HYPOVENTILATION

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10/8/14
HYPOVENTILATION

1. Physiology of hypoventilation
2. Can’t vs Won’t breathe
3. Common and emerging causes
4. Consequences: pulmonary hypertension, sodium avid state/edema, neurocognitive dysfunction, mortality
5. Permissive effects of sleep
6. Treatments: PAP, weight loss surgery, oxygen, thyroid replacement, narcotic modification, phrenic pacing
7. Cases
Hypoventilation mechanisms

\[
PCO_2 = \frac{0.863 \times VC02}{VE \times (1 - VD/VT)}
\]

VE

PC02

VC02

VD/VT
Hypoventilation mechanisms

PC02

PC02

P02

VE

Increasing VD/VT VC02

3.5

7

40

80

aa

b

a
Clinical Categories of Hypoventilation

• *Can’t breathe*: dyspnea due to mechanical restraint, weakness, or excessive ventilation.

• *Won’t breathe*: no dyspnea. Depressed drive due to congenital or acquired controller error.
Can’t breathe

-Airway Obstruction
  • COPD, asthma, cystic fibrosis

-Restrictive
  • Obesity
  • Kyphoscoliosis

-Weakness
  • ALS/myopathies
Kyphoscoliosis
Angle > 90°

COPD Fev1 < 30%

Obesity + OSA
Ventilatory drive

High HCO3 + low drive

High HCO3
Low Drive
Normal

JAP 100:1737
Permissive effects of sleep COPD; N=54

O'Donoghue FJ, European Respiratory Journal 2003;21(6):977-984
Treatable Causes of Mechanical Restraint

- Upper airway obstruction - tracheostomy
- Lower airway obstruction - bronchodilators
- Obesity - surgery
- Kyphoscoliosis - PAP
Consequences of Hypercapnia/Hypoxemia

Renal:
• ~30% reduction in GFR
• ~30% reduction in sodium clearance

Cardiovascular:
• Increased sympathetic
• Pulmonary hypertension

Neurocognitive:
• Impairment
• Encephalopathy
Hypoxemia + Hypercapnia $\rightarrow$ Pulmonary Hypertension
Post-Hospitalization Mortality

Won’t breathe

• *Exogenous*: narcotics, sedatives.

• *Endogenous*: Leptin resistance$^{1-5}$, alkalosis, myxedema, adaptation, genetic$^{6-10}$, structural.

In chronic disease, “won’t breathe” may represent an adaptation that can be reversed with treatment.
Voluntary Hyperventilation

Leech JA, Chest 1987; 92:807–813
Two areas of rapid acceleration:

Obesity
Prescribed Narcotics
Weight Loss in Obesity

Small case series with improvement in gas exchange (6-15mmHg)$^{1,2}$ with surgical weight loss

$^1$Sugerman HJ. *Chest.* 1986;90:81-6
Deaths from prescribed opioids

Substance Abuse and Mental Health Services Administration 2007
Opioid Deaths

Narcotic Dosing Adjustments?

Hypoventilation dynamically worsens with acute narcotic dosing
Hypoventilation worsens if sedative added to narcotic
Hypoventilation is partially-corrected after 6 weeks of stable methadone dosing
Can’t + Won’t the leptin story
Leptin resistance in OSAH

<table>
<thead>
<tr>
<th></th>
<th>PCO₂&lt;45 (106)</th>
<th>PCO₂&gt;45 (79)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>32.5 ± 0.3</td>
<td>33.2 ± 0.8</td>
<td>NS</td>
</tr>
<tr>
<td>FEV₁/FVC, %</td>
<td>84.2 ± 0.6</td>
<td>85.4 ± 1.7</td>
<td>NS</td>
</tr>
<tr>
<td>PaCO₂, mm Hg</td>
<td>40.9 ± 0.3</td>
<td>46.6 ± 0.4</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>AHI</td>
<td>52.9 ± 2.2</td>
<td>47.4 ± 2.8</td>
<td>NS</td>
</tr>
<tr>
<td>Leptin, ng/mL</td>
<td>9.0 ± 0.4</td>
<td>14.3 ± 1.0</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>


Leptin resistance in obesity

leptin CSF/serum ratio is fourfold higher in lean individuals compared to obese subjects

Caro JF. . Lancet 1996; 348:159–161
Hypoventilation Diagnosis

1. There is an increase in the arterial PaCO2 (or surrogate) to a value > 55 mm Hg for ≥ 10 minutes

2. There is ≥ 10 mm Hg increase in PaCO2 (or surrogate) during sleep (in comparison to an awake supine value) to a value exceeding 50 mm Hg for ≥ 10 minutes.

<table>
<thead>
<tr>
<th>Awake PaCO2</th>
<th>Sleep PaCO2</th>
<th>Change in PaCO2</th>
<th>Benefits</th>
<th>Challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>50</td>
<td>10</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>45</td>
<td>10</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>55</td>
<td>5</td>
<td>yes</td>
<td></td>
</tr>
</tbody>
</table>

Benefits-removes false positive classifications
Challenges-instrumentation reliability
Hypoventilation in Children

Scope:
Infant-13 years
13-18 years discretion

Hypoventilation:
>25% of the total sleep time as measured by either the arterial PCO2 or surrogate is spent with a PCO2 >50 mm Hg
Pediatric Respiratory Rules
Reminders

dend-tidal PCO2

- Alternative apnea sensor
- Hypoventilation sensor during diagnosis
- RERA definition
Pediatric Respiratory Rules

end-tidal PCO2
PAP TREATMENT

CPAP Effective ~99%
PAP TREATMENT

Bilevel modes
- Support and control modes
- Fixed-Pressure
- Adjustable-Assured volume
- Adjustable-EPAP
PAP TREATMENT

Sleep study not required:
• Neuromuscular disease
• COPD in support mode
Sleep study not required:
• Neuromuscular disease
• COPD in support mode
• Adaptation that can be reversed with treatment [6 week]
• Sleep is permissive
Hypoventilation in OHS/OSA

n=54 BMI 44± 9

de Llano LAP, Chest 2005;128:587 - 594
PAP in restrictive disease

Simonds AK Thorax 1995;50:604-609
PAP in restrictive disease
level III evidence

• Improvement in hypoventilation (PC02)

• Improvement in muscle power

• Improvement in sleepiness

• Improvement in mortality
Case #1

32 year-old female with previous thyroidectomy admitted with somnolence and hypercapnia.

Hypoventilation PCO2 128, PO2 115, pH 7.13, HCO3 45

Weight 506 lbs with massive edema

PSG: Hypoventilation and sleep apnea (AHI 25). Oxygen saturation baseline 88%; nadir 63% and tcPC02 baseline 56mmHg and zenith 86mmHg
Low Drive State
Reversible Hypoventilation
in Hypothyroidism

PC02 128 mmHg
36-year-old thin male with a longstanding history of wheezing. He has been noncompliant with medical therapy for asthma and presents with dyspnea and severe right heart failure with peripheral edema worsening over two weeks.

Hypoventilation: Awake PaO2 50 mmHg PCO2 63 mmHg

Spirometry: FeV1 1.2 L

Echo: Pulmonary hypertension 60 mmHg + right atrial pressure with dilated right ventricle, atrium and tricuspid insufficiency

PSG: AHI 16 SpO2 nadir 79%; PtCO2 90 asleep; initiated on bilevel PAP 18/6 with PCO2 80-90 mmHg. No clinical improvement.
Bilateral vocal cord paralysis
Inspiratory flow < 1 L/sec
Bilateral Vocal Cord Paralysis

- Multisystem atrophy
- Shy-Drager
- Machado-Joseph

Case #3

46 y/o female with pulmonary hypertension [60+RA] and increasing peripheral edema occurring over 3 years referred for intermittent hypoxemia:

- normal chest xray
- negative pulmonary angiogram
- ECHO: no PFO
- FeV1/VC  2.3/2.6 VC 80%pred
Hypoxemia during day 78% when bicycling; extreme fatigue, persistent edema

• PCO2 55-65
• O2 sat 93%--→30% with breath hold
Adult presenting with Congenital Central Hypoventilation
→ Phox 2b mutation with 25 alanine repeats

4 adults 17-55 y/o with hypoventilation with phox B alanine repeats presenting with
• pulmonary hypertension
• hypoxemia during anesthesia
• respiratory failure during daytime
• respiratory failure during sleep
Chromosome 4p12

- Hirshprung’s
- Neuroblastoma
- Autonomic abnormalities
• Sildenafil
• BPAP at night
• Oxygen daytime
• FeedbackSpO2 during exercise
Non-PAP Therapy
Stimulants for Hypoventilation

- Progesterone- modestly lowers $\text{PCO}_2^1$; improves hypoventilation$^2$ but not OSA$^3$
- Acetazolamide- may worsen OSA, less effective than progesterone in hypoventilation$^1$
- Thyroid replacement in myxedema

$^1$Skatrud JB. Progress in Clinical & Biological Research. 136:87-95, 1983
$^3$Cook W. Chest 1989;96(2):262-6
Phrenic Pacing
HYPOVENTILATION SYNDROMES

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