ASTHMA AND COPD
SIMILARITIES AND DIFFERENCES

Nicola A. Hanania, MD, Marc Peters, MD, Golden, MD
The Overlap Between Asthma and COPD

COPD=chronic obstructive pulmonary disease.

The Dutch Hypothesis

- Various forms of airway obstruction are different expressions of a single disease
  - Chronic nonspecific lung disease (CNSLD)
- Host and environmental factors play a role in pathogenesis
  - Host factors: atopy and AHR
    - Other endogenous factors: sex and age
  - Exogenous factors: allergens, viral infections, smoking (pollutants)
- Diffuse airway obstruction = common pathophysiologic characteristic

The British Hypothesis

- Asthma and COPD are distinct entities caused by different mechanisms
  - Differences in inflammation
  - Airway remodeling vs alveolar remodeling
  - Epidemiology
Outline:
Are There Relationships Between Asthma and COPD?

- Definitions
- Impact
- Risk factors
- Pathophysiology
- Pulmonary function and disease progression
- Clinical presentation
- Treatment strategies
Are There Relationships Between Asthma and COPD?

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## What Is Asthma? What Is COPD?

<table>
<thead>
<tr>
<th>Asthma&lt;sup&gt;1&lt;/sup&gt;</th>
<th>COPD&lt;sup&gt;2&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>• A <strong>chronic inflammatory disorder</strong> of the airways in which many cells and factors play a role</td>
<td>• A <strong>preventable and treatable disease</strong></td>
</tr>
<tr>
<td>• Inflammation results in</td>
<td>• Associated with significant <strong>extrapulmonary effects</strong> and important <strong>comorbid conditions</strong></td>
</tr>
<tr>
<td>– <strong>Recurrent symptoms</strong></td>
<td>• Characterized by airflow limitation that is</td>
</tr>
<tr>
<td>– Variable <strong>airflow obstruction</strong> that is mostly reversible</td>
<td>– <strong>Not fully reversible</strong></td>
</tr>
<tr>
<td>– Increase in existing <strong>bronchial hyperresponsiveness</strong></td>
<td>– <strong>Usually progressive</strong></td>
</tr>
<tr>
<td></td>
<td>– Associated with an <strong>abnormal inflammatory response</strong> to noxious particles or gases</td>
</tr>
</tbody>
</table>

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Are There Relationships Between Asthma and COPD?

- Definitions
- Impact
- Risk factors
- Pathophysiology and
- Pulmonary function and disease progression
- Clinical presentation
- Treatment strategies
The Burden of Asthma

- Asthma is one of the most common chronic diseases worldwide with an estimated 300 million affected individuals.
- Prevalence increasing in many countries; estimated that there may be an additional 100 million persons with asthma by 2025.
- Each year 180,000 deaths worldwide are attributable to asthma; many of the deaths are preventable, being due to suboptimal long-term medical care and delay in obtaining help during the final attack.
- A major cause of school/work absence
- Health care expenditures very high; developed economies might expect to spend 1-2 percent of total health care expenditures on asthma. Developing economies likely to face increased demand
COPD: Global Burden

- An estimated 210 million people worldwide have COPD.
- COPD is a leading cause of morbidity and mortality worldwide.
- COPD ranks 12th as a burden of disease; by 2020 it is projected to rank 5th.
- More than 3 million people died of COPD in 2005; this represented 5% of all deaths worldwide.
- Total deaths from COPD are projected to increase by >30% over the next 10 years without interventions to decrease risk, particularly exposure to tobacco smoke.
- COPD will become the third-leading cause of death worldwide by 2030.

Are There Relationships Between Asthma and COPD?

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Interactions Between Asthma and COPD

Genetic susceptibility

Environmental factors
(Allergy, infection, smoking, air pollution)

Bronchial Inflammation
Bronchial Hyperresponsiveness

Asthma

COPD
Genetic Associations that Suggest a Common Origin in COPD & Asthma

- IgE
- BHR
- Rate of FEV1 decline
- Airway thickness

## Precipitating Factors for Asthma and COPD: Similarities and Differences

### Asthma
- Genetic susceptibility
- Airway hyperresponsiveness
- Environmental
  - Allergen exposures
  - Viral respiratory infections
  - Tobacco smoke and air pollution
- Disease triggers
  - Exercise
  - Changes in weather
  - Exposure to cold air
  - Emotional factors
- Endocrine factors

### COPD
- Host factors
  - $\alpha_1$-Antitrypsin deficiency
  - Other genetic factors (?) not yet identified
  - Airway hyperresponsiveness
  - Lung growth: reduced maximal attained pulmonary function
- Environmental factors
  - Tobacco smoke
  - Occupational dusts and chemicals
  - Outdoor and indoor air pollution
  - Infections: history of severe respiratory infection in childhood
  - Socioeconomic factors
Outline:
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Inflammatory Cascade Differs Between Asthma and COPD

**Asthma**
- Allergens
- Epithelial Cells
- CD4+ Cell (Th2)
- Mast Cell
- Eosinophils
- Bronchoconstriction and airway hyperresponsiveness
  - Eotaxin, IL-4, IL-5, IL-13

**COPD**
- Cigarette Smoke
- Epithelial Cells
- Alveolar macrophage
- CD8+ cell (Tc1)
- Neutrophils
- Small airway fibrosis and alveolar destruction
  - TNF-α, IL-8, IL-1β, IL-6

**Reversible**

**Airflow Limitation**

**Not Fully Reversible**

IL = interleukin; TNF = tumor necrosis factor.
Pathophysiologica Changes in Asthma and COPD
Contrasting Histopathology of Asthma and COPD

Asthma
- Inflammation
- Airway Smooth Muscle
- Basement Membrane
- Fibrosis
- Alveolar Disruption

COPD

Structural Changes in Asthma and COPD
### Inflammatory Phenotypes in Asthma vs. COPD

<table>
<thead>
<tr>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Eosinophils and mast cells</td>
<td>- Macrophages and neutrophils</td>
</tr>
<tr>
<td>- Neutrophils (severe)</td>
<td>- Eosinophils (exacerbations)</td>
</tr>
<tr>
<td>- CD 4+ T(_H2) cells</td>
<td>- CD 8+ T cells,</td>
</tr>
<tr>
<td>- LTC4, D4, E4</td>
<td>- LTB4, Interferon (\gamma)</td>
</tr>
<tr>
<td>- Cytokines</td>
<td>- Cytokines</td>
</tr>
<tr>
<td>- IL 4, IL 5, IL 13</td>
<td>- IL 8, IL-1</td>
</tr>
<tr>
<td>- RANTES, eotaxins, MCP-1</td>
<td>- TNF-(\alpha)</td>
</tr>
</tbody>
</table>

Site of Airway Obstruction in Asthma and COPD:
Asthma in Medium Sized Airways, COPD in the Small Airways

Asthma

Emphysema

Chronic Bronchitis

trachea

bronchi

alveoli
However,

- Asthma is often a progressive process with partially reversible component that can involve small peripheral airways.
- CT scans demonstrating increased airway wall thickness like COPD:
  - Volume of lung in density range c/w emphysema: 5% in mild and 23% severe asthmatics.

Sciurba FC Chest 2004:126:17S
Inflammation- Similarities

1. Alveolar inflammation demonstrated in asthma *
2. Severe asthma- BAL with neutrophils **
3. COPD: tissues eosinophils during exacerbations
   – Pts with eosinophils have better response to steroids ***

* Kraft M. Am J Respir Crit Care Med 1996:154:1505
** Wenzel S Am J Respir Crit Care Med 1999:160:1001
*** Chanez P Am J Respir Crit Care Med 1997:155:1529
Pathophysiology of Asthma

- Inflammation in asthma is characterized by eosinophils, CD4+ T-lymphocytes, macrophages and mast cells.
- Prominent pathological features of asthma include:
  - airway hyperresponsiveness
  - episodic bronchospasm in the large airways
  - vasodilation and angiogenesis
- Severe asthma can be classified into two subtypes: eosinophil (+) and eosinophil (-)
- Neutrophils are found in severe, corticosteroid-dependent asthma.
Pathophysiology of COPD

- COPD is a disease characterized by inflammation in:
  - airways
  - systemic circulation
- COPD is a systemic disease that can cause weight loss and muscle weakness
- Prominent pathological features of COPD include:
  - mucus hypersecretion
  - small airway fibrosis
  - alveolar destruction
  - extrapulmonary effects
Outline:
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Pulmonary Function

- Classically
  - Asthma reversible airway obstruction
  - COPD partially reversible
Spirometry Is Essential in Both Asthma and COPD

Asthma

• Necessary to establish a diagnosis\textsuperscript{1}
• Low FEV\textsubscript{1} is strongly predictive of risk for exacerbations\textsuperscript{1,2}
• Important in assessing control\textsuperscript{1}

COPD

• Essential for diagnosis\textsuperscript{3}
• Used to determine severity, which is linked to
  – Treatment decisions
  – Prognosis

Acute Bronchodilator Response Does not Differentiate Between Asthma and COPD: Changes in Responder Classification After Albuterol and Ipatroprium Bromide

Numbers in circles refer to the total classified as positive responders at that visit and those in squares are the nonresponders on the same occasion.

*Reversible defined as ≥12% and 200-mL increase in FEV₁ following 4 puffs (360 mcg) of albuterol.

<table>
<thead>
<tr>
<th>Physiologic Differences Between Asthma and COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elastic recoil</td>
</tr>
<tr>
<td>Asthma: Normal</td>
</tr>
<tr>
<td>COPD: Decreased</td>
</tr>
<tr>
<td>Diffusion capacity ($D_{LCO}$)</td>
</tr>
<tr>
<td>Asthma: Normal or Increased</td>
</tr>
<tr>
<td>COPD: Decreased</td>
</tr>
<tr>
<td>Lung volume</td>
</tr>
<tr>
<td>Asthma: Normal</td>
</tr>
<tr>
<td>COPD: Hyperinflation</td>
</tr>
<tr>
<td>Bronchodilator response</td>
</tr>
<tr>
<td>Asthma: Flow-dominant</td>
</tr>
<tr>
<td>COPD: Volume-dominant</td>
</tr>
</tbody>
</table>

Sciurba FC. *Chest*. 2004;126:117S-124S.
Lung Volumes

- Nonreversible COPD pts 83% had improvement in lung volumes
  - Those with most severe disease > improvement
- Asthma study 15% reversibility in lung volumes not FEV-1

O’Donnel C Eur Respir J 2001:18:914
Smith HR Chest 1992:101:1577
Pulmonary Function

- Comparing spirometry, lung volumes & DLCO in COPD vs incompletely reversible asthma (nonsmokers)
  - DLCO best discriminator
    - COPD - 58-67% predicted
    - Asthma - 85-99% predicted
    - However, for individuals DLCO 80% predicted 77% sensitive and 71% specific in discriminating asthma from COPD

Boulet L Can Respir J 1998:5:270
Fabbri LM Am J Respir Crit Care Med 2003:167:418
Airway Hyperresponsiveness

- Positive Methacholine occurs in nearly all asthmatics, < 5% normals
- 63% of men and 87% of women with COPD show AHR with < 25 mg/ml of metacholine
  - Lower PFT’S associated with >AHR, decline in lung function and mortality
  - Smoking cessation has positive effect on AHR and improves FEV1 greater in those with AHR

Natural History of Asthma

FEV1/Ht^3
(L/m^3)

Normal
Asthma
Smokers with Asthma

Age (Yrs.)

Peat JK. Eur J Respir Dis. 1987
Natural History of COPD

Mannino DM. *Chest.* 2002;121:121S-126S.

Fletcher and Peto, 1977
Physiologic Differences

### Asthma
- Normal DLCO
- Normal lung volume
- Normal elastic recoil
- Flow dominant BD response

### COPD
- Abnormal DLCO
- Hyperinflation
- Decreased elastic recoil
- Volume dominant BD response

Sciurba FC, CHEST 2004;117S-124S
Outline:
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The Clinical Spectrum of Asthma and COPD

- **Asthma**: Symptoms caused by variable airflow obstruction that may be progressive
- **COPD**: Symptoms caused by chronic (progressive) airflow obstruction with superimposed exacerbations

Key Differences in Clinical Presentation Between Asthma and COPD

COPD
- Onset in mid-life.
- Symptoms slowly progressive.
- Long smoking history.
- Dyspnea during exercise.

Asthma
- Onset early in life (often childhood).
- Symptoms vary from day to day.
- Symptoms at night/early morning.
- Allergy, rhinitis, and/or eczema also present.
- Family history of asthma.
## Asthma Imitates Mild/Moderate COPD With Increasing Age

<table>
<thead>
<tr>
<th>Asthma in young age</th>
<th>Asthma in old age</th>
</tr>
</thead>
<tbody>
<tr>
<td>±80% extrinsic</td>
<td>Mainly intrinsic</td>
</tr>
<tr>
<td>Often normal FEV₁</td>
<td>Often reduced FEV₁</td>
</tr>
<tr>
<td>Often reversible obstruction</td>
<td>(60% of patients)</td>
</tr>
<tr>
<td>Remission likely (60%–70% patients)</td>
<td>Often less reversible obstruction</td>
</tr>
<tr>
<td></td>
<td>Remission unlikely (20% patients)</td>
</tr>
</tbody>
</table>

Asthma Clinical Course

Symptoms

Severe

Mild

Time
COPD: Clinical Course

Dyspnea
Exercise Limitation
Exacerbations
Hospitalizations

Systemic Effects
Respiratory Failure
Cardiovascular Disease
COPD Phenotypes

- Biomarkers/Genetics
- Comorbidities (Depression, Cardiac Dis)
- Hyperinflation
- Mucus Hypersecretion
- Airway disease
- Emphysema
- Fibrosis
- Inflammation
- Lung Function - Airflow Limitation
- Exacerbations
- Muscles/Body Mass Index
- Exercise/Activity
- Shortness of Breath Quality of Life
- Emphysema
- Inflammation
Systemic Consequences of COPD

- Weight loss with decreased fat-free mass
- Muscle wasting and weakness
- Cardiac co-morbidity
- Other systemic effects:
  - osteoporosis
  - anemia
  - depression
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<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Controlled (All of the following)</th>
<th>Partly controlled (Any present in any week)</th>
<th>Uncontrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime symptoms</td>
<td>None (2 or less / week)</td>
<td>More than twice / week</td>
<td></td>
</tr>
<tr>
<td>Limitations of activities</td>
<td>None</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td>Nocturnal symptoms / awakening</td>
<td>None</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td>Need for rescue / “reliever” treatment</td>
<td>None (2 or less / week)</td>
<td>More than twice / week</td>
<td></td>
</tr>
<tr>
<td>Lung function (PEF or FEV₁)</td>
<td>Normal</td>
<td>&lt; 80% predicted or personal best (if known) on any day</td>
<td></td>
</tr>
<tr>
<td>Exacerbation</td>
<td>None</td>
<td>One or more / year</td>
<td>1 in any week</td>
</tr>
</tbody>
</table>
### COPD Staging: GOLD Guidelines

<table>
<thead>
<tr>
<th>GOLD Stage</th>
<th>Symptoms</th>
<th>FEV(_1)/FVC*</th>
<th>FEV(_1) (Predicted)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I: Mild</strong></td>
<td>+/−</td>
<td>&lt;70%</td>
<td>≥80%</td>
</tr>
<tr>
<td><strong>II: Moderate</strong></td>
<td>+/−</td>
<td>&lt;70%</td>
<td>≥50%, &lt;80%</td>
</tr>
<tr>
<td><strong>III: Severe</strong></td>
<td>+/−</td>
<td>&lt;70%</td>
<td>≥30%, &lt;50%</td>
</tr>
<tr>
<td><strong>IV: Very severe†</strong></td>
<td></td>
<td>&lt;70%</td>
<td>&lt;30%</td>
</tr>
</tbody>
</table>

*Postbronchodilator values.
†Or FEV\(_1\) <50% plus chronic respiratory failure.

FEV\(_1\) = forced expiratory volume in 1 second; FVC = forced vital capacity.
GOALS OF THERAPY

COPD
- Prevent disease progression
- Relieve symptoms
- Improve exercise tolerance
- Improve health status
- Prevent and treat complications
- Prevent and treat exacerbations
- Reduce mortality

Asthma
- Achieve normal lung function
- No symptoms
- Maintain normal quality of life
- Prevent and treat exacerbations
- Prevent mortality
Nonpharmacologic Approaches

**ASTHMA**
- Identifying and avoiding triggers
  - Allergens, irritants (smoke)
- Vaccination
- Treat underlying conditions that may result in asthma control
  - Allergic rhinitis, sinusitis, gastroesophageal reflux (GERD)
- Asthma education

**COPD**
- All stages of disease
  - Smoking cessation
  - Avoidance of indoor and outdoor occupational exposures
- Vaccinations
- Optimizing nutrition
- Oxygen
- Pulmonary rehabilitation
- Surgical interventions (LVRS, transplantation)
Pharmacologic Therapy

• Two different sets of guidelines
• Two different treatment paradigms
• Similar pharmacologic agents
Medications for Asthma and COPD

**Asthma**
- Anti-inflammatory drugs
  - Corticosteroids
  - Antileukotrienes
  - Cromones
  - Theophylline (?)
- Bronchodilators
  - Short and Long-acting β-agonists
  - Short-acting Anticholinergic
- ICS/LABA combination
- Anti IgE

**COPD**
- Bronchodilators
  - Short and Long-acting β-agonists
  - Short and Long-acting Anticholinergics
  - Theophylline
- Anti-inflammatory drugs
  - Corticosteroids
- ICS/LABA Combination
- Mucoactive drugs
- Antibiotics
- Vaccination
GINA Management Approach Based on Control
Children Aged >5 Years, Adolescents, and Adults

<table>
<thead>
<tr>
<th>Level of Control</th>
<th>Treatment Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controlled</td>
<td>Maintain and find lowest controlling step</td>
</tr>
<tr>
<td>Partly controlled</td>
<td>Consider stepping up to gain control</td>
</tr>
<tr>
<td>Undercontrolled</td>
<td>Step up until controlled</td>
</tr>
<tr>
<td>Exacerbation</td>
<td>Treat as exacerbation</td>
</tr>
</tbody>
</table>

Treatment Steps

Reduce

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
<th>Step 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma Education</td>
<td>Environmental Control</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As-needed rapid-acting $\beta_2$-agonist

Controller options

<table>
<thead>
<tr>
<th>Controller options</th>
<th>Select one</th>
<th>Select one</th>
<th>Add one or more</th>
<th>Add one or both</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-dose inhaled ICS</td>
<td>Low-dose ICS plus LABA</td>
<td>Medium- or high-dose ICS plus LABA</td>
<td>Oral glucocorticosteroid (lowest dose)</td>
<td></td>
</tr>
<tr>
<td>Leukotriene modifier</td>
<td>Medium- or high-dose ICS</td>
<td>Leukotriene modifier</td>
<td>Anti-IgE treatment</td>
<td></td>
</tr>
<tr>
<td>Low-dose ICS plus leukotriene modifier</td>
<td>Sustained-release theophylline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-dose ICS plus sustained-release theophylline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Alternative reliever treatments include inhaled anticholinergics, short-acting oral $\beta_2$-agonists, some long-acting $\beta_2$-agonists, and short-acting theophylline. Regular dosing with short- and long-acting $\beta_2$-agonists is not advised unless accompanied by regular use of an inhaled glucocorticosteroid.

Global Initiative for Asthma. ginasthma.com/Guidelineitem.asp??l1=2&l2=1&intId=60.
### Gold Guidelines
**Stepwise Approach for Managing COPD**

<table>
<thead>
<tr>
<th>Stage</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FEV₁/FVC &lt;0.70</td>
<td>FEV₁/FVC &lt;0.70</td>
<td>FEV₁/FVC &lt;0.70</td>
<td>FEV₁/FVC &lt;0.70</td>
</tr>
<tr>
<td></td>
<td>FEV₁ ≥80% predicted</td>
<td>50% ≤ FEV₁ &lt; 80% predicted</td>
<td>30% ≤ FEV₁ &lt; 50% predicted</td>
<td>FEV₁ &lt; 30% predicted or FEV₁ &lt; 50% predicted plus chronic respiratory failure</td>
</tr>
</tbody>
</table>

#### Golden Guidelines
- **Stage I**: FEV₁/FVC <0.70 or FEV₁ <50% predicted
- **Stage II**: FEV₁/FVC <0.70 or 50% ≤ FEV₁ <80% predicted
- **Stage III**: FEV₁/FVC <0.70 or 30% ≤ FEV₁ <50% predicted
- **Stage IV**: FEV₁/FVC <0.70 or FEV₁ <30% predicted or FEV₁ <50% predicted plus chronic respiratory failure

#### Active Reduction of Risk Factors
- Active reduction of risk factor(s); influenza, pneumococcal, and other vaccinations as needed
- *Add* short-acting bronchodilator (when needed)

#### Additional Treatments
- *Add* regular treatment with one or more long-acting bronchodilators (when needed); *Add* pulmonary rehabilitation
- *Add* inhaled glucocorticosteroids if repeated exacerbations
- *Add* long-term oxygen if chronic respiratory failure; *Consider* surgery

Response to Bronchodilators

- **ASTHMA**
  - **SABA**
    - Tolerance
    - Dosed PRN
  - **LABA**
    - Monotherapy assoc. with increased frequency of exacerbations
    - Little tolerance
  - **Anticholinergic**
    - Efficacious in acute attack

- **COPD**
  - **SABA**
    - No tolerance
    - Regularly dosed
  - **LABA**
    - Monotherapy assoc. with decreased frequency of exacerbations
    - Little tolerance
  - **Anticholinergic**
    - Efficacious in acute and stable disease

Donohue JF, CHEST 2004;125S-137S
Response to Inhaled corticosteroids

- **ASTHMA**
  - First line therapy even in mild persistent disease
  - Improve lung function and symptoms and health status, decrease exacerbations,
  - Decrease mortality
  - Significant anti-inflammationary effects
  - Decreased response in smokers

- **COPD**
  - Modest effect on long-term deterioration in lung function
  - Significant decrease in exacerbations (30%)
  - Significant improvement in health status
  - No effect on mortality
  - Recommended by guidelines for severe disease and in patients with recurrent exacerbations
  - ? Increase risk of pneumonia
Acute Exacerbations of Asthma & COPD
Differences in Management of Acute Asthma and COPD

**Acute Asthma**
- Mostly treated in ED or outpatient
- Short-acting bronchodilators
- Systemic corticosteroids
- Oxygen therapy
- No need for antibiotics
- Non-invasive ventilation usually not effective

**Acute COPD**
- Low threshold for admission
- Short-acting bronchodilators
- Systemic corticosteroids
- Controlled oxygen therapy
- Antibiotics
- Non-invasive ventilation
  - Level A indication
Novel Therapeutic Targets: Asthma

New Corticosteroids
New Bronchodilators

PDE4 Inhibitors

Transcription Factor & Kinase Inhibitors
- NF-κB
- NF-AT
- GATA3
- P38 MAP kinase
- JNK
- Syk

Cell Adhesion Blockers
- ICAM1
- VLA4

Mediator Antagonists
- antihistamines
- leukotriene
- prostaglandins
- endothelin
- adenosine
- tryptase
- NO

Vasodilation & Angiogenesis

CD4+ Th2 Cell

Mast Cell

Eosinophil

Airway Hyperresponsiveness

Epithelial Denudation
Subepithelial Fibrosis

Macrophage / Dendritic Cell

Allergen

Immunotherapy
- Specific AG
- T-cell peptides
- BCG, CpG

Anti-Allergy Drugs
- anti-IgE
- anti-CD23

Interleukin Inhibitors
- IL-5, 4, 13
- IL-9
- IL-1

TNF-α Inhibitors

Cytokines
- IL-10
- IFN-γ
- IL-12/18

Chemokine Receptor Inhibitors
- CCR2, 3, 4 & 8

Novel Therapeutic Targets: COPD

Smoking Cessation

New Bronchodilators

PDE4 Inhibitors

Transcription Factor & Kinase Inhibitors
  • NFkB
  • P38 MAPK
  • PI3Kγ

Mediator Antagonists
  • CXCR2
  • CCR2
  • TNF-α

Anti-Fibrotic Therapy
  • TGF-β1

Anti-Oxidants
  • iNOS Inhibitors

Protease Inhibitors
  • NE
  • MMP
  • SLPI
  • α1-AT

Muco-Regulators
  • EGF rec kinase

Alveolar Repair
  • retinoids

Similarities Between Asthma and COPD

- Common disorders
- Both associated with significant morbidity, mortality, and health care cost/utilization
- Often under-diagnosed (misdiagnosed), under-treated
- Airway obstruction and hyperresponsiveness underly pathophysiology
- Inflammation plays a key role for both
- Complex interaction between genetic predisposition and the environment, may have common susceptibility genes
- Associated with progressive loss of lung function
- Heterogeneous (variable) natural history & clinical course
- The presence or absence of reversibility of FEV1 does not distinguish COPD from asthma
## Differences Between Asthma and COPD

**Asthma**
- Usually intermittent airflow obstruction but sometimes has a less reversible obstruction
- High levels of bronchial responsiveness
- Cellular inflammation including eosinophils, mast cells, T lymphocytes, in severe disease neutrophils
- Broad inflammatory mediator responses
- Airway remodeling (epithelial injury and fibrosis)
- Significant response to corticosteroids
- Improvement in airway obstruction with bronchodilators and corticosteroids

**COPD**
- Progressive airflow obstruction
- Most patients have increased bronchial responsiveness
- Cellular inflammation including neutrophils, macrophages, eosinophils and mast cells may occur in exacerbations
- Cytokine, chemokine, protease responses
- Emphysema (lung destruction) frequent
- Poor response to ICS
- Smaller bronchodilator and corticosteroid response
- Systemic consequences

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Bleecker ER. *Chest.* 2004;126(suppl 2):93S-95S.