2. SLEEP RELATED BREATHING DISORDERS

Most patients tested in sleep centers are diagnosed with sleep related breathing disorders. The majority of these patients have obstructive sleep apnea syndrome. The *ICSD-2* defines 13 types of sleep related breathing disorders. We will lump these into 3 categories: 1) central sleep apnea syndromes (problems with the effort to breathe) 2) obstructive sleep apnea (continued effort to breathe but an obstructed upper airway), and 3) hypoventilation and hypoxemia (problems with gas exchange). We will briefly discuss some of the sub-types within these categories.

1. CENTRAL SLEEP APNEA

Central sleep apnea syndromes are defined by episodes of not breathing during which there is no indication of effort to breathe in the signals that are recorded during a sleep study. Airflow channels and respiratory effort channels are flat during central apneas. All central sleep apnea diagnoses require a sleep study according to the diagnostic criteria in *ICSD-2*.

In the previous chapter we used Spielman's 3 factor model to help us think about what causes insomnia. In this section we will use the temperature control of a house as a model of how the brain controls breathing. In this model, the house is the body, the furnace is the lungs and the thermostat is in the brain. This is shown in Figure 6.

The house sits on a quiet street in a suburban Midwest neighborhood. It is February and there is snow on the ground. The house has good insulation, but the air temperature is well below zero outside and the temperature in the house slowly falls. A sensor in the living room registers the drop in temperature and sends a signal to the thermostat. The environmentally-conscious homeowners have set the thermostat at 68 degrees. As the temperature drops below 66 degrees the thermostat signals the furnace to start up. Gradually the air in the living room warms to 70 degrees. The temperature sensor tells the thermostat that it is nice and warm now (if you are wearing a sweater), and the thermostat tells the furnace to shut off.

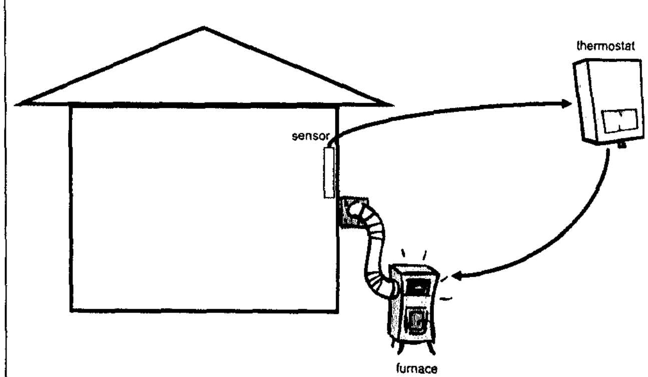
It is important for the system that the thermostat is not *too* sensitive, so that it's not turning on and shutting off every few minutes. In our model house, the thermostat is set so that the temperature can vary by 4 degrees (from 66 to 70 degrees). A smaller range may be too sensitive. For example, if the thermostat were set to signal the furnace to go on when the temperature was 68.1 degrees and off at 67.9 degrees, the room would cool by a tenth of a degree very quickly and the furnace would cycle on and off very rapidly. This would not be energy efficient. It takes some time for the furnace to heat up each time it starts. Instead, the furnace rests for a while, and while it rests the temperature starts dropping. When it falls below 66 degrees, the cycle begins again. This is a feedback loop – the sensor feeds information to the thermostat, which changes the temperature by turning on the furnace, which is monitored by the sensor and feeds back into the thermostat.

Breathing is more complicated than heating a house, but the concept of a feedback loop is the same in both. Sensors monitor the level of carbon dioxide in the blood. These sensors signal a part of the brain when the carbon dioxide level is too high or too low. Carbon dioxide is produced by the body as a result of using energy. When the level of carbon dioxide in the blood starts to increase, action is required -- just like when the air in the living room starts to get too cold. The brain sends a signal to the diaphragm to increase breathing. This can result in faster breathing or an increase the amount of air with each breath. Both of these changes increase the amount of air that passes through the lungs per minute (minute ventilation). This "blows off" the excess carbon dioxide and returns carbon dioxide to a lower level. When the carbon dioxide level decreases, the brain sends a signal to slow the breathing rate.

Disorders can affect breathing in ways that can be understood using the house heating model. For example, imagine that the owners put a skylight in the living room of the house. The sun may come out and heat the air in the living room (which has a skylight) to 75 degrees. The temperature sensor tells the thermostat that the air is fine, so the furnace doesn't come on for a long time. When the carbon dioxide level is really low the brain may stop the signal to breathe. In the body, this may result in times when there is no effort to breathe.

At bedtime, most people set the thermostat for a lower temperature like 62 degrees. This makes the furnace stay off for a longer time until the temperature drops to below

Figure 6. Control of the temperature in a house.



60 degrees or so. In much the same way, sleep changes the way the brain responds to carbon dioxide levels. As you fall asleep, the acceptable level for carbon dioxide moves upward. This means that a level of carbon dioxide that produces normal breathing during waking may be too low for sleep. At sleep onset, the brain may stop sending the signal for breathing until carbon dioxide rises. This may produce 1 or more episodes of central apnea at sleep onset, or in relaxed wakefulness prior to sleep, such as is shown in Figure 7.

A few central sleep apneas at sleep onset are considered normal. When does central sleep apnea become abnormal? The *ICSD-2* requires a minimum of 5 apneas per hour of sleep averaged over the entire night plus 1 of the following: excessive daytime sleepiness; frequent arousals or a complaint of insomnia; or awakening short of breath.

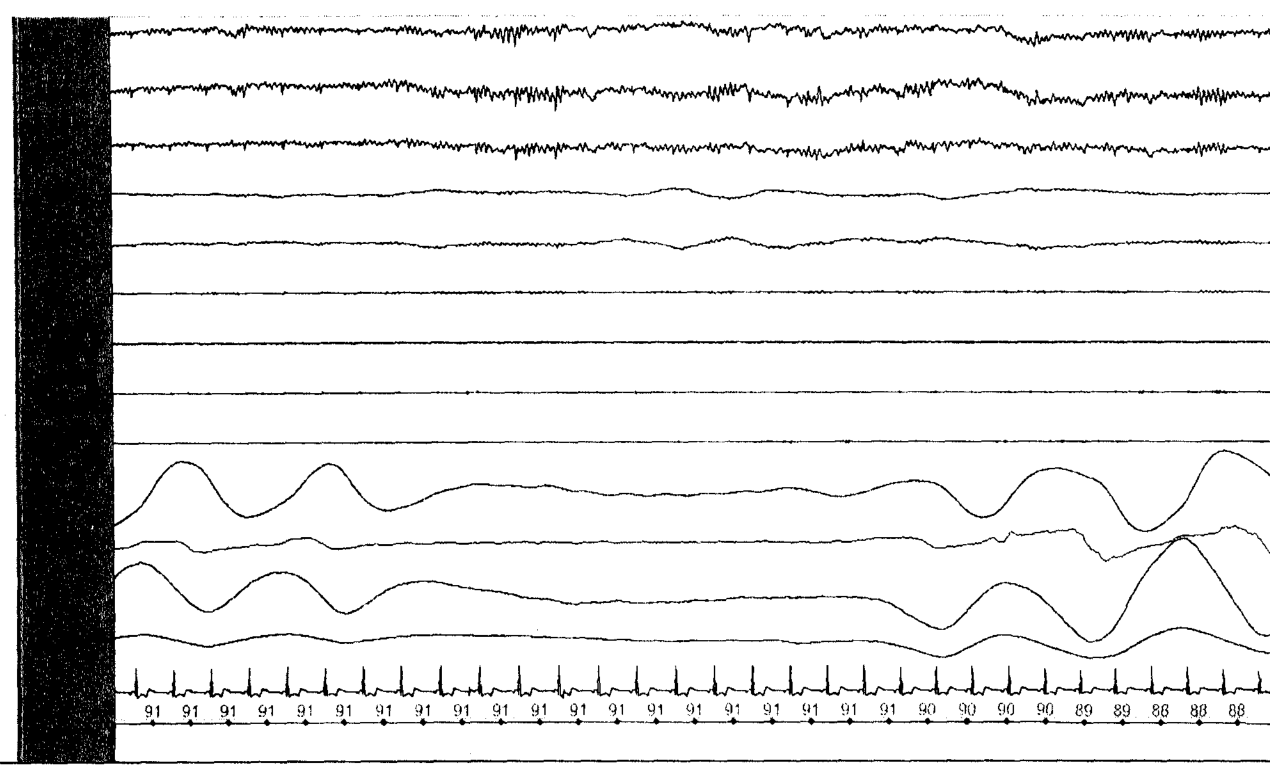
Primary central sleep apnea. There are several conditions that can result in central apneas on a sleep study. "Primary" central sleep apnea is thought to be due to increased sensitivity to carbon dioxide levels. There is speculation that the primary form of central sleep apnea is genetic, but there is little data to support this. Like the thermostat that is set to go on at 68 and off at 67, the patient with primary central apnea has a small range of acceptable carbon dioxide levels. When the carbon dioxide level drops below the "apnea threshold" breathing is no longer stimulated. This happens more quickly in patients with primary central apnea than in normal breathers. Apneas cause carbon dioxide levels to rise to more acceptable levels. However, apneas also result in decreased oxygen saturation, which may lead to an arousal. The arousal may produce the symptoms necessary to meet the *ICSD-2* criteria for a diagnosis of central sleep apnea.

What is seen on a sleep study when the patient has primary central sleep apnea? The study shows 5 or more central apnea events per hour of sleep. The study often shows sleep fragmentation (frequent arousals) which is associated with decreased N3 sleep. The apneas usually continue past the sleep onset portion of the recording, occurring during N1 and N2. Central apneas are less common during R.

How is primary central sleep apnea treated? Usually primary central sleep apnea is not treated. In the past, some clinicians have used hypnotics as a treatment. This sounds like a bad idea since some hypnotics are known to decrease breathing effort. The thinking is that hypnotics help patients pass through the sleep onset transition more quickly and reduce awakenings during the night. There are a few reports in the literature suggesting that it helped people. Central sleep apnea may also be treated with medications that increase respiratory effort, and there are some studies that have shown improvement with continuous positive airway pressure (CPAP) therapy.

What happens to primary central sleep apnea patients? The long term prognosis for central sleep apnea patients is unknown. Some patients develop heart or lung problems,

Figure 7. Central apnea prior to sleep onset.



suggesting that they didn't really have a primary form of central sleep apnea.

Cheyne Stokes breathing pattern. This breathing pattern was named after 2 English physicians, John Cheyne and William Stokes. It is defined by periods of breathing too fast followed by slowed breathing, at times with central apneas. It is thought to be caused by a slowing of the response to changes in carbon dioxide level in the blood. Using the Midwestern house model, it is as if the thermostat in the house has been replaced by an old guy who looks at a thermometer and runs over to the furnace and turns it on when the room temperature is too low (Figure 8).

What is the effect of replacing the thermostat, which responds quickly, with an old guy watching a thermometer? It takes much longer for the furnace to be turned on and the house to start heating up. Let's say the thermostat is set at 68 degrees, and we want the furnace to go on when the temperature gets below 66 degrees. The thermostat turns the furnace on as soon as the temperature hits 66 degrees. But the old man has to wake up, look at the thermometer, find his cane, walk over to the furnace and turn it on. This allows the temperature to drop another 4 degrees, to 62 degrees. The same thing happens when it's time to turn the furnace off: the temperature hits 70 degrees, the old guy finally wakes up and looks at the thermometer, he stands up, finds his cane and walks to the furnace. By the time he turns off the furnace, the room is at 74 degrees and is too warm.

In the body, the delay in responding to carbon dioxide changes is usually caused by heart failure. This slows the pumping of blood throughout the body, and the blood with high carbon dioxide takes a longer time to reach the body sensors. This means that the carbon dioxide level continues to rise before the signal to increase breathing is triggered. This is shown in Figure 9.

Figure 8. The thermostat is replaced by an old guy watching a thermometer.

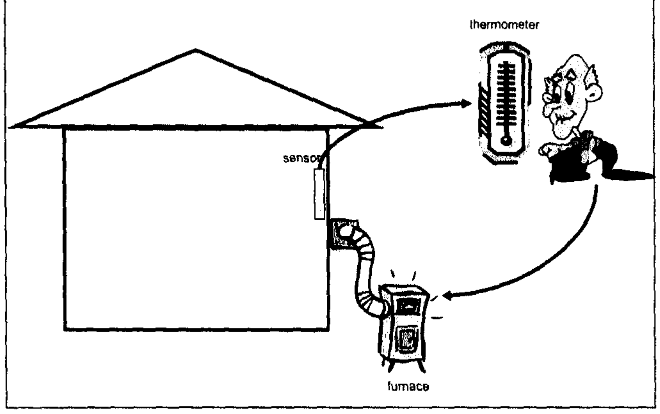


Figure 9. Change in breathing pattern with slowed response to carbon dioxide.

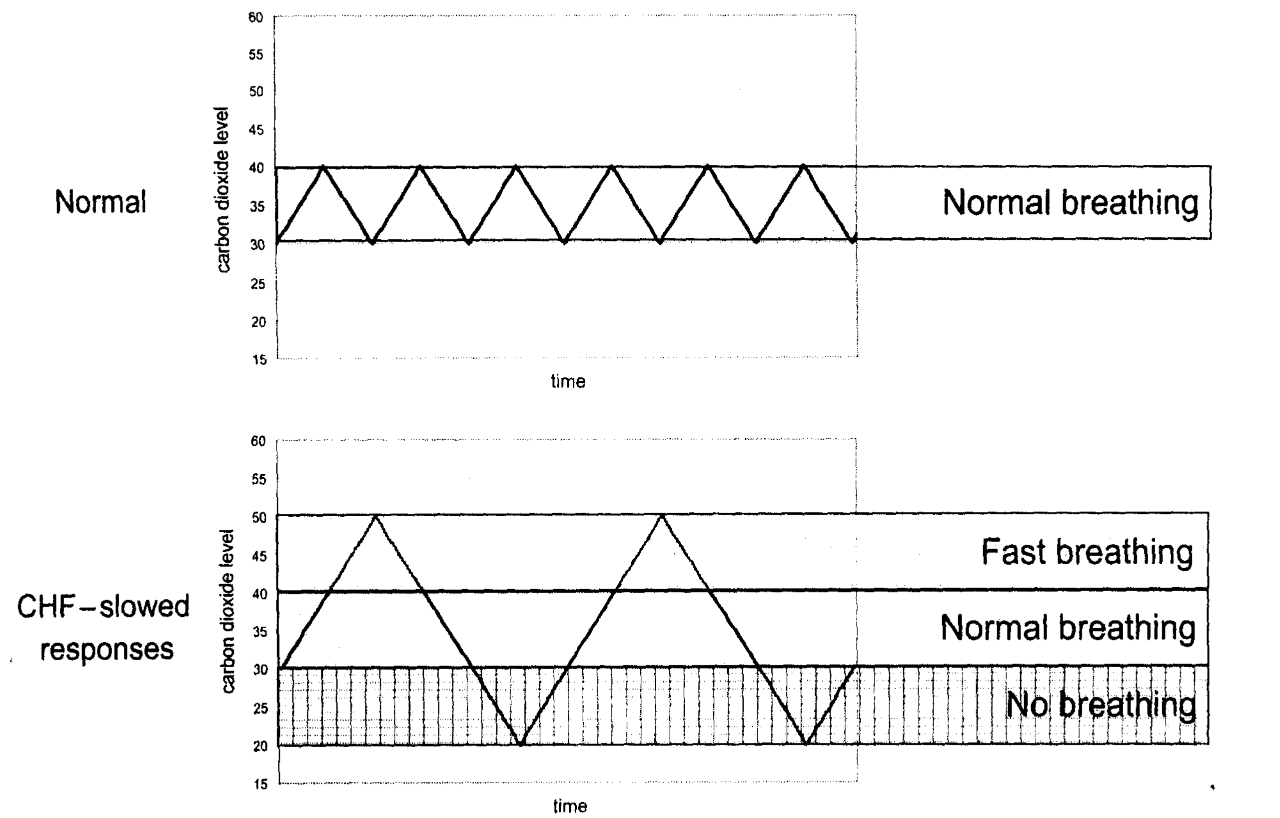
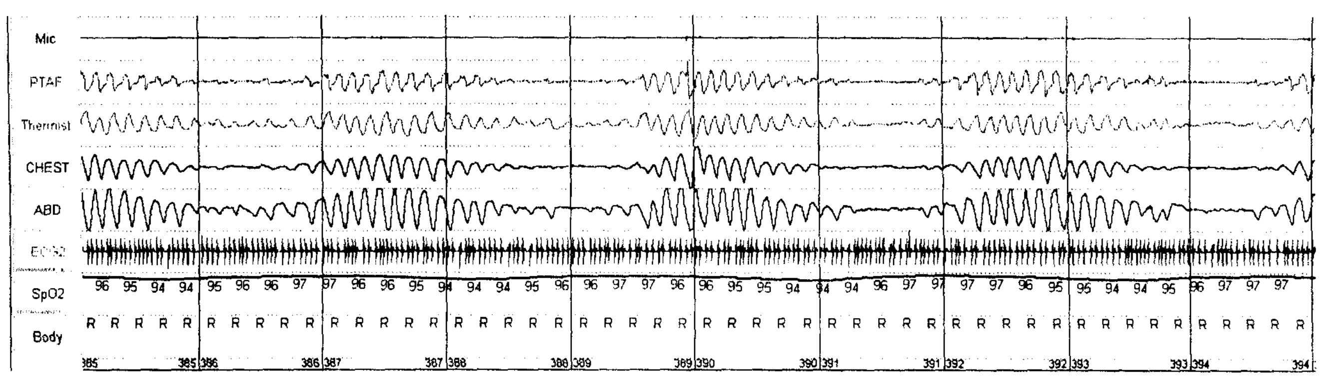


Figure 10. Cheyne Stokes breathing pattern in a heart failure patient.



What is seen when a patient with Cheyne Stokes breathing pattern has a sleep study?

Figure 10 is a 5 minute sample of a sleep study showing a typical Cheyne Stokes breathing pattern. The amplitude of the breathing signals increases slowly, reaches a peak, decreases slowly and on some occasions stops completely. In this patient, the time between the fastest breathing points is about 80 seconds. In this disorder, the time between periods of fast breathing is almost always more than 45 seconds. This can be used to tell the difference between repeated episodes of primary central sleep apnea and Cheyne Stokes breathing pattern. A second difference is that Cheyne Stokes breathing pattern is usually associated with an arousal at the time of the fastest breathing rate. In central apnea the arousal, if it happens, usually occurs at the end of the apnea. In both cases there are some mild increases and decreases in oxygen saturation that follow the breathing pattern. This is shown in the SpO_2 channel near the bottom of Figure 10.

An example of a patient with Cheyne Stokes breathing pattern:

Mr. Kingfisher is an 80 year old man with heart failure, sent by his cardiologist to the Cardinal City Sleep Center for evaluation of his sleep problems. He reports feeling short of breath at night, and feels that he does not sleep deeply. His wife does not feel that he snores, although she is aware of something wrong with his breathing during sleep. Sometimes she will wake in the middle of the night and wait for him to start breathing again. He is sleepy during the day and has fallen asleep at the dining room table while reading the newspaper. Dr. Robin notes that Mr. Kingfisher is wearing bedroom slippers. When questioned, Mr. Kingfisher reports that his feet are swollen and he cannot fit them into his regular shoes. This indicates to Dr. Robin that Mr. Kingfisher's heart failure is not under good control.

Mr. Kingfisher has a sleep study that shows frequent Cheyne Stokes breathing pattern during N1 and N2 sleep, and a central sleep apnea index of 12 per hour of sleep. Breathing was nearly normal during R, with some mild desaturation but without central apneas or Cheyne Stokes breathing pattern. He had no N3 sleep, but this is not unusual in a gentleman of his age.

Most episodes of Cheyne Stokes breathing pattern occur during N1 and N2 sleep, especially at the transition from waking to sleep. The transitions are when central apneas of all types are most frequent. Cheyne Stokes breathing pattern tends to go away during R sleep. This is because the body's response to changes in blood gas levels is decreased during R. It's as if the furnace no longer pays attention to the thermostat. Instead, the furnace cycles on and off every 15 minutes no matter what the temperature is in the room. This comparison isn't exact; breathing becomes more irregular during R, but not as a result of changes in the level of carbon dioxide in the blood. Cheyne Stokes breathing pattern can also occur during waking. However, in patients with Cheyne Stokes breathing pattern during wake, the "wake" may not be "fully alert wake." In some patients, the level of consciousness may improve and worsen with the breathing rate, so that patients appear to wake up for a few seconds at the fastest breathing rate when oxygen saturation is highest. They will then fall asleep and breathing stops.

How is Cheyne Stokes breathing pattern treated? One way to reduce or eliminate Cheyne Stokes breathing pattern is to treat the congestive heart failure or other medical causes. This may be more or less effective depending on how much the blood cycle time can be improved. A variety of treatments for central sleep apnea have been tried in patients with Cheyne Stokes breathing pattern. Positive airway pressure (PAP) has been shown to be effective in reducing the apnea hypopnea index in patients with Cheyne Stokes breathing pattern. Various forms of pressure support have been used with mixed success. Treatments have included bi-level PAP and positive pressure ventilation. Adaptive servo ventilation (where the pressure changes based on breath-to-breath changes in lung volume) may also be effective. Increasing the amount of carbon dioxide in the air has also been shown to reduce the apnea hypopnea index in patients with Cheyne Stokes breathing pattern. Supplemental oxygen may be helpful in some cases.

What happens to patients with Cheyne Stokes breathing pattern? In patients with congestive heart failure, the appearance of Cheyne Stokes breathing pattern usually signals a worsening of the disease. There is some data to suggest that the abnormal breathing pattern actually contributes to the worsening of the disease. Most studies of treatment effects have focused on the number of apneas or measures of heart failure. Additional research is needed to determine if any or all of the treatments also improve the quality of life or extend lifespan in patients with Cheyne Stokes breathing pattern.

High-altitude periodic breathing. The breathing system responds to carbon dioxide levels during sleep (room temperature in the house model), but it also monitors and responds to oxygen levels. The level of oxygen in the air at high altitudes is less than it is at sea level. In order to keep the level of oxygen in the blood constant, breathing rate must increase as you climb to altitudes higher than 4,000 meters. With increases of the breathing rate, the level of carbon dioxide in the blood decreases. At times, the level of carbon dioxide goes so low during N sleep that there is no stimulus to breathe. This results in an apnea. The apnea causes the oxygen level to drop and the carbon dioxide level to rise. This provides a stimulus to breathe. During the sleep study in patients at high altitude, apneas occur periodically. They begin at sleep onset and usually repeat every 12 to 34 seconds. This is shorter than the cycle of patients with Cheyne Stokes breathing pattern. The diagnosis can be made with 5 or more central apneas per hour of sleep. The apneas usually go away during R.

High altitude periodic breathing is a normal response to changes in the amount of oxygen in the air. It usually indicates proper functioning of the breathing system. Most people do not have symptoms during the day. There may be some disruption of sleep during the night, but this is usually mild. No treatment is needed, and the breathing pattern becomes normal when the patient returns to a lower altitude.

Central sleep apnea due to drug or substance. Several medications, especially opioids, can affect the breathing system. These medications include methadone, hydrocodone and time-release morphine. Lower doses can cause central apneas during sleep. High doses can cause respiration to stop completely (respiratory arrest). Medication-induced central apneas are a temporary problem and usually go away as the patient adapts to continued use of the medication. Central apneas also typically go away when the medication is stopped. The diagnostic criteria require an index of 5 or more central apneas per hour of sleep and the use of a medication for at least 2 months.

2. OBSTRUCTIVE SLEEP APNEA

The diagnosis of obstructive sleep apnea is used for a range of disorders that are a result of blockage of the flow of air in the upper airway. At 1 end of this range is complete obstruction of the upper airway resulting in no air flow. This is called apnea. Partial obstruction is called "hypopnea." A mild form of obstruction is a need for increased effort to maintain flow resulting in frequent arousals called respiratory effort related arousal (RERA). Criteria for scoring each of these events can be found in the *Manual.* Snoring may represent the mildest form of obstruction, but is not considered part of the obstructive sleep apnea syndrome.

The tendency to have apnea or hypopnea is thought to depend on properties of the upper airway. If the airway starts out narrow, it will be more likely to collapse. Collapse may also be caused by poor muscle tone. If the upper airway were made of pasta, it would be a rigatoni. Before cooking the rigatoni is rigid and will not collapse. Breathing through such a tube is easy. When it is cooked *al dente* it is flexible but still unlikely to collapse. This is the typical condition of the upper airway. Cook the rigatoni to death and it becomes floppy. Attempting to breathe through floppy rigatoni will not be successful because the tube will collapse. In addition, big tonsils or a large tongue may act like a flap valve at the upper end of the airway and cause collapse.

Using the house heating model, obstructive sleep apnea is caused by the cat sitting on the air vent from the furnace and blocking the hot air from entering the house. The room remains cold, the sensor reports that the room is cold to the thermostat, and the thermostat keeps the furnace running. Eventually the cat gets too hot and moves off the vent, allowing the furnace to heat the room. When the pre-set temperature is reached, the furnace turns off. Then the cat goes back to sitting on the vent.

Obstructive sleep apnea occurs in cycles as well. Current evidence suggests that low oxygen levels trigger the awakening, which results in increased muscle tone in the upper airway. This eventually overcomes the obstruction. A partial obstruction may need to go on for a longer time to produce the arousal.

The current measure to differentiate between mild and severe obstructive sleep apnea is not based on the degree of obstruction or amount of oxygen desaturation. In fact, most patients with obstructive sleep apnea have a combination of apnea, hypopnea and upper airway resistance. The severity is usually determined by the apnea hypopnea index (AHI), which is the number of apnea and hypopnea events per hour of sleep. A respiratory disturbance index (RDI) may also be used as a measure of severity. It is often defined as the number of apneas, hypopneas and RERAs per hour of sleep. There is, at present, no consensus on definitions of these measures. An additional index that is often calculated is the number of oxygen desaturations per hour of sleep (ODI), which is usually based on 3% or 4% criteria.

The *ICSD*-2 diagnosis of obstructive sleep apnea is based on sleep study findings and symptoms. A diagnosis is made when the AHI is 15 or more and there is respiratory effort during at least a portion of all events. A diagnosis can also be made if there is an AHI of 5 or more and the patient has 1 of the following: 1) daytime sleepiness; 2) waking up choking; or 3) either loud snoring or witnessed apnea.

Figure 11 shows a typical episode of obstructive sleep apnea. The oronasal thermistor channel (THERM) and nasal pressure transducer signal (PRESS) both go nearly flat during the beginning of the event. The chest and abdomen show paradoxical movements, indicating continued effort without change in volume of the lungs. The EEG channels show an arousal at the end of the event. Note that there is snoring in the 2 breaths prior to the start of the apnea. This indicates increased airway resistance even before the apnea occurs. Snoring returns near the end of the apnea. This indicates that the airway has partially opened. Not shown in this sample is oxygen desaturation that typically accompanies the apnea. Desaturations are recorded with a delay of 10 seconds or more and would be outside of the window shown in Figure 11.

Figure 11. Typical obstructive apnea.

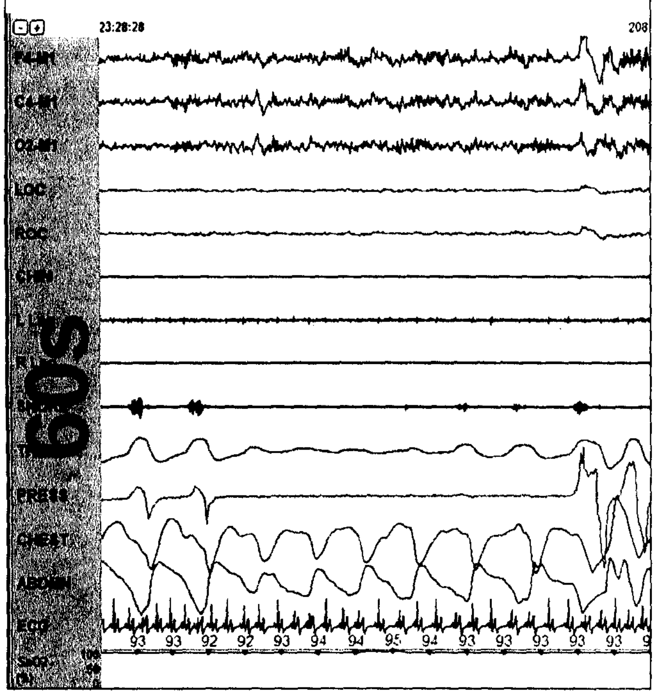
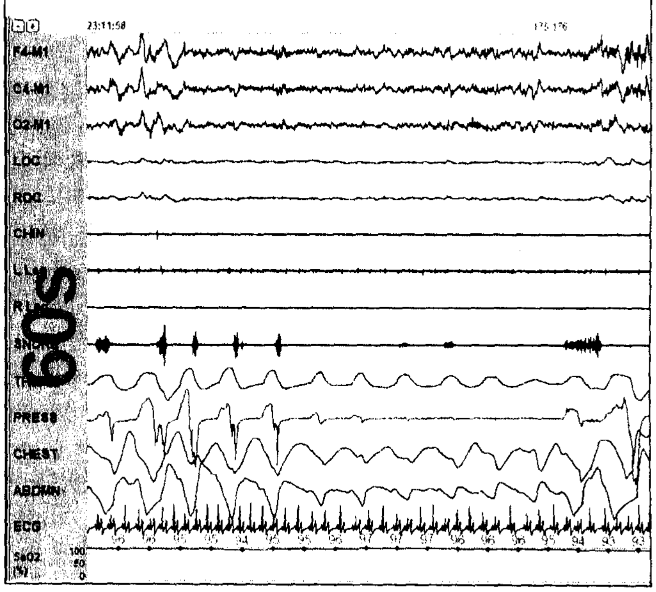


Figure 12 shows a similar respiratory event. In this event, the flow signal is reduced but continues in the oronasal thermal sensor channel (THERM). The nasal pressure signal is mostly flat (PRESS). This means a hypopnea is scored rather than an apnea. Snoring is recorded before the event, at reduced volume during the event and again at the end of the event. Respiratory effort continues throughout the event. Oxygen saturation drops from 97% to 93% and to 89% at 10 seconds after the event. There is an arousal at the end of the event. The *Manual* provides a measureable cut off between these 2 types of events. Apnea is scored with a 90% or greater reduction in the amplitude of the oronasal thermal signal. Hypopnea is scored with a 30% or greater reduction in amplitude of the nasal pressure signal with a 4% reduction in oxygen saturation. An alternative definition for hypopnea is a 50% reduction in nasal pressure signal with a 3% reduction in oxygen saturation or an arousal.

There is speculation that drawing a line between apneas and hypopneas may be artificial and unnecessary. Both types of events seem to contribute to consequences of obstructive sleep apnea such as daytime sleepiness and increased risk of high blood pressure. However, the clinical significance of events without desaturations is not known. There is evidence to suggest that RERAs are similar to hypopneas. RERAs require more sensitive sensors for proper detection. A flatten-

Figure 12. Typical hypopnea.



ing of the nasal pressure signal accompanied by an arousal can be used to score RERAs. For an interesting discussion of this controversy, see the review article that accompanies the *AASM Manual for the Scoring of Sleep and Associated Events* (Redline et al, *Journal of Clinical Sleep Medicine*, 2007:3(2);169-200).

Leaving the details of scoring sleep studies and moving to the clinical diagnosis, *ICSD-2* lumps all of these obstructive sleep disordered breathing events together in the criteria for obstructive sleep apnea syndrome. They are all called "scoreable" respiratory events. There are studies that document a relationship between the diagnosis of obstructive sleep apnea and medical consequences such as hypertension. Similar studies of RERAs do not exist. It is easy to diagnose the patients who have a combination of apnea, hypopnea and RERA. Studies show that scoring RERAs results in only a 5% increase in the AHI in patients with obstructive sleep apnea syndrome. But there are also some patients who have only RERAs and no apneas or hypopneas. These patients are said to have upper airway resistance syndrome. Most sleep specialists feel that these patients have a form of obstructive sleep apnea. Some insurers do not reimburse for treatment of upper airway resistance syndrome. There are strong opinions on both sides of this argument. More research is needed to determine the best approach.

A typical patient with obstructive sleep apnea:

Dr. Robin's nurse, Ms. Ibis, opens the door to the waiting room and calls out for Mr. Puffin. Ms. Puffin stands up and shakes the sleeping obese gentleman in the chair next to hers. Mr. Puffin wakes with a start, and proceeds to the examination room. He is 37 years old, 5'7" tall and weighs 225 pounds. He has a 22" neck. Ms. Ibis finds that his blood pressure is 160/95. Mr. Puffin settles into the chair and waits for Dr. Robin. He promptly falls back to sleep. When Dr. Robin enters the room, Ms. Puffin turns to wake Mr. Puffin, but Dr. Robin signals to let him sleep for a bit. They listen for a few minutes to Mr. Puffin's loud snoring, which is so loud that it causes the glass panes in the medical cabinet to vibrate. With a gulp, the snoring suddenly stops. Dr. Robin consults his watch and notes that the episode of not snoring lasts 45 seconds. It ends with a huge gasp and several quick breaths. Dr. Robin then gently wakes Mr. Puffin and asks him why he has come to the sleep center.

"I came for her," Mr. Puffin states, pointing as Ms. Puffin. "It's our 15th anniversary, and when I asked Polly what she wanted, she said she wanted me to see the doctor about my snoring. It doesn't bother me at all. But she insisted, so here I am."

Dr. Robin asks, "Do you have any trouble staying awake during the day?"

"I think of it this way: I have a talent for catching up on my sleep when things get boring. It's not a problem for me. I have some trouble at night because I wake up a lot. I go to the bathroom 4 or 5 times a night, just like everyone else my age. " replies Mr. Puffin. Ms. Puffin reminds him of the driving accident he had last month. "OK, except when I drive. My new car is so darned comfortable that I can't help falling asleep. Cars just shouldn't be that comfortable."

To use a basketball analogy made famous by a recent director of the CIA, Mr. Puffin is a "slam dunk" when it comes to the diagnosis of obstructive sleep apnea. Sleep medicine specialists call this a "high pretest probability." He is at a high risk because he is a middle-aged male who has severe daytime sleepiness, obesity, loud snoring and high blood pressure. A neck size greater than 17" is also a risk factor. He has frequent nocturnal awakenings. This is not normal for a 37 year old, despite what he claims. He also provided Dr. Robin and Ms. Puffin with an opportunity to witness an episode of apnea, complete with gasping for air. Nevertheless, he still needs a sleep study. The diagnosis of obstructive sleep apnea requires documentation of a minimum of 5 scoreable respiratory events per hour of sleep.

Mr. Puffin is in deep denial of his symptoms. He does not see his frequent napping as a problem, even though he has had car accidents as a result of falling asleep at the wheel. This is fairly common in patients with obstructive sleep apnea, and may be a result of the gradual onset of symptoms. If Mr. Puffin were normal 1 day and had the symptoms he describes the next, he would surely realize that something was wrong. In patients with severe obstructive sleep apnea, the problem can often be traced back many years or even decades. Mr. Puffin may have even been a loud snorer as a child, infuriating his bunk mates at sleep-away camp.

A not-so-typical case of obstructive sleep apnea:

Ms. Hawk is a 27 year old former professional tennis player. She was a star of the Stanford University tennis team and for a time was on tour and ranked in the top 50 nationally. She retired from the tour at age 24 and took a job as the tennis coach at the University of Oregon. Her transition from player to coach was accompanied by increasing fatigue and lack of energy. She feels that this is due to a 5 pound weight gain and getting less exercise during the day. She spends most of her day reviewing film, working on strokes and attending a distressing number of faculty and alumni donor meetings. Despite this, she manages a 3 mile run several times a week.

She was referred to the sleep center by her new boyfriend, Dr. Crane. He is an ENT doctor at the University Health Center. He recently spent the night with Ms. Hawk and noted loud snoring and witnessed brief apneas. Dr. Crane has sent Dr. Robin a note describing the apneas and asking Dr. Robin to take a good look at Ms. Hawk's upper airway. Ms. Hawk is 5'9" tall and 130 pounds, and is in excellent physical condition. Her neck size is 14". Her blood pressure is 118/78 and her pulse rate is 47 beats per minute. When asked about her level of daytime sleepiness, Ms. Hawk reports that the faculty meetings, which are usually about how to spend alumni donations to the football team, can cause her to zone out for minutes at a time. She has not had a car accident or fallen asleep in social situations.

Dr. Robin examines Ms. Hawk's upper airway. He notes that she has rather large tonsils and a narrow airway. He notes that the tissue in her upper airway is reddened and the uvula appears to be somewhat swollen. He also thinks that she has a small jaw and that her bottom teeth do not line up properly with her upper teeth.

Ms. Hawk is not middle-aged, male, obese, hypertensive or particularly sleepy during the day. She has a normal sized neck. However, she does have some risk factors for obstructive sleep apnea. The most important of these is that she has had witnessed episodes of apnea. More than 50% of patients with witnessed apnea are diagnosed with obstructive sleep apnea when they have a sleep study.

A narrow airway, especially with a small jaw (called "retrognathia") is also a risk factor for obstructive sleep apnea. The small airway is more likely to collapse. Large tonsils contribute to the suspicion of apnea. Unlike Mr. Puffin, Ms. Hawk has noted a recent change in her level of alertness. She describes this as fatigue and lack of energy. In addition, her level of exercise has changed, going from the extreme rigors of professional sports to a lower level that would be more than normal for most patients. This change may result in a decrease in muscle tone and may include mild fat deposition. This may contribute to the risk of upper airway collapse.

What is seen on the sleep study of a patient with obstructive sleep apnea? Episodes of obstructive apnea (Figure 11), hypopnea (Figure 12) and RERAs are necessary for the diagnosis in patients with obstructive sleep apnea. If these events are not recorded, the diagnosis cannot be made. Loud snoring is often recorded using a microphone taped to the patient's neck. Many patients with obstructive sleep apnea will fall asleep quickly, but a minority will have trouble with falling or staying asleep and will complain of insomnia. Most patients have frequent brief awakenings during the night. Frequent urination is common (like Mr. Puffin). Other symptoms associated with sleep apnea are sleepwalking, bedwetting and erectile dysfunction.

Obstructive apneas are usually worst when the patient sleeps on their back. This is thought to be due to the tongue falling back and reducing the size of the upper airway. Gravity contributes to the collapse of the airway. Apneas also increase in frequency and last longer during R sleep. Muscle tone is reduced during R and the response to changes in carbon dioxide and oxygen is blunted, increasing the likelihood of apneas and hypopneas. In some patients, frequent apneas result in awakenings from R and reduce the amount of R sleep during the night. In other cases, apneas and hypopneas are only seen during R and breathing during the other sleep stages is nearly normal.

Other effects of obstructive sleep apnea on patients can be recorded during a sleep study. We have already discussed the decrease of oxygen saturation during apnea. Apneas also result in an increase in carbon dioxide level. Carbon dioxide level can be measured either by end tidal or transcutaneous sensors. Increased carbon dioxide levels in the morning may contribute to headaches. Airway obstruction and oxygen desaturation during sleep contribute to changes in heart rate during sleep. These changes include slowing of heart rate during apnea and an increased frequency of arrhythmias. Immediate blood pressure increases can be seen during apnea if blood pressure is monitored during the sleep study. The end of the apnea is almost always accompanied by an arousal, including an increase in heart rate.

How is obstructive sleep apnea treated? The most frequently used treatment for obstructive sleep apnea is continuous positive airway pressure (CPAP). The positive pressure provides an air splint that keeps the upper airway open. CPAP is recommended by the AASM as the first line treatment of obstructive sleep apnea. Other forms of positive airway pressure (bi-level and various forms of auto-PAP) should be used if CPAP is not tolerated. When all types of PAP are a failure, the patient should be offered oral appliance therapy, behavioral therapy (position training) or surgical therapy. These options are not thought to be as effective as PAP therapy.

Patients undergo CPAP titration studies to determine the optimal pressure that reduces the AHI to an acceptable level. At times, the best pressure may require a compromise between the level needed to keep the airway open and a level that does not produce central apneas or cause discomfort due to high flow volumes. But CPAP failure usually does not result from a failure of the pressure to keep the airway open. Failure of CPAP is most often due to inability of the patient to use the device on a regular basis. This may be due to a poorly-fitting mask, irritation of the bridge of the nose, nasal dryness or claustrophobia. Studies have shown that as many as 50% of patients who have been prescribed CPAP are unable or unwilling to use it regularly. However, changing to a different mask or completing a program of mask "desensitization" can be helpful in getting the patient to use the treatment. Warming the air and adding moisture can also improve patient's compliance with CPAP.

Oral appliances pull the lower jaw forward, thereby opening the upper airway. These are usually made of plastic and are fitted by a dentist. Some are adjustable, so that a position can be found that reduces the AHI but does not cause jaw discomfort. Evidence-based reviews have supported the use of oral appliance therapy as an effective treatment for obstructive sleep apnea.

The goal of positional therapy is to reduce the number of apneas by reducing the amount of time spent sleeping on the back. This works best in people who have most of their apneas when they sleep on their back. There are some devices to help people learn not to sleep on their backs. These range from electronic sensors that make a noise or give a small electrical shock when the patient rolls onto their back to t-shirts with a vertical pocket on the back that fits 3 or 4 tennis balls and causes discomfort when the patient tries to sleep on their back. Success rates for positional therapy are poor.

A variety of surgeries have been developed to open the upper airway. In children, removal of the tonsils and adenoids has been shown to reduce or eliminate apnea in most patients. However, the apnea continues in as many as 20% of children after the surgery. Removal of the uvula and extra tissue in the upper airway can have an effect on the AHI. Overall, surgical therapies have been shown to have limited success in treating obstructive sleep apnea. Some recent data suggests that a multi-stage approach may be the best surgical option for treatment of obstructive sleep apnea.

In some patients weight loss or medication may improve obstructive sleep apnea. Extremely obese patients who undergo surgery for weight loss are often reported to have improvement of their obstructive sleep apnea. These treatments are not as effective as CPAP and are useful only in selected patients.

What happens to obstructive sleep apnea patients? Untreated sleep apnea increases the risk of dying. In 1 study, untreated obstructive sleep apnea was associated with a 3.8 times higher rate of death over an 18 year follow up period. The frequency of cardiovascular related death was 5.2 times higher in patients with untreated obstructive sleep apnea than in patients with normal breathing during sleep. Data regarding the effect of CPAP treatment on mortality is somewhat more mixed, but there is some data that shows that regular CPAP use extends the lifespan of patients with obstructive sleep apnea. Short term use of CPAP has been shown to improve blood pressure and daytime sleepiness and reduce the risk of heart attack. There are many unanswered questions, such as how many hours per night of CPAP use is enough to result in these improvements and what level of AHI improvement is necessary. However, despite these limitations, there is ample data to show that treatment of obstructive sleep apnea with CPAP is effective.

A positive response to CPAP:

Mr. Puffin spends a night in the Cardinal City Sleep Center. The technologist prepares him for the possibility that he will have CPAP treatment as part of his sleep study. The technologist shows him a variety of masks, and he elects to be fitted with nasal pillows. Mr. Puffin is surprised that he falls asleep relatively quickly despite the electrodes and sensors. He is awakened at 1:30 AM by the technologist and the CPAP treatment is applied. Mr. Puffin has some mild difficulty with the headgear and straps but falls asleep quickly once he gets comfortable. He wakes in the morning and remembers an especially vivid dream about a watercolor set that he received as a gift for his 10th birthday. In the dream he elected to take a walk in the woods and look for birds to paint. The dream seemed to last hours and included several finished paintings. He notes that he hasn't remembered many dreams lately. After taking off the electrodes and sensors, the technologist asks Mr. Puffin how he feels. He reports that he feels good, and notes that he doesn't have his usual morning headache. He feels that the night was better than his usual night of sleep. Mr. Puffin asks the technologist if he could take the CPAP machine home with him.

This type of clinical response is associated with a high probability of successful CPAP therapy. Mr. Puffin was minimally aware of his symptoms prior to the "split night" study. Immediately in the morning, with only a few hours of CPAP therapy, he remembers a vivid, prolonged dream for the first time in a while. He also reports that he doesn't have a headache, which was not even a complaint during his clinic visit.

Figure 13. Sleep hypnogram of Mr. Puffin, a patient undergoing a "split night" study.

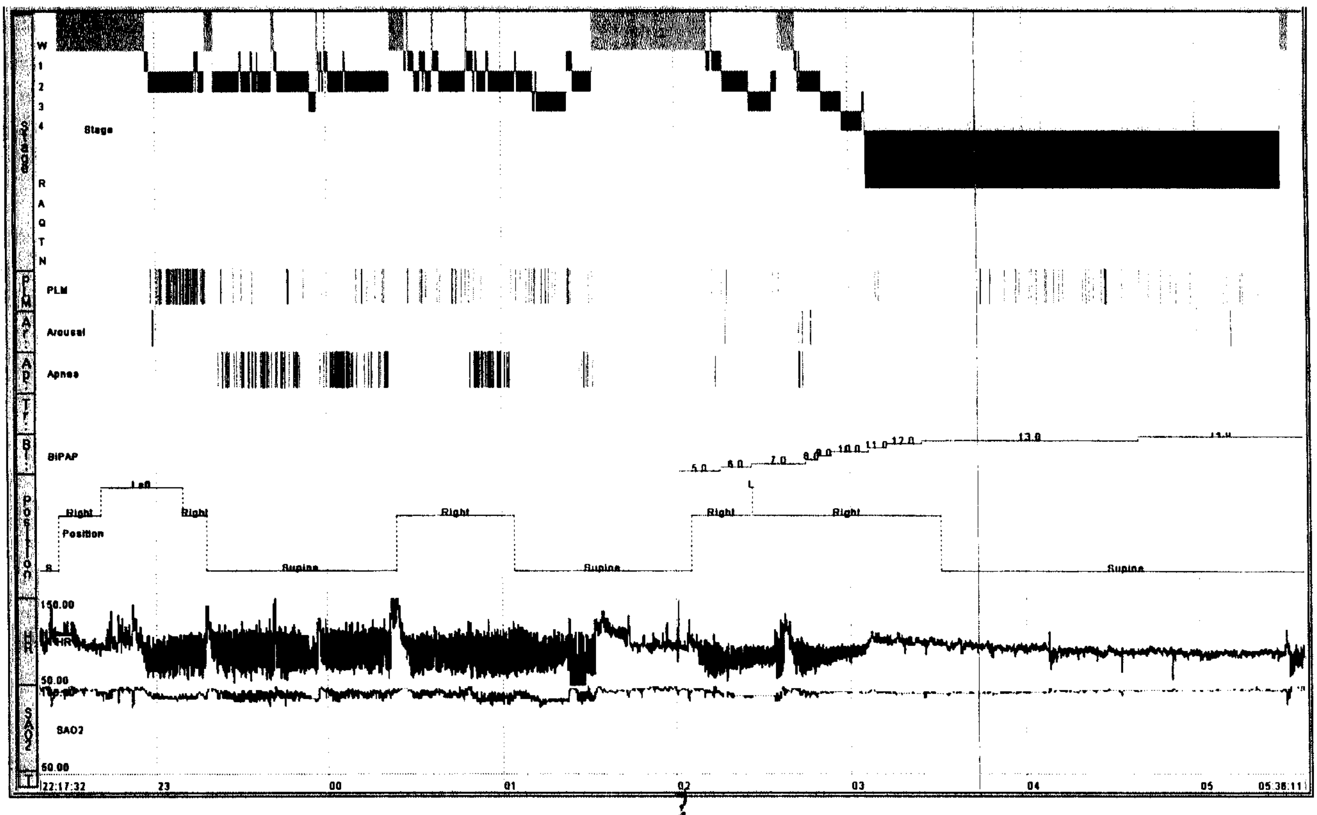


Figure 13 shows Mr. Puffin's positive response to CPAP during a "split night" study – half without CPAP and half with CPAP. The left hand side of the figure, showing the pre-CPAP portion of the night, shows fragmented sleep, frequent apneas, marked changes in heart rate (HR) and mild oxygen desaturations. In the right hand portion of the recording CPAP is applied. At about 10 cm pressure a bout of R begins that lasts more than 2 hours. According to the technologist's notes, snoring was eliminated at 14 cm of CPAP pressure. Heart rate stabilized and oxygen saturation stayed above 90% at this pressure. The patient was awakened by the technologist at 5:30 AM to end the study. He went on to use his CPAP regularly through the period in which he was followed by the physician.

Not all patients respond this way and careful monitoring of patient CPAP use by a physician is recommended. Newer CPAP units contain microprocessors and memory that tracks when the machine is in use. This monitoring has revealed a large difference between the amount of usage reported by the patient and actual CPAP use. Early machines tracked how long the power switch was on, but patients were found who turned on the machine and left it in a closet overnight in an attempt to fool the physician into thinking it was in use. Now machines only track time when the pressure rises and falls in a pattern that is consistent with breathing. Some machines have an alarm that wakes the patient if the mask falls off.

Patients who do not use their CPAP regularly should be encouraged to try different masks. If this is not effective, alternative treatment should be offered.

3. SLEEP RELATED HYPOVENTILATION/HYPOXEMIA

Hypoventilation is a reduction of the amount of air flow. Hypoxemia is a low oxygen level. Sleep related hypoventilation and hypoxia can occur without apnea or hypopnea for the following reasons:

1. Impaired gas exchange between the alveoli and blood
2. Failure of inhaled air to reach the entire lung
3. Failure of the lungs to properly inflate

There is also a diagnosis of an unexplained form of hypoventilation in adults. An interesting genetic form of hypoventilation is called congenital central alveolar hypoventilation syndrome. It is usually diagnosed in infancy or childhood. Hypoventilation syndromes are not exclusively disorders of sleep, although the hypoventilation and hypoxemia are often prominent during sleep and often worst during R sleep. On occasion, the initial diagnosis of these disorders occurs as a result of review of findings from a sleep study.

Gas exchange occurs at the intersection of the alveoli (small sacs in the lungs) and the capillaries (small blood vessels). Oxygen crosses the barrier and attaches to the blood cells. Diseases that cause inflammation or excess connective tissue around the alveoli can block or slow this transfer. These diseases include cystic fibrosis, pneumocystis pneumonia and lupus. The lungs fill with air, but the proper amount of oxygen is not transferred to the blood cells. This is similar to increasing the distance between the furnace and the living room in our house in the Midwest. The heat tends to dissipate during the time it travels through the air ducts and fails to get from the furnace to the room.

The airways are narrowed in chronic obstructive pulmonary disease (COPD) and emphysema. This is another problem that reduces the amount of air that can get to the alveoli. The problem is usually one of breathing out – the lungs do not empty properly. Reduced flow means reduced oxygen exchange and low oxygen saturation. This is equivalent to using narrow ventilation air ducts to carry the heat from the furnace to the room. Less warm air flowing into the living room means it will take longer for the room to heat up.

Neuromuscular disorders can also decrease the amount of air pumped into and out of the lungs. Disorders such as amyotrophic lateral sclerosis (ALS or "Lou Gehrig's disease"), muscular dystrophy and polio often affect the muscles that move the diaphragm. When the diaphragm does not move properly the air flow to the lungs is reduced. A more common problem leading to reduced air flow is obesity. Extreme weight can produce a condition called obesity-hypoventilation syndrome. Excess weight on the chest and abdomen makes it more difficult for the muscles of the diaphragm to move. This problem may be made even worse by upper airway obstruction.

What is seen when a patient with hypoventilation has a sleep study? Patients with these disorders have low oxygen levels and high carbon dioxide levels during sleep. They may have episodes of central or obstructive apnea that cause brief additional changes in oxygen and carbon dioxide. But the hypoventilation and hypoxia continue even during times when breathing seems normal. The breathing rate is often faster than normal in an attempt to compensate for the poor transfer of oxygen to the blood. The *Manual* requires that carbon dioxide levels be used to diagnose hypoventilation on a sleep study. An increase of at least 10 mm Hg compared to the waking levels is required for diagnosis.

Frequent arousals occur in hypoventilation patients. This may be due to low oxygen levels. High carbon dioxide levels can also cause arousals as well as headaches. Breathing in hypoventilation patients is at its worst during R, often resulting in a reduced amount of R sleep.

How is hypoventilation treated? Some of the disorders that result in hypoventilation may not be improved by the increase air flow that PAP can provide. The group that stands to benefit the most from PAP therapy are those with neuromuscular or chest wall disorders, including obesity-hypoventilation. The positive pressure reduces the burden on muscles to inflate the lungs. Oxygen levels often increase during the night and sleep quality is often improved when PAP is used in these patients.

What happens to hypoventilation patients? Outcome is usually directly related to the underlying disease. Patients with COPD or ALS have progressive diseases with no known cures. Treatment may produce short term increases in breathing and quality of life, but have no effect on the progression of the disorder. Other causes of hypoventilation, such as post-polio syndrome, may not worsen with time. There is no data to evaluate the effects of treatment on these patients, but the assumption is that treatment will, at a minimum, improve some or all of the symptoms of these disorders.

A brief note on congenital central alveolar hypoventilation syndrome.

Congenital central alveolar hypoventilation syndrome (CCHS) is a rare disorder that is associated with an impaired response to increased carbon dioxide levels as well as other medical problems. Many patients with this disorder breathe normally while awake. During sleep they have hypoventilation or may stop breathing altogether. It is caused by a genetic abnormality. In the past it was thought that all patients with CCHS were either diagnosed and treated in infancy or died. However, more recently patients have been diagnosed as adults with the genetic abnormality and a much milder form of the disorder. These patients may not be diagnosed until they are adolescents or even adults. Sleep studies show reduced breathing or periods of central apnea. Often there are no arousals even with very high levels of carbon dioxide or low levels of oxygen.

CHAPTER 2 STUDY QUESTIONS

1. Mr. Redstart is hospitalized with heart failure. Dr. Robin visits and finds him asleep. His breathing looks abnormal. For a time he breathes very quickly, then his breathing slows down and stops altogether for a time. It starts up again quite slowly, and then gets faster. Each cycle takes more than a minute. He doesn't snore. When Dr. Robin wakes him up his breathing seems completely normal. The most likely *ICSD-2* diagnosis is:
   a. Obstructive sleep apnea
   b. Sleep related hypoventilation due to neuromuscular and chest wall disorders
   c. Central sleep apnea due to drug or substance
   d. Central sleep apnea due to Cheyne Stokes breathing pattern
   e. Heart failure

2. Ms. Gnatcatcher says that her new boyfriend is a wonderful human being. He is sweet, attentive and says that he likes watching movies that deal with feelings. But at night he drives her crazy. He is an extremely loud snorer, and from time to time the snoring stops for 20 to 30 seconds. It seems like someone has put a cork in his mouth. He struggles a bit, flops around, and then suddenly gasps for air. Come to think of it, says Ms. Gnatcatcher, he is more than a bit overweight. He also takes medication for high blood pressure. Maybe he's not such a great boyfriend after all. The most likely *ICSD-2* diagnosis is:
   a. Smith-Magenis syndrome
   b. Obstructive sleep apnea
   c. Primary central sleep apnea
   d. Congenital central hypoventilation syndrome
   e. Environmental insomnia

3. Mr. Ptarmigan says that he was fascinated with snowboarding but sleep problems kept him from achieving total mastery of the sport. Every time he went snowboarding he woke up so many times during the night in the hotel where he stayed that he was sleepy during the day and couldn't focus on perfecting his moves. He also complained of being short of breath at night, but never has this problem when at home in New Orleans. The most likely *ICSD-2* diagnosis is:
   a. Central sleep apnea due to high altitude periodic breathing
   b. Idiopathic insomnia
   c. Obstructive sleep apnea
   d. Half-pipe syndrome
   e. Central sleep apnea due to Cheyne Stokes breathing pattern

4. Ms. Vireo is in front of Dr. Robin in the airport security line. She has a canvas tote with the logo of a CPAP manufacturer on it. Dr. Robin asks her about it and she says she just started using CPAP and is having trouble adjusting to it. She complains of terrible nightmares since she started using CPAP. Dr. Robin tells her:
   a. She is probably on too much pressure
   b. She probably needs a new mask
   c. The nightmares are probably a result of more R sleep, which is a good thing
   d. The nightmares probably mean that she is depressed and she should ask her internist for an anti-depressant
   e. She probably doesn't have sleep apnea after all

5. Central sleep apneas at sleep onset are most likely due to:
   a. Hypocretin levels changing in the hypothalamus at sleep onset
   b. Partial obstruction of the upper airway caused by relaxation of the sphincter muscles
   c. Changes in the threshold for response to carbon dioxide levels at sleep onset
   d. Sensor malfunction
   e. Reverberation of thalamo-cortical neural networks