Allergic Rhinitis and Its Impact on Asthma

Rhinitis: A Risk Factor for Asthma?

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Aarhus University Hospital,
Denmark
Rhinitis and asthma

- **Rhinitis**
  - SIT-SLIT Evidence A

- **SIT**
  - Evidence ?

- **SLIT**
  - Evidence B

- **Asthma**
  - SIT-SLIT Evidence A
  - Evidence ?
Onset of asthma and allergic rhinitis

49-64% rhinitis present before asthma

21-25% rhinitis and asthma started simultaneous

Settipane 1986
Maternowski 1962
Allergic Rhinitis and Asthma: Adults

• Rhinitis is a significant risk factor for asthma
  – risk of developing asthma is increased in patients with:
    • persistent or severe allergic rhinitis symptoms
    • physician-documented sinusitis
  – risk of developing asthma is 3 to 5 times higher than normal for patients with allergic rhinitis

**Allergic Rhinitis Precedes Asthma: The Allergic March**

<table>
<thead>
<tr>
<th>Population</th>
<th>Outcome</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK&lt;sup&gt;1&lt;/sup&gt; (n = 7,225)</td>
<td>Asthma at 7 years</td>
<td>7.1</td>
</tr>
<tr>
<td>USA&lt;sup&gt;2&lt;/sup&gt; (n = 770)</td>
<td>Asthma at 5–9 years</td>
<td>2.9</td>
</tr>
<tr>
<td>Australia&lt;sup&gt;3&lt;/sup&gt; (n = 8,585)</td>
<td>Asthma at 7 years</td>
<td>3.9</td>
</tr>
<tr>
<td>USA&lt;sup&gt;4&lt;/sup&gt; (n = 1,021)</td>
<td>Asthma life 23-year follow-up</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Cumulative incidence rate of asthma

![Cumulative incidence rate of asthma graph]

### Number at risk

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>3163</td>
<td>3158</td>
<td>3153</td>
<td>3064</td>
<td>2967</td>
</tr>
<tr>
<td>Atopy, no rhinitis</td>
<td>704</td>
<td>701</td>
<td>698</td>
<td>669</td>
<td>642</td>
</tr>
<tr>
<td>Non-allergic rhinitis</td>
<td>1377</td>
<td>1396</td>
<td>1358</td>
<td>1268</td>
<td>1199</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>1217</td>
<td>1208</td>
<td>1194</td>
<td>1093</td>
<td>1038</td>
</tr>
</tbody>
</table>

### Probability of developing asthma, % (95% CI)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Atopy, no rhinitis</th>
<th>Non-allergic rhinitis</th>
<th>Allergic rhinitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0.2 (0.1–0.5)</td>
<td>0.5 (0.3–0.9)</td>
<td>0.8 (0.5–1.2)</td>
</tr>
<tr>
<td>2</td>
<td>0.6 (0.2–1.5)</td>
<td>1.1 (0.6–2.3)</td>
<td>1.9 (1.1–3.2)</td>
<td>1.9 (1.1–3.2)</td>
</tr>
<tr>
<td>4</td>
<td>0.9 (0.5–1.5)</td>
<td>1.7 (1.1–2.5)</td>
<td>2.2 (1.5–3.1)</td>
<td>3.1 (2.3–4.1)</td>
</tr>
<tr>
<td>6</td>
<td>1.6 (1.0–2.4)</td>
<td>2.5 (1.7–3.5)</td>
<td>3.0 (2.2–4.1)</td>
<td>3.8 (2.9–5.1)</td>
</tr>
</tbody>
</table>

*Lancet 2008; 372: 1049–57*
Baseline characteristics of participants with and without asthma onset

<table>
<thead>
<tr>
<th></th>
<th>No asthma onset (n=6321)</th>
<th>Asthma onset (n=140)</th>
<th>p†</th>
<th>Crude RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women, n (%)</td>
<td>3263 (50.2)</td>
<td>91 (65.0)</td>
<td>0.0005</td>
<td>1.84 (1.30-2.66)</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>34.2 (7.3)</td>
<td>34.5 (8.7)</td>
<td>0.591</td>
<td>1.06* (0.90-1.25)</td>
</tr>
<tr>
<td>Body-mass index, kg/m², mean (SD)</td>
<td>23.8 (3.8)</td>
<td>25.0 (5.9)</td>
<td>0.017</td>
<td>1.28* (1.12-1.47)</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td></td>
<td></td>
<td>0.607</td>
<td></td>
</tr>
<tr>
<td>Non-smokers</td>
<td>2669 (43.2)</td>
<td>63 (45.7)</td>
<td>1.00 (reference)</td>
<td></td>
</tr>
<tr>
<td>Ex-smokers</td>
<td>1235 (20.0)</td>
<td>31 (22.5)</td>
<td>1.17 (0.75-1.83)</td>
<td></td>
</tr>
<tr>
<td>Moderate smokers</td>
<td>1397 (22.6)</td>
<td>25 (18.1)</td>
<td>0.86 (0.56-1.30)</td>
<td></td>
</tr>
<tr>
<td>Heavy smokers</td>
<td>882 (14.3)</td>
<td>19 (13.8)</td>
<td>0.85 (0.45-1.60)</td>
<td></td>
</tr>
<tr>
<td>Total IgE, mean (SD)</td>
<td>81.7 (195.8)</td>
<td>135.5 (300.7)</td>
<td>0.017</td>
<td>1.33* (1.11-1.60)</td>
</tr>
<tr>
<td>Atopy, n (%)</td>
<td>1859 (29.4)</td>
<td>62 (44.3)</td>
<td>0.0001</td>
<td>1.91 (1.37-2.66)</td>
</tr>
<tr>
<td>Asthma-like symptoms, n (%)</td>
<td>1307 (20.7)</td>
<td>51 (36.4)</td>
<td>&lt;0.0001</td>
<td>2.20 (1.56-3.10)</td>
</tr>
<tr>
<td>Family history of asthma, n (%)</td>
<td>657 (10.4)</td>
<td>30 (21.4)</td>
<td>&lt;0.0001</td>
<td>2.35 (1.57-3.52)</td>
</tr>
<tr>
<td>Respiratory infection in childhood, n (%)</td>
<td>539 (9.0)</td>
<td>17 (13.4)</td>
<td>0.085</td>
<td>1.57 (0.94-2.61)</td>
</tr>
<tr>
<td>FEV₁ L/s ‡, mean (SD)</td>
<td>3.78 (0.47)</td>
<td>3.57 (0.54)</td>
<td>&lt;0.0001</td>
<td>0.64* (0.55-0.76)</td>
</tr>
<tr>
<td>Bronchial hyper-responsiveness, n (%)</td>
<td>414 (7.7)</td>
<td>27 (25.2)</td>
<td>&lt;0.0001</td>
<td>4.06 (2.63-6.28)</td>
</tr>
</tbody>
</table>

FEV₁=forced expiratory volume in 1 s. *Relative risk per roughly 1 SD increase (7.1 year for age, 3.8 kg/m² for body-mass index, 1.58 for log total IgE, and 0.47 L for FEV₁). †For difference between groups using t test for continuous variables and χ² for categorical variables. ‡FEV₁=residual FEV₁+ mean FEV₁.
Serum ECP predicts asthma in allergic rhinitis

- 67 seasonal allergic rhinitis (grass)
- 7 years follow up
- S- ECP > 17 μg/l had a 5.4 increased risk of asthma development

- A question of degree of allergic inflammation?

LP Nielsen et al. Allergy 2009; 64: 733-7
The Allergic March

Atopic Dermatitis → Allergic Rhinitis (x 2.5) → Asthma (x 4.9)

Plaschke P et al. *AJRCCM* 2000;162:920-4
Period prevalence of wheezing after stratification into rhinitis phenotypes at different ages

Stratification at the age of 2 years

Stratification at the age of 5 years

Control group (C) ⊗ Non-allergic rhinitis (R)
Atopy without rhinitis (A) ⋄ Allergic rhinitis (AR)

Probability of remaining free of wheezing stratified by rhinitis phenotypes at different ages

Stratification at the age of 2 years

Stratification at the age of 5 years

Development of asthma: Continuing smokers and nonsmokers combined

<table>
<thead>
<tr>
<th>Pack years</th>
<th>OR (multivariate analysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-10 vs 0</td>
<td>2.05 (0.99 – 4.27)</td>
</tr>
<tr>
<td>11 – 20 vs 0</td>
<td>3.71 (1.77 – 7.78)</td>
</tr>
<tr>
<td>≥21</td>
<td>5.05 (1.93 – 13.2)</td>
</tr>
</tbody>
</table>

J Allergy Clin Immunol 2008;121:1428-34.
Cigarette smoking is associated with a greater risk of incident asthma in allergic rhinitis

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<tr>
<td>Smokers vs non smokers</td>
<td>2.98 (1.81 – 4.92)</td>
</tr>
<tr>
<td>Male vs female</td>
<td>0.34 (0.20 – 0.55)</td>
</tr>
</tbody>
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J Allergy Clin Immunol 2008;121:1428-34.
PAT study 10 year data
Risk of Asthma after 10 years

Coseasonal SLIT reduces the development of asthma in children with allergic rhinitis.

Novembre E. et al, JACI 2004

<table>
<thead>
<tr>
<th>SLIT</th>
<th>NO SLIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>37</td>
<td>26</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NO ASTHMA</th>
<th>ASTHMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>18</td>
</tr>
</tbody>
</table>

79 children
Allergic rhinitis only
Follow-up: 3 yrs

Novembre E. et al, JACI 2004
Intranasal and inhaled fluticasone propionate for pollen-induced rhinitis and asthma

Assessed for eligibility (n=275)
- Excluded (n=13)
  - Protocol violation (n=2)
  - Consent withdrawn (n=2)
  - Lost to follow-up (n=1)
  - Other (n=8)

Randomised (n=262)
- Placebo (n=66)
  - Withdraw n from study (n=6)
    - Adverse event (n=1)
    - Lack of efficacy (n=2)
    - Protocol violation (n=2)
    - Other (n=1)
  - Completed study (n=60)
- INFP (n=70) (FP intranasal)
  - Withdraw n from study (n=7)
    - Adverse event (n=2)
    - Consent withdrawn (n=1)
    - Lack of efficacy (n=1)
    - Protocol violation (n=1)
    - Other (n=2)
  - Completed study (n=63)
- IHFP (n=61) (Inhaled FP)
  - Withdraw n from study (n=6)
    - Adverse event (n=3)
    - Lack of efficacy (n=1)
    - Lost to follow-up (n=1)
    - Other (n=1)
  - Completed study (n=55)
- INFP + IHFP (n=65) (FP intranasal + inhaled FP)
  - Withdraw n from study (n=7)
    - Adverse event (n=2)
    - Protocol violation (n=1)
    - Other (n=4)
  - Completed study (n=58)

Allergy 2005; 60: 875-81
Nasal symptoms are reduced by intranasal steroid.

% patient with no nasal blockage/congestion

Placebo  INFP  IHFP  INFP + IHFP

□ = baseline, ■ = weeks 1-6;
* p<0.05, ** p<0.01 and *** <0.001 vs intranasal or inhaled placebo.

Allergy 2005; 60: 875-81
Nasal symptoms are reduced by intranasal steroid

% patients with no sneezing

baseline (□) and after 4 weeks treatment (■)

*** = p<0.001 IHFP ± INFP vs. INFP or placebo

Allergy 2005; 60: 875-81
Nasal symptoms are reduced by intranasal steroid

baseline (□) and after 4 weeks treatment (■)

*** = p<0.001 IHFP± INFP vs. INFP or placebo

Allergy 2005; 60: 875-81
Protection from increase in BHR by inhaled but not intranasal steroid

baseline (☐) and after 4 weeks treatment (■)

*** = p<0.001 IHFP± INFP vs. INFP or placebo

Allergy 2005; 60: 875-81
Rhinitis is a major risk factor for asthma

• Allergic rhinitis is a higher risk than nonallergic rhinitis for asthma
• Those with signs of peripheral airways inflammation may be at especially high risk (s-ECP; FeNO, sputum eosinophilia?)
• Smoking in rhinitics increase the risk for asthma further
• Allergen specific immunotherapy may reduce the risk by 50%
• Preventive value of pharmacological treatments are not know
Thank you for your attention