Sleep Apnea and Asthma

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Obstruction at 2 Ends of the Respiratory Tract

Obstructive Sleep Apnea

Asthma
Asthma and OSA

Common risk factors
Common symptoms
Identifying and treating one may help the other
Objectives

• Nocturnal asthma and effects of sleep on the respiratory system
• Overview of obstructive sleep apnea (OSA) in adults and children
• Interactions of OSA and Asthma
• Management of co-existent OSA and asthma
CASE

• 8 yo AA boy presented for evaluation of asthma
• Dx with asthma age 5, no prior hospitalizations
• PMH of eczema. SH- 2\textsuperscript{nd} hand smoke exposure
• Sx:
  - frequent cough and wheezing, occasional sx with exercise
  - frequent night time arousals (cough, gasping for breath)
• Loud snorer
• Worsening aggressive behavior, poor school performance
• Meds: ICS, prn albuterol, previously had been on ADHD therapy
• PE:
  - 25\% for height and 110\% for weight
  - Enlarged tonsils
  - Lungs CTA
Background

**Asthma**
- Variable (lower) airflow obstruction
- Bronchial hyper-responsiveness
- Airway inflammation/mucus
- Highly prevalent in both children and adult populations
- Adverse effects on QOL, school, work, cost of medical care, etc

**Obstructive Sleep Apnea (OSA)**
- Episodic (upper) airflow obstruction associated with irregular respiratory patterns during sleep
- Signs of poor sleep as well as daytime (awake) consequences
- Very high prevalence in adults
- Adverse effects on school/job performance
- Significant effects on CV system, risk of diabetes, and all cause mortality
# 2007 NAEEEP Guidelines

## Classification of Asthma Severity

### Components of Severity

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Classification of Asthma Severity (Youths ≥12 years of age and adults)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Persistent</strong></td>
</tr>
<tr>
<td></td>
<td>Intermittent</td>
</tr>
<tr>
<td></td>
<td>≤2 days/week</td>
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<tr>
<td></td>
<td>≤2x/month</td>
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<td>≤2 days/week</td>
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### Nighttime awakenings

<table>
<thead>
<tr>
<th>Normal FEV₁/FVC:</th>
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<tbody>
<tr>
<td>8–19 yr     85%</td>
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<tr>
<td>20–39 yr     80%</td>
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<tr>
<td>40–59 yr     75%</td>
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<td>60–80 yr     70%</td>
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<table>
<thead>
<tr>
<th>Interference with normal activity</th>
</tr>
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<tbody>
<tr>
<td>None</td>
</tr>
<tr>
<td>Minor limitation</td>
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<tr>
<td>Some limitation</td>
</tr>
<tr>
<td>Extremely limited</td>
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<table>
<thead>
<tr>
<th>Lung function</th>
<th>Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal FEV₁ between exacerbations</td>
<td>FEV₁ &gt;80% predicted</td>
</tr>
<tr>
<td>FEV₁ &gt;80% predicted</td>
<td>FEV₁/FVC normal</td>
</tr>
<tr>
<td>FEV₁/FVC normal</td>
<td>FEV₁ &lt;60% but &lt;80% predicted</td>
</tr>
<tr>
<td>FEV₁/FVC reduced 5%</td>
<td>FEV₁ &lt;60% predicted</td>
</tr>
<tr>
<td>FEV₁/FVC reduced &gt;5%</td>
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<table>
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<tr>
<th>Risk</th>
<th>Exacerbations requiring oral systemic corticosteroids</th>
</tr>
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<tr>
<td></td>
<td>0–1/year (see note) ≥2/year (see note)</td>
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Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.

Relative annual risk of exacerbations may be related to FEV₁.
Nocturnal Asthma

- Asthma-related sleep disruptions have been reported in up to 80% of adult patients. Also very high in children.
- Characterized by 15% decrease in FEV1 between bedtime and awakening
- Nocturnal symptoms of cough, wheezing, SOB, gasping for breath may represent asthma or other conditions (OSA)
- Worsening of sx between midnight and 8am
  - More ER visits
  - More calls to physicians
  - High percentage of asthma-related deaths
Circadian Alterations in Lung Function

Sutherland, J Allergy Clin Immunol, 2005; 116:1179-86
Factors contributing to worsening asthma during sleep

- Increased airway resistance due to activation of cholinergic pathways
- Decreased lung volumes
- Enhanced airway inflammation
- Nocturnal GERD
- Increased pulmonary capillary blood volume
- Reduced mucociliary clearance
- Diurnal variation in beta2-adrenergic and corticosteroid receptor sensitivity
- Melatonin secretion associated with increased production of pro-inflammatory cytokines
- Allergic rhinosinusitis
- Environmental allegries (indoor pets)
Mean changes in peak expiratory flow rate (PEFR) and the plasma concentrations of cortisol, epinephrine, cyclic AMP, and histamine over a 24-hour period in patients with nocturnal asthma. The nadir in PEFR, which occurs at 4 AM, is associated with low levels of cortisol and epinephrine and high levels of the bronchoconstrictor mediator, histamine.

Nocturnal Asthma

Timing of dyspneic episodes in asthma

Time course of dyspneic episodes in 3129 mainly asthmatic patients. Most of the episodes occurred at night.

Adapted from Dethlefsen, U, Repgas, R, Clin Med 1985; 80:4...
Obstructive Sleep Apnea

Upper airway occlusion

Respiratory cessation (apnea) or suppression (hypopnea)

Oxygen desaturation

Airway obstruction terminated by arousal from sleep

Obstructive sleep apnea occurs when muscles at the back of the throat relax and obstruct airflow. These muscles normally support your tonsils and tongue, the soft palate on the roof of your mouth, and the uvula, which hangs from the soft palate at the back of your mouth.

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Adult Sleep Apnea

- 25% of adults are at high risk for OSA
- Risk factors:
  - **OBESITY**
  - Male sex
  - **Large neck size** (circumference >40cm)
  - Craniofacial, nasal, throat soft tissue abnormalities
  - Smokers
  - Advancing age
  - Family History
  - HTN, DM

“King Kong Bundy”
Clinical Manifestations:
- Snoring
- Excessive daytime sleepiness
- Restless sleep
- Poor concentration/work performance
- Increased risk of car accidents!
- Sensing nocturnal dyspnea, choking, gasping
- Insulin resistance and profound cardiovascular effects
  - HTN
  - Congestive Heart Failure
  - Increased risk of strokes, MI
Sleep Disordered Breathing and Mortality: Eighteen-Year Follow-up of the Wisconsin Sleep Cohort

Terry Young, PhD¹; Laurel Finn, MS¹; Paul E. Peppard, PhD¹; Mariana Szklo-Coxe, PhD¹; Diane Austin, MS¹; F. Javier Nieto, PhD¹; Robin Stubbs¹, BS; K. Mae Hla, MD²

Prospective population-based study of 1546 patients who underwent formal PSG

Random sample of men and women (30-60) recruited from state employment records

Cox proportional hazard regression used to estimate all-cause and CV mortality
Chronic Hypoxia and High Fat Diet Causes Atherosclerosis in Mice

Savransky, AJRCCM 2007; 175: 1290-1298
Diagnosis of OSA--- Polysomnography

PSG
- EEG to determine sleep stage
- Microphone (snoring?)
- Measurements of airflow
- Thoracic/abdominal/leg movement
- Oxygenation
- Ventilation (etCO2)
- Others (pH probe, extended EEG)

Apnea-Hypopnea Index (AHI):

#total number of apneas or hypopneas
hr of sleep
Diagnosis of OSA--- Polysomnography
Diagnosis of OSA--- Polysomnography
Diagnosis of OSA--- Polysomnography
Treatment of Adult OSA- CPAP
Less Effective Treatments for Adult OSA

- Surgery
- Dental Appliances
Pediatric Obstructive Sleep Apnea

- 7-9% children snore
- OSA in 2% of 4-5 year olds
- Risk Factors
  - Adenotonsilar hypertrophy (snoring)
  - Obesity
  - Congenital abnormalities affecting jaw
  - Cerebral palsy, Down Syndrome
  - Family history
  - History of low birth weight
Pediatric Airway Abnormalities

- Pierre-Robin Syndrome
- Down’s Syndrome
- Cleft Palate
Severity of Medical Complications

- Nocturnal enuresis
- Sinus arrhythmia
- Growth Failure – FTT
- Systemic hypertension
- Aspiration
- Seizures
- Pulmonary hypertension
- Cor pulmonale
- Coma
- SIDS
- Death

Behavioral Complications

- Developmental delay
- Poor school performance
- Attention-deficit and hyperactivity disorder
- Aggressive behavior
- Excessive daytime somnolence
- Mood swings and irritability
- Learning disability

Gozal, D. et al. Pediatrics 102;87: 616-620
Sleep-Disordered Breathing and School Performance in Children

- Children with OSAS treated with T&A had significant improvement in grades.

sleep-associated gas exchange abnormalities (SAGEA); TR, treated. NT, not treated. PS, primary snorer. CO, control.

Treatment of Pediatric OSA

• Treatment
  - Adenotonsillectomy!!
  - Nocturnal positioning/weight loss
  - CPAP in some cases
Tonsillectomy

- Mouth Gag
- Tongue
- Endotracheal Tube for Anesthesia
- Right Tonsil
- Tonsillar Bed
- Anterior Pillar
- Soft Palate
- Uvula
- Upper Incisors

www.ghorayeb.com
Adenotonsillectomy Outcomes in Treatment of Obstructive Sleep Apnea in Children
A Multicenter Retrospective Study

Rakesh Bhattacharjee¹, Leila Kheirandish-Gozal¹,⁹, Karen Spruyt¹,⁹, Ron B. Mitchell², Jungrak Promchiarak³, Narong Simakajornboon³, Athanasios G. Kaditis⁴, Deborah Spleinard⁵, Mark Spleinard⁵, Lee J. Brooks⁶, Carole L. Marcus⁶, Sanghun Sin⁷, Raanan Arens⁷, Stijn L. Verhulst⁸, and David Gozal¹,⁹

Multicenter retrospective review of 578 children who underwent AT for treatment of OSA

- Analyzed pre- and post-AT sleep studies
- Significant improvement in AHI and other sleep parameters
- Obesity and Asthma were risk factors for AT treatment failure

Post-surgical PSG recommended for these “high risk” patients
## Key Differences: Adult vs. Pediatric OSA

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<thead>
<tr>
<th></th>
<th>Adults</th>
<th>Children</th>
</tr>
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<tbody>
<tr>
<td><strong>Peak Age</strong></td>
<td>Elderly</td>
<td>Preschoolers</td>
</tr>
<tr>
<td><strong>Etiology</strong></td>
<td>Obesity/neck size</td>
<td>Adenotonsillar hypertrophy</td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td>Obese</td>
<td>Variable</td>
</tr>
<tr>
<td><strong>Common Daytime</strong></td>
<td>Daytime Hypersomnolence</td>
<td>Hyperactivity</td>
</tr>
<tr>
<td><strong>Features</strong></td>
<td>Cognitive impairment</td>
<td>Developmental Delay</td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
<td>AHI&gt;5</td>
<td>AHI&gt;1</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>CPAP</td>
<td>Adenotonsillectomy</td>
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</tbody>
</table>
OSA and asthma

• Studies have demonstrated that asthma is associated with:
  • Decreased sleep quality
  • Snoring
  • Early awakening
  • Difficulty maintaining sleep
  • Daytime hypersomnolence

Does this occur directly because of asthma?
Are asthmatics particularly at risk for sleep disordered breathing (OSA)?
Evidence that OSA and asthma are linked

- Share common risk factors (obesity, allergic rhinitis, etc.)
- Prevalence of both conditions increasing

- Bronchial hyper-responsiveness has been described in OSA patients without asthma or atopic disease.

  **AND**

- Treatment with CPAP can improve this hyper-reactivity
  
  Lin, Lung 1995; 173:117-126

- Improved asthma control in OSA-asthma patients treated with CPAP
  
  Chan, Am Rev Resp Dis 1988; 137:1502-1504
• PSG performed on 26 patients with severe asthma, 26 with moderate asthma, and 26 non-asthma controls (matched for age and body size)
• OSA diagnosis:
  - 23/26 (88%) of severe asthmatics
  - 15/26 (58%) of moderate asthmatics
  - 8/26 (31%) of controls
• AHI values, oxygen saturations,
• No correlation between severity of OSA and asthma severity, lung function, or self-reported asthma control

Julien, J Allergy Clin Immunology 2009; 124:371-6
Evidence that Pediatric Asthma and OSA are Linked

• Children with wheezing are more likely to have tonsillar hypertrophy

• Asthma increases the risk of snoring and OSA

  Redline, AJRCCM 1999; 159:1527-32

• Treatment of OSA has been shown to improve the quality of nocturnal asthma

  Chan; Am Rev Respir Dis 1988; 137:1502-4

• Insomnia in children with asthma may reflect underlying OSA

  Levine, Sleep 1987; 10:590-9

• Asthma is a risk factor for increased respiratory complications after adenotonsillectomy in children with snoring and physical signs of upper airway obstruction

  Kalra, Ann Allergy Asthma Immunol 2005; 94: 549-52
Mechanisms of OSA *Worsening* Asthma

- Upper airway edema
- Systemic inflammation
- Sleep deprivation
- Cardiac dysfunction
- Increased GERD and microaspiration
- CPAP may increase airway reactivity
- Obesity
  - Asthma control improves in obese patients who lose weight
  - Medications commonly used for comorbid conditions (beta-blockers, ACE-I) may worsen asthma control
Inflammation and OSA

- Snoring itself may cause vibratory trauma in upper airway and trigger immune response
- CRP is elevated in OSA
- Increased production of reactive oxygen species
- Endothelial cell damage and dysfunction
- Circadian rhythm of TNF-alpha secretion abnormal in OSA
- Obesity associated with leptin, adiposectin, TNF-alpha, IL-6
- Increased levels of IL-6 and IL-8 in exhaled breath condensate of OSA patients
- Increased PMNs in upper airway mucosa

Kasabeh, Sleep Medicine Reviews 2007; 11:47-58
Thickened/reactive airways in OSA patients

Bronchial hyperreactivity and airway wall thickening in obstructive sleep apnea patients

Nesrin Sarıman · Ender Levent · Rahmi Çubuk · Şirin Yurtlu · Fehime Benli Aksungar

Sleep Breath 2010 (Epup)
Mechanisms of Asthma *Worsening* OSA

- Systemic inflammation
- Steroid therapy
  - Effects of prolonged steroid use on upper airway integrity
  - Metabolic alkalosis can induce apneic periods
- Allergic rhinitis/nasal congestion
Treatment of OSA in the asthmatic patient

- **Adults**
  - CPAP
  - Weight loss/exercise

- **Children**
  - Adenotonsillectomy
    - Asthma is a risk factor for increased respiratory complications following surgery in children who snore who have physical findings of potential upper airway obstruction.
  - CPAP in some cases
  - Weight loss/exercise
• Inhaled corticosteroid/long-acting beta agonist products
• Chronotherapy of PO steroids (3pm)
• Theophylline
• Treatment of GERD
• Treatment of allergic rhinitis
8 yo AA boy presented to clinic for evaluation of asthma and possible OSA
Dx with asthma age 5, no prior hospitalizations
PMH of eczema. SH- 2nd hand smoke exposure
Sx:
- frequent cough and wheezing, occasional sx with exercise
- frequent night time arousals (cough, gasping for breath)
Loud snorer
Worsening aggressive behavior, poor school performance
Meds: ICS, prn albuterol, previously had been on ADHD therapy
PE:
- 25% for height and 110% for weight
- Enlarged tonsils
- Lungs CTA
Case: Initial PSG

AHI of 21.5 events/hr, lowest O2 sat 68%
• Underwent adenotonsillectomy
• Improved snoring and daytime sleepiness
• Asthma improved but still sub-optimally controlled on ICS/LABA
• Repeat PSG
AHI: 12.6 events/hr, lowest O2 sat 80%
On nCPAP of 13cmH20, normalized AHI and no oxygen desaturation
Case Conclusion

- Nasal CPAP initiated
- Improved daytime somnolence, behavior, school performance
- One year later- asthma sx much improved

- Improved compliance?
- Better environment (less smoke exposure)?
- Older?
- Treatment of the OSA?
- Did control of OSA lead to his improved asthma?
OBSTRUCTIVE SLEEP APNEA

The Expert Panel recommends that clinicians consider evaluating patients who have unstable, not-well-controlled asthma, particularly those who are overweight or obese, to ascertain whether they have symptoms that suggest OSA (Evidence D).
Conclusions

• OSA is a prevalent co-morbid condition which may have significant impact on asthma control
• Clinicians should have a high index of suspicion for OSA
  • Formal sleep studies (PSG) for patients with symptoms
• Prospective, randomized-controlled studies needed to see if successful treatment of OSA improves asthma control (and vice versa)
Questions?

Common risk factors
Common symptoms
Identifying and treating one may help the other