CONTROL OF BREATHING DURING WAKEFULNESS AND SLEEP

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Why do we have to breathe?
Breathing = Life

"Breathing should provide oxygen transport into the cells and tissues, and should transport carbon dioxide out of the cells and tissues"
Every cell in the human body needs a continuous supply of **oxygen**. The oxygen is used in a process that captures the energy locked in the foods we eat.

**Carbon dioxide** is one of the waste products of this process, and the body needs to dispose of carbon dioxide.
The lungs inflate and deflate in response to the actions of the diaphragm and the pleura.

The diaphragm is the large, dome-shaped muscle underneath the lungs. The pleura are membranes that surround the lungs. The parietal pleura is the outside membrane. It is attached at its base to the diaphragm. The pleural cavity is the space between the parietal pleura and the visceral pleura, which covers the outside of the lungs.

Inhalation begins as the diaphragm contracts. When the diaphragm contracts and flattens, the parietal pleura begins to stretch.

In children older than newborns, the intercostal muscles also contract. This raises the ribs and stretches the parietal pleura even more. As the pleura stretches, the air pressure in the pleural cavity gets lower.
The lungs follow the pleura as it stretches. This is because the lowered pressure in the pleural cavity sucks the lungs outward, like a vacuum.

As the lungs stretch, the air pressure inside them gets lower, so air gets sucked into the lungs. This is because the atmospheric pressure in the air outside the body is higher than the air pressure in the lungs, and air moves from an area of higher pressure toward an area of lower pressure.

Exhalation begins as the diaphragm and intercostal muscles relax. The diaphragm returns to its dome shape, the ribs descend, and the pleura returns to its unstretched state. The lungs, like a stretched spring, recoil back to their unstretched state, and the air is squeezed out.
What is the role of the brain in the control of breathing?

- Brain - generates basic respiratory rhythm

(Design by Professor Julian F. R. Paton, University of Bristol, UK.)
BRAIN - transmits basic respiratory rhythm into the pattern of the respiratory motoneuron activity
Brain – adapts and modulates pattern of respiratory motoneuron activity with acid base balance.

Nucleus tractus solitarius, NTS

Acid base balance; Peripheral and central chemoreceptors
....finally

- BRAIN - coordinates respiratory movements with the body activity such as running, walking, talking, sleeping, eating etc.
What parts of the brain participate in the neuronal control of breathing?
Is there a respiratory center in the brain?


- PreBotzinger complex
- retrotrapezoid nucleus/parafacial respiratory group (RTN/pFRG)
Respiratory neurons

I. A. RYBAK, J.F.R. PATON, AND J.S. SCHWABER

A

early-I
ramp-I
late-I
dec-E
post-I
con-E2
E 2
Phr.

t(s)

INSPIRATION EXPIRATION
Neurotransmitters involved in a neuronal control of breathing

- **Neurotransmitter that act as:**
  - **EXCITATORY** enhances breathing process
  - **INHIBITORY** attenuates breathing process

Neurotransmitters help signals travel from one brain cell to another.
Which neurotransmitters participate in the neuronal control of breathing?

- Glutamate
- Acetylcholine
- Serotonin
- GABA
- Glycine
What is going on with the breathing during the sleep?

- It changes dramatically depending on the sleep stage that we are in during sleep
1 “train” = 1 sleep cycle
1 night = 4 to 6 cycles
90 - 120 minutes
70 - 100 minutes

Your body rests and manufactures antibodies and growth hormones.

You feel relaxed.
You feel like you’re on a cloud.
You get your teddy bear.
You hear noises in the house but don’t feel like responding to them.
You can still understand the conversations you overhear.
You can still hear, but you can’t understand.
You no longer hear anything. You’re cut off from the world.
You are sleeping very deeply.
You either wake up or begin another cycle.
This is dream sleep.
Your brain recharges its batteries and records what it has learned during the day.

(Adapted from Samara/Sommeil Primitam. Cradess)
Breathing control- beginning of the sleep

- $pCO_2$ increases while the ventilation slows down
- At the begging some kind of transition between wakefulness and stage 1 and 2 is going on
NREM sleep

- Breathing is stable with no changes in breathing frequency and amplitude.
- Air flow during inspiration decreases, while the inspiratory phase duration as well as total respiratory cycle duration does not change.
- **Thoracic muscle activity and abdominal muscle activity**
  - Activity of the diaphragm moderately increases, or sometimes does not change, while the activity of abdominal muscles increases.
- **Resistance of the upper airway**
  - Increases for about 230%.
  - Resistance increases at the level of epiglottis.
  - Tonic activity of the pharyngeal dilatators muscles decreases.
- **Arterial blood**
  - $pCO_2$ increases for 3-7 mmHg, $pO_2$ decreases for 3-9 mmHg, while $SaO_2$ decreases for 2% or less.
- **Pulmonary arterial pressure**
  - Periodically changes in either direction.
REM sleep

- **Ventilation**
  - Irregular breathing, with sudden changes in breathing frequency and amplitude
  - Frequently could be interrupted with *central apneas that last between 10-30 seconds (Physiological change)*
- Rapid eye movements in the EOG are present
- **Thoracic muscle activity and abdominal muscle activity**
  - Activity of the intercostals muscles is decreased in this sleep stage
  - Alpha motoneurons activity is been inhibited and specific type of depression of fusimotoric activity happens
  - Activity of the diaphragm increases in REM sleep
- **Upper airway resistance**
  - It reaches maximum because of almost complete atony of the pharyngeal muscles
- **Arterial blood**
  - Same changes occurs as in NREM sleep stage
- **Pulmonary arterial pressure**
  - Changes, and usually increase during REM sleep stage.
Breathing disorders during sleep

- Syndrome of central apneas
  - Primary central apneas
  - Secondary central apneas (related to some other disorders of the CNS)
  - Central apnea as a result of drug abuse
    (combination of sedatives and alcohol is the most common cause of no intentional suicide)
Obstructive sleep apnea (OSA)

- Obstructive sleep apnea in childhood

- Obstructive sleep apnea in adults
Obstructive sleep apnea, OSA

- It is a life threatening condition
- “Apnea” literally means “no air”
- People who have OSA do not breathe from 10 seconds to even few minutes for several hundred times per night
- OSA is often unrecognized and undiagnosed
- Nearly 18 million people in USA suffer from OSA
Apneas during sleep

- **Central apnea** there is no command delivered from the respiratory neurons to the respiratory muscles
- **Obstructive apnea** (2% women, 4% men over 35 years of age), there is command from the brainstem to breathe but upper airway is obstructed
- **Mixed apnea**
Most common places of upper airway obstruction
Neurotransmitters and neuromodulators in the neuronal control of breathing during sleep

**Figure 3**

![Diagram](image-url)
OSA symptoms

- Excessive daytime sleepiness
- Snoring
- Struggling with breathing and air during night
- Nocturnal- frequent nocturnal diuresis
- Morning headaches
- Tiredness after the night of “sleep”
Symptoms of OSA in children

- Hyperactivity
- Attention disorder (aggression)
- Loud breathing and snoring during sleep
- Unusual body position during sleep
Risk factors for OSA

- Age (40-60 years)
- Increased body weight
- Male gender (men: women=8:1)
- Upper airway obstruction
- Craniofacial malformations
- Drugs (sedatives, sleep pills)
- Hypothyroidism
- Acromegaly
In physical exam

- Increased neck circumference
- Increased body weight
- Narrowing of the upper airway
- “crowded oropharyngeal region
- Increased tonsillar tissue
- Increased uvula
- Micro/retrognatia
Consequences of unrecognized OSA

- Social
- 31% patients with OSA have increased risk for repeated car accidents
- Respiratory/cardiovascular/neurological/psychiatric
- Changes of personality and behavior
- Decreases work efficiency, affects learning and memory capabilities
- Increases risk for metabolic syndrome development (diabetes, thyroid dysfunction, ovarian disorders and infertility)
Respiratory consequences

- Hypoxemia
- Hypercapnia
- Acidosis
- Pulmonary hypertension
Cardiovascular consequences

- 33% patients with OSA has arterial hypertension
- 33% patients with arterial hypertension has OSA
- 10% patients with OSA has arterial hypertension
- Myocardial infarction
- Cerebrovascular infarction
- Sudden death
- Arrhythmias
Cardiovascular disorders

Metabolic syndrome

Neurocognitive disfunction

OSA Coomorbidities
Top 10 Diagnoses by Internists

- Allergic rhinitis
- Asthma
- Hypothyroidism
- Esophageal disorder
- Depressive disorder
- Routine medical exam
- Hypercholesterolemia
- Hyperlipidemia
- Diabetes Mellitus
- Hypertension

Percentage of visits

Source: IM news, 6/1/05

Charles Atwood, MD, FCCP
VA Pittsburgh Healthcare System
UPMC Sleep Medicine Center
Pittsburgh Mind–Body Center
Core D:
“the sleep core”
How sleep problems relate to the top 10 diagnoses

- Sleepiness, fatigue
- OSA, fatigue
- Insomnia, poor quality sleep

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How can we recognize who is at risk of having OSA?

- Anamnesis (quality of sleep and sleep hygiene)
- Physical exam
- Questionnaires:
  - STOP
  - Berlin
  - Epworth sleepiness scale
How can we diagnose OSA?

- Only in specialized sleep laboratories where polysomnography should be done
- **POLYSOMNOGRAPHY INCLUDES:**
  - EEG
  - EOG
  - ECG
  - EMG - chin and legs
  - Respiratory effort – thoracic and abdominal belt
  - SaO$_2$
  - Video recordings
  - Body position
**Opstructive apnea** - there is no airflow and there are no thoracic and abdominal muscles activity
Primary snoring
Central apnea - no airflow and thoracic and abdominal muscle activity
What is the main outcome that we are looking for after polysomnography?

- **Apnea Hypopnea Index, AHI** – number of apneas and hypopneas during one hour of sleep

- **Respiratory disturbance index (RDI)** - includes apneas and hypopneas, and may also include other respiratory disturbances such as snoring arousals, hypoventilation episodes, desaturation events, etc. They are often identical, but depending upon what is scored, the RDI may be larger than the AHI.
QUICK STEPS TO READING SLEEP STUDY REPORTS

1. Sleep Efficiency
   Normal Ranges: Young adults > 90%
                  Geriatrics 80-85%
   *NOTE: Efficiency decreases with age

2. Sleep Architecture
   Normal Ranges:
   
   Stage 1: 5%
   Stage 2: 45%
   Stage 3: 12%
   Stage 4: 13%
   Total non-REM: 75%

3. AHI (Apnea-Hypopnea Index)
   Severity Scale:
   
   AHI (events/hr):
   30 - Severe Apnea
   15 - Moderate
   5 - Mild
   0 - Normal

4. Lowest Oxygen Desaturation
   Normal Range: > 88%

5. PLM Index (Periodic Limb Movement)
   Normal Range: < 5.0 (PLM/hr)

RECOMMENDATIONS

IF: THEN:

AHI > 15 CPAP titration
5 > AHI > 15 AND daytime sleepiness
AHI > 30 CPAP titration (urgent)
Low AHI AND daytime sleepiness MSLT (multiple sleep latency test)
PLM Arousal Index > 5 Drug therapy, follow-up sleep study

WHAT TO DO NEXT?
If necessary, sign/fax follow-up prescription. We will contact patient and schedule patient for follow-up therapy.
Treatment of OSA

- Change of sleep habits should be advised
- Mechanical assistance
- Surgery procedures (optional)
- Pharmacology treatment (optional)
Changes of sleep and lifestyle habits

- Decrease body weight if it is increased
- Try to avoid sleeping in a prone position, sleep on a side should be advised
- Sew a small pocket to the back of the pajamas and place a tennis ball or other small ball into it

**AVOID**
- Sedatives,
- Alcohol should be avoided 4 hours before sleep
- Avoid meals before sleep,
- Smoking,
- Sleep deprivation
Mechanical device therapy

- CPAP (Continuous Positive Airway Pressure) in patients who have AHI more than 30 (in Croatia)
Dental medical doctors

Oral devices
Results of CPAP therapy

- Decreases risk for myocardial and cerebrovascular infarction
- Decreases risk for traffic accidents
- Decreases excessive daytime sleepiness and tiredness
- Increases learning capabilities, mood, etc.
Surgical treatment

FIGURE 1. Macroglossia and tongue ridging in a patient with OSA.
Pharmacological treatment

- Numerous pharmacologic agents have been investigated as potential primary therapies for patients with OSA.
- However, no agent has been identified that prevents or overcomes upper airway obstruction enough to justify pharmacologic therapy as a primary therapy in the routine management of patients with OSA.
- It is unknown whether pharmacologic agents used concurrently with positive airway pressure therapy lowers the amount of airway pressure required to treat the disorder..
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