months.
- ▶ Baseline changes

# QUESTIONS

- ▶ References available upon request
- ▶ E-Mail [juliarogersnp@gmail.com](mailto:juliarogersnp@gmail.com)