Upper Airway Dysfunction in Sleep Apnea

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OSA PREDISPposing FACTORS

- Age (40 - 60 years)
- Male Gender (8 : 1 male : female)
- Ethnicity (e.g., matched for age and BMI, Asians vs. Caucasians have more severe OSA)
- Hypothyroidism
- Medications, Alcohol
- Obesity
- Anatomic Abnormalities
Approximately 5% of OSA in patients are estimated to be directly due to nasal obstruction, but has indirect contributions to OSA severity.

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NASAL ANATOMY

A = Lateral nasal wall
B = Medial aspect of the inferior turbinate
C = Nasal septum

NASAL RESISTANCE DURING SLEEP

Modified from Olsen et al., 1981

Day
Night

Subjects
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**NASAL RESISTANCE DURING SLEEP**

 Modified from Olsen et al., 1981

Mean Values Per Sleep Hour

<table>
<thead>
<tr>
<th>Awakenings</th>
<th>Sleep Stage Changes</th>
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<tbody>
<tr>
<td>2</td>
<td>6</td>
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**APNEA AND NASAL RESISTANCE**

 Modified from McNicholas et al., 1982

Change Obstructive Apneas/Hour vs. Percent Change in Nasal Resistance
CONSEQUENCES OF INCREASED NASAL RESISTANCE

24 Rhesus monkeys studied at birth, 3 months, and 6 months with plugs placed in their nares had a significant nasal resistance increase.


- The increase in nasal resistance halted growth of the maxillo-mandibular skeleton, and induced changes in the naso-maxillary, mandible, and pharyngeal airway space.
- Development of mouth breathing in association with an increase in nasal resistance, led to mouth opening and mouth breathing during the day and night.
- This obligate mouth breathing and alteration in craniofacial growth are associated with OSA.

A tendency to have a retruded mandible (p=0.05)
- A greater inclination of the mandibular and occlusal planes (p<0.01)
- A tendency to have greater inclination of the upper incisors (p=0.08)
OBESITY, CRANIOFACIAL DYSMORPHISM, AND OSA

Watanabe et al; Am J Respir Crit Care Med. 2002;165:260–265
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CONTRIBUTORS TO AN ABNORMAL UPPER AIRWAY

- Excess, erythematous pharyngeal tissue
- Enlarged, erythematous uvula
- Macroglossia
- Congested nasal passages
- Maxillomandibular protrusion
- Low-lying soft palate
- High arched hard palate
- Retrognathia
• Infants with apneas had family members with OSA, and small upper airways were a common familial feature

• Relatives of OSA patients reported more OSA symptoms and sleep-related breathing disorders, plus more evidence of craniofacial dysmorphism, compared to controls

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FAMILIAL CHARACTERISTICS OF OSA

• Prior studies have shown that OSA occurs in genetically-related subjects \(^1\)
• Autosomal dominant inheritance in two small families with OSA \(^2\)
• Specific HLA markers were more frequent in Japanese OSA patients compared to selected populations \(^3\)


CANDIDATE GENES FOR CRANIOFACIAL DYSMORPHISM

• Mutations in genes belonging to the following have been identified as causes of cleft lip/palate, craniosynostosis, and other facial abnormalities:
  – fibroblast growth factor (e.g., FGFR1, FGFR2, FGFR3)
  – transforming growth factor beta (e.g., TGFBR1, TGFBR2)
  – homeobox (e.g., MSX1, MSX2)
  – sonic hedgehog (e.g., PTCH, SHH)
• Other candidate genes known to play a role in craniofacial development include the retinoic acid receptors, genes on the endothelin pathway (e.g., ECE1, EDN1 and EDNRA), and TCOF1, the cause of Treacher Collins syndrome

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PATENCY OF THE UPPER AIRWAY

Dilating Force

• Neuromuscular tone

Collapsing Forces

• Negative inspiratory force
• Gravity effects (supine)
• Sleep (REM)
• Neuromotor function (decreased tone, reflex and chemosensitivity)
• Physical characteristics
### OSA PHENOTYPES

- **Anatomy**
  - Craniofacial dysmorphism
  - Obesity
- Decreased tone of upper airway dilator muscles (HGNS)
- Low (sedatives) and high arousal threshold
- Ventilatory control stability (high loop gain) (O2)
- Fluid retention (diuretics, HOB elevation)