Asthma

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Objectives

1. Understand the approach to asthma
2. Defining asthma goals, severity and control
3. Basic pharmacological management of asthma
4. Non pharmacological management of asthma
5. Advanced therapies including monoclonal antibody therapy
Definition of asthma

Asthma is characterized by chronic airway inflammation.

It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.
Asthma

• Asthma manifests with episodic cough, chest tightness, shortness of breath, and wheezing.

• Patients with asthma have increased nonspecific airway responsiveness that results in increased sensitivity to inhaled bronchoconstrictive agents and airway obstruction that is typically reversible.

• An underlying problem in asthma is airway inflammation, which is often related to allergies.

• Uncontrolled inflammation or repeat exacerbations can potentially be associated with development of structural airway changes known as remodeling.
Asthma triad

Airway (chronic) inflammation

Bronchial hyper responsiveness
= Broncho constriction

Intermittent reversible airflow obstruction
Pathologic Changes in Asthma

- Airway inflammation
  - Eosinophils
  - Mast cells
  - Lymphocytes
  - Neutrophils
- Smooth muscle hypertrophy / hyperplasia
- Bronchoconstriction
- Airway hyperreactivity

- Mucous hypersecretion
  - Goblet cell metaplasia
  - Submucosal gland hypertrophy
- Impaired mucous clearance
- Edema
- Subepithelial matrix protein deposition
- Collagen deposition
Acute Allergen Induced airways Inflammation

Before

10 Minutes After
In 2010, one in 12 people (about 26 million, or 8% of the U.S. population) had compared in 2001 with 1 in 14 (about 20 million, or 7%).
Implications of Uncontrolled Asthma (U.S- 2009/2010)

13.9 million
People experience asthma attacks

10.6 million
Asthma physician office visits

2.1 million
Emergency department visits

479,300
Hospitalizations

3,388
Asthma-related deaths

More fun facts

- 1 in 11 children & 1 in 12 adults have asthma
- 52% of asthmatics have an attack each year
- Asthma mortality is 44% higher in females and three times higher in African Americans
- 9 people die from asthma every day
- The 3 main classes of drugs used were discovered in the 1960s
Higher Cost of Severe Asthma (U.S.)

Higher healthcare costs with asthma severity

Severe asthma (persistent state) versus controlled asthma

1. Higher annual mean number of **work days lost** (7.1 Vs 0.4)
2. Higher annual mean number of **school days lost** (9.1 Vs 0.1)
3. Higher annual mean number of **physician visits** (5.6 Vs 2.4)
4. Higher **limitation for outdoor activities** (OR 2.58)
5. Increased **daily activity limitation** (66% more)
6. Increased risk of progression to **fixed airflow obstruction** (sputum eosinophilia)
7. Increased risk for **asthma exacerbations** (6 fold increased risk)

High Risk (of Death !!!) Patients

- ≥ 1 hospitalization or ED visit for asthma in the past month
- ≥ 2 hospitalizations for asthma in the past year
- ≥ 3 ED visits for asthma in the past year
- ≥ 1 previous severe exacerbation (intubation or ICU admission)
- ≥ 2 MDI short acting beta\(_2\) agonist canister use per month
- Current or recent withdrawal from systemic steroids
- Patients with symptom perception issues
Approach to asthma

2 Goals
1. Reduce impairment
2. Reduce risk

Initial assessment
A. Clinical probability
B. Rule out Co-morbidities / mimickers
C. Adjunctive testing: PFT, MCT, Allergy testing
D. Trial of therapy

Initial profiling
A. Severity classification
B. Phenotyping

Initial therapy
A. Non pharmacological
B. Control co-morbid conditions
C. Pharmacological
   I. Exacerbation
   II. Prior asthma therapy
   III. New to therapy

High probability
I. Asthma in childhood
II. Episodic symptoms
III. Triggers
IV. Personal or family history of atopy

Low probability
I. Failure of asthma therapy
II. Age >50 years
III. Cardiac history
IV. Cigarette smoking
Diagnosis of asthma – symptoms

• *Increased* probability that symptoms are due to asthma if:
  • More than one type of symptom (wheeze, shortness of breath, cough, chest tightness)
  • Symptoms often worse at night or in the early morning
  • Symptoms vary over time and in intensity
  • Symptoms are triggered by viral infections, exercise, allergen exposure, changes in weather, laughter, irritants such as car exhaust fumes, smoke, or strong smells

• *Decreased* probability that symptoms are due to asthma if:
  • Isolated cough with no other respiratory symptoms
  • Chronic production of sputum
  • Shortness of breath associated with dizziness, light-headedness or peripheral tingling
  • Chest pain
  • Exercise-induced dyspnea with noisy inspiration (stridor)
Diagnosis of asthma – physical examination

- Physical examination in people with asthma
  - Often normal
  - The most frequent finding is wheezing on auscultation, especially on forced expiration

- Wheezing is also found in other conditions, for example:
  - Respiratory infections
  - COPD
  - Upper airway dysfunction
  - Endobronchial obstruction
  - Inhaled foreign body

- Wheezing may be absent during severe asthma exacerbations (‘silent chest’)

GINA 2014
Typical spirometric tracings

Note: Each FEV$_1$ represents the highest of three reproducible measurements
<table>
<thead>
<tr>
<th>Condition</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD</td>
<td>Airway obstruction is less reversible; typically seen in older patients with smoking history</td>
</tr>
<tr>
<td>Vocal cord dysfunction</td>
<td>Abrupt onset and end of symptoms; monophonic wheeze; more common in younger patients; confirm with laryngoscopy or flow-volume loop</td>
</tr>
<tr>
<td>Heart failure</td>
<td>Dyspnea and often wheezing; crackles on auscultation; limited response to asthma therapy; cardiomegaly; edema; elevated BNP; other features of heart failure</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>Cough productive of large amount of purulent sputum; rhonchi and crackles are common; may have wheezing and clubbing; confirmed by CT imaging</td>
</tr>
<tr>
<td>Allergic bronchopulmonary aspergillosis</td>
<td>Recurrent infiltrates on chest radiograph; eosinophilia; high IgE levels; frequent need for corticosteroid treatment</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>Cough productive of large amount of purulent sputum; rhonchi and crackles are common; prominent clubbing; may have wheezing</td>
</tr>
<tr>
<td>Mechanical obstruction</td>
<td>More localized wheezing; if central in location, flow-volume loop may provide a clue</td>
</tr>
</tbody>
</table>
Methacholine Challenge

• Typical symptoms + Response to therapy
• Abnormal PFT

• Does this patient really have asthma?
• eg. Symptoms consistent with asthma but no response to treatment, chronic cough, occupational asthma, screening like scuba divers & military personnel
## Methacholine Challenge

### Table 3-4. Interpretation of Bronchoprovocation Challenge Testing

<table>
<thead>
<tr>
<th>Test Result</th>
<th>History Suggestive of Asthma</th>
<th>History Not Suggestive of Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Diagnosis of asthma confirmed</td>
<td>Up to 10% of nonatopic, nonasthmatic subjects (26% of all smokers) have reactive airways but are asymptomatic</td>
</tr>
<tr>
<td></td>
<td>? PC_{20} of 4mg/ml</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>Atopic patient with seasonal asthma symptoms tested “out of season”</td>
<td>Diagnosis of asthma ruled out</td>
</tr>
<tr>
<td></td>
<td>Patient with occupational asthma tested long after exposure to the etiological agent</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Recent glucocorticoid use</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other conditions mimicking asthma such as vocal cord dysfunction and central airway obstruction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>? PC_{20} of 8mg/ml</td>
<td></td>
</tr>
</tbody>
</table>

ATS Board review: Le, Khosa, Pasnick, Wang: 2015
Goals of Management

- Achieve and maintain control of symptoms
- Maintain normal activity levels, including exercise
- Maintain pulm. function as close to normal levels as possible
- Prevent asthma exacerbations
- Avoid adverse effects from asthma medications
- Prevent asthma mortality
## Classifying Asthma Severity and Initiating Treatment in Youths ≥12 Years of Age and Adults

### Assessing severity and initiating treatment for patients who are not currently taking long-term control medications

<table>
<thead>
<tr>
<th>Components of Severity</th>
<th>Classification of Asthma Severity (≥12 Years of Age)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intermittent</td>
</tr>
<tr>
<td>Symptoms</td>
<td>≤2 days/week</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤2×/month</td>
</tr>
<tr>
<td>Short-acting β₂-agonist use for symptom control (not prevention of EIB)</td>
<td>≤2 days/week</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
</tr>
<tr>
<td>Lung function</td>
<td>Normal FEV₁/FVC: 85% 8–19 yr 85% 20–39 yr 80% 40–59 yr 75% 60–80 yr 70%</td>
</tr>
<tr>
<td>Exacerbations requiring oral systemic corticosteroids</td>
<td>0–1/year</td>
</tr>
<tr>
<td>Risk</td>
<td>Consider severity and interval since last exacerbation</td>
</tr>
</tbody>
</table>

### Recommended Step for Initiating Treatment

- **Step 1**: In 2 to 6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.

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EIB = exercise-induced bronchospasm; FEV₁ = forced expiratory volume in 1 second; FVC = forced vital capacity.

## Assessing asthma control in youths greater than or equal to 12 years of age and adults

<table>
<thead>
<tr>
<th>Components of control</th>
<th>Classification of asthma control (youths ≥12 years of age and adults)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Well controlled</td>
</tr>
</tbody>
</table>
| Impairment
Symptoms       | ≤2 days/week    | >2 days/week        | Throughout the day     |
| Nighttime awakenings | ≤2x/month       | 1 to 3x/week        | ≥4x/week               |
| Interference with normal activity | None           | Some limitation     | Extremely limited      |
| Short-acting beta₂-agonist use for symptom control (not prevention of EIB) | ≤2 days/week | >2 days/week        | Several times per day |
| FEV₁ or peak flow  | >80 percent predicted/personal best | 60 to 80 percent predicted/personal best | <60 percent predicted/personal best |
| Validated questionnaires |
| ATAQ                | 0              | 1 to 2             | 3 to 4                 |
| ACQ                 | ≤0.75*         | ≥1.5               | N/A                    |
| ACT                 | ≥20            | 16 to 19           | ≤15                    |
| Risk
Exacerbations      | 0 to 1/year    | ≥2/year (see footnote) | Consider severity and interval since last exacerbation |
| Progressive loss of lung function | Evaluation requires long-term follow-up care |
| Treatment-related adverse effects | Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk. |
ERS & ATS Definition Of Severe Asthma

**ASTHMA MEDICATION REQUIREMENTS (1)**

1. GINA Step 4-5 medication (High dose ICS + LABA): Example 1 puff of Fluticasone-Salmeterol 500-50 BID
2. Treatment with systemic steroids for ≥ 50% of previous year

**UNCONTROLLED ASTHMA (1)**

1. Poor symptom control: ACQ 1.5, ACT <20
2. Frequent exacerbations: ≥ 2 bursts of systemic steroids (≥ 3 days) in previous year
3. History of serious exacerbation: ≥ 1 hospitalization/ ICU stay/ intubation
4. Airflow limitation: FEV$_1$ <80%
Persistent asthma: Daily medication
Consult with asthma specialist if step 4 care or higher is required.
Consider consultation at step 3.

Step 1
Preferred: SABA PRN
Alternative: Cromolyn, LTRA, Nedocromil, or Theophylline

Step 2
Preferred: Low-dose ICS + LABA
Alternative: Medium-dose ICS

Step 3
Preferred: Medium-dose ICS + LABA
Alternative: Low-dose ICS + either LTRA, Theophylline, or Zileuton

Step 4
Preferred: High-dose ICS + LABA AND
Consider Omalizumab for patients who have allergies
Alternative: Medium-dose ICS + either LTRA, Theophylline, or Zileuton

Step 5
Preferred: High-dose ICS + LABA + oral corticosteroid AND
Consider Omalizumab for patients who have allergies

Step 6
Step up if needed
(first, check adherence, environmental control, and comorbid conditions)
Assess control
Step down if possible
(and asthma is well controlled at least 3 months)

Each step: Patient education, environmental control, and management of comorbidities.
Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

Quick-relief medication for all patients
- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.
Early LABA + ICS versus Maximizing ICS

• GOAL: 1 year, randomized, DB-PC evaluating step wise approach using Salmeterol-Fluticasone (max: 50-500µg) Vs Fluticasone (max 500 µg) alone for asthma control

• 3 Patient strata
  1. ICS naïve
  2. ICS dose ≤ 500µg of Beclomethasone equivalent
  3. ICS dose > 500µg but less that ≤ 1000µg Beclomethasone equivalent

Beta Agony !!! Chronic use

- **SABA: Increased risk of asthma related death**
  
  1. Initial small study found 2 fold increase in fatal episodes
  2. A retrospective study (n = 12,300) showed similar findings
  3. Case-control (500 each group) no difference at 4-12 month BUT possible increase mortality 1-5 year

- **LABA: Increased death**
  
  1. FDA meta analysis (~61000 patients) : increased asthma events
  2. Death mitigated (somewhat with concomitant ICS use)
  3. SMART Trial: Salmeterol Vs placebo
     - 26,355 patient, 28 weeks
     - Higher risk of asthma events in Salmeterol
     - Worse in African Americans

**Bottom line: FDA black box warning.**

4. Age and risks of FDA-approved long-actingβ₂-adrenergic receptor agonists. McMahon AW, Levenson MS, McEvoy BW, Mosholder AD, Murphy D
“Because there is no gold standard for the definition of asthma, there can be no gold standard for the assessment of asthma control, and no single primary endpoint can be recommended for the assessment of treatment response in asthma.”
How good are we at assessing control?

1 page questionnaire – 5 parameters (Eg: Daytime symptoms, Night time symptoms)
Filled by patients and handed over to their primary care physicians

10,428 patients/ 354 physicians

Guideline classification: 59% were uncontrolled, 19% well controlled, 23% totally controlled

Physicians: 42% were uncontrolled

• Up to 50% of asthma patients are “uncontrolled”
• Physicians tend to overestimate control

Short term loss of control → Increased risk of exacerbations

• 12 week study, 292 patient

• Each 1-point increase in ACQ was associated with a 50% increased risk of exacerbation (hazard ratio, 1.50; 95%CI, 1.03-2.20)

• Evaluation of individual ACQ components also demonstrated a similar trend, though each to a lesser degree than the full composite ACQ

1. In the past 4 weeks, how much of the time did your **asthma** keep you from getting as much done at work, school or at home?

<table>
<thead>
<tr>
<th>All of the time</th>
<th>Most of the time</th>
<th>Some of the time</th>
<th>A little of the time</th>
<th>None of the time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

2. During the past 4 weeks, how often have you had shortness of breath?

<table>
<thead>
<tr>
<th>More than once a day</th>
<th>Once a day</th>
<th>3 to 6 times a week</th>
<th>Once or twice</th>
<th>Not at all</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

3. During the past 4 weeks, how often did your **asthma** symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?

<table>
<thead>
<tr>
<th>4 or more nights a week</th>
<th>2 or 3 nights a week</th>
<th>Once a week</th>
<th>Once or twice</th>
<th>Not at all</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?

<table>
<thead>
<tr>
<th>3 or more times per day</th>
<th>1 or 2 times per day</th>
<th>2 or 3 times per week</th>
<th>Once a week or less</th>
<th>Not at all</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

5. How would you rate your **asthma** control during the past 4 weeks?

<table>
<thead>
<tr>
<th>Not controlled at all</th>
<th>Poorly controlled</th>
<th>Somewhat controlled</th>
<th>Well controlled</th>
<th>Completely controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
Severe asthma control – ATS/ERS 2014

<table>
<thead>
<tr>
<th></th>
<th>Well controlled</th>
<th>Not well controlled</th>
<th>Poorly controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACQ</strong></td>
<td>≤ 0.75</td>
<td>≥ 1.5</td>
<td>N/a</td>
</tr>
<tr>
<td><strong>ACT</strong></td>
<td>≥ 20</td>
<td>16-19</td>
<td>≤ 15</td>
</tr>
</tbody>
</table>
Non pharmacological measures

- Asthma management partnership with patient (i.e. MANAGE THEIR EXPECTATIONS)

- Triggers
  - Direct face to face: Monitoring
    - Routine monitoring: 1-6 months based on severity
    - Changing “steps”: 2-6 week for level of control (more so for step up than step down)
    - Vaccinate, vaccinate, vaccinate (low risk of autism)

- Inhaler use
  - https://www.cdc.gov/asthma/inhaler_video/default.htm
    - 12 steps for Metered Dose Inhaler without a spacer
    - 15 steps for Metered Dose Inhaler with a spacer or chamber
    - Dry Powered Inhaler: 11 steps for a Aerolizer, 8 steps for a Diskhaler, 4 steps for Diskus, 12 steps for Handihaler, 15 steps for Twisthaler
    - When in doubt, consider nebulizers short term
    - Inhaler reminder program: decreased ACT scores and exacerbation frequency *

$ NAEPP-EPR 3: 2007

* Foster, Inhaler reminders improve adherence with controller treatment in primary care patients with asthma134;6JACI.Dec.2014.
<table>
<thead>
<tr>
<th>Doing Well</th>
<th>Take these long-term control medicines each day (include an anti-inflammatory).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicine</td>
<td>How much to take</td>
</tr>
<tr>
<td>When to take it</td>
<td></td>
</tr>
<tr>
<td>-------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>

**Asthma Action Plan**

**Green Zone**
- No cough, wheeze, chest tightness, or shortness of breath during the day or night
- Can do usual activities

And, if a peak flow meter is used,
- Peak flow: more than (80% or more of my best peak flow)
- My best peak flow is: __________
- Before exercise: __________

**Yellow Zone**
- Cough, wheeze, chest tightness, or shortness of breath, or
- Waking at night due to asthma, or
- Can do some, but not all, usual activities
- Peak flow: __________ to __________ (60 to 79% of my best peak flow)

**Medical Alert!**
- Very short of breath, or
- Quick-relief medicines have not helped, or
- Cannot do usual activities, or
- Symptoms are same or get worse after 24 hours in Yellow Zone
- Peak flow: less than __________ (60% of my best peak flow)

**Red Zone**
- Take this medicine:
- ____________ 4 or 6 puffs or Nebulizer
- ____________ mg per day. For: ____________ (3–10) days

Then call your doctor NOW. Go to the hospital or call for an ambulance it:
- You are still in the red zone after 15 minutes AND
- You have not reached your doctor.

**Danger Signs**
- Trouble walking and talking due to shortness of breath
- Lips or fingernails are blue
- Take 4 or 6 puffs of your quick-relief medicine AND
- Go to the hospital or call for an ambulance ____________ NOW!
• Validated more in the pediatric population and if set up with an “Alert pathway” (hospital network EHR-EMR alert/ telephone alerts / web based alert systems)

• Did not show benefit in subspecialty clinic (Pulmonary or Allergy) trial*

  ➢ 407 children and adults/ randomized to plan Vs no plan (written action plan)

  ➢ No effect on asthma symptom frequency, ER visits, asthma QOL at 12 months

Peak Flow

• Theoretical advantage, needs insight for use (cognitive component)

• Needs a established best to monitor trends: 2-4 times per day for 2 weeks

• Role in patient at extremes of age, occupational asthma and patients with issues of symptom perceptions (pregnant asthmatics)

• Established short comings

1. Long term adherence is poor (In a study setting): 1st month-63%, 6 months – 50%, 12 months ~ 30%.

2. In another study (patient were blinded to a computer chip in flow meter) 22% of data entered were “invented”

3. There can be substantial variability between measurements (20-60 L/min)

4. Outcome improvement (healthcare utilization and QOL) noted only when it is part of a comprehensive management plan.


<table>
<thead>
<tr>
<th>Reasons of poor control</th>
<th>Variables</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease-related</td>
<td>Comorbidities</td>
<td>Rhinitis, rhinosinusitis, gastroesophageal reflux, obstructive sleep apnoea, and obesity</td>
</tr>
<tr>
<td></td>
<td>Triggers</td>
<td>House dust mite, pets, occupational exposure, exercise, drug, passive smoking, new allergens, aspirin, and beta-blockers</td>
</tr>
<tr>
<td></td>
<td>Asthma type</td>
<td>Aspirin-sensitivity, neutrophilic activity, and severe therapy-resistant</td>
</tr>
<tr>
<td>Patient related</td>
<td>Sociodemographic factors</td>
<td>Female sex, education below secondary level, adolescence, and elderly age</td>
</tr>
<tr>
<td></td>
<td>Adherence</td>
<td>Undertreatment, overtreatment, irregular visits to healthcare providers, insufficient monitoring of symptoms, and no modifications in lifestyle</td>
</tr>
<tr>
<td></td>
<td>Psychiatric comorbidity</td>
<td>Anxiety and depressive disorders</td>
</tr>
<tr>
<td></td>
<td>Psychological characteristics</td>
<td>Alexithymia (a personality trait characterized by difficulty in identifying and verbally expressing feeling) and inadequate coping strategies</td>
</tr>
<tr>
<td></td>
<td>Perceptions</td>
<td>Tendency to tolerate symptoms, exacerbations and lifestyle limits as an inevitable consequence of asthma</td>
</tr>
<tr>
<td></td>
<td>Expectations</td>
<td>Low expectations and aspirations about the achievable degree of control</td>
</tr>
<tr>
<td></td>
<td>Behaviours</td>
<td>Smoking habits</td>
</tr>
<tr>
<td></td>
<td>Knowledge</td>
<td>Inadequate information about the disease’s treatment.</td>
</tr>
<tr>
<td>Doctor related</td>
<td>Misdiagnosis</td>
<td>Limited awareness of asthma prevalence inadequate assessment</td>
</tr>
<tr>
<td></td>
<td>Knowledge of current guidelines</td>
<td>Lack of consciousness and familiarity about guidelines availability</td>
</tr>
<tr>
<td></td>
<td>Attitude towards guidelines</td>
<td>Difficulty in accepting a particular document or the concept itself of the guidelines</td>
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<tr>
<td></td>
<td>Guidelines implementations</td>
<td>Lack of confidence in personal abilities to put the recommendations into practice</td>
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<tr>
<td></td>
<td></td>
<td>Expectations of failure in following guidelines</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Difficulty changing deep-seated routines</td>
</tr>
<tr>
<td>Trigger</td>
<td>Description</td>
<td></td>
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<td></td>
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<tr>
<td>Inhaled allergen</td>
<td></td>
<td></td>
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<tr>
<td>Respiratory infections (viruses)</td>
<td></td>
<td></td>
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<tr>
<td>Respiratory irritants (Smoke)</td>
<td></td>
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<tr>
<td>Weather</td>
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<tr>
<td>Medications</td>
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<tr>
<td>Food</td>
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<tr>
<td>Emotional states</td>
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</tbody>
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Asthma beyond ICS and LABA
Spiriva Respimat

1.25 mcg

2 puffs once a day
1. Adding LAMA to ICS alone or LABA + ICS

2. Adding LAMA to on an ICS **INSTEAD** of a LABA
Monoclonal antibodies
Omalizumab: Anti-IgE therapy

- All 5 criteria (GINA treatment step 5-6)
  1. ≥ 12 years age
  2. Moderate to severe persistent asthma
  3. Inadequate control despite ICS (high dose ICS not a requirement in US)
  4. Total serum IgE between 30-700 IU
  5. (+) Skin test or in vitro testing for allergen specific IgE to a perennial allergen

- Prospective, multicenter, DB-PC, RCT
- 850 patients, high doses ICS + LABA ± other controller => Omalizumab (n = 427) Vs Placebo (n= 423)
- At 48 weeks, Omalizumab
  - Lower rate of AE-asthma (0.66 Vs 0.88 per patient; P= 0.006)
  - Improved mean AQLQ scores (0.29 point, CI 0.15 – 0.43)
  - Reduced mean daily albuterol puffs ( -0.27 puffs per day, CI -0.49 to -0.04)
  - Decreased asthma symptoms score (TASS score) ( -0.26, CI -0.42 to -0.10)

- Key limitation: Early patient discontinuation

Mepolizumab- Anti-IL-5 therapy

- Severe, eosinophilic asthma (generally $\geq 150/\mu L$), SC dose, every 4 weeks

**Dose ranging efficacy and safety with Mepolizumab in severe asthma (DREAM)**

- 621 patients, severe asthma, evidence of eosinophilic inflammation (serum, sputum, FeNO)
- IV Mepolizumab 75mg , 250 mg, 750mg => all group has lower exacerbation rates, lowest with 750mg (52% reduction)

**Steroid reduction in mepolizumab (SIRIUS) trial**

- 135 patients, severe asthma, eosinophilia, 5-35mg of Prednisone (or equivalent)
- Rx arm had a 2.39 greater likelihood in reduction of steroid dose
- Rx also had decrease in exacerbations and symptom score

**Mepolizumab as adjunctive in patients with severe asthma (MENSA) trial**

- 576 patients, severe asthma, eosinophilia, high dose ICS ± oral steroids
- IV Mepolizumab Vs SC Mepolizumab Vs Placebo
  - Exacerbation reduced by 47% in IV and 53% in SC group compared to placebo
Reslizumab- Anti IL-5 Antibody

- **Eosinophilic phenotype, ≥ 400/µL, IV infusion**
- **Medium** to high doses of ICS patients and poorly controlled

**2011 study**

- ACQ score, IV Reslizumab (53 patients) Vs Placebo (53 patients) x 12 weeks
- Decreased sputum eosinophils, improved airflow. Failed to meet MCID for ACQ

**2015 trial**

- DB-PC, 2 duplicate trials (~220 centers), above criteria
- Iv Reslizumab (477 patients) Vs IV placebo (476 patients) Q4 weeks x 1 year
- Study group; significant reduction in AE-asthma. Also improved FEV1, QOL and ACQ

---

Others

• Bronchial thermoplasty

- Your guess is as good as mine!
- Awaiting discovery of the right phenotype
Conclusion

• Guidelines are guide-lines and not substitute for clinical judgement

• Monitoring control is paramount--> short term loss of control results in increased risk of exacerbations

• Severe Asthma refer to a specialist→ Screen and consider monoclonals when severe asthma loses control

• Do you best with non pharmacological interventions but don’t put all your efforts into it

• Call as needed
COPD
“COPD, a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases.”

*The Global Initiative for Chronic Obstructive Lung Disease (2014 update)*
Problem Statement

• Affects estimated 32 million people in the US
• Fourth leading cause of death in the US
• Estimated US prevalence = 10.1%
• Global prevalence = 7-19%
• BOLD study = 10.1% global prevalence
Pathophysiology

Changes occur in:
• large (central) airways,
• small (peripheral) bronchioles,
• lung parenchyma.

Most changes are caused by noxious stimuli.
Chronic Bronchitis

• Mucous gland hyperplasia (histologic hallmark)
• Airway structural changes
  • Atrophy
  • Focal squamous metaplasia
  • Ciliary abnormalities
  • Airway smooth muscle hyperplasia
  • Inflammation
  • Bronchial wall thickening
Mucosal Gland Hyperplasia
Airway Structural Changes
Emphysema

• Permanent enlargement of airways distal to the terminal bronchioles
• Decline in alveolar surface area
• Airflow limitations
  • Decrease in elastic recoil (alveolar wall loss)
  • Airway narrowing (support structures loss)
Emphysema
Cigarette and COPD

- ~15% get clinically significant disease
- FEV1 declines faster in smokers (20 vs 60ml/y)
- Mortality depends on:
  - Age of initiation
  - Total pack-years
  - Current smoking status
Cigarette and COPD

Second-hand smoke effects:
• increases the risk of respiratory infections
• augments asthma symptoms
• causes a measurable reduction in PFT
Worth a mention...

“...lung function deviation and lung structural changes are present in cigarette smokers before the clinical signs of airway obstruction reveal.”

Etiology

- Cigarette smoking
- Environmental factors
- Airway hyper-responsiveness (Dutch hypothesis)
- Alpha 1-antitrypsin deficiency
- Intravenous drug abuse
- Immunodeficiency syndromes
- Vasculitis syndromes
- Connective tissue disorders
Diagnosing COPD – Key Indicators

- Dyspnea
  - Progressive
  - Worse with exercise
  - Persistent
- Chronic cough (may be intermittent/dry)
- Chronic sputum production (any pattern)
- History of exposure to risk factors
- Family history of COPD
Most importantly...

**Spirometry** is required to establish a diagnosis of COPD.

Post-bronchodilator FEV1/FVC < 0.70  
(GOLD definition)

ATS $\rightarrow$ LLN
Assessment of COPD

Assess the following aspects separately:

• Symptoms
• Degree of airflow limitation (spirometry)
• Risk of exacerbations
• Comorbidities
Assessing Symptoms

Validated questionnaires

• COPD Assessment Test (CAT)

• Modified British Medical Research Council (mMRC) breathlessness scale
<table>
<thead>
<tr>
<th>Statement</th>
<th>Scale</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>I never cough</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I cough all the time</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>I have no phlegm(mucus) in my chest at all</td>
<td></td>
<td></td>
</tr>
<tr>
<td>My chest is full of phlegm(mucus)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>My chest does not feel tight at all</td>
<td></td>
<td></td>
</tr>
<tr>
<td>My chest feels very tight</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>When I walk up a hill or one flight of stairs I am not breathless</td>
<td></td>
<td></td>
</tr>
<tr>
<td>When I walk up a hill or one flight of stairs I am very breathless</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>I am not limited doing any activities at home</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I am very limited doing activities at home</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>I am confident leaving my home despite my lung condition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I am not at all confident leaving my home because of my lung condition</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>I sleep soundly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I don't sleep soundly because of my lung condition</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>I have lots of energy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I have no energy at all</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>I have no energy at all</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>
Modified MRC (mMRC) Questionnaire

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. □
Assessing Airflow Limitation/Spirometry
GOLD

<table>
<thead>
<tr>
<th>Classification of Severity of Airflow Limitation in COPD (Based on Post-Bronchodilator FEV1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients with FEV1/FVC &lt; 0.70:</td>
</tr>
<tr>
<td>GOLD 1</td>
</tr>
<tr>
<td>GOLD 2</td>
</tr>
<tr>
<td>GOLD 3</td>
</tr>
<tr>
<td>GOLD 4</td>
</tr>
</tbody>
</table>
## Table 7. Severity of any spirometric abnormality based on FEV₁*

<table>
<thead>
<tr>
<th>Severity</th>
<th>FEV₁ (% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>&gt;70</td>
</tr>
<tr>
<td>Moderate</td>
<td>60 - 69</td>
</tr>
<tr>
<td>Moderately severe</td>
<td>50 - 59</td>
</tr>
<tr>
<td>Severe</td>
<td>35 - 49</td>
</tr>
<tr>
<td>Very severe</td>
<td>&lt;35</td>
</tr>
</tbody>
</table>

*Adapted from Pellegrino et al.⁶
Assessing Risk of Exacerbations

**Exacerbation**: An *acute* event characterized by a *worsening* of the patient’s respiratory symptom that is *beyond normal* day-to-day variations, and leads to a *change* in medication.

**Best predictors:**
- History of previous treated events
- Worsening airflow limitation
Assessing Comorbidities

May influence mortality and hospitalizations:
• Cardiovascular diseases
• Osteoporosis
• Depression and anxiety
• Skeletal muscle dysfunction
• Metabolic syndrome
• Lung cancer
Assessment of COPD Severity

When assessing risk, choose the highest risk according to GOLD grade or exacerbation history.

<table>
<thead>
<tr>
<th>Patient Category</th>
<th>Characteristics</th>
<th>Spirometric Classification</th>
<th>Exacerbations Per Year</th>
<th>mMRC</th>
<th>CAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Low Risk, Less Symptoms</td>
<td>GOLD 1-2</td>
<td>1</td>
<td>0-1</td>
<td>&lt;10</td>
</tr>
<tr>
<td>B</td>
<td>Low Risk, More Symptoms</td>
<td>GOLD 1-2</td>
<td>1</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>C</td>
<td>High Risk, Less Symptoms</td>
<td>GOLD 3-4</td>
<td>2</td>
<td>0-1</td>
<td>&lt;10</td>
</tr>
<tr>
<td>D</td>
<td>High Risk, More Symptoms</td>
<td>GOLD 3-4</td>
<td>2</td>
<td>2</td>
<td>10</td>
</tr>
</tbody>
</table>
### Combined Assessment of COPD

<table>
<thead>
<tr>
<th>Symptoms:</th>
<th></th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less</td>
<td>mMRC 0-1/CAT &lt; 10</td>
<td>A or C</td>
</tr>
<tr>
<td>More</td>
<td>mMRC &gt; 2/CAT ≥ 10</td>
<td>B or D</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Airflow limitation:</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>Gold 1 or 2</td>
<td>A or B</td>
</tr>
<tr>
<td>High risk</td>
<td>Gold 3 or 4</td>
<td>C or D</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exacerbations:</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>≤ 1 per year</td>
<td>A or B</td>
</tr>
<tr>
<td>High risk</td>
<td>≥ 2 per year</td>
<td>C or D</td>
</tr>
</tbody>
</table>
## Combined Assessment of COPD

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Characteristic</th>
<th>Spiro Class</th>
<th>Exacer/y</th>
<th>CAT</th>
<th>mMRC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong></td>
<td>Low risk Less symptoms</td>
<td>GOLD 1-2</td>
<td>≤ 1</td>
<td>&lt; 10</td>
<td>0-1</td>
</tr>
<tr>
<td><strong>B</strong></td>
<td>Low risk More symptoms</td>
<td>GOLD 1-2</td>
<td>≤ 1</td>
<td>≥ 10</td>
<td>≥ 2</td>
</tr>
<tr>
<td><strong>C</strong></td>
<td>High risk Less symptoms</td>
<td>GOLD 3-4</td>
<td>≥ 2</td>
<td>&lt; 10</td>
<td>0-1</td>
</tr>
<tr>
<td><strong>D</strong></td>
<td>High risk More symptoms</td>
<td>GOLD 3-4</td>
<td>≥ 2</td>
<td>≥ 10</td>
<td>≥ 2</td>
</tr>
</tbody>
</table>
Management of Stable COPD

- Reduce symptoms
  - Relieve symptoms
  - Improve exercise tolerance
  - Improve health status
- Reduce risk
  - Prevent disease progression
  - Prevent and treat exacerbations
  - Reduce mortality
Approach Considerations

- Smoking cessation
- Management of inflammation (steroid/macrolide)
- Management of infection
- Management of sputum viscosity & clearance
- PPIs for exacerbations
- Oxygen for hypoxemia
- Vaccination (pneumococcal/influenza)
- AAT treatment (reduces neutrophil elastase burden)
- Pulmonary rehabilitation
Major Medication Classes

• Bronchodilators
  • Anticholinergics
  • B-2 agonists
  • Methylxanthines

• Corticosteroids & Phosphodiesterase-4 inhibitors
  • Inhaled corticosteroids
  • Oral corticosteroids
  • Roflumilast
<table>
<thead>
<tr>
<th>Group</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; choice</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt; choice</th>
<th>Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>SAMA prn Or SABA prn</td>
<td>LAMA or LABA Or SAMA and SABA</td>
<td>Theophylline</td>
</tr>
<tr>
<td>B</td>
<td>LAMA or LABA</td>
<td>LAMA or LABA</td>
<td>SAMA and/or SABA</td>
</tr>
<tr>
<td>C</td>
<td>ICS+LABA Or LAMA</td>
<td>LAMA and LABA</td>
<td>PDE-4i SAMA and/or SABA Theophylline</td>
</tr>
<tr>
<td>D</td>
<td>ICS+LABA Or LAMA</td>
<td>ICS and LAMA, or ICS+LABA+LAMA, or ICS+LABA+PDE-4i, or LAMA+LABA, or LAMA+PDE-4i</td>
<td>Carbocysteine SAMA and/or SABA Theophylline</td>
</tr>
</tbody>
</table>

Legend: SAMA – short acting muscarinic antagonist; SABA – short acting beta agonist; LAMA – long acting muscarinic antagonist; LABA – long acting beta agonist; ICS – inhaled corticosteroid; PDE4i – phosphodiesterase inhibitor
LAMA + LABA Vs LABA-ICS for frequent exacerbators

- FLAME Trial: 52 week, DB, non inferiority trial
- COPD + at least one exacerbation in previous year
- Indacaterol + Glycopyrronium (Qd) Vs Salmeterol + Fluticasone (BID)

- 1680 patients in LABA + LAMA
- 1682 patients in LABA + ICS

- Annual rate of exacerbation was 11% lower
- Time to first exacerbation was longer
- Severe exacerbation rates were lower
- Adverse effects were similar
Oxygen Therapy in COPD

Long-term oxygen therapy improves survival ≥ 2 folds in hypoxemic patients with COPD.

*Reference: BMRC Study, and US NHLBI NOTT Trial*

Oxygen therapy recommendations:

- PaO2 < 55 mm Hg
- PaO2 < 59 mm Hg, with evidence of polycythemia or cor pulmonale
- Maintain PaO2 at 60-65 mm Hg
- Re-evaluate 1-3 months after initiating oxygen
Non-Invasive Positive Pressure Ventilation

Canadian Critical Care Trials Group and the Canadian Critical Care Society Noninvasive Ventilation Guidelines Group:

• NIPPV should be the first-line choice for supporting patients with a severe exacerbation of COPD.

• In facilities with extensive NIPPV experience, patients with COPD can be considered for a trial of early extubation to NIPPV.

• Patients with hypoxemia or acute respiratory distress after undergoing surgery or in immunosuppression can be considered for a trial of NIPPV.

• Routine use of helium-oxygen is not recommended with NIPPV in patients with severe exacerbation of COPD.
Invasive Options
Surgical/Interventional Options

- Bullectomy
- Lung Volume Reduction Surgery
- Lung Transplant
- End-of-life Care
Transplant candidates

1. BODE index $\geq 7$ (BMI, Obstruction FEV1, Dyspnea MMRC, Exercise 6MWT)
2. FEV1 <15-20 % pred
3. $\geq 3$ exacerbations per year
4. Moderate to severe pulmonary hypertension
"Nocardiosis! Does that mean his heart is gone??"
Pulmonary Function Test
Patient Instructions Prior to Testing

- Should not drink alcohol for four hours prior to test
- Should not smoke at least one hour before test
- Do not eat a large meal two hours prior to test
- No vigorous exercise 30 minutes before test
- Do not wear tight form fitting clothes
- May need to remove loose dentures for test
- Should wait at least one month post MI, consider impact of problems that may affect results (chest/abdominal pain, oral or facial pain, stress incontinence, dementia, physical deformities or medical conditions)
- Bring a list of all medications – potentially withhold bronchodilators, corticosteroids
Lung Volume Terminology

- **Total lung capacity**
  - **Inspiratory reserve volume**
  - **Tidal volume**
  - **Expiratory reserve volume**
  - **Residual volume**
  - **Inspiratory capacity**
  - **Vital capacity**
Spirogram Patterns

- Normal
- Obstructive
- Restrictive
- Mixed Obstructive and Restrictive
Spirometry

Predicted Normal Values
Predicted Normal Values

Affected by:

✓ Age
✓ Height
✓ Sex
✓ Ethnic Origin
Criteria for Normal
Post-bronchodilator Spirometry

• FEV₁: % predicted ≥ 80%

• FVC: % predicted ≥ 80%

• FEV₁/FVC: > 0.7 - 0.8, depending on age
Normal Trace Showing \( FEV_1 \) and FVC

\[
\begin{align*}
FEV_1 &= 4 \text{L} \\
FVC &= 5 \text{L} \\
\frac{FEV_1}{FVC} &= 0.8
\end{align*}
\]
SPIROMETRY

OBSTRUCTIVE DISEASE
Spirometry: Obstructive Disease

- **FEV₁** = 1.8L
- **FVC** = 3.2L
- **FEV₁/FVC** = 0.56

Normal

- Obstructive
Spirometric Diagnosis of COPD

- COPD is confirmed by post–bronchodilator FEV\(_1\)/FVC < 0.7

- Post-bronchodilator FEV\(_1\)/FVC measured 15 minutes after 400µg salbutamol or equivalent
### Bronchodilator Reversibility Testing

<table>
<thead>
<tr>
<th>Bronchodilator*</th>
<th>Dose</th>
<th>FEV$_1$ before and after</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salbutamol</td>
<td>200 – 400 µg via large volume spacer</td>
<td>15 minutes</td>
</tr>
<tr>
<td>Terbutaline</td>
<td>500 µg via Turbohaler®</td>
<td>15 minutes</td>
</tr>
<tr>
<td>Ipratropium</td>
<td>160 µg** via spacer</td>
<td>45 minutes</td>
</tr>
</tbody>
</table>

Some guidelines suggest nebulised bronchodilators can be given but the doses are not standardised. “There is no consensus on the drug, dose or mode of administering a bronchodilator in the laboratory.” Ref: ATS/ERS Task Force: Interpretive strategies for Lung Function Tests *ERJ* 2005;26:948
Figure 5.1-6. Bronchodilator Reversibility Testing in COPD

GOLD Report (2009)

**Preparation**
- Tests should be performed when patients are clinically stable and free from respiratory infection.
- Patients should not have taken inhaled short-acting bronchodilators in the previous six hours, long-acting bronchodilator in the previous 12 hours, or sustained-release theophylline in the previous 24 hours.

**Spirometry**
- FEV₁ should be measured before a bronchodilator is given.
- The bronchodilator should be given by metered dose inhaler through a spacer device or by nebulizer to be certain it has been inhaled.

**Figure 5.1-6. Bronchodilator Reversibility Testing in COPD**

- The bronchodilator dose should be selected to be high on the dose/response curve.
- Possible dosage protocols are 400 μg β₂-agonist, up to 160 μg anticholinergic, or the two combined. FEV₁ should be measured again 10-15 minutes after a short-acting bronchodilator is given; 30-45 minutes after the combination.

**Results**
- An increase in FEV₁ that is both greater than 200 ml and 12% above the pre-bronchodilator FEV₁ is considered significant. It is usually helpful to report the absolute change as well as the % change from baseline to set the improvement in a clinical context.
Preparation

• Tests should be performed when patients are clinically stable and free from respiratory infection

• Patients should not have taken:
  
  ✓ inhaled short-acting bronchodilators in the previous six hours
  
  ✓ long-acting bronchodilator in the previous 12 hours
  
  ✓ sustained-release theophylline in the previous 24 hours
Spirometry

• FEV$_1$ should be measured (minimum twice, within 5% or 150mls) before a bronchodilator is given.

• The bronchodilator should be given by metered dose inhaler through a spacer device or by nebulizer to be certain it has been inhaled.

• The bronchodilator dose should be selected to be high on the dose/response curve.

(.....continued)
Spirometry (continued)

• Possible dosage protocols:
  ✓ 400 µg β₂-agonist, or
  ✓ 80-160 µg anticholinergic, or
  ✓ the two combined

• FEV₁ should be measured again:
  ✓ 15 minutes after a short-acting bronchodilator
  ✓ 45 minutes after the combination
Results

• An increase in FEV$_1$ that is both greater than 200 ml and 12% above the pre-bronchodilator FEV$_1$ (baseline value) is considered significant.

• It is usually helpful to report the absolute change (in ml) as well as the % change from baseline to set the improvement in a clinical context.
SPIROMETRY

RESTRICTIVE DISEASE
Spirometry: Restrictive Disease

- **Normal**
- **Restrictive**

**FEV<sub>1</sub> = 1.9L**
**FVC = 2.0L**
**FEV<sub>1</sub>/FVC = 0.95**
Mixed Obstructive/Restrictive

- $\text{FEV}_1$: < 80% predicted
- $\text{FVC}$: < 80% predicted
- $\text{FEV}_1 / \text{FVC}$: < 0.7
Restrictive and mixed obstructive-restrictive are difficult to diagnose by spirometry alone; full respiratory function tests are usually required (e.g., body plethysmography, etc).
Flow Volume Curve

- Standard on most desk-top spirometers
- Adds more information than volume time curve
- Less understood but not too difficult to interpret
- Better at demonstrating mild airflow obstruction
Flow Volume Curve

- Expiratory flow rate (L/sec)
- Inspiratory flow rate (L/sec)
- Maximum expiratory flow (PEF)
- TLC
- FVC
- RV
Flow Volume Curve Patterns
Obstructive and Restrictive

Obstructive
- Reduced peak flow, scooped out mid-curve

Severe obstructive
- Steeple pattern, reduced peak flow, rapid fall off

Restrictive
- Normal shape, normal peak flow, reduced volume
Spirometry: Abnormal Patterns

**Obstructive**
- Slow rise, reduced volume expired; prolonged time to full expiration

**Restrictive**
- Fast rise to plateau at reduced maximum volume

**Mixed**
- Slow rise to reduced maximum volume; measure static lung volumes and full PFT’s to confirm
PRACTICAL SESSION

Performing Spirometry
Spirometry Training

• Training is essential for operators to learn correct performance and interpretation of results

• Training for competent performance of spirometry requires a minimum of 3 hours

• Acquiring good spirometry performance and interpretation skills requires practice, evaluation, and review

• Spirometry performance (who, when and where) should be adapted to local needs and resources

• Training for spirometry should be evaluated
Obtaining Predicted Values

- Independent of the type of spirometer
- Choose values that best represent the tested population
- Check for appropriateness if built into the spirometer

Optimally, subjects should rest 10 minutes before performing spirometry
Withholding Medications

Before performing spirometry, withhold:

- Short acting $\beta_2$-agonists for 6 hours
- Long acting $\beta_2$-agonists for 12 hours
- Ipratropium for 6 hours
- Tiotropium for 24 hours

Optimally, subjects should avoid caffeine and cigarette smoking for 30 minutes before performing spirometry.
Performing Spirometry - Preparation

1. Explain the purpose of the test and demonstrate the procedure

2. Record the patient’s age, height and gender and enter on the spirometer

3. Note when bronchodilator was last used

4. Have the patient sitting comfortably

5. Loosen any tight clothing

6. Empty the bladder beforehand if needed
Performing Spirometry

- **Breath in** until the lungs are full
- Hold the breath and **seal the lips tightly** around a clean mouthpiece
- Blast the air out **as forcibly and fast as possible**. Provide lots of encouragement!
- **Continue blowing** until the lungs feel empty
Performing Spirometry

• **Watch** the patient during the blow to assure the lips are sealed around the mouthpiece

• **Check** to determine if an adequate trace has been achieved

• **Repeat the procedure** at least twice more until ideally 3 readings within 100 ml or 5% of each other are obtained
Reproducibility - Quality of Results

Three times FVC within 5% or 0.15 litre (150 ml)
Spirometry - Possible Side Effects

• Feeling light-headed
• Headache
• Getting red in the face
• Fainting: reduced venous return or vasovagal attack (reflex)
• Transient urinary incontinence

Spirometry should be avoided after recent heart attack or stroke
Spirometry - Quality Control

• Most common cause of inconsistent readings is poor patient technique
  ✓ Sub-optimal inspiration
  ✓ Sub-maximal expiratory effort
  ✓ Delay in forced expiration
  ✓ Shortened expiratory time
  ✓ Air leak around the mouthpiece

• Subjects must be observed and encouraged throughout the procedure
Spirometry – Common Problems

- Inadequate or incomplete blow
- Lack of blast effort during exhalation
- Slow start to maximal effort
- Lips not sealed around mouthpiece
- Coughing during the blow
- Extra breath during the blow
- Glottic closure or obstruction of mouthpiece by tongue or teeth
- Poor posture – leaning forwards
Lung Volumes

TLC < 80% > 70% of predicted mild restriction

TLC < 70% > 60% of predicted moderate restriction

TLC < 60% of predicted severe restriction
Diffusion Capacity (DLCO)

- >60 % predicted and <LLN – mild
- 40-60% predicted – moderate
- <40% predicted – severe
**Interpreting Pulmonary Function Tests**

Confirm validity (consistent, reproducible effort and flow loops)

- **FVC/FVC**
  - Adults: < LLN (ATS criteria)
  - or < 70% (GOLD criteria)
  - 5 to 18 years of age: < 85% of predicted

  - Yes
    - FVC: Adults: < LLN
    - 5 to 18 years of age: < 85% of predicted
      - Yes
        - **Obstructive defect**
          - Grade severity (Table 3)
          - **Bronchodilator therapy**
            - Increase in FVC or FEV₁: Adults: > 12% and ≥ 200 ml.
            - 5 to 18 years of age: > 10% of predicted
              - Yes
                - Reversible obstruction (asthma)
              - No
                - Irreversible obstruction
                  - Consider differential diagnosis (Table 4)
          - **Bronchodilator therapy**
            - Increase in FVC: Adults: > 12% of predicted
            - 5 to 18 years of age: > 80% of predicted
              - Yes
                - Reversible obstruction with air trapping (likely chronic obstructive pulmonary disease)
              - No
                - Consider differential diagnosis (Tables 4 and 5)
      - No
        - Mixed pattern
          - Grade severity (Table 3)
          - **Bronchodilator therapy**
            - Increase in FVC: Adults: > 12% and ≥ 200 ml.
            - 5 to 18 years of age: > 10% of predicted
              - Yes
                - Reversible obstruction (asthma)
              - No
                - Irreversible obstruction
                  - Consider differential diagnosis (Table 4)
          - **Bronchodilator therapy**
            - Increase in FVC: Adults: > 12% of predicted
            - 5 to 18 years of age: > 80% of predicted
              - Yes
                - Reversible obstruction with air trapping (likely chronic obstructive pulmonary disease)
              - No
                - Consider differential diagnosis (Tables 4 and 5)
    - No
      - Mixed pattern
        - Grade severity (Table 3)
        - **Bronchodilator therapy**
          - Increase in FVC: Adults: > 12% and ≥ 200 ml.
          - 5 to 18 years of age: > 10% of predicted
            - Yes
              - Reversible obstruction (asthma)
            - No
              - Irreversible obstruction
                - Consider differential diagnosis (Table 4)
          - **Bronchodilator therapy**
            - Increase in FVC: Adults: > 12% of predicted
            - 5 to 18 years of age: > 80% of predicted
              - Yes
                - Reversible obstruction with air trapping (likely chronic obstructive pulmonary disease)
              - No
                - Consider differential diagnosis (Tables 4 and 5)

- No
  - **Restrictive pattern**
    - Grade severity (Table 3)
    - **Bronchodilator therapy**
      - Increase in FVC: Adults: > 12% and ≥ 200 ml.
      - 5 to 18 years of age: > 10% of predicted
        - Yes
          - Reversible obstruction (asthma)
        - No
          - Irreversible obstruction
            - Consider differential diagnosis (Table 4)
      - **Bronchodilator therapy**
        - Increase in FVC: Adults: > 12% of predicted
        - 5 to 18 years of age: > 80% of predicted
          - Yes
            - Reversible obstruction with air trapping (likely chronic obstructive pulmonary disease)
          - No
            - Consider differential diagnosis (Tables 4 and 5)
    - No
      - Mixed pattern
        - Grade severity (Table 3)
        - **Bronchodilator therapy**
          - Increase in FVC: Adults: > 12% and ≥ 200 ml.
          - 5 to 18 years of age: > 10% of predicted
            - Yes
              - Reversible obstruction (asthma)
            - No
              - Irreversible obstruction
                - Consider differential diagnosis (Table 4)
          - **Bronchodilator therapy**
            - Increase in FVC: Adults: > 12% of predicted
            - 5 to 18 years of age: > 80% of predicted
              - Yes
                - Reversible obstruction with air trapping (likely chronic obstructive pulmonary disease)
              - No
                - Consider differential diagnosis (Tables 4 and 5)

- Normal
  - If there is still concern for asthma, order bronchoprovocation
ATS PFT Interpretation
THANK YOU