Pulmonary Complications
Pediatric Obesity

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Outline

- Obstructive Sleep Apnea
  - Definition of Obstructive Sleep apnea, Pathophysiology and Consequences.
  - Interactions of Sleep Apnea and Obesity
  - Diagnosis & Treatment

- Asthma
  - Pathophysiology
  - Diagnosis and Management

- Comparison of OSA and Asthma in Obesity
Primary Snoring

- Primary Snoring
  - Snoring is noted but no polysomnographic abnormalities
  - Several studies suggest that some patients may have neurobehavioral consequences.
  - Habitual snoring in 3-12% of the population and 1-3% have OSA

Katz et. al. 2005
Definitions

- Upper Airway Resistance Syndrome
  - Brief repetitive, respiratory related arousals during sleep in the absence of overt apnea, hypopnea, or gas exchange abnormalities
  - It has been linked to significant cognitive and behavioral sequelae in children including learning disabilities, attention deficit, hyperactivity, and aggressive behavior.

Katz et. al. 2005
Definitions

- **Obstructive Sleep Apnea Syndrome**
  - Recurrent episodes of partial or complete airway obstruction resulting in hypoxemia, hypercapnia, and/or respiratory arousal.
  - Children with OSA can develop a combination of oxidative stress, inflammation, autonomic activation, and disruption of sleep homeostasis.
  - OSA may produce metabolic, cardiovascular, and neurocognitive side effects.

Katz et. al. 2005
Epidemiology

- Sample size greater than 1000 with representative questionnaire based studies and whether objective testing was performed
  - 27% snored sometimes.
  - 11.7% snored ≥ to 3 times a week
  - 10.9% almost always snored
  - 4.2% always snored
  - 2.2 to 3.8% OSA determined objectively
<table>
<thead>
<tr>
<th>Epidemilologic Risk Factors</th>
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<tbody>
<tr>
<td><strong>↑ Size Adenoids, Tonsils</strong></td>
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<tr>
<td>Obesity</td>
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<tr>
<td>Race (African Amer)</td>
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<tr>
<td>Gender (Male)</td>
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<tr>
<td>Prematurity</td>
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<tr>
<td>Craniofacial Abnorm</td>
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<tr>
<td>Neurologic D/O</td>
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<tr>
<td>Nasal Pharyngeal Inflam.</td>
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<tr>
<td>Socio/Economic/Environ</td>
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<td>FH of OSA</td>
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</table>
Pathophysiology of Pediatric OSA

Airway Narrowing

Abnormal Neuromuscular Control

Obstructive Sleep Apnea

Obesity

Genetics
Cross-Section of Oropharynx

- Nasal obstruction
- Micro- or retrognathia
- Tonsillar hypertrophy
- Large tongue
Neuromuscular Compensation, Arousal, and Ventilatory Control

- Upper airway muscles, such as the genioglossus, increased both the luminal size and the stiffness of the airway.
Airway Mechanics

- The critical closing pressure is the luminal pressure at which airway collapse occurs.
- The critical closing pressure (Pcrit) is higher in children with OSA.
  - In patients with OSA after T & A, the Pcrit in these patients is still higher than controls suggesting subtle anatomic and neuromuscular control abnormalities.
Neuromuscular Compensation, Arousal, and Ventilatory Control

- Children with OSAS have increased genioglossus activity compared to controls.
- At sleep onset, pharyngeal dilator activity is reduced, ventilatory variability increases, apneic threshold increases in non REM sleep.
- Airway collapse is offset by increased pharyngeal dilatory activity in non REM sleep.
Neuromuscular Compensation, Arousal, and Ventilatory Control

- Arousals from sleep immediately open the airway and normalize gas exchange abnormalities.
  - Potentiates obstructive cycling by augmenting ventilatory overshoot
  - Interferes with sleep homeostasis.
- REM sleep further reduces pharyngeal dilator activity which is a cause of disproportionate severity of OSA in REM.
Consequences of Obstructive Sleep Apnea

- Metabolic
- Cardiovascular
- Neurocognitive
Neurocognitive Sequelae of Pediatric OSA

- Decreased Quality of Life
- Aggressive Behavior
- Poor school performance
- Depression
- Attention Deficit
- Hyperactivity
- Moodiness
Metabolic Sequelae of Pediatric OSA

- Elevated CRP
- Possible Insulin Resistance
- Hypercholesterolemia
- Elevated Transaminases
- Decreased insulin like growth factor
- Decreased or altered growth hormone secretion
Cardiovascular Sequelae of Pediatric OSA

- Autonomic Dysfunction
- Systemic Hypertension
- Absent Blood Pressure Dipping
- Left Ventricular Dysfunction
- Pulmonary Hypertension
- Abnormal Heart Rate Variability
- Elevated Vascular Endothelial Growth Factor.
Obesity and Sleep

- Short sleep times has been associated with being overweight and obese.
  - Systematic review has shown an inverse relationship between sleep duration and obesity risk.
  - Ages 2 thru 6, if less than 10 hours sleep 4.2 times likely to be overweight
Obesity and Obstructive Sleep Apnea.

- 46 to 59% patients of patients with obesity have OSA.
- Factors increasing chances OSA
  - Adenotonsillar hypertrophy
  - Fat deposition lateral fat pads, uvula, and tongue
  - Increased collapsibility of the pharynx
  - Truncal obesity associated with increase work of breathing and hypoxia.
Relationship of Obesity and Obstructive Sleep Apnea.

- OSA may predispose patients to obesity by derangement in adipose hormone functioning.
- May have an impact on contributing to leptin resistance.
- Sleep fragmentation and daytime sleepiness could have an impact as well.
- OSA is a low grade inflammatory process and coexistence with obesity may augment that process.
Relationship of Obesity and Obstructive Sleep Apnea.

- However not every patient with OSA will go onto develop metabolic dysfunction.
- This finding suggests other environmental and genetic factors.
- This area is in need of trials to assess the relationship between OSA, obesity and metabolic syndrome.
- These hypothesis are being assessed in clinical trials.
Obesity and Obstructive Sleep Apnea

**Figure 31-1** Schematic diagram illustrating the potential interactions between sleep, obstructive sleep apnea, obesity, and metabolic dysfunction in children.
OSA, Obesity and Metabolic Syndrome

- Includes insulin resistance, dyslipidemia, elevated blood pressure, and obesity.
- Insulin resistance and glucose intolerance were independently associated with OSA in adults. Pediatric Data is not as consistent.
- Variability in the association SDB and low HDL
- OSA has consistently been shown to be associated with elevated diastolic BP
Obesity and Metabolic Syndrome.

**Figure 17-1** Potential contributions of obstructive sleep apnea to the metabolic syndrome. TG, triglycerides; HDL, high-density lipoprotein; BP, blood pressure; SNS, sympathetic nervous system; HIF-1, hypoxia-inducible factor-1; OSA, obstructive sleep apnea.
OSA, Obesity and Metabolic Syndrome

- Interventional studies with T&A or CPAP have shown to be beneficial in some cases
  - In Pediatric Studies, glucose metabolism improves with treatment.
  - Interventional studies have shown improvement in total cholesterol, HDL and LDL.
  - Diastolic hypertension has consistently shown to improve with either T&A or CPAP.
  - Longitudinal study of weight after T and A did not show an improvement in weight.
History – Nocturnal Symptoms

- Sleep history
  - Snoring: unlikely to have sleep apnea if no history of snoring
    - Older patients may be the exception and history may not be accurate.
  - Respiratory pauses while sleeping
  - Increased work of breathing
  - Paradoxical respirations
  - Enuresis
  - Restless sleep
History - Nocturnal Symptoms

● Sleep history
  ● Choking while sleeping
  ● Restless sleep
  ● Hyper extended neck
  ● Frequent awakenings
  ● Mouth breathing or dry mouth
  ● Increase in parasomnias such as sleep walking
  ● Quality of sleep.
History – Diurnal Symptoms

- Sleep Excessive daytime sleepiness: 7.5% of patients with history of OSA syndrome have this complaint
  - Napping
  - Morning headaches
  - Difficulty arousing during sleep
- Upper Airway
  - Mouth breathing
  - Nasal congestion
  - Frequent otitis media or sinusitis
  - Nasal speech
History – Diurnal Symptoms

- Neurocognitive.
  - Poor school performance
  - Aggressive behavior
  - Attention deficit disorder
  - Hyperactivity
  - Depression
  - Moodiness
Obesity is associated with other Sleep disorders.

- Narcolepsy
  - Rapid weight gain with the presentation of narcolepsy is a common presentation.
  - Animal models have shown hypersomnolence with weight gain on restricted diet has been demonstrated when hypocretin (orexin) neurons in the hypothalamus ablated.
  - Specific cause unknown but is likely a complex set of relationships involving neurotransmitters feeding and metabolism.
Obesity is associated with other Sleep disorders.

- Sleep-related eating disorder
  - Recurrent episodes of nocturnal awakening with associated eating without recollection.
  - A parasomnia like Sleepwalking

- Inadequate Sleep Hygiene
Physical Exam

- General
  - Sleepiness
  - Obesity
  - Failure to Thrive
  - Neck Size > 17” associated with OSA in Adults

- Cardiovascular
  - Hypertension
  - Loud P2

- Extremities
  - Clubbing
  - Edema

- Neurologic
  - Increased tone
  - Developmental Delay
Physical Exam: HEENT

- Swollen nasal mucosa
- Deviated Septum
- Adenoidal Facies
  - Infraorbital darkening
  - Elongated Face
  - Mouth Breathing
- Tonsillar Hypertrophy
- High Arched Palate
- Overbite

- Crowded Oropharynx
- Macroglossia
- Glossoptosis
- Midfacial Hypoplasia
- Micrognathia
- Retrognathia
Facial Findings: Midface Hypoplasia
Facial Findings: Micrognathia/Retrognathia
Facial Findings: Adenoidal Facies, Long Face Syndrome

- Infraorbiatal darkening
- Mouth Breathing
- Elongated Midface
- Nasal Atrophy
Nasal Findings: Edematous Nasal Turbinates
Nasal Findings: Deviated Septum
Mouth Findings: Overbite
Mouth Findings: High Arched Palate
Mouth Findings: Scoring Tonsils
Mouth Findings: Mallampati Score

Class I

Class II

Class III

Class IV
Syndromes Associated with OSA

- Down’s Syndrome
- Prader Willi
- Achondroplasia
- Treacher Collins
- Hunter’s/Hurler’s
- Pierre Robin
- Cleft Palate/Lip
- Muscular Dystrophy
- Spinal Muscular Atrophy
- Cerebral palsy
- Sickle Cell disease
- Spina Bifida
Recognition of OSA in Children

- Difficult to predict diagnosis of sleep apnea based on awake evaluation
  - Parents may miss night time symptoms
  - Daytime symptoms in children can be subtle
  - Presence of snoring is helpful but only predictive that will have snoring on the sleep study.
- Physical Exam can be normal
- 50/50 chance correct diagnosis based on clinical assessment.
Diagnostic Studies

- The gold standard for the diagnosis of obstructive sleep apnea is polysomnography.
- Ancillary data such as xrays, Hct, serum bicarbonate, EKG, echocardiogram, and neurocognitive testing are non specific.
- Home video recordings can be helpful with sensitivity of 92% but specificity of 29% as it misses subtler forms of OSA.
Pediatric Polysomnography

EEG

EOG

Nasal EtCO2

Chin EMG (2)

Sao2

Respiratory Effort

Nasal Oral Airflow

Microphone

EKG

Leg EMG (2)

EEG

EOG

Nasal EtCO2

Chin EMG (2)

Sao2

Respiratory Effort

Nasal Oral Airflow

Microphone

EKG

Leg EMG (2)

Tech Observer

Documents arousals, parasomnias, abnormal sleeping position, and attends to any technical problem

Video Camera

Record behavior

Courtesy of Dr. Carol Rosen
Obstructive Apnea
Obstructive Hypopneas
Central Apnea
Polysomnogram: Normals

- What is normal for children is different than adults.
- It is has taken some time to sort out what normals are for children.
- Also, if there are abnormalities on the the PSG what should the intervention be.
Polysomnogram: Normals

- **Respiratory Parameters**
  - Obstructive Apnea Index/h TST 0.0 ± 0.1
  - Apnea Hypopnea Index/h TST 0.1 ± 0.1
    - Includes Central, Obstructive, Hypopneic
  - Central Apnea Index/h TST 0.5 ± 0.5
  - %TST ET CO2 > than 50 2.8 ± 11.3
  - Peak ET CO2 46 ± 3
  - Oxygen Saturation < 90% (%TST) 0.05 ± 0.2
### Classification of OSA

#### TABLE 28.4 Diagnostic Classification and Severity of SDB

<table>
<thead>
<tr>
<th></th>
<th>APNEA INDEX (Events/h)</th>
<th>SpO₂ NADIR (%)</th>
<th>Pₑ₇CO₂ PEAK (Torr)</th>
<th>Pₑ₇CO₂ &gt; 50 Torr (%TST)</th>
<th>AROUSALS (Events/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Snoring</td>
<td>≤1</td>
<td>&gt;92</td>
<td>&lt;53</td>
<td>&lt;10%</td>
<td>EEG &lt;11</td>
</tr>
<tr>
<td>Upper Airway Resistance Syndrome</td>
<td>≤1</td>
<td>&gt;92</td>
<td>&lt;53</td>
<td>&lt;10%</td>
<td>RERA &gt;1, EEG &gt;11</td>
</tr>
<tr>
<td>Mild OSAS</td>
<td>1–4</td>
<td>86–91</td>
<td>&gt;53</td>
<td>10–24%</td>
<td>EEG &gt;11</td>
</tr>
<tr>
<td>Moderate OSAS</td>
<td>5–10</td>
<td>76–85</td>
<td>&gt;60</td>
<td>25–49%</td>
<td>EEG &gt;11</td>
</tr>
<tr>
<td>Severe OSAS</td>
<td>10</td>
<td>≤75</td>
<td>&gt;65</td>
<td>≥50%</td>
<td>EEG &gt;11</td>
</tr>
</tbody>
</table>

*Arterial oxygen saturation, SpO₂; End tidal Pco₂, Pₑ₇CO₂; EEG, electrocortical; RERA, respiratory effort related arousal; Total sleep time, TST*
Problems with Diagnosis of OSA based on Single Night PSG

- Although single night studies seem to be adequate, sometimes a repeat study is indicated.

- Reasons for an inadequate study
  - Inadequate REM sleep
  - Inadequate time in the supine position
  - Technical limitations in key channels
  - Parent report that not a typical night
Problems with Diagnosis of OSA based on Polysomnograms

- Efforts were made to gauge severity using variables such as AHI
  - Mild 1-5/h, Moderate 5-10/h, Severe > 10/hr
  - Gas exchange
  - Sleep fragmentation.
- Problem is that threshold of OSA associated with adverse consequences varies widely among children.
  - Patients with mild OSA may be severely affected by their OSA and vice versa may not be true.
- Efforts underway to use polysomnographic data with symptoms, biomarker, genomic profile to come up with plan.
Limits of Polysomnography

- Dilemmas
  - Treating every habitual snorer is excessive
  - The PSG alone will not guide us on how to treat these patients.
  - Not treating patients who are affected is wrong as well
  - However the treatment has measureable morbidity and mortality.
  - Unclear how to identify the vulnerable Primary Snorer.
Model of Pediatric OSA

Environmental
- Food
- Exercise
- Pollution
- Literacy

Severity of Sleep Disordered Breathing

Individual Susceptibility
- ApoE
- TNF-alpha
- FABP4
- Polymorphisms
- Genetic Disorders

Age
- Obesity
- Prematurity

Gozal 2012
Decision Making on Treatment

- History and Physical is important to look for possible areas of end organ involvement.
- PSG by itself is not adequate to assess for Pediatric OSA but need to use in combination with History and Physical.
- In patients with primary snoring or mild sleep apnea, need to have discussions around these issues and come up with a plan.
Treatment of Pediatric OSA

- Make decisions on etiology, severity, therapeutic options
- Adenotonsillectomy is first line treatment.
- CPAP would be appropriate for some patients depending on the etiology.
- Some medical treatments have shown some effectiveness in mild obstructive sleep apnea
Adenotonsillectomy

- Initial studies had that this procedure was curative of OSA, but subsequent studies have shown that a smaller percentage
- Possible predictors of failure
  - Obesity
  - Severe OSA on initial PSG
  - Asthma is also associated, possibly related to the inflammation that it produces.
  - Craniofacial disorders, Genetic Syndromes, and Neurologic disorders more likely to have persistent findings
Adenotonsillectomy

- For this reason, many patients in these groups will need to have a PSG after T and A to see if there is resolution of their symptoms.
- Also these patients seem to have more perioperative complications as well.
OSA, Obesity and Treatment

- In patients with obesity, a T&A was curative (AHI less than 1) in only 12%.
  - In the general population it is closer 70 to 80%.
- CPAP is an alternative treatment for some patients and can be used effectively.
- Weight loss is also very important.
  - Evidence is that although can decrease OSA unusual for resolution.
Children on CPAP
Positive Airway Pressure
CPAP Therapy

- The likelihood that a tonsillectomy and adenoidectomy will resolve sleep apnea in obese patients is low.
- After tonsillectomy and adenoidectomy, it is important to repeat sleep studies to assess for that.
- For severe sleep apnea, CPAP therapy is initiated before any surgical intervention to help in the postoperative phase.
Non Obstructive Hypoventilation

- Respiratory parameters during sleep.
  - Sleep related oxygen desaturations
  - During sleep decreased oxygen saturations < 90 during the study for periods greater than 5 minutes with Nadir less than 85 without evidence of obstruction
  - Elevated end tidal CO2 during sleep
    - PaCO2 greater than 45 or abnormally increased from waking
    - Pediatrics ETCO2 greater than 50 for 10% of study or ETCO2 greater than 53
  - Waking ABG may be normal or abnormal
Obesity and Non obstructive Hypoventilation

- It is important to proceed with sleep studies but also to monitor end tidal CO2 which is an important marker for hypoventilation.

- Servo ventilation devices or BiPAP with a rate are options in these patients.
Asthma

- Phenotypes
- Characteristics of Asthma in obese patients
- Treatment options
Phenotypes in Asthma

- One definition is as follows
  - “a feature, or more usually, a cluster of features which leads to the separation of a specific group from generality of wheezing at a given time.”

- Goals
  - Insight into pathophysiology of disease
  - Possible need for different treatment options

- Renewed interest in this aspect
  - Tools looking at inflammation are improved
  - New environmental factors such as obesity.
Categories of Asthma under investigation

- Episodic viral wheezing in preschool children
- Inflammatory phenotypes
  - Eosinophilic
  - Neutrophilic
- Steroid responsiveness and wheezing types
- Severe/Refractory asthma
- Obesity and asthma
Links between Asthma and obesity

- Asthma and obesity are likely to be linked in a multifactorial fashion.
- The data in adults appears to be more consistent among studies.
- In Pediatrics, there have not been as many studies and the studies at times conflict one another.
Obesity and Asthma

• Adult literature
  • Increase prevalence of obese subjects with asthma when compared to the normal populations.
  • Finding is consistent across different ethnic groups
  • The association is more prominent in non atopic disease (neutrophilic inflammation)
  • More difficult to control asthma
  • Reduced response to inhaled corticosteroids.
  • Variable Hyper responsiveness
Obesity and Asthma

- **Pediatric Literature**
  - The link has not been as consistent in pediatric literature. Some of the studies that were done had methodological concerns.
  - Even so, two prospective analyses of school age children show that asthma prevalence and incidence are increased by the presence of obesity.
Links between Asthma and obesity

- Genetics
- Environment
- Inflammation
- Airway hyper responsiveness
- Mechanical effects
Figure 1.
Proposed pathways for the association between childhood asthma and obesity. ANS, autonomic nervous system; FCR, functional residual capacity; FEV$_1$, forced expiration volume in 1 second; FVC, forced vital capacity; IL-6, interleukin-6.
Management of Asthma in Obese patients.

- No consensus on the best way to manage these patients at this time.
- Cochrane Report: “Weight loss was also associated with improvement in symptoms, reduction in need for reliever medication in the short term, and some improvement in lung function. . . Better designed and reported studies are needed, especially in children “
My Approach to Obesity and Asthma

- Continue to use the asthma guidelines as for any other patient with asthma.
- Look for possibility of co morbidities including Obstructive Sleep Apnea, GERD, Allergies, Rhinitis which may impact a patient’s asthma.
- Aggressive treatment for exercise induced symptoms with bronchodilators and may use combination therapy with an inhaled steroids and Long Acting Beta agonist.
My Approach to Obesity and Asthma

- Concerns if needing multiple course of oral steroids and will increase therapy in attempt to avoid exposure to oral steroids.
- Discuss with the families that weight loss will likely improve their symptoms.
Obesity

Asthma

OSA

Inflammation
Airway Narrowing
Conclusions

- Obstructive Sleep apnea in children causes significant Metabolic, Cardiovascular and Neurologic problems in children.

- Obstructive Sleep Apnea is an important Comorbidity in patients with Obesity and it is important to screen for it in our clinics, especially in patients who have developed metabolic syndrome.

- Sleep studies are the gold standard diagnostic study and can be used with the History and Physical to decide on the best treatment options.
Conclusions

- There appears to be a distinct form of asthma associated with overweight children which tends to be non atopic, more difficult to control, and needing increased therapy compared to similar non obese patients.
- Asthma guidelines still apply for this population but important to look for co-morbidities such as OSA and GER.
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