ALLERGIC PHENOTYPES: ASTHMA

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Chronic inflammatory disease of airways in which multiple mechanisms and cells are involved

Bronchial hyperresponsiveness causes recurrent episodes of cough, dyspnea, chest tightness and wheezing, specially at night or early morning

Episodes associated with variable airflow obstruction, reversible spontaneously or with treatment

Hipocrates (460-360 BC) defined asthma as “a disease commonly seen in fishermen, taylors and metal workers”
• 300 million people worldwide


  o **6-7 yrs:**
    o Boys: increase from 7% to **10.7 %**
    o Girls: increase from 5.3% to **8.2 %**

  o **13-14 yrs**: no changes (9 %)

  o **80%** is IgE mediated (allergic asthma)
  o Some countries: stable

More frequent in **developed countries**, more **populated areas** and specially **urban environment**

- **Comorbidities:**
  - Rhinitis
  - Polyposis
  - CRS

- Major cause of **work and school loss**

- **High cost** in hospitalization & medication

- **Allergic asthma** most common

*Global Initiative for Asthma (GINA Updated 2014)*
Global Initiative for Asthma (GINA Updated 2014)
ASTHMA

MULTIFACTORIAL DISEASE

GENETIC FACTORS

ENVIRONMENTAL FACTORS
NATURAL HISTORY

50% <10 yrs old
33% < 40 yrs old

DIFFERENT PHENOTYPES
MAIN CHARACTERISTICS

Inflammation

Airway Hyperreactivity

Reversible airflow obstruction

DIFFERENT TYPES OF INFLAMMATION

NOT ALWAYS REVERSIBLE (FIXED)

NOT EXCLUSIVE
ASTHMA PHENOTYPES
Clinicians are already familiar with the phenotyping exercise consisting of identifying visible properties associated with asthma. Yet, phenotypic descriptions in clinical notes and medical publications are often imprecise and frequently over-lapping.

Agache I. Curr Opin Allergy Clin Immunol 2013, 13:249–256

Different approaches (cluster analysis, biomarkers, clinical presentation....)

Different underlying disease mechanisms

NO strong relationship between pathological features and clinical patterns/treatment response except for some forms of severe asthma

Global Initiative for Asthma (GINA Updated 2014)
According to GINA 2014, many phenotypes have been identified.

Some of the most common are:

- Allergic Asthma
- Non-Allergic Asthma
- Late-Onset Asthma
- Asthma with Fixed Airflow Limitation
- Asthma with Obesity

Severe Asthma?
NERD?
Overlap Asthma/COPD?
ALLERGIC ASTHMA:

- Starts in childhood
- Associated with family history of allergic disease (eczema, allergic rhinitis, food/drug allergy)
- Eosinophilic airway inflammation
- Respond well to ICS treatment

NON-ALLERGIC ASTHMA:

- Not associated with allergy
- Adults
- Neutrophilic/eosinophilic/paugranulocytic inflammation
- Respond less well to ICS
ASTHMA PHENOTYPES

LATE-ONSET ASTHMA:
- Adults
- Women
- Non allergic
- Require higher doses of ICS/relatively refractory to ICS

ASTHMA WITH FIXED AIRFLOW LIMITATION:
- Long-standing asthma
- Airway wall remodeling

ASTHMA WITH OBESITY:
- Obese patients
- Prominent respiratory symptoms
- Little eosinophilic airway inflammation
"IN VITRO" DIAGNOSIS
OCCUPATIONAL ASTHMA

INFLAMMATION
BRONCHIAL HYPERREACTIVITY
BRONCHIAL OBSTRUCTION
OCCUPATIONAL ASTHMA

- Spirometry
- Bronchodilator Test
- BHR (Metacholine)
- Nitric Oxide
- Induced Sputum
- PEF Variability
OCCUPATIONAL ASTHMA

SPECIFIC INHALATION CHALLENGE (CHAMBERS)

SPECIFIC INHALATION CHALLENGE (WORKPLACE)
SEVERE ASTHMA PHENOTYPES

**Clinical Phenotypes**
- Asthma with frequent severe exacerbations
- Asthma with fixed airflow obstruction
- Corticosteroid-dependent asthma

**Inflammatory Phenotypes**
- Persistent severe eosinophilic asthma
- Noneosinophilic severe asthma with increased neutrophils
- Severe paucigranulocytic asthma

**Clinical Phenotypes of Childhood Asthma**
- According to age range:
  - Wheezing in preschool children (0-5 years)
  - School-aged children (6-11 years)
  - Adolescents (12 to 17 years)
- According to treatment response
- According to the course of the disease
  - Rare but severe exacerbations
  - Brittle asthma
  - Severe asthma with sensitization to fungi
- Inflammatory phenotypes
  - In stable asthma
  - In acute asthma
SEVERE ASTHMA ENDOTYPES

• Classification where asthma is divided into different entities with specific biological causal mechanisms (asthma endotypes)
• An asthma endotype can encompass various phenotypes, and a specific phenotype may be present in several endotypes
• Cluster analyses

<table>
<thead>
<tr>
<th>PRACTALL Consensus(^a)</th>
<th>Wenzel(^b)</th>
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</thead>
<tbody>
<tr>
<td>• Aspirin-sensitive asthma</td>
<td>• Early-onset allergic asthma</td>
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<tr>
<td>• Allergic bronchopulmonary mycosis</td>
<td>• Persistent eosinophilic asthma</td>
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<tr>
<td>• Allergic asthma (adults)</td>
<td>• Allergic bronchopulmonary mycosis</td>
</tr>
<tr>
<td>• Preschoolers with wheezing and positive asthma</td>
<td>• Obese female</td>
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<td>predictive indices</td>
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<tr>
<td>• Severe late-onset hypereosinophilic asthma</td>
<td>• Neutrophilic asthma</td>
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<td>• Asthma in cross-country skiers</td>
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Treatment

- Education
- Triggers
- Follow-up
- Immunotherapy
- Pharmacotherapy
DIAGNOSIS

PERSONALIZED MANAGEMENT

PHENOTYPE

MECHANISMS

ASTHMA

DIAGNOSIS
PHENOTYPE-ORIENTED TREATMENT

• Add-on treatment without phenotyping:
  Add controller meds (Teophyline/LTRs)

• Sputum-guided treatment:
  Adjust ICS based on sputum results

• Phenotype-guided add-on treatment:
  – NERD: LTRs (evidence B)
  – Severe allergic with high IgE: Omalizumab (evidence A)
Thank you for your attention

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