COPD - 2018

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Duke University Medical Center
Durham NC

COPD - 2018
- Definitions and pathophysiology
- Clinical picture, prevalence, impact
- Diagnosis and staging
- Evidence based management guidelines
- Barriers to implementation

Human Airways: Health and Disease
- Normal:
  - 23 branched tube structure
  - Proximal generations have cartilage, smooth muscle, mucus glands; Distal generations are membranous and held open by tethering forces
- Airway inflammatory diseases:
  - Inflammation narrows airways (asthma, bronchitis), reducing airflow
  - More distal involvement can also create alveolar destruction (emphysema)

Tracheobronchial Tree
Consequences of airway inflammation

- Patho-physiology:
  - Airway obstruction – increased work to breathe, mucus
  - Hyperinflation – collapsing narrowed airways trap gas
  - Alveolar destruction (emphysema) – direct alveolar damage
  - Abnormal gas exchange –
    - Hypercapnia – muscle overload, dead space
    - Hypoxemia – hypoventilation, V/Q mismatch

COPD is a systemic disease

- Chronic airway inflammation “spills” inflammatory cytokines into the circulation
  - ASCVD
  - Renal insufficiency
  - Neuro-myopathy
  - Osteoporosis
  - Cachexia, debility may be product of this

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COPD spectrum

- Proximal predominant (large airways)
  - mucus gland hypertrophy (cough/sputum)
  - reduced respiratory drive
  - airway hyper-reactivity
- Distal predominant (small airways/alveoli)
  - dyspnea - active respiratory drive
  - reduced DLCO

COPD: the clinical spectrum

Emphysema  Bronchitis
Clinical COPD Is Just The Tip Of The Iceberg

- 2 Million "severe"
- 10 Million Dx
- ? Millions at risk


COPD Projected to Be the Third-Leading Cause of Death by 2020

- Proportion of 1965-1998 Rate, Percentage Change in Age-Adjusted Death (US)

COPD: Direct Cost

Morbidity and Mortality: 2002 Chart Book on Cardiovascular, Lung, and Blood Diseases. NIH/NHLBI. May 2002

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Diagnosis of COPD

EXPOSURE TO RISK FACTORS

AND/OR

SYMPTOMS

sputum

cough

dyspnea

wheezing

SPIROMETRY

Adapted with permission from the GOLD web site. Available at www.goldcopd.com.

Spirometry

Spirometry

COPD: the spirogram

Normal

Obstructed

Restricted

Global Obstructive Lung Disease (GOLD) Consortium Staging

I: Mild
- FEV₁/FVC < 70%
- FEV₁ ≥ 80%
- With or without symptoms

II: Moderate
- FEV₁/FVC < 70%
- 50% ≤ FEV₁ < 80%
- With or without symptoms

III: Severe
- FEV₁/FVC < 70%
- 30% ≤ FEV₁ < 50%
- With or without symptoms

IV: Very Severe
- FEV₁ < 30%
- FEV₁ < 70%
- With or without symptoms
- Presence of chronic respiratory failure or right heart failure

www.goldcopd.com
More to COPD than just airway obstruction

- Anatomic
  - Spirometry insensitive to:
    - Alveolar destruction/emphysema
    - Trapped gas
    - Chest CT scanning
- Functional
  - Exercise intolerance:
    - Dyspnea vs cough vs hypoxemia
  - Risk of exacerbations

Spirometry can miss emphysema

In COPDgene, 357 of 858 smokers with normal spirometry had emphysema on CT

Symptoms/function as important as FEV1 on survival

BODE: Dyspnea, 6MWT, BMI, FEV1

Frequency of severe acute exacerbations predicts mortality

*Acute exacerbations of COPD prior to entry to study requiring hospital management*
GOLD 2017: Combined Assessment of COPD

- Diagnose COPD
  - Spirometry not enough
  - Radiology (hyperinflation, emphysema) and DLCO alternate diagnostic tools

- Two components determine severity of disease
  - Symptom assessment
  - Risk of exacerbations

CAT = COPD assessment test; mMRC = modified Medical Research Council.

GOLD 2017

1) Diagnose
2) Obstruction Severity
3) Impact

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Global Strategy for Diagnosis, Management and Prevention of COPD
Manage Stable COPD: Non-pharmacologic

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<tr>
<th>Patient Group</th>
<th>Essential</th>
<th>Recommended</th>
<th>Depending on local guidelines</th>
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<tr>
<td>A</td>
<td>Smoking cessation (can include pharmacologic treatment)</td>
<td>Physical activity</td>
<td>Flu vaccination, Pneumococcal vaccination</td>
</tr>
<tr>
<td>B, C, D</td>
<td>Smoking cessation (can include pharmacologic treatment) Pulmonary rehabilitation</td>
<td>Physical activity</td>
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Smoking Cessation

- “First thing you have to do to get out of hole is stop digging”
- Nicotine is incredibly addictive – spontaneous quit rates <5%/year
- What can help?
  - Nicotine replacement
  - Welbutrin
  - Varenicline
  - Formal programs (ALA, ACS)

Pulmonary rehabilitation

- Education
  - chronic management
  - acute management
- Exercise
  - deconditioning common
  - may need bronchodilators/O2
- Psycho-social support
**Global Strategy for Diagnosis, Management and Prevention of COPD**

**Manage Stable COPD: Non-pharmacologic**

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**Current Inhaled Medications for COPD**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand</th>
<th>Usual Starting Dose</th>
<th>Duration</th>
</tr>
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<tbody>
<tr>
<td>β₂-Agonists</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol</td>
<td>ProAir, Proventil, Ventolin</td>
<td>2 puffs q 4-6 hrs PRN</td>
<td>4-6 h</td>
</tr>
<tr>
<td>Levalbuterol</td>
<td>Xopenex HFA</td>
<td>2 puffs q 4-6 hrs PRN</td>
<td>4-6 h</td>
</tr>
<tr>
<td>Pulmicort</td>
<td>Maxair/Autohaler</td>
<td>2 puffs q 4-6 hrs PRN</td>
<td>5 h</td>
</tr>
<tr>
<td>Long-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formoterol</td>
<td>Foradil, Albuterol, Perforomist, Brovana</td>
<td>1 inhaled capsule bid</td>
<td>12+ h</td>
</tr>
<tr>
<td>Indacaterol</td>
<td>Astra NeoBaler</td>
<td>1 inhaled capsule daily</td>
<td>24+ h</td>
</tr>
<tr>
<td>Salmeterol</td>
<td>Serevent Diskus</td>
<td>1 puff bid</td>
<td>12+ h</td>
</tr>
</tbody>
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HFA = hydrofluoroalkane.
### Current Inhaled Medications for COPD Cont’d

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<thead>
<tr>
<th>Medication</th>
<th>Brand</th>
<th>Usual Starting Dose</th>
<th>Duration</th>
</tr>
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<tbody>
<tr>
<td><strong>Anticholinergics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipratropium bromide</td>
<td>Atrovent</td>
<td>2 puffs qid</td>
<td>6-8 h</td>
</tr>
<tr>
<td>Long-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aclidinium</td>
<td>Tudorza Pressair</td>
<td>1 puff bid</td>
<td>24+ h</td>
</tr>
<tr>
<td>Tiotropium bromide</td>
<td>Spiriva Handihaler</td>
<td>1 inhaled capsule daily</td>
<td>24+ h</td>
</tr>
<tr>
<td><strong>Combination Bronchodilators</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol/ipratropium</td>
<td>Combivent</td>
<td>2 puffs q 4-6 hrs PRN</td>
<td>4-6 h</td>
</tr>
<tr>
<td>Umeclidinum/Vilanterol</td>
<td>Amoro Ellipta</td>
<td>1 puff daily</td>
<td>24 h</td>
</tr>
</tbody>
</table>

* NEW: Tiotropium/olodaterol (Stiolto)

* HFA = hydrofluoroalkane; PDE4 = phosphodiesterase 4.

**The latest compounds and formulations - 2018**

- **LABAs**
  - Oladaterol SMI (Stiverdi)

- **LAMAs**
  - Glycopyronium DPI (Seebri)
  - Umeclidium DPI (Incruse)

- **LABA/ICS**
  - Formoterol/beclamethasone MDI and DPI (Fostair)
  - Formoterol/mometasone MDI (Dulera)

**The latest compounds and formulations - 2018**

- **LAMA/LABA**
  - Formoterol/acidinium DPI (Genuair)
  - Formoterol/glycopyronium MDI* (Bevespi)
  - Indacaterol/glycopyronium DPI (Ultibro)
  - Oladaterol/tiotropium SMI (Stiolto)

- **LAMA/LABA/ICS**
  - Trelegy Ellipta

* co-suspension technology

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### Current Oral Medications for COPD

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<tr>
<th>Medication</th>
<th>Brand</th>
<th>Usual Starting Dose</th>
<th>Duration</th>
</tr>
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<tbody>
<tr>
<td>Corticosteroids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td></td>
<td>4-48mg/day depending on disease and response</td>
<td>12-24 h</td>
</tr>
<tr>
<td>Prednisolone</td>
<td></td>
<td>5-60mg/day depending on disease and response</td>
<td>12-24 h</td>
</tr>
<tr>
<td>Prednisone</td>
<td></td>
<td>5-60mg/day depending on disease and response</td>
<td>12-24 h</td>
</tr>
<tr>
<td>PDE4 Inhibitor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roflumilast</td>
<td>Daliresp</td>
<td>One 500 mcg tablet daily</td>
<td>17+ h</td>
</tr>
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HFA = hydrofluoroalkane; PDE4 = phosphodiesterase 4.


### Global Strategy for Diagnosis, Management and Prevention of COPD

#### Manage Stable COPD: Pharmacologic Therapy
(Medications in each box are mentioned in alphabetical order, and therefore not necessarily in order of preference.)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Recommended First choice</th>
<th>Alternative choice</th>
<th>Other Possible Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>SAMA pm or SABA pm</td>
<td>LAMA or LABA or SABA and SAMA</td>
<td>Thalidomide</td>
</tr>
<tr>
<td>B</td>
<td>LAMA or LABA</td>
<td>LAMA and LABA</td>
<td>SABA or/ SAMA Thalidomide</td>
</tr>
<tr>
<td>C</td>
<td>ICS + LABA or LAMA</td>
<td>LAMA and LABA or LAMA and PDE4-inh, or LABA and PDE4-inh.</td>
<td>SABA or/ SAMA Thalidomide</td>
</tr>
<tr>
<td>D</td>
<td>ICS + LABA and/or LAMA</td>
<td>ICS + LABA and LAMA or ICS+LABA and PDE4-inh, or LAMA and LABA or LAMA and PDE4-inh.</td>
<td>Carbamazepine or/ SAMA Thalidomide</td>
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### Other Management Issues

- Oxygen
- Nocturnal NIV for hypercapnia
- Lung volume reduction procedures
- Action plan for AECOPD
Other Management Issues

- Oxygen
  - Survival benefit in patients with resting hypoxemia
  - Improves exercise function in patients with exercise hypoxemia. Effect does NOT “carry over” to improve long term outcomes (NIH LOTT study)
  - Target should be SpO2 89.93, NOT > 95
- Nocturnal NIV for hypercapnia (high pressure)
- Lung volume reduction procedures
- Action plan for AECOPD

Other Management Issues

- Oxygen
- Nocturnal NIV for hypercapnia may improve long term outcomes
  - Resting muscles at night vs normalizing PCO2?
    - Lancet Resp Med 2014; Sept 2: 298
    - JAMA 2017;317:2177
- Lung volume reduction procedures
- Action plan for AECOPD

Other Management Issues

- Oxygen
- Nocturnal NIV for hypercapnia
- Lung volume reduction procedures
- Action plan for AECOPD

- Bronchodilators/antibiotics/steroids/hot line
Addressing the “end of the road”

- Options for disease “modification” are limited
  - Most medications and management strategies alleviate symptoms, improve function
  - True disease modification today involve reducing pro-inflammatory agents (cigarettes) and reducing exacerbations
- COPD is a progressive disease and we need to be realistic when end stage is present
  - Advanced directives addressing futility of aggressive support when underlying disease irreversible

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Barriers to Implementing Effective Management Strategies

- Clinician barriers
  - Proper diagnosis/staging/prescribing per guidelines
- Patient barriers
  - Understanding complex medication regimens
  - Adherence to treatment plans (both pharmaceutical and non-pharmaceutical)
- System barriers
  - Costs of medications
  - Clinical support structures

SPR Performance 2006-2012

- Spirometry: HMO

HMO = health maintenance organization.
COPD Often Unrecognized During Hospitalization.

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PCE Performance 2008–2012

Pharmacotherapy: Corticosteroids (HMO)

Pharmacotherapy: Bronchodilators (HMO)
LABA Adherence

- N = 1014 COPD in health plan given new LABA
- Prescription filling over 1 year:
  - >80%: 26%
  - 60-70%: 14%
  - 40-50%: 20%
  - 20-30%: 21%
  - <20%: 19%

Cost Differences Between Baseline and Follow-up

- LAMA/LABA
- LABA/ICS
- LAMA/LABA/ICS

Why aren’t patients adherent?

- Lack of understanding of importance
- Maintenance vs rescue
- Ineffective use of devices
  - Breathing maneuvers, device operation
- Costs
  - The “donut hole” and drugs running several hundred $/month

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- Patient barriers
  - Understanding complex medication regimens
  - Adherence to treatment plans (both pharmaceutical and non-pharmaceutical)
- System barriers
  - Costs of medications
  - Clinical support structures
System Barriers – Clinical Support Structures

- Access to clinicians
  - Priority scheduling
  - Hot lines
  - Home visits
  - Education
- Discharge planning
  - Medications
  - Follow-up plans
- Pulmonary rehabilitation centers

Barriers to pulm rehab

- Less than 2% of COPD patients use PR (COPD 2014; July 1)
- Why not more?
  - Limited number of programs
  - Cost/reimbursement issues (now CMS reimbursed)
  - Logistics (transport, timing)
  - Motivation
- Future – home-based programs with telemedicine technology

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