Allergic Rhinitis and Asthma - the link

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The Global Burden of Asthma

- Asthma is one of the most common chronic diseases in the world, especially in children.
- An estimated 300 million people are affected worldwide.
- Asthma prevalence increases as communities adopt western lifestyles and become urbanised.
- Asthma mortality is also increasing and is alarmingly high.

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Allergic rhinitis

- Allergic rhinitis is a global health problem affecting 10 to 50% of the population.
- Its prevalence is increasing.
- Although it is not usually a severe disease, rhinitis alters social life and affects school performance and work productivity.
- Costs incurred by rhinitis are substantial.
- Most importantly, Allergic rhinitis is a risk factor for asthma.

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International Study of Asthma & Allergies in Childhood (ISAAC III)

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Impairment Due to Allergic Rhinitis: work productivity and activity impairment questionnaire

- Ability to do daily activities: 96%
- Work productivity: 91%
- Classroom productivity: 93%
- Any work time missed: 23%
- Any classroom time missed: 23%

AR markedly impairs the QOL of patients


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ASIAN SURVEY: Impact of AR on Asthma in Child’s Quality of Life

Most patients (73%) had pre-existing AR when diagnosed with asthma. Most troublesome symptom was wheezing (17%) and coughing (17%).

Erkka V and Pawankar R, 2007

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Asthma and Rhinitis

- Common Triggers
- Epidemiological Link
- Common inflammatory processes
- Pathophysiological links
- Treatment Outcomes
Allergic Rhinitis Is a Risk Factor for Asthma

- 80% of asthmatics have rhinitis and 40% of rhinitis patients have asthma

23-year follow-up of college freshmen undergoing allergy testing; data based on 738 individuals (69% male) with average age of 40 years. Adapted from Settipane RJ et al Allergy Proc 1994;15:21-25.

% of patients who developed asthma

<table>
<thead>
<tr>
<th>Condition</th>
<th>% of Patients Who Developed Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>No allergic rhinitis at baseline (n=528)</td>
<td>3.6</td>
</tr>
<tr>
<td>Allergic rhinitis at baseline (n=162)</td>
<td>10.5</td>
</tr>
</tbody>
</table>

p<0.002
Allergic Rhinitis: Risk Factor for Asthma Development

Perennial rhinitis often precedes asthma

10 year prognosis for childhood (3-17 years old) allergic rhinitis

Allergic rhinitis as a risk factor for the development of asthma

Incidence of asthma over an 8-year period in the Copenhagen Allergy Study

Linneberg et al. Allergy 2002;57:1048

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Risk factor in Children

- Physician diagnosed allergic rhinitis in children
  - By 6 years of age 42%
  - Began in first year 77%
  - Began after first year 57%
  - Prick skin test positive * 20%
- Development of asthma by 6 years
  - When rhinitis began in first year 23% (p<.005)
  - When rhinitis began after first year 13%


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**Allergic Rhinitis and Asthma Have Common Triggers**

- **Outdoor allergens**
  - Pollens
  - Molds

- **Indoor allergens**
  - House–dust mites
  - Animal dander
  - Insects (e.g., cockroach allergen)

- **Nonsteroidal Anti-inflammatory Drugs (NSAIDs)** (e.g., aspirin)
Early and Late Phase Responses in Allergic Rhinitis and Asthma

Upper Airways (Allergic rhinitis)

Score for nasal symptoms
- Sneezing
- Nasal pruritus
- Congestion
- Rhinorrhea

Immediate (early) phase

Late phase

Time postchallenge (hours)

0 1 2 3 4 5 6 7 8 9 10 11 12 24

Time (hours)

0 1 2 3 4 5 6 7 8 9 10 11 12 24

FEV<sub>1</sub> (% change)

Lower Airways (Asthma)


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Common Inflammatory Cells and Mediators


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Bronchial biopsies in patients with SAR

Chakir et al, Allergy Clin Immunol 2000

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Eosinophilic inflammation in submucosa

Chanez et al, Am J Respir Crit Care Med 1999
Nasal provocation results in bronchial inflammation

Nasal provocation results in bronchial inflammation

Baseline: n = 14, p = 0.03

Sputum eosinophils (%)

0 0.5 1 1.5 2

Baseline 24 hrs after nasal allergen challenge

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**Bronchial Allergen Challenge Produced Nasal Inflammation**

- **Blood** (N = 16)
  - Eosinophils ($10^6$ Cells/mm$^2$)
  - $T_0 = 0$ vs control ($T_0$);
  - $T_{24} = 24$-hr postchallenge.
  - * $P <.05$ vs control ($T_0$);
  - † $P <.01$ vs allergic patients ($T_0$).

- **Bronchial Subepithelium** (N = 16)
  - Eosinophils (No. Cells/mm$^2$)
  - $T_0$ vs control ($T_0$);
  - * $P <.05$ vs allergic patients ($T_0$).

- **Nasal Lamina Propria** (N = 16)
  - Eosinophils (No. Cells/mm$^2$)
  - $T_0$ vs control ($T_0$);
  - * $P <.05$ vs allergic patients ($T_0$).

- $T_0 = 0$ before challenge; $T_{24} = 24$-hr postchallenge.


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Correlation between nasal and bronchial inflammation


There exists nasal inflammation in asthma despite the presence of allergic rinitis in atopic individuals (20 to 66 yr old)

EOS in nasal mucosa (asthmatics)

EOS in bronchial mucosa (asthmatics)

r = 0.851, p < 0.001

(n = 17)
Nasal Steroids Reduced Asthma Symptoms in Patients With Seasonal AR and Seasonal Asthma


<table>
<thead>
<tr>
<th>Treatment</th>
<th>Placebo (n = 14)</th>
<th>Flunisolide (n = 19)</th>
<th>Cromolyn (n = 14)</th>
<th>BDP (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma Chest Symptom* Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Weekly Difference From Baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7/11</td>
<td>-5</td>
<td>0</td>
<td>-5</td>
<td>0</td>
</tr>
<tr>
<td>7/17</td>
<td>-5</td>
<td>0</td>
<td>-5</td>
<td>0</td>
</tr>
<tr>
<td>7/24</td>
<td>-5</td>
<td>0</td>
<td>-5</td>
<td>0</td>
</tr>
<tr>
<td>7/31</td>
<td>-5</td>
<td>0</td>
<td>-5</td>
<td>0</td>
</tr>
<tr>
<td>8/7</td>
<td>-5</td>
<td>0</td>
<td>-5</td>
<td>0</td>
</tr>
<tr>
<td>8/14</td>
<td>-5</td>
<td>0</td>
<td>-5</td>
<td>0</td>
</tr>
<tr>
<td>8/21</td>
<td>-5</td>
<td>0</td>
<td>-5</td>
<td>0</td>
</tr>
<tr>
<td>8/28</td>
<td>-5</td>
<td>0</td>
<td>-5</td>
<td>0</td>
</tr>
<tr>
<td>9/4</td>
<td>-5</td>
<td>0</td>
<td>-5</td>
<td>0</td>
</tr>
<tr>
<td>9/11</td>
<td>-5</td>
<td>0</td>
<td>-5</td>
<td>0</td>
</tr>
<tr>
<td>9/18</td>
<td>-5</td>
<td>0</td>
<td>-5</td>
<td>0</td>
</tr>
</tbody>
</table>

*chest tightness and wheezing

Daily Ragweed Pollen Count (Grain/m^3)

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Antihistamine Improved Asthma Symptoms in Patients With Seasonal AR and Asthma

* P <.05 vs placebo.
Inhibition of the bronchial allergic reaction by an antileukotriene and an antihistamine

% inhibition of the allergen induced drop in FEV₁

N = 16

early late

montelukast
loratadine
montelukast and loratadine

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Percentage of Children After 3 Years of SIT vs. Control With or Without Asthma


Odds ratio 2.52

<table>
<thead>
<tr>
<th>% of patients</th>
<th>SIT</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma (-)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma (+)</td>
<td></td>
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</tr>
</tbody>
</table>

N=151

SIT = allergen-specific immunotherapy

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Asthma and allergic rhinitis – Two related conditions linked by one common airway

**Anatomy/Physiology**
- Upper and lower airways are contiguous
- Functional linkage - nose vs. mouth breathing
- Similar histology

**Same mediators**
- IgE
- Cytokines
- Histamine
- Leukotrienes

**Same cells**
- Mast cells
- Eosinophils
- Th2 cells
- CD34 stem cells (the bone marrow connection)

**Same drugs**
- Anti-IgE
- Steroids (ICS/INS)
- Antihistamines (?)
- Antileukotrienes

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Increased Risk of ER Visits for Asthma in AR Patients

Patients with AR and asthma had an increased risk of ER visits

Bousquet J, et al. Poster presented at the (EAACI) 2004 (Post hoc analysis of medical resource use/asthma attacks in asthmatic patients with and without concomitant allergic rhinitis over 52 weeks)
Increased Risk of Hospitalization for Asthma in AR Patients

Patients with AR and asthma had an increased risk of hospitalization.


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Treating Allergic Rhinitis Decreased Asthma-Related Resource Utilization

Retrospective cohort study of costs over a period of up to one year incurred by patients 12 to 60 years of age with both allergic rhinitis and asthma. Adapted from Crystal-Peters J et al J Allergy Clin Immunol 2002;109(1):57-62.

Patients untreated for allergic rhinitis (n=1357) vs Patients treated for allergic rhinitis (n=3587)

61% fewer hospitalizations in patients treated for AR
Asthma and Allergic Rhinitis – Two Related Conditions Linked by One Common Airway

Module 1: The underlying mechanisms of the United Airway concept

Asthma and Allergic Rhinitis: WAO Online Lecture Series
Interactions Nose – Lower Airways: Possible Mechanisms of Relationship

- Central sensitization and nasopharyngo-bronchial reflexes
- Drainage of inflammatory material
- Mouth breathing
- ↓ Air warming & humidification
- ↓ Particle/irritant trapping
- (↓ Nitric oxide)
- Systemic propagation of (para)nasal inflammation

Adapted from Togias A. JACI 2003  Ruby Pawankar, NMS
Link between Rhinitis and Asthma

- **Allergic Rhinitis**
  - Allergen
  - Histamine, Tryptase, Cys LTs, PGs, IL-4, IL-5, IL-6, IL-13, GM-CSF, TNF-α

- **Th2**
  - IL-4, IL-5, IL-6, IL-13, RANTES, Eotaxin
  - CCR3, CCR4, CCR5

- **Bone marrow**
  - CysLT₁ R, CysLT₂ R, IL-5 R, IL-3 R, GM-CSF R

- **Eosinophil**
  - Eo /Ba progenitor
  - IL-4, IL-5, IL-6, IL-13, GM-CSF

- **Asthma**
  - Blood vessel
  - Upregulated Adhesion Molecules & chemoattractants
  - VLA-4, VCAM-1

Asthma and Rhinitis

One Airway, One Disease?

Togias: ‘Asthma and rhinitis are manifestations of one syndrome, the chronic allergic respiratory syndrome’

JACI 2003

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We look forward to welcoming you to the
2011 World Allergy Congress
CANCÚN, MÉXICO
4-8 December 2011
www.worldallergy.org/wac2011

A meeting of the
In collaboration with

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# 2nd MIDDLE EAST - ASIA ALLERGY ASTHMA IMMUNOLOGY CONGRESS

**Advances in Allergy, Asthma & Clinical Immunology:**
Towards Optimal Patient Care

28 April – 1 May 2011
Grand Hyatt, Dubai - UAE

[www.MEAAIC.org](http://www.MEAAIC.org)

## Objectives
- To Provide Insights into the Fundamentals of Allergy, Asthma & Clinical Immunological Diseases
- To Highlight the most Recent Advances and Developments in Allergy, Asthma & Clinical Immunological Diseases Leading to Optimal Patient Care

## Key Reasons to Attend MEAAIC
- Attend State of the Art Lectures by the "Who's Who" in the field of Allergy, Asthma and Clinical Immunology
- Participate in Practical, Clinic-Friendly Workshops on Asthma, Anaphylaxis, Spirometry, Rhinoscopy, Bronchoscopy, Immunotherapy, Sleep Apnea & more
- Network with Others in your field/area of interest
- Receive CME Credits
- Present your own Original Work to Key International Opinion Leaders

## Topics

| Immunotherapy - Subcutaneous & Sublingual | Immune Deficiency |
| Allergic Rhinitis - Mechanisms, Quality of Life & Evidence Based Treatment | Food Allergy |
| Asthma - Phenotypes, Endotypes, Severe Asthma & Evidence Based Treatment | Anaphylaxis |
| Allergy Testing - Skin vs Serum IgE | Rhinosinusitis and Rhinoconjunctivitis |
| Atopic Dermatitis & Urticaria | Asthma vs COPD |
| | Sleep Apnoea |

## Who Should Attend
Delegates from the Middle East - Asia region and beyond. Clinicians, researchers, and other allied health professionals with interests in:
- Asthma
- Allergy
- Clinical Immunology
- Pediatrics
- Pulmonology
- Ophthalmology
- Dermatology
- ENT

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**International & Regional Faculty to be Announced Shortly**

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