Upper Airway Dysfunction in Sleep Apnea

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Founding and Immediate Past President, World Sleep Society

OSA PREDISPOSING 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

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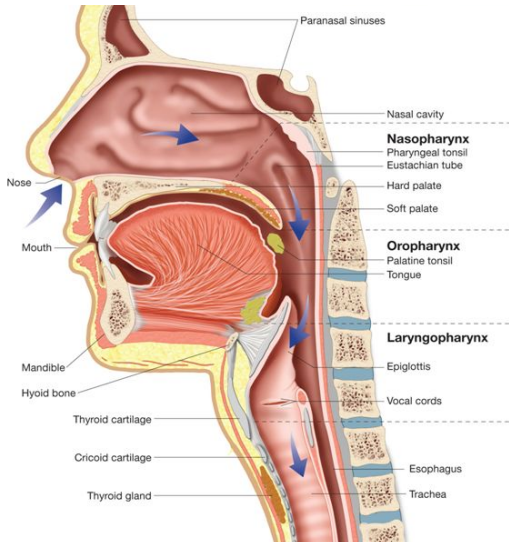
UPPER AIRWAY ANATOMY



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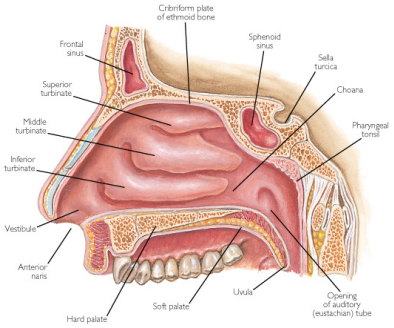
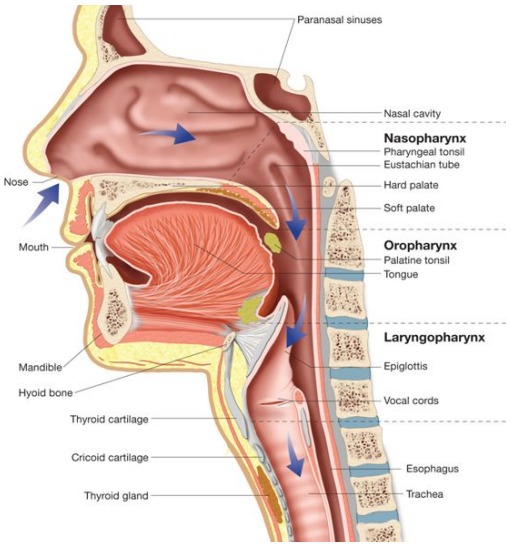
NASAL ANATOMY



Approximately 5% of OSA in patients are estimated to be directly due to nasal obstruction, but has indirect contributions to OSA severity.



Rama A, Tekwani S, Kushida CA. Sites of obstruction in obstructive sleep apnea. Chest. 2002;122(4):1139-47.

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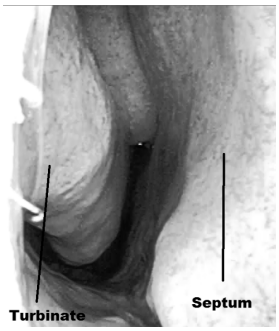
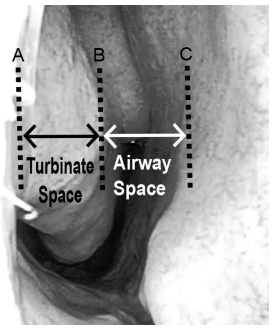
NASAL ANATOMY





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

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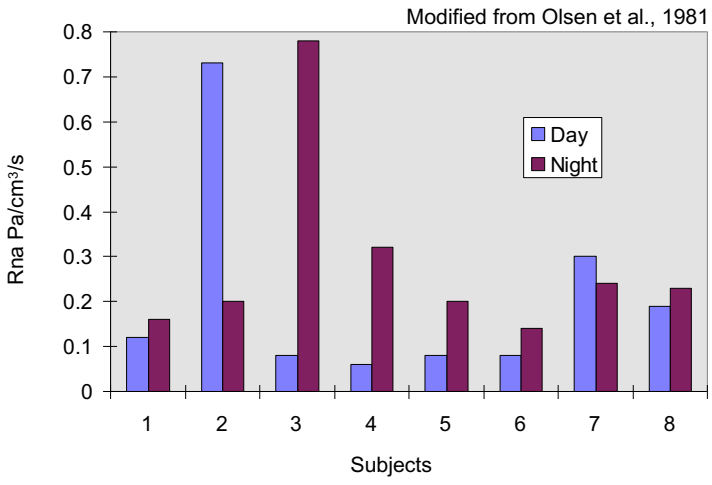
NASAL RESISTANCE DURING SLEEP



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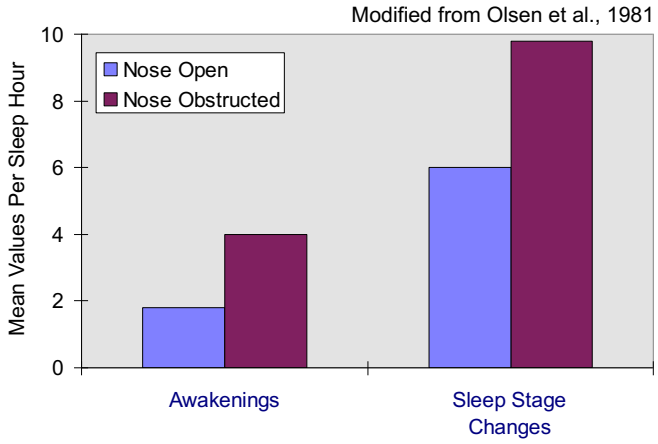
NASAL RESISTANCE DURING SLEEP



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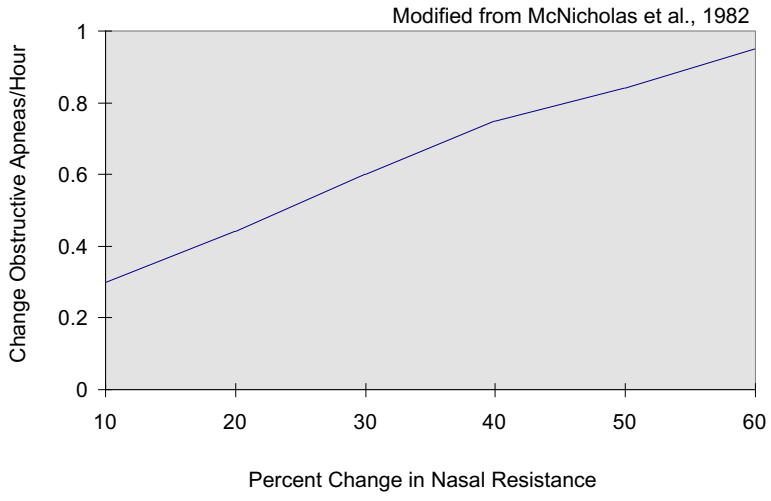
APNEA AND NASAL RESISTANCE



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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

Harvold, E, et al. Primate Experiments on oral respiration. Am J Orthod 1981:79(4);359-372

CONSEQUENCES OF INCREASED NASAL RESISTANCE

- 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.

Harvold, E, et al. Primate Experiments on oral respiration. Am J Orthod 1981:79(4);359-372

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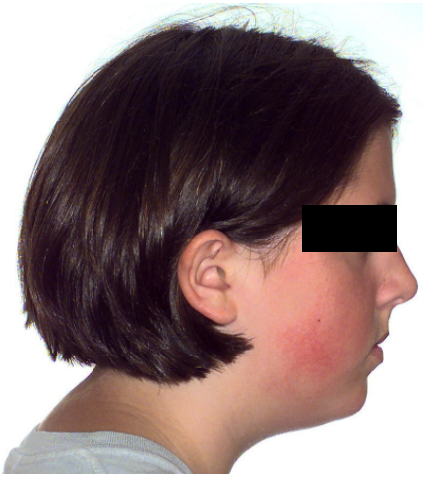
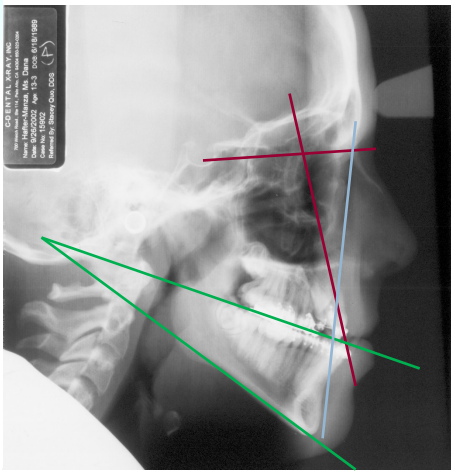
CONSEQUENCES OF INCREASED NASAL RESISTANCE





- 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)

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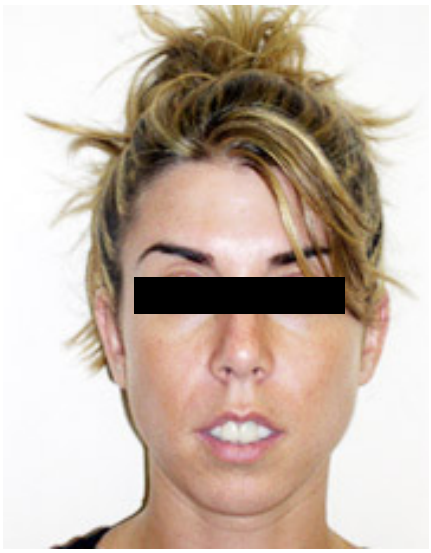
CONSEQUENCES OF INCREASED NASAL RESISTANCE



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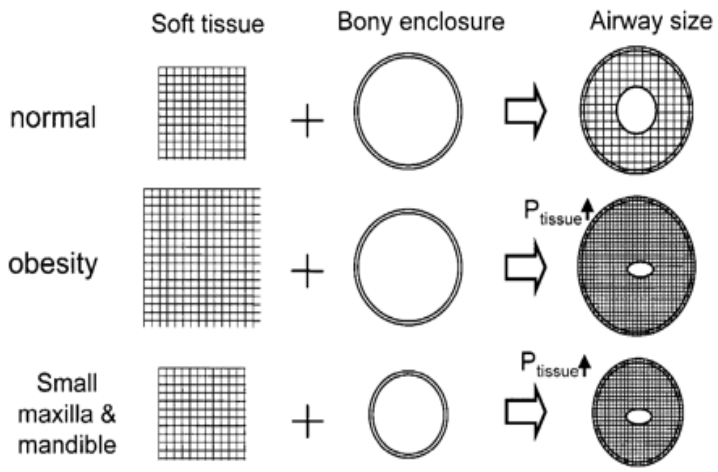
OBESITY, CRANIOFACIAL DYSMORPHISM, AND OSA



Watanabe et al; *Am J Respir Crit Care Med*. 2002;165:260–265

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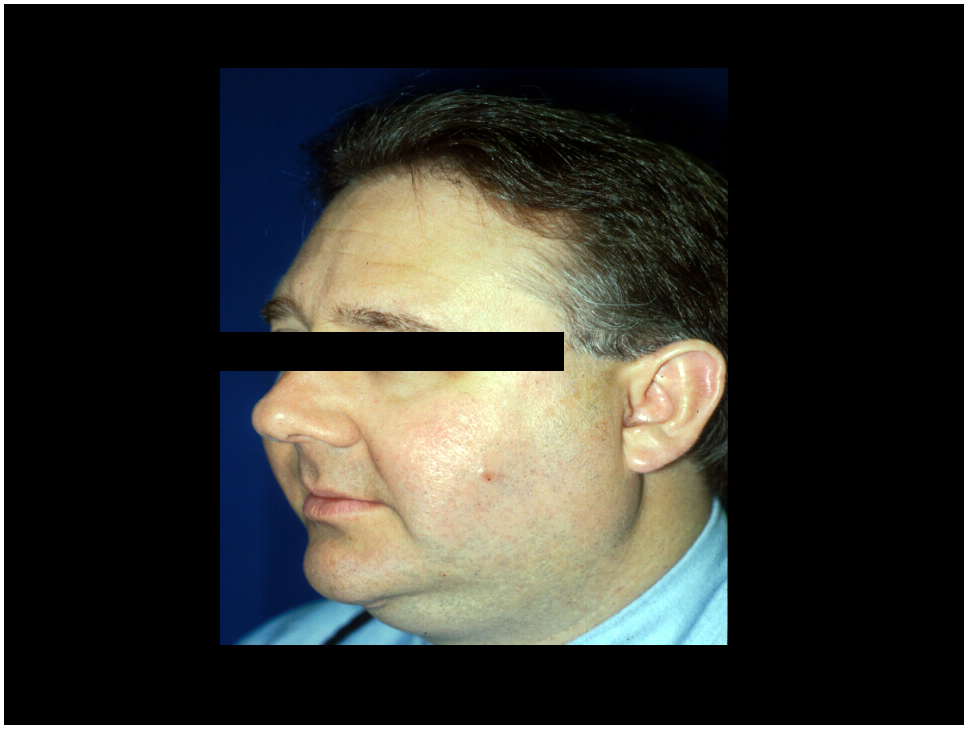
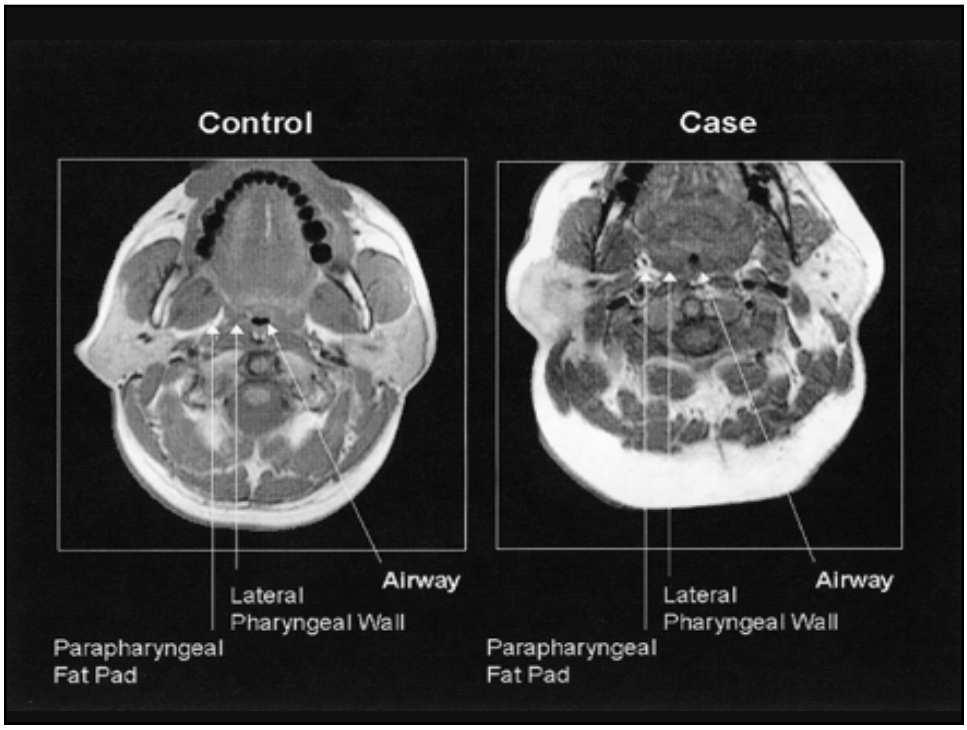
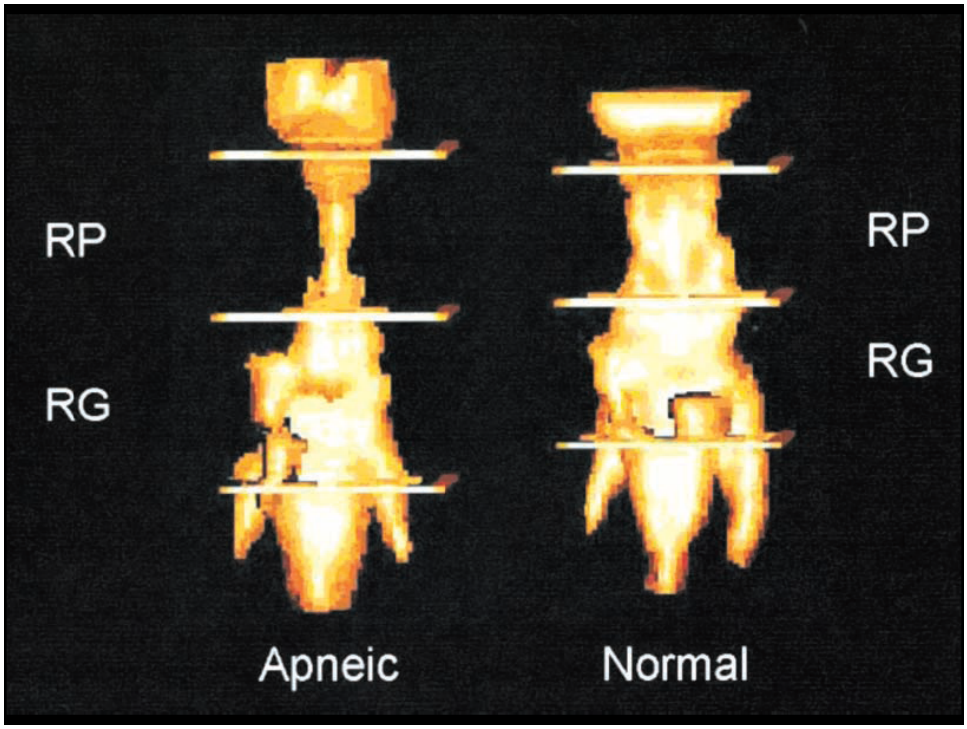
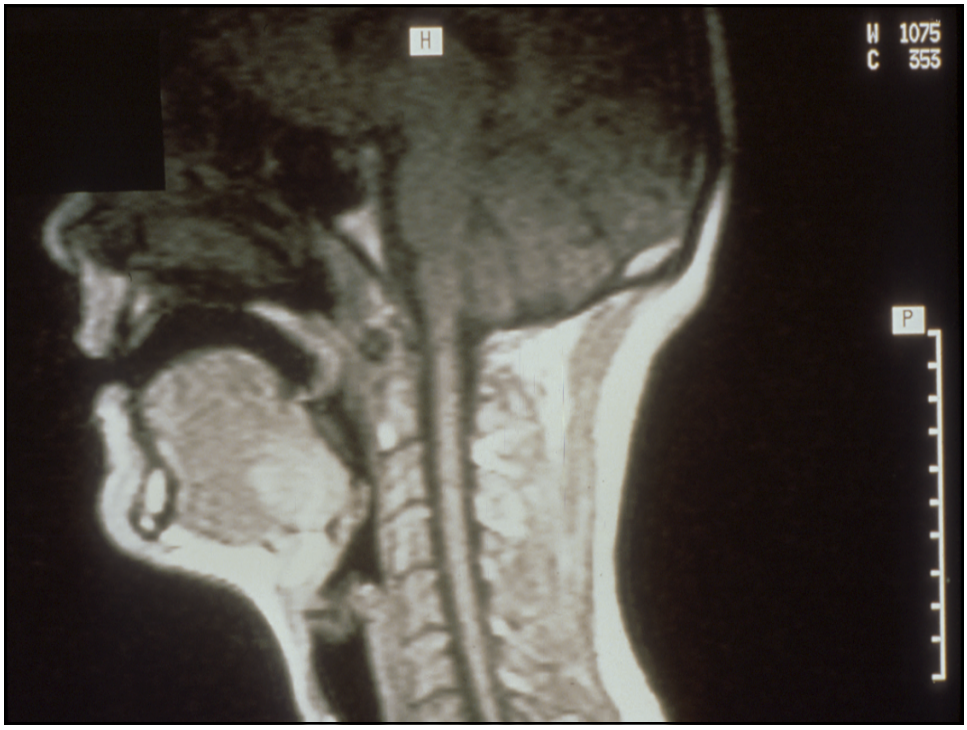



Control
Case
Airway
Lateral
Pharyngeal Wall
Parapharyngeal
Fat Pad
Airway
Lateral
Pharyngeal Wall
Parapharyngeal
Fat Pad


RP
RG
RP
RG
Apneic
Normal



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

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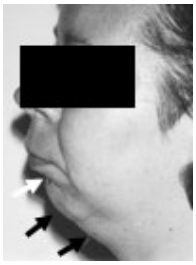
CRANIOFACIAL DYSMORPHISM AND OSA



- 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

Guilleminault, et al., 1986. Mathur and Douglas, 1995; Guilleminault, 1995

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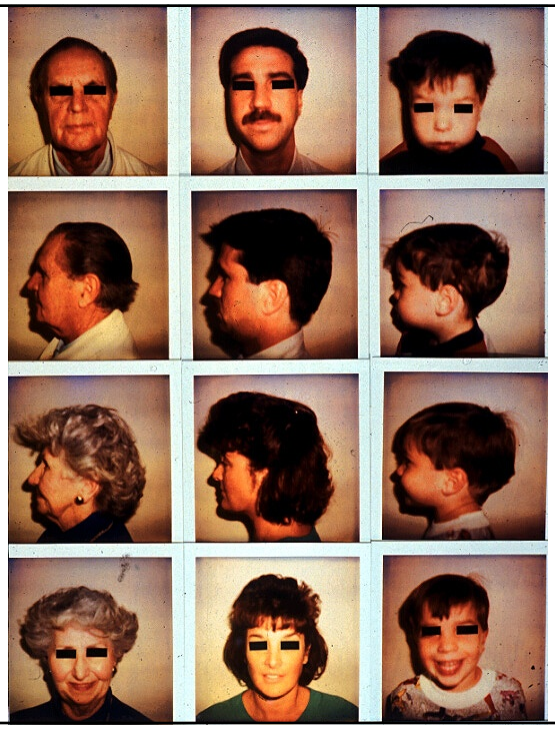

FAMILIAL CHARACTERISTICS OF OSA

- 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]

[1]Strohl, et al., 1978; Wittig, et al., 1988; Redline, et al., 1992; Mathur and Douglas, 1995; Pillar and Lavie, 1995. [2]Manon-Espaillat, et al., 1988; El Bayadi, et al., 1990. [3]Yoshizawa, et al., 1993

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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

Patel SR, Tishler PV. Familial and genetic factors. In: Kushida CA, Obstructive Sleep Apnea, 2007.

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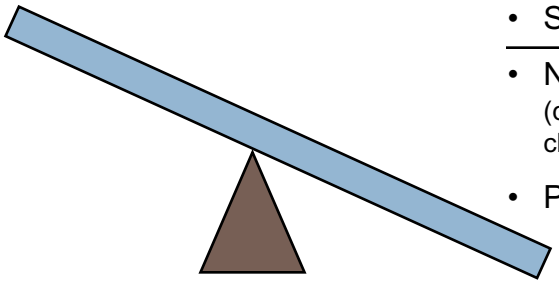
PATENCY OF THE UPPER AIRWAY

Dilating Force

- Neuromuscular tone



Collapsing Forces

- Negative inspiratory force
- Gravity effects (supine)
- Sleep (REM)

- Neuromotor function (decreased tone, reflex and chemosensitivity)
- Physical characteristics

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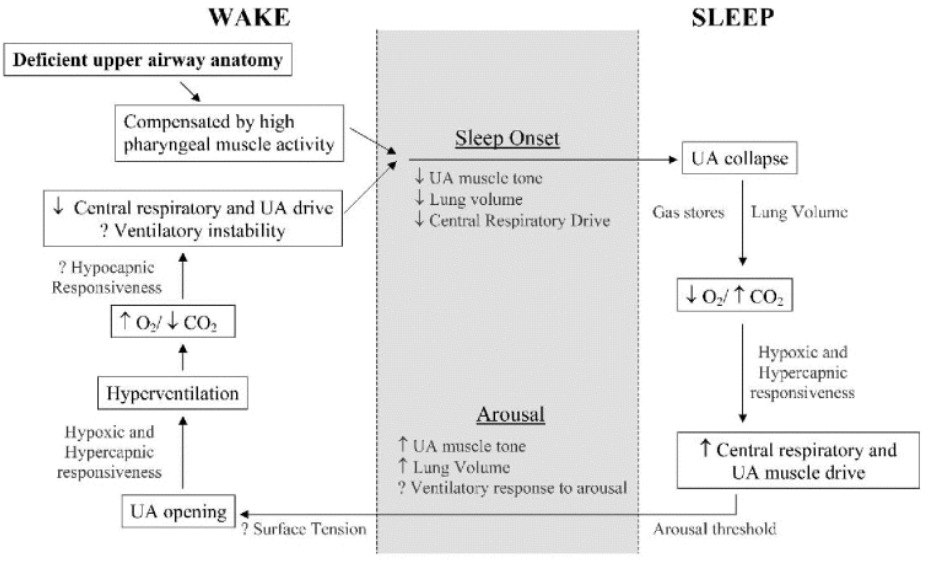

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OSA PHENOTYPES

- 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)

Subramani Y, Singh M, Wong J, Kushida CA, Malhotra A, Chung F. Understanding phenotypes of obstructive sleep apnea: Applications in anesthesia, surgery, and perioperative medicine. *Anesth Analg*. 2017 Jan;124(1):179-191.

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