Central Apnea
Disclosures

- No financial disclosure
- Past President, American Academy of Sleep Medicine
- Member, ABIM Board of Directors
At the end of this presentation, the learner will be able to:

1. Describe the etiology and risk factors of central apnea in different patient population.
2. Describe the relationship between central and obstructive apnea.
3. Outline a management approach, including diagnosis and treatment.
• 86 year old male
• Evaluation of snoring, fragmented sleep and dyspnea on exertion.
• Previous smoking history
• PFTs: Poor effort and mild airflow obstruction
• Echocardiography: EF = 40%
Question #1
What is the underlying mechanism of the phenomenon indicated by the arrow?

A. Upper Airway obstruction
B. REM sleep
C. Hypocapnia
D. Diaphragmatic dysfunction
Question # 1
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A. Upper Airway obstruction
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Effect of NREM sleep on Ventilation

The hypocapnic apneic threshold

NREM sleep unmasks a reproducible, highly sensitive, hypocapnic apneic threshold

Skatrud et al. JAP. 55:813-22, 1983
Upper airway changes

1. Reduced activity of upper airway dilators
2. Loss of load compensation
3. Reduced pharyngeal caliber
4. Reduced tidal volume ($V_T$)
Classification of Central Apnea

• Central sleep apnea with Cheyne-Stokes breathing
• Central sleep apnea due a medical disorder without Cheyne-Stokes breathing
• Central sleep apnea due to high altitude periodic breathing
• Central sleep apnea due to a medication or substance
• Primary central sleep apnea
• Treatment-emergent central sleep apnea
<table>
<thead>
<tr>
<th>Hypoventilation</th>
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</thead>
<tbody>
<tr>
<td>Sleep related hypoventilation: CNS, neuromuscular or chest wall disease</td>
</tr>
<tr>
<td>Inadequate ventilatory reserve: hypercapnia not required</td>
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<tr>
<td>May not meet the criteria for “central” or apnea”</td>
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<table>
<thead>
<tr>
<th>Post- hyperventilation</th>
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<tbody>
<tr>
<td>No daytime alveolar hypoventilation</td>
</tr>
<tr>
<td>Hyperventilation</td>
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<tr>
<td>The most common type of central apnea</td>
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• 86 year old male
• Evaluation of snoring, fragmented sleep and dyspnea on exertion.
• Previous smoking history
• PFTs: Poor effort and mild airflow obstruction
• Echocardiography: EF= 40%

• AHI=60/hour of sleep
• CAI= 20/hour of sleep
• ABGs: $P_aO_2$ = 82 torr, $P_aCO_2$ = 34 torr
Question # 2
What is/are the potential underlying mechanism(s) of recurrent central apnea?

A. Impaired arousal response
B. Low loop gain
C. Hypercapnia
D. High controller gain
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A. Impaired arousal response
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Recurrent Central Apnea: Apnea
Hyperventilation

Hypocapnia

Central apnea

ΔPaO2, PaCO2

Δ Sleep State
Hyperventilation

Hypocapnia

Central apnea

$\Delta P_{aO_2}, P_{aCO_2}$

$\Delta$ Sleep State

Apnea Begets Apnea
The Loop Gain: An engineering Construct

- Diffusion, Mixing, Circulation

\[ \Delta PCO_2 \]
Plant Gain

Airways, Lung, Chest wall
“Plant”

Central Pattern Generator
“Controller”

\[ \Delta \text{Ventilation} \]
Controller gain
Mechanisms of hypocapnic Central Apnea
Loop Gain

<table>
<thead>
<tr>
<th>Reducing PCO2</th>
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<tbody>
<tr>
<td><strong>Plant gain</strong></td>
</tr>
<tr>
<td>Input = VE</td>
</tr>
<tr>
<td>Output= PaCO2</td>
</tr>
<tr>
<td>Plant gain: ( \Delta \text{PaCO2} / \Delta \text{VE} )</td>
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</tbody>
</table>

| Changing ventilation: |
| **Controller gain (CG) or chemoreflex sensitivity** |
| Input parameter = PaCO2 |
| Output parameter= VE |
| CG= \( \Delta \text{VE} / \Delta \text{PaCO2} \) |

Effect of Chemoreceptor Sensitivity

$V_E, \text{L/min}$  
Isometabolic line

$P_{aCO_2} \text{mm Hg}$

CO2 Reserve
Effect of Prevailing PaCO2

\( \text{Effect of Prevailing PaCO2} \)

\( V_E, \text{ L/min} \)

Isometabolic line

Ventilatory Reserve
Effect of Prevailing PaCO2

VE, L/min

Isometabolic line

Low PaCO2

Eucapnia

PaCO2 mm Hg

A

B

52 34 36 38 40 44

0 2 4 6 8 10

0 1 2 3 4
Effect of Prevailing PaCO2

\[ V_E, \text{ L/min} \]

Isometabolic line

Low PaCO2

Eucapnia

\[ P_a \text{CO}_2 \text{ mm Hg} \]
Effect of Prevailing PaCO2

![Graph showing the effect of prevailing PaCO2 on ventilatory response (VE, L/min) against PaCO2 (mm Hg). The graph illustrates the isometabolic line and two regions: Low PaCO2 and Eucapnia.]
Question # 3
The effect of decreased steady state PaCO₂ on susceptibility to central apnea is:

A. No effect- unchanged chemo-sensitivity
B. Increased- PaCO₂ closer to the hypocapnic apneic threshold.
C. Decreased- decreased plant gain.
D. Increased- decreased CO₂ stores.
Question # 3
The effect of decreased steady state $\text{PaCO}_2$ on susceptibility to central apnea is:

A. No effect- unchanged chemo-sensitivity
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C. Decreased- decreased plant gain.
D. Increased- decreased CO2 stores.
CENTRAL APNEA RISK FACTORS

• Age, gender and menopause
• Medical Conditions
  • CHF, CVA, Atrial fibrillation ?
  • Narcotics
  • Endocrine: Hypothyroidism, Acromegaly
• Idiopathic central apnea ?
**Question # 4:**

Which sleep state is least prone to central apnea

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>A</td>
<td>N1</td>
</tr>
<tr>
<td>B</td>
<td>N2</td>
</tr>
<tr>
<td>C</td>
<td>N3</td>
</tr>
<tr>
<td>D</td>
<td>REM</td>
</tr>
</tbody>
</table>
Question # 4:
Which sleep state is least prone to central apnea

A. N1  
B. N2  
C. N3  
D. REM
• Congestive Heart Failure
• Opiate analgesics
• Obstructive sleep apnea
  • Treatment-Emergent Central Apnea
Polysomnographic findings in male heart failure patients with either central (CSA) or obstructive (OSA) sleep apnea.

Baseline: Pre-CPAP
On CPAP
Question #5
Which of the following statements regarding treatment-emergent central sleep apnea (TECSA) is correct

A. TECSA develops in the majority of patients undergoing split-night titration
B. Indicates the need for BPAP therapy.
C. Only patients with central apnea in the baseline study develop TECSA
D. The majority will experience complete resolution over a few weeks to months.
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B. Indicates the need for BPAP therapy.
C. Only patients with central apnea in the baseline study develop TECSA.
D. The majority will experience complete resolution over a few weeks to months.

Question #5
Which of the following statements regarding treatment-emergent central sleep apnea (TECSA) is correct?
Change in CSAI in ith CPAP-related CSA

- CSA
- CPAP-Emergent
- N=14

• 86 year old male
• Evaluation of snoring, fragmented sleep and dyspnea on exertion.
• Previous smoking history
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• AHI=60/hour of sleep
• CAI= 20/hour of sleep
• ABGs: $P_aO_2= 82$ torr, $P_aCO_2= 34$ torr
• What is your treatment recommendations
Which of the following is considered as STANDARD treatment for central sleep apnea related to heart failure

A. BPAP
B. CPAP
C. ASV
D. Oral acetazolamide
Which of the following is considered as STANDARD treatment for central sleep apnea related to heart failure

A. BPAP
B. CPAP
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D. Oral acetazolamide
Treatment of Central Apnea

• There is no specific treatment for central apnea
• Most modalities dampen post apneic overshoot.
• Positive Pressure
  • CPAP, BPAP, ASV
• Altering chemical stimuli
  • Supplemental O2 or CO2
• Sleep State: hypnotics
• Ventilatory Drive: Acetzolamide
• Phrenic nerve Stimulation
Does nasal CPAP ameliorate central apnea?

• Association with OSA
• Decreasing overshoot: Plant Gain
  • Opening the upper airway
  • Increasing $O_2$ stores
• CPAP has been used for CSR in CHF
• Improvement in intermediate outcome
Treatment of Central Apnea

- Central Apnea
- Central Hypopnea
- Upper airway obstruction
- Breathing Instability
Oropharyngeal airway occlusion during spontaneous CSA
The Canadian Continuous Positive Airway Pressure trial (Can PAP)

N = 258
NCPAP: 128 No-CPAP: 130
2-year Follow up

Heart-Transplantation-free Survival

• CPAP vs. placebo at 3 months
  ▪ AHI
  ▪ EF
  ▪ Mean nocturnal oxyhemoglobin saturation
  ▪ Plasma nor-epinephrine levels
  ▪ Six-minute walk,
• N-CPAP had no effect on survival
Effect of Bi-level PAP on central apnea index

ASV Pressure (cm H$_2$O)

Reduction in respiratory effort

Resumption of respiratory effort

PS = 11 cm H$_2$O
PS = 3 cm H$_2$O
PEEP = 4 cm H$_2$O

Flow

Time

Comfortable, minimal pressure support when breathing is stable
ASV algorithms respond to central hypopnea/apnea
ASV responds when breathing effort resumes
Adaptive Pressure Support Servo-Ventilation

- Small and variable ventilatory support
- The hydrostatic benefits of low levels of nasal CPAP (5 cm H2O)
- Baseline pressure swing is 4 cm H2O
- Increases to provide 90% of the long-term average VE.
- No hyperventilation

Teschler et al. AJRCCM, 164, 4, 614-619, 2001
Adaptive Pressure Support Servo-Ventilation

- Prospective, randomized, cross-over design
- N=16; gender?
- Desaturation index (3%) > 15/h
- Five consecutive nights
  - CPAP
  - Supplemental O2 @ 2L/NC
  - Bi-level –ST mode
  - ASV

Teschler et al. AJRCCM, 164, 4, 614-619, 2001
Adaptive Pressure Support Servo-Ventilation

Teschler et al. AJRCCM, 164, 4, 614-619, 2001

Central Apnea Index

Total Arousal Index

21/NC ST mode
Which of the following treatments is associated with increased mortality risk in patients with predominantly central apnea

A. CPAP in patients with Heart failure and preserved EF
B. BPAP in patients with opioid-associated central sleep apnea
C. Adaptive-Servo ventilation in patients with heart failure and reduced ejection fraction
D. CPAP in patients with heart failure and reduced ejection fraction
Cumulative Incidence Curves for the Primary End Point, Death from Any Cause, and Cardiovascular Death.

- N=1325 patients
- HF-rEF
- AHI≥15/hour of sleep
- Predominance of central apnea
Which of the following treatments is associated with increased mortality risk in patients with predominantly central apnea

A. CPAP in patients with Heart failure and preserved EF
B. BPAP in patients with opioid-associated central sleep apnea
C. Adaptive-Servo ventilation in patients with heart failure and reduced ejection fraction
D. CPAP in patients with heart failure and reduced ejection fraction
• N=20, 9 weeks
• AHI 30.0 ± 18.1 to 13.5 ± 13.3 (p =0.001),
• CAHI 26.0 ± 17.2 to 7.1 ± 11.8 (p <0.001)
• Arousals 24.0 ± 11.6 to 15.1 ± 7.7 (p <0.001)
• ESS 13 ± 5 to 8 ± 5 (p < 0.001).
• OSA increased in 3 patients
• In the absence of a randomized, controlled trial, zolpidem cannot be recommended for treatment of ICSA at this time.
Effect of Supplemental Oxygen on AHI in Patients with CHF

![Chart showing the effect of supplemental oxygen on AHI in patients with CHF. The chart compares the means and standard deviations (SD) of the apnea-hypopnea index (AHI) in different studies. The studies are labeled as follows: Hanly (n=9), Walsh (n=7), Staniforth (n=11), Franklin (n=7), Andreas (n=22), and Javaheri (n=29). The p-values for the comparison between room air and oxygen are indicated as follows: P<0.01, P<0.05, P<0.01, P=0.02, P<0.001, and P<0.001 respectively.]}
Costanzo MR et al. Transvenous neurostimulation for central sleep apnoea: a randomised controlled trial. 2016 Sep 3;388(10048):974-82
• Similar principles in CSA and PAP-emergent CSA
• Treat the underlying condition
• Initiate CPAP is the initial treatment
• No ASV or BPAP for CSA with HFrEF (EF<45%)
• CPAP failure/intolerance in HFrEF patients with CSA
  • Nocturnal oxygen
  • Medical management of heart failure.

Our Approach
When Data are few; experts are many!
• Patients with HFpEF or primary CSA
  • A trial of CPAP
  • A trial of ASV
  • A trial of BPAP with a back-up respiratory rate
  • Intolerant of PAP: A trial of acetazolamide
Questions?