Sleep, Rhinitis, Asthma and Obesity

Timothy J. Craig
Professor of Medicine and Pediatrics
Distinguished Educator
Penn State University
Presentation Overview

- Obesity and asthma
- OSA and asthma
- Obesity and rhinitis
- Rhinitis and OSA
- Sleep and inflammation
- What we need to do
Conflicts of interest with this presentation

- Merck - consultant and research
- GSK - research
- Genentech - research
- Novartis - research
Presentation Overview

- Obesity and asthma
- OSA and asthma
- Obesity and rhinitis
- Rhinitis and OSA
- Sleep and inflammation
- What we need to do
Increase incidence of asthma correlates with?

• 1. High HDL
• 2. Waist Hip Ratio
• 3. Low triglycerides
• 4. Metabolic Syndrome

Answer:
Increase incidence of asthma correlates with?

- 1. High HDL
- 2. Waist Hip Ratio
- 3. Low triglycerides
- 4. Metabolic Syndrome

Answer: 4
R.V. Fenger\textsuperscript{a,*}, A. Gonzalez-Quintela\textsuperscript{b}, A. Linneberg\textsuperscript{a}, L.L.N. Husemoen\textsuperscript{a}, B.H. Thuesen\textsuperscript{a}, M. Aadahl\textsuperscript{a}, C. Vidal\textsuperscript{b}, T. Skaaby\textsuperscript{a}, J.C. Sainz\textsuperscript{c}, E. Calvo\textsuperscript{c}

The relationship of serum triglycerides, serum HDL, and obesity to the risk of wheezing in 85,555 adults

\begin{tabular}{|c|c|c|}
\hline
Rhinitis symptoms & Absent & 9.3 (4561/48791) \\
& Present & 29.9 (10243/34295) \\
\hline
BMI & \textless 18.5 kg/m\textsuperscript{2} & 18.1 (257/1421) \\
& 18.5–25 kg/m\textsuperscript{2} & 16.0 (6239/38918) \\
& 25–30 kg/m\textsuperscript{2} & 18.1 (5816/32120) \\
& \textgeq 30 kg/m\textsuperscript{2} & 24.1 (2999/12463) \\
\hline
WC & Normal\textsuperscript{b} & 17.0 (11074/65329) \\
& High\textsuperscript{b} & 24.5 (2701/11025) \\
\hline
S-Triglycerides & \textless 150 mg/dl & 16.7 (11448/68472) \\
& 150–400 mg/dl & 23.9 (3200/13416) \\
& \textgeq 400 mg/dl & 28.6 (269/942) \\
\hline
S-HDL & Normal\textsuperscript{b} & 17.2 (11308/65728) \\
& Low\textsuperscript{b} & 22.2 (3361/15167) \\
\hline
S-LDL & Normal\textsuperscript{b} & 18.0 (13600/75564) \\
& High\textsuperscript{b} & 18.3 (1829/9991) \\
\hline
S-glucose & Normal\textsuperscript{b} & 17.8 (13456/75510) \\
& High\textsuperscript{b} & 19.6 (1973/10045) \\
\hline
Blood pressure & Normal\textsuperscript{b} & 17.5 (9098/52097) \\
& High\textsuperscript{b} & 18.9 (6331/33458) \\
\hline
Metabolic syndrome & Absent\textsuperscript{b} & 17.2 (10892/63149) \\
& Present\textsuperscript{b} & 25.4 (2113/8334) \\
\hline
\end{tabular}
The relationship of serum triglycerides, serum HDL, and obesity to the risk of wheezing in 85,555 adults

<table>
<thead>
<tr>
<th>Rhinitis symptoms</th>
<th>Absent</th>
<th>Present</th>
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<tbody>
<tr>
<td></td>
<td>9.3</td>
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<td>(4561/48791)</td>
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<tr>
<th>BMI</th>
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<th>S-glucose</th>
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<tbody>
<tr>
<td>Normal b</td>
<td>17.8</td>
<td>(13456/75510)</td>
</tr>
<tr>
<td>High b</td>
<td>19.6</td>
<td>(1973/10045)</td>
</tr>
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<table>
<thead>
<tr>
<th>Blood pressure</th>
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<tbody>
<tr>
<td>Normal b</td>
<td>17.5</td>
<td>(9098/52097)</td>
</tr>
<tr>
<td>High b</td>
<td>18.9</td>
<td>(6331/33458)</td>
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<table>
<thead>
<tr>
<th>Metabolic syndrome</th>
<th>Absent</th>
<th>Present</th>
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<tbody>
<tr>
<td></td>
<td>17.2</td>
<td>25.4</td>
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<tr>
<td></td>
<td>(10892/63149)</td>
<td>(2113/8334)</td>
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</table>
The relationship of serum triglycerides, serum HDL, and obesity to the risk of wheezing in 85,555 adults

Figure 1  Risk of wheezing per standard deviation of s-HDL and s-TG by level of BMI. Diamonds: s-HDL; squares: s-TG. Odds ratio estimates with 95% confidence intervals indicated by error bars were obtained in one single logistic regression model adjusted for age, sex, adiposity, occupation, alcohol, and physical activity during working hours. S-TG, serum triglyceride; s-HDL, serum high density lipoprotein.

Respiratory Medicine (2013) 107, 816–824
With increase BMI there is increase asthma but only in those that do not have rhinitis.
In conclusion, we found that high s-TG and low s-HDL were significantly associated with the risk of wheezing in 85,555 Spanish workers and these associations persisted after adjusting in several ways for adiposity. The finding that these associations were mainly seen in individuals without rhinitis symptoms may support the notion that only specific types of asthma are associated with low-grade systemic inflammation.
Study of 351 asthma children in PR compared to 327 controls
Erick Forno, MD, MPH,a Edna Acosta-Perez, PhD, MSc,b John M. Brehm, MD,a Juan Celedon, MD,*

<table>
<thead>
<tr>
<th></th>
<th>Asthma</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>0.69 ± 1.19*</td>
<td>0.51 ± 1.12</td>
</tr>
<tr>
<td>PBF</td>
<td>0.29 ± 0.86§</td>
<td>0.22 ± 0.77</td>
</tr>
<tr>
<td>WC</td>
<td>0.03 ± 1.04§</td>
<td>−0.03 ± 0.95</td>
</tr>
<tr>
<td>WHR</td>
<td>0.001 ± 0.85</td>
<td>−0.001 ± 1.13</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Pulmonary function tests, mean ± SD</th>
<th>Asthma</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁ (L)</td>
<td>1.88 ± 0.67*</td>
<td>2.05 ± 0.74</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>2.33 ± 0.82*</td>
<td>2.47 ± 0.88</td>
</tr>
<tr>
<td>FEV₁/FVC (%)</td>
<td>80.9% ± 9.0%*</td>
<td>83.5% ± 8.9%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Asthma severity</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of ED/UC visits for asthma†</td>
<td>10 (5-20)</td>
<td>NA</td>
</tr>
<tr>
<td>Severity scores, past year†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisone courses (0-4)</td>
<td>2 (1-2)</td>
<td>NA</td>
</tr>
<tr>
<td>Exercise symptoms (0-3)</td>
<td>1 (1-3)</td>
<td>NA</td>
</tr>
<tr>
<td>Missed school days (0-3)</td>
<td>1 (0-2)</td>
<td>NA</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Atopy measures</th>
<th></th>
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<tbody>
<tr>
<td>Total serum IgE level (IU/mL)†</td>
<td>346 (116-881)*</td>
<td>158 (44-600)</td>
</tr>
<tr>
<td>Allergic rhinitis (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>STR to (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dust mite</td>
<td>55.4*</td>
<td>41.6</td>
</tr>
<tr>
<td>Cockroach</td>
<td>39.4*</td>
<td>26.3</td>
</tr>
</tbody>
</table>

Increase obesity in asthma compared to controls
Lower FEV₁
Increase allergies
Conclusions:

• Adiposity indicators are associated with asthma, asthma severity/control, and atopy in Puerto Rican children.

• Atopy significantly mediates the effect of adiposity on asthma outcomes.

• Longitudinal studies are needed to further investigate the causal role, if any, of adiposity distribution and atopy on “obese asthma” in childhood.

Followed 6,267 participants (elderly) for obesity and asthma.
### Increase in BMI correlated with increase in asthma

- **Age, years**:
  - Nonasthma: 73.6 ± 4.9
  - Asthma: 73.5 ± 4.7
  - Mean ± SD or %
  - Value: 0.59

- **Women, %**:
  - Nonasthma: 60.0
  - Asthma: 62.7
  - Mean ± SD or %
  - Value: 0.19

- **Center, %**:
  - Bordeaux: 22.1
  - Dijon: 51.2
  - Montpellier: 26.7
  - Mean ± SD or %
  - Value: 0.90

- **Educational level, %**:
  - No school or primary ≤ diploma:
    - Nonasthma: 32.6
    - Asthma: 33.6
    - Mean ± SD or %
    - Value: 0.14
  - Secondary without baccalaureate:
    - Nonasthma: 30.2
    - Asthma: 26.7
    - Mean ± SD or %
    - Value: 0.14
  - Baccalaureate or university:
    - Nonasthma: 37.2
    - Asthma: 39.7
    - Mean ± SD or %
    - Value: 0.14

- **Smoking status, %**:
  - Never:
    - Nonasthma: 61.1
    - Asthma: 60.6
    - Mean ± SD or %
    - Value: 0.002
  - Former:
    - Nonasthma: 33.0
    - Asthma: 36.5
    - Mean ± SD or %
    - Value: 0.002
  - Current:
    - Nonasthma: 5.9
    - Asthma: 2.9
    - Mean ± SD or %
    - Value: 0.002

- **BMI, kg/m²**:
  - Nonasthma: 25.7 ± 4.0
  - Asthma: 26.1 ± 4.1
  - Mean ± SD or %
  - Value: 0.02

- **% Normal**:
  - Nonasthma: 47.1
  - Asthma: 41.5
  - Mean ± SD or %
  - Value: 0.01

- **Overweight**:
  - Nonasthma: 39.8
  - Asthma: 42.6
  - Mean ± SD or %
  - Value: 0.01

- **Obese**:
  - Nonasthma: 13.1
  - Asthma: 15.9
  - Mean ± SD or %
  - Value: 0.01

- **Waist circumference, cm**:
  - Nonasthma: 88.7 ± 12.4
  - Asthma: 90.7 ± 12.5
  - Mean ± SD or %
  - Value: <0.001

- **% <94/80**:
  - Nonasthma: 88.7
  - Asthma: 31.6
  - Mean ± SD or %
  - Value: <0.001

- **94/80–102/88**:
  - Nonasthma: 30.0
  - Asthma: 28.2
  - Mean ± SD or %
  - Value: <0.001

- **≥102/88**:
  - Nonasthma: 9.0
  - Asthma: 40.2
  - Mean ± SD or %
  - Value: <0.001

- **Metabolic syndrome, %**:
  - Nonasthma: 39.1
  - Asthma: 25.9
  - Mean ± SD or %
  - Value: 0.25

- **Cardiovascular disease history, %**:
  - Nonasthma: 4.0
  - Asthma: 10.3
  - Mean ± SD or %
  - Value: 0.14

- **β-Blockers, %**:
  - Nonasthma: 17.6
  - Asthma: 11.3
  - Mean ± SD or %
  - Value: <0.001

- **Dyspnea, %**:
  - Nonasthma: 45.7
  - Asthma: 26.5
  - Mean ± SD or %
  - Value: <0.001

- **Troubled with shortness of breath when hurrying on the level ground or walking up a slight hill (strenuous exercise)**:
  - Nonasthma: 43.3
  - Asthma: 46.1
  - Mean ± SD or %
  - Value: <0.001

- **Walks slower than people of the same age on the level ground because breathlessness**:
  - Nonasthma: 9.4
  - Asthma: 20.0
  - Mean ± SD or %
  - Value: <0.001

- **Breathlessness when dressing or undressing or at rest**:
  - Nonasthma: 1.6
  - Asthma: 7.4
  - Mean ± SD or %
  - Value: <0.001
In patients with the mean age of 72 years with asthma compared to without asthma there is:

1. Increase BMI
2. Increase waist size
3. Increase obesity
4. Increase dyspnea
To conclude, abdominal overweight and obesity were found to be independently and strongly related to asthma prevalence and incidence in a large population-based study in the elderly. Given the parallel increase in the prevalence of elderly persons and of abdominal obesity in industrialized countries, an increasingly obese elderly population will undoubtedly require more attention by researchers and clinicians. Studies aiming to understand the origin of late-onset asthma and the mechanisms involved in the obesity–asthma link are needed.
Visceral adipose tissue secretes inflammatory mediators and results in which of the following?

• 1. Decrease levels of Leptin
• 2. Increase levels of adiponectin
• 3. Increase sputum eosinophils
• 4. Increase TNF, IL-1, IL-6 and IL-8

• Answer:
Visceral adipose tissue secretes inflammatory mediations and results in which of the following?

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• 4. Increase TNF, IL-1, IL-6 and IL-8

• Answer: 4
Obesity and Asthma

Allergy Asthma Immunol Res. 2014
May;6(3):189-195.
Sutherland- summary of asthma and obesity

Table 1. Notable characteristics of asthma in obese individuals

- In epidemiological studies, obesity significantly increases the risk for asthma.
- Obesity alters lung physiology in ways that mimic asthma, possibly confounding clinical evaluation of obese patients with respiratory symptoms.
- A substantial body of literature has identified potential inflammatory pathways by which obesity increases asthma risk, including increased allergic sensitization and airway hyperresponsiveness, redistribution of lung eosinophils, altered macrophage phenotype and function, and neurogenic pathways.
- Obese asthmatics have increased healthcare use and worsened health status.
- Cluster analyses have identified a number of important characteristics that differ between obese and lean asthmatics, including symptom severity, airway inflammation, age of asthma onset, sex, and treatment responsiveness.
- Both adult and pediatric studies indicate that obese asthmatics are less responsive to glucocorticoids, the mainstay of asthma controller therapy.
- Small studies have suggested that weight loss improves clinical and physiologic aspect of asthma, although the impact of weight loss on inflammatory pathways remains unknown.

Presentation Overview

- Obesity and asthma
- OSA and asthma
- Obesity and rhinitis
- Rhinitis and OSA
- Sleep and inflammation
- What we need to do
The correlation of sleep apnea and asthma is mainly in:

- 1. men
- 2. females
- 3. children
- 4. independent of BMI
The correlation of sleep apnea and asthma is mainly in?

• 1. men
• 2. females
• 3. children
• 4. independent of BMI

• Answer: 2
Obstructive sleep apnea and asthma: Associations and treatment implications

Bharati Prasad\textsuperscript{a,b,*}, Sharmilee M. Nyenhuis\textsuperscript{a}, Terri E. Weaver\textsuperscript{b}
Asthma and sleep apnea

Fig. 1. Obstructive sleep apnea and asthma: pathophysiologic links.
The OSA and asthma correlation was mainly in females.
Practice points

1) Obstructive sleep apnea (OSA) and asthma are highly prevalent respiratory disorders that frequently overlap in patients.
2) A high index of suspicion is warranted for overlap of OSA and asthma, particularly in the presence of obesity, rhinitis, gastroesophageal reflux (GER), and in patients poorly responsive to therapy.
3) Individualized therapy addressing moderating factors such as weight gain, GERD, nasal obstruction, and cardiovascular disease is warranted for optimal outcomes.
Moderate to severe OSA patients and the proportion with REM-related OSA.
AH1 in and out of REM sleep in patients with OSA with and without asthma.
<table>
<thead>
<tr>
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<th>Co-variables in asthmatic children with OSAS</th>
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<tr>
<td></td>
<td>Yes (n = 9)</td>
<td>No (n = 53)</td>
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<tr>
<td><strong>Atopy</strong></td>
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<tr>
<td>Max% REM SAO2 desaturation mean (SE)</td>
<td>14.2 (1.2)</td>
<td>11.7 (0.8)</td>
<td></td>
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</tr>
<tr>
<td>REM AHI mean (SE)</td>
<td>27.5 (10.6)</td>
<td>20.4 (3.3)</td>
<td></td>
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<tr>
<td>Non-REM AHI mean (SE)</td>
<td>3.9 (1.2)</td>
<td>5.3 (1.1)</td>
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<tr>
<td><strong>Rhinitis</strong></td>
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<tr>
<td>Max% REM SAO2 desaturation mean (SE)</td>
<td>11.7 (1.4)</td>
<td>12.4 (1.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>REM AHI mean (SE)</td>
<td>24.3 (5.0)</td>
<td>19.7 (3.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-REM AHI mean (SE)</td>
<td>5.69 (1.3)</td>
<td>4.38 (1.3)</td>
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</table>
These results demonstrate that asthma is associated with REM-related breathing abnormalities in children with moderate–severe OSA. The link between asthma and REM-related OSA is independent of asthma control and obesity. Further research is needed to delineate the REM-sleep biological mechanisms that modulate the phenotypical expression of OSA in asthmatic children. *Pediatr Pulmonol. 2013; 48:592–600.* © 2012 Wiley Periodicals, Inc.
Presentation Overview

- Obesity and asthma
- OSA and asthma
- Obesity and rhinitis
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- Sleep and inflammation
- What we need to do
The true statement about obesity and rhinitis is?

- 1. no correlation
- 2. In obesity there is an increase in allergic rhinitis
- 3. In obesity there is an increase in chronic rhinosinusitis and allergic rhinitis
- 4. In obesity there is an increase in chronic rhinosinusitis

• Ans:
The true statement about obesity and rhinitis is?

• 1. no correlation
• 2. In obesity there is an increase in allergic rhinitis
• 3. In obesity there is an increase in chronic rhinosinusitis and allergic rhinitis
• 4. In obesity there is an increase in chronic rhinosinusitis

• Ans: 3
Objectives/Hypothesis: Determine whether adult obesity is associated with chronic rhinosinusitis (CRS) and/or allergic rhinitis (AR).

Study Design: Cross-sectional analysis of medical panel survey.

Methods: The Medical Expenditure Panel Survey, a large-scale household-based survey of health care utilization in the United States (2008 and 2010) was examined, identifying adult cases of CRS and AR. The presence or absence of obesity (body mass index $\geq 30$ kg/m$^2$) was determined. Adjusting for age, sex, race, geographic region, insurance coverage, and Charlson Comorbidity Index, odds ratios for the presence of CRS and/or AR in the presence of obesity were determined. The relations between body mass index as a linear variable and the presence of CRS and AR were determined.

Results: A total of $17.6 \pm 0.6$ million adults reported AR ($7.7\% \pm 0.3\%$) and $13.0 \pm 0.5$ million reported CRS ($5.7\% \pm 0.2\%;$ weighted estimates). Additionally, $64.9 \pm 1.4$ million adults ($29.0\% \pm 0.4\%$) were classified as obese based on body mass index. The adjusted odds ratio for AR when obesity was present was $1.22$ ($P < .001$, 95% confidence interval $= 1.12-1.33$). The adjusted odds ratio for CRS when obesity was present was $1.31$ ($P < .001$, 95% confidence interval $= 1.18-1.45$). Increasing body mass index as a continuous variable was significantly associated with the presence of both AR (odds ratio $= 1.023$, $P < .001$) and CRS (odds ratio $= 1.022$, $P < .001$).

Conclusions: The current data demonstrate an increased prevalence of adult obesity associated with both AR and CRS.

Key Words: Obesity, epidemiology, chronic rhinosinusitis, allergic rhinitis, prevalence, body mass index.

Level of Evidence: 2b

Laryngoscope, 123:1840-1844, 2013
17 million adults with allergic rhinitis and 13 million adults with chronic rhino-sinusitis. Also 64 million adults with obesity.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Allergic Rhinitis</th>
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<th>Chronic Rhinosinusitis</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio</td>
<td>95% CI</td>
<td>P</td>
<td>Odds Ratio</td>
<td>95% CI</td>
<td>P</td>
</tr>
<tr>
<td>Obese</td>
<td>1.218</td>
<td>1.117–1.328</td>
<td>&lt;.001</td>
<td>1.309</td>
<td>1.184–1.448</td>
<td>&lt;.001</td>
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<td>Age, mean yr</td>
<td>1.001</td>
<td>0.998–1.003</td>
<td>.535</td>
<td>0.990</td>
<td>0.987–0.994</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.601</td>
<td>0.550–0.657</td>
<td>&lt;.001</td>
<td>0.538</td>
<td>0.482–0.601</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>Reference</td>
<td></td>
<td></td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race/ethnicity, %</td>
<td></td>
<td></td>
<td>&lt;.001</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.889</td>
<td>0.775–1.042</td>
<td></td>
<td>0.396</td>
<td>0.312–0.502</td>
<td></td>
</tr>
<tr>
<td>Black not Hispanic</td>
<td>0.614</td>
<td>0.521–0.723</td>
<td></td>
<td>0.484</td>
<td>0.396–0.592</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>0.767</td>
<td>0.628–0.938</td>
<td></td>
<td>0.203</td>
<td>0.125–0.331</td>
<td></td>
</tr>
<tr>
<td>Other not Hispanic</td>
<td>Reference</td>
<td></td>
<td></td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Allergic rhinitis vs. BMI

Bhattacharyya: Obesity and Sinonasal Disease
Chronic rhinosinusitis vs. BMI

Bhattacharyya: Obesity and Sinonasal Disease
CONCLUSION

The current data demonstrate an increased prevalence of obesity in the setting of CRS or ARS. Given the current findings, further research is warranted to determine if a potential causal relation between obesity and AR and CRS exists, especially given the projected future population demographics with respect to overweight and obese patients in the United States.
Presentation Overview

- Obesity and asthma
- OSA and asthma
- Obesity and rhinitis
- Rhinitis and OSA
- Sleep and inflammation
- What we need to do

Reviewed 443 manuscripts

18 articles met quality to include in the meta-analysis

**Figure 2.** Sleep disorders assessed in included studies.

This report represents the first systematic review of existing literature on the association of AR and SDB. This review supports a correlation between AR and SDB. However, the majority of the studies included in this review had evidence Levels of 3 or 4. Further higher quality studies should be carried out in the future to better determine the relationship between AR and SDB in children.
The link between rhinitis and rapid-eye-movement sleep breathing disturbances in children with obstructive sleep apnea

Shehlanoor Huseni, M.D.,1 Maria J. Gutierrez, M.D.,2,3 Carlos E. Rodriguez, M.D., M.Sc.,4,5,6 Cesar L. Nino, Ph.D.,7 Geovanny F. Perez, M.D.,1 Krishna Pancham, M.D.,1 and Gustavo Nino, M.D.1,8

Conclusion: Rhinitis is highly prevalent in children with OSA. Although OSA is not more severe in children with rhinitis, they do have a distinct OSA phenotype characterized by more REM-related OSA. Further research is needed to delineate the link between REM-sleep and the physiology of the nose during health and disease.

(Am J Rhinol Allergy 28, e56–e61, 2014; doi: 10.2500/ajra.2014.28.3994)
<table>
<thead>
<tr>
<th>Factors/Variables</th>
<th>Total (n = 145)</th>
<th>OSA only (n = 82, 57%)</th>
<th>OSA with Rhinitis (n = 63, 43%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td>0.57</td>
</tr>
<tr>
<td>Female</td>
<td>55 (38%)</td>
<td>34 (41%)</td>
<td>21 (33%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>90 (62%)</td>
<td>48 (59%)</td>
<td>42 (67%)</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>6.26 (3.1)</td>
<td>6.14 (3.1)</td>
<td>6.4 (3.0)</td>
<td>0.61</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td>0.95</td>
</tr>
<tr>
<td>White</td>
<td>96 (62%)</td>
<td>55 (67%)</td>
<td>41 (65%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>49 (37%)</td>
<td>27 (33%)</td>
<td>22 (35%)</td>
<td></td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>20.4 (6.3)</td>
<td>20.5 (6.3)</td>
<td>20.1 (6.5)</td>
<td>0.71</td>
</tr>
<tr>
<td><strong>Sleep study parameters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OSA severity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD) OAHI (mild)</td>
<td>2.62 (0.9)</td>
<td>2.65 (0.9)</td>
<td>2.58 (0.9)</td>
<td>0.70</td>
</tr>
<tr>
<td>Mean (SD) OAHI (moderate–severe)</td>
<td>18.8 (16.6)</td>
<td>18.04 (19)</td>
<td>20 (12.6)</td>
<td>0.61</td>
</tr>
<tr>
<td>TST, mean (SD)</td>
<td>518.6 (53)</td>
<td>515.7 (54)</td>
<td>522.6 (53)</td>
<td>0.50</td>
</tr>
<tr>
<td>TST supine, %; mean (SD)</td>
<td>41.0 (18.5)</td>
<td>44.6 (20.5)</td>
<td>38.8 (17)</td>
<td>0.24</td>
</tr>
<tr>
<td>REM (%), mean (SD)</td>
<td>19.6 (4.2)</td>
<td>19 (6)</td>
<td>20.1 (3.3)</td>
<td>0.38</td>
</tr>
</tbody>
</table>

(Am J Rhinol Allergy 28, e56–e61, 2014; doi: 10.2500/ajra.2014.28.3994)
Rhinitis and OSA in REM and NREM Sleep
95% CI for the Mean

p = 0.04 *

p = NS

(Am J Rhinol Allergy 28, e56-e61, 2014; doi: 10.2500/ajra.2014.28.3994)
The link between rhinitis and rapid-eye-movement sleep breathing disturbances in children with obstructive sleep apnea

Shehlanooor Huseni, M.D.,¹ Maria J. Gutierrez, M.D.,²,³ Carlos E. Rodriguez, M.D., M.Sc.,⁴,⁵,⁶ Cesar L. Nino, Ph.D.,⁷ Geovanny F. Perez, M.D.,¹ Krishna Panchar, M.D.,¹ and Gustavo Nino, M.D.¹,⁸

Conclusion: Rhinitis is highly prevalent in children with OSA. Although OSA is not more severe in children with rhinitis, they do have a distinct OSA phenotype characterized by more REM-related OSA. Further research is needed to delineate the link between REM-sleep and the physiology of the nose during health and disease.

(Am J Rhinol Allergy 28, e56–e61, 2014; doi: 10.2500/ajra.2014.28.3994)
Key Points: Allergy and Sleep-Disordered Breathing

- Allergic rhinitis significantly contributes to sleep-disordered breathing through multiple mechanisms, with the greatest impact mediated primarily through nasal obstruction.
- Sleep impairment is very common in patients with allergic rhinitis, chronic rhinosinusitis, and nasal polyposis, and has a significant impact on disease-specific and general health quality of life measures.
- The degree of sleep disturbance is directly related to the severity of the allergic disease at a given time.
- Nasal obstruction also demonstrates circadian rhythm and positional variability, with worsening in the overnight hours and in the supine position.
- Nasal obstruction increases the likelihood of snoring, obstructive sleep apnea, and intolerance to medical device therapies for sleep apnea.
Presentation Overview

- Obesity and asthma
- OSA and asthma
- Obesity and rhinitis
- Rhinitis and OSA
- Sleep and inflammation
- What we need to do
Sleep Disturbance and Inflammation
Similarities between the two

**Obese man with severe OSA**
- Increase in IL-1
- Increase in TNF
- Increase in IL-6
- Increase in T-helper 2 cytokines
- Decrease in T-helper 1 cytokines

**A young girl snoring and with rhinitis**
- Increase in IL-1
- Increase in TNF
- Increase in IL-6
- Increase in T-helper 2 cytokines
- Decrease in T-helper 1 cytokines

Craig et al AAAI 2014
Allergic Patients Experience More Apnea/Hypopnea than Non-allergic Controls

Allergic patients had more apnea/hypopnea episodes than non-allergic controls

\[ P<0.001 \]

AHI=apnea/hypopnea index, determined as the total number of apnea and hypopnea episodes (assessed by polysomnography) divided by hours of sleep.

**Allergic Rhinitis Symptoms are Associated with Sleep Disorders**

Prevalence of Sleep Disorders in Patients with Allergic Rhinitis and Controls

![Bar chart showing prevalence of sleep disorders in AR patients compared to controls.](image)

- **Insomnia**: 35.8% for AR patients, 16% for controls. *P≤0.003 vs controls.
- **Severe Insomnia**: 23.2% for AR patients, 10.4% for controls.
- **Sleep Apnea Syndrome**: 3.8% for AR patients, 0.5% for controls. *P≤0.003 vs controls.
- **Hypersomnia**: 32.6% for AR patients.

Pathophysiology of Allergic Rhinitis and Impact on Sleep

**Early-Phase Response**
- Mast Cell
  - Allergen
  - Degranulation
  - Neosynthesis
    - CysLTs
    - Prostaglandins
    - PAF
    - Bradykinin
    - ILs
    - TNF-α
    - GM-CSF
  - Chemotactic factors
    - (CysLTs, PAF, IL-5)

**Late-Phase Response**
- Cellular Infiltration/Inflammation
  - Eosinophil
    - CysLTs
    - GM-CSF
    - TNF-α
    - IL-1
    - IL-3
    - PAF
    - ECP
    - MBP
  - Basophil
    - Histamine
    - CysLTs
    - TNF-α
    - IL-4
    - IL-5
    - IL-6
  - Monocyte
    - CysLTs
    - TNF-α
    - PAF
    - IL-1
    - IL-10
  - Lymphocyte
    - IL-4
    - IL-13
    - IL-5
    - IL-3
    - GM-CSF
    - IL-6

Multiple Pro-Inflammatory Factors in Allergic Rhinitis Affect Sleep and Symptoms

<table>
<thead>
<tr>
<th>Mediator</th>
<th>Effect on Sleep</th>
</tr>
</thead>
</table>
| Histamine  | Balance between wakefulness and sleep, arousal; 
|            | ↑ nasal obstruction, rhinorrhea, & pruritus                                      |
| CysLT      | ↑ Slow-wave sleep, ↑ Sleep-disordered breathing; ↑ Nasal obstruction, rhinorrhea |
| IL-1       | ↑ Latency to REM and ↓ REM duration                                              |
| IL-4       |                                                                                   |
| IL-10      |                                                                                   |
| Bradykinin | ↑ Sleep apnea; ↑ Nasal obstruction & rhinorrhea                                   |
| Substance P| ↑ Latency to REM, arousal; ↑ Nasal obstruction                                    |

Effect of sleep restriction on IL-6

Changes of TNF over 24 hour clock before and with sleep restriction

Nurses Health Study: Snoring Increases the Risk of Associated Diseases

<table>
<thead>
<tr>
<th>Condition</th>
<th>Increased Risk with More Frequent Snoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary Heart Disease¹</td>
<td>√</td>
</tr>
<tr>
<td>Stroke¹</td>
<td>√</td>
</tr>
<tr>
<td>Hypertension²</td>
<td>√</td>
</tr>
<tr>
<td>Diabetes³</td>
<td>√</td>
</tr>
</tbody>
</table>

Nurses Health Study: Snoring Increases Risk of CV Disease

Age-Adjusted Odds Ratio for CV Disease by Snoring Category

N=71,779 subjects.

Nurses Health Study: Snoring Increases Risk of Hypertension

Multivariate-Adjusted Odds Ratio for Hypertension by Snoring Category

Adjusted Odds Ratio for Hypertension

Baseline
8-Year Follow-up

N=73,231 subjects.

Nurses Health Study: Snoring Increases Risk of Type II Diabetes

Multivariate-Adjusted Odds Ratio for Type II Diabetes by Snoring Category

Adjusted Odds Ratio for Type II Diabetes

P<0.0001 for trend

N=69,582 subjects.

Presentation Overview

- Obesity and asthma
- OSA and asthma
- Obesity and rhinitis
- Rhinitis and OSA
- Sleep and inflammation
- What we need to do
For weight loss what is the recommendation in minutes per day?

• 1. 30 minutes
• 2. 45 minutes
• 3. 60 minutes
• 4. 90 minutes
• 5. 120 minutes

• ans
For weight loss what is the recommendation in minutes per day?

• 1. 30 minutes
• 2. 45 minutes
• 3. 60 minutes
• 4. 90 minutes
• 5. 120 minutes

• Ans: 3
2013 AHA/ACC/TOS Obesity Guideline

EXERCISE

Increased physical activity: Comprehensive lifestyle intervention programs typically prescribe increased aerobic physical activity (such as brisk walking) for \( \geq 150 \) minutes/week (equal to \( \geq 30 \) minutes/day, most days of the week). Higher levels of physical activity, approximately 200 to 300 minutes/week, are recommended to maintain lost weight or minimize weight regain long-term (\( \geq 1 \) year).

30 minutes for healthy people and 60 minutes for weight loss and to maintain weight loss
What is the importance of exercise in the mouse model with asthma
Effect of exercise on inflammatory mediators of asthma

A  Sedentary, OVA

B  Exercised, OVA

C

<table>
<thead>
<tr>
<th></th>
<th>Sedentary, OVA</th>
<th>Exercised, OVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>pv lymph cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pb lymph cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td>epi hyper</td>
<td></td>
<td></td>
</tr>
<tr>
<td>goblet/mucin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pastva. J Immunol 2004;172;4520-4526
Exercise decreased VCAM-1 surface expression in the lungs of OVA-sensitized mice.
The number of total cells, eosinophils and epithelial cells in the bronchoalveolar lavage
Exercise Improves Asthma Outcomes
“Symptom Free Days”

Mendes. CHEST / 138 / 2 / AUGUST, 2010
Exercise Improves Asthma Outcomes
“Oxygen consumption”

Mendes. CHEST / 138 / 2 / AUGUST, 2010
Exercise Improves Asthma Outcomes
“Quality of Life”

<table>
<thead>
<tr>
<th></th>
<th>Control Group</th>
<th>Exercise Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (n=12)</td>
<td>Week 12 (n=11(^{†}))</td>
</tr>
<tr>
<td>ACQ Questionnaire</td>
<td>0.90±0.15</td>
<td>0.99±0.16(^{†})</td>
</tr>
<tr>
<td>ACQ with Spirometry</td>
<td>1.06±0.10(^{#})</td>
<td>0.80±0.14</td>
</tr>
<tr>
<td>Perceived Asthma Control</td>
<td>2.33±0.19</td>
<td>2.25±0.18(^{†})</td>
</tr>
<tr>
<td>Mini-AQLQ</td>
<td>5.79±0.15</td>
<td>5.90±0.17(^{†})</td>
</tr>
<tr>
<td>Maximal VO(_{2})</td>
<td>2.66±0.27</td>
<td>2.77±0.29</td>
</tr>
<tr>
<td>Submaximal VO(<em>{2}/VO(</em>{2})</td>
<td>23.21±0.73</td>
<td>23.64±0.80</td>
</tr>
<tr>
<td>Maximal VO(<em>{2}/VO(</em>{2})</td>
<td>28.46±0.88</td>
<td>28.65±1.39</td>
</tr>
<tr>
<td>Submaximal DI</td>
<td>0.42±0.03</td>
<td>0.42±0.02</td>
</tr>
<tr>
<td>Maximal DI</td>
<td>0.68±0.04</td>
<td>0.69±0.04</td>
</tr>
</tbody>
</table>

ACQ: Asthma Control Questionnaire; AQLQ: Asthma Quality of Life Questionnaire; VO\(_{2}\): Oxygen uptake; VO\(_{2}\): Ventilation; DI: Dyspnea Index

\(^{†}\)n=12 for paper measurements only; \(^{‡}\)n=17 for paper measurements only; \(^{#}\) significant differences at baseline between control and exercise group; \(^{*}\)p<0.05 between groups from T1 to T2; **p<0.05 within exercise group from T2 to T3; ***p<0.05 within exercise group from T1 to T3; \(^{^}\) statistical trend from T1 to T2; p<0.10.

*Dogra. ERJ June 7, 2010*
Exercise in *children*: all compared to open label conventional treated group

<table>
<thead>
<tr>
<th>author</th>
<th>duration</th>
<th>frequency</th>
<th>type</th>
<th>P value</th>
<th>Subject #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basaran 2006</td>
<td>2 months</td>
<td>1 hour, 3X a week</td>
<td>Aerobic, moderate</td>
<td>0.001</td>
<td>62</td>
</tr>
<tr>
<td>Fanelli 2007</td>
<td>4 months</td>
<td>1.5 hours, 2X a week</td>
<td>Aerobic to 70%</td>
<td>0.03</td>
<td>38</td>
</tr>
<tr>
<td>Flapper 2008</td>
<td>3 months</td>
<td>2.5 hours, 1 time a week</td>
<td>Aerobic</td>
<td>0.02</td>
<td>36</td>
</tr>
<tr>
<td>Moreira 2008</td>
<td>3 months</td>
<td>50 minutes, 2X weekly</td>
<td>Aerobic</td>
<td>0.004</td>
<td>34</td>
</tr>
</tbody>
</table>

Exercise in **adults**: all compared to open label conventional treated group

<table>
<thead>
<tr>
<th>author</th>
<th>duration</th>
<th>frequency</th>
<th>type</th>
<th>P value</th>
<th>Subject #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turner 2010</td>
<td>6 weeks</td>
<td>1.5 hour, 3X a week</td>
<td>Aerobic, moderate</td>
<td>0.04</td>
<td>34</td>
</tr>
<tr>
<td>Goncalves 2008</td>
<td>3 months</td>
<td>0.5 hours, 2X a week</td>
<td>Aerobic to 70%</td>
<td>0.001</td>
<td>20</td>
</tr>
<tr>
<td>Mendes 2010</td>
<td>3 months</td>
<td>0.5 hours, 2X a week</td>
<td>Aerobic to 70%</td>
<td>0.001</td>
<td>101</td>
</tr>
</tbody>
</table>

D. Pacheco, J of Asthma, 2012
Exercise in *Adults, non aerobic*: all compared to open label conventional treated group

<table>
<thead>
<tr>
<th>author</th>
<th>duration</th>
<th>frequency</th>
<th>type</th>
<th>P value</th>
<th>Subject #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sabina 2005</td>
<td>1 month</td>
<td>1.5 hour, 2X a week</td>
<td>Yoga</td>
<td>NS</td>
<td>62</td>
</tr>
<tr>
<td>Thomas 2009</td>
<td>1 and 6 months</td>
<td>3 sessions</td>
<td>Breathing exercises</td>
<td>NS</td>
<td>183</td>
</tr>
<tr>
<td>Vempati 2009</td>
<td>2 months</td>
<td>1.5 hours, daily</td>
<td>Yoga</td>
<td>0.013</td>
<td>57</td>
</tr>
</tbody>
</table>

Correct statement for treatment for OSA?

• 1. Weight loss is just as effective as CPAP
• 2. CPAP is better than weight loss
• 3. CRP is reduced more with CPAP than Weight loss
• 4. No one is adherent anyway so why try

• Ans:
Correct statement for treatment for OSA?

• 1. Weight loss is just as effective as CPAP
• 2. CPAP is better than weight loss
• 3. CRP is reduced more with CPAP than Weight loss
• 4. No one is adherent anyway so why try

• Ans:
Correct statement for treatment for OSA?

• 1. Weight loss is just as effective as CPAP
• 2. CPAP is better than weight loss
• 3. CRP is reduced more with CPAP than Weight loss
• 4. No one is adherent anyway so why try

• Ans: 1
Adverse Impact of obesity on allergic diseases

- Obesity is associated with increase risk of asthma
- OSA and asthma overlap
- Obesity is associated with increased risk of rhinitis
- Rhinitis is associated with increase in OSA
- Impaired sleep causes an inflammatory state
- Sleep impairment in allergic diseases can be caused by
  - Inflammatory mediators
  - Symptoms, primarily ocular itch and rhinorrhea
  - Congestion
- Impaired sleep adversely affects performance, productivity and social functioning, and increases the risk of associated diseases and obesity
- Best treatment is weight loss and exercise
Thank you for your participation

- Stephanie Teets
- Stan Golden
- Josh Berlin
- Sujani Kukumanu
- Katherine Hughes
- Casey Glass
- Joel Torretti
- Faina Gurevich
- Wenxin Wei
- Jeff McCann
- Chris Hanks
- Carah Santos
- Niti Sardana
Thank you

Have a great day.