Complex Sleep Apnea
Can we do better?
David Weed D.O., FCCP, FAASM
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“If you don’t know where you are going, you’ll end up somewhere else.”

Yogi Berra
Objectives

- Discuss what syndromes comprise mixed sleep disordered breathing pathology
- Discuss treatment options
“Complex” Sleep Apnea??

- When central apneas emerge during a PAP titration for a patient with obstructive sleep apnea
  - Can also occur with a dental appliance
  - Many have central apneas on baseline study

- Both obstructive sleep apnea and Cheyne Stokes breathing

- Both obstructive sleep apnea and central sleep apnea (due to narcotic use, idiopathic)

- Mixed apneas??
“Complex” Sleep Apnea

- Have obstructive sleep apnea on baseline
- Most have a hint that centrals may appear with PAP
  - scattered mixed and central apneas
  - Cheyne Stokes pattern
- As obstructive events are eliminated, more central events occur; note differences between events in REM vs NREM
Clinical Heterogeneity for Comp SAS

- 150 patients studied
- 65% had a risk factor for Comp SAS:
  - CHF 21%
  - Stroke 13%
  - Opioids 18.7%
  - Atrial fibrillation 10.7%
- 35.3% had no risk factor

Kuzniar T et al; Sleep Breath 2012
Sleep Disordered Breathing Syndromes

- Obstructive sleep apnea disorders
  - Adult; pediatric
- Central sleep apnea disorders
- Sleep related hypoventilation syndromes
- Sleep related hypoxemia disorders
From ICSD-3:

Central Sleep Apnea Syndromes

- Central Sleep Apnea with Cheyne-Stokes Breathing
- Central Apnea Due to 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
- Primary Central Sleep Apnea of Infancy
- Primary Central Sleep Apnea of Prematurity
- Treatment-Emergent Central Sleep Apnea
Central Sleep Apnea

- A diagnosis of **central sleep apnea (CSA)** requires all of the following:
  - An apnea hypopnea index > 5
  - Central apneas/hypopneas > 50% of the total apneas/hypopneas
  - Central apneas or hypopneas ≥ 5 times per hour
  - Symptoms of either excessive sleepiness or disrupted sleep
Pathophysiology of Central Sleep Apnea

- Events are common at sleep onset in normal individuals
  - CO2 the key driver of respiration during sleep
  - Resetting of CO2 set point
  - Worse at high altitude
Central sleep apnea subtypes

**Hypercapnic**
- Decreased ventilatory output
- Marginal ventilatory status in wakefulness; Lost at sleep onset
- Usually chronic respiratory failure
- Frequently have already developed cor pulmonale
- \[\downarrow \downarrow \text{PO}_{2}, \uparrow \text{PCO}_{2}\]

**Normocapnic**
- Transient instability of drive
- Sleep state oscillation between wakefulness and early sleep – may be normal
- Cheyne-Stokes respirations
- Most common in heart failure
- Also seen in stroke
Central Sleep Apnea

Types:
- Primary – idiopathic
- Cheyne Stokes (CS)
- High altitude periodic breathing
- Due to neurologic or medical condition (not CS) – usually secondary to a structural CNS lesion
- Due to drug - opioids
Central Sleep Apnea with Cheyne-Stokes Breathing (CS)

- ICD-9CM
  - 780-04 – Cheyne-Stokes respiration
- ICD-10CM
  - R06.3 – Periodic breathing
Cheyne-Stokes Respiration (CS)

- First described by Cheyne (1818) then Stokes (1854)
- Best studied in relation to CHF
  - Found in 25-40%
- Risk factors for CSR in CHF
  - male gender
  - atrial fibrillation
  - age > 60
  - hypocapnia
- Associated with increased mortality in CHF
- Seen following acute stroke (26-50%)
Transplant free survival: CSR vs No CSR

Sin et al, Circulation 2000;102:61-6
Cheyne Stokes: Diagnostic Criteria

(A or B) + C + D satisfy the criteria

A. The presence of one or more of the following:
   - Sleepiness
   - Difficulty initiating or maintaining sleep, frequent awakenings, or nonrestorative sleep
   - Awakening short of breath
   - Snoring
   - Witnessed apneas

B. The presence of atrial fib/flutter, congestive heart failure, or a neurological disorder

C. PSG (during diagnostic or PAP titration) shows all of the following:
   - Five or more central apneas and/or central hypopneas per hour of sleep
   - The total number of central apneas and/or central hypopneas is > 50% of the total number of apneas and hypopneas
   - The pattern of ventilation meets criteria for Cheyne-Stokes breathing (CSB)

D. The disorder is not better explained by another current sleep disorder, medication use (e.g., opioids), or substance use disorder
Scoring Cheyne Stokes

- Score a respiratory event as Cheyne-Stokes breathing if BOTH of the following are met:
  - There are episodes of $\geq 3$ consecutive central apneas and/or central hypopneas separated by a crescendo and decrescendo change in breathing amplitude with a cycle length of $\geq 40$ seconds.
  - There are $\geq 5$ central apneas and/or central hypopneas per hour of sleep associated with the crescendo/decrescendo breathing pattern recorded over $\geq 2$ hours of monitoring.
Cycle length

Circulation time
Mechanisms thought to cause CSR in CHF

- Increased awake ventilation
- Increased sensitivity of respiratory drive
- Circulation delay – reduced CO
  - Heart failure
  - Sleep onset
  - Hypoxemia from CSR
    - (increased PAP → RV → dec LV filling)
  - Supine position
adapted from Leung et al. Am J Respir Crit Care Med 2001;164(12):2147-65
CSA due to a medical or neurologic condition without CS breathing

- ICD-9CM
  - 327.27 – Central sleep apnea in conditions classified elsewhere

- ICD-10CM
  - G47.37 – Central sleep apnea in conditions classified elsewhere
CSA due to a medical or neurologic condition without CS breathing

- **Criteria A-C must be met**
  
  A. The presence of one or more of the following:
     - Sleepiness
     - Difficulty initiating or maintaining sleep, frequent awakenings, or non restorative sleep
     - Awakening short of breath
     - Snoring
     - Witnessed apneas
  
  B. PSG shows all of the following:
     - Five or more central apneas and/or central hypopneas per hour of sleep
     - The number of central apneas and/or central hypopneas is > 50% of the total number of apneas and hypopneas
     - Absence of CSB
  
  C. The disorder occurs as a consequence of a medical or neurological disorder but is not due to medication use or substance use
CSA due to a medical or neurologic condition without CS breathing

- Brainstem lesions of developmental, vascular, neoplastic, degenerative, demyelinating, or traumatic origin
  - Chiari malformation
  - Post stroke
  - Brain neoplasm
  - Multiple system atrophy
- due to dysfunction of central ventilatory control centers to initiate ventilatory effort
Primary Central Sleep Apnea

- ICD-9CM
  - 327.21 – Primary central sleep apnea
- ICD10-CM
  - G47.31 – Primary central sleep apnea
Primary Central Sleep Apnea

- **Criteria A-D must be met**
  
  **A.** The presence of at least one of the following:
  - Sleepiness
  - Difficulty initiating or maintaining sleep, frequent awakenings, or non restorative sleep
  - Awakening short of breath
  - Snoring
  - Witnessed apneas
  
  **B.** PSG demonstrates all of the following:
  - Five or more central apneas and/or central hypopneas per hour of sleep (PSG).
  - The number of central apneas and/or central hypopneas is > 50% of the total number of apneas and hypopneas
  - Absence of CSB
  
  **C.** There is no evidence of daytime or nocturnal hypoventilation
  
  **D.** The disorder is not better explained by another current sleep disorder, medical or neurologic disorder, medication use, or substance use disorder
Central Apnea  These are central apneas (2) with minimal oxygen desaturation. Both of these events range between 13-16 seconds in duration.
Central sleep apnea due to drug or substance

- ICD-9CM
  - 327.29 – Other organic sleep apnea
- ICD10-CM
  - G47.39 – Other sleep apnea
Central sleep apnea due to a drug or substance

- **Criteria A-E must be met**
  - A. The patient is taking an opioid or other respiratory depressant
  - B. The presence of one or more of the following:
    - Sleepiness
    - Difficulty initiating or maintaining sleep, frequent awakenings, or non restorative sleep
    - Awakening short of breath
    - Snoring
    - Witnessed apneas
  - C. PSG (diagnostic or on positive airway pressure) shows all of the following:
    - Five or more central apneas and/or central hypopneas1 per hour of sleep (PSG)
    - The number of central apneas and/or central hypopneas is > 50% of the total number of apneas and hypopneas
    - Absence of CSB
  - D. The disorder occurs as a consequence of an opioid or other respiratory depressant
  - E. The disorder is not better explained by another current sleep disorder
Ataxic Breathing Pattern

- Methadone
- • Oxycontin
- • Fentanyl patch
- • Suboxone
Treatment Emergent Central Sleep Apnea

- ICD-9CM
  - 327.29 – Other organic sleep apnea
- ICD-10CM
  - G47.39 – Other sleep apnea
Treatment Emergent Sleep Apnea

- Persistence or emergence of central apneas or hypopneas upon exposure to CPAP when obstructive events have disappeared
  - Also described after nasal and maxillofacial surgery, with dental appliance, after tracheostomy
- These patients have predominately obstructive or mixed apneas during the diagnostic sleep study occurring at ≥ 5 times per hour
Treatment Emergent Sleep Apnea

- Diagnostic polysomnography (PSG) shows predominantly obstructive respiratory events with five or more obstructive respiratory events (i.e., obstructive or mixed apneas, obstructive hypopneas) per hour of sleep.

- Polysomnography during use of positive airway pressure without back-up rate shows significant resolution of obstructive events and emergence or persistence of central apnea or central hypopnea with all of the following:
  - Apnea hypopnea index ≥ 5/hour;
  - Central apnea - central hypopnea index [CAHI] ≥ 5/hour;
  - Number of central apneas and central hypopneas is ≥ 50% of total number of apneas and hypopneas.

- The central sleep apnea is not better explained by another central sleep apnea disorder (e.g. central sleep apnea with Cheyne-Stokes breathing or central sleep apnea due to Drug or Substance).
Baseline: has recurrent events as seen here
CPAP: continues to have similar events at all pressures
Characteristics of TE sleep apnea

- A high number of arousals persist on PAP treatment and the AHI is often higher during NREM than REM sleep
- Treatment emergent central apneas invariably occur during NREM sleep
- Pressures that are effective in controlling obstructive events during REM sleep prove ineffective during NREM sleep due to emergence of central apneas
- In N3, central apneas often decrease until interrupted by an arousal which precipitates another run of central events
- Persistent sleep fragmentation on CPAP treatment and may report little benefit from therapy
Treatment-emergent Sleep Apnea

- Development of CSA during therapy for OSA
  - Unmasking previously-existing CSA
  - Over titration of CPAP
    - Hering-Breuer reflex
  - More effective ventilation with relief of obstruction
- Can occur with other forms of therapy as well!

Compared with controls, OSA patients:

Have a lower ETCO2 during sleep

Therefore, live closer to their apneic threshold

Have a similar apneic threshold

In sum, have a heightened chemosensitivity

Salloum et al, AJRCCM 2010; 181: 189-93.
- 310 pts, full CPAP or split night PSG
- 245 used a nasal mask
- Divided into CAI > 5 vs CAI < 5
  - No difference in age, gender, BMI, AHI
  - Measured leak

![Bar chart showing median and maximum leak for CAI < 5 and CAI > 5]
TREATMENT OF CENTRAL SLEEP APNEA SYNDROME IN ADULTS

The Treatment of Central Sleep Apnea Syndromes in Adults: Practice Parameters with an Evidence-Based Literature Review and Meta-Analyses

R. Nisha Aurora, MD¹; Susmita Chowdhuri, MD²; Kanan Ramar, MD³; Sabin R. Bista, MD⁴; Kenneth R. Casey, MD, MPH⁵; Carin I. Lamm, MD⁶; David A. Kristo, MD⁷; Jorge M. Maliea, MD⁸; James A. Rowley, MD⁹; Rochelle S. Zak, MD¹⁰; Sharon L. Tracy, PhD¹¹
Therapy Options

- Determine if there is an etiology for centrals
  - Atrial fibrillation
  - CHF
  - Opioids or other depressant medication
  - Stroke/TIA in history
- If no obvious reason, consider CNS imaging
Chiari I Malformation

Figure 3. MRI findings on patients with Chiari I malformation and central sleep apnea. (A) Sagittal T1W image of the brain demonstrating method of measurement of the tips of the cerebellar tonsils below the foramen magnum. (B) Sagittal T2-weighted image shows the low-lying cerebellar tonsils (block arrow) with attenuation of the cerebrospinal fluid along their dorsal aspect and the T2-hyperintense syrinx in the cervical and upper thoracic cord (straight arrows). (C) Axial T2-weighted images shows the crowding around the foramen magnum with absence of cerebrospinal fluid along the dorsal aspect of the cerebellar tonsils (arrows).
Chiari I Malformation

- 1:1000-5000
- Downward displacement of cerebellar tonsils through foramen magnum
- Both central and obstructive apneas described
- SDB may be related to compression of brainstem structures
- Decompressive surgery has been shown to reduce both OSA and CSA
Etiology of CSA

- Atrial fibrillation
  - Cardioversion
  - Ablation
- CHF
  - Maximize therapy
  - Pacemaker
- Opioids – reduce dose
- Chiari malformation - surgery
Therapy Options

- Determine if there is an etiology for centrals
- If specific etiology found, may target that initially
- Consider drug trial
  - Hypnotics
  - Acetazolamide
Acetazolamide for CSA

- 2 non-randomized treatment studies reported on the use of acetazolamide for primary CSA
  - 250 mg/day decreased the AHI from $37.2 \pm 23.2$ to $12.8 \pm 10.8$ in 14 patients at 1-month follow-up
  - 1000 mg/day - CAI decreased $54 \pm 29$ to $12 \pm 20$ in 6 patients after 1 week of therapy
- 1 study in CS/CHF
  - Randomized crossover with reduction in AHI
- Considered a **low evidence level option**
- Side effects: paresthesias, tinnitus, GI symptoms, metabolic acidosis, electrolyte imbalance
Hypnotics for CSA

- Zolpidem
  - decreased AHI from $30.0 \pm 18.1$ to $13.5 \pm 13.3$ ($P = 0.0001$) over 9 wks in 20 pts
  - Also has been used in high altitude without much improvement

- Triazolam
  - decreased AHI ($P = 0.05$), decreased CAI in 5 pts

**Low evidence level option**
Therapy Options

- Determine if there is a potential etiology for centrals
- If specific etiology found, may target that initially
- Consider drug trial (low level evidence)
- Gases
  - CO2/dead space
  - Oxygen
Gases – Carbon Dioxide

- Low CO2 levels (hypocapnia) drive most CSA
  - 1-4% inhalation of CO2 resolves CSA
    - 6 pts Comp SAS - quick abolition of sleep-disordered breathing
    - cost of device, the need for a continuous supply of medical-grade CO2, and potential adverse effects of CO2 therapy limit applicability
- Addition of dead space also been shown to help but cannot be individualized
Gases – Oxygen

- Stabilizes respiratory drive
- CPAP + Oxygen reduces SDB
- Oxygen can help CSB

Problem:
- Usually cannot justify payment
- Not as effective as ASV
- No long term outcome studies
Therapy Options

- Determine if there is a potential etiology for centrals
- If specific etiology found, may target that initially
- Consider drug trial (low level evidence)
- Gases
- PAP therapy
  - Best CPAP and re-evaluate; monitor leak
  - ASV
CompSAS may go away or start with CPAP therapy

- Prospective study
- Utilized full PSG (no split nights, no HST)
- 675 pts
- Polysomnography
  - Baseline
  - On therapeutic CPAP
  - 3 months after CPAP therapy
CompSAS may go away or start with CPAP therapy

Eur Respir J 2011;38:329-37
Adaptive Servo-ventilation

- bilevel positive airway pressure that introduced for treatment of central / Comp SAS
- provides variable pressure support (PS) in response to a servo mechanism-based assessment
- Measures or estimates patient’s respiratory output (tidal exhalation, flow, minute ventilation)
- Increase PS during hypopnea, reduce PS during hyperpnea, timed breaths during central apnea
- In US, 2 companies provide:
  - ResMed – VPAP Adapt SV
  - Phillips Respironics – BIPAP Auto SV (advanced)
Two Different ASV Machines

VPAP Adapt
- Variable inspiratory support is given to maintain the target ventilation (90% of recent average ventilation)
- Variable learned backup rate

BiPAP auto SV Advanced
- Variable inspiratory support is given to maintain the average peak flow over the prior 4 minutes
- Auto backup rate will not allow patient to go below 8 BPM
- Clinician can also set backup rate
Adaptive Servo Ventilation

ASV counterbalances the shift between hyperventilation and hypoventilation by applying variable inspiratory support and thus overcomes the ventilatory overshoot.
Average Volume Assured Pressure Support

Intelligently changing pressure support to maintain alveolar ventilation

Pressure increases to meet target alveolar ventilation

Pressure decreases to meet target alveolar ventilation
## Characteristics of ASV Devices

<table>
<thead>
<tr>
<th>ASV Feature</th>
<th>BIPAP-AutoSV (Philips Respironics)</th>
<th>BIPAP-AutoSV Advanced (Philips Respironics)</th>
<th>VPAP-AdaptSV (Resmed)</th>
<th>SOMNOvent CR (VM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expiratory pressure range, cm H₂O</td>
<td>EPAP, 4-25 cm H₂O</td>
<td>EPAP&lt;sup&gt;min&lt;/sup&gt;, 4-25 cm H₂O</td>
<td>EEP, 4-15 cm H₂O</td>
<td>EEPAP, from 6-17 cm H₂O</td>
</tr>
<tr>
<td>Inspiratory pressure (pressure support) range, cm H₂O</td>
<td>IPAP&lt;sup&gt;max&lt;/sup&gt;, 4-30 cm H₂O</td>
<td>PS&lt;sup&gt;max&lt;/sup&gt; 0-26 cm H₂O, total pressure does not exceed 30 cm H₂O</td>
<td>0-25 cm H₂O, total pressure does not exceed 25 cm H₂O</td>
<td>From (EEFAP +5 cm H₂O)-14 cm H₂O, total pressure does not exceed 20 cm H₂O</td>
</tr>
<tr>
<td>Breath rate, min</td>
<td>4-30</td>
<td>4-30</td>
<td>Auto</td>
<td>8-20</td>
</tr>
<tr>
<td>Breathing backup rate</td>
<td>Spontaneous, auto, set</td>
<td>Spontaneous, auto, set</td>
<td>Auto</td>
<td>Spontaneous, auto, set</td>
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<tr>
<td>Expiratory relief</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Timed inspiration</td>
<td>0.5-3.0 s</td>
<td>0.5-3.0 s</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Ramp feature</td>
<td>Yes (0-45 min)</td>
<td>Yes (0-45 min)</td>
<td>No</td>
<td>Yes (5-30 min)</td>
</tr>
<tr>
<td>Compliance card</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No. PC software WM support</td>
</tr>
</tbody>
</table>

ASV = adaptive servoventilation; EEP = end expiratory pressure; EEPAP = end expiratory positive airway pressure; EPAP = expiratory positive airway pressure; IPAP = inspiratory positive airway pressure; max = maximum; min = minimum; PS = pressure support; VM = Weinmann Geräte für Medizin GmbH+Co. KG.
Prescription Settings

**VPAP Adapt (ASV mode)**
- EPAP
- PS min (lowest 3cmH2O)
- PS max

**SPAP Adapt (ASVauto mode)**
- EPAP min/max
- PS min (lowest 0 cmH2O)
- PS max

PS = pressure above APAP min at all times in VPAP Adapt ASVauto mode

**BiPAP auto SV Advanced**
- EPAP min/max
- PS min (lowest 0 cmH2O)
- PS max
- Max Pressure
- Rate: Auto or BPM
- I-Time (with fixed rate)
### Coding Guidelines for Equipment and Accessories

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
<th>Payment Category/Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>EO470</td>
<td>Respiratory assist device, Bi-level pressure capability, <em>without backup rate feature</em>, used with noninvasive</td>
<td>Capped Rental</td>
</tr>
<tr>
<td></td>
<td>interface, e.g., nasal or facial mask (intermittent assist device with continuous positive airway pressure device). BiPAP Pro with Bi-Flex, BiPAP Pro 2 with Bi-Flex, BiPAP Plus, BiPAP Auto with Bi-Flex M Series, BiPAP Plus with Bi-Flex M Series</td>
<td>• Rental payment can be made for up to 13 months of continuous use.</td>
</tr>
<tr>
<td>EO471</td>
<td>Respiratory assist device, bi-level pressure capability, <em>with backup rate feature</em>, used with noninvasive</td>
<td>On or After 04/01/06:</td>
</tr>
<tr>
<td></td>
<td>interface, e.g., nasal or facial mask (intermittent assist device with continuous positive airway pressure device). BiPAP S/T, BiPAP Synchrony S/T, BiPAP autoSV.</td>
<td>• Capped rental only</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Rental payment can be made for up to 13 months of continuous use.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prior to 04/01/06: Items requiring frequent and substantial servicing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Equipment is provided to the beneficiary on a monthly rental basis until medical necessity ends.</td>
</tr>
</tbody>
</table>
Adaptive Servo-Ventilation (ASV): Novel Treatment for Cheyne-Stokes Respiration in Heart Failure

(A) Typical 5-min polygraph recording on the diagnostic night with desaturations and arousals.

(B) Typical 5-min polygraph recording on the adaptive servo-ventilation night.
ASV in CSR patients

- 29 male patients, LVEF < 40%
- Tx’d ~ 6 months with ASV; no control group
- AHI at baseline = 37.4; min SpO2 80.9%
- Used Embletta PM device
- CSR defined as >80% of respiratory events were central apneas with CSR
- AHI > 15 to be enrolled
- Avg ASV setting: IPAP 8-12; EPAP 4-7
ASV in CSR patients

- AHI improved (3.7)
- Min SpO2 improved (86.9%)
- NYHA class decreased (2.43 to 1.93)
- BNP levels fell (2285 to 1061)
- CPX testing improved
- LVEF improved (28.2 to 35.2)
NPPV vs ASV

- Somnovent
  - Bilevel PAP with backup rate; EPAP to eliminate OA, IPAP to optimal treatment of CA
  - ASV to maintain flow and minute ventilation
- 30 patients completed study

Randomized Controlled Trial of Noninvasive Positive Pressure Ventilation (NPPV) Versus Servoventilation in Patients with CPAP-Induced Central Sleep Apnea (Complex Sleep Apnea)

Dominic Deliweg, MD; Jens Kerl, PhD; Ekkehard Hoehn; Markus Wenzel, MD; Dieter Koehler, PhD
## Table 3
Polygraphic and polysomnographic data of the two treatment arms during continuous positive airway pressure treatment prior to randomization as well as during titration to the randomized treatment and 6 weeks after commencement of noninvasive positive pressure ventilation or servventilation.

<table>
<thead>
<tr>
<th>Variables</th>
<th>CPAP after 6 weeks, randomized to NPPV</th>
<th>CPAP after 6 weeks, randomized to SV</th>
<th>P</th>
<th>NPPV first night</th>
<th>SV first night</th>
<th>NPPV after 6 weeks</th>
<th>SV after 6 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>15</td>
<td>15</td>
<td></td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Breathing during sleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apnea-hypopnea index, events/h</td>
<td>28.6 ± 6.5</td>
<td>27.7 ± 9.7</td>
<td>0.76</td>
<td>9.1 ± 4.3</td>
<td>9 ± 6.4</td>
<td>16.5 ± 8</td>
<td>7.4 ± 4.2</td>
</tr>
<tr>
<td>Apnea index, events/h</td>
<td>19 ± 5.6</td>
<td>21.1 ± 8.6</td>
<td>0.43</td>
<td>2 ± 3.1</td>
<td>3.5 ± 4.5</td>
<td>10.4 ± 5.9</td>
<td>1.7 ± 1.9</td>
</tr>
<tr>
<td>Central apnea index, events/h</td>
<td>16.7 ± 5.4</td>
<td>18.2 ± 7.1</td>
<td>0.51</td>
<td>2 ± 3.1</td>
<td>2.5 ± 3.9</td>
<td>10.2 ± 5.1</td>
<td>1.5 ± 1.7</td>
</tr>
<tr>
<td>Obstructive apnea-hypopnea index, events/h</td>
<td>11.9 ± 3.3</td>
<td>9.4 ± 7.3</td>
<td>0.25</td>
<td>7.1 ± 3.8</td>
<td>6.4 ± 3.6</td>
<td>6.3 ± 4.1</td>
<td>5.9 ± 3.1</td>
</tr>
<tr>
<td>Mean oxygen saturation, %</td>
<td>93.9 ± 2</td>
<td>93.9 ± 1.9</td>
<td>0.93</td>
<td>93.3 ± 2.6</td>
<td>94.3 ± 1.9</td>
<td>93.6 ± 2.2</td>
<td>94.1 ± 2.1</td>
</tr>
<tr>
<td>Minimum oxygen saturation, %</td>
<td>80.7 ± 11.1</td>
<td>80.7 ± 9.9</td>
<td>0.97</td>
<td>81.1 ± 5.1</td>
<td>84.2 ± 4.9</td>
<td>84 ± 5.8</td>
<td>86.8 ± 4</td>
</tr>
<tr>
<td>Oxygen desaturation index, events/h</td>
<td>17.5 ± 13.1</td>
<td>24.3 ± 11.9</td>
<td>0.15</td>
<td>10.1 ± 4.5</td>
<td>8.9 ± 8.4</td>
<td>21.1 ± 9.2</td>
<td>4.8 ± 3.4</td>
</tr>
<tr>
<td>Sleep characteristics</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Arousal index events/h</td>
<td>33.8 ± 20</td>
<td>27.6 ± 15.5</td>
<td>0.4</td>
<td>25 ± 20.1</td>
<td>25.6 ± 15.7</td>
<td></td>
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</tr>
<tr>
<td>Respiratory arousal index/h</td>
<td>18.4 ± 15</td>
<td>13.7 ± 7</td>
<td>0.36</td>
<td>8.5 ± 9.9</td>
<td>8.7 ± 7.1</td>
<td></td>
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</tr>
<tr>
<td>Total sleep time, min</td>
<td>252 ± 90</td>
<td>235 ± 84</td>
<td>0.63</td>
<td>277 ± 82</td>
<td>277 ± 103</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>63.3 ± 22.1</td>
<td>61 ± 22.1</td>
<td>0.81</td>
<td>68.4 ± 21</td>
<td>64.4 ± 20.4</td>
<td></td>
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</tr>
<tr>
<td>Rapid eye movement sleep %</td>
<td>11.8 ± 9.3</td>
<td>9.3 ± 8</td>
<td>0.48</td>
<td>10.8 ± 5.7</td>
<td>12.6 ± 9</td>
<td></td>
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</tr>
<tr>
<td>Slow wave sleep, %</td>
<td>11.4 ± 7.7</td>
<td>8.7 ± 9.6</td>
<td>0.46</td>
<td>16.9 ± 8.2</td>
<td>14.6 ± 7.1</td>
<td></td>
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</tr>
<tr>
<td>Nightly use, h</td>
<td>5.0 ± 0.9</td>
<td>5.3 ± 1.3</td>
<td>0.53</td>
<td>4.8 ± 1.4</td>
<td>5.5 ± 1.1</td>
<td></td>
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</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation. Significance was determined by one-way analysis of variance. Post hoc analysis was carried out using the Scheffé procedure in case of equal variances and the Games-Howell test in case of unequal variances. *P < 0.05 compared with CPAP treatment. #P < 0.05 compared with NPPV titration. **P < 0.05 compared with servventilation titration. *P < 0.05 compared with NPPV after 6 weeks. #P < 0.05 compared with servventilation after 6 weeks. CPAP, continuous positive airway pressure; NPPV, noninvasive positive pressure ventilation; SV, servventilation.
ASV to treat Opioid induced CSA

- 5 articles, 127 patients; on opioids > 6 months
- Dosage ranged from 10 - 450 mg daily (morphine equivalent)
- CPAP mostly ineffective
- Bilevel PAP with and without supplemental oxygen achieved elimination of central apneas in 62%
- ASV: conflicting results - 58% central apnea index <10/hour
- Ataxic breathing predicted poor response to PAP
ASV caveats

- No long term trials to show a mortality reduction
- Cost is much higher than CPAP
- Excellent choice for CS alone or CS with OSA
  - Not as effective for CSA secondary to opioids or without CS
- Acceptable AHI is higher than with CPAP – 10?; converts apneas to hypopneas
Take Home Points

- Complex sleep apnea is a confusing term
  - Look for etiology for central events and address those if possible
  - Many patients with treatment emergent CSA will improve with time
  - ASV appears to be better than NPPV (bilevel PAP) for persistent CSA/CS
Words From A Great Philosopher…

“Somebody has to do something, and it's just incredibly pathetic that it has to be us!”

Jerry Garcia