Obesity Hypoventilation Syndrome and Obstructive Sleep Apnea

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Educational Objectives:

1. Review the key difference in examination, laboratory values, and diagnostic testing between obesity hypoventilation syndrome (OHS) and obstructive sleep apnea (OSA).
2. Understand the different treatment options for OHS and OSA.
3. Review different non-invasive ventilation techniques available.

Scenario:

A 45-year old morbidly obese man with mild persistent asthma presents for a yearly visit in the pulmonary clinic. He denies any recent wheezing, cough, or shortness of breath, but complains of fatigue that has been slowly worsening over the past year. He is embarrassed because he recently fell asleep during an important meeting at work. His wife made the trip with him today because she is concerned about him "zoning out" while driving.

<u>Question 1:</u> What other questions are vital to ask to determine the cause of his sleepiness?

It is important to ask about following questions for specified reasons.

History	Rationale
# Snoring # Nocturnal awakening due to gasping/choking	**# Sleep Apnea:** Sleep apnea can lead to poor quality of sleep. It is important to ask about snoring, nocturnal choking/gasping for air, witnessed apneas (if there is bed partner), and non-restorative sleep. Snoring is the most common symptom of OSA and occurs in 70-95% of patients with OSA.[2,3] # Suspicion of OSA can be calculated from simple tool like STOP-BANG (See below) *
# Sleep schedule and naps (bedtime, wakeup time, number of times waking after sleep, sleep latency)	**# Total sleep time:** Insufficient sleep contributes to sleepiness. Sleep plays a key role in optimal health. The consensus recommendation from the American Academy of Sleep Medicine (AASM) and Sleep Research Society (SRS) recommend 7 or more hour of sleep per night on regular bases for adults.[1] **# Sleep Fragmentation:** If patient does sleep for 8-9 hours per night but is woken up frequently, he/she may not be getting N3 or REM sleep. Additionally, asking what wakes him/her up (i.e., wheezing, need to urinate, chest pain, heart burn, cough from post-nasal drip, coughing/gasping for air, etc.) can help you identify other diagnoses that may be the primary problem.
# Screen time (phone, TV, tablets etc.) prior to sleep and during sleep time	Excessive screen time may be correlated with insomnia and poor-quality sleep.
# Leg pain/movements	**# Restless Legs Syndrome:** Does the patient have trouble falling asleep due to uncomfortable sensation or pain in his/her legs that usually occurs at night and is relieved with movement? The criteria required for identification of RLS are: (1) an urge to move the legs often accompanied by unpleasant sensations; (2) the urge is worsened during rest or inactivity; (3) the urge is improved with leg movement; and (4) the urge is worsened in the evening or night.[4] # Sleep apnea patient also have leg movement but no specific urge to move the legs.
# Morning headache	# May happen due to unrefreshed sleep, but excessive headache may point towards obesity hypoventilation syndrome (OHS)
# Sleep paralysis, Cataplexy, hypnogogic hallucinations	**# Narcolepsy:** Weakness during periods of strong emotions is known as cataplexy which is almost pathognomonic symptoms for narcolepsy although every narcolepsy patient does not have cataplexy.
# Excessive daytime sleepiness/Tiredness/ unrefreshed sleep	# Number of conditions can cause excessive daytime sleepiness (EDS) including OSA, sleep fragmentation, insufficient sleep (most common for young people including residents and fellows), medication usage, and narcolepsy. # Severity of EDS can be objectively evaluated by tool like Epworth Sleepiness Scale (ESS), see below. **

*** Suspicion of OSA (STOP-BANG)[22]**
S – Snoring Loudly
T – Tiredness
O – Observed Apnea
P – Pressure (HTN)
B – BMI $\geq$ 35 kg/m2
A – Age $\geq$ 50 years
N – Neck circumference ($\geq$16 inch/40 cm)
G – Gender (male)
Score <3 predicts low-likelihood of OSA and score $\geq$3 predicts high-likelihood of OSA.

**** Severity of Sleepiness:** We often estimate the amount of sleepiness using the Epworth Sleepiness Scale (image to the right).[5] It can be useful to quantify the degree of daytime sleepiness and also monitor response to treatment. The score ranges from 0 to 24 and scores >10 are consistent with pathologic sleepiness.

TABLE 1. *The Epworth sleepiness scale*

THE EPWORTH SLEEPINESS SCALE

Name: _____

Today's date: _____ Your age (years): _____

Your sex (male = M; female = F): _____

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently try to work out how they would have affected you. Use the following scale to choose the *most appropriate number* for each situation:

0 = would *never* doze
1 = *slight* chance of dozing
2 = *moderate* change of dozing
3 = *high* chance of dozing

Situation	Chance of dozing
Sitting and reading	_____
Watching TV	_____
Sitting, inactive in a public place (e.g. a theater or a meeting)	_____
As a passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after a lunch without alcohol	_____
In a car, while stopped for a few minutes in the traffic	_____

Figure 1 (above). Epworth Sleepiness Scale Questionnaire. Johns MW, Sleep 1991.

Scenario continued:

This **45-year old male** complains of sleepiness for at least a year. It is worst when he is sedentary and he often falls asleep while reading or watching television. Recently, he has **fallen asleep several times at his job** as a software engineer, including during an important meeting. On days when he is especially tired, he uses his lunch break to take a quick nap in his car before returning to work. He has **difficulty staying awake while driving longer distances**, and recently, he dozed off momentarily and hit the rumble strips on the side of the highway. He usually gets into bed at 10:30 PM (though he often falls asleep earlier while watching TV) and falls asleep "instantly." He occasionally **awakens feeling as if he is choking or suffocating**. This sensation goes away quickly once he is awake. **He also wakes up 3-4x per night to urinate.** He does not notice nocturnal wheezing and does not have nocturnal leg cramps. He wakes up in the morning at 6:30 AM using the alarm clock, but often hits the snooze until around 7 AM. He usually **feels in the morning as if he "barely slept."** He often has a **dry mouth** when he awakens. His wife notes that he **snores loudly.** Because of his snoring, she sometimes moves to the guest bedroom to sleep. On the weekends, he sleeps until 8:30 AM or 9 AM and tries not to nap but often finds himself dozing off for up to an hour if he is not keeping active. No matter how long he sleeps, he rarely feels rested. **His Epworth Sleepiness Score is 13.** He does get headaches, but these do not necessarily occur in the morning. With regards to his asthma, he denies any exercise limitation ("it's my knees and my weight that keep me from walking more, doc"), recent episodes of wheezing or significant cough. He uses his rescue inhaler infrequently (less than once weekly). He does not smoke cigarettes.

Exam:

BP 145/85, HR 75, RR 18, **Weight 345 lbs, Height 5'10"**
General: Morbidly obese middle-aged man, face somewhat flushed, in no distress
Neck circumference 19 inches, BMI 49.5 kg/m^2
HEENT: PERRL, **injected conjunctiva, large uvula, narrowing of the peritonsillar lateral walls and tongue ridging**
Exam Continued:
Lungs: breath sounds clear to auscultation throughout, no rales, rhonchi or wheezes
Cards: heart sounds regular, no murmurs, gallops, rubs
Abdomen: soft, non-tender, obese, bowel sounds present
Extremities: no clubbing or cyanosis, trace pedal edema
Neuro: non-focal exam, DTRs intact

<u>Question 2:</u> What is the most likely diagnosis for his sleepiness? What are his risk factors for each?

The patient likely has obstructive sleep apnea. He gets approximately 8 hours of sleep on the weekdays and 10 hours of sleep on the weekends. The quantity of sleep is sufficient. He denies symptoms related to restless legs syndrome. Additionally, he does not have any REM-disturbance symptoms such as hypnogogic hallucination or sleep paralysis. Narcolepsy, though can be diagnosed in 40s, it is less likely – especially in this patient given other symptoms.

Obesity hypoventilation syndrome cannot be ruled out just based on the information available.

His risk factors for OSA include increased age, male gender, and obesity.

Symptoms that point towards OSA are: loud snoring, nocturnal choking/gasping for air, nocturnal polyuria (increased release of atrial natriuretic peptide (ANP) secondary to increased negative intrathoracic pressure due to inspiratory effort against a closed airway and in turn increased venous return), dry mouth, non-restorative sleep, excessive daytime sleepiness.

Signs that points towards OSA are: obesity, large neck, crowded upper airway, hypertension.

STOP BANG Score = 6, High likelihood of OSA.

Other risk factors that are associated with OSA include:

- Age: Prevalence of OSA increases from adulthood through 6-7th decade of life.[6]
- Male gender: It is 2-3x more common in man than women. This gender gap does narrow after menopause in women[7,8]
- Obesity: 10% increase in weight has shown to be associated with 6-fold increase in incidence of OSA.[9] In a population-based study, prevalence of moderate to severe OSA was demonstrated to be 63% with BMI > 30 kg/m^2. [10]
- Craniofacial and upper airway abnormalities
- Nasal congestion in adults doubles the risk for OSA compared to controls.[7]

<u>Question 3:</u> What diagnostic tests will be necessary?

There are three different types of sleep studies that could be ordered for this patient:

1. Diagnostic polysomnography (PSG): reports electroencephalogram (EEG), electrooculogram (EOG), electromyogram (EMG) for chin and legs, airflow signals, respiratory effort signals for chest and abdomen, oxygen saturation, body position, and electrocardiogram (ECG).

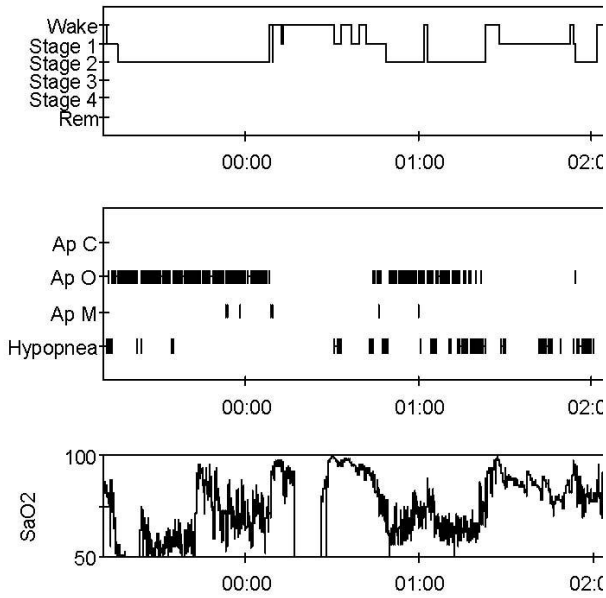
   It can be used to diagnose OSA, central sleep apnea (CSA), sleep-related hypoventilation disorders, REM behavior disorder, parasomnias, narcolepsy and hypersomnia (PSG would be followed by Multiple Sleep Latency Test), periodic limb movement disorder, bruxism, etc.

2. Split-night study: reports the same parameters as the diagnostic PSG, however, the study is split into first diagnostic half and then if sufficient apneas are seen (if the criteria are met for a split night study), the second treatment part is initiated the same night. It is mainly used to diagnose sleep disordered breathing and treat them at the same time.

3. Type 3, unattended, home sleep apnea test (HSAT): reports airflow signals, respiratory effort signals (single or dual), oxygen saturation, ECG, sleep/wake or monitoring time, and snoring. As per American Academy of Sleep Medicine, HSAT is to diagnose only OSA in uncomplicated adults presenting with signs and symptoms that indicate an increased risk of moderate to severe OSA.[11] It is important to note the relative contraindications of HSAT like central sleep apnea, HFrEF, Severe pulmonary disease like COPD or ILD, patients on Home Oxygen, recent stroke etc. In our patient, HSAT would have been sufficient as he has high likelihood of OSA and absence of comorbid factors listed above.

The patient underwent a sleep study that demonstrated the following: his latency to sleep onset was <2 minutes; his sleep efficiency was 89%. He had fragmented sleep with 61 arousals/hour. His Apnea-Hypopnea Index (AHI) was 90 events/hour. There were no periodic limb movements.

His tracing is shown to the right.



<u>Question 4:</u> What do the tracings demonstrate?

This type of tracing is known as Hypnogram. The top panel shows different stages of sleep. Note that this patient never attains N3 or REM sleep. Also, this is an old tracing; stages 3 and 4 are now combined. He also has multiple awakenings. The middle panel demonstrates that patient has multiple obstructive sleep apneas and hypopneas as soon as he falls asleep. The bottom panels show desaturation events throughout the study. During obstructive apneas and hypopneas, individuals have collapse of the upper airway, which leads to oxyhemoglobin desaturation and/or arousal from sleep. Thus, accompanying the many sleep-disordered breathing events observed in this patient (apnea graph), cyclical desaturations are recorded by the SaO2 graph. He has severe OSA based on AHI of 90/hour.

Figure 2. Obstructive sleep apnea severity ratings.

<u>Question 5:</u> How will you treat this patient?

Treatment options include:

1. **Continuous positive airway pressure (CPAP):** first-line, most effective therapy, but not tolerated by all patients. CPAP essentially increases the intraluminal pressure so that it is greater than the pharyngeal transmural pressure, keeping the airway open.[12] Most recent meta-analysis with 35 randomized control trials show that CPAP was more effective compared to sham in reducing AHI and improving sleepiness based on ESS.[13]
   As of the time this script was authored, the Philips PAP machines were recently recalled because of polyester-based polyurethane (PE-PUR) to control sound and vibration which possibly caused release of toxic particles and gasses that patients may inhale or swallow. Although replacement machines are now being delivered.

2. **Behavior modification:**
   a. Weight loss – weight loss and exercise should be recommended for all patients with OSA. Weight loss rarely cures OSA unless there is significant amount of weight loss, ie., from a bariatric procedure. Weight loss does reduce AHI.
   b. Positional therapy – if patient is found to have strong positional component, i.e., much higher AHI in supine position, sleeping in non-supine position can improve AHI. Several over the counter devices exist such as Zzoma pillows.
   c. Alcohol avoidance – alcohol can exacerbate OSA symptoms, cause sleep fragmentation, and can depress the respiratory system.
   d. Sedative avoidance – any of the sedatives can also exacerbate the OSA symptoms and also depress the respiratory system

Figure 3. Zzoma pillow.

3. **Oral appliance:** this is often used as second like therapy in patients with moderate to severe OSA who cannot tolerate PAP therapy. It can be used as first line therapy in patients with mild OSA and no other comorbidities. AASM recommends repeating the sleep study once the patient is fit with an oral mandibular device.

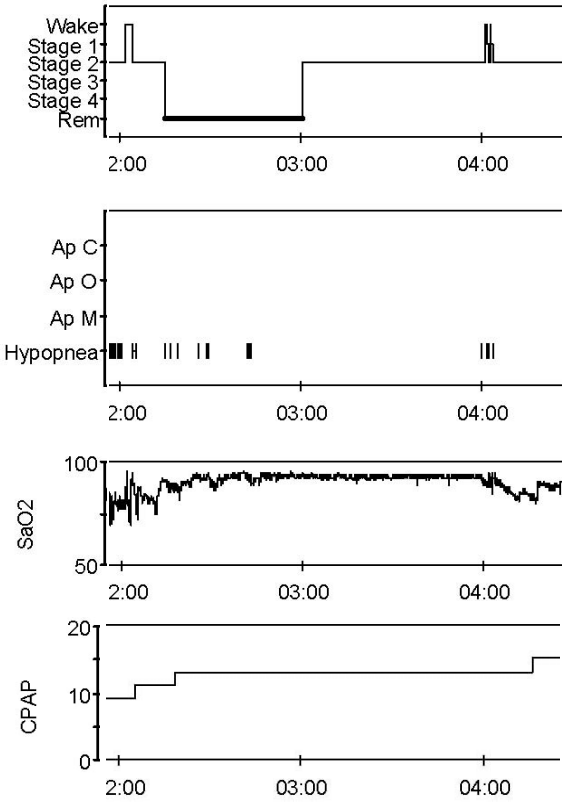
4. **Upper airway surgery:** It is difficult to predict which patient would benefit from an upper airway surgery.

5. **Hypoglossal Nerve Stimulation:** Also used as second line therapy for OSA. Patients will often need drug-induced sleep endoscopy to determine the pattern of airway collapse. This modality can be used in patients with OSA who have ineffective pharyngeal dilator muscles.

6. **Oxygen:** can improve oxygen saturation but may prolong apneas and does not decrease the number of events; therefore, in general, oxygen alone is not considered to be effective therapy.

7. **Tonsillectomy and adenoidectomy** are the mainstay of treatment in non-obese children with OSA, but these are rarely effective treatments in adults.

<u>Question 6:</u> What does the tracing below demonstrate?



The tracing shows a split night study. CPAP titration begins just before 2 AM. Initially, the patient still has lots of events. However, during the REM sleep period, CPAP increased to 13 cm H_2O, at which pressure nearly all breathing events are abolished. However, his oxygen saturation remains close to 90% and often below that (15% of the night with saturation <88%). So, at CPAP of 15 cm H_2O where his apneas are eliminated, he remains hypoxic.

During the second half of the sleep study, he is treated with continuous positive airway pressure. When he is titrated to a pressure of 13 cm H_2O, his apnea-hypopnea index is reduced to 5 events/hour. At this setting, his arousal index decreases to 2 events/hour and his sleep is much more consolidated. He awakens feeling refreshed early the next morning ("better than I've slept in years").

However, in reviewing his study, you notice that although his AHI appears to have been normalized by CPAP, his oxyhemoglobin saturations remain low (15% of time at 13 cm H_2O, patient still had oxyhemoglobin saturations between 80-90%).

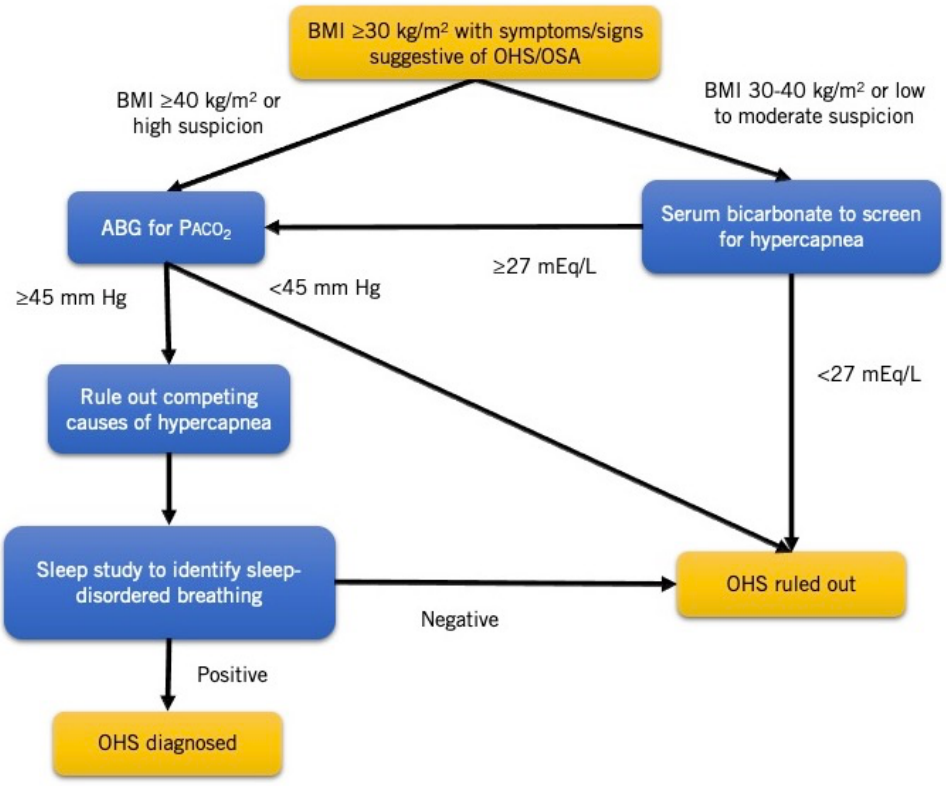
Question 7: Has your diagnosis changed?

He likely has obesity hypoventilation syndrome (OHS). OHS is defined by BMI > 30 kg/m^2, a resting $PaCO_2$ of more than 45 mmHg, and absence of an alternative cause of alveolar hypoventilation. It is often associated with worsened nocturnal hypercapnia, nocturnal hypoxemia, and OSA.[14-17]

OHS is a diagnosis of exclusion and other conditions commonly associated with hypercapnia should be ruled out. In 90% of patients with OHS, the sleep-disordered breathing is obstructive sleep apnea. The other 10% may have sleep-related hypoventilation (an increase in $PaCO_2$ of > 10 mm Hg above that of wakefulness or significant oxygen desaturations) that is not the result of obstructive apneas or hypopneas.

Question 8: Would you like to order additional diagnostic tests?

You can check an arterial blood gas, which would likely show a chronic respiratory acidosis, with elevated PCO_2 and borderline PaO_2. You can also check serum chemistry, which would likely show an elevated HCO_3. Early diagnosis of OHS can improve outcome and one such way to work up OHS patient is mentioned below[23]



Abbreviations: ABG, arterial blood gas; BMI, body mass index; OHS, obesity hypoventilation syndrome; OSA, obstructive sleep apnea.

<u>Question 9:</u> How will you treat the patient?

In a prospective trial, 57% of ambulatory patients with severe OHS can be successfully treated with CPAP alone while the remaining 43% of patients failed CPAP titration due to persistent hypoxemia at therapeutic pressure.[18] Bilevel PAP (BPAP) should be instituted if the patient is intolerant
of higher CPAP pressures (>15 cmH2O) that are required to resolve apneas and hypopneas or if the hypoxemia persists despite elimination of apneas and hypopneas with adequate CPAP pressures. During BPAP titration, IPAP should be 8-10cmH2O above EPAP to increase ventilation. BPAP S/T can also be used. BPAP S/T allows us to add back up rate to bilevel positive airway pressure to help maintain ventilation. Adherence to PAP therapy has shown to improve PaCO2, PaO2, and decrease the need for oxygen therapy.[19-21] See figure to the right.[18]

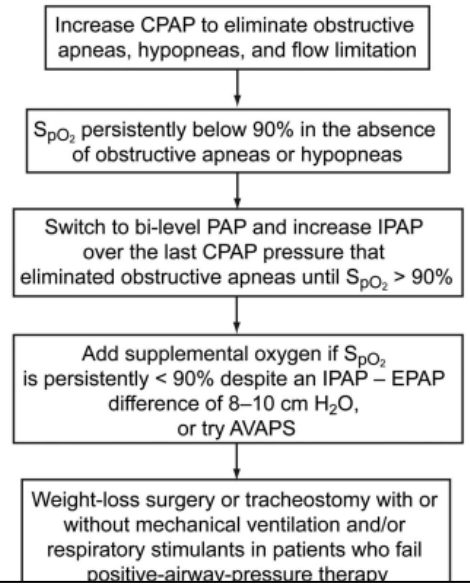


Figure 4. Suggested therapeutic algorithm during CPAP titration in patients with OHS. Borrowed from Mokhlesi B. Respir Care 2010.

"BiPAP" should not be used when referring to this type of PAP therapy as this is a brand name of bilevel positive airway pressure. Also, BPAP in the outpatient setting is not an FDA approved ventilator due to lack of alarms and does not have a built in back up rate (see table below).

	CPAP	**BPAP**	**ASV**
Definition	Continuous positive airway pressure; uses single pressure above ambient pressure.	Bilevel positive airway pressure; uses IPAP which is experienced during inspiration and EPAP which is experienced during expiration.	Adaptive servo ventilation; provides variable amounts of pressures that alternate between expiratory and inspiratory phases.
Prescription	CPAP	IPAP/EPAP (back up respiratory rate if S/T)	EPAP, PS (min and max), back up rate
Indications	OSA	OSA, hypoventilation, neuromuscular diseases Pulmonary edema, COPD exacerbation	Hypoventilation, CSA, complex apnea

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