(Almost) Everything You Need to Know to Pass the Sleep Medicine Boards:

Sleep Disordered Breathing

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Sleep Medicine Board Topic Blueprint

Medical Content Category	% of Exam
Normal Sleep and Variants	16%
Circadian Rhythm Sleep-Wake Disorders	10%
Insomnia	17%
Central Disorders of Hypersomnia	12%
Parasomnias	7%
Sleep-Related Movements	8%
Sleep-Related Breathing Disorders	20%
Sleep in Other Disorders	5%
Instrumentation and Testing	5%
	100%

Sleep Disordered Breathing

Sleep-Related Breathing Disorders	20% of Exam
Obstructive sleep apnea	9%
Adult obstructive sleep apnea	
Pediatric obstructive sleep apnea	
Central sleep apnea syndromes	7.5%
Central sleep apnea with Cheyne-Stokes breathing	
Central sleep apnea due to a medical disorder without Cheyne-Stokes breathing	
Central sleep apnea due to high-altitude periodic breathing	
Central sleep apnea due to medications or substances	
Primary central sleep apnea	
Primary central sleep apnea of infancy	
Primary central sleep apnea of prematurity	
Treatment-emergent central sleep apnea	
Sleep-related hypoventilation disorders	2.5%
Obesity-hypoventilation syndrome	
Congenital central alveolar hypoventilation syndrome	
Late-onset central hypoventilation with hypothalamic dysfunction	
Idiopathic central alveolar hypoventilation	
Sleep-related hypoventilation due to medications or substances	
Sleep-related hypoventilation due to medical disorders	
Sleep-related hypoxemia disorder	<2%
Isolated symptoms and normal variants	<2%
Snoring	
Catathrenia	

Question

As compared to younger individuals, which one of the following statements is correct regarding obstructive sleep apnea in individuals over the age of 60?

A) Associated with higher mortality

B) Stronger association with obesity

C) More likely to tolerate oral appliance therapy

D) Oxygen desaturations are less severe

Answer

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OSA and Increased Age

- Prevalence of OSA increases with age
  - SHHS: 26.4% had RDI ≥ 15; 60% had RDI ≥ 5 (Age > 60)
- BMI and gender become less important with age
  - BMI not an independent risk factor for OSA over the age of 60
  - No gender specificity after women go through menopause
- OSA commonly associated with EDS and may contribute to HTN, cardiovascular disease, nocturia, cognitive impairment and reduced QOL
- Most studies suggest that OSA does not increase the risk of mortality in older adults
- Oxygen desaturations less severe in older adults
- Central apneas become more common
- CPAP can improve symptoms, cognitive function and QOL
- Older age is associated with a less favorable response to oral appliance therapy

Question

- A 50 year old male who presents with snoring and daytime sleepiness (Epworth = 14) is recently diagnosed with severe OSA (AHI = 35) on an HST and started on CPAP therapy at 10 cm H_20.
- PMHx: DM, obesity, atrial fibrillation
- PE:
  - BP: 120/80 mm hg, P: 80 R: 12
  - Cardiac: Irregular rate and rhythm
  - Remainder of exam normal

Question

When he returns for his initial 3 month office visit, which one of the following outcomes is CPAP therapy most likely to improve?

A) Blood pressure

B) Atrial fibrillation

C) Daytime sleepiness

D) Glucose control

Answer

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CPAP Outcomes Summary: Patients with Daytime Symptoms

	AHI	Sleep Architecture	Subjective Sleepiness	Objective Sleepiness	Neuro-cognitive and Mood	Quality of Life	Cardiovascular Risk Reduction
Severe/Moderate OSAS	+	+/-	+	+/-	+/-	+/-	+/-
Mild OSAS	+	+/-	+/-	-	-	+/-	NA

OSA, CV Disease and Treatment (CPAP): The Bottom Line: Data is Inconclusive

- CPAP may reduce cardiovascular mortality in severe OSA with EDS
  - Prospective observational studies
- CPAP can reduce blood pressure, but reductions in BP are small and results are inconsistent across studies
  - EDS and uncontrolled HTN may predict a more robust BP response
  - Better adherence = Better BP response
  - Antihypertensive medication better than CPAP
  - CPAP may improve BP in patients with resistant HTN and OSA
  - CPAP better than oxygen in patients with CV disease or CV risk factors
- CPAP does not reduce the incidence of HTN or cardiovascular diseases in patients with OSA and no daytime sleepiness
- Limited data for reductions of arrhythmias with CPAP
- CPAP improves LVEF in patients with CHF with systolic dysfunction and OSAS
- Minimal to no data concerning:
  - Mild OSAS
  - Long-term RCTs on other cardiovascular outcomes

Other CPAP Outcomes

- CPAP use associated with reductions in motor vehicle accidents
- CPAP use not associated with weight loss
  - May be associated with mild weight gain
- Improvements in DM, lipids and metabolic syndrome are inconsistent and debatable
  - Weight loss better than CPAP for improving these outcomes
- Benefits for patients without symptoms not clear across spectrum of disease severity

AASM Practice Parameter and Clinical Guideline Recommendations Still Supported by the Data

- CPAP Indications (Standards):
  - Treatment of moderate - severe OSAS
  - Improving subjective sleepiness
- CPAP Recommendations (Options):
  - Treatment of mild OSAS
  - Improving quality of life
  - As an adjunctive anti-hypertensive therapy

Kushida, C et al. Sleep 2006; 29:375-380
Gay, P et al. Sleep 2006;29:381- 401
Epstein, L et al. J Clin Sleep Med 2009;5:263-276

Question

Which one of the following has been associated with lower adherence to PAP therapy?

A) Severe OSA (AHI > 30)

B) Excessive daytime symptoms

C) Pressures < 12 cm H_2O

D) Lower socioeconomic status

Answer

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A) Severe OSA (AHI > 30)

B) Excessive daytime symptoms

C) Pressures < 12 cm H_2O

D) Lower socioeconomic status

Predictors of Adherence Inconsistent: The Bottom Line

- Possibly daytime sleepiness and more severe disease associated with improved adherence
- African American race and/or lower socioeconomic class associated with lower adherence
- Pressure level not predictive

Question

Which one of the following interventions has been associated with improved PAP adherence?

A) AutoPAP

B) Eszopiclone

C) Nasal steroids

D) PSG titration

Answer

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A) AutoPAP

B) Eszopiclone

C) Nasal steroids

D) PSG titration

AASM Practice Parameters and Clinical Guideline Adherence Recommendations

- Interventions to Improve Adherence:
  - Heated humidification (*Standard*)
  - Education (*Standard*)
- Follow up:
  - CPAP usage should be objectively monitored (*Standard*)
  - Initial follow up in first few weeks (*Standard*)
  - Yearly and as needed follow-up thereafter (*Option*)

Kushida, C et al. Sleep 2006; 29:375-80
Gay, P et al. Sleep 2006;29:381- 401
Epstein, L et al. J Clin Sleep Med 2009;5:263-276

Impact of Supportive, Educational and Behavioral Therapies on CPAP Compliance

Therapy	Interventions	Evidence Quality	Mean Improvements in Nightly CPAP Adherence
Supportive	• Increased practical support • Encouragement • Telemedicine • Relaxation prior to CPAP	Low to moderate	.85 hours
Education	• Video • Face-to-face sessions • Group sessions • Written material • Phone calls • Home follow up	Low to moderate	.6 hours
Behavioral Therapies	• Motivational interviewing • Written feedback • CBT with education	Very low to low	1.44 hours

Wozniak D et al. Cochrane Database Review 2014

Data on Heated Humidification and PAP Adherence: Inconsistent and Not Very Strong

Study	N	Interventions	Outcomes
Massie 1999	38	• CPAP with heated, cold pass and no humidification • Duration: 3 weeks	• **Heated humidification improved adherence** • **No difference in adherence with cold pass or no humidification** • Reduced upper airway dryness with HH • No differences in Epworth between groups
Neill 2003	42	• CPAP with and without heated humidification • Duration: 3 weeks	• **Small increase in adherence** • Reduced upper airway symptoms • No change in sleepiness or satisfaction
Mador 2005	98	• CPAP with and without heated humidification • Durations: 12 months	• **No differences in adherence** • No differences in daytime sleepiness, QOL • Reduced upper airway dryness with HH
Salgado 2008	39	• APAP with and without heated humidification • Durations: 30 days	• **No differences in adherence** • No differences in nasal symptoms
Worsnop 2010	54	• Heated vs no humidification • Durations: 12 weeks	• **No differences on adherence** • Reduced nasal symptoms

Massie C et al. Chest. 1999;116:403-8
Neill A et al. Eur Respir J. 2003 Aug;22(2):258-62
Mador M et al. Chest 2005;128:2151-8
Salgado S et al. J Bras Pneumol. 2008;34:690-4
Worsnop C et al. Intern Med J 2010;40:650-656

Hypnotics and CPAP Adherence

Study	Hypnotic and Intervention	n	Main Findings
Bradshaw (2006)	Zolpidem 10 mg vs placebo vs standard care x 14 days	72	No differences in adherence, either nights used or hours per night after 30 days
Lettieri (2008)	Eszopiclone 3 mg prior to PSG titration vs placebo	226	Eszopiclone improves the quality of titration and reduces need for repeat studies
Lettieri (2009)	Eszopiclone 3 mg vs Placebo x 14 days	160	Eszopiclone improved adherence, both nights used and hours per night after 6 months
Park (2013)	Zaleplon 10 mg vs placebo for split-night titration	134	No differences in adherence or other symptoms after 30 days

- Conclusions:
  - Short term eszopiclone may improve titration efficacy and 6 month adherence
  - Other hypnotics not associated with improved adherence

Adherence Interventions and Outcomes Summary: The Bottom Line

Intervention	Outcomes	Comments
Education/Supportive Care	Beneficial	• Various interventions helpful in most patients • Best intervention, or combination, not clear
Behavioral Therapies	Beneficial	• Various interventions improve adherence • Low quality supporting data data
Heated humidification	Inconsistent/Controversial	• Some, but not the majority of data support improved adherence • Nasal congestion or rhinitis may be associated with improved adherence with heated humidification
Advanced PAP (Flex, Bilevel and APAP)	No benefit	• Not associated with improved adherence or other outcomes • Biflex, may be the exception, in CPAP nonadherent
Nasal Steroids	No Benefit	• Not associated with improved adherence or nasal symptoms

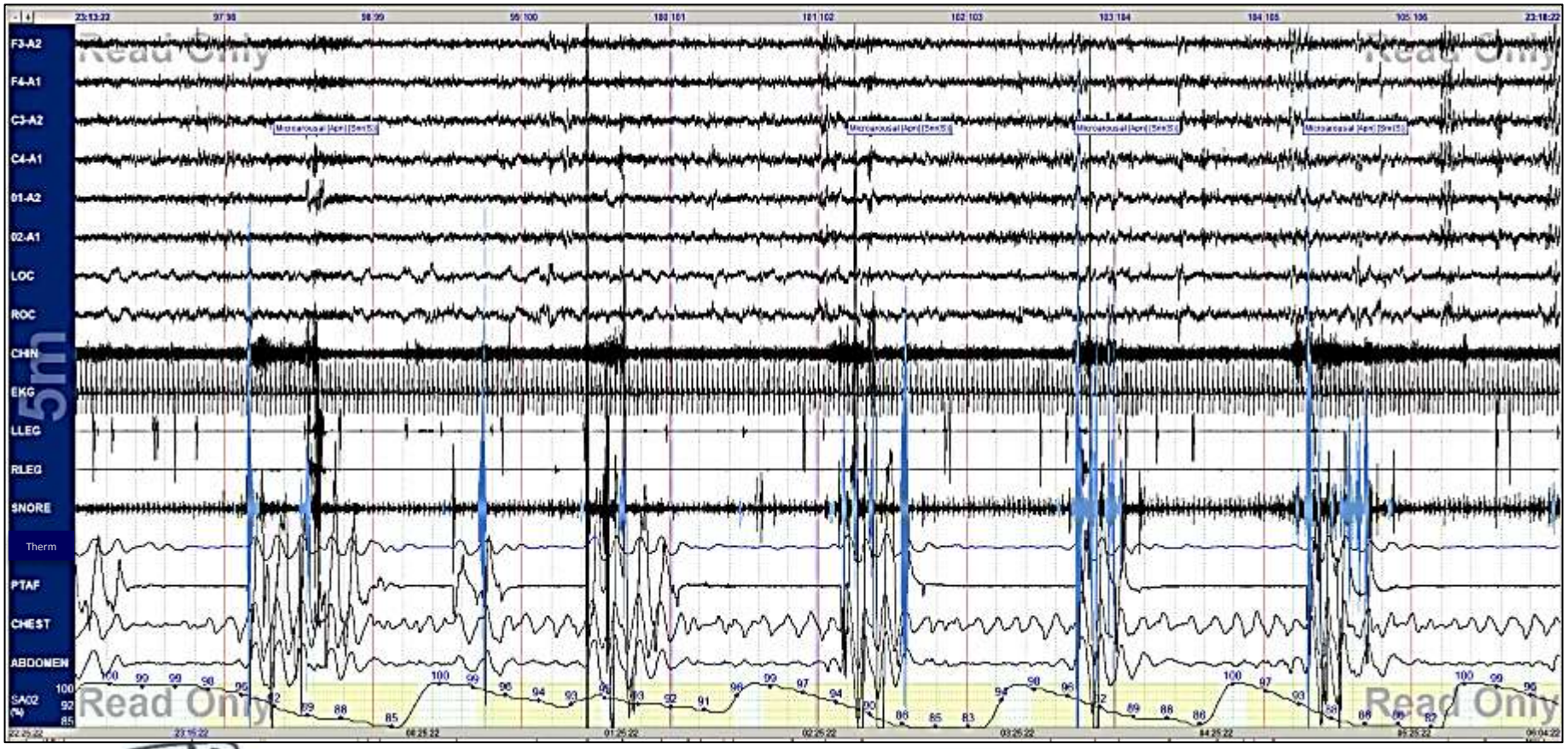
Adherence Interventions and Outcomes Summary: The Bottom Line

Intervention	Outcomes	Comments
Mask Type	Controversial	• Best mask type is not clear and is patient dependent • Changing mask type may alter effective PAP pressure
Hypnotics	Controversial	• Eszopiclone may improve PAP titration efficacy and 6 month adherence • Data do not support other hypnotics
Telemedicine	Unclear	• Limited data suggest benefit, other not supportive • More data required
Compliance Monitoring	Unclear	• No clear data to guide therapy or determine which patients may benefit from this intervention
Sleep Specialist Care	Unclear	• Observational studies support • RCTs show mixed results in uncomplicated moderate/severe OSA

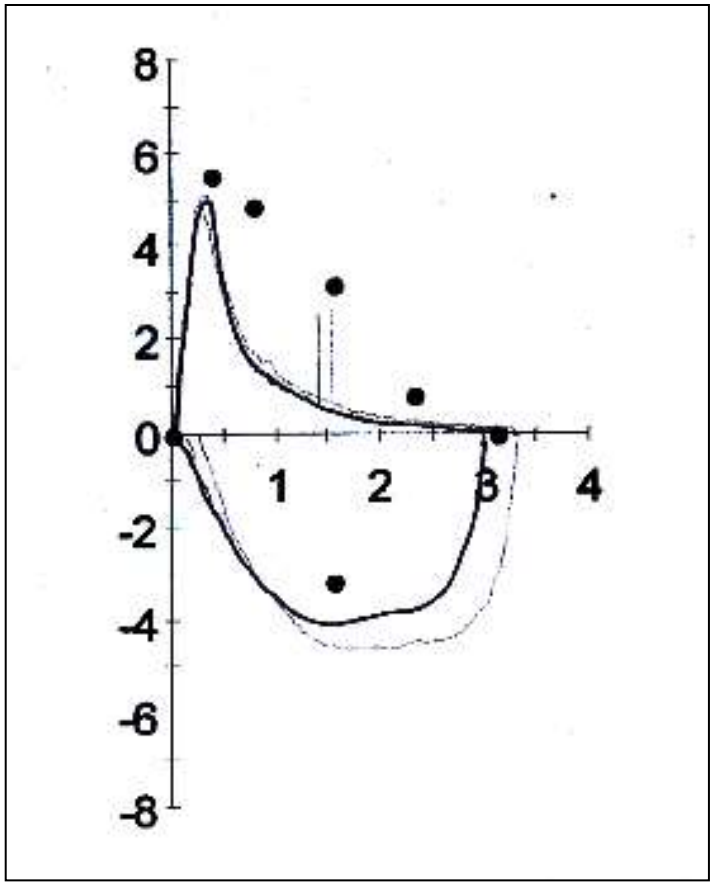
Question

According to the most recent AASM Practice Parameter recommendations, treatment with AutoCPAP would be best indicated for which one of the following patients?

A) A 45 year old obese male with snoring, witnessed apneas, daytime sleepiness (EPWORTH = 14) and an AHI of 40. A five minute epoch of the main PSG respiratory findings are shown below:

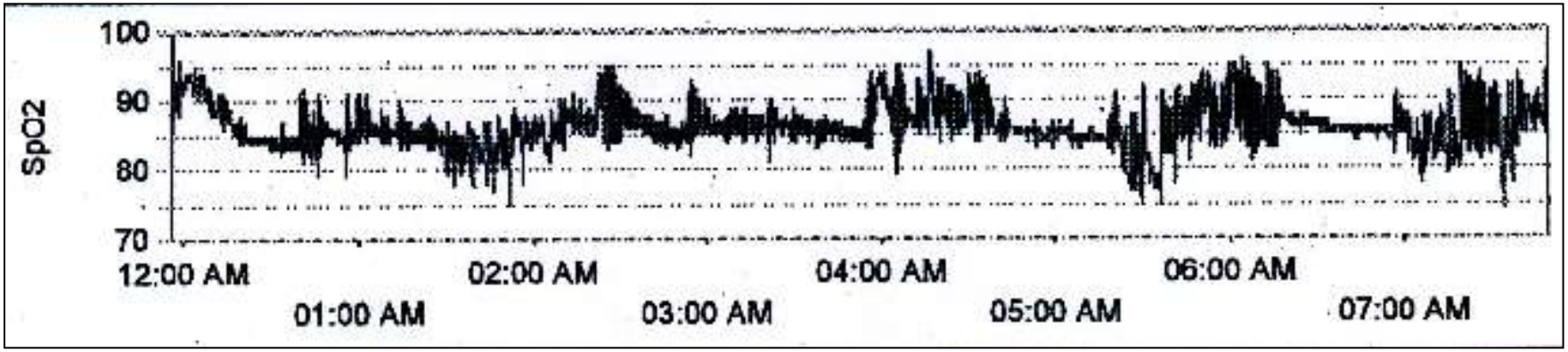


B) A 45 year old obese male with snoring, witnessed apneas, daytime sleepiness (EPWORTH = 14), and an AHI of 40. His spirometry is shown below:



C) A 45 year old obese male with snoring, witnessed apneas, daytime sleepiness (EPWORTH = 14) and an AHI of 40. His room air ABG and overnight oximetry are shown below:

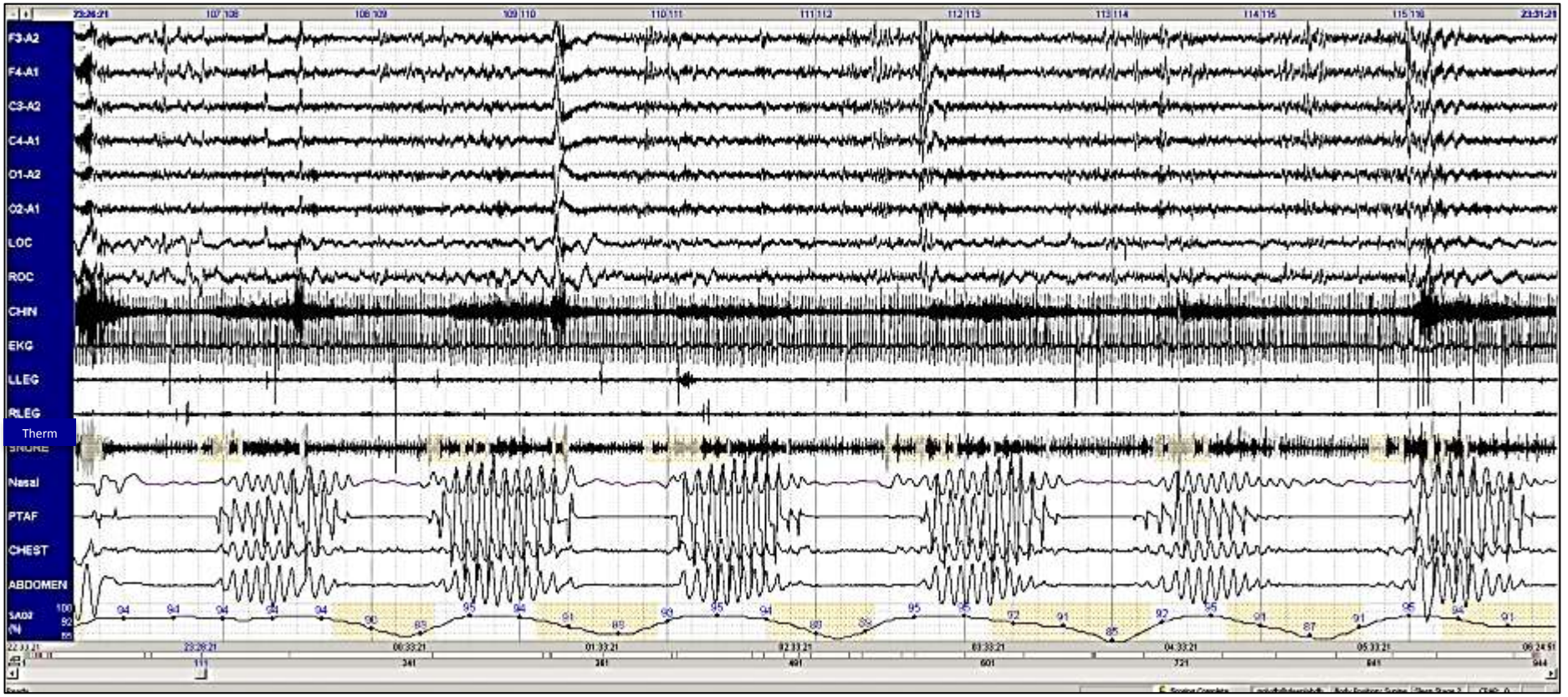
Overnight Oximetry



Room Air ABG

Ph	7.34
PCO2 (mm Hg)	60
PO2 (mm Hg)	62
HCO3 (mmol/L)	34

D) A 45 year old obese male with snoring, witnessed apneas, daytime sleepiness (EPWORTH = 14) and an AHI of 40. A five minute epoch of the main PSG respiratory findings are shown below:



5 Minute Epoch

Question

According to the most recent AASM Practice Parameter recommendations, treatment with AutoCPAP would be best indicated for which one of the previous patients?

A, B, C or D

Answer

According to the most recent AASM Practice Parameter recommendations, treatment with AutoCPAP would be best indicated for which one of the following patients?

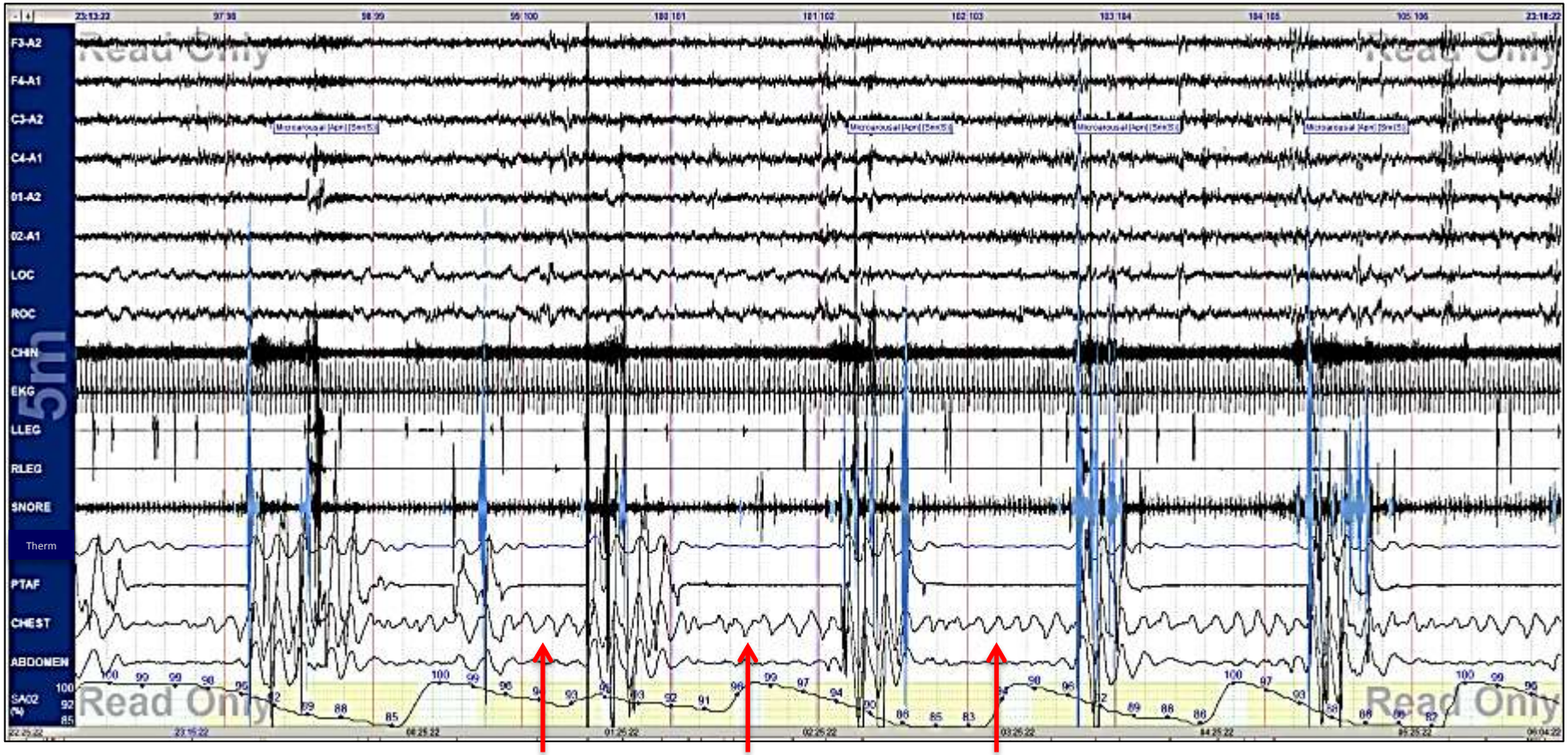
The correct answer is A

Who is a Potential Candidate for APAP?

- **Clear Candidates**
  - **Un**complicated moderate to severe OSAS
- **Unclear Groups**
  - REM-related OSAS
  - Position dependent
  - High pressures (>10)
  - CPAP intolerant

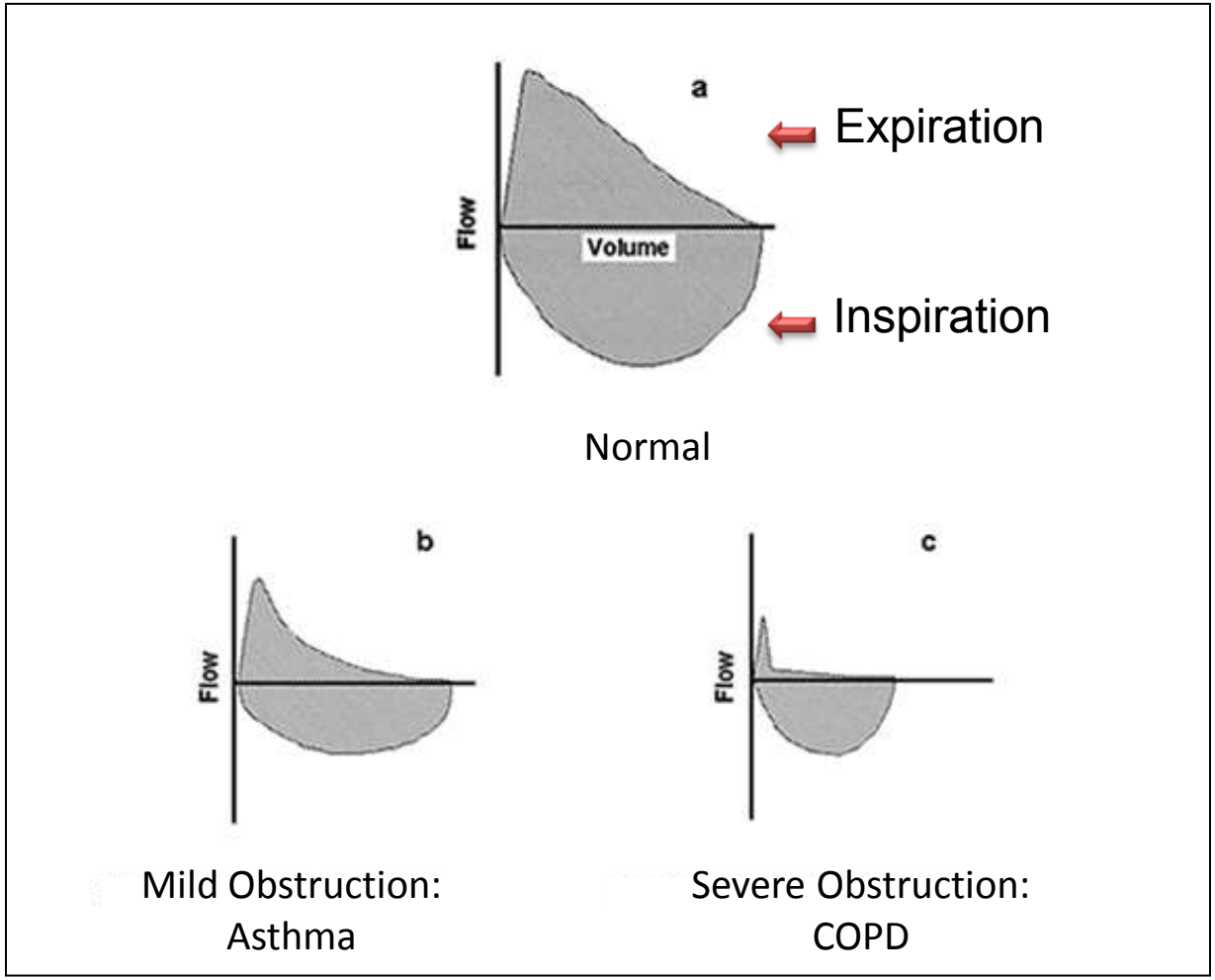
- **Not APAP Candidates (**AASM Standard**)**
  - Congestive heart failure
  - COPD and chronic lung disease
  - Obesity Hypoventilation Syndrome
  - Other hypoventilation syndromes
  - Lack of snoring

Patient “A” has Uncomplicated Severe OSAS



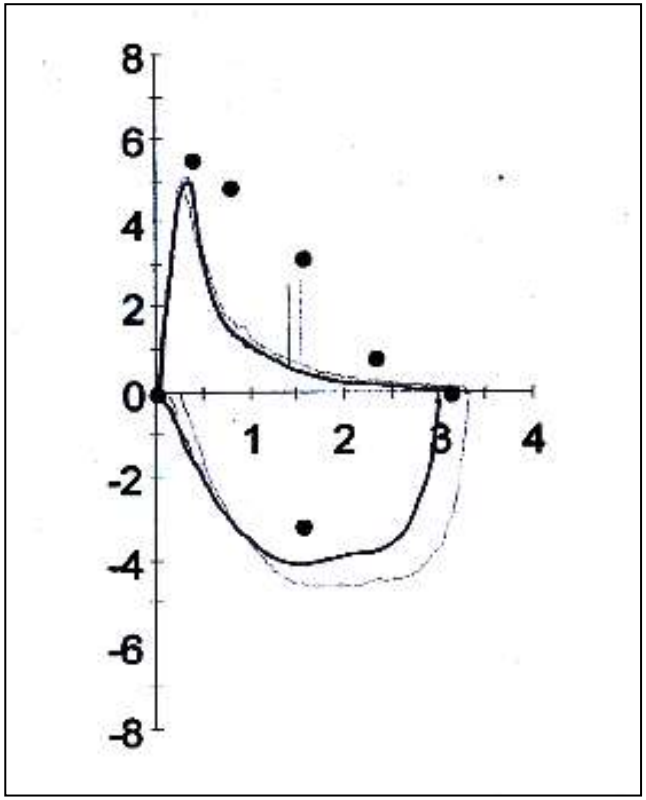
Recurrent Obstructive Apneas
with Associated Oxygen Desaturations

Flow Volume Loops:
Normal and Degrees of Obstruction

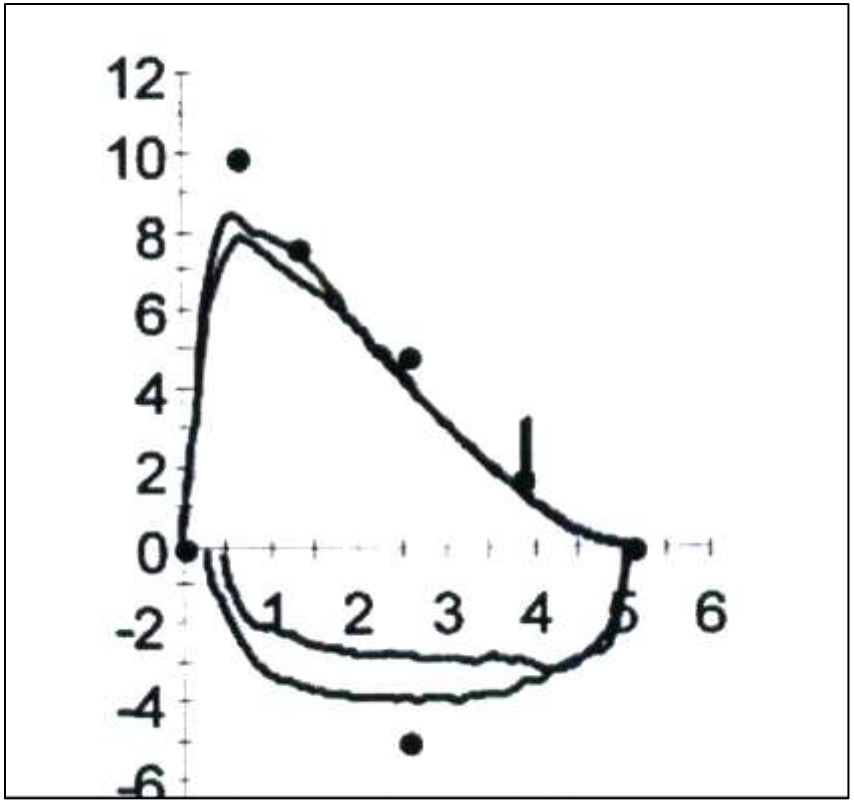


Patient “B” has Obstructive Lung Disease

Obstructed Spirometry

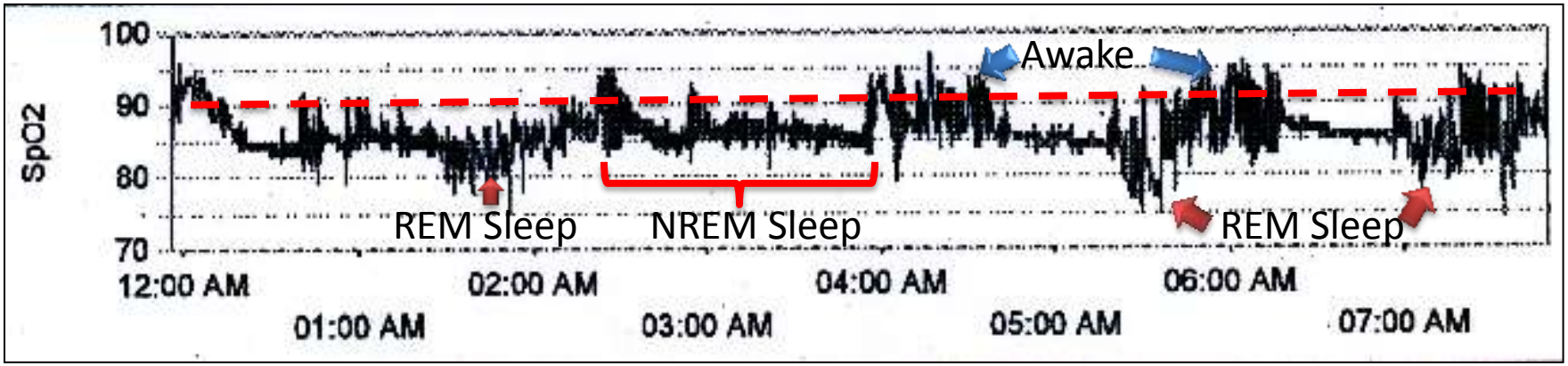


Normal Spirometry



Patient “C” Has Hypoventilation with Hypercapnea

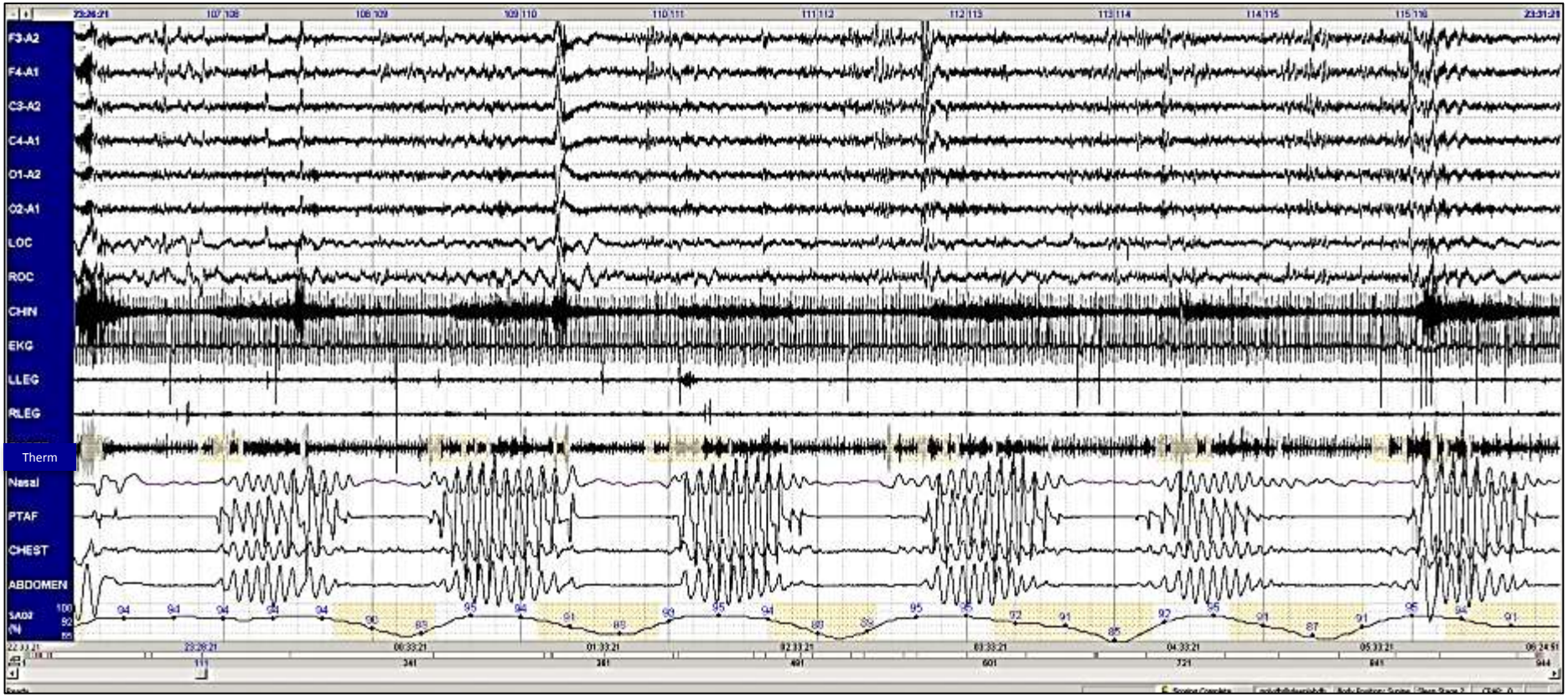
Overnight Oximetry is Most Consistent with Hypoventilation and REM Related Events



Room Air ABG Consistent with Chronic Hypercapnea

Ph	7.34	Low
PCO2 (mm Hg)	60	High
PO2 (mm Hg)	62	Low
HCO3 (mmol/L)	34	High

Patient “D” Has Central Apneas with a Cheyne Stokes Pattern



APAP: The Bottom Line

- Recommended for patients with moderate to severe uncomplicated OSA
- Not recommended for OSA with comorbidities:
  - CHF, hypoventilation syndromes, COPD, non-snorers (UPPP)
- Outcomes:
  - Lower mean pressures with APAP
  - Similar outcomes to CPAP
  - APAP is as effective as CPAP for uncomplicated moderate to severe OSA
- AASM 2008 Indications:
  - Standard:
    - Not recommended for OSA diagnosis or split-night studies
  - Guideline:
    - To determine fixed CPAP in an attended setting
  - Options:
    - Stand alone therapy
    - To determine fixed CPAP in an unattended setting

Question

Which one of the following statements is correct regarding oral appliance (OA) therapy for the treatment of OSA?

A) OA therapy results in improvements in blood pressure similar to CPAP
B) OA therapy reduces the AHI better than CPAP
C) OA therapy improves oxygenation better than CPAP
D) CPAP improves daytime sleepiness better than OA therapy

Answer

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Oral Appliance Therapy for OSA

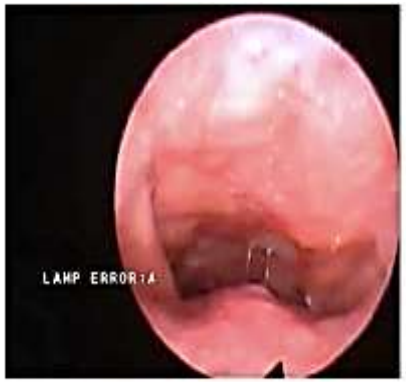
- AASM Guidelines:
  - Indicated for mild-to-moderate OSA
  - Severe OSA should have initial trial with CPAP
- Typically well tolerated
- Difficult to predict success
- CPAP more effective for reducing AHI and improving oxygenation
- OAs = CPAP for improving sleepiness
- Role in reducing blood pressure is not clear, though data suggest benefits similar to CPAP

Question

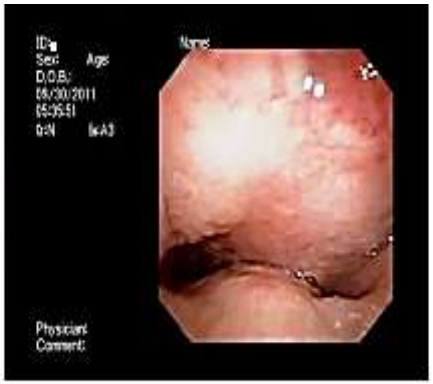
- A 55 year old male with severe OSA (AHI = 40) who is intolerant to CPAP therapy is interested in treatment with hypoglossal nerve stimulation.
- He undergoes a drug induced sedated endoscopy (DISE) to determine if he is a candidate for this procedure.

Which one of the following DISEs would exclude the patient for HGNS treatment?

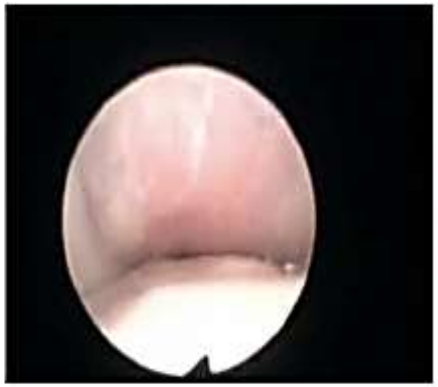
A



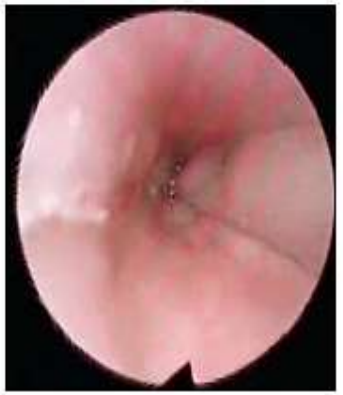
B



C



D



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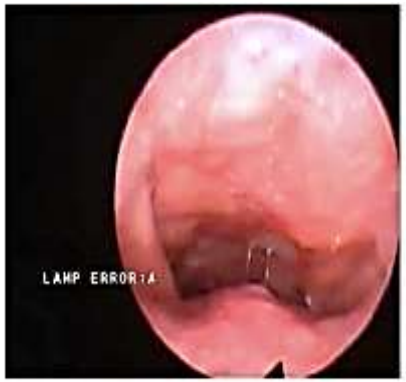
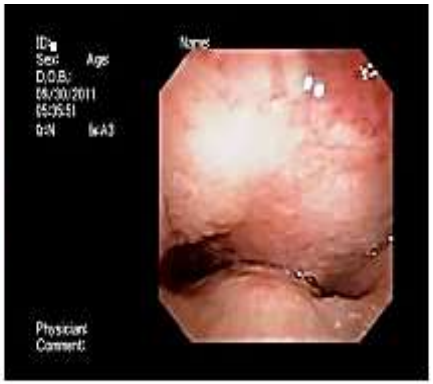
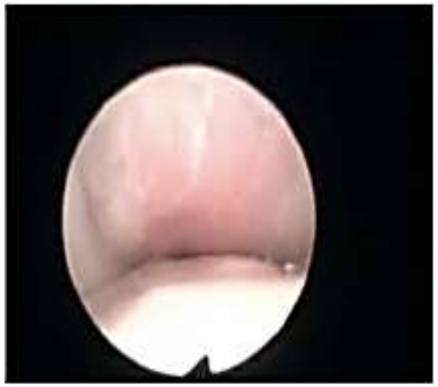


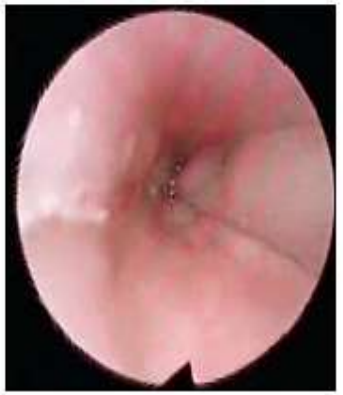
B



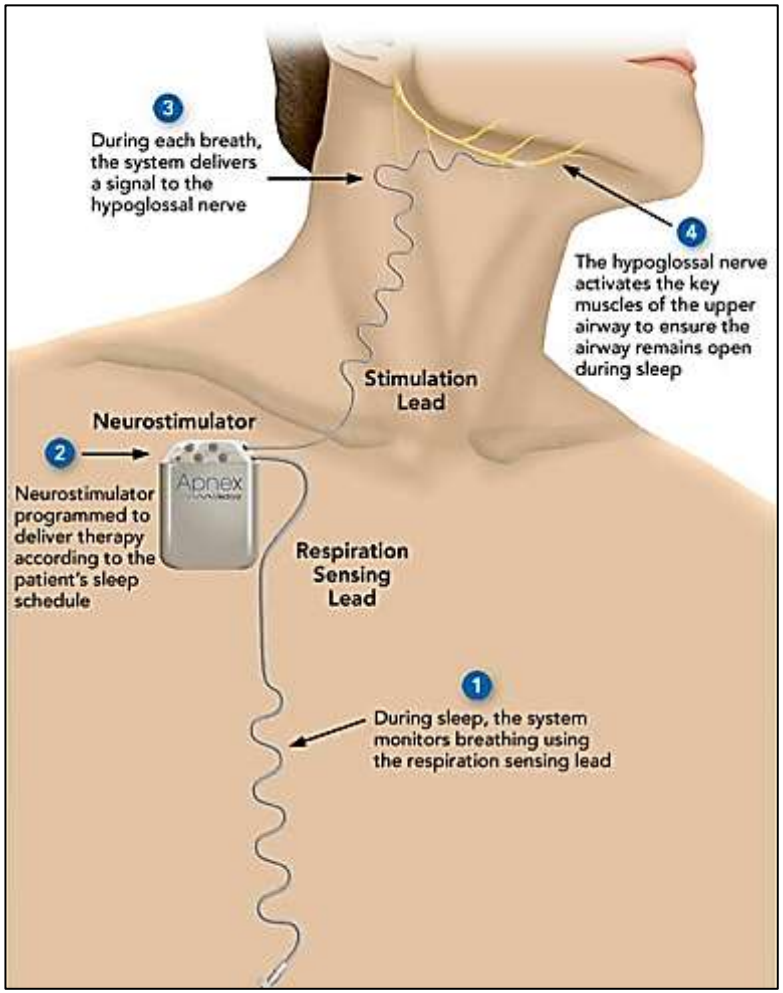
C



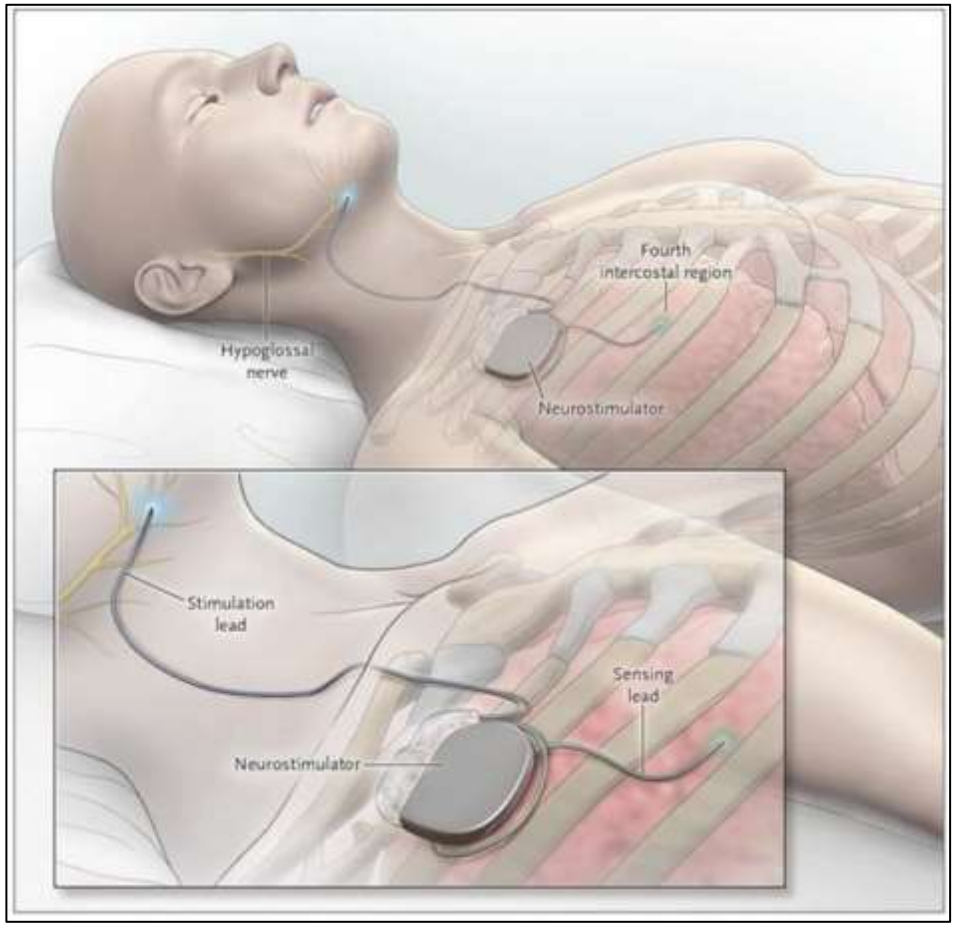
D



Hypoglossal Nerve Stimulation Devices



Kezirian E et al.J Sleep Res 2014;23:77-83



Strollo P et al. NEJM 2014;370:139-149

STAR Trial Study Design

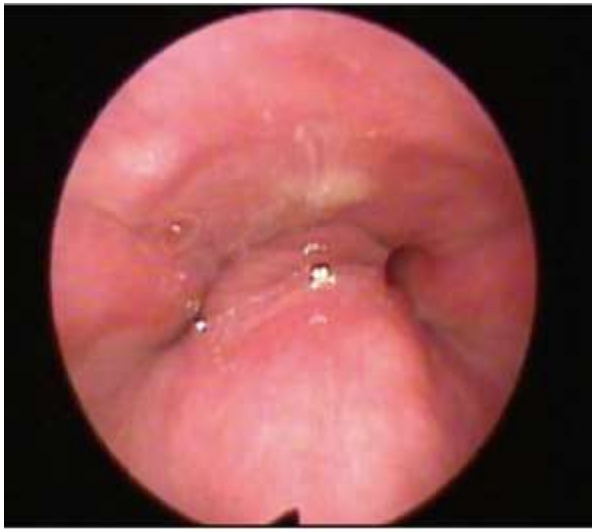
- Multicenter (22), prospective, single group design with participants serving as their own controls
- Inclusion Criteria
  - Moderate to severe OSA intolerant to CPAP
- Exclusion Criteria
  - BMI > 32 kg/m^2
  - AHI < 20 or > 50 events
  - Central or mixed apneas > 25% of the AHI on PSG
  - Neuromuscular disease, severe obstructive or restrictive lung disease, moderate to severe pulmonary HTN, NYHA class 3 or 4 CHF, recent AMI, uncontrolled HTN, acute psychiatric disease, tonsillar hypertrophy, concentric pharyngeal collapse on DISE

Strollo P et al. NEJM 2014;370:139-149

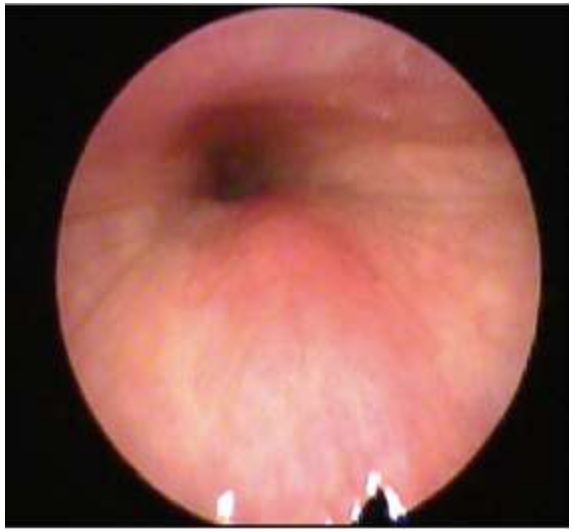
Drug Induced Sedated Endoscopy (DISE)

- Initially described by Croft and Pringle in 1991
- Goal: Examination of the upper airway under conditions that are similar to sleep state
- Generally safe and well tolerated

AP Collapse



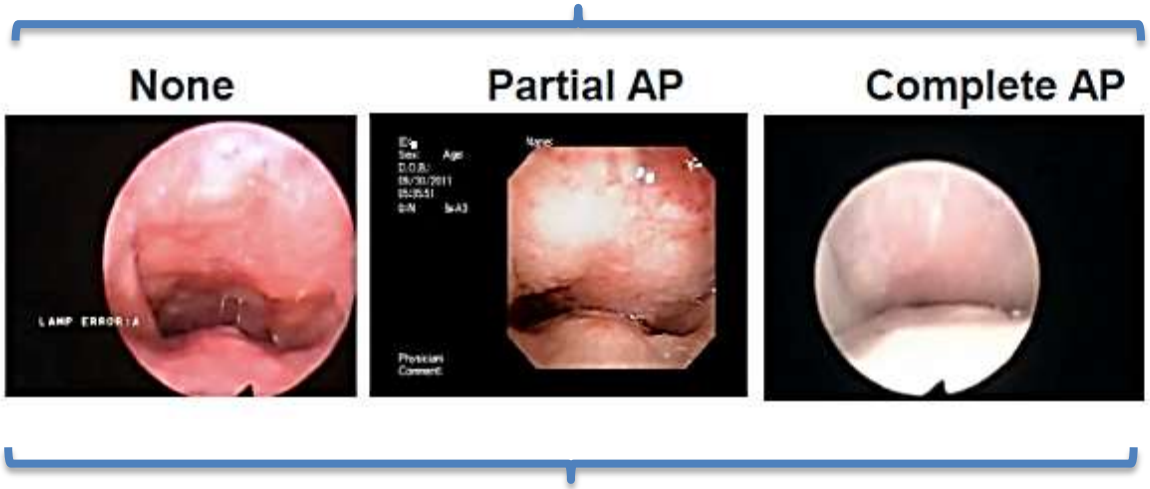
Concentric Collapse



Vanderveken O et al. J Clin Sleep Med 2013;9: 433- 438

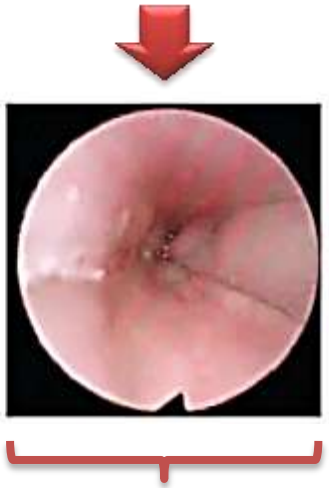
Complete Concentric Collapse on DISE is a Contraindication to HGNS Therapy

Spectrum of AP Collapse



Potential Candidates for Procedure

Concentric Collapse



Contraindication for Procedure

Credit: Ryan Soose, MD UPMC

Hypoglossal Nerve Stimulation Treatment for OSA

- Inspire device is FDA approved for patients with moderate to severe OSA who fail or can't tolerate CPAP therapy
- Exclusions:
  - BMI > 32 kg/m^2, AHI < 20 or > 50, central apneas, concentric upper airway collapse on DISE
- Current supporting data:
  - Overweight and mildly obese (BMI $\leq$ 32 kg/m^2) patients with moderate to severe OSA who are CPAP intolerant
  - Improved OSA, daytime sleepiness and QOL
    - Mean 68% reduction in AHI over a year (AHI 29.3 to 9)
  - Low complication rate: < 2%
  - Appears to be a viable long-term treatment option based on 3 year follow up data
- Up to 33% may not respond to therapy
  - Though more recent data suggest improved outcomes as surgical technique evolves
- Role in the routine management of OSA yet to be determined
  - Cost will continue to be the major barrier

Strollo P et al. NEJM 2014;370:139-149

Central Sleep Apnea Syndromes:(ICSD 3)

- Central Sleep Apnea with Cheyne Stokes Breathing
- Central Sleep Apnea due to Medical Condition without Cheyne Stokes
- Central Sleep Apnea due to High Altitude Periodic Breathing
- Central Sleep Apnea due to Medication or Substance
- Primary Central Sleep Apnea
- Primary Sleep Apnea of Infancy
- Primary Central Sleep Apnea of Prematurity
- Treatment Emergent Central Sleep Apnea

Question

The chemoreceptors for oxygen are located in which one of the following structures?

A) Pons
B) Carotid body
C) Medulla
D) Right atrium

Answer

The chemoreceptors for oxygen are located in which one of the following structures?

A) Pons

B) Carotid body

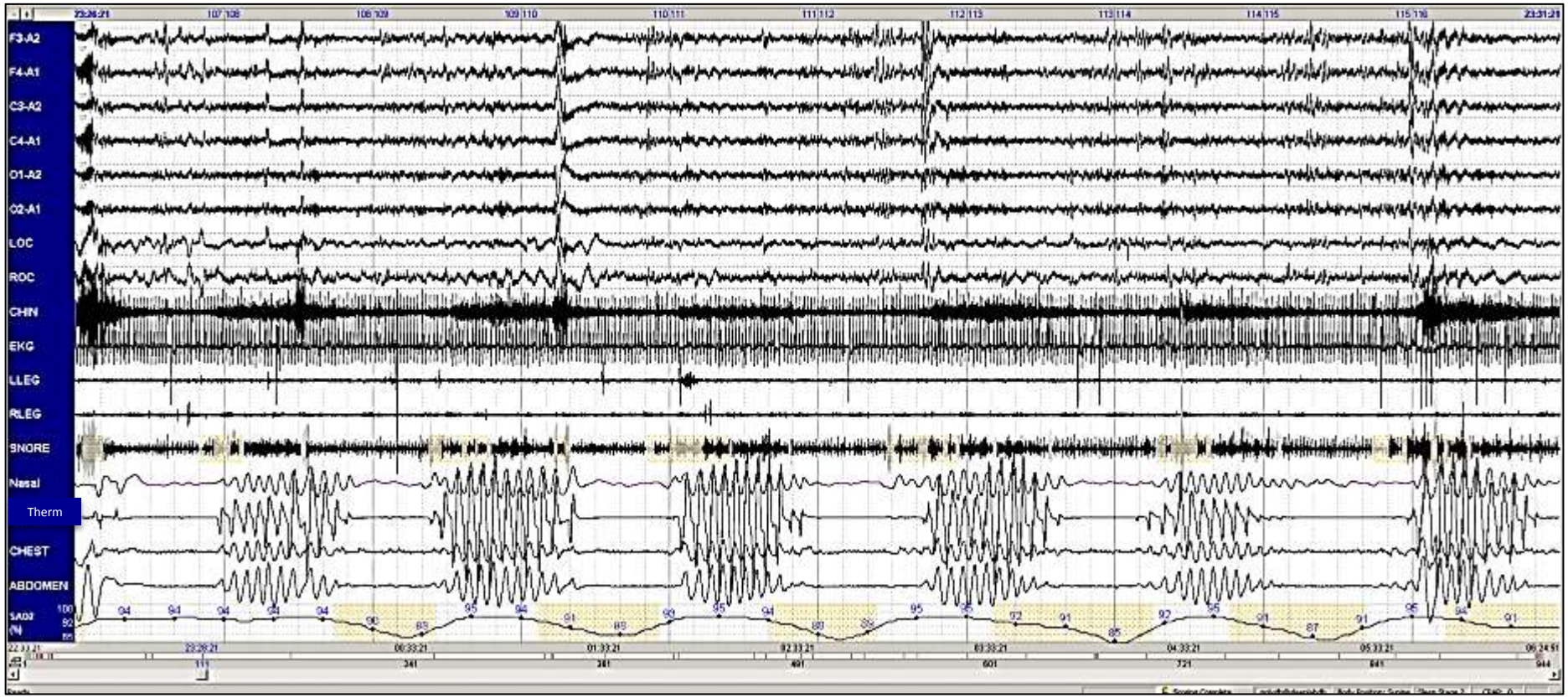
C) Medulla

D) Right atrium

Control of Breathing During Sleep

	Things to Know for the Boards
NREM Sleep	• Under metabolic control • Regular rate and rhythm • Reduced response to CO_2 and O_2
REM Sleep	• Less dependent on metabolic drive • Regular respiration during tonic REM • Irregular respiration during phasic REM • Further reduced response to CO_2 and O_2
Chemoreceptors for CO_2	• Centrally located in the brain stem • Modify respiration in response to CO_2 and H^+
Chemoreceptors for O_2	• Carotid and aortic bodies
Brain Control of Breathing	• Pons and Medulla

The following breathing pattern is associated with which one of the following?



Question

The previous breathing pattern is associated with which of the following?

A) Typical cycle duration of 15 to 30 seconds

B) Female gender

C) Waking hypercapnea

D) Increased chemoreceptor responsiveness to CO_2

Answer

The previous breathing pattern is associated with which of the following?

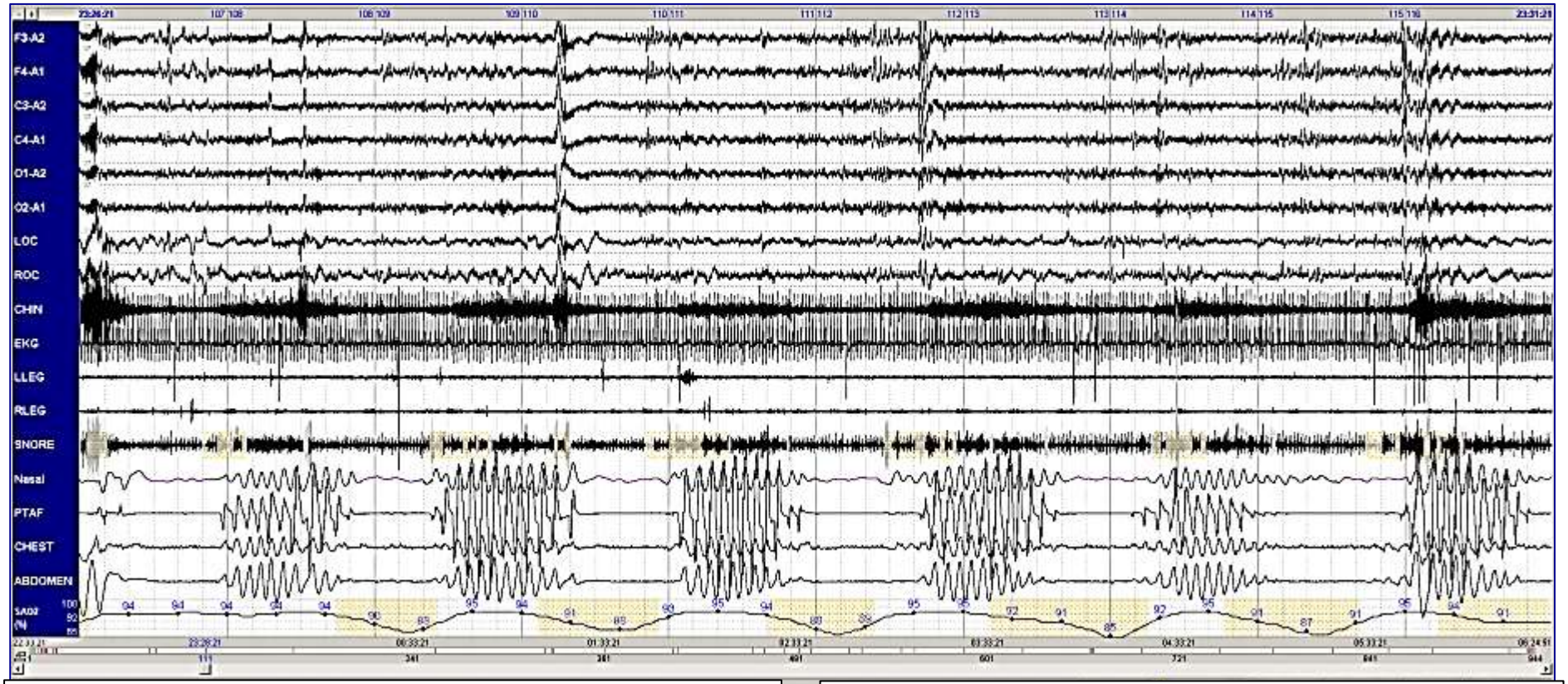
A) Typical cycle duration of 15 to 30 seconds

B) Female gender

C) Waking hypercapnea

D) Increased chemoreceptor responsiveness to CO_2

Cheyne Stokes CSA



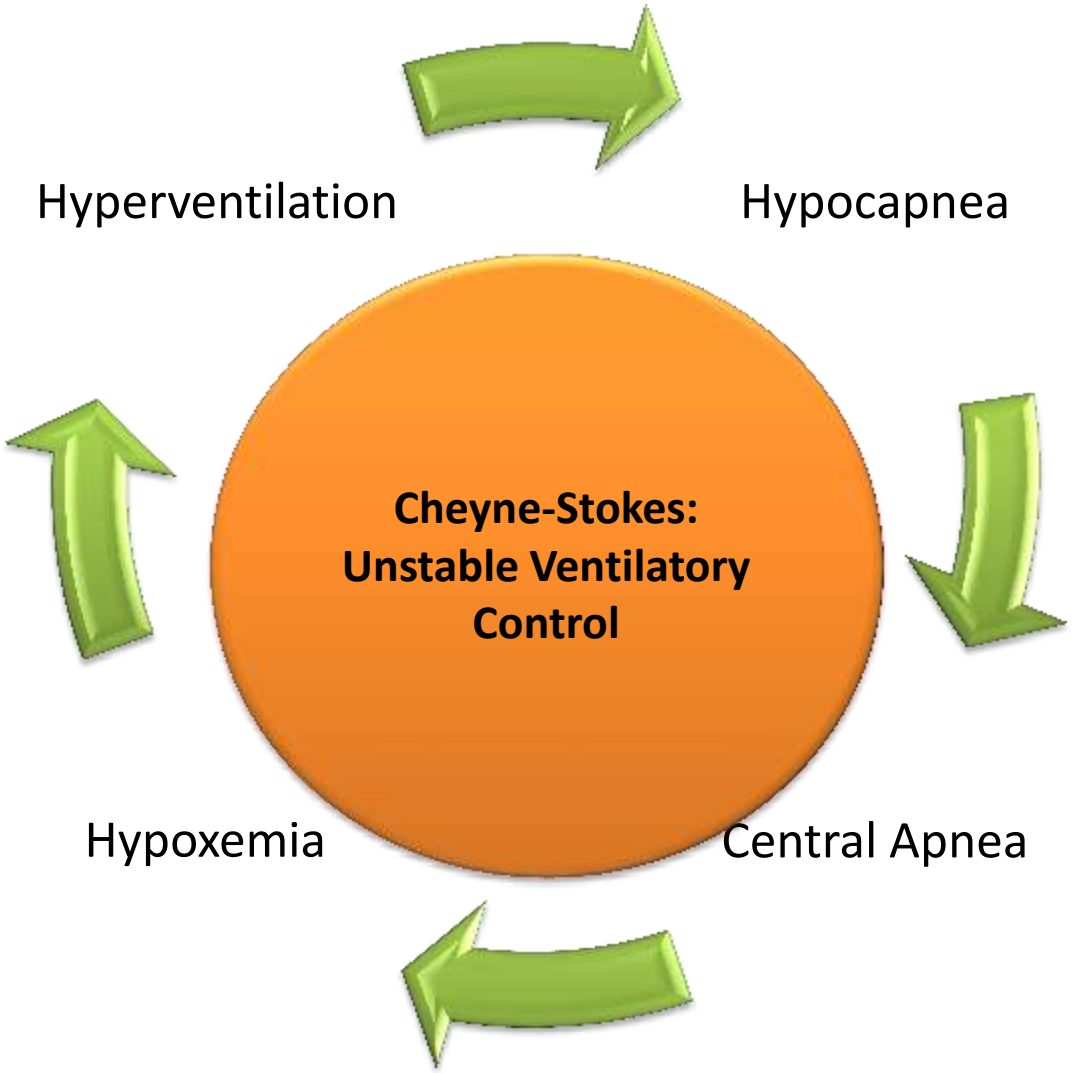
- Crescendo decrescendo pattern
- Cycle duration:
  - –Typically 60-90 secs
  - –Proportional to circulation time
  - –Inversely proportional to LVEF

- More common in stages 1 and 2 sleep
  - -Absent in REM sleep
- Arousal during hyperpnea
  - –Typically during the peak of hyperpnea
- Delayed oxygen desaturation

Risk Factors for the Cheyne Stokes Breathing Pattern in CHF

- Male
- Age > 60
- Hypocapnea during wakefulness
- Atrial fibrillation

Increased Chemoreceptor Responsiveness to CO2



High Ventilatory Drive

Increased Circulatory Time

Low Oxygen Stores\Pulmonary Edema

Cheyne Stoke Breathing Pattern

- Mechanisms: High Loop Gain!
  - Increased chemoreceptor responsiveness to CO2
  - Increased ventilatory drive
  - Increased circulatory time
  - Decreased oxygen stores
- Results:
  - Sleep fragmentation = EDS
  - Sympathetic activation

Question

Which one of the following patients has the lowest left ventricular ejection fraction (LVEF)?

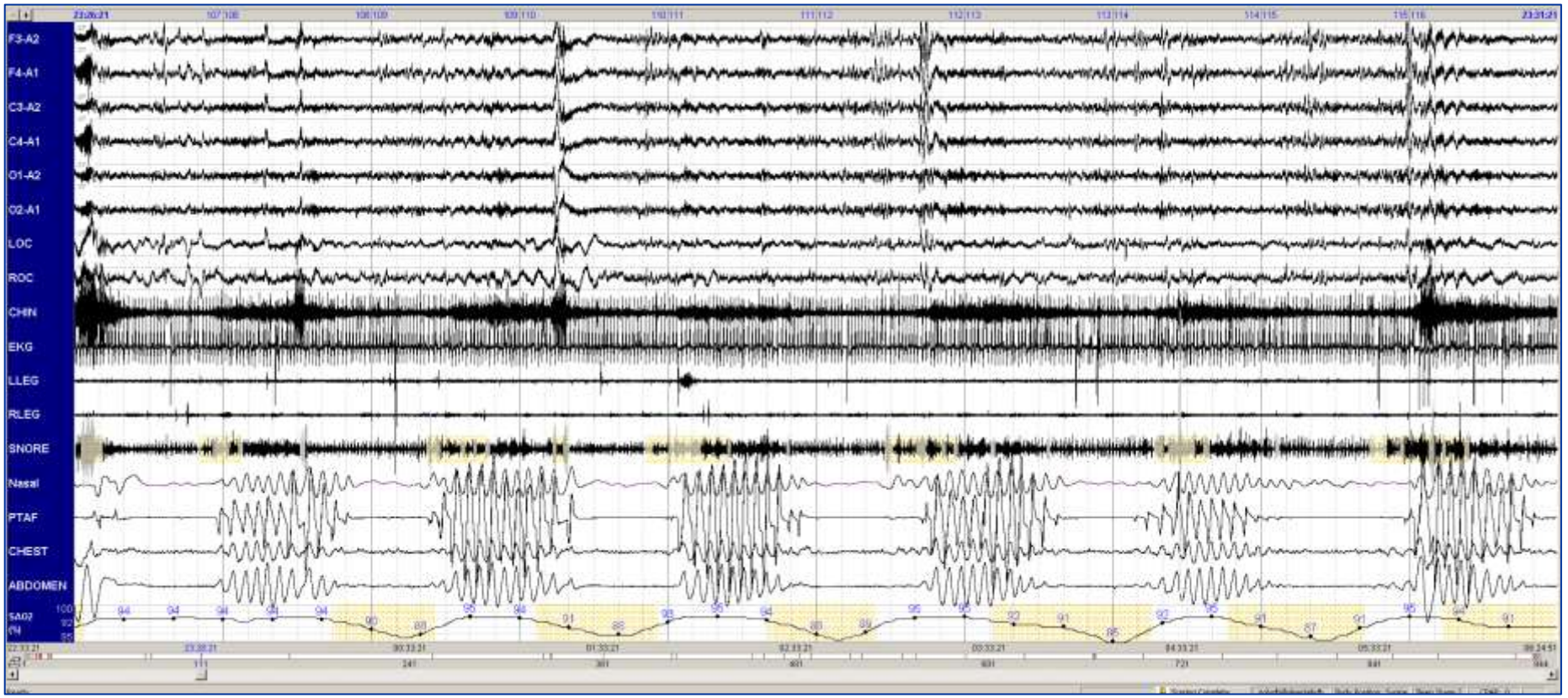
A) A

B) B

C) C

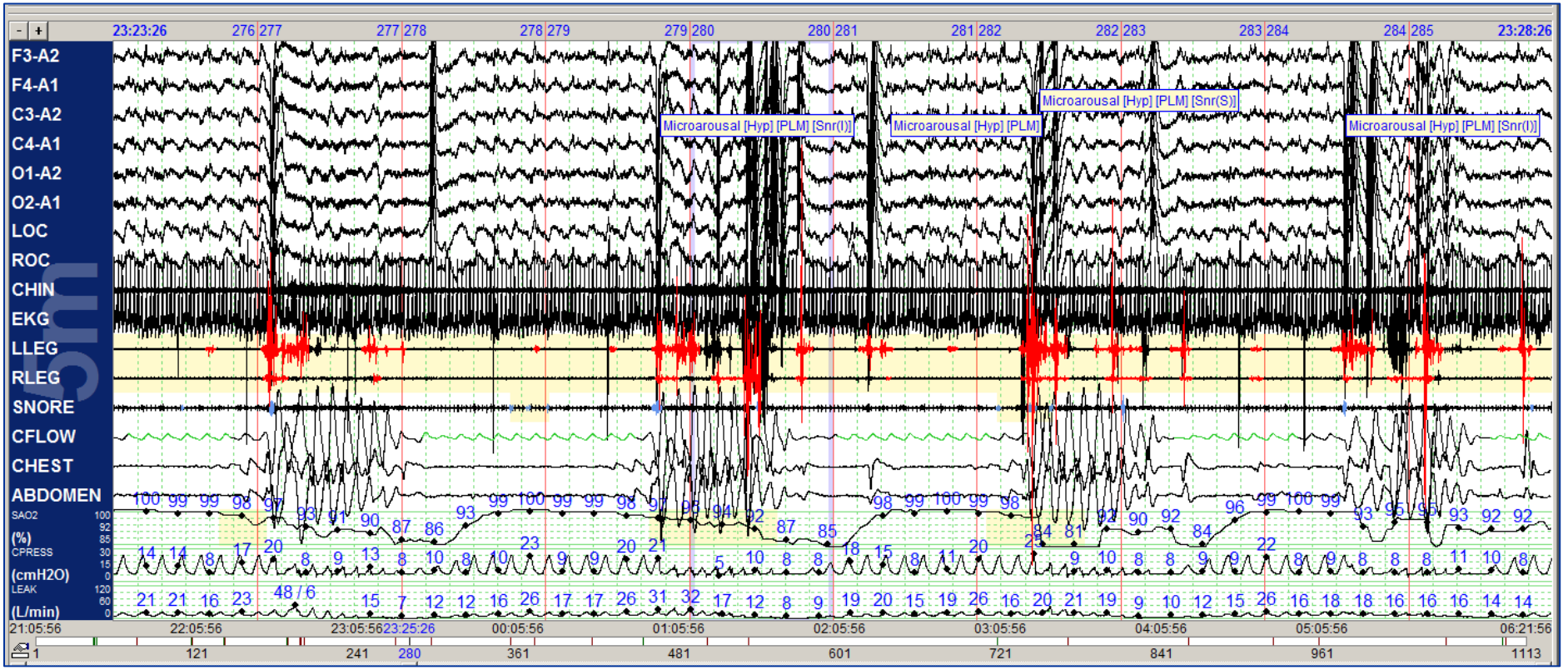
D) D

Patient A



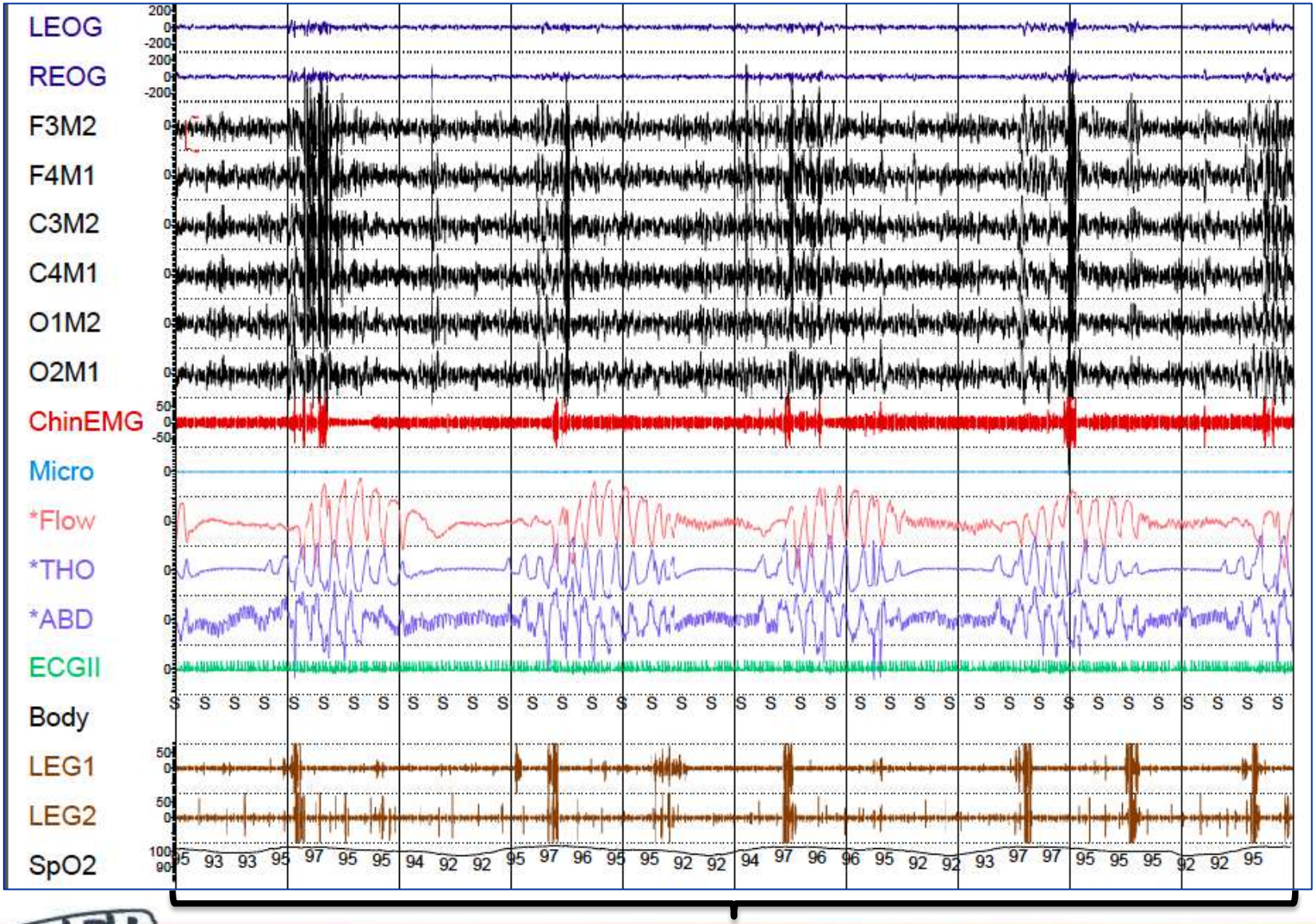
5 Minute Epoch

Patient B

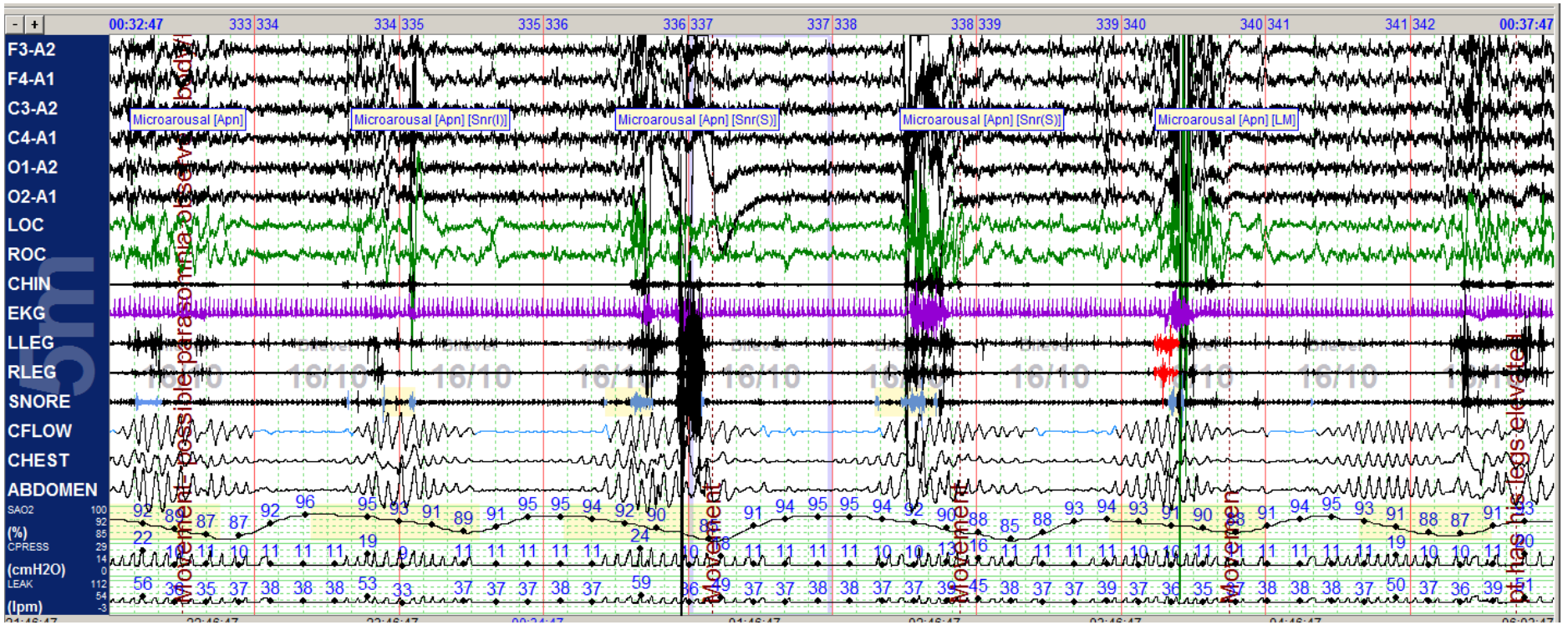


5 Minute Epoch

Patient C



Patient D



5 Minute Epoch

Question

Which one of the previous patients has the lowest left ventricular ejection fraction (LVEF)?

A) A

B) B

C) C

D) D

Answer

Which one of the following patients has the lowest left ventricular ejection fraction (LVEF)?

A) A

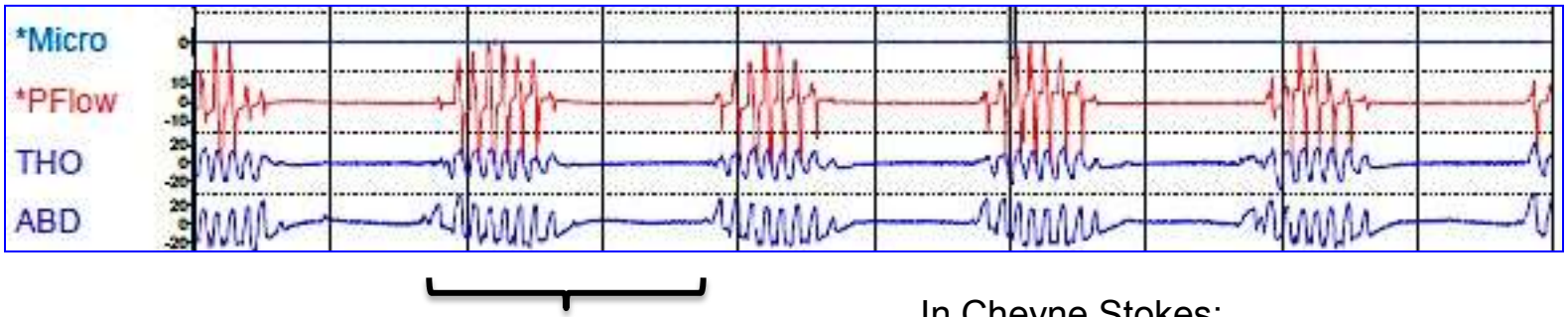
B) B

C) C

D) D

CSA Cycle Length

30 Second Epoch



Cycle Length:
Beginning of an event
to the end of the event

In Cheyne Stokes:

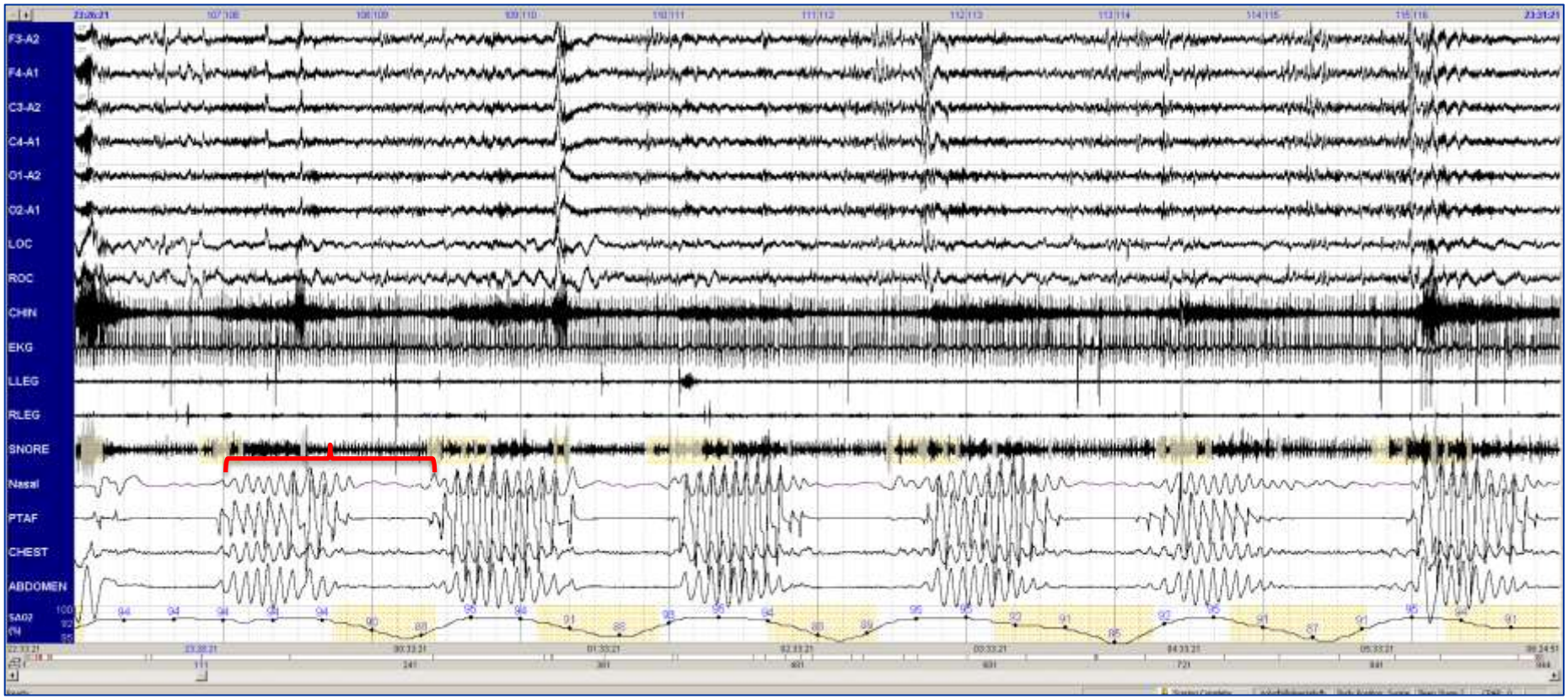
- Typically longer than other CSA syndromes
- Typically 45 to 90 seconds
- Inversely proportional to systolic function (LVEF)
- Proportional to circulation time

Table 9—Variation in cycle length in Cheyne-Stokes breathing with different severities of heart failure

	LVEF (%)				
	> 50	40-49	30-39	20-29	< 20
Cycle length	49.1 ± 17.4	58.9 ± 13.4	60.5 ± 10.5	73.9 ± 16.2	85.7 ± 23.1

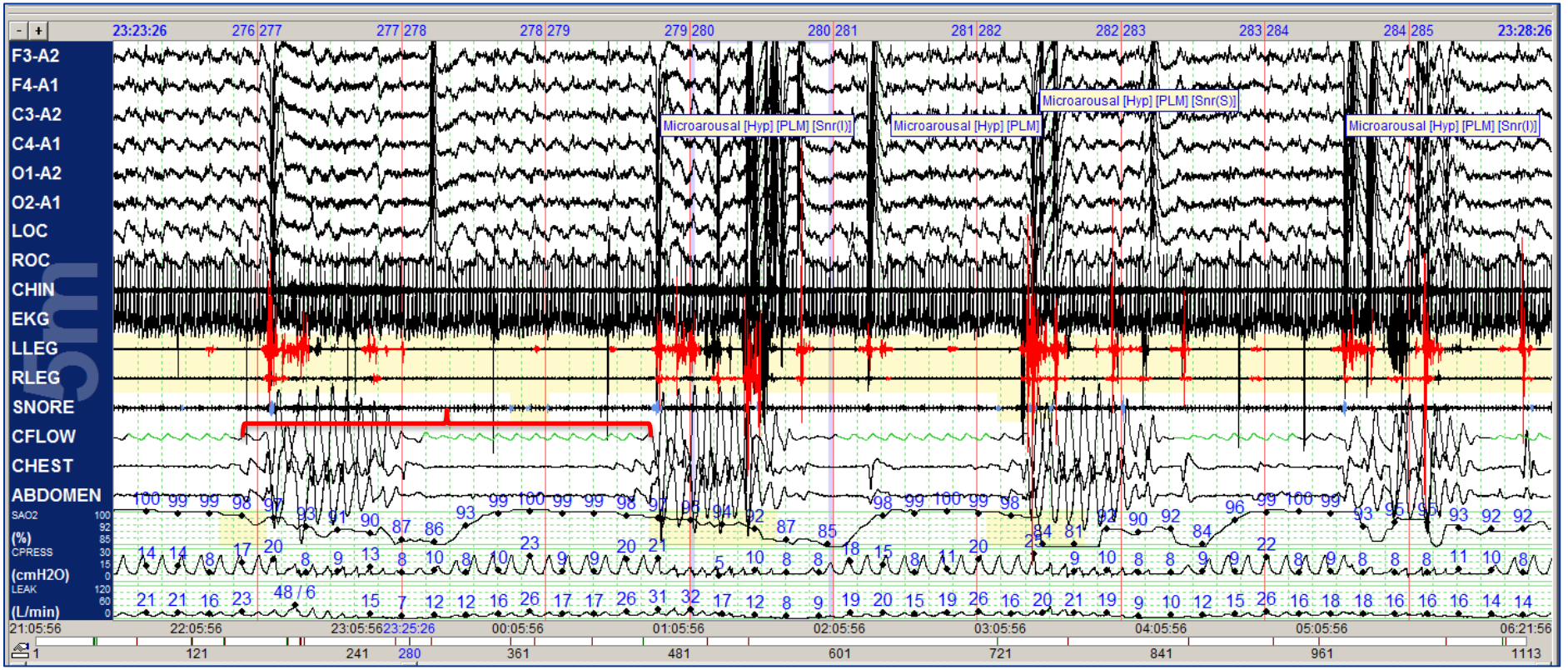
Data from Wedewardt et al.[106] Values are Mean ± SD in seconds. LVEF, left ventricular ejection fraction; SD, standard deviation.

Patient A: Cycle Length ≈ 45 Seconds



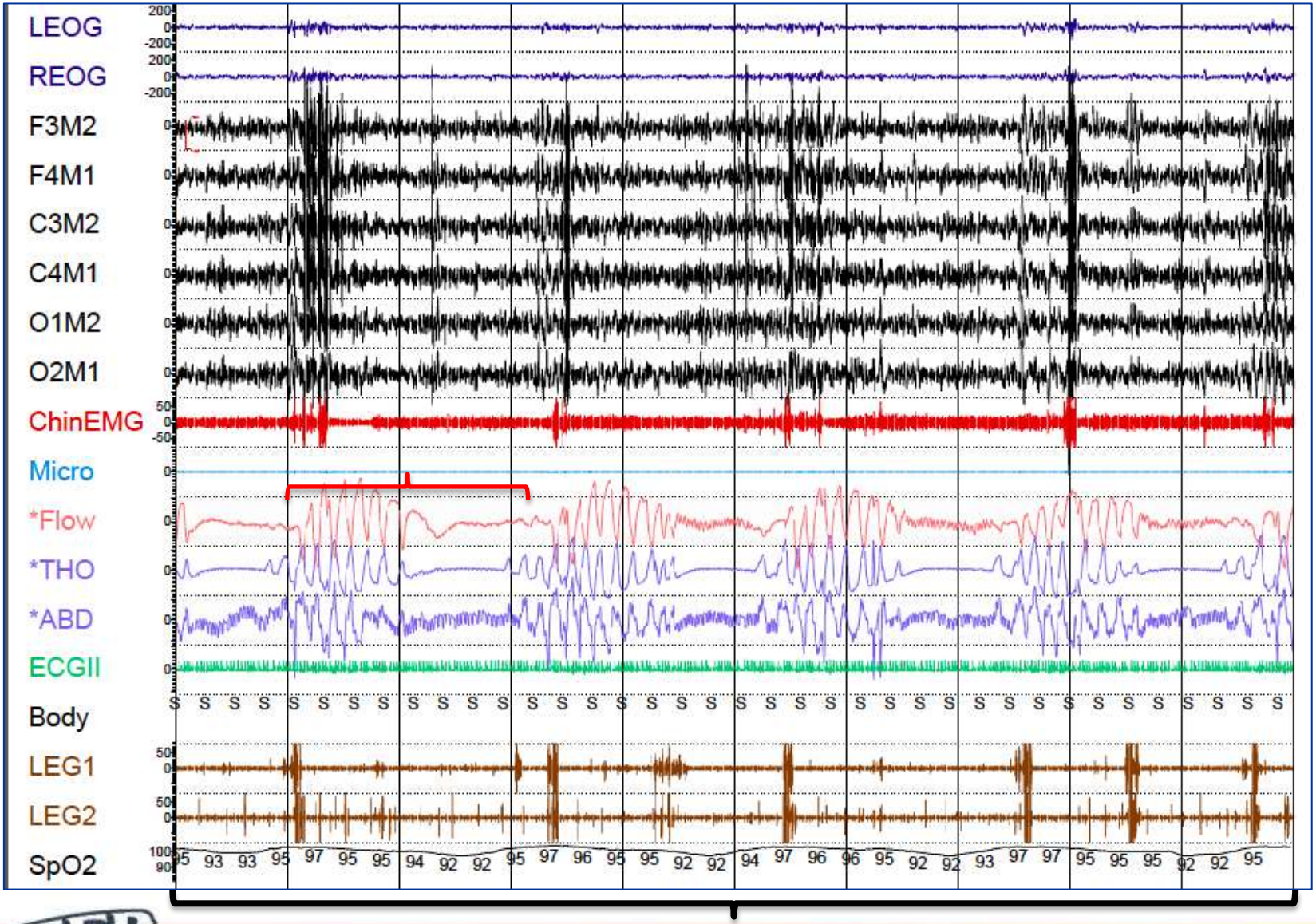
5 Minute Epoch

Patient B: Cycle Length ≈ 85 Seconds

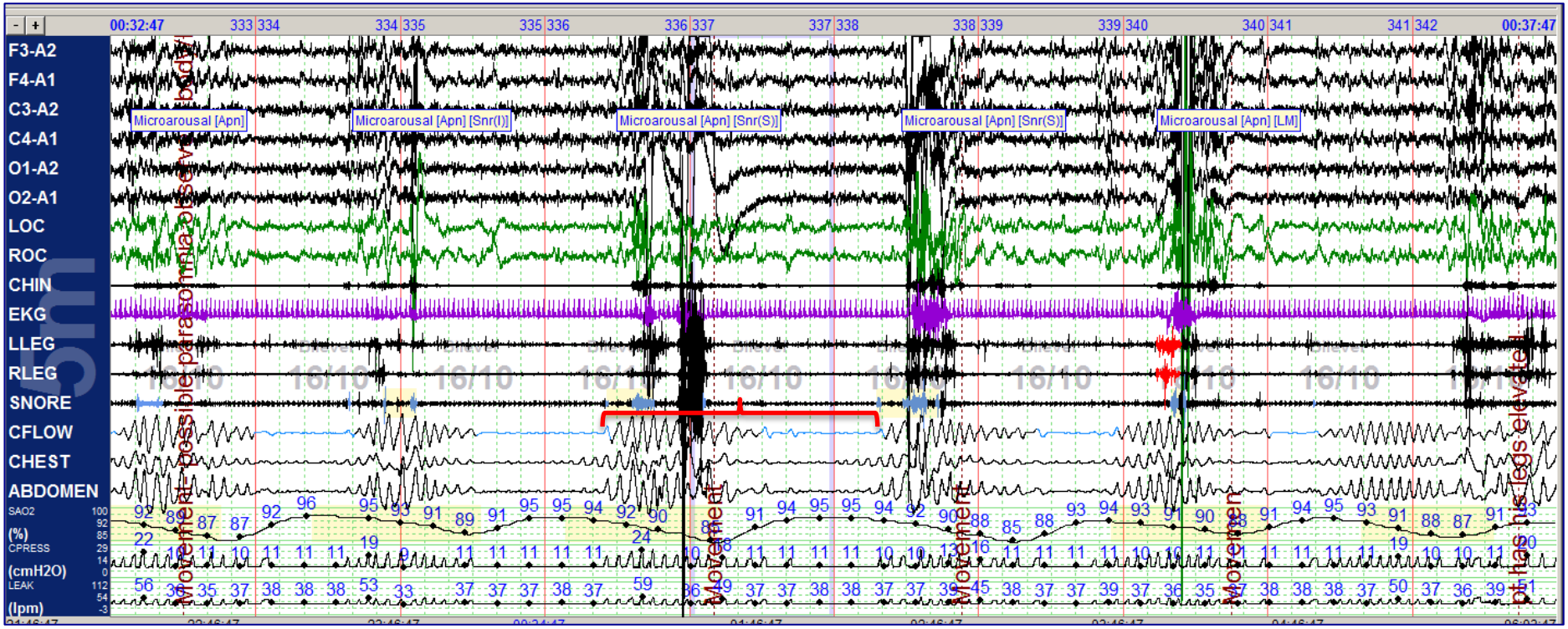


5 Minute Epoch

Patient B: Cycle Length ≈ 65 Seconds



Patient D: Cycle Length ≈ 50 Seconds

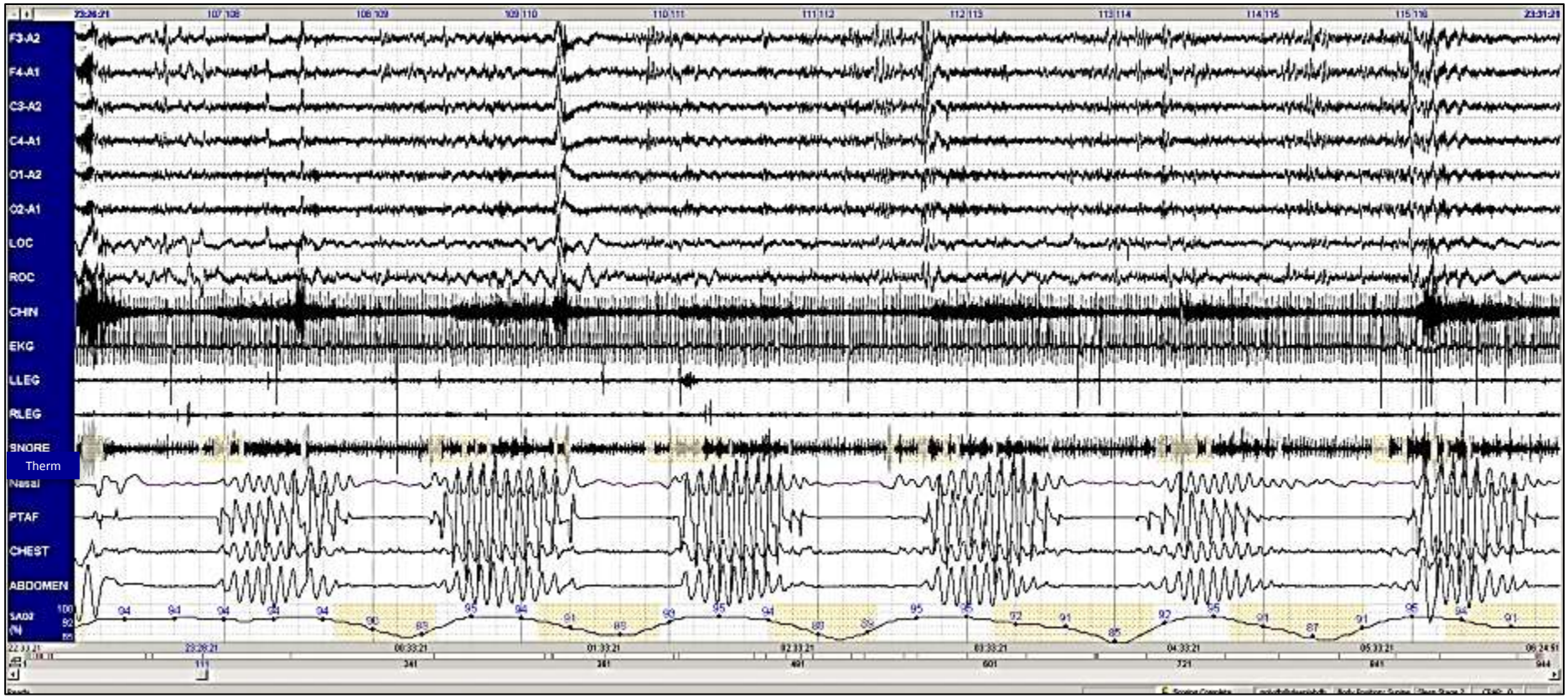


5 Minute Epoch

Case

- A 55 year old male with a history of CHF (EF 35%) presents with symptoms of frequent awakenings and daytime sleepiness.
- His wife notes intermittent snoring and periods of apnea.
- Medications: Carvedilol, furosemide, digoxin, potassium
- Exam: No distress, mallampati score of 3, lungs clear and 1+ bilateral LE edema
- An overnight attended PSG demonstrated the following:

Main PSG Finding: 5 Minute Epoch



Question

Which of the following would be the best initial treatment for this patient?

A) CPAP

B) Oxygen

C) Adaptive servo ventilation (ASV) Bilevel

D) Ace inhibitor

E) AutoCPAP

Answer

Which of the following would be the best initial treatment for this patient?

A) CPAP

B) Oxygen

C) Adaptive servo ventilation (ASV) Bilevel

D) Ace inhibitor

E) AutoCPAP

Cheyne Stokes Management in CHF

Maximize Medical Therapy

1) Improves survival
2) Reduces hospitalizations
3) Improves LVEF

The Treatment of CSA Syndromes in Adults: AASM Practice Parameters 2012

- Standards:
  - CPAP therapy targeted to normalize the AHI is indicated for the initial treatment of CSAS related to CHF
  - ASV targeted to normalize the AHI is indicated for the treatment of CSAS related to CHF
  - Nocturnal oxygen therapy is indicated for the treatment of CSAS related to CHF
- Options:
  - BPAP in ST mode targeted to normalize the AHI
    - May be considered only if there is no response to adequate trials of CPAP, ASV and oxygen therapies
  - Acetazolamide and theophylline
    - Limited supporting evidence

CANPAP: CPAP Does Not Affect Survival In CHF with Predominantly Central Apneas

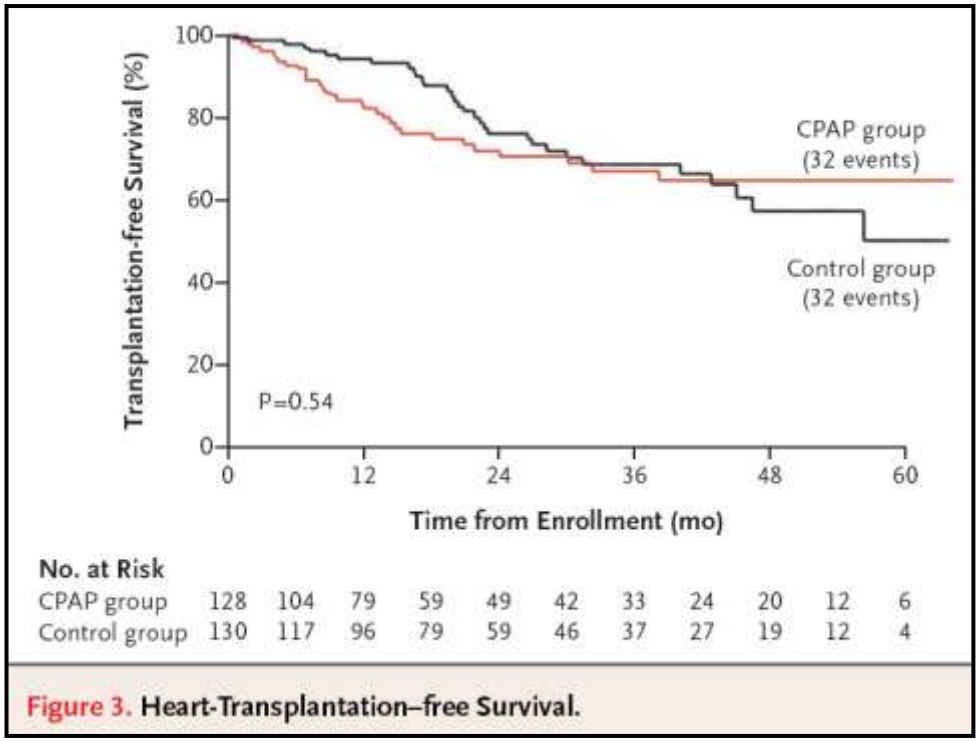


Figure 3. Heart-Transplantation–free Survival.

- Modest Improvements:
  - LVEF (2.2%)
  - Exercise tolerance
  - Catecholamines
- No affect on:
  - Hospitalizations
  - Transplant-free survival
- Limitations
- Post hoc analysis suggested benefits in CPAP responders

Bradley, T et al. NEJM 2005;353:2025-33

Resmed SERVE HF Trial: ASV Contraindicated for CSA with CHF and LVEF ≤ 45%

- RCT to assess the role of ASV combined with medical management vs medical management alone in patients with symptomatic chronic CHF (NYHA class 2-4), LVEF ≤ 45% and predominantly moderate to severe CSA (AHI > 15)
- Results:
  - No change in unplanned hospitalizations
  - Increased all-cause-mortality in the ASV group
    - Relative 28% increase per year in the ASV
  - Increased cardiovascular mortality in the ASV group:
    - Absolute 2.5% increase per year in ASV group (7.5% vs 10%)
    - Relative 34% increase per year in ASV group
- Conclusions and recommendations:
  - ASV offers no meaningful benefits and is contraindicated in this group of patients

Cowie M et al. N Engl J Med 2015; 373:1095-1105

SPECIAL ARTICLES

Updated Adaptive Servo-Ventilation Recommendations for the 2012 AASM Guideline: "The Treatment of Central Sleep Apnea Syndromes in Adults: Practice Parameters with an Evidence-Based Literature Review and Meta-Analyses"

R. Nisha Aurora, MD, MHS[1]; Sabin R. Bista, MD[2]; Kenneth R. Casey, MD, MPH[3]; Susmita Chowdhuri, MD[4]; David A. Kristo, MD[5]; Jorge M. Mallea, MD[6]; Kannan Ramar, MD[7]; James A. Rowley, MD[8]; Rochelle S. Zak, MD[9]; Jonathan L. Heald, MA[10]

- **Standard** level recommendation against the use of use of ASV to treat CHF-associated CSAS in patients with an LVEF of ≤ 45% and moderate or severe CSAS

- **Option** level recommendation for the use of ASV in the treatment CHF-associated CSAS in patients with an LVEF > 45% or mild CHF-related CSAS

N Aurora et al. J Clin Sleep Med 2016;12(5):757–761.

Other Attempted Treatments for CSA in CHF

- Oxygen
  - May decrease AHI and improve oxygen sats
  - High levels (100%) may worsen CHF
  - No long term follow data to prove efficacy on important outcomes
- Inhaled CO_2
  - Findings inconsistent
- Theophylline
  - Short term studies show decrease in AHI
- Cardiac pacing
  - Atrial pacing not effective
  - Cardiac resynchronization therapy (CRT)
- Phrenic nerve pacing
  - May reduce AHI, though significant residual AHI
  - More data required, not FDA approved
- Transplant
  - Improves CSR, but may be delayed

APAP Not Indicated for Central Apneas of Any Type

- APAP only indicated for:
  - Uncomplicated moderate to severe OSA
- Not indicated for:
  - CHF
  - Hypoventilation
  - COPD
  - Obesity hypoventilation
  - Non-snorers (s/p UPPP)

Morganthaler, TI et al. Sleep 2008;31:141-47

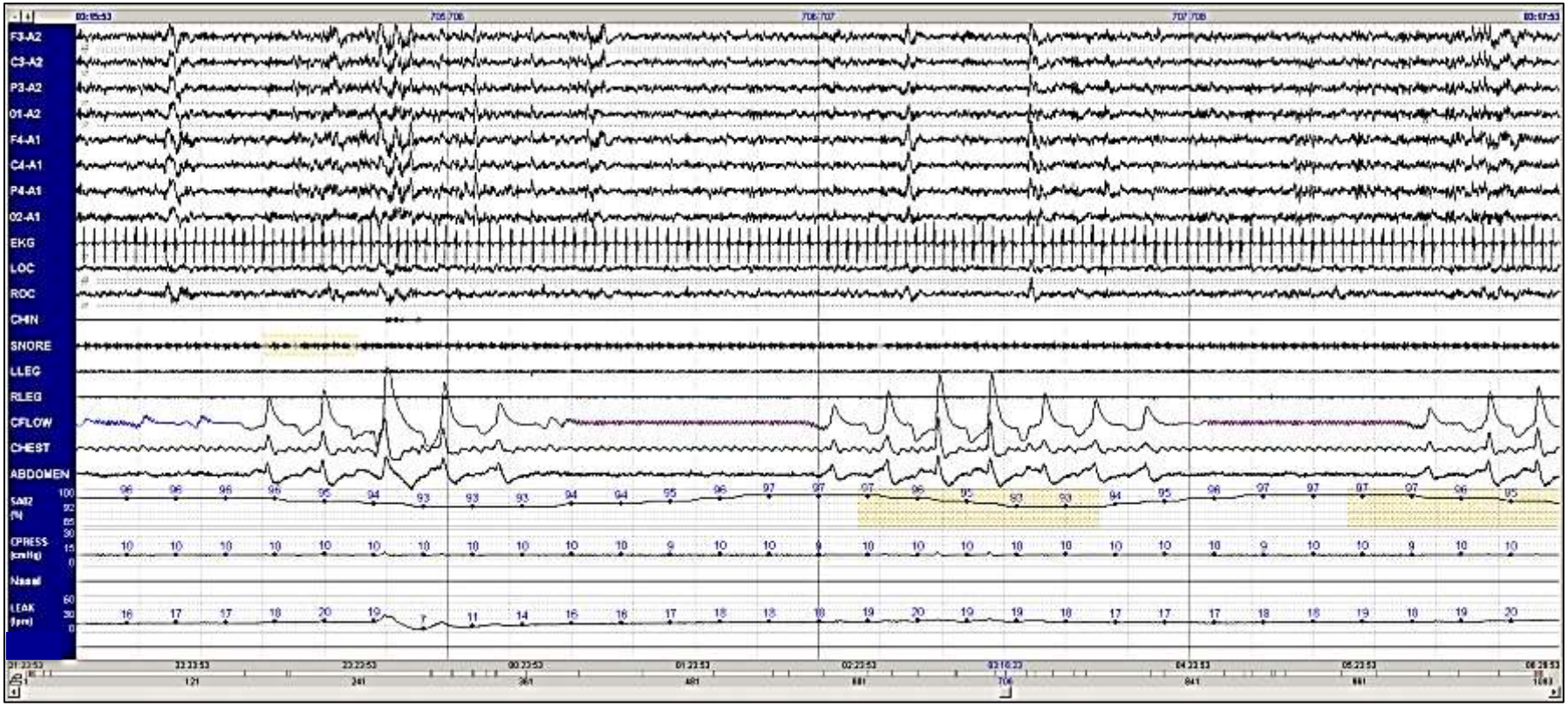
The Bottom Line: Cheyne Stokes CSA

- Characteristics:
  - Cycle length:
    - Typically 60 to 90 secs
    - Proportional to circulation time
    - Inversely proportional to LVEF
  - Arousal during hyperpnea
  - Delayed desaturation
  - Common in NREM and resolves in REM sleep
- Mechanisms: High Loop Gain!
  - Increased chemoreceptor responsiveness to CO_2
  - Increased ventilatory drive
  - Delayed circulatory time
- Associated with increased mortality in CHF with systolic dysfunction
- Initially managed with maximized medical therapy
- AASM Practice parameters recommend CPAP and oxygen as treatment options (Standards)
  - Little data to support these therapies in these patients at this time
- ASV therapy contraindicated in patients with CSA and CHF and LVEF < 45%

Case

- 68 year old male presents with snoring, witnessed apneas and daytime sleepiness
- PMHx: HTN, atrial fibrillation, type 2 DM
- Medications: Valsartan, warfarin, metoprolol, metformin
- Aside from obesity, unremarkable exam
- Undergoes an attended split-night PSG which demonstrates severe OSA with an AHI of 42 events per hour and oxygen desaturation to a nadir of 75%
- During the CPAP titration portion of the study, the following is observed:

CPAP PSG Titration Findings



2 Minute Epoch

Question

Obstructive events are resolved in supine REM sleep at a CPAP pressure of 10 cm H_20, but the previous PSG findings persist in NREM sleep. Which one of the following therapies should you recommend for home treatment?

A) APAP 8 to 12 cm H_2O

B) Bilevel PAP IPAP 12 cm H_2O and EPAP 8 cm H_2O

C) CPAP at 10 cm H_2O

D) ASV bilevel PAP therapy

E) I don't know

Answer

Obstructive events are resolved in supine REM sleep at a CPAP pressure of 10 cm H_20, but the previous PSG findings persist in NREM sleep. Which one of the following therapies should you recommend for home treatment?

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C) CPAP at 10 cm H_2O

D) ASV bilevel PAP therapy

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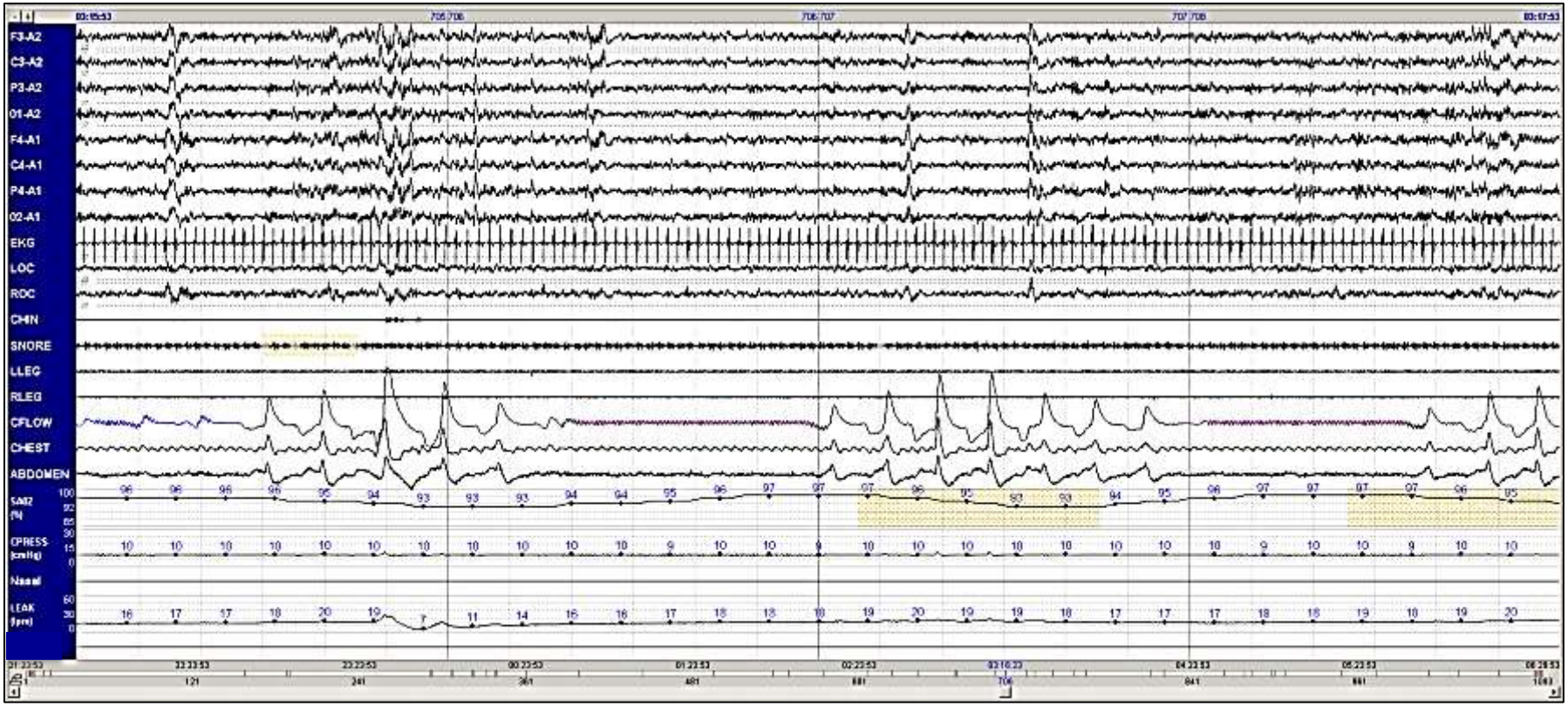
Treatment Emergent Central Sleep Apnea



2 Minute Epoch

Treatment-Emergent Central Sleep Apnea

- ICSD 3 Diagnostic Criteria: Must meet all criteria
  - **A)** Diagnostic PSG shows five or more obstructive respiratory events per hour of sleep
  - **B)** PSG during use of PAP without a backup rate shows significant resolution of obstructive events and emergence or persistence of central apneas or central hypopneas with all of the following:
    - Central apnea-central hypopnea index (CAHI) ≥ 5 /hour
    - Number of central apneas and hypopneas is ≥ 50% of the total number of apneas and hypopneas
  - **C)** Central sleep apnea is not better explained by another CSA disorder
- Alternate name: Complex sleep apnea

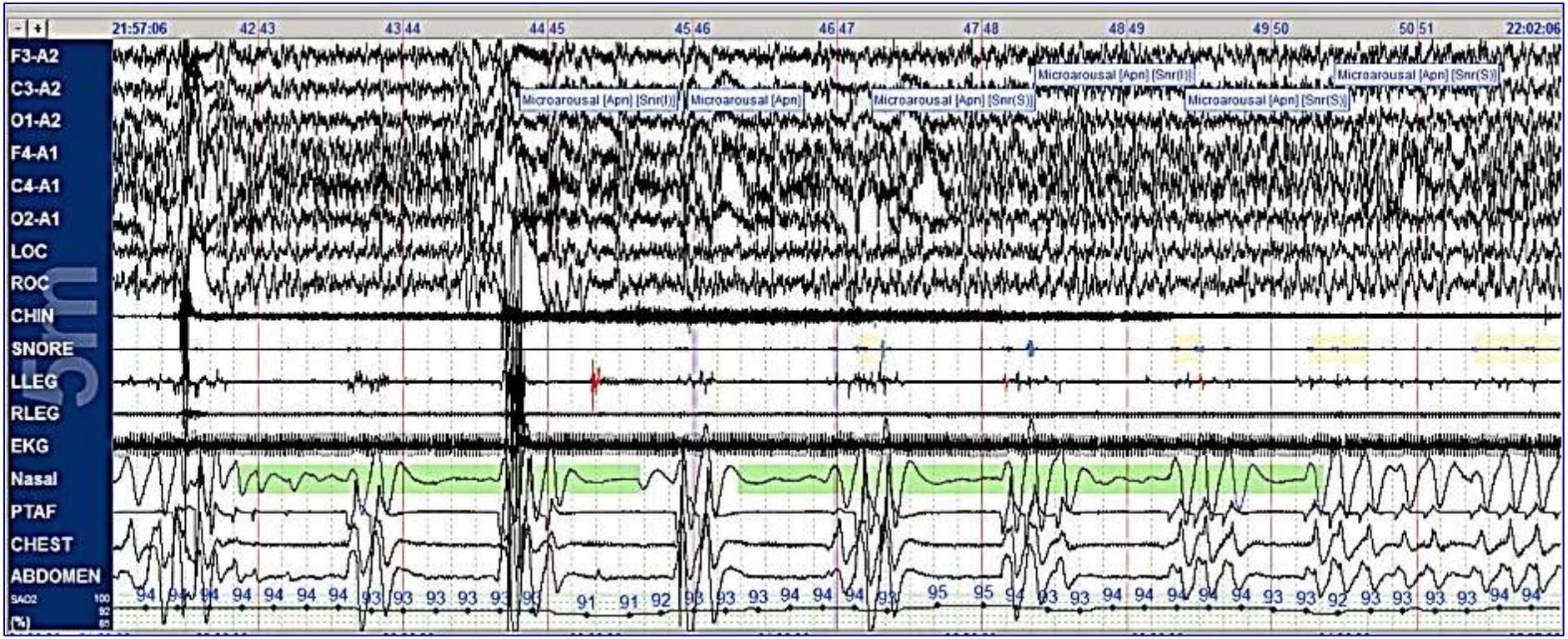
Treatment-Emergent CSA: Summary

- Prevalence 5% to 20%
- Pathophysiology not well defined
- Associated conditions: Severe OSA, opioids, CHF, stroke, NMD
- Note: Not limited to PAP therapy
- Central events may persist on CPAP (AHI > 10) in up to 36%
  - Though most studies suggest central events resolve with time
- ASV bilevel therapy resolves central events and reduces the AHI better than CPAP
- No difference between ASV and CPAP in regards to important outcomes after 3 months of therapy
- Optimal treatment approach and role for ASV bilevel therapy not well defined. Consider a trial of ASV if:
  - Non-adherent to CPAP
  - Remain symptomatic on CPAP
  - Have persistent severe sleep apnea on CPAP

Case

- A 20 year old female presents with fragmented sleep, witnessed apneas and daytime sleepiness.
- She also notes intermittent headaches and neck pain that are precipitated by coughing and sneezing.
- Physical Exam: Normal
- A PSG demonstrates the following

PSG: 5 Minute Epoch



Question

Based on the history and PSG findings, the best initial recommendation would be which one of the following?

A) CPAP

B) ASV bilevel therapy

C) MRI of the brain

D) Lumbar puncture

Answer

Based on the history and PSG findings, the best initial recommendation would be which one of the following?

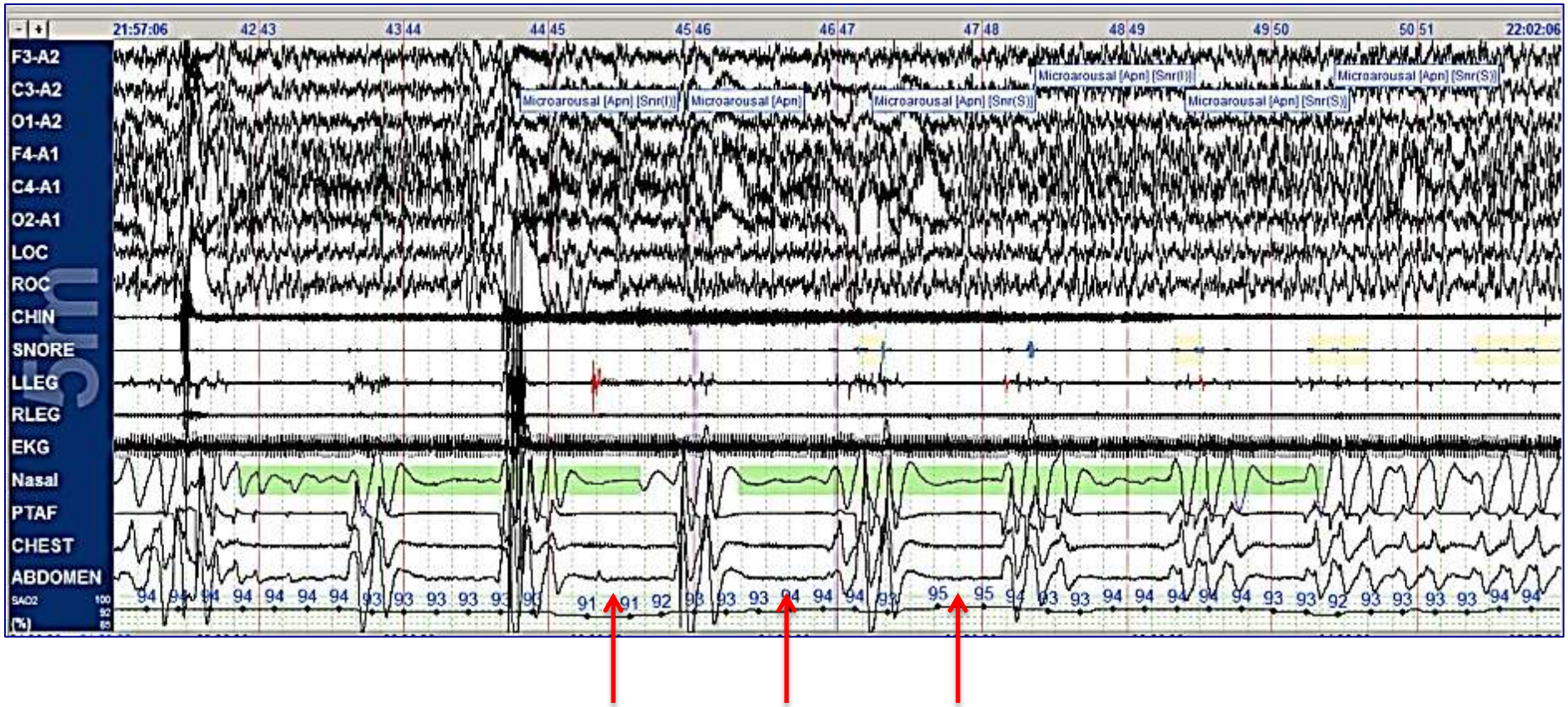
A) CPAP

B) ASV bilevel therapy

C) MRI of the brain

D) Lumbar puncture

PSG: Central Sleep Apnea Without Cheyne Stokes Breathing



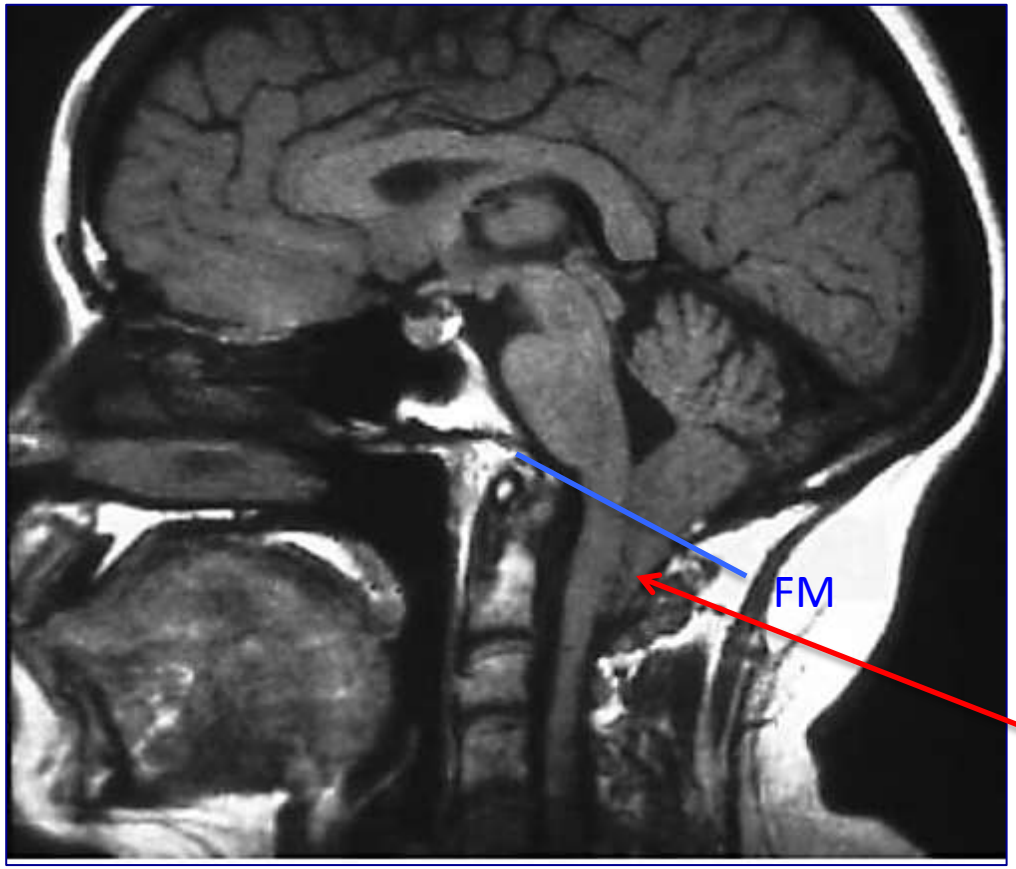
CSA due to a Medical Disorder without Cheyne-Stokes Breathing: ICSD 3 Diagnostic Criteria

- The presence of 1 or more of the following:
  - Sleepiness
  - Difficulty initiating or maintaining sleep, frequent awakenings or nonrestorative sleep
  - Awakening short of breath
  - Snoring
  - Witnessed apneas
- PSG shows CSA fulfilling AASM scoring criteria without evidence of Cheyne Stokes breathing
- Occurs as a consequence of a medical or neurologic disorder but is not due to medication or substance use

CSA due to a Medical Disorder without Cheyne-Stokes Breathing: Common Disorders

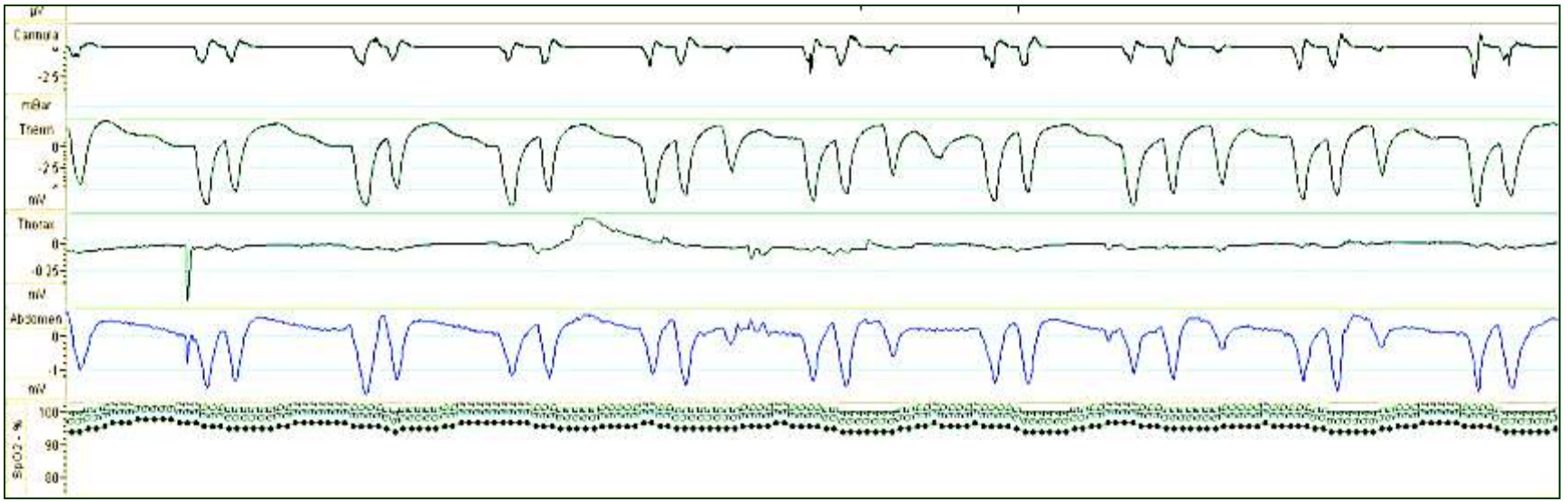
- Chiari 1 malformation
  - Age 20 to 40 presenting with daytime sleepiness and headaches
    - Also: Neck pain, vertigo, unsteady gait, dysphagia, dysphonia
  - PSG demonstrates CSA +/- OSA
    - Can exhibit CSA, OSA and or mixed apneas
  - Diagnosis: Brain MRI
  - Treatment: Base of skull surgery
- Post stroke
  - May resolve or improve over time
- Brain stem damage due to trauma, increased ICP or tumor

Chiari 1 Malformation



- Definition:
  - Abnormally shaped cerebellar tonsils that are displaced below the level of the foramen magnum (FM)
    - (≥ 5 mm below the FM)

Biot's Pattern



- Also referred to as **clustered respiration**:
  - Characterized by groups of quick, shallow inspirations followed by regular or irregular periods of apnea
- Other associations:
  - Brain stem damage due to strokes, trauma or increased ICP

Question

Which one of the following statements regarding high altitude periodic breathing is correct?

A) Occurs predominantly in REM sleep
B) Typical cycle length is > 60 seconds
C) Primary mechanism is hypoxemia
D) CPAP is the best treatment

Answer

Which one of the following statements regarding high altitude periodic breathing is correct?

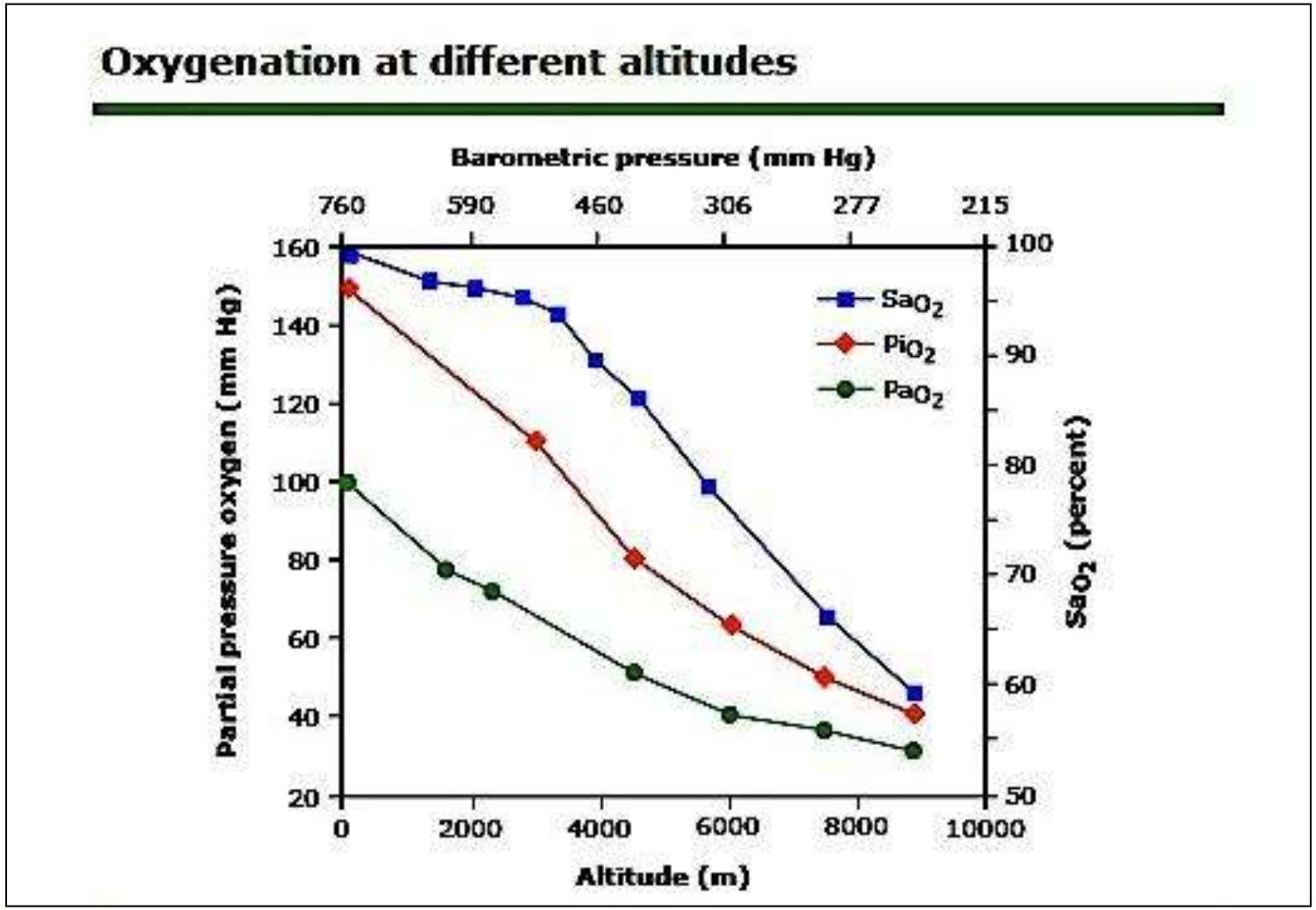
A) Occurs predominantly in REM sleep

B) Typical cycle length is > 60 seconds

C) Primary mechanism is hypoxemia

D) CPAP is the best treatment

CSA due to High Altitude Periodic Breathing



Altitude CSA/Periodic Breathing

- NREM associated CSA
- Associated symptoms required for ICSD 3 diagnosis
- Typically does not occur below 2500 meters
  - Increased prevalence at higher altitudes
  - May occur at lower altitudes with comorbidities
- Mechanism:
  - Hypoxemia
  - More common in patients with enhanced ventilatory responses to hypoxemia
- Shorter cycle duration than Cheyne Stokes
  - Commonly < 40 seconds and typically < 20 seconds
- Treatment:
  - Oxygen
  - Acetazolamide

Central Sleep Apnea: The Bottom Line

- Typically occurs in NREM sleep and resolves in REM sleep
- Clinical significance beyond sleep disruption and associated symptoms not clear
  - Affect on cardiovascular disease or other outcomes not known
- Pathophysiology depends on the CSA syndrome
  - Cheyne Stokes:
    - Increased chemoreceptor responsiveness to CO_2
    - Increased ventilatory drive
    - Delayed signal transport to central CO_2 and peripheral oxygen receptors
  - High altitude CSA
    - Hypoxemia during sleep
  - Medication and medical problem related
    - Altered signal perception and respiratory drive
- Treatment is syndrome dependent
  - Best treatments <u>not</u> clear for most syndromes

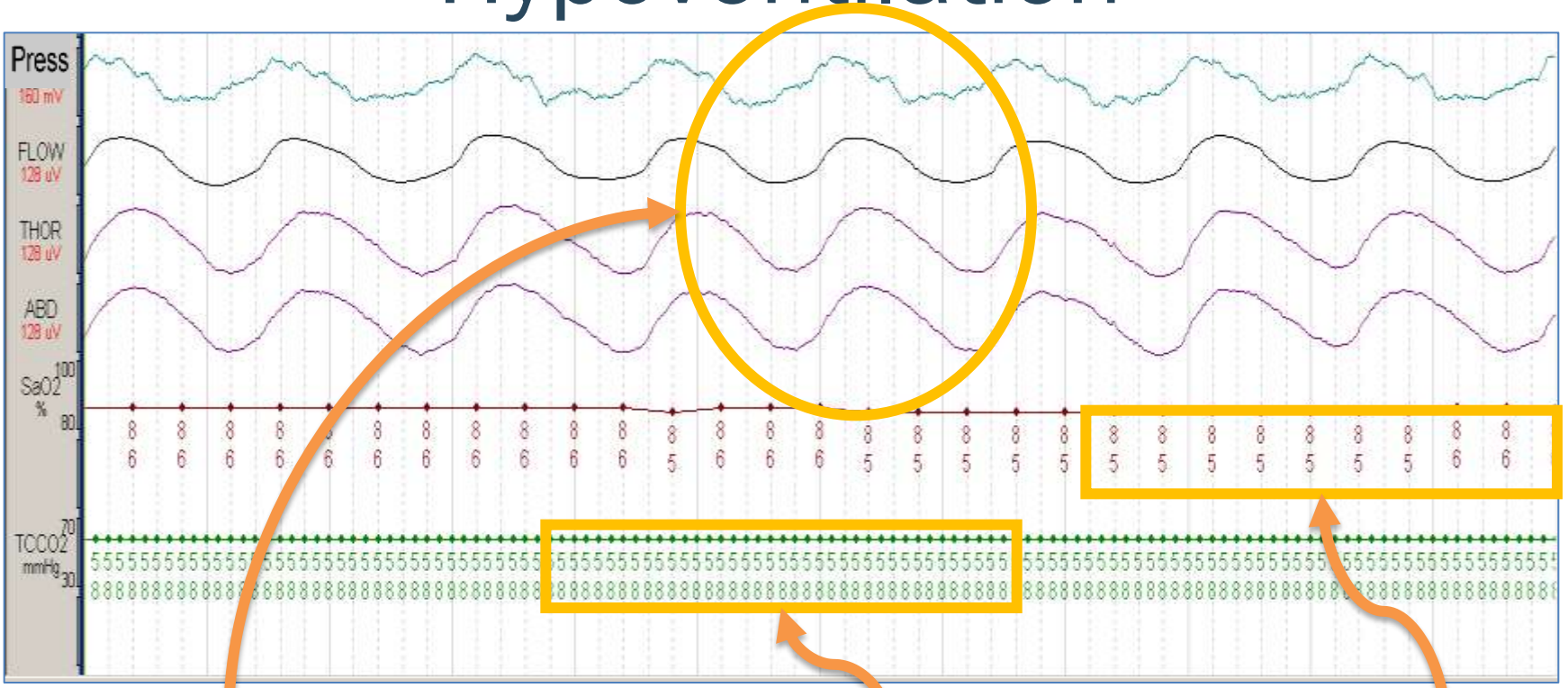
Sleep Related Hypoventilation Disorders: ICSD 3

- Obesity hypoventilation syndrome
- Congenital central alveolar hypoventilation syndrome
- Late-onset central hypoventilation with hypothalamic dysfunction
- Idiopathic central alveolar hypoventilation
- Sleep related hypoventilation due to medication or substance
- Sleep related hypoventilation due to a medical disorder

Hypoventilation: AASM Scoring Manual

- Monitoring hypoventilation is optional
- If monitoring for hypoventilation, recommended monitoring includes:
  - Diagnostic study: Arterial PCO_2, transcutaneous or end-tidal CO_2
  - PAP titration: Arterial PCO_2 or transcutaneous CO_2
  - ****DON'T USE $ETCO_2$ with PAP***
  - Best monitoring device or method ($ETCO_2$, etc..) not clear
- Hypoventilation is scored if either of the following occur:
  - Increase of PCO_2 or surrogate to value > 55 mm Hg for ≥ 10 minutes or
  - Increase of PCO_2 or surrogate during sleep (in comparison to awake supine value) to a value > 50 mm HG for ≥ 10 minutes
- Other things to know:
  - Persistent oxygen desaturation alone is not sufficient
  - Duration of event not defined

Hypoventilation

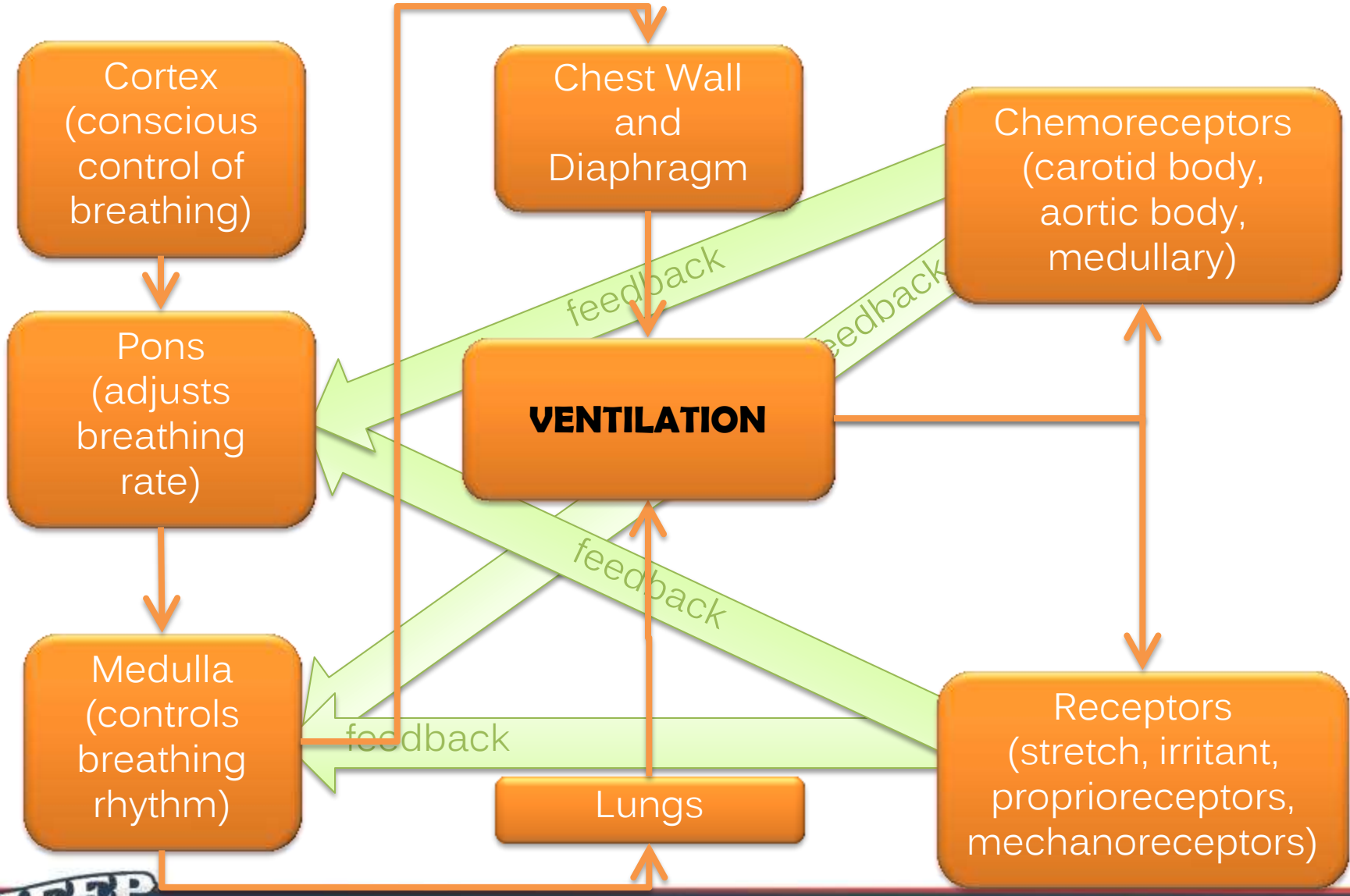


Breathing is regular – no apnea, hypopnea, RERA or flattening of nasal pressure.

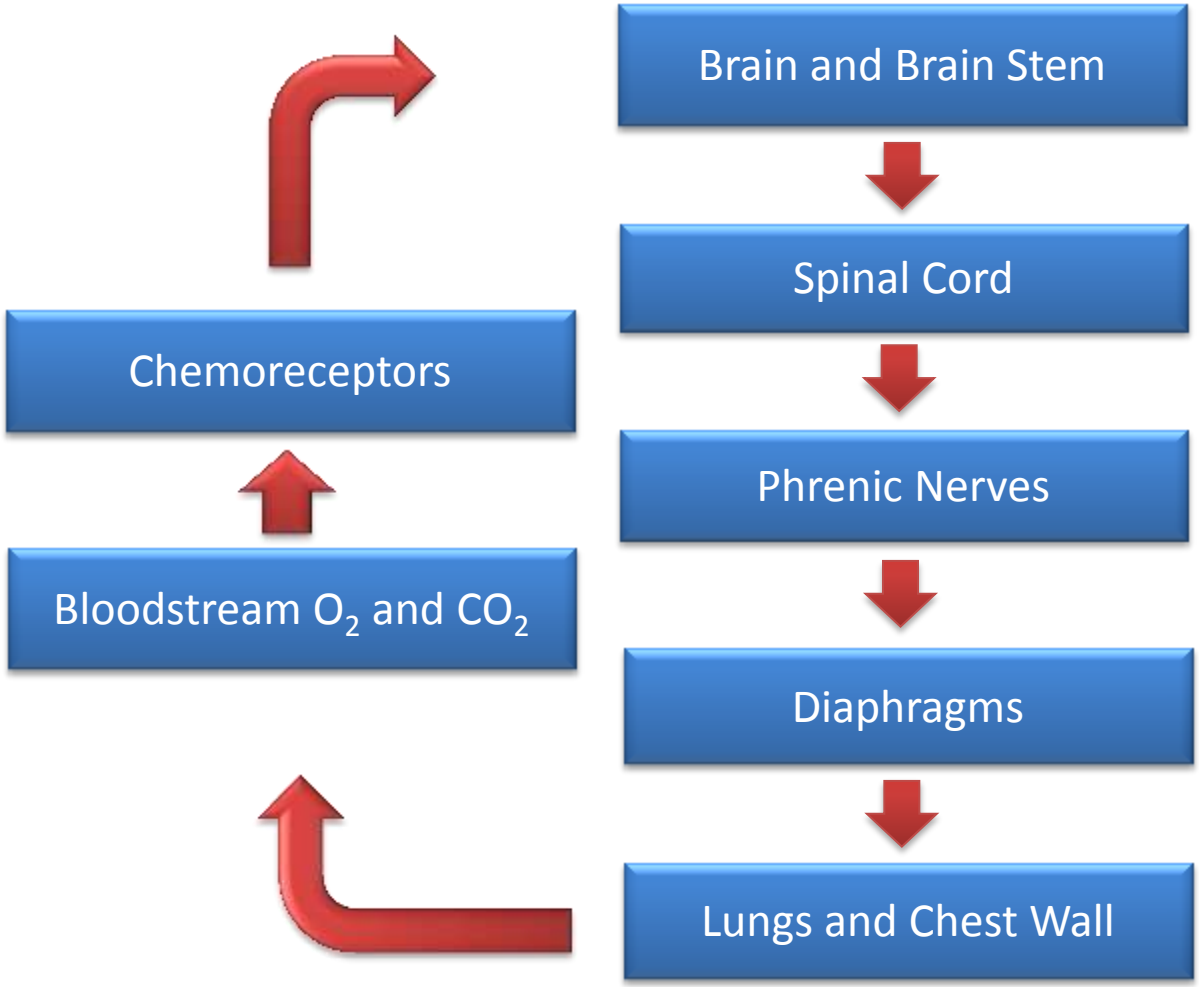
The event is scored based on high $TCCO_2$ level. Lying down during waking, the patient was at 32 mm Hg. The reading of 58 mm Hg is abnormally high.

Oxygen saturation is low at 85%.

A “Simple” Diagram of the Control of Breathing



Ventilation Pump System and Control of Breathing

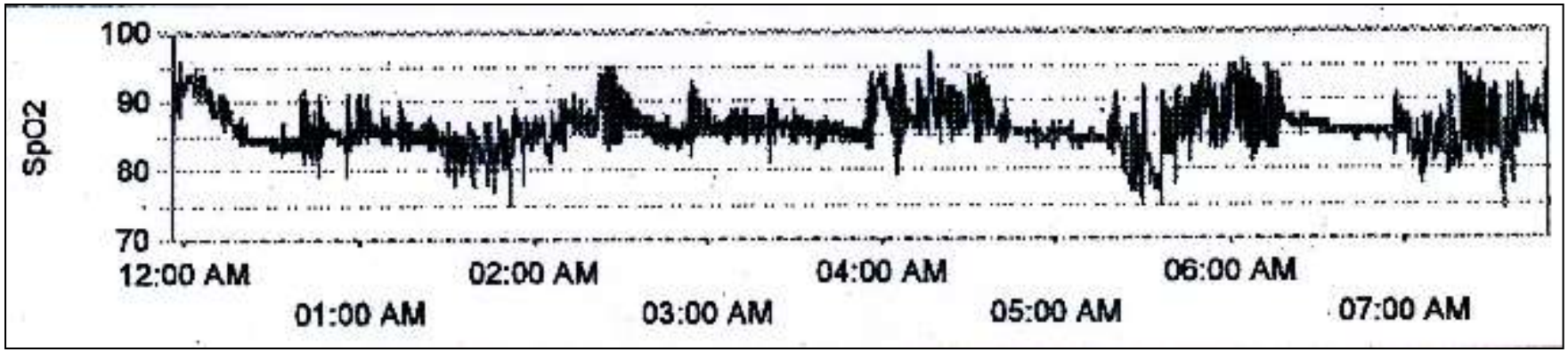


Case

- 65 year old morbidly obese female with symptoms of intermittent awakenings, daytime sleepiness and LE edema.
- PMHx: Morbid obesity, HTN, IDDM. Denies COPD
- SHx: Nonsmoker
- Exam: BMI 46 kg/m^2, Normal vitals, Pulse ox 91% on RA
  - Lungs clear, normal cardiac exam, 1+ LE edema bilaterally
- Labs: Hb = 18 g/dL and HCO_3 = 34 mmol/L
- Spirometry: FVC 55% without obstruction, FEV1 60%

Overnight Oximetry and Daytime ABG

Overnight Oximetry on Room Air



Room Air Awake ABG

Ph	7.34
PCO_2 (mm Hg)	60
PO_2 (mm Hg)	62
HCO_3 (mmol/L)	34

Question

Based on the history, exam and data presented, the best initial recommendation should be:

A) Add oxygen at 2 l/min at night

B) HST with home APAP trial

C) PSG with CPAP titration

D) PSG with ASV titration

Answer

Based on the history, exam and data presented, the best initial recommendation should be:

A) Add oxygen at 2 l/min at night

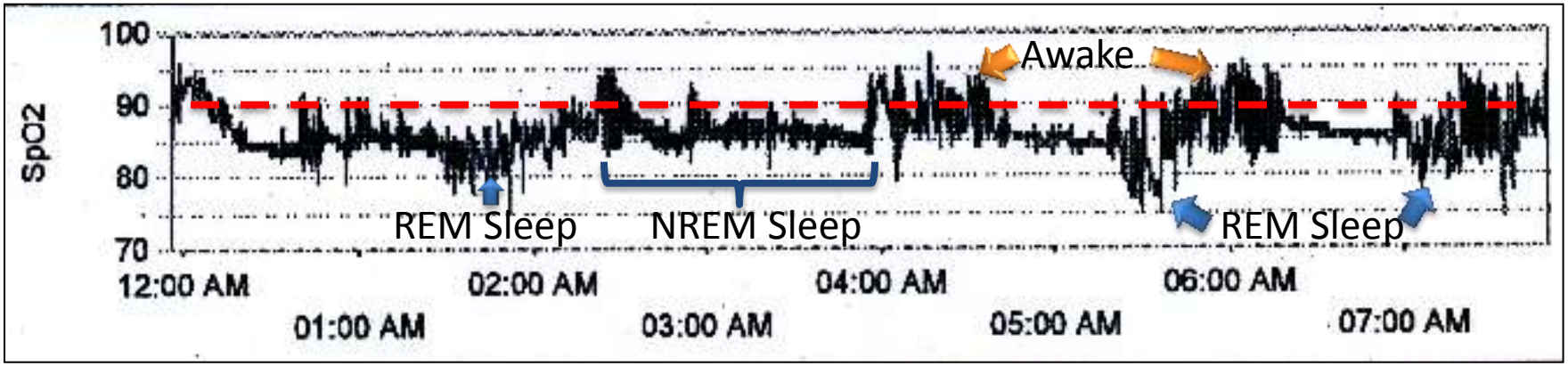
B) HST with home APAP trial

C) PSG with CPAP titration

D) PSG with ASV titration

Oximetry and ABG Consistent with Hypoventilation with Hypercapnea

Oximetry Suggestive of Hypoventilation



Room Air ABG Consistent with Chronic Hypercapnea

Ph	7.34	Low
PCO_2 (mm Hg)	60	High
PO_2 (mm Hg)	62	Low
HCO_3 (mmol/L)	34	High

Obesity Hypoventilation Syndrome (OHS) Diagnostic Criteria: ICSD 3

- Diagnostic Criteria: All must be met
  - Presence of hypoventilation during wakefulness ($PaCO_2$ > 45 mm Hg) as measured by arterial PCO_2, end-tidal PCO_2 or transcutaneous PCO_2
  - Presence of obesity
    - BMI > 30 kg/m2
    - > 95 percentile for age and sex for children
  - Hypoventilation is <u>not</u> primarily due to other etiologies
    - Lung disease, chest wall disorders (other than mass loading from obesity), medication use, neurologic disorders, muscle weakness, congenital disease, or idiopathic central alveolar hypoventilation syndrome
- Alternate names:
  - Hypercapnic sleep apnea
  - Sleep related hypoventilation associated with obesity

Obesity Hypoventilation Syndrome (OHS)

- Most patients have coexisting OSA
  - 90% with AHI ≥ 5
  - 10% pure sleep related hypoventilation
- Actual prevalence not well defined
- Increased risk for cardiovascular morbidity, hospitalizations and death vs eucapnic OSA or eucapnic obese
- Risk factors for hypercapnea:
  - More severe OSA (AHI, % of TST < 90%)
  - Greater lung restriction
  - Greater BMI
    - ≈ 50% of individuals with a BMI > 50 m/kg^2 have OHS

Kaw R, Mokhlesi, B. Chest. 2009; 136:787-96

OHS Summary

- OHS is under-recognized and is a diagnosis of exclusion
- ABG currently required for diagnosis and initiation of bilevel PAP therapy with a backup rate
- HCO_3 > 27 mmol/L may be helpful in identifying patients with chronic hypercapnea
- HST not indicated for diagnosis
- Best PAP treatment is not clear:
  - May be effectively treated with CPAP, bilevel therapy with or without a back up rate or AVAPS
  - APAP and ASV therapy have no role
- Oxygen should not be primary therapy for OHS and should only be used after PAP therapy maximized
  - Reevaluate need for oxygen based on clinical improvement

Case

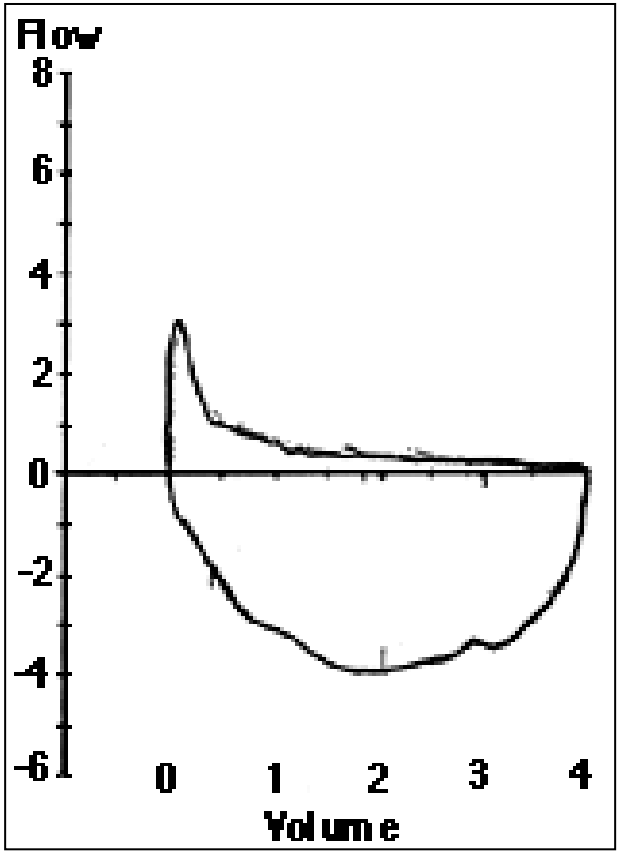
- 72 year old female presents with complaints of dyspnea on exertion and a longstanding morning cough productive of sputum.
- She notes intermittent awakenings as well as some sleep maintenance insomnia.
- She denies snoring, witnessed apneas or RLS symptoms.
- Epworth = 11
- PMHx: HTN
- MEDS: Metoprolol QD and albuterol prn

Case

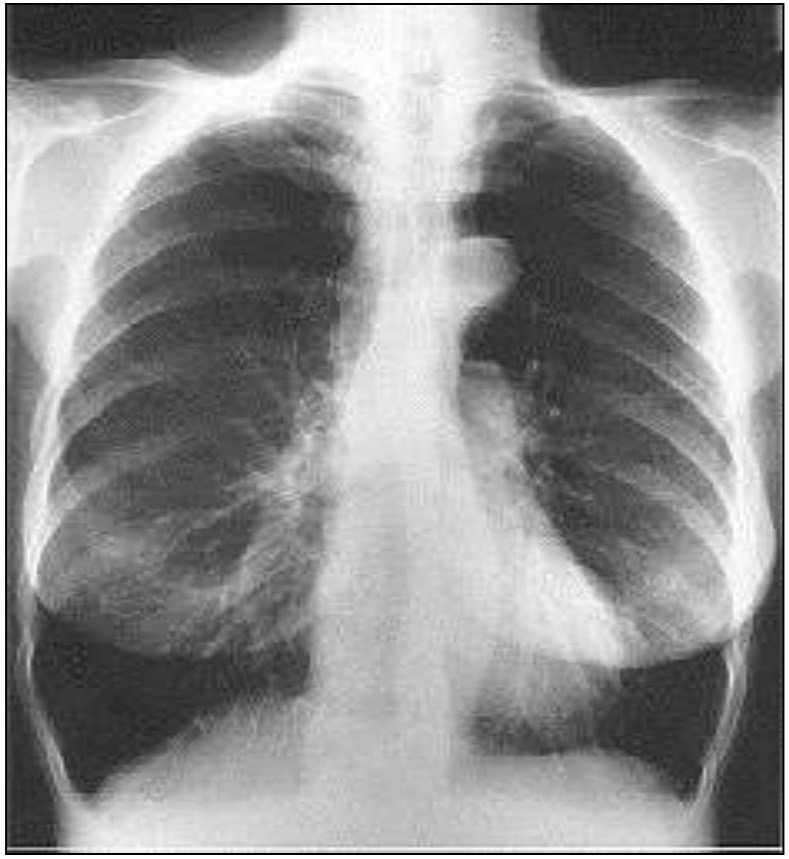
- Physical exam:
  - BMI 24 kg/m²
  - Resting room air pulse ox 92%
  - Diminished breath sounds bilaterally
  - Distant heart sounds
  - 1+ LE edema bilaterally
  - Remainder of exam normal

Case

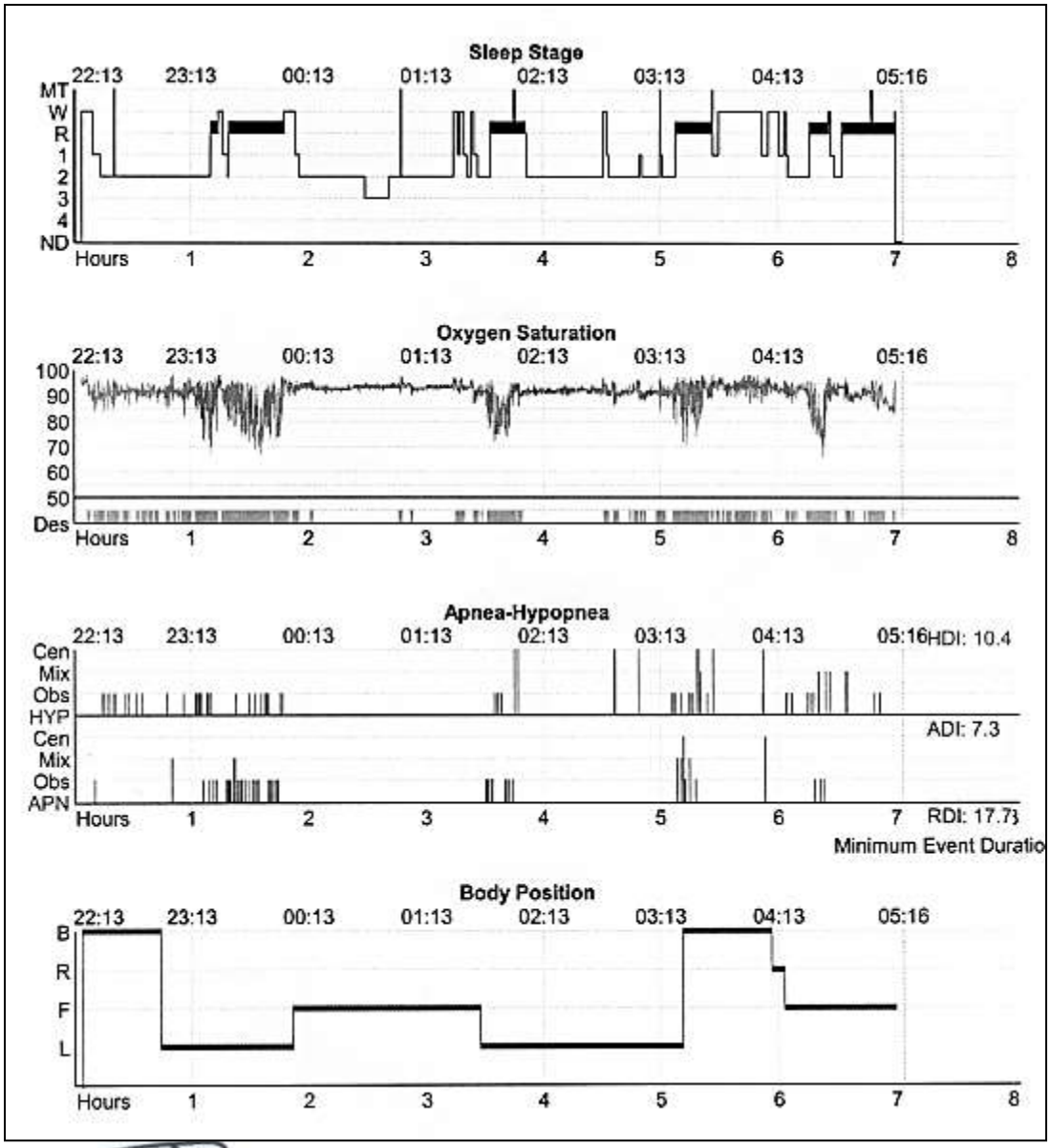
Flow Volume Loop



Chest Xray



ABG (RA): Ph 7.40, PCO_2 43, PO_2 68, HCO_3 25



PSG AHI = 17

Question

Based on the information provided, which one of the following treatments has been associated with improved survival?

A) Bilevel S

B) Oxygen

C) CPAP

D) Bilevel VAPS

Answer

Based on the information provided, which one of the following treatments has been associated with improved survival?

A) Bilevel S

B) Oxygen

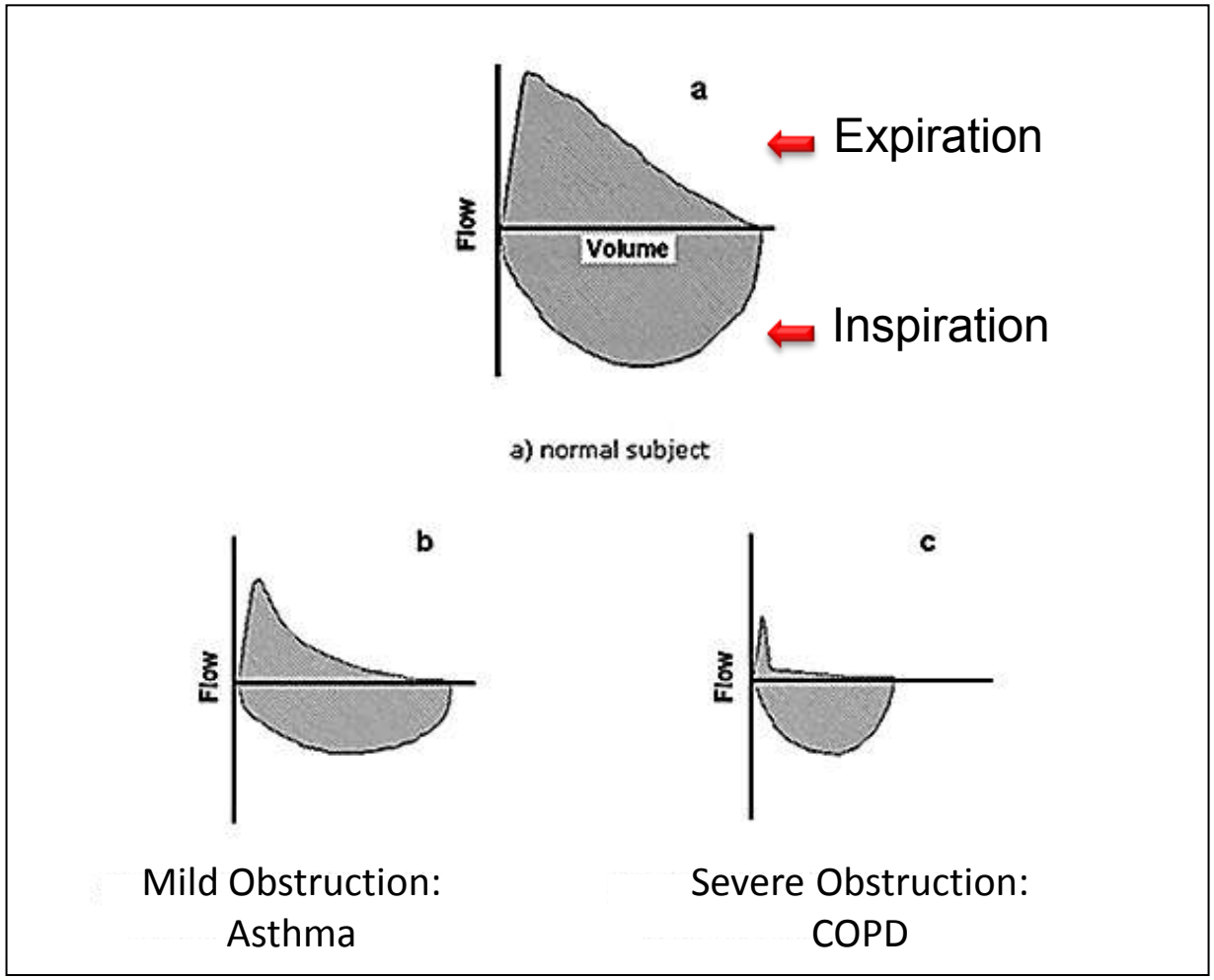
C) CPAP

D) Bilevel VAPS

Chronic Obstructive Pulmonary Disease (COPD)

- Definition:
  - Chronic obstructive lung disease
  - Post bronchodilator FEV1/FVC < 70%
- Chronic bronchitis:
  - Chronic productive cough for three months in each of two successive years in a patient in whom other causes of chronic cough have been excluded
- Emphysema:
  - Emphysema is defined by abnormal and permanent enlargement of the airspaces that are distal to the terminal bronchioles. This is accompanied by destruction of the airspace walls, without obvious fibrosis
- Asthma (chronic obstructive)

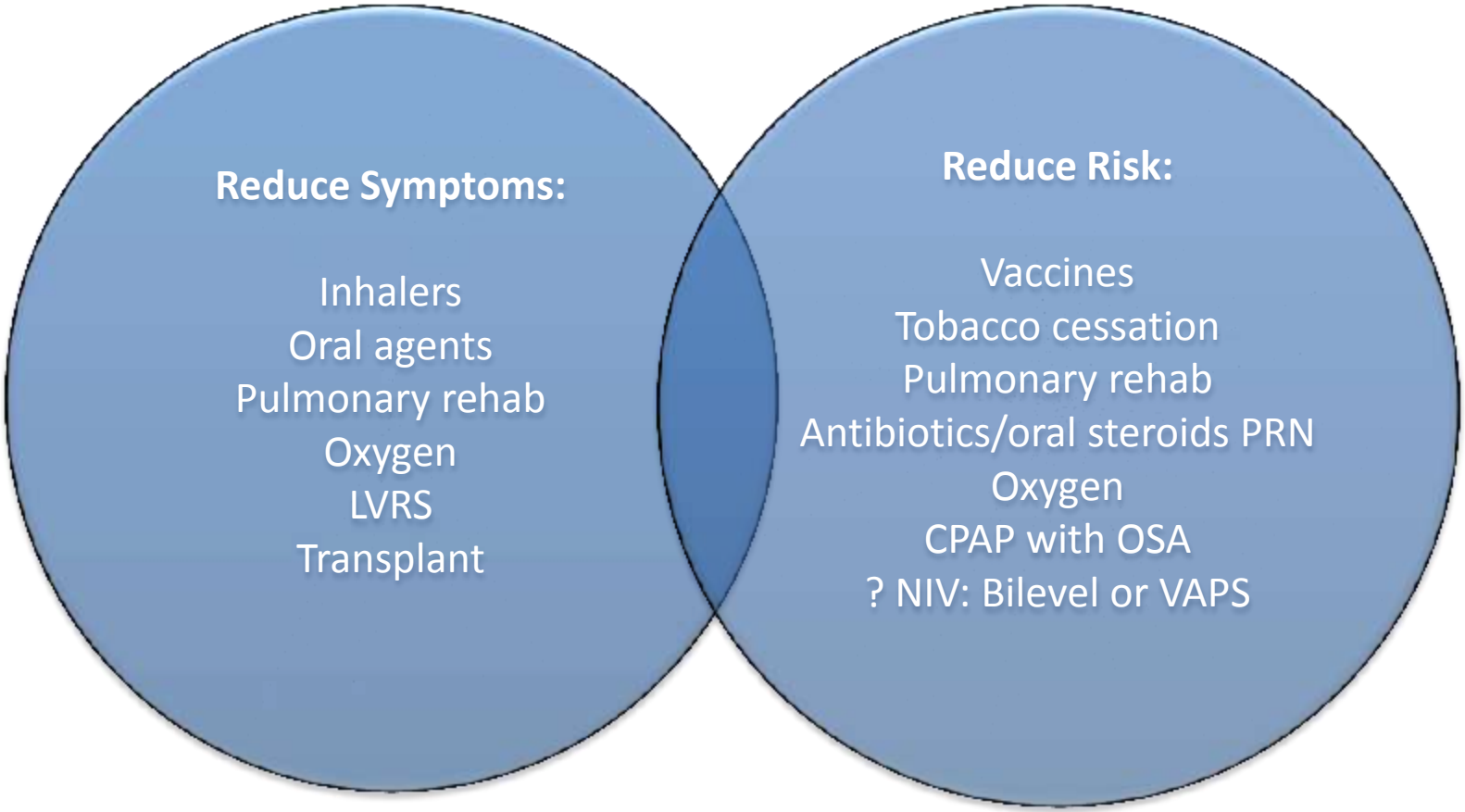
Flow Volume Loops: Normal and Degrees of Obstruction



Mild Obstruction: Asthma

Severe Obstruction: COPD

COPD Treatment



COPD Treatment: Oxygen

- Improves survival in patients with resting hypoxemia ($PaO_2 \leq 60$ mm Hg)
  - More (duration) = Better outcomes
    - Nocturnal Oxygen Therapy Trial (NOTT)
    - Medical Research Council (MRC) Trial
- No data to support improved survival in patients with normal resting oxygen saturations
  - Ambulatory oxygen:
    - Improves post exercise dyspnea and fatigue domain of QOL
    - No evidence that ambulatory oxygen improves exercise capacity or survival
  - Nocturnal oxygen:
    - Role unclear
    - No data to support improved survival

Stege Resp Med 2008;102:801-814
Kryger, Sleep Breath 2009;13:79-84
Amer. F. Cochrane Database Syst. Reviews 2014
NOTT Trial. Ann Intern Med 1980;93:391
MRC Trial. Lancet 1981;1:681

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 27, 2016 VOL. 375 NO. 17

A Randomized Trial of Long-Term Oxygen for COPD with Moderate Desaturation

The Long-Term Oxygen Treatment Trial Research Group*

- In patients (n = 738) with stable COPD and resting (89% to 93%) or exercise-induced moderate desaturation (≥ 80% to < 90%), the prescription of long-term supplemental oxygen:
  - Did **not** result in a longer time to death or first hospitalization than no long-term supplemental oxygen
  - Nor did it provide sustained benefit with regard to any of the other measured outcomes (QOL, depression, 6 MW, COPD exacerbations)

Overlap Syndrome

- Coexistence of COPD and OSA
- Prevalence of OSA similar to general population
- Associated with lower nocturnal mean oxygen saturations and lower oxygen desaturations compared to COPD patients without OSA
- Increased risk of death and severe COPD exacerbation leading to hospitalization if OSA untreated compared to group without concomitant OSA
- Risks of death or hospitalization reduced with CPAP treatment
  - Outcomes no different than COPD group alone
  - Improved CPAP adherence = Better survival
  - Older age associated with reduced survival

Marin, J et al. AJRCCM 2010;182:325-331
Morganthaler, TI et al. Sleep 2008;31:141-47
Stranchina M et al. J Clin Sleep Med 2013;9(8):767-772

Patients with COPD are Not Candidates for APAP

- **Clear Candidates**
  - **Un**complicated moderate to severe OSAS
- **Unclear Groups**
  - REM-related OSAS
  - Position dependent
  - High pressures (>10)
  - CPAP intolerant

- **Not APAP Candidates (**AASM Standard**)**
  - Congestive heart failure
  - COPD and chronic lung disease
  - Obesity hypoventilation syndrome
  - Other hypoventilation syndromes
  - Lack of snoring

Is There A Role for Nocturnal NIPPV in Patients with COPD?

Does Nocturnal NIPPV Improve Meaningful Outcomes in Stable COPD?

- Cochrane Database Review (2013): Limited data suggest no benefit on meaningful outcomes:
  - 7 RCTs with 245 patients used for ≥ 3 months in hypercapnic patients with stable COPD
    - Gas exchange
    - Exercise tolerance (6MWD)
    - HRQOL
    - Lung function or respiratory muscle strength
    - Sleep efficiency
  - 2 studies with up to 12 month follow up demonstrated similar outcomes

Struik FM et al. Cochrane Database Syst Rev. 2013 Jun;6:CD002878.

Nocturnal NIPPV May Improve Survival in Stable Hypercapnic COPD

- Methods:
  - 195 patients with stable GOLD stage IV,
  - PCO_2 > 52 mm Hg and ph > 7.35
  - NIV targeted to reduce PCO_2 by 20% or < 48 mm Hg
  - Randomized to NIPPV or medical therapy
  - Outcome: 12 month all-cause mortality
- Results: Mortality reduced in NIPPV group
  - Mortality 12% in NIPPV group vs 33% in control group
  - HR = 0.24 (p = 0.0004)
- Conclusions:
  - The addition of long-term NIPPV to standard treatment improves survival of patients with hypercapnic, stable COPD when NIPPV is targeted to reduce hypercapnia

Kohnlein T et al. The Lancet Respiratory Medicine, Early Online Publication, 25 July 2014 doi:10.1016/S2213-2600(14)70153-5

Effect of Home Noninvasive Ventilation With Oxygen Therapy vs Oxygen Therapy Alone on Hospital Readmission or Death After an Acute COPD Exacerbation

- Methods:
  - RCT of pts with COPD with persistent hypercapnea ($PaCO_2$ > 53 mm Hg, resting hypoxemia and a ph > 7.30), 2 to 4 weeks after an acute exacerbation of COPD
  - Randomized 1:1 NIV with O_2 vs O_2 alone
- Results:
  - N = 116 (2021 screen/1905 excluded)
    - 53% female, FEV1 = 0.6L, $PaCO_2$ = 59 mm Hg
  - Median NIV settings (IPAP 24, EPAP 5, rate 14)
  - 12 month risk of readmission or death was 63.4% in NIV vs 80% in O_2
  - Deaths: 16 in NIV + O_2 vs 19 in O_2 alone
- Conclusions:
  - NIV plus oxygen may prolong the time to readmission or death within 12 months of a COPD exacerbation with in patients with persistent hypercapnea

Is There A Role for Nocturnal NIPPV in Patients with Stable COPD?

- No role for patients without hypercapnea
- Role for patients with stable COPD and hypercapnea unclear:
  - Conflicting results based on limited data
  - NIPPV targeted to reduced $PaCO_2$ may improve survival
  - Role of VAPs vs Bilevel S or ST unclear

Answer

Based on the information provided, which one of the following treatments has been associated with improved survival?

A) Bilevel S

B) Oxygen

C) CPAP

D) Bilevel VAPS

Treating COPD and Outcomes

- Most treatments improve symptoms and functional capacity, but not mortality
- Treatments:
  - Oxygen improves survival in COPD with resting hypoxemia
  - CPAP improves survival and decreases exacerbations and hospitalizations in those with the overlap syndrome
    - Better outcomes associated with greater CPAP adherence
  - NIPPV targeted to reduce $PaCO_2$ may improve survival in patients with stable COPD and hypercapnea ($PaCO_2$ > 52 mm Hg)
  - Current data does not support the use of chronic NIPPV in patients with COPD to reduce readmissions or improve survival after an acute episode of acute respiratory failure

Case

- A 10 year old previously healthy female has recently undergone an outpatient surgery with general anesthesia.
- Post operatively she is difficult to extubate due to persistent hypoxemia and hypercapnea.
- After extubation she demonstrates recurrent sleep related hypoventilation requiring nocturnal ventilatory support.
- FH: Her younger brother requires ventilatory support at night.
- PE: Normal BMI and neurologic exam

Question

Which one of the following is the most likely etiology for patients respiratory abnormalities?

A) Late onset hypoventilation with hypothalamic dysfunction
B) Idiopathic central alveolar hypoventilation
C) Congenital central alveolar hypoventilation syndrome
D) Sleep related hypoventilation due to substance or drug

Answer

Which one of the following is the most likely etiology for patients respiratory abnormalities?

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C) Congenital central alveolar hypoventilation syndrome
D) Sleep related hypoventilation due to substance or drug

Congenital Central Alveolar Hypoventilation Syndrome (CCHS)

- ICSD 3 diagnostic criteria:
  - Presence of sleep related hypoventilation
  - Mutation of the *PHOX2B* gene is present
    - Autosomal dominant
    - Poly-alanine repeat expansion mutations (PARMs)
- Also known as congenital central hypoventilation syndrome
  - Previously known as Ondine's curse
- Other:
  - Daytime CO_2 may be elevated or normal
  - Hypoventilation most severe in NREM > REM > Wake

Congenital Central Alveolar Hypoventilation Syndrome for the Boards

- Typically presents at birth or in early childhood with sleep related hypoventilation
- Severity of illness determined by *PHOX2B* mutation type:
  - More poly-alanine repeats = More severe disease
- May present in adulthood with respiratory failure after anesthesia or a respiratory illness
  - Typically due to a mild mutation of the *PHOX2B* gene
- Associated with Hirschspung's disease, neural crest tumors and autonomic dysfunction
- Increased risk for neuroblastoma
- Treatment:
  - Ventilatory support at night
  - Case reports of diaphragmatic pacing

Late-Onset Central Hypoventilation with Hypothalamic Dysfunction

- Diagnostic Criteria:
  - Presence of sleep related hypoventilation
  - Symptoms absent during the first few years of life
  - At least 2 of the following:
    - Obesity
    - Endocrine abnormalities of hypothalamic origin
    - Severe emotional and behavioral disturbances
    - Tumor of neural origin
      - 40% with neural crest tumors
  - Mutation of *PHOX2B* is not present
  - Not better explained by other disorders
- Also known as ROHHAD:
  - Rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation
- Treatment: Ventilatory support

Rationale

- CHHS is the most likely etiology given the + family history of sleep related hypoventilation and onset with exposure to anesthesia
- Late onset central hypoventilation (ROHHAD) is unlikely given the absence of obesity and endocrine dysfunction.
- Idiopathic central alveolar hypoventilation is possible, but is less likely
- Sleep related hypoventilation due to drug or substance is unlikely given the persistence of symptoms after the exposure to anesthesia has been completed

Thank You and Good Luck

Question

Which of the following is true of narcotic-induced central apnea?

A) Independent of dose of narcotic

B) Generally resolves with ongoing narcotic therapy

C) ASV bilevel therapy is the treatment of choice

D) Most commonly associated with methadone

Answer

Which of the following is true of narcotic-induced central apnea?

A) Independent of dose of narcotic

B) Generally resolves with ongoing narcotic therapy

C) ASV bilevel therapy is the treatment of choice

D) Most commonly associated with methadone

CSA due to Medication or Substance: ICSD 3 Diagnostic Criteria

- The patient is taking an opioid or other respiratory depressant
- The presence of 1 or more of the following:
  - Sleepiness
  - Difficulty initiating or maintaining sleep, frequent awakenings or non-restorative sleep
  - Awakening short of breath
  - Snoring
  - Witnessed apneas
- PSG shows CSA fulfilling AASM scoring criteria without evidence of Cheyne Stokes breathing
- Occurs as a consequence of an opioid or other respiratory suppressant
- Not better explained by another sleep disorder

CSA due to Medication or Substance

- Opioid related sleep disordered breathing:
  - Central apneas including Biot's pattern
  - Prolonged obstructive hypoventilation
  - Obstructive apneas and hypopneas
  - Mixed pattern of sleep disordered breathing
- Most commonly associated with long acting opioids, methadone most common
- Dose dependent relationship with narcotics
- Typically does not resolve spontaneously
  - Natural history not well defined
- Optimal treatment not clear
  - May respond best to a reduction in dose of opioids
  - ASV bilevel treatment data inconsistent

Case

An 85 year old male presents to the ER with altered mental status and an oxygen saturation of 86% on room air. His room air (RA) ABG demonstrates the following:

- Ph: 7.24
- PCO_2: 60 mm Hg
- PaO_2: 58 mm Hg
- HCO_3: 24 mmol/L

Question

Which one of the following is the most likely etiology that explains the patient's hypoxemia?

A) Aspiration pneumonia
B) Congestive heart failure
C) Narcotic overdose
D) Pulmonary embolism

Answer

Which one of the following is the most likely etiology that explains the patient's hypoxemia?

A) Aspiration pneumonia

B) Congestive heart failure

C) Narcotic overdose

D) Pulmonary embolism

Calculate A – a Gradient

- A – a (alveolar to arterial) oxygen gradient
  - A- a gradient = $PAO_2 – PaO_2$
    - PaO_2 measured by blood gas
    - PAO_2 is calculated using the alveolar gas equation
    - Simplified alveolar gas equation for the sleep boards:
      - $PAO_2 = FiO_2 (713) – PCO_2/0.8$
      - On room air with a PCO_2 of 40, PAO_2 should = 100 mm Hg
        - » .21(713) – 40/0.8 = 150 - 50 = 100
- Normal A-a gradient:
  - Age dependent and increases with age
  - Normal 5 -10 mm Hg in young adults
  - Increases by 1 mm Hg for each decade of life

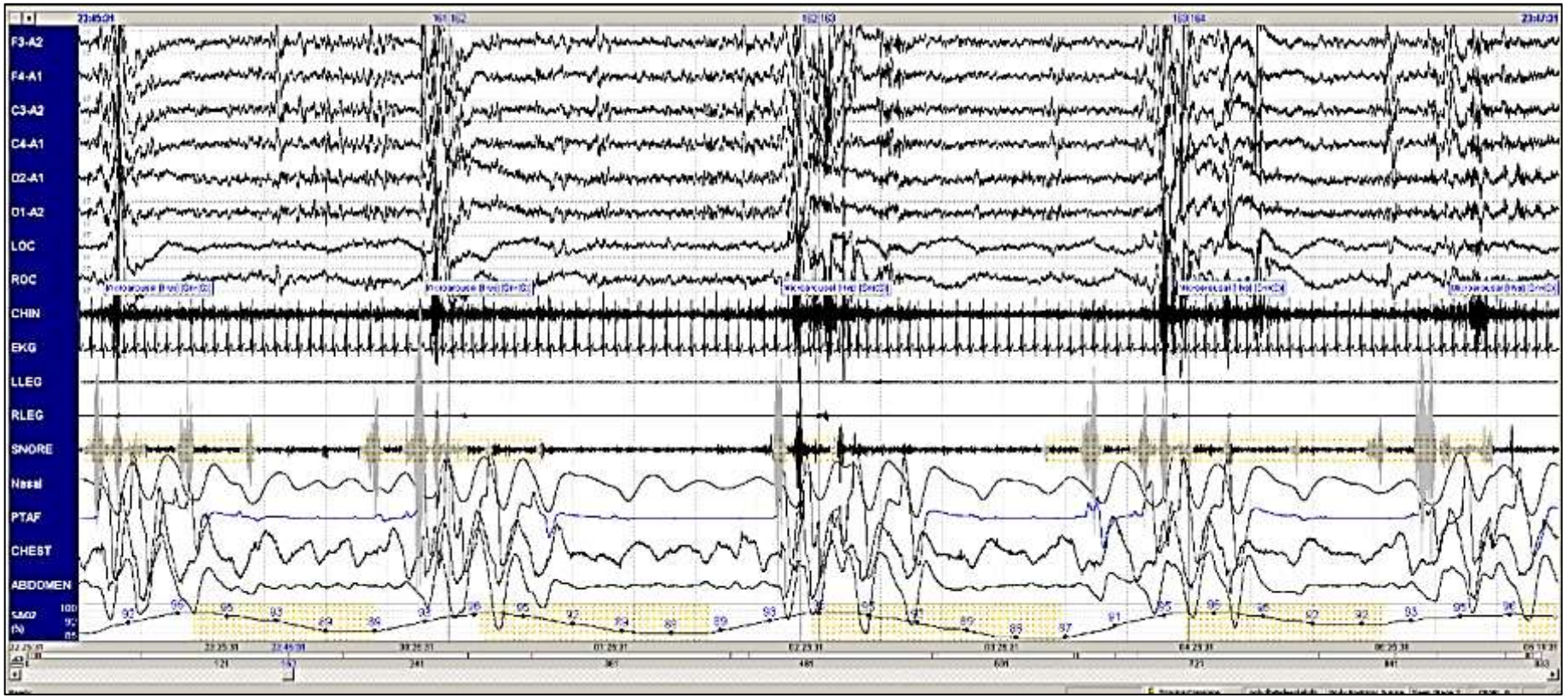
Case Rationale

- Alveolar gas equation:
- Calculate A – a gradient:
  - PAO_2: FiO_2 (713) – PCO_2/0.8
    - PAO2 = 150 – 75 = 75 mm Hg
  - PaO_2 = 58 mm Hg
  - PAO_2 – PaO_2 = 17 mm Hg (Relatively normal for age)
- A – a gradient is relatively normal for age, thus a narcotic overdose leading to hypoventilation is the most likely etiology

Case

- A 55 year old male with a history of CHF (EF 35%) presents with symptoms of frequent awakenings and daytime sleepiness.
- His wife notes intermittent snoring and periods of apnea.
- Medications: Carvedilol, valsartan, furosemide, digoxin, potassium
- Exam: No distress, mallampati score of 3, lungs clear and 1+ bilateral LE edema
- An overnight attended PSG demonstrated the following:

Now the PSG Demonstrates the Following:



2 Minute Epoch

Question

Which of the following would be the best initial treatment for this patient?

A) CPAP
B) Oxygen
C) Adaptive servo ventilation (ASV) Bilevel
D) Ace inhibitor

Answer

Which of the following would be the best initial treatment for this patient?

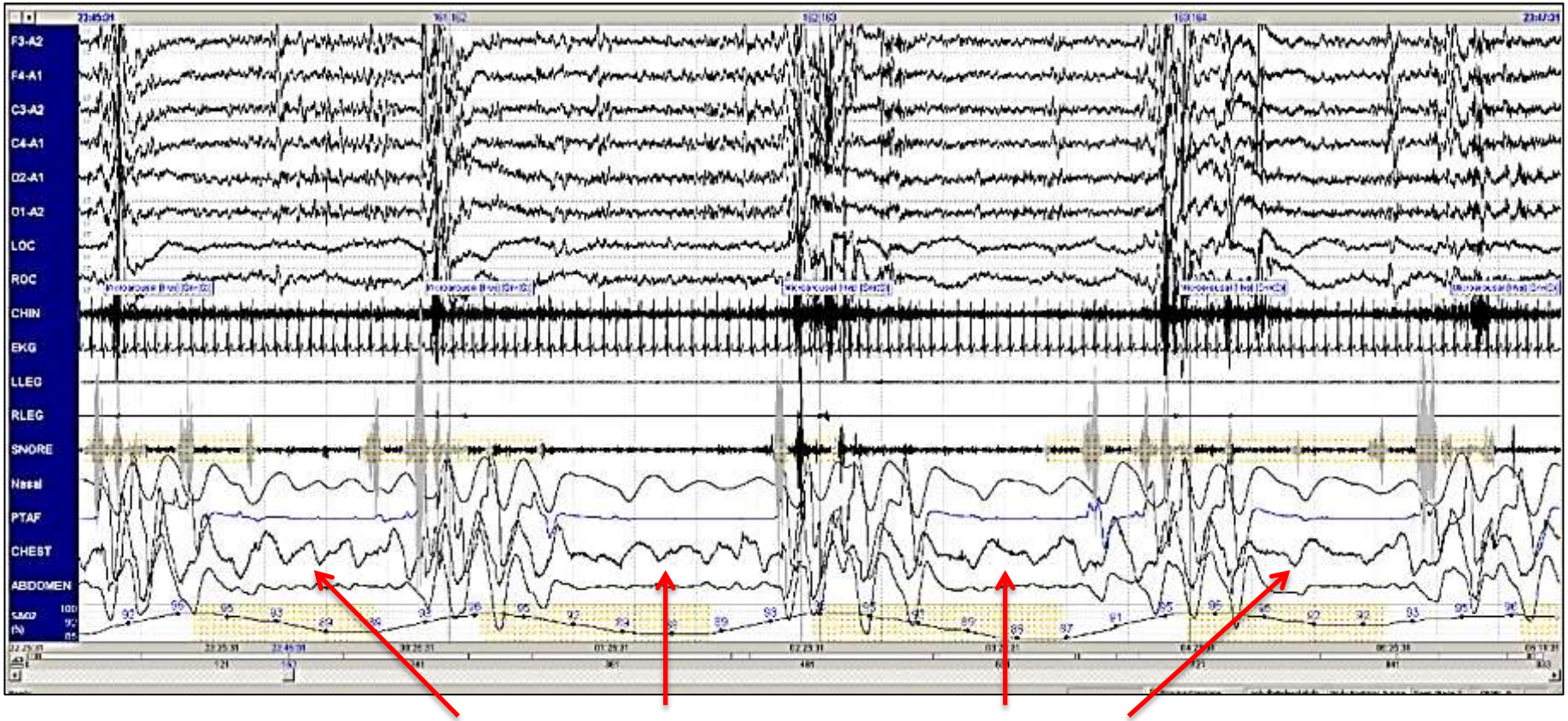
A) CPAP

B) Oxygen

C) Adaptive servo ventilation (ASV) Bilevel

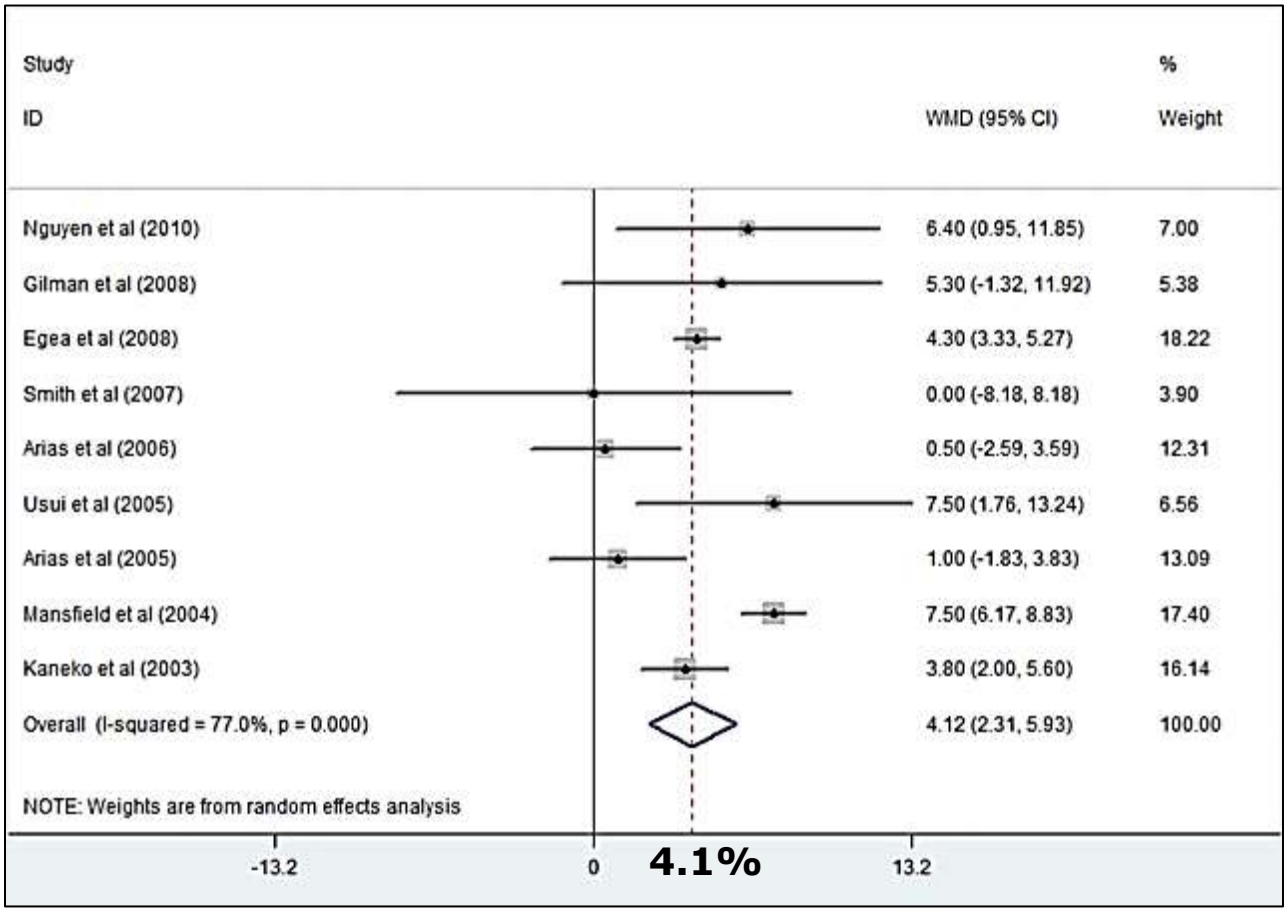
D) Ace inhibitor

The PSG Demonstrates OSA



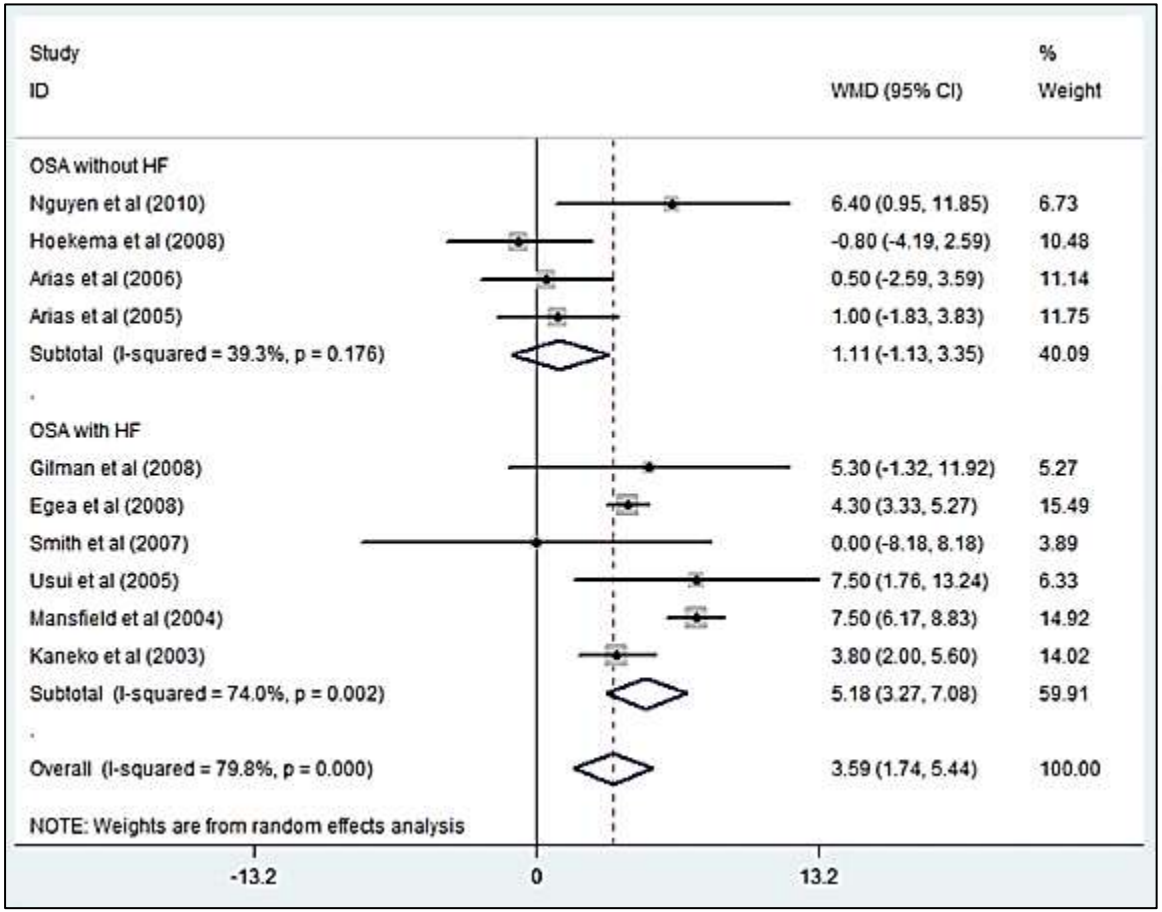
Recurrent Obstructive Hypopneas

CPAP Improves LVEF in Patients with CHF & OSA



Sun H et al. PLoS One 2013;8:e62298

LVEF Improvements Most Pronounced in Patients with Reduced LVEF at Baseline



Diastolic CHF: 1% improvement in LVEF with CPAP

Systolic CHF: 5% improvement in LVEF with CPAP

***CPAP not associated with reductions in LVEF

Sun H et al. PLoS One 2013;8:e62298

Preparing for Sleep Medicine Certification 2017

Part I: Everything you need to know about sleep apnea
– Neil Freedman MD

Part II: Everything else
– Teofilo Lee-Chiong MD

SLEEP 2017
Boston, MA
June 6, 2017

Nearly
Everything else in one hour

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Disclosure

- Research funding: Philips Respironics
- Consulting: Elsevier, CareCore National
- Chief Medical Liaison: Philips Respironics
- Royalties: Oxford, Lippincott, Elsevier, Wiley, CreateSpace
- I will not be discussing off-label uses

Biology

Physiology

Testing

Populations

Medications

Disorders

The story of wake neurons

Main characters

Glutamate
Dopamine
Hypocretin
Norepinephrine
Serotonin
Histamine
Acetylcholine

The story of wake neurons

Main characters

The story of wake

neurons

Glutamate

Dopamine

Hypocretin

Norepinephrine

Serotonin

Histamine

Acetylcholine

Main CNS excitatory neurotransmitter

Main characters

The story of wake

neurons

Glutamate

Dopamine

Hypocretin

Norepinephrine

Serotonin

Histamine

Acetylcholine

Main CNS excitatory neurotransmitter

"Going-to-mate" is exciting

Main characters

The story of wake

neurons

Glutamate

Dopamine

Hypocretin

Norepinephrine

Serotonin

Histamine

Acetylcholine

Dope to get high

Main characters

The story of wake

neurons

Glutamate

Dopamine

Hypocretin

Norepinephrine

Serotonin

Histamine

Acetylcholine

Never sleep when hungry

Main characters

The story of wake neurons

Glutamate
Dopamine
Hypocretin
Norepinephrine
Serotonin
Histamine
Acetylcholine

Or angry

Main roles

Motor activation	Acetylcholine Dopamine
Alertness and attention	Acetylcholine Histamine Norepinephrine
Emotional arousal	Dopamine Norepinephrine Serotonin

Main locations

Glutamate	Ascending reticular formation
	Excitatory = ascending

Main locations

Glutamate	Ascending reticular formation Excitatory = ascending
Dopamine	Substantia nigra, vPAG Dope = substance

Main locations

Glutamate	Ascending reticular formation Excitatory = ascending
Dopamine	Substantia nigra Dope = substance
Hypocretin	Hypothalamus (perifornical) Hypocretin = hypothalamus

Main locations

Norepinephrine Locus ceruleus

No loco

Main locations

Norepinephrine	Locus ceruleus No loco
Serotonin	Raphe nuclei Se raphim

Main locations

Norepinephrine	Locus ceruleus No loco
Serotonin	Raphe nuclei Se raphim
Histamine	Tuberomammillary nucleus His mama

The story

His mama sent an
excited ascending
seraphim so that he
will do
no loco such as
dope substance
to get high-high

Wake neurotransmitters: clinical correlates

Dopamine	Agonists increase wakefulness – amphetamine Antagonists promote sleep – haloperidol
Histamine	
Catecholamine	
Stimulants	

Wake neurotransmitters: clinical correlates

Dopamine	
Histamine	Receptor blockers cause sedation – diphenhydramine, low dose doxepin, low dose mirtazapine
Catecholamine	
Stimulants	

Wake neurotransmitters: clinical correlates

Dopamine	
Histamine	
Catecholamine	Agonists increase arousal and wakefulness – isoproterenol
Stimulants	

Wake neurotransmitters: clinical correlates

Dopamine	
Histamine	
Catecholamine	
Stimulants	Increase in dopamine and norepinephrine – amphetamine, cocaine and methylphenidate Increase in hypocretin and dopamine – modafinil and armodafinil

The photo of sleep

neurons

The photo of sleep neurons

GABA
Adenosine
Glycine
Acetylcholine

http://veryverychic.typepad.com

GABA	Basal forebrain
Adenosine	Basal forebrain
Glycine	
Acetylcholine	Basal forebrain

GABA	Basal forebrain, VLPO
Adenosine	Basal forebrain
Glycine	Spinal cord
Acetylcholine	Basal forebrain, PPT/LDT

Sleep neurotransmitters: clinical correlates

GABA	GABA-A receptor agonists cause sleepiness – benzodiazepines Alcohol facilitates GABA and inhibits glutamate – sedating at high doses
Adenosine	
Acetylcholine	

Sleep neurotransmitters: clinical correlates

GABA	
Adenosine	Receptor blockers increase wakefulness and decrease EEG SWA – caffeine
Acetylcholine	

Sleep neurotransmitters: clinical correlates

GABA	
Adenosine	
Acetylcholine	Agonists increase REM sleep – physostigmine Antagonists decrease REM sleep – tricyclic antidepressants

Glutamate Main CNS excitatory neurotransmitter

Glutamate Main CNS excitatory neurotransmitter

GABA Main CNS inhibitory neurotransmitter
Main NREM neurotransmitter

Glutamate Main CNS excitatory neurotransmitter

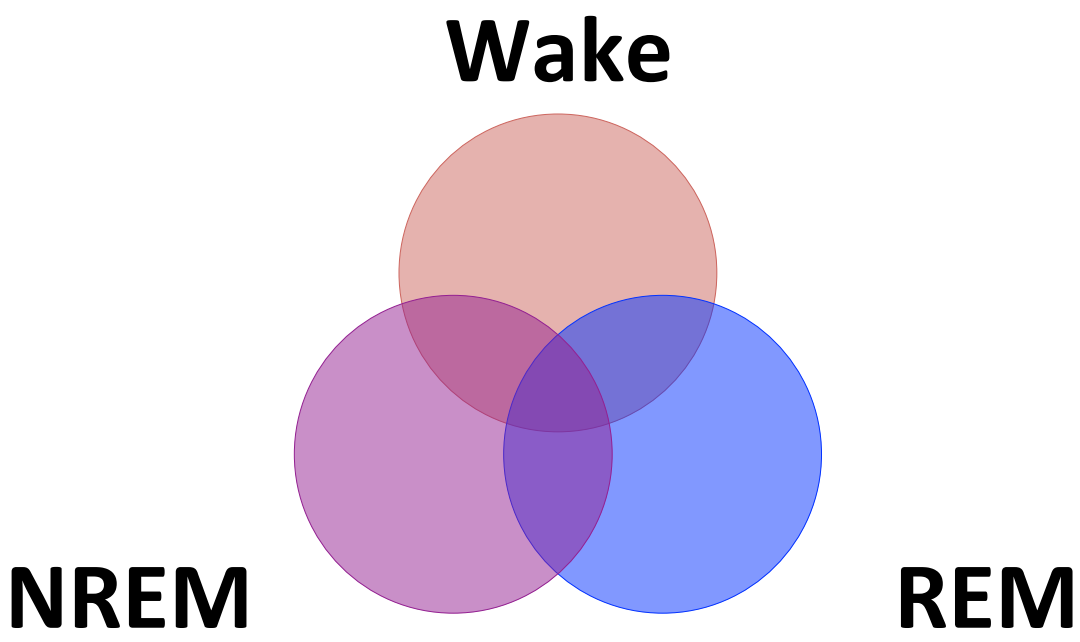
GABA Main CNS inhibitory neurotransmitter
Main NREM neurotransmitter

Acetylcholine Main REM sleep neurotransmitter

Glutamate	Main CNS excitatory neurotransmitter
GABA	Main CNS inhibitory neurotransmitter Main NREM neurotransmitter
Acetylcholine	Main REM sleep neurotransmitter
Glycine	Main spinal cord inhibitory neurotransmitter Responsible for REM muscle atonia

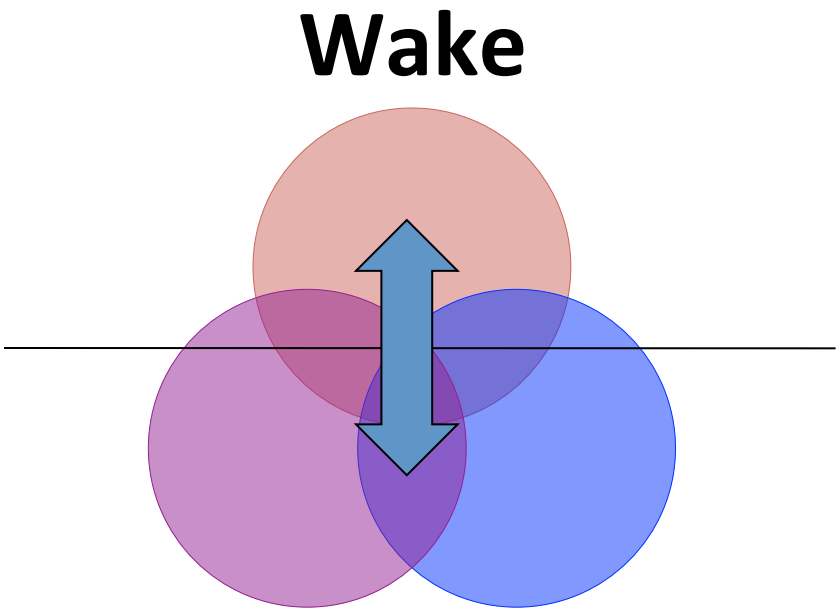
Glutamate	Main CNS excitatory neurotransmitter
GABA	Main CNS inhibitory neurotransmitter Main NREM neurotransmitter
Acetylcholine	Main REM sleep neurotransmitter
Glycine	Main spinal cord inhibitory neurotransmitter Responsible for REM muscle atonia
Adenosine	Responsible for homeostatic sleep drive

Neurobiology of sleep

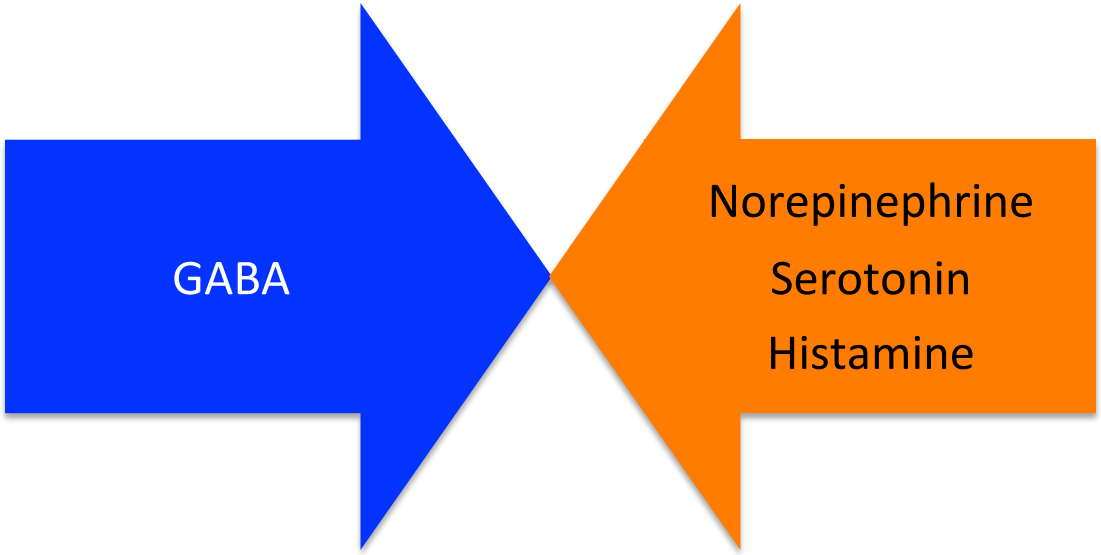


Wake-Sleep Switch

NE, 5HT, HA

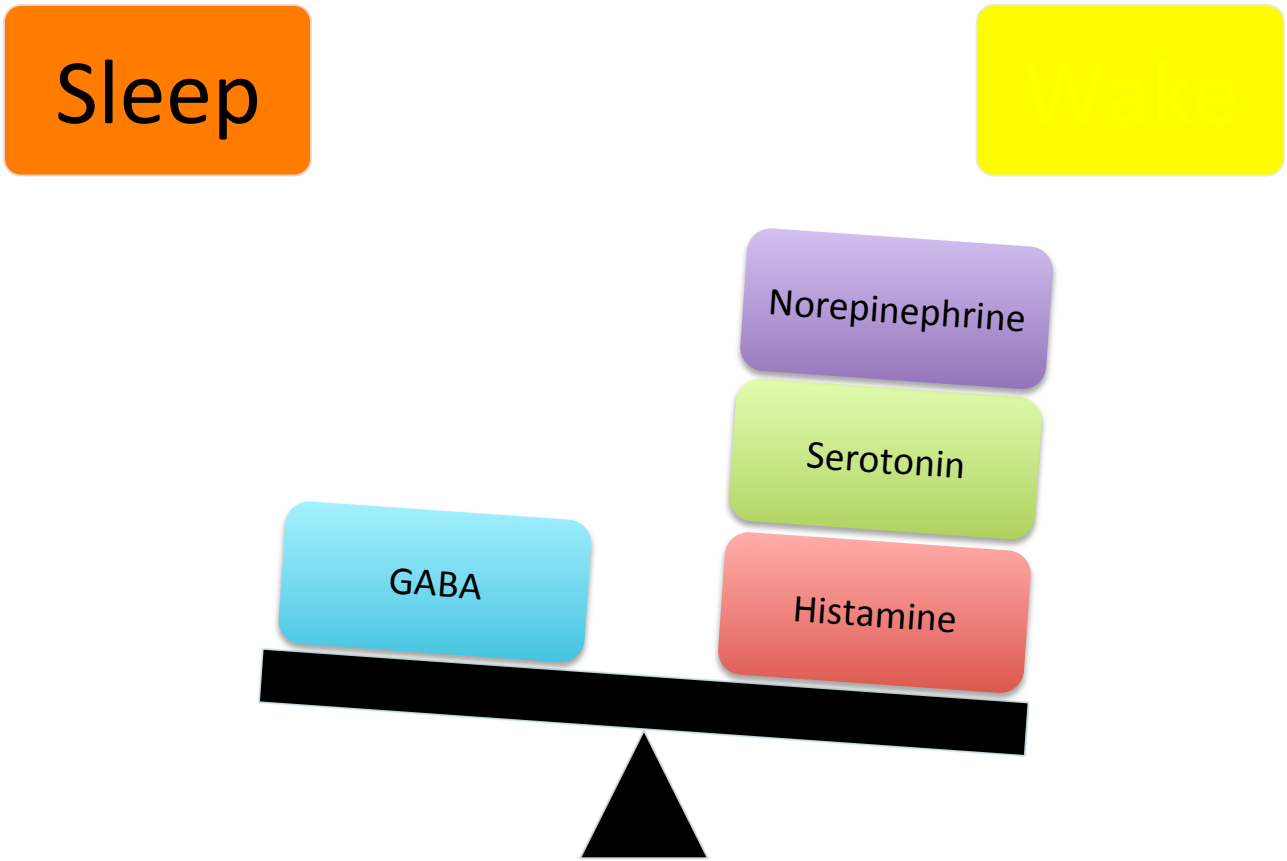


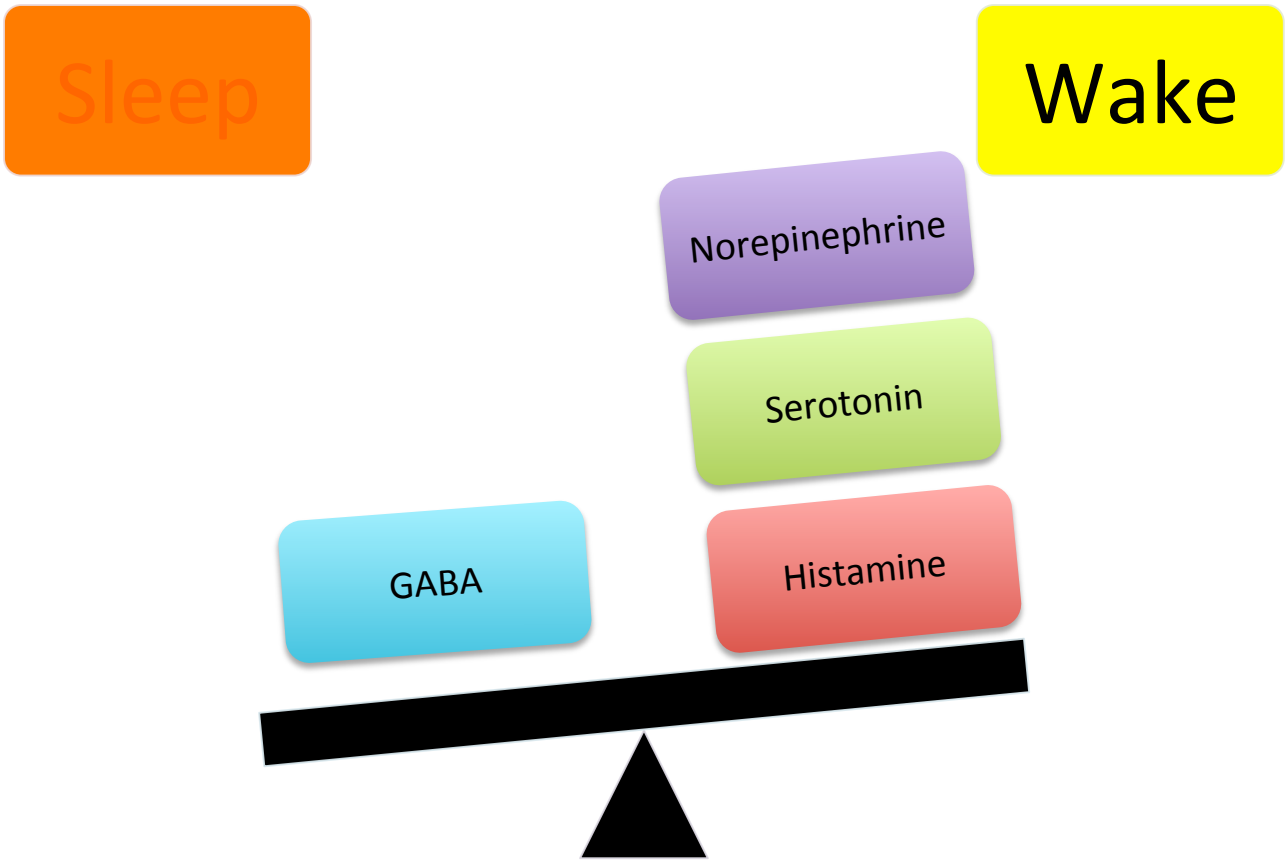
GABA (VLPO)



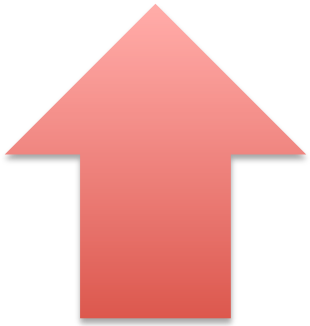
Bidirectional reciprocal inhibitory interactions between GABA (sleep) and N-S-H (wake)

Activation of GABA neurons produces coordinated inhibition of arousal systems



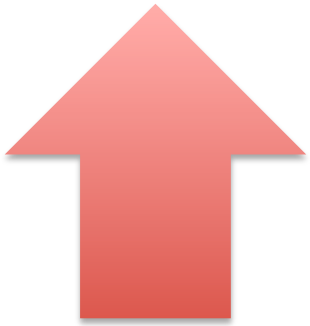


Hypocretin neurons are active during wake



Cortex

Locus ceruleus, dorsal raphe and tuberomamillary nuclei

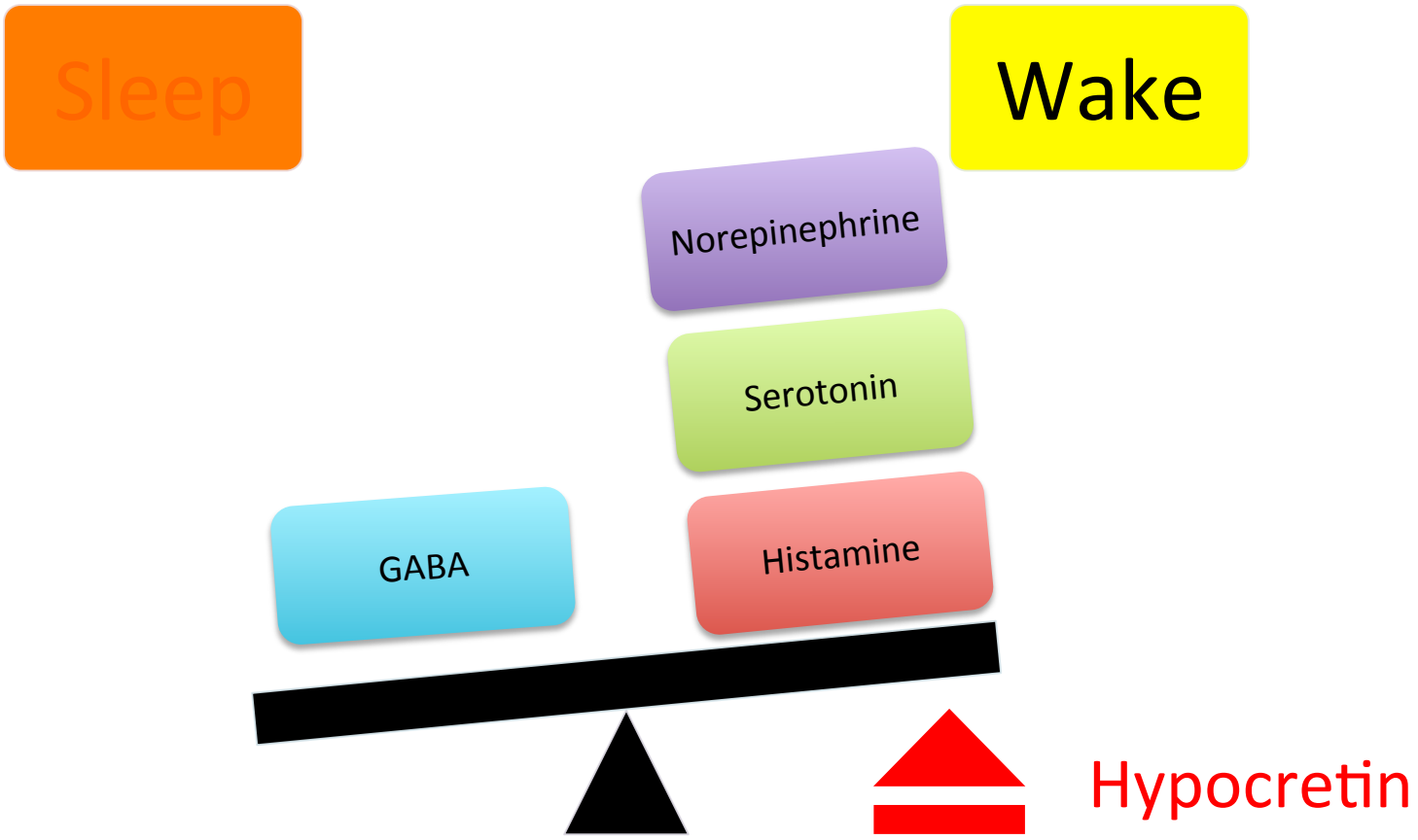


Cortex

Locus ceruleus, dorsal raphe and tuberomamillary nuclei

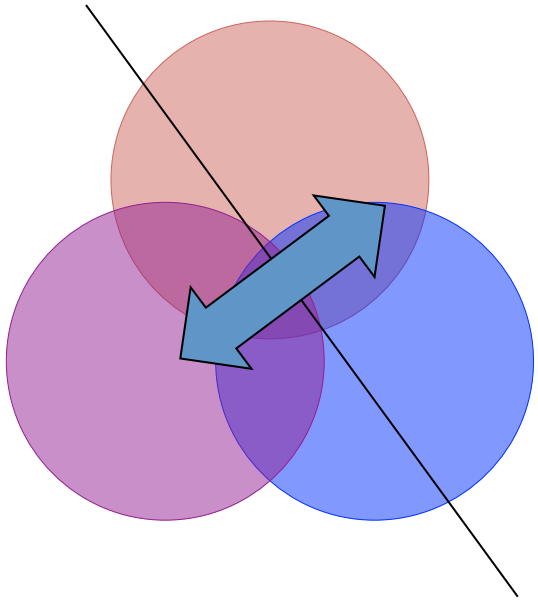
Hypocretin neurons suppress REM sleep

Hypocretin stabilizes the sleep-wake switch.



Thalamocortical circuit switch

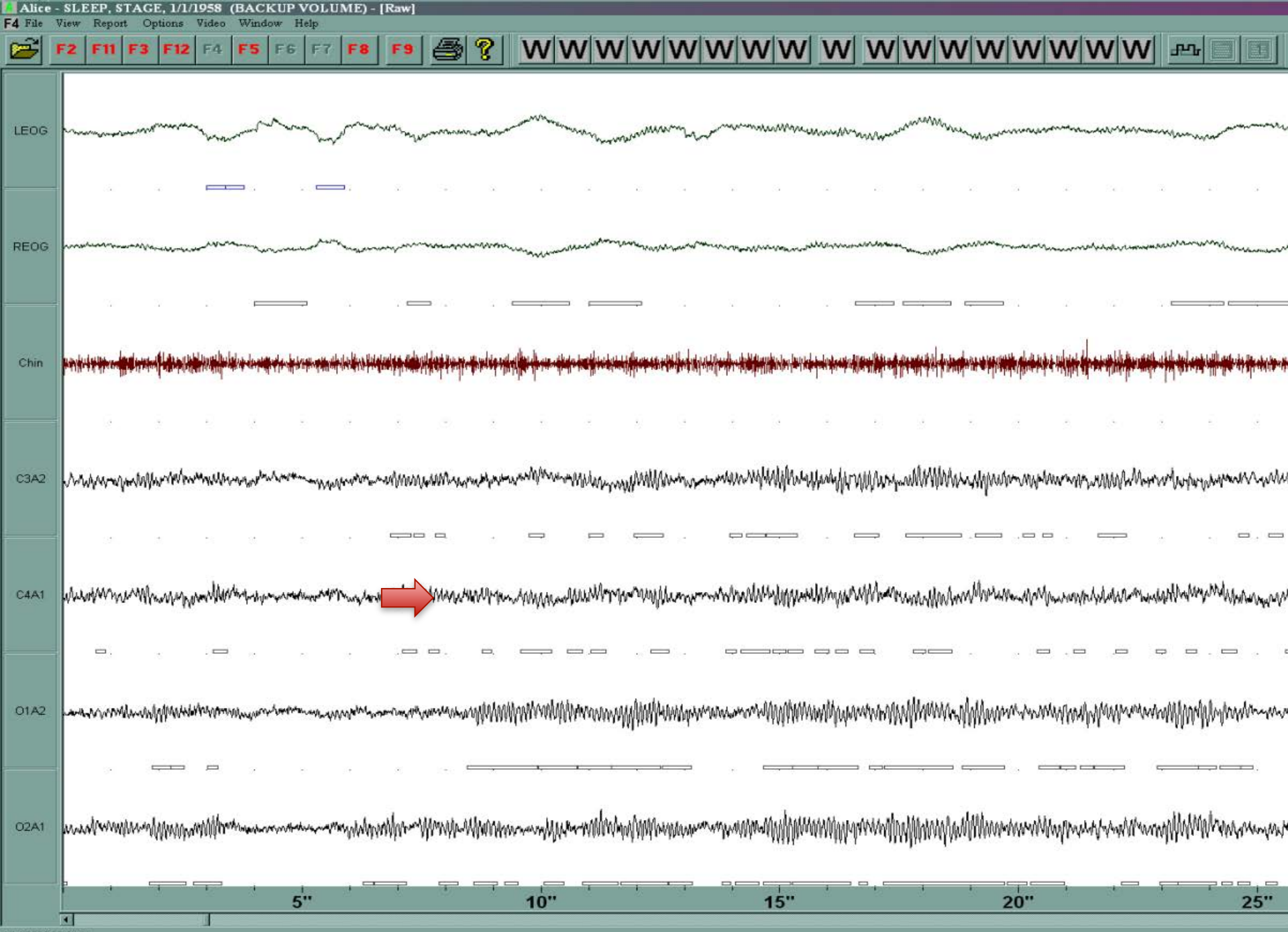
NREM

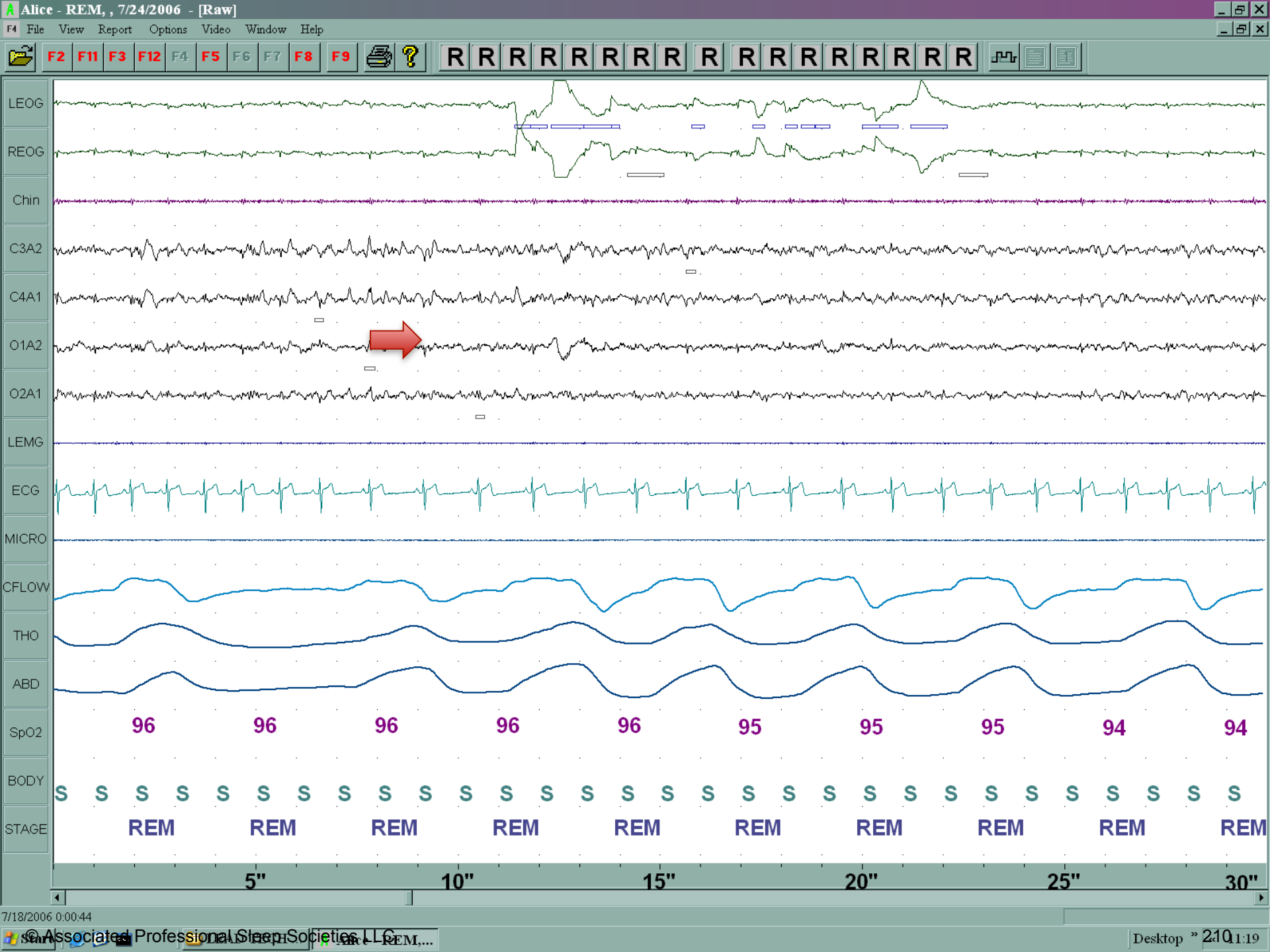


Wake/REM

Wake/REM sleep

Presence
of excitatory inputs
(Ach, etc.)
⇓
Depolarization
(excitation) of
thalamocortical
neurons



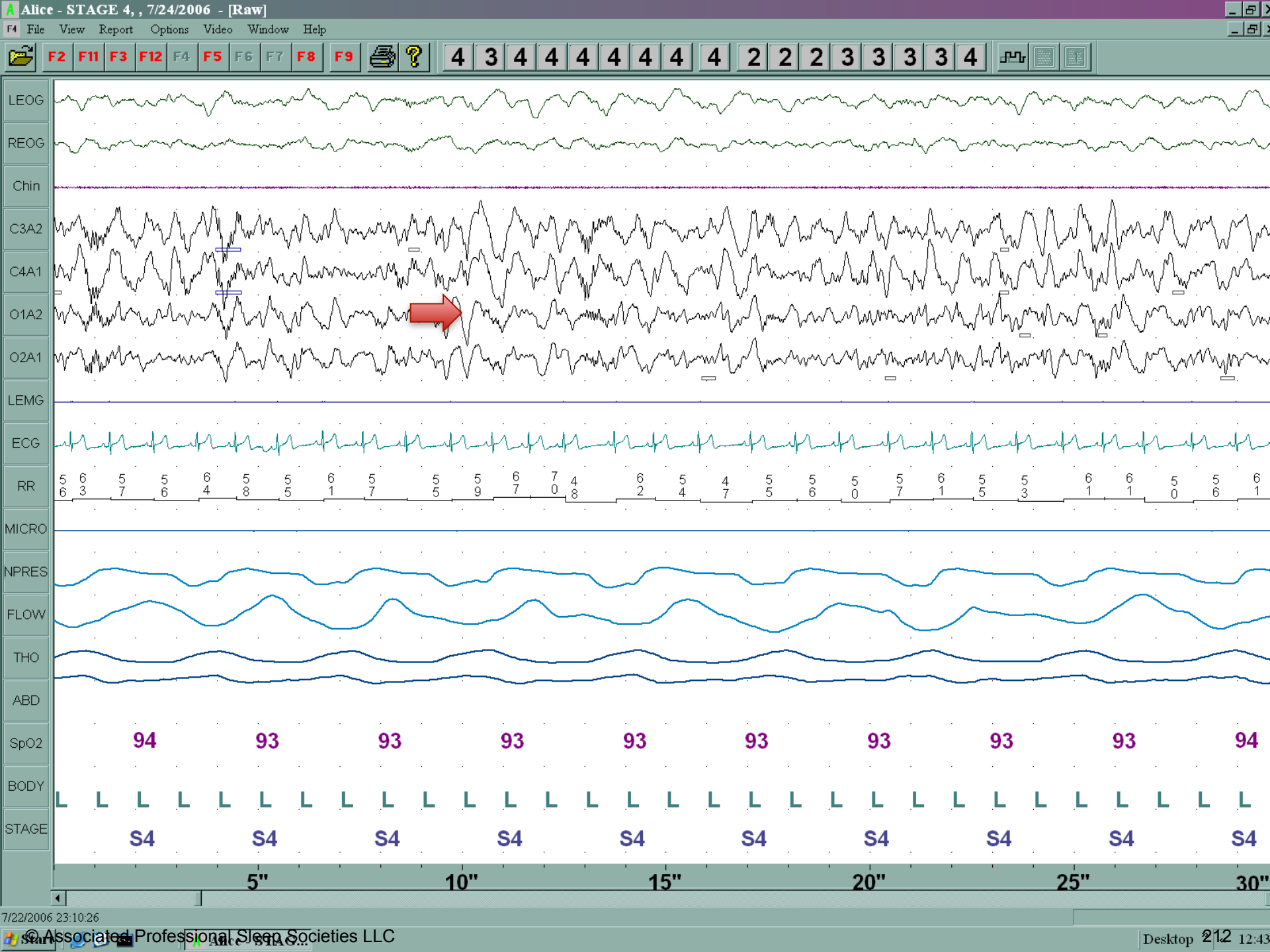


Wake/REM sleep

Presence
of excitatory inputs
(Ach, etc.)
⇓
Depolarization
(excitation) of
thalamocortical
neurons

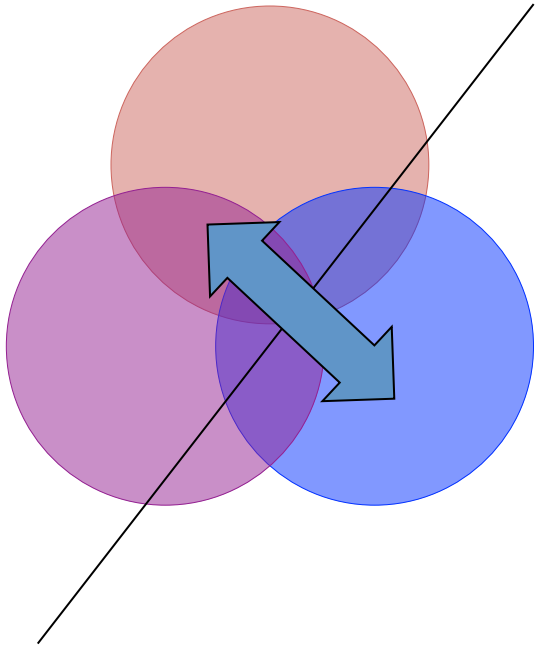
NREM sleep

Removal
of excitatory inputs by
GABA
⇓
Hyperpolarization
(inhibition) of
thalamocortical
neurons



REM-on/REM-off switch

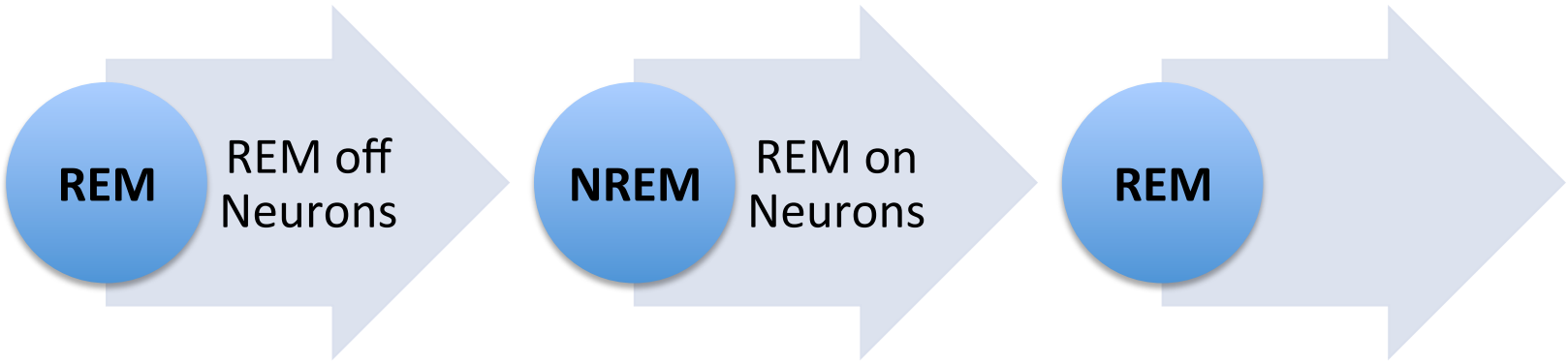
NREM



REM

"REM-on" neurons – acetylcholine

"REM-off" neurons – N-S-H



REM-on neurons are inhibited by REM-off neurons

Bottom Line: Neurotransmitters

	Wake	NREM	REM
Acetylcholine	⇑⇑	X	⇑
Glutamate	⇑	X	⇑

Bottom Line: Neurotransmitters

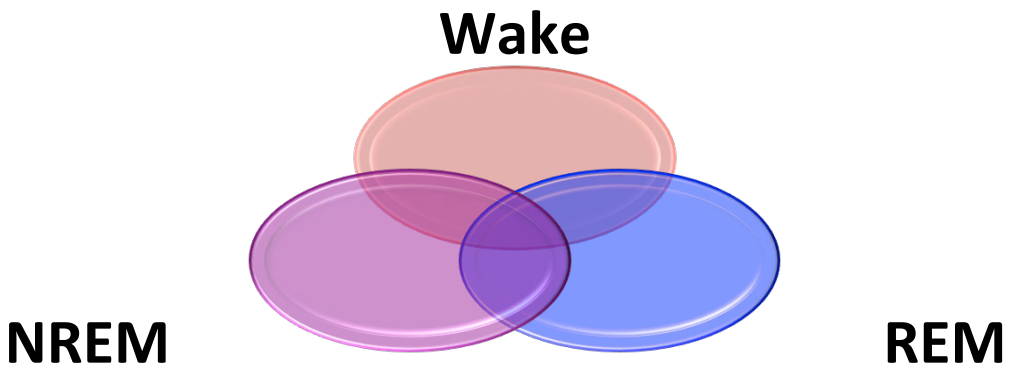
	Wake	NREM	REM
Norepinephrine	⇑	X	X
Serotonin	⇑	X	X
Histamine	⇑	X	X
Hypocretin	⇑	X	X

Bottom Line: Neurotransmitters

	Wake	NREM	REM
GABA	X	⇑	⇑

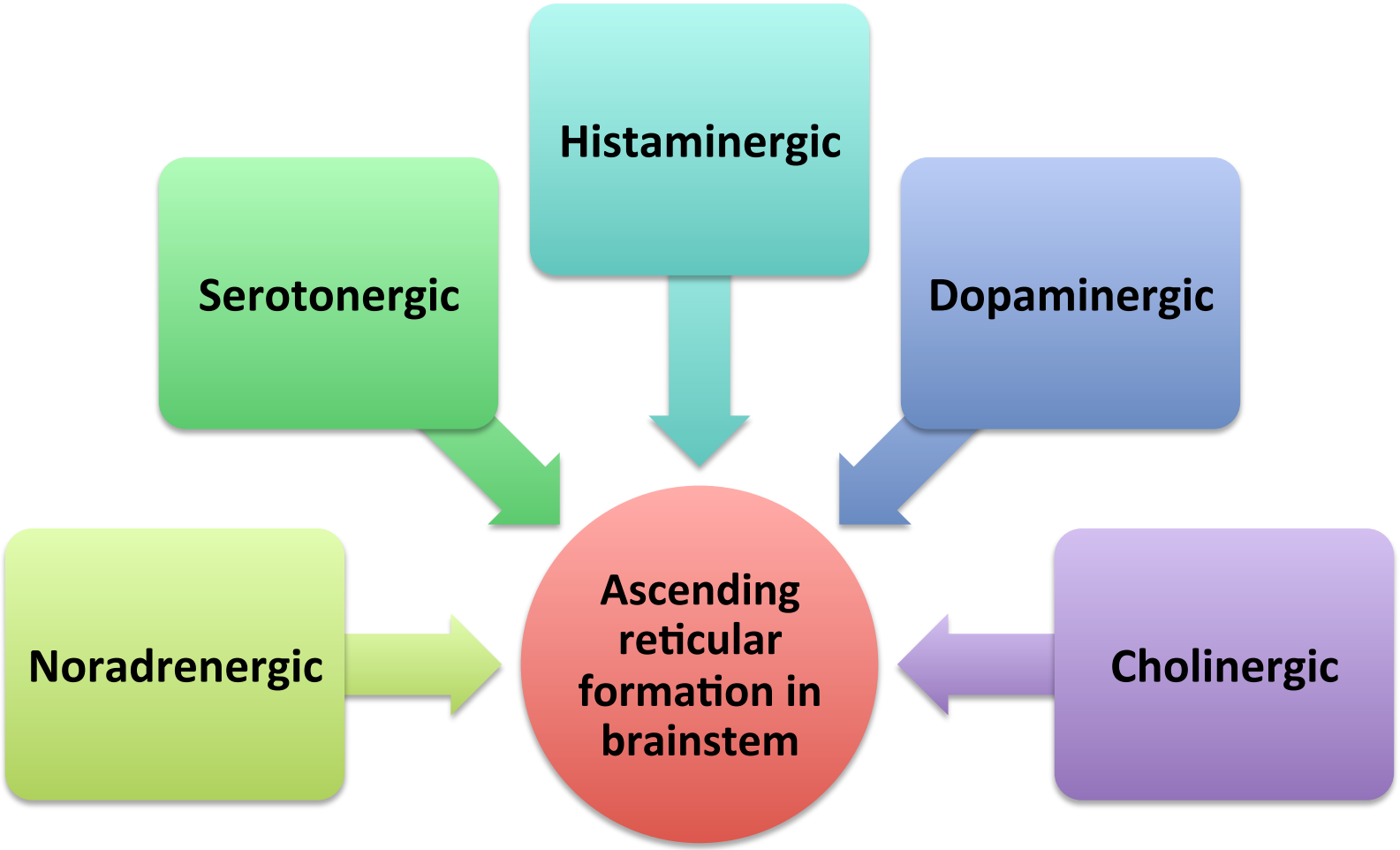
Bottom Line: Neurotransmitters

	Wake	NREM	REM
Acetylcholine	⇑⇑	X	⇑
Glutamate	⇑	X	⇑
Norepinephrine	⇑	X	X
Serotonin	⇑	X	X
Histamine	⇑	X	X
Hypocretin	⇑	X	X
GABA	X	⇑	⇑

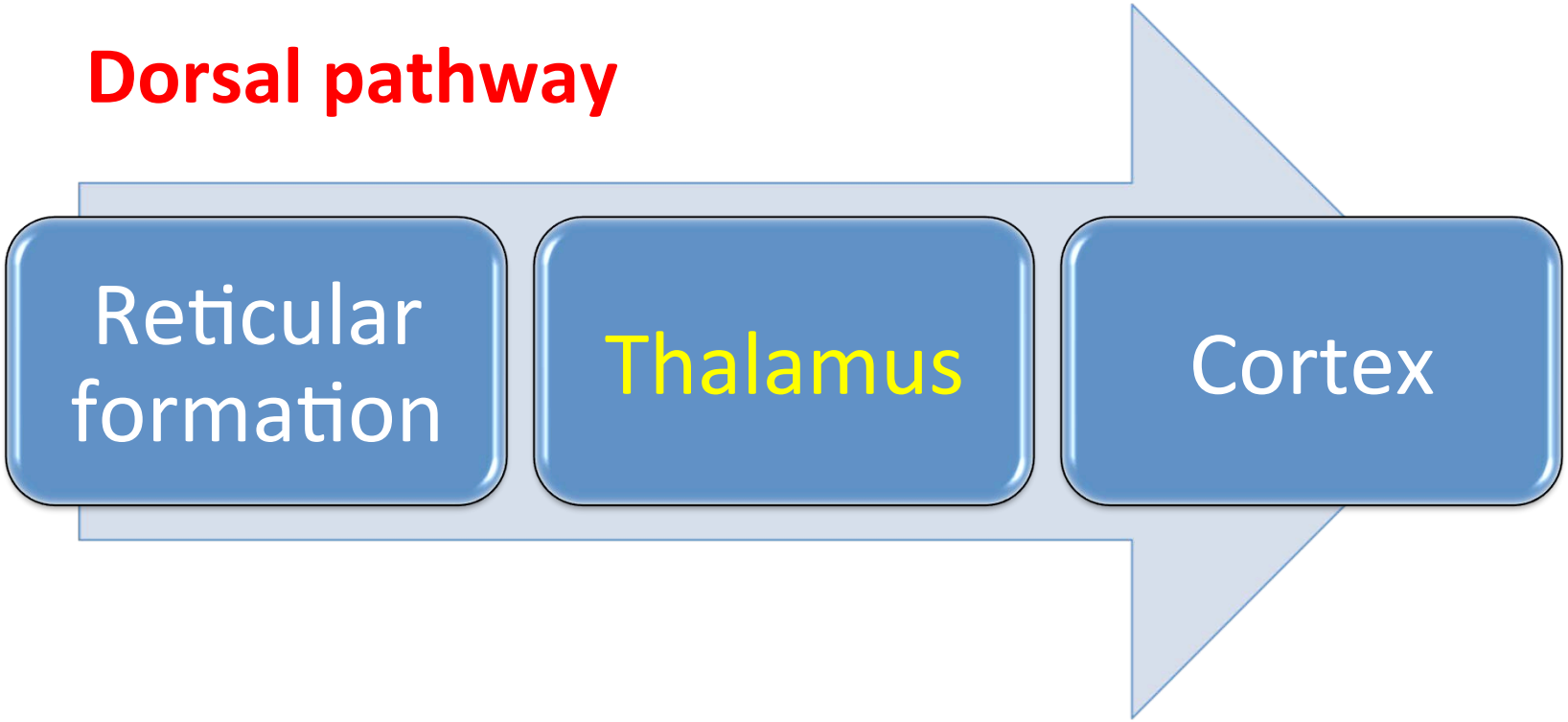


≥ 7 transmitters to form the stages
3 switches to control the changes
In the land of sleep
Where the shadows lie

Neural regulation of waking



RF: Ascending Pathways



RF: Ascending Pathways

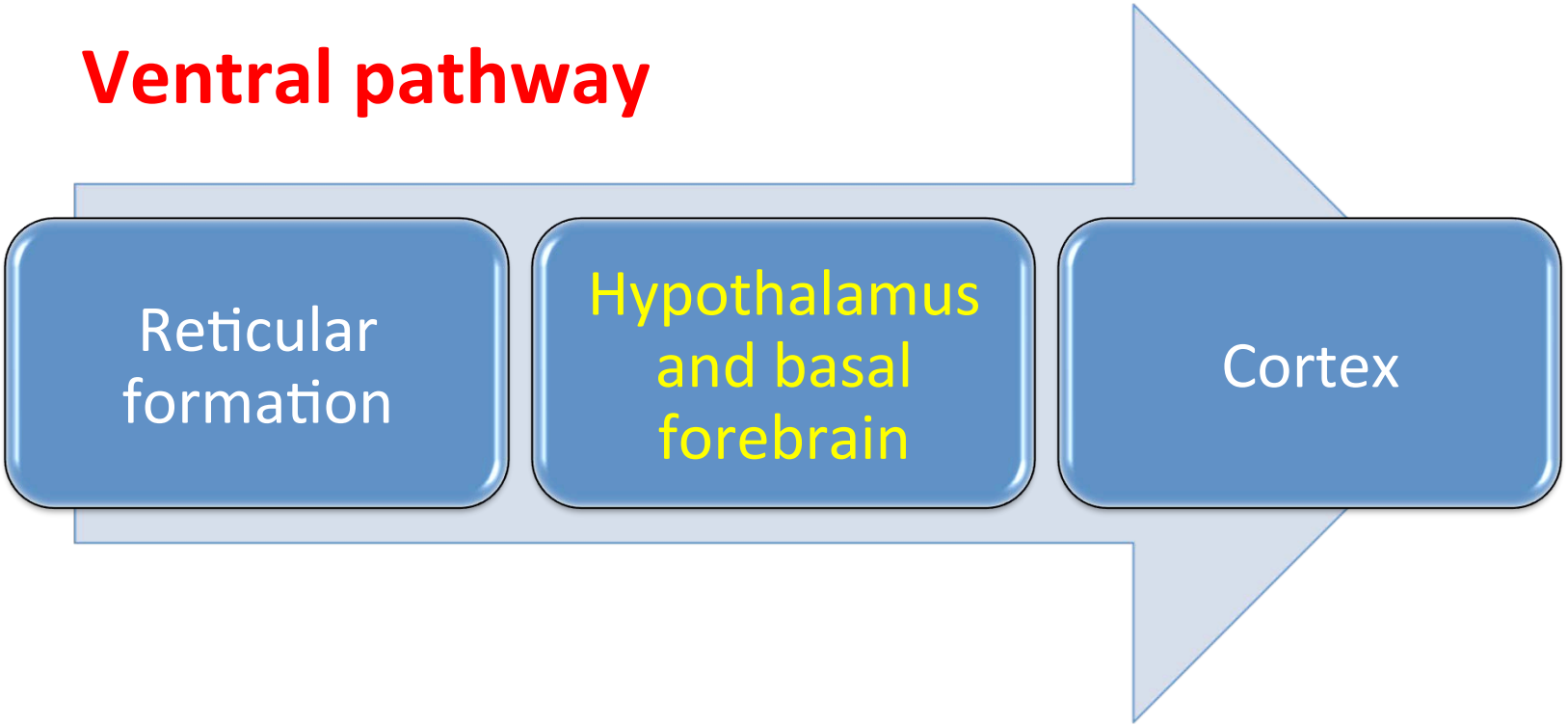
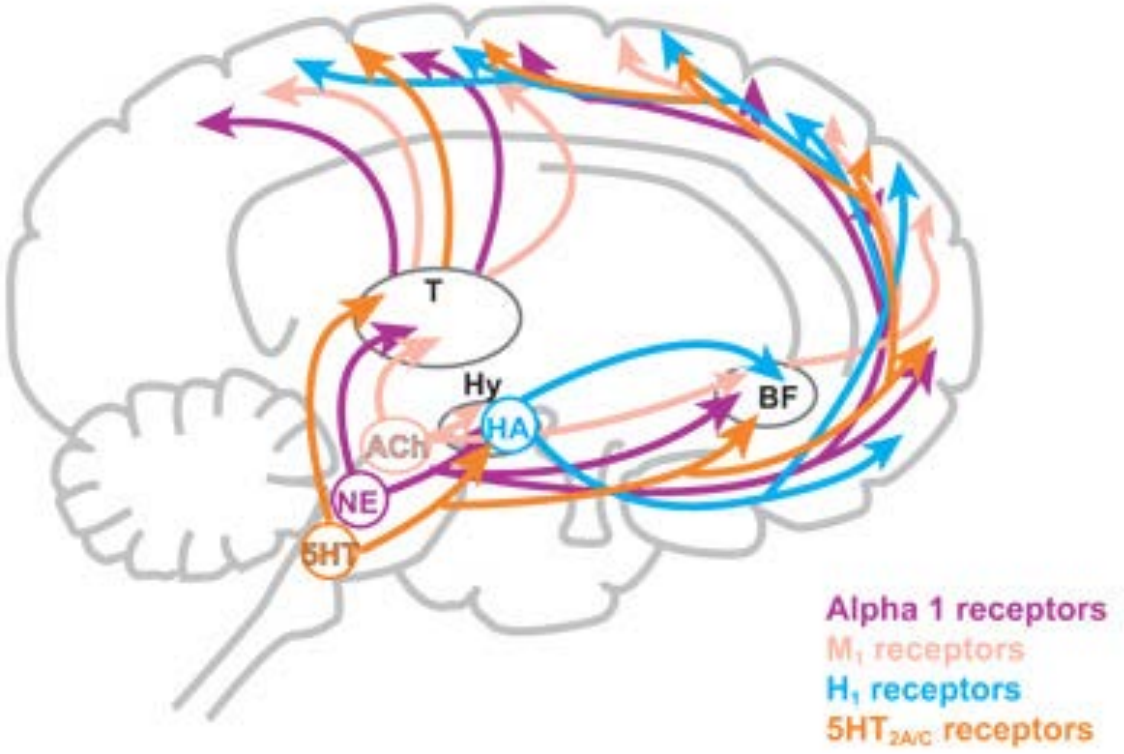


FIGURE 1.
Cortical Arousal



T=thalamus; Hy=hypothalamus; ACh=acetylcholine; HA=histamine; BF=basal forebrain; NE=norepinephrine; 5-HT=serotonin; M=muscarinic; H=histamine.

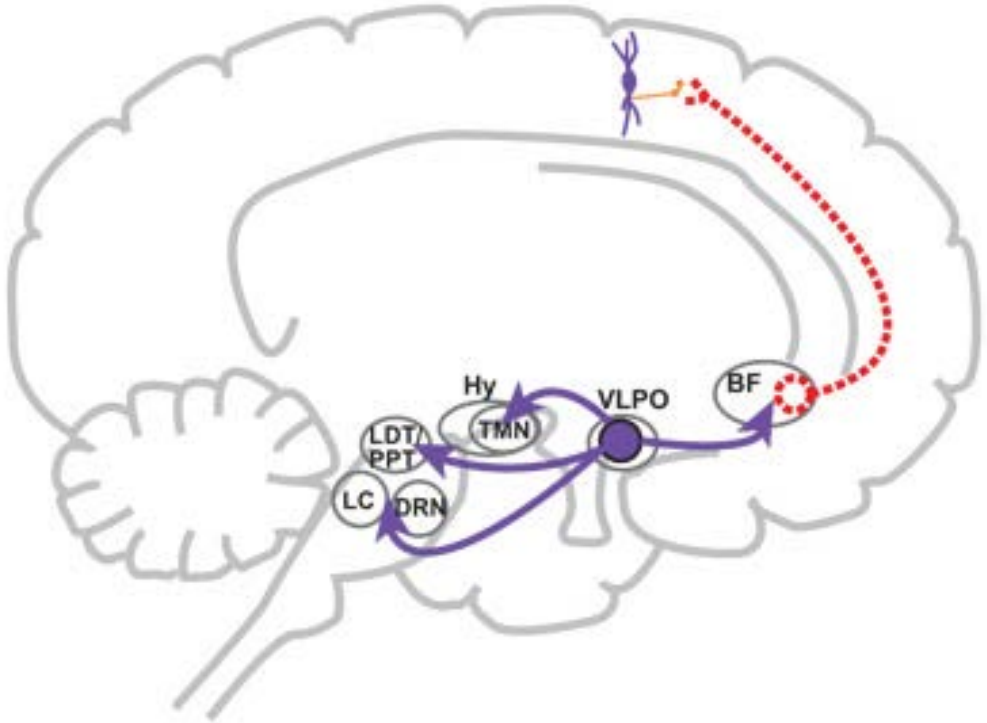
Stahl SM. *CNS Spectr.* Vol 13, No 12. 2008.

Neural regulation of sleep

VLPO – GABA NREM
REM

PPT/LDT – Ach REM

FIGURE 2.
Sleep-promoting GABA system

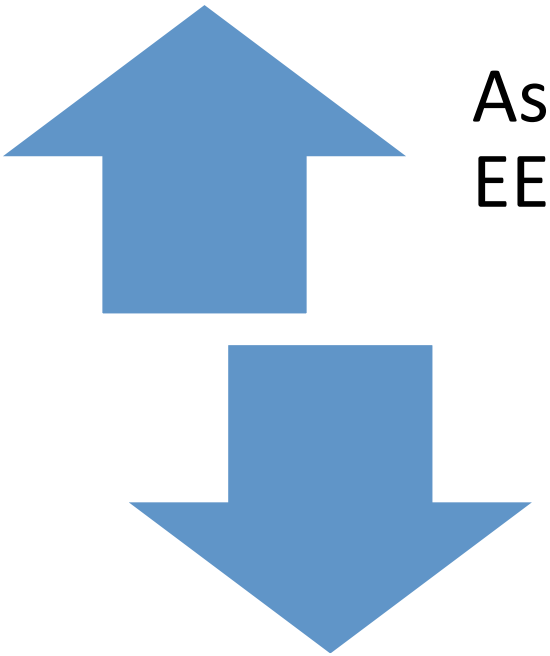


GABA=□-aminobutyric acid; Hy=hypothalamus; BF=basal forebrain; LDT=laterodorsal tegmental; PPT=peduncolopontine tegmental; TMN=tuberomamillary nucleus; VLPO=ventrolateral preoptic nucleus; LC=locus coeruleus; DRN=dorsal raphe nucleus.

Stahl SM. *CNS Spectr.* Vol 13, No 12. 2008.

Pontine LDT/PPT

REM-on neurons



Ascending: produce EEG desynchrony

Descending: produce muscle atonia

Pons (perilocus coeruleus of the pontine tegmentum)

⇓

Lateral tegmento-reticular tract

⇓

Medullary magnocellularis neurons

⇓

Ventrolateral reticulospinal tract

⇓

Motor neurons of the anterior horn cells of the spinal cord

(neurotransmitter: glycine)

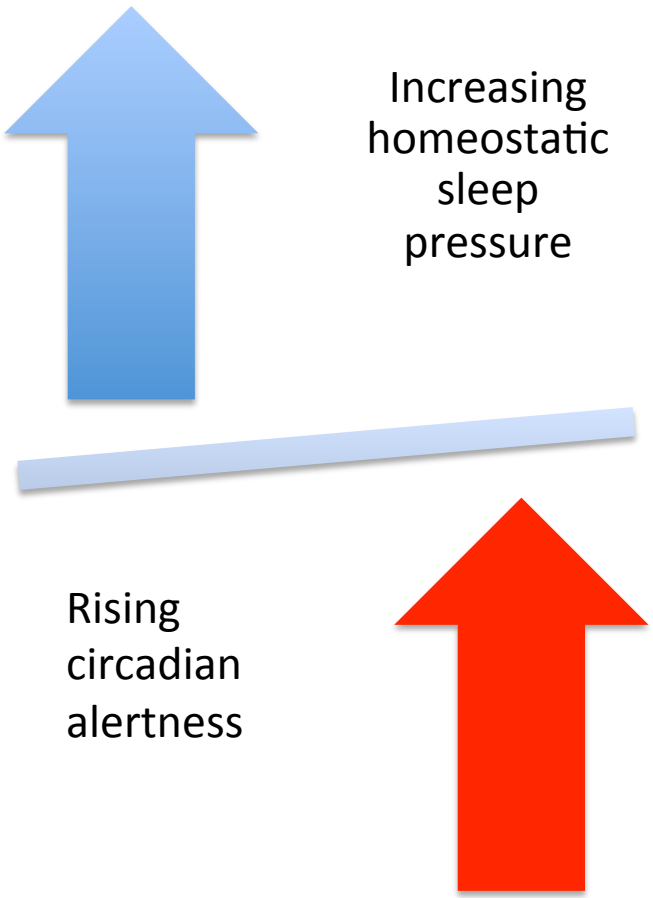
Two processes control the timing of sleep and wake

Sleep homeostasis - dependent on the sleep-wake cycle

Circadian rhythm - independent of the sleep-wake cycle

Sleep pressure that increases with prior wakefulness and declines with sleep	Sleep homeostasis
Main role is to promote wakefulness	Circadian rhythm

Waking period



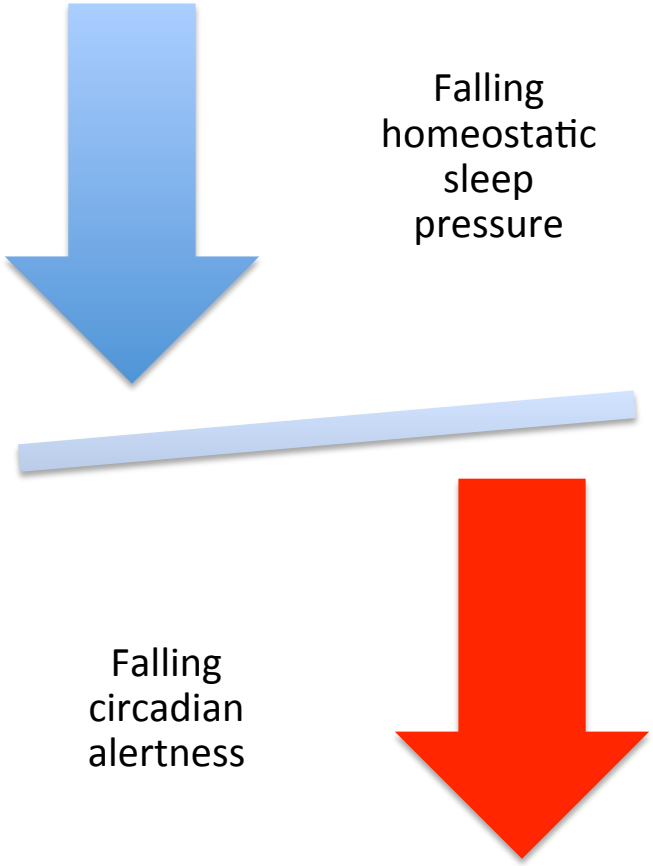
Constant alertness throughout the waking period

- Increase in homeostatic sleep pressure is opposed by rising circadian alertness

Sleep period

Constant sleepiness throughout the sleep period

- Decreasing homeostatic sleep pressure is opposed by falling circadian alerting tendency



Free running

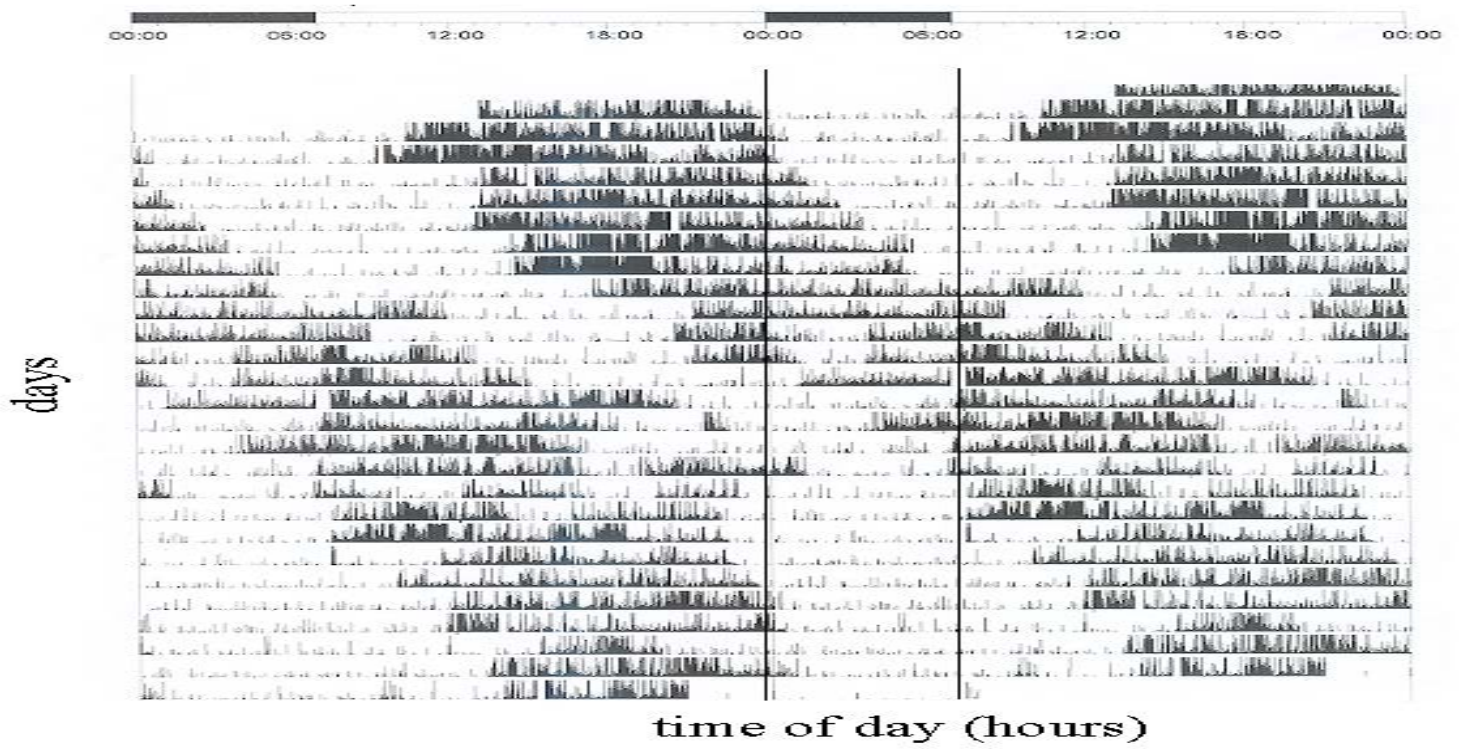
Circadian rhythms free-run at a genetically-determined frequency in the absence of environmental time cues (*tau*)

Free running

Most human circadian rhythms are not exactly 24 hours

Commonly about

tau 24.2 hours



Moore R et al. Sleep: A comprehensive handbook. Wiley 2006

Entrainment

Process by which external cues adjust the phase of the intrinsic circadian rhythms

Synchronizes the intrinsic circadian cycle to the environmental 24-hour period

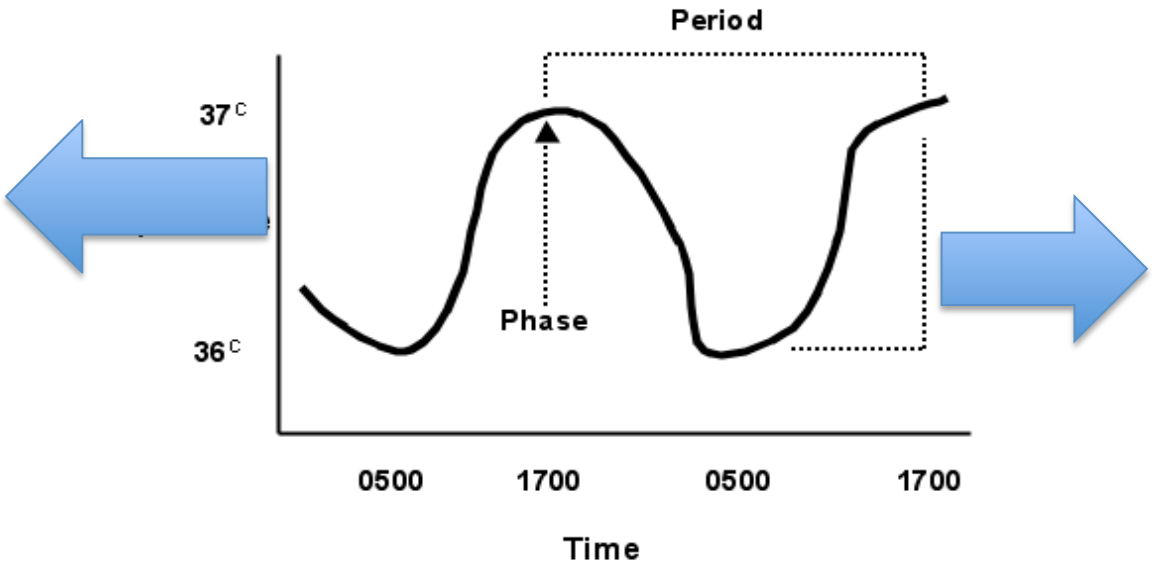
Entrainment

Process by which external cues adjust the phase of the intrinsic circadian rhythms

Synchronizes the intrinsic circadian cycle to the environmental 24-hour period

Forward or backward

Phase is the cycle's position in time relative to an external measurement, such as clock time.



Phase advancement

Phase delay

Sleep: a comprehensive handbook, 2006

	Maximum	Minimum
Gastric acid secretion	Between 10 PM and 2 AM	Between 5 AM and 11 AM
Cortisol	8-9 AM	12 AM
Thyroid stimulating hormone	Between 9 PM and 6 AM	Between 10 AM and 7 PM

Circadian timing systems

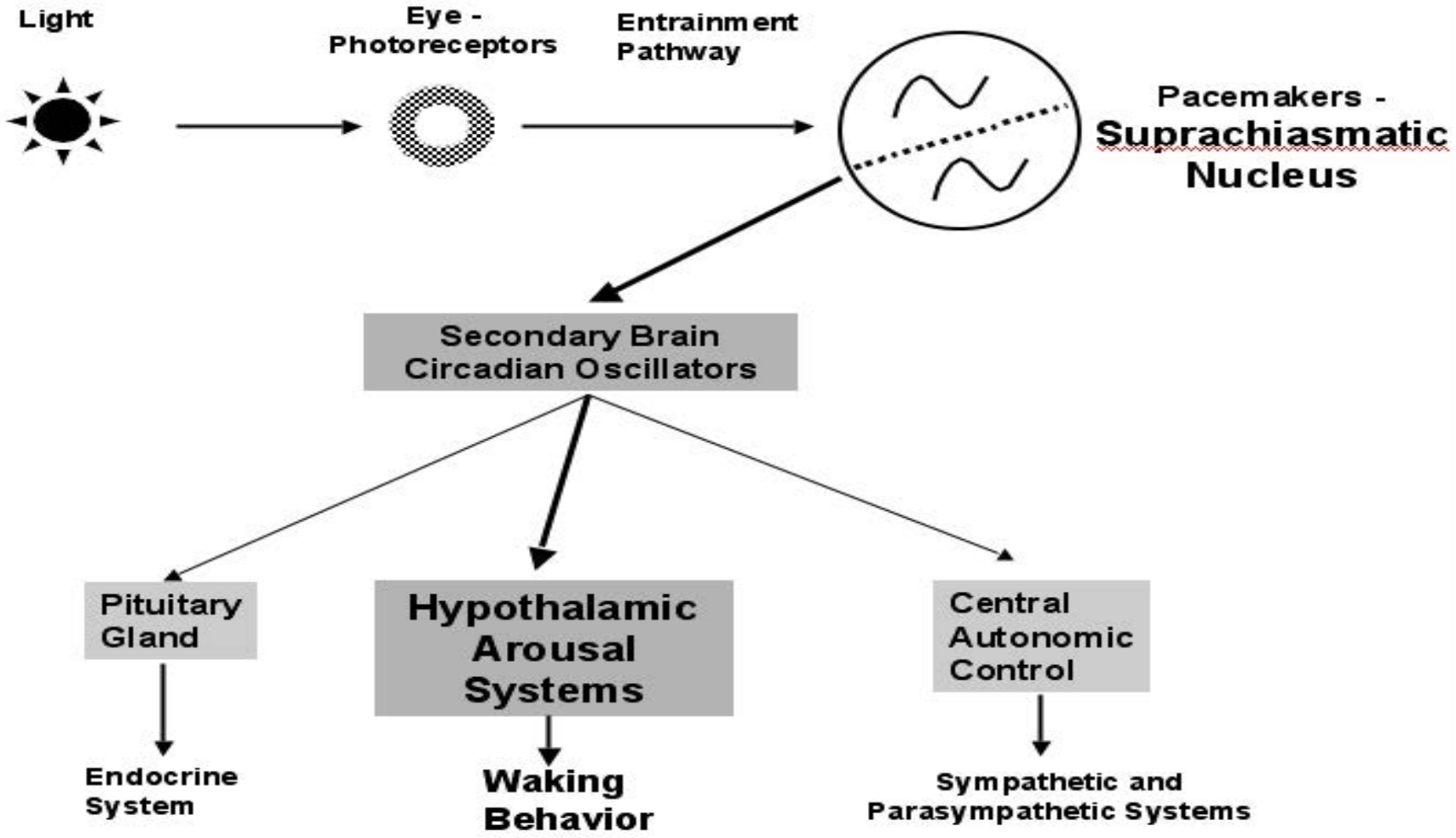
Suprachiasmatic nucleus is the master circadian rhythm generator in mammals

Circadian timing systems

Suprachiasmatic nucleus is the master circadian rhythm generator in mammals

Promotes wakefulness during the day

Consolidates sleep during the night



Sleep: a comprehensive handbook, 2006

Afferent SCN pathways

Glutamatergic

Retina ganglion cells with
melanopsin
(most sensitive to
blue to blue-green light)
⇓
Retinohypothalamic tract
⇓
SCN

Alternate

Afferent SCN pathways

Glutamatergic

Alternate

Eyes

⇓

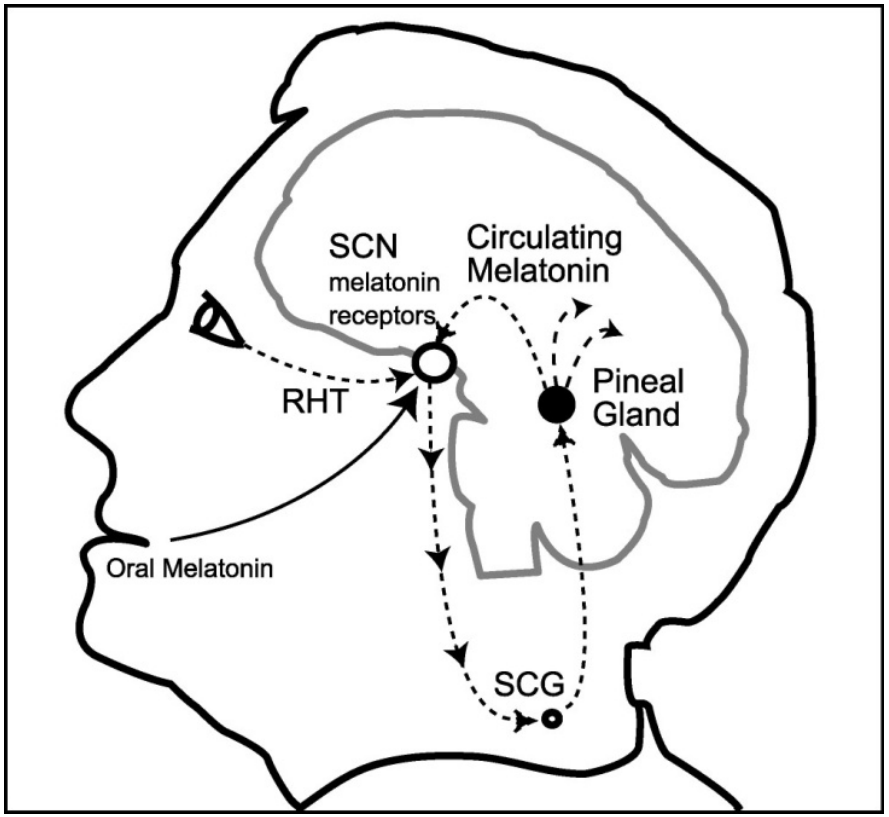
Lateral geniculate nuclei

⇓

Geniculohypothalamic tract

⇓

SCN



Sleep: a comprehensive handbook, 2006

Suprachiasmatic nucleus

⇓

Hypothalamus (para/ subventricular nuclei)

⇓

Medial forebrain bundle

⇓

Spinal cord (intermediolateral gray column neurons)

⇓

Superior cervical ganglion

⇓

Pineal gland

Biological markers

DLMO	CTmin
Dim light melatonin onset	Minimum core body temperature
2-3 hours before bedtime	2-3 hours before wake time

Biological markers

DLMO CTmin

before bedtime before wake time

Melatonin

Synthesized and released by the pineal gland

Melatonin

- Greatest secretion at night
- Secretion suppression by light exposure

Melatonin

Two melatonin receptors

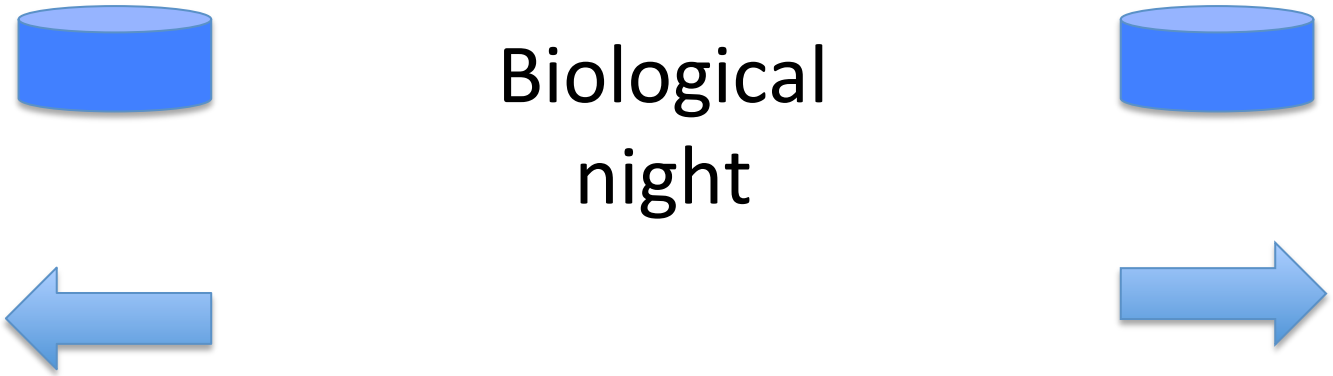
MT1	Inhibits firing of SCN
MT2	Phase-shifting action

*Also possess mild hypnotic properties

Melatonin

Taken in the evening ⇒ phase advances circadian rhythms

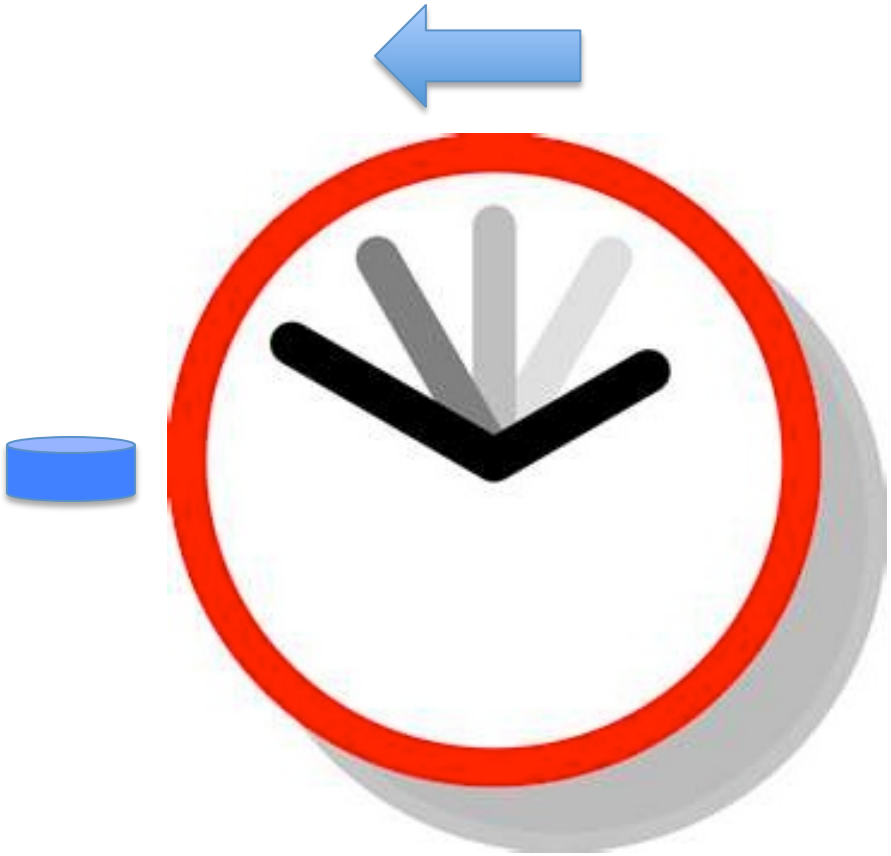
Taken in the morning ⇒ phase delays circadian rhythms



Melatonin

Evening melatonin phase advances circadian sleep-wake rhythms

Melatonin = Magnet (pulls sleep towards it)



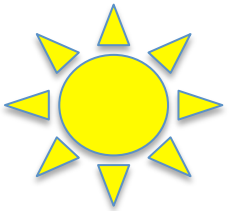
Evening melatonin

Light exposure

Before CTmin ⇒
phase delays
circadian rhythms

After CTmin ⇒
phase advances
circadian rhythms

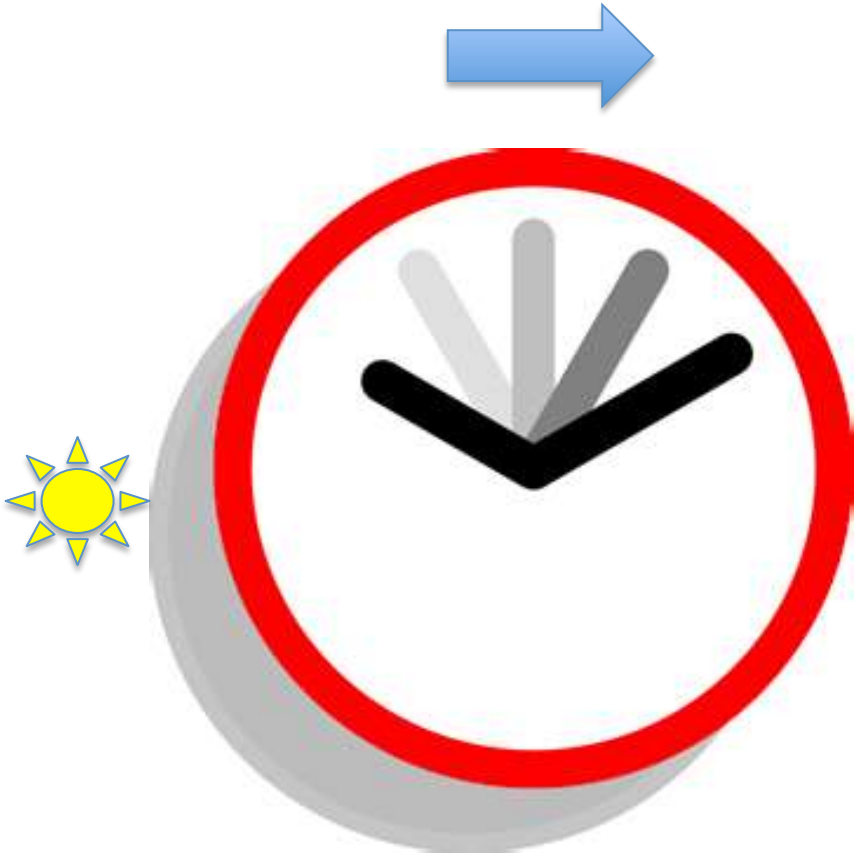
2-3 hours
before
wake time



Light exposure

Evening light exposure (before CTmin) ⇒ phase delays circadian rhythms

Phototherapy = phush (pushes sleep away from it)



Evening light

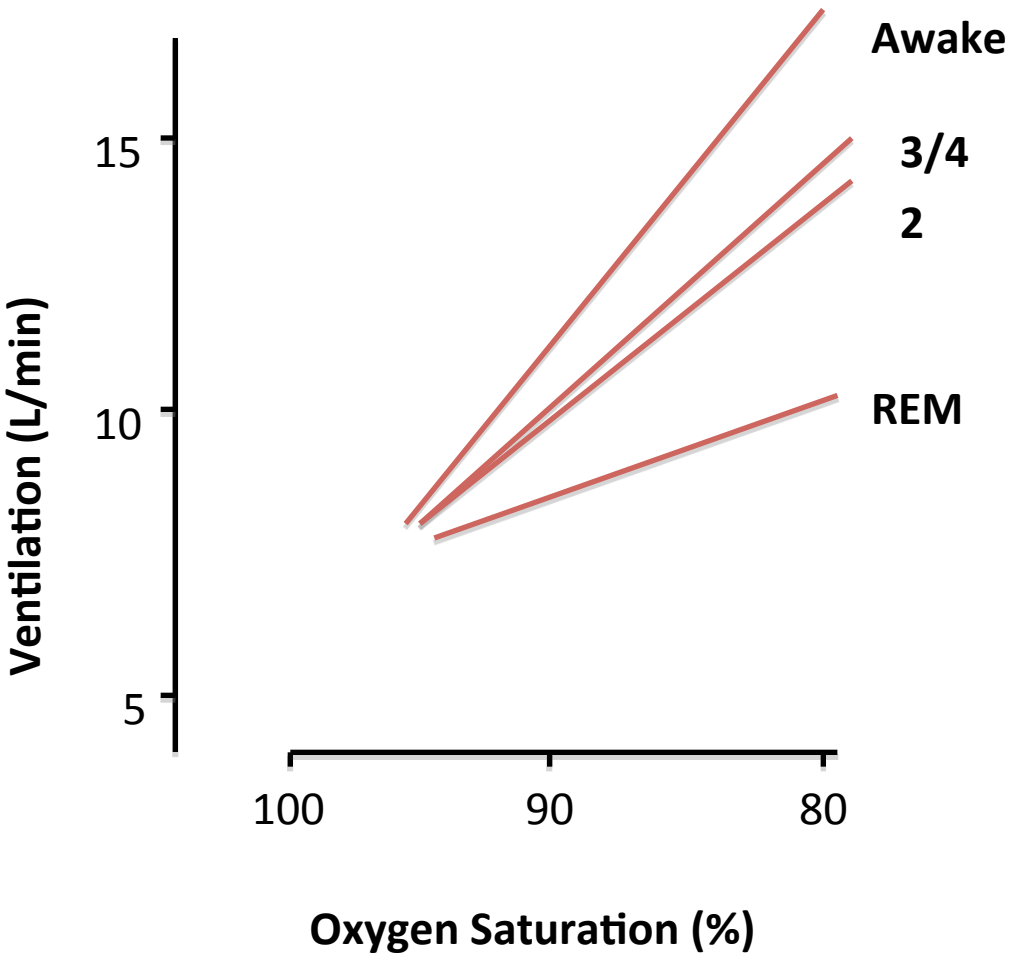
Sleep physiology

What goes down during sleep

Respiratory system

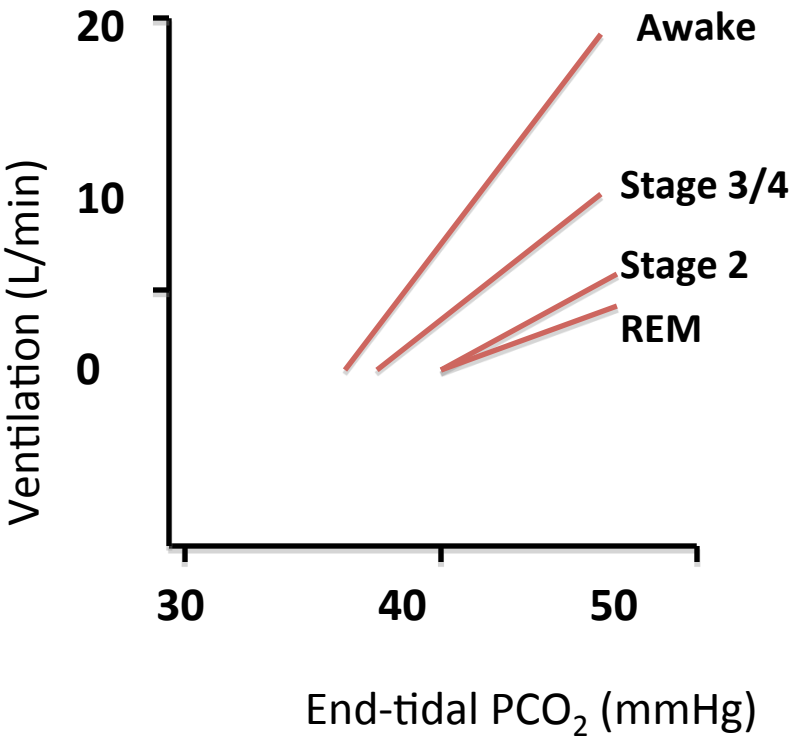
- PaO2 and SaO2
- Tidal volume and minute ventilation
- UA dilator muscle tone
- Activity of accessory muscles of respiration
- Hypoxic and hypercapnic ventilatory responses

Ventilatory response to hypoxia



Douglas NJ. Clin Chest Med 1985;6:563
Principles and Practice of Sleep Med 2010

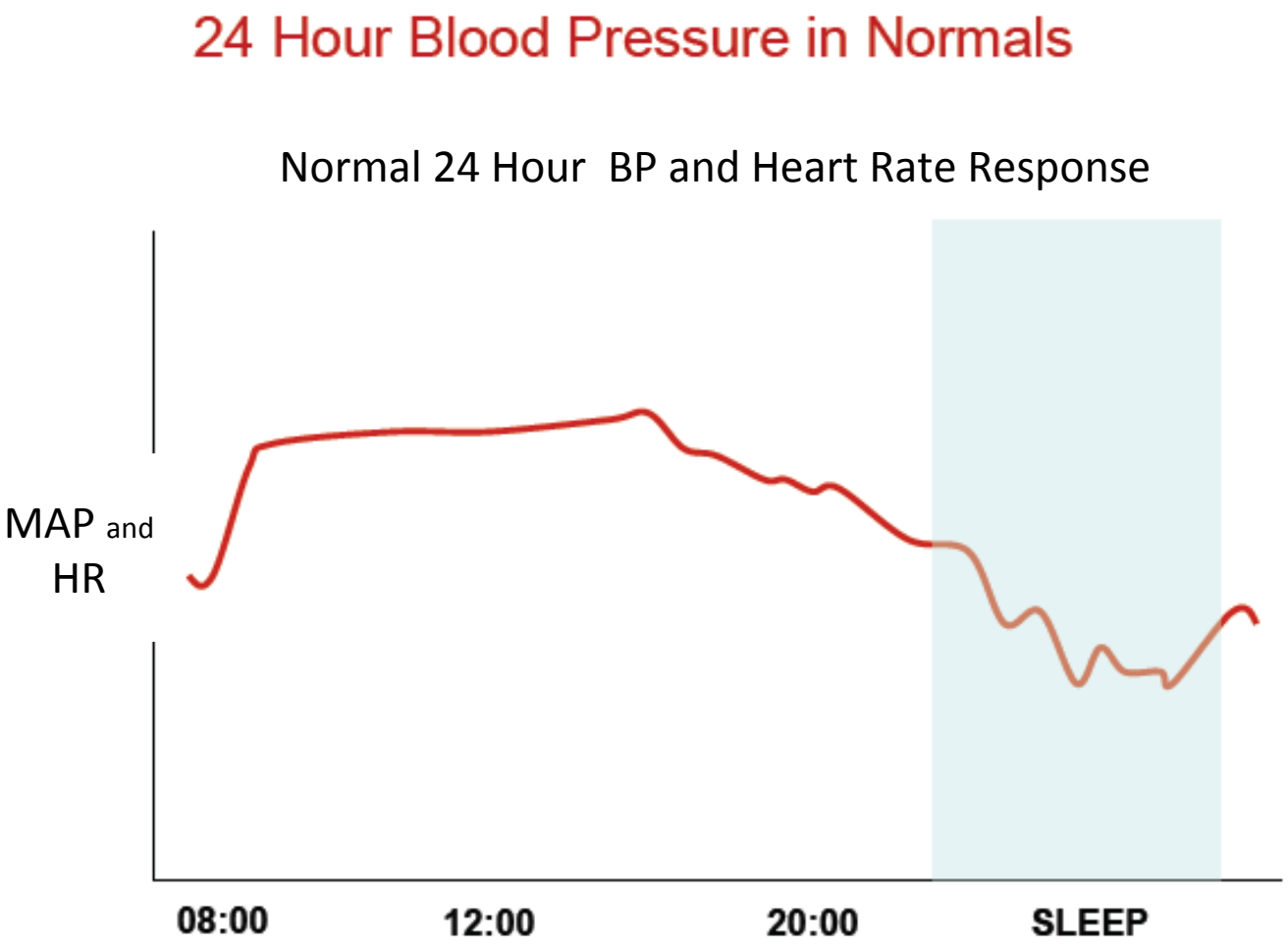
Ventilatory response to hypercapnia



Douglas NJ Clin Chest Med 1985

	What goes down during sleep
Cardiovascular system	HR, CO and BP (NREM and tonic REM sleep) Frequency of PVCs
Gastrointestinal system	Swallowing rate and salivary production Esophageal and intestinal motility
Renal system	Glomerular filtration

BP and HR during sleep



What goes down during sleep

Endocrine system	Cortisol (in N3 sleep) Insulin secretion
Other	Sympathetic activity Muscle tone Core body temperature and thermoregulatory responses Metabolic rate (in NREM)

Physiology goes down
when you lay down
to sleep

Thus, it might be easier to
remember what goes up…..

What goes up during sleep

Growth hormone	Endocrine
Prolactin	system
Renin	
Antidiuretic hormone	
Testosterone	
Parasympathetic activity	Others
PaCO2	
Renal water reabsorption	

Hormone secretion during sleep

	Linked primarily to:
Cortisol	Circadian rhythms
Growth hormone	Sleep (in N3 sleep)
TSH	Both sleep and circadian rhythms

Hormone secretion during sleep

	Linked primarily to:
Cortisol	**C**ircadian rhythms
Growth hormone	Sleep (in N3 sleep)
TSH	Both sleep and circadian rhythms

Immunity and sleep

Pro-inflammatory cytokines —IL-1β and TNF-α	Increases sleepiness
Anti-inflammatory cytokines —IL-4, IL-10	Decreases sleepiness

Immunity and sleep

Pro-inflammatory cytokines
—IL-1β and TNF-α

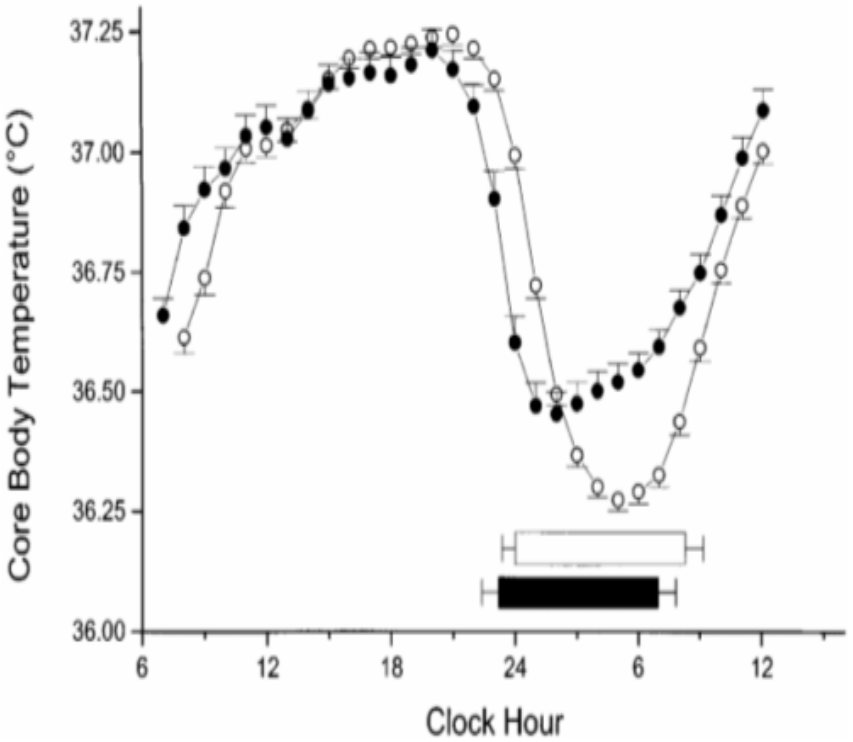
Pro-sleep

Anti-inflammatory cytokines
—IL-4, IL-10

Anti-sleep

Thermoregulation during sleep

- CT peaks in the late afternoon and early evening: 6-8 pm
- Falls at the onset of sleep
- Nadir at 2 hours prior to usual wake time: 4-5 am



Baker FC et al 2001

Thermoregulation during sleep

Sleep occurs during the falling phase of the temperature rhythm (after CTmax)

Waking occurs during the rising phase of the temperature rhythm (after CTmin)

Thermoregulation during sleep

Sleep occurs during the falling phase of the temperature rhythm (after CTmax)

Cool down to sleep sound

Waking occurs during the rising phase of the temperature rhythm (after CTmin)

Heat up to wake up

Thermoregulation during sleep

Initiating sleep during the falling phase of the temperature rhythm

↓ SOL
↑ TST
↑ N3

Thermoregulation during sleep

Falling asleep is faster during the falling phase of the temperature rhythm

↓ SOL
↑ TST
↑ N3

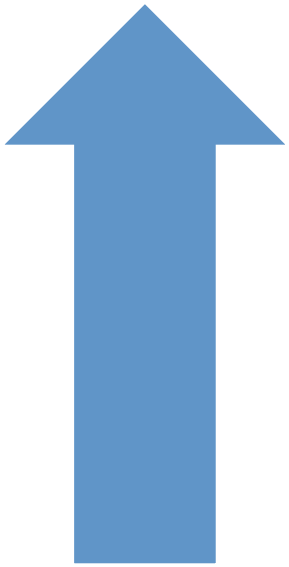
Sleep deprivation

SD ≠ SR

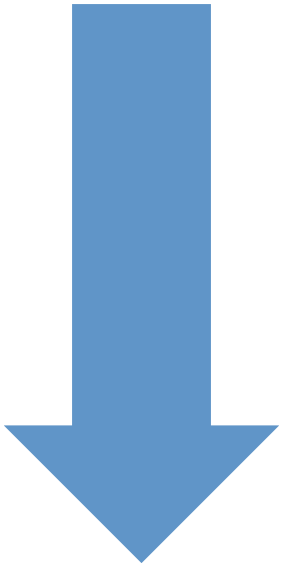
- Vulnerability to SD varies within individuals across time and between individuals
- Consequences of total SD appear to differ those of chronic sleep restriction

SD ≠ SR

Persons often underestimate the negative impact of SD on cognition and performance



- Sympathetic activity
- Insulin resistance
- Cortisol
- Metabolic rate
- Mortality



- Vigilance / cognition
- Growth hormone
- Seizure threshold
- Resistance to infection
- Pain tolerance

Sleep deprivation

Sleep PSG

Shortened SOL
Increased TST
Greater N3 sleep
- 1st night after SD
Greater REM sleep
- 2nd night after SD

Sleep deprivation

Wake EEG	Shift to slower EEG frequencies (theta and delta waves)

Ghrelin	Leptin
Gastric cells	Lipid cells
Gorge	Less food
Gain weight	Lose weight
Ginormous	Lean
Greater levels in SD	Less levels in SD

Ghrelin	Leptin
Gastric cells	Lipid cells
Gorge	Less food
Gain weight	Lose weight
Ginormous	Lean
Greater levels in SD	Less levels in SD

Pediatric sleep

Pediatric sleep architecture

Initial sleep episode

Active sleep – < 3 months of age

Quiet sleep – > 3-4 months of age

Pediatric sleep architecture

Proportion of NREM-REM sleep

50:50 in infants

75:25 among adolescents and adults

Pediatric sleep architecture

Percentage of REM sleep

50% of TST in infants

25% of TST in adolescents and adults

Pediatric sleep architecture

NREM-REM cycle length

50-60 minutes in infants

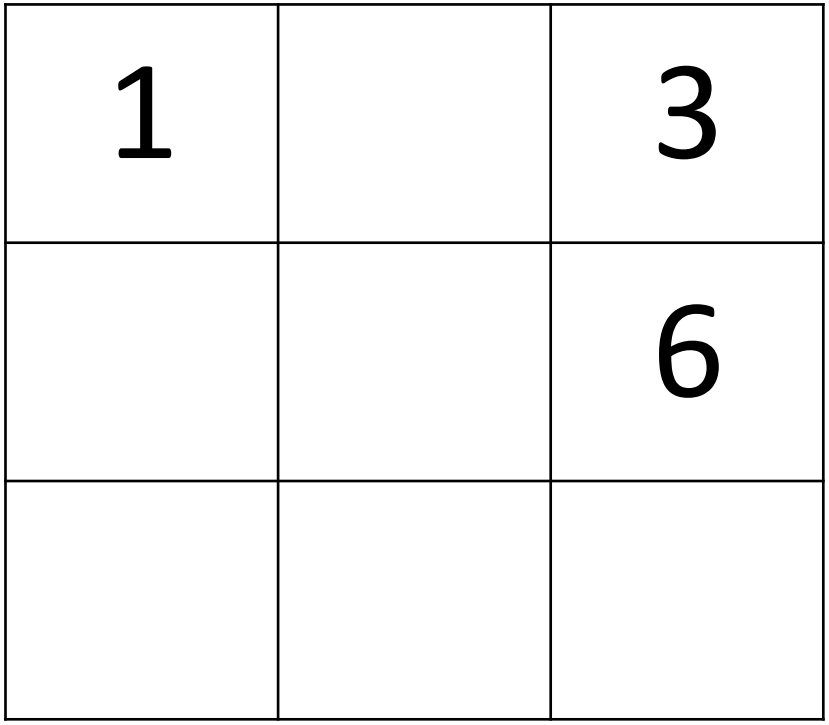
90-120 minutes in adults

Age at which specific EEG features first develop

1 month	Sleep spindles
3 months	Delta waves
6 months	K complexes

Age at which specific EEG features first develop

1 month	SO
3 months	DO
6 months	KU



Age at which specific EEG features first develop

28-30	Active sleep
	Quiet sleep
32	Trace' discontineau
36	Trace' alternant

*weeks of gestation

	Age at which specific behaviors first develop
6 weeks	Longest sleep period occurring at night
6-9 months	Ability to sleep through the night
3-6 years	Cessation of daytime napping

Age at which specific behaviors first develop

6 weeks	Mostly night
6 months	All night
6 years	Only night

TST gradually decreases throughout childhood

< 1 month	19 hours
< 1 year	15 hours
1-3 years	12 hours
3-5 years	10 hours
> 5 years	9 hours

TST gradually decreases throughout childhood

< 1 month	19	hours
< 1 year	15	(19 minus 4)
1-3 years	12	(15 minus 3)
3-5 years	10	(12 minus 2)
> 5 years	9	(10 minus 1)

Colic

Sustained episodes of crying > 3 hours
Onset generally at 3 weeks of age
Usually resolves by 3 months of age

Colic

Lasts 3 hours

Starts 3 weeks

Ends 3 months

2-4 months	Place a child to bed while drowsy but still awake
3 months	Transition infant to final sleep environment
≥ 6 months	Discontinue nighttime feedings in children

EDS: consider in any child > 5 years of age if

Nap during the day, especially if unplanned

Weekend sleep ≥ 2 hours more vs. weekdays

Inappropriate sleep (times or situations)

Hyperactivity, inattentiveness, irritability, or impulsiveness

Sleep in women

OSA is less common in pre-menopausal Women than in men

OSA is less common in pre-menopausal Women than in men.

- Less neck soft tissue volume
- Shorter pharyngeal airway length
- Lower pharyngeal compliance during sleep

Women are generally more symptomatic at comparable AHIs than men

Women are generally more symptomatic at comparable AHIs than men.

Fewer snoring and witnessed apneas

More insomnia and sleepiness

Greater mood disturbance

Women have different PSG findings

Women have different PSG findings.

- Lower AHI (at same BMI)
- Less supine position dependency
- Less O_2 desaturation

Women have worse survival than men with similar AHIs

Women have worse survival than men with similar AHIs.

More endothelial dysfunction

Greater myocardial injury

Less risk of stroke

Pregnancy

Sleep disturbance = 3rd > 1st > 2nd trimester

Increase in risk for OSA, RLS, nocturnal leg cramps, EDS

Menopause

Greater subjective complaints of sleep disturbance

Increased prevalence of insomnia and OSA

Consider gabapentin for treatment of hot flashes

M > F

Gender differences

SRBD[2]
(SRBD/S-RBD)

SRBD = Sleep related breathing disorders
- OSA (adult)
- CSA/CSB (in HF)
- OHS
- Snoring

S = Sleepiness
- Narcolepsy
- Kleine-Levin syndrome

RBD = REM behavior disorder

Gender differences

F > M

G-I-RLS

I = Insomnia

I = Idiopathic hypersomnia

RLS = Restless legs syndrome (adults)

Aging

Sleep requirements

Aging: The same

Nocturnal sleep disturbance

Excessive daytime sleepiness

Napping

Tolerance to sleep deprivation

Prevalence of insomnia, OSA, CSA, RLS, PLMD, RBD and ASPS

What goes up

Aging:

N3 sleep
Melatonin secretion
Amplitude of circadian sleep-wake rhythms
Homeostatic sleep drive
Arousal threshold
GH secretion during sleep
Tolerance to shift work and jet lag

Aging:
What goes down

Aging physiology itself (not major cause)
Menopause
Medical disorders (nocturia)

Causes of sleep disturbance in older adults

Neurological disorders (dementia, PD)
Psychiatric disorders (depression)
Adverse effects of medications
Primary sleep disorders

Aging and OSA

- Less sleepiness
- Weaker association with obesity
- Milder sleep O_2 desaturation
- Lower risk of CV diseases and HTN

Aging and OSA

AHI is less able to predict mortality risk

Less sleepiness

Weaker association with obesity

Milder sleep O_2 desaturation

Lower risk of CV diseases and HTN

Polysomnography

Diagnosis of SDB
PAP titration for SDB
Follow-up after UA surgery or dental devices for OSA

PSG: indications

Evaluation of
- Narcolepsy
- Periodic limb movement disorder
- Atypical or injurious parasomnias
- Nocturnal seizures

Derivation is the difference in voltage between 2 electrodes

Polygraph

Bipolar Two standard electrodes are matched to each other

Referential A standard electrode is matched to a reference electrode

Amplifiers

AC amplifiers are use for high-frequency (fast) variables

- EEG, EOG, EMG, ECG

DC amplifiers are used for low-frequency (slow) variables

- SaO2, CPAP levels

Can use either AC or DC amplifiers

- Airflow and respiratory effort

Fast = Accelerate

AC amplifiers are use for high-frequency (fast) variables

- EEG, EOG, EMG, ECG

Slow = Dccelerate

DC amplifiers are used for low-frequency (slow) variables

- SaO2, CPAP levels

Can use either AC or DC amplifiers

- Airflow and respiratory effort

Electro encephalography

F = frontal
C = central
P = parietal
O = occipital
M = mastoid

Electrode placement is based on the International 10-20 system

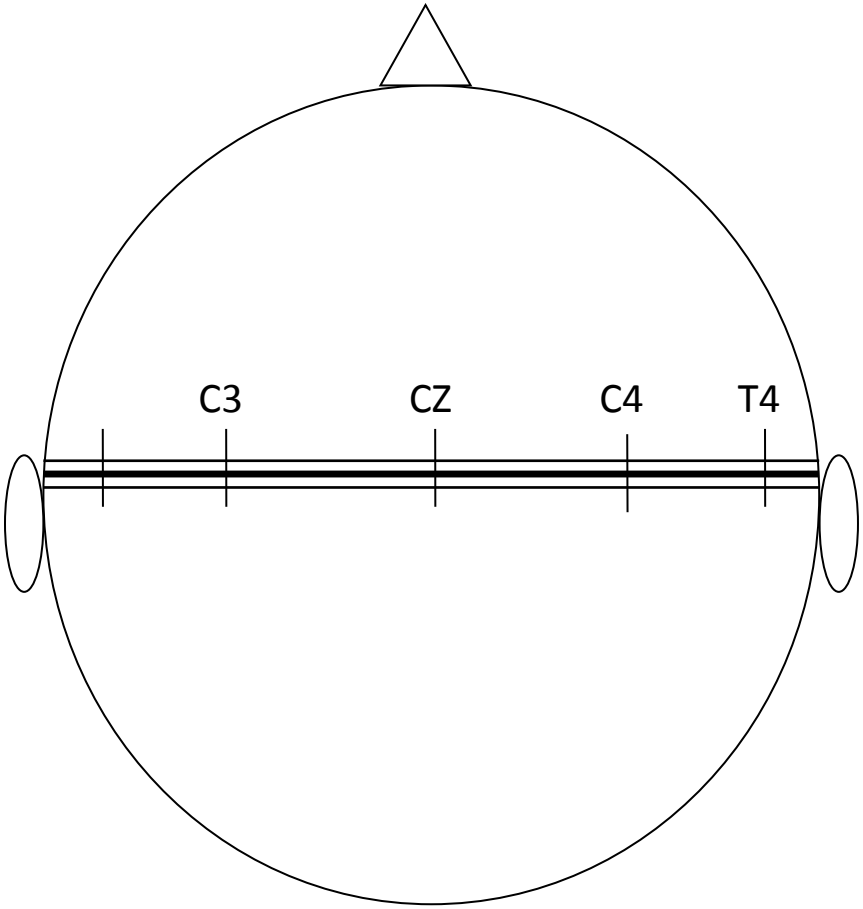
Electro encephalography

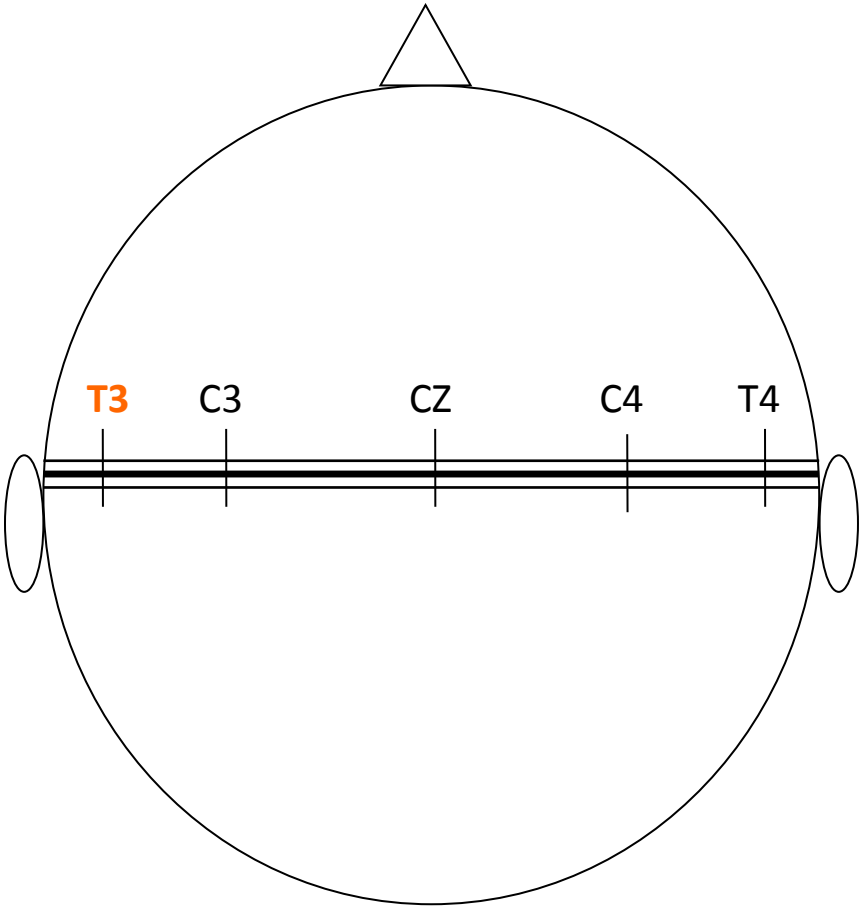
Odd numbers = left-sided electrodes
Even numbers = right-sided electrodes
Z = midline electrodes

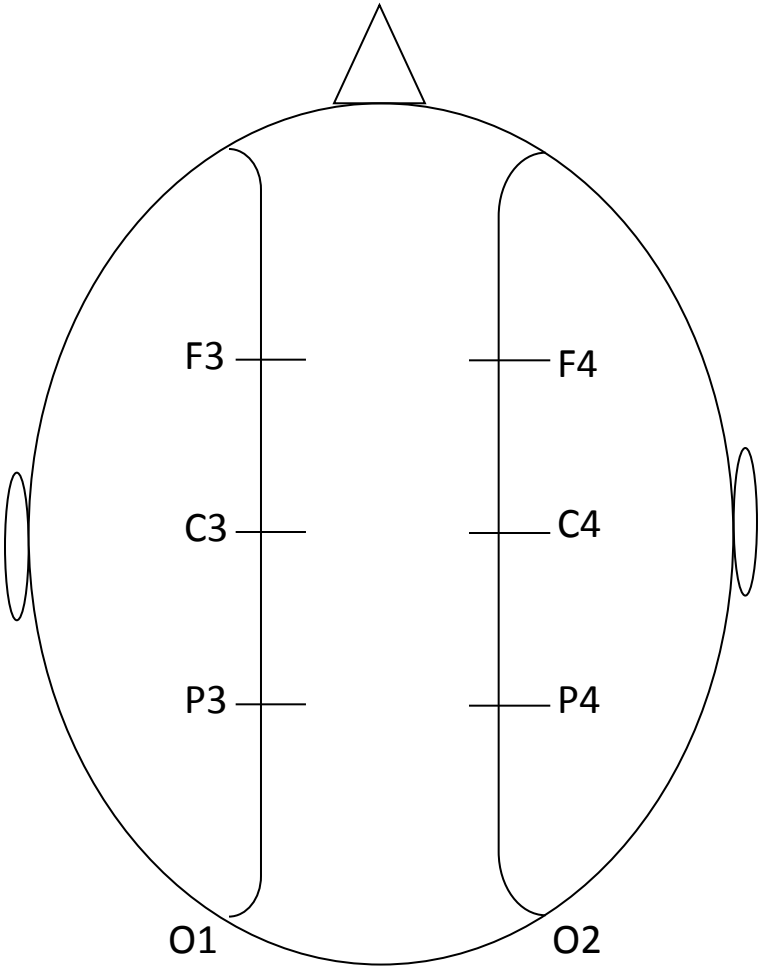
Electro encephalography

Most are right handed,
So left handed is odd

Odd numbers = left-sided electrodes
Even numbers = right-sided electrodes
Z = midline electrodes







Electroencephalography

Recommended electrode placements are

F4M1
C4M1
O2M1

Note: Left (odd) mastoid

Basic EEG Wave frequencies [Hz]

< 4	Delta
4-7	Theta
8-13	Alpha
> 13	Beta

Basic EEG Wave frequencies [Hz]

< 4	Do
4-7	The
8-13	Alpha
> 13	Bet

Basic EEG Wave frequencies [Hz]

N3 sleep	Delta
N1, N2, R sleep	Theta
Drowsiness	Alpha
Alert wakefulness	Beta

Best place to look for

Alpha waves	Occipital
Spindles	Central
SWS	Frontal
K complex	Frontal

Originate in the

Spindles Thalamus

SWS Cortex

Electrooculography

Difference in potentials (dipole) between the cornea (positive) and the retina (negative)

Electro oculography

dipole

CO-PO

(cornea = positive charge)

RE-NE

(retina = negative charge)

Electro oculography

Dipole changes with eye movements

Negative voltage (upward deflection) when the eye moves away from an electrode

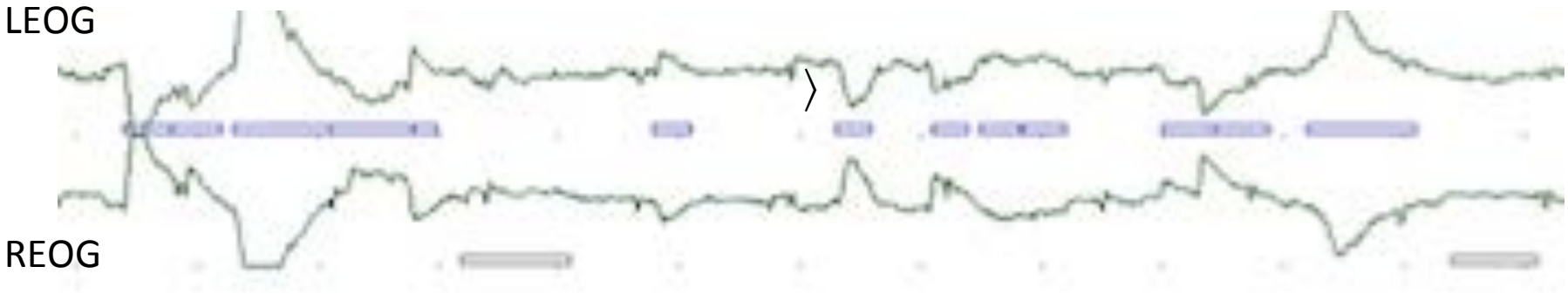
Positive voltage (downward deflection) when the eye moves toward an electrode

Electro oculography

Negative voltage (upward deflection) when the eye moves away from an electrode

PO-DO-TO

Positive voltage (downward deflection) when the eye moves toward an electrode



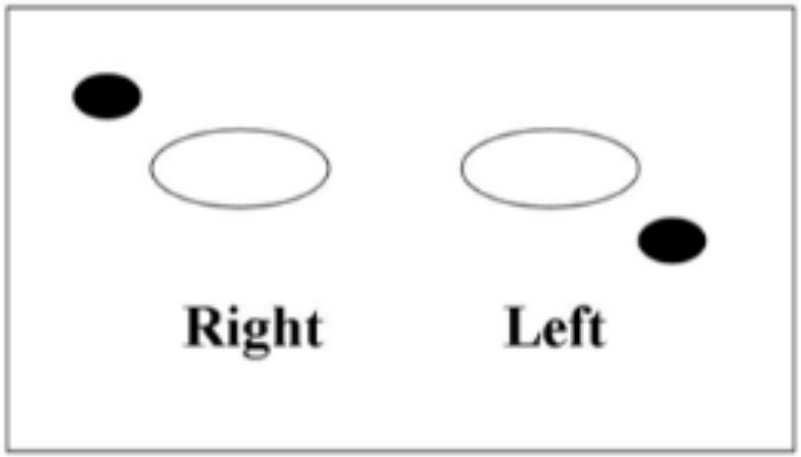
What goes down is pointing towards eye

Electrooculography

Recommended electrode placements

E1M2

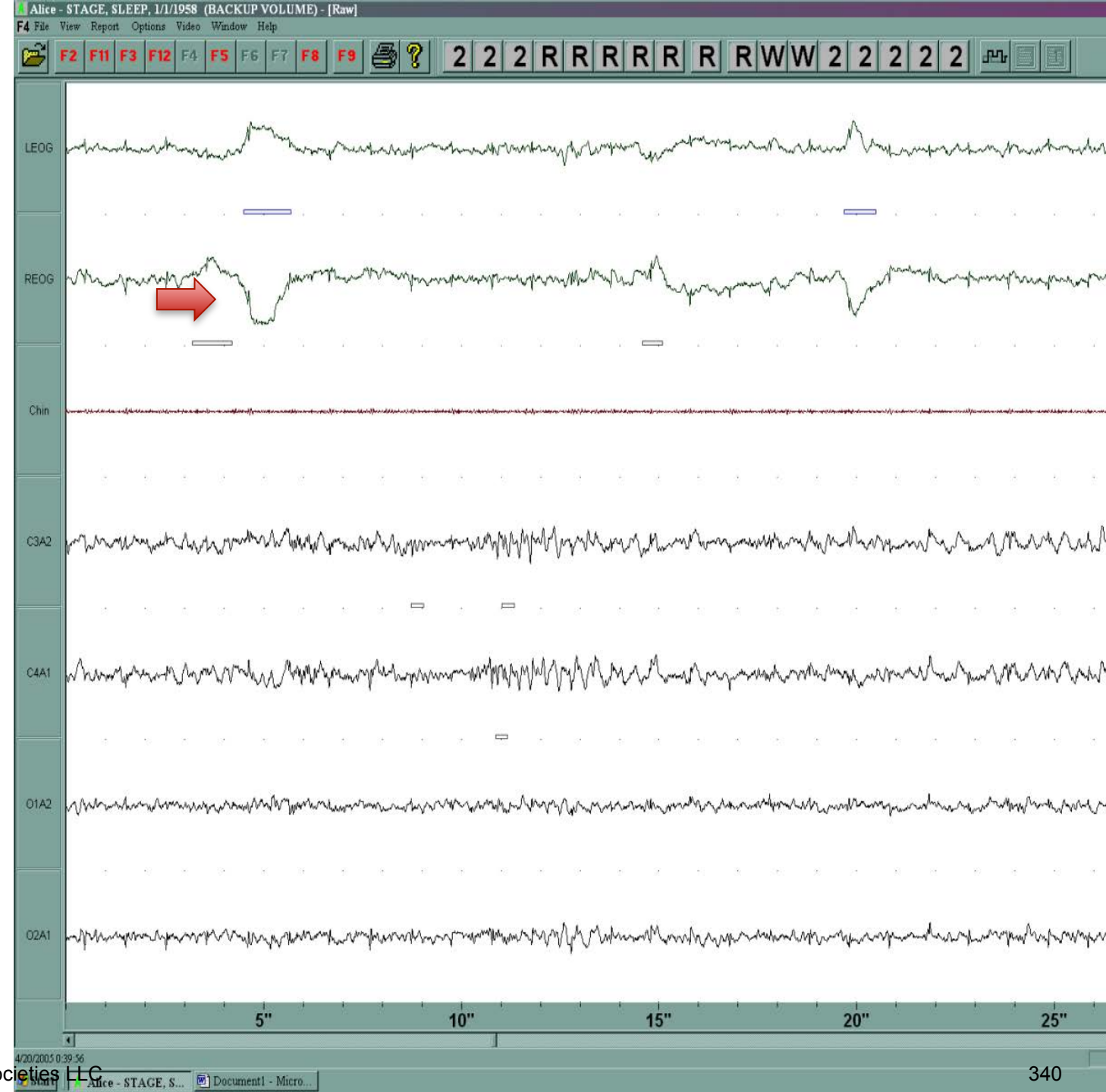
E2M2



Note: the other mastoid

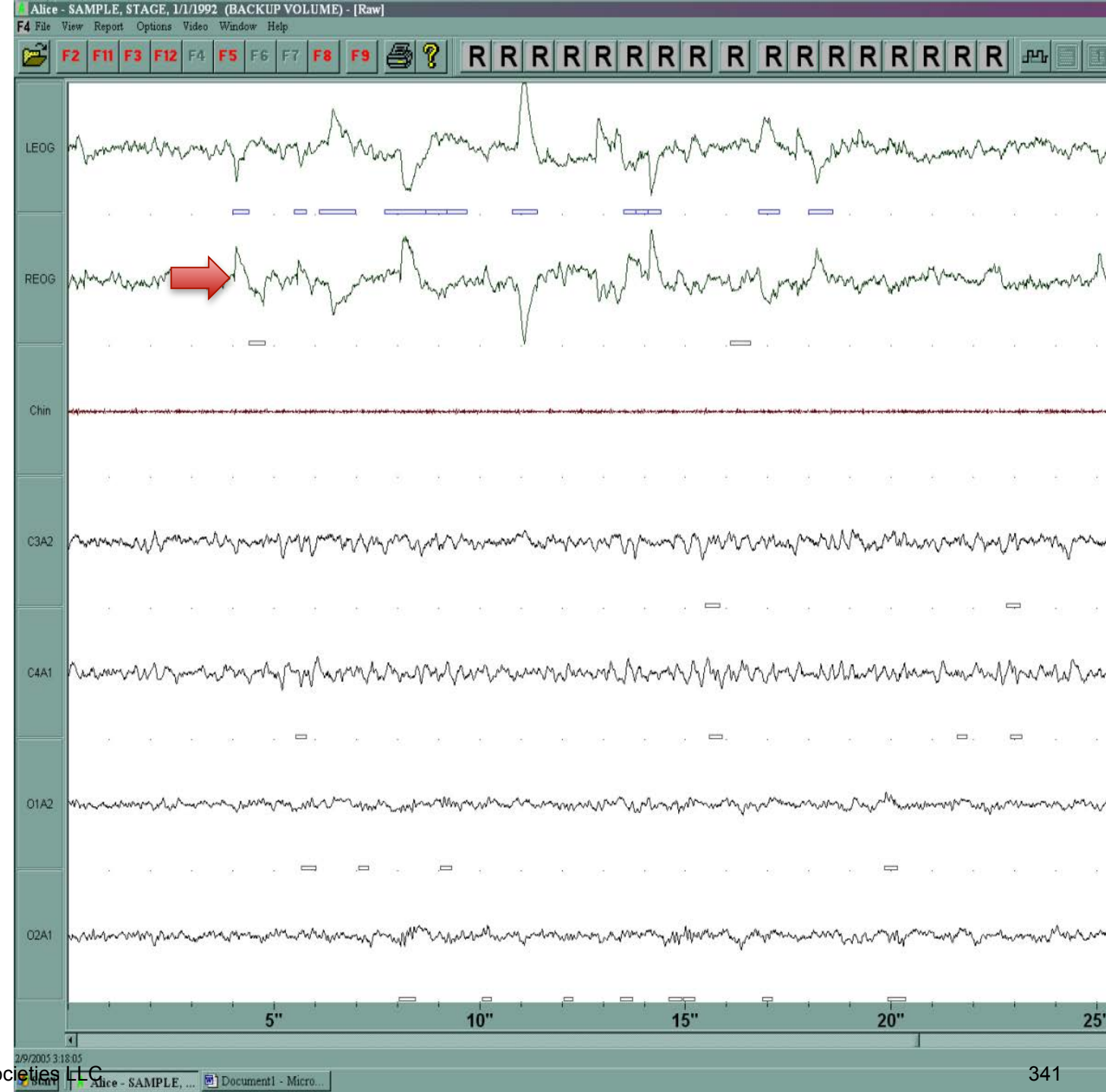
Slow rolling movements

Drowsiness with closed eyes,
N1 sleep,
or
brief awakenings

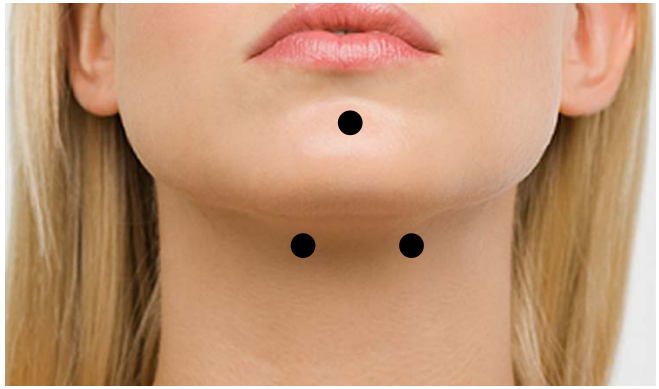


Rapid eye movements

Wake with open eyes (eye blinks) or REM sleep



Electromyography



Newbeauty.com

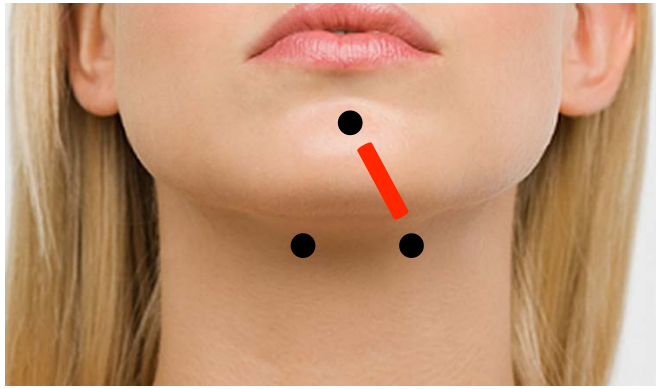
Location of three electrodes

Midline, above the mandible

Right of midline,
below the mandible

Left of midline,
below the mandible

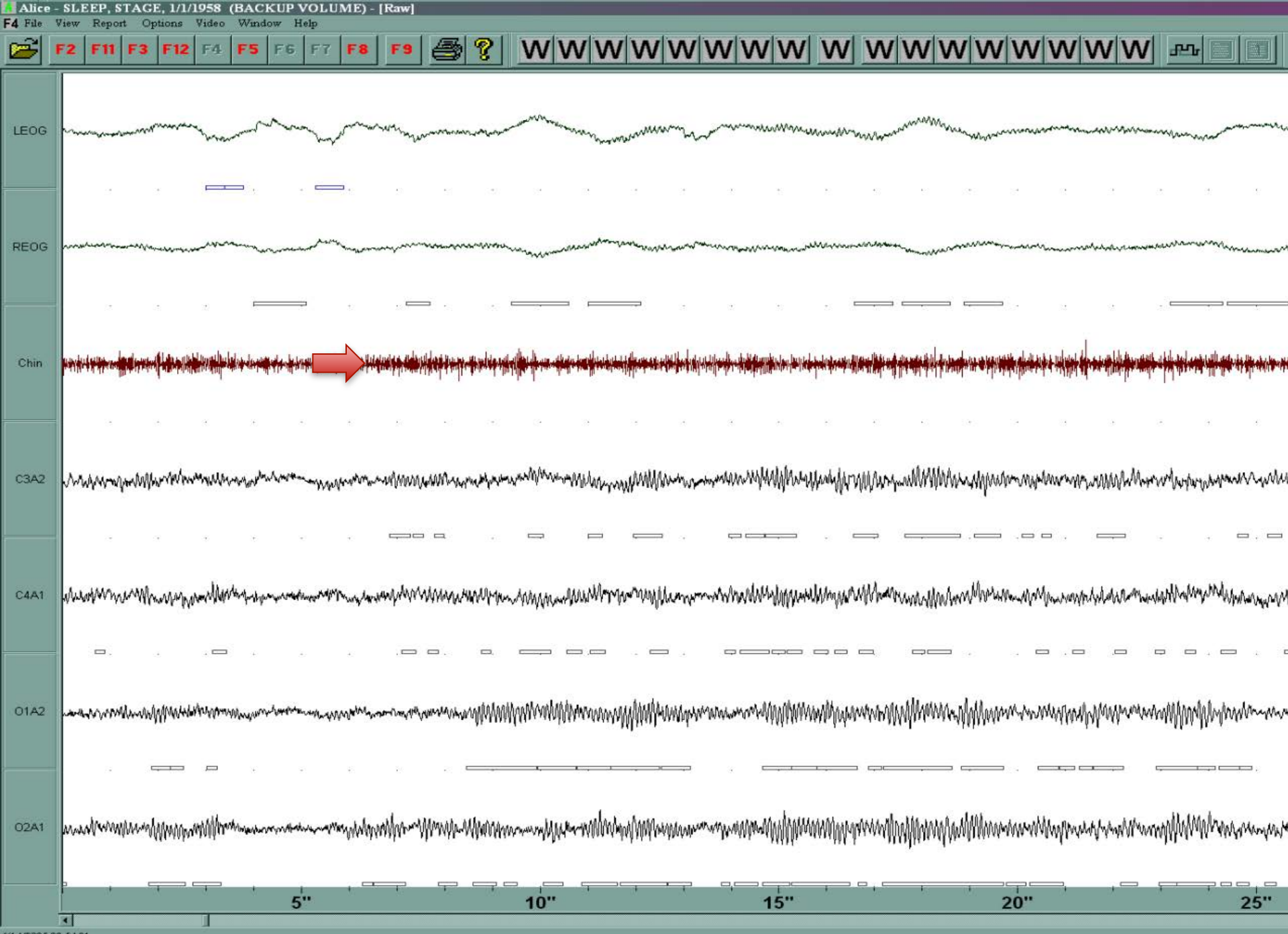
Electromyography

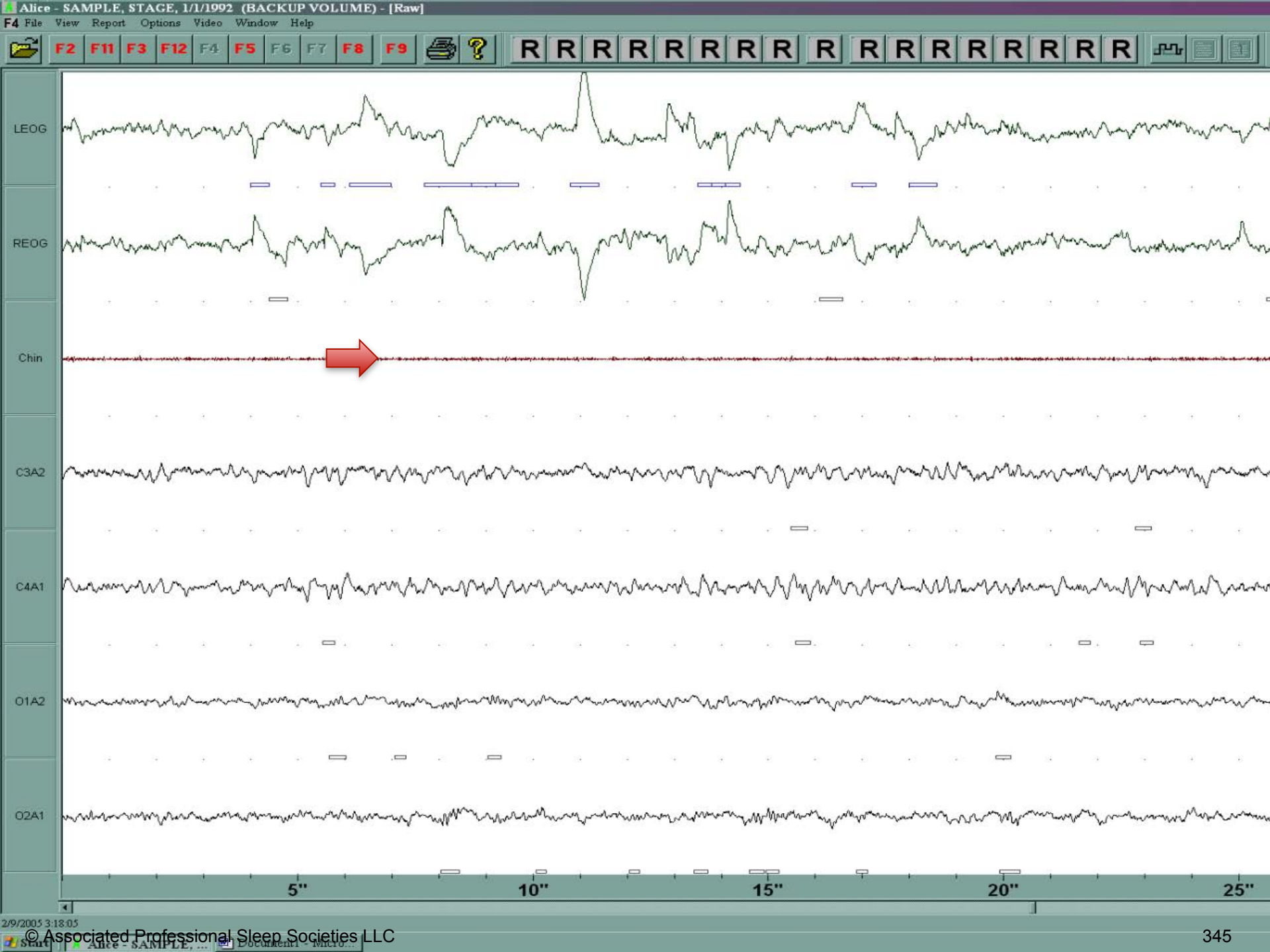


Newbeauty.com

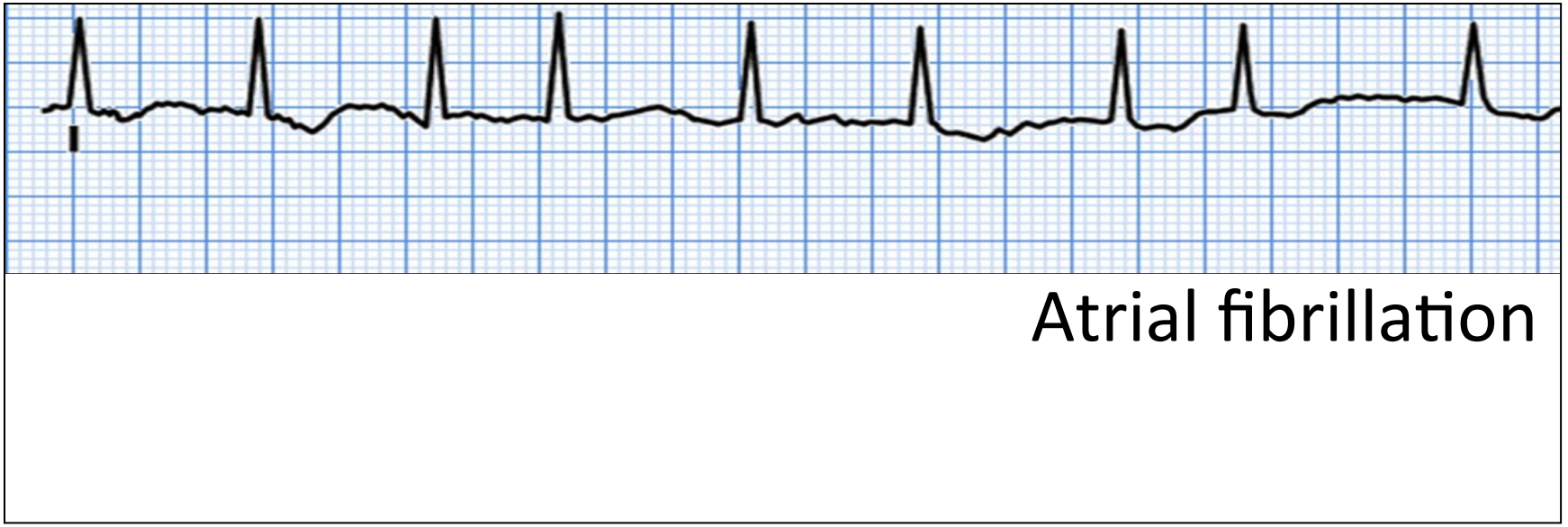
Location of three electrodes

Derivation consists of one electrode below and one electrode above the mandible



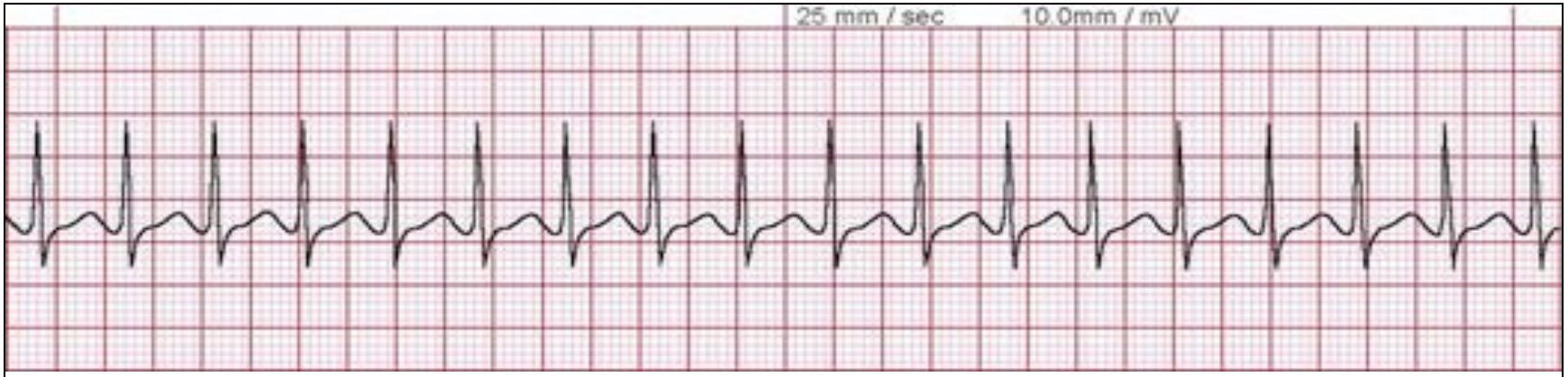


Electrocardiography



Yamashita T et al. Am J Cardiol 1998;82:1364-1367

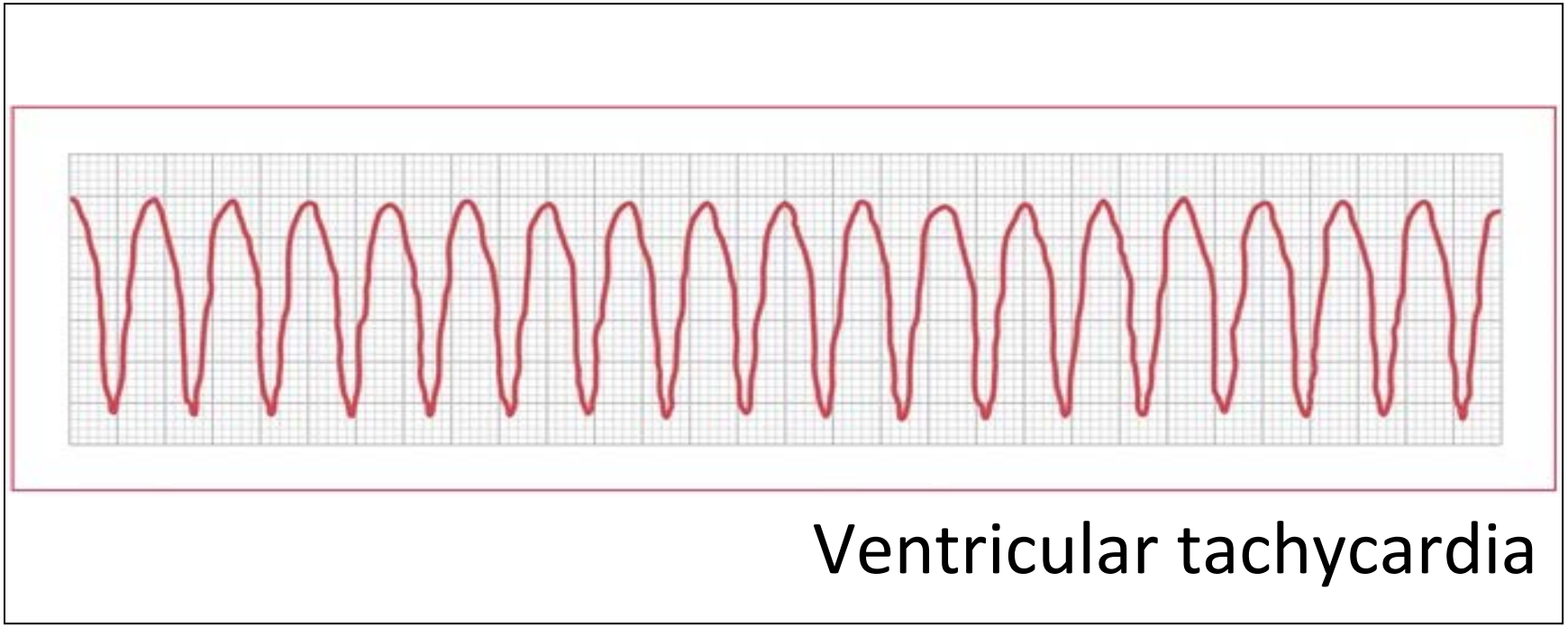
Electrocardiography



Supraventricular tachycardia

Yamashita T et al. Am J Cardiol 1998;82:1364-1367

Electrocardiography



Ventricular tachycardia

Yamashita T et al. Am J Cardiol 1998;82:1364-1367

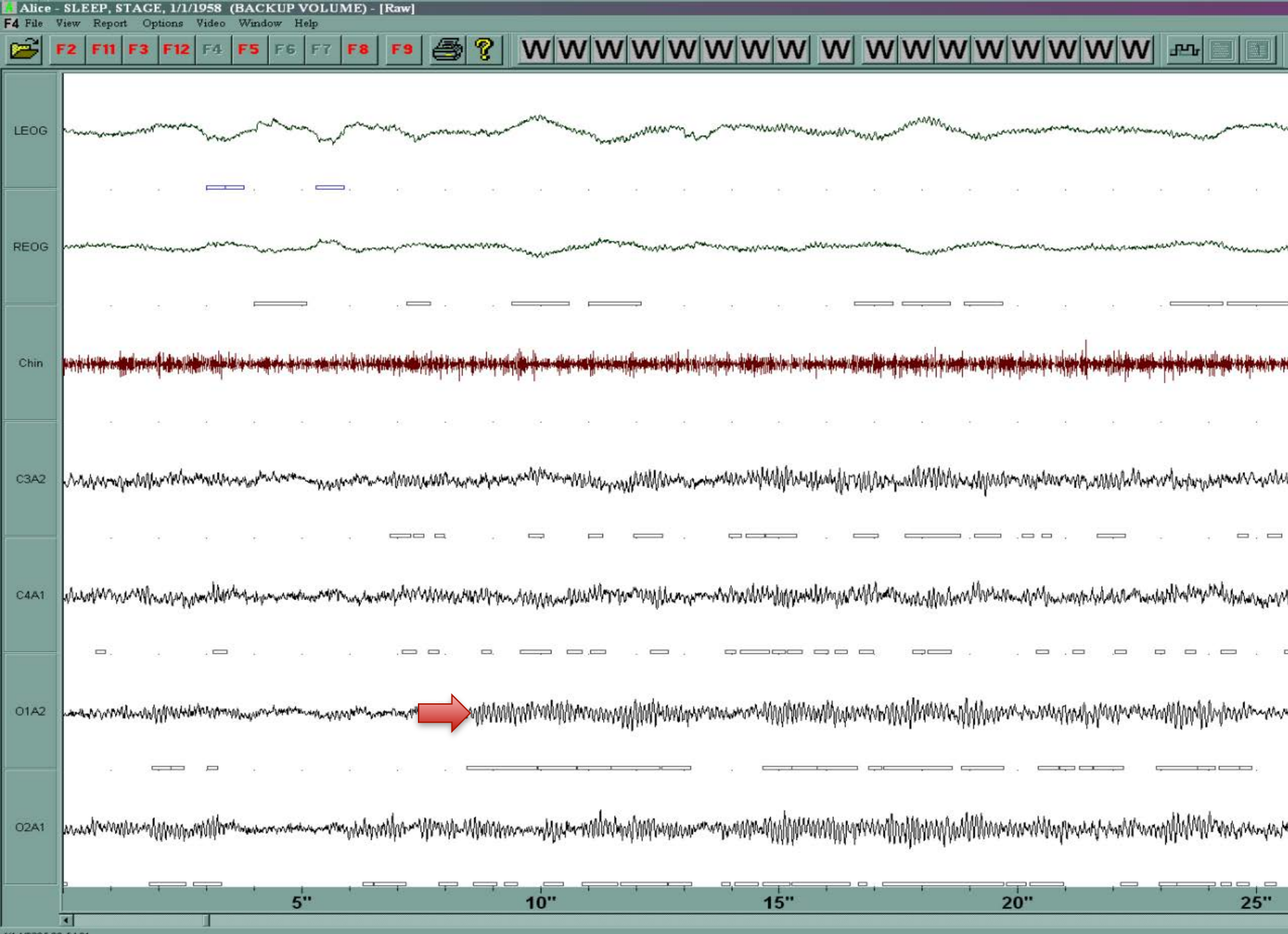
Scoring adult sleep stages

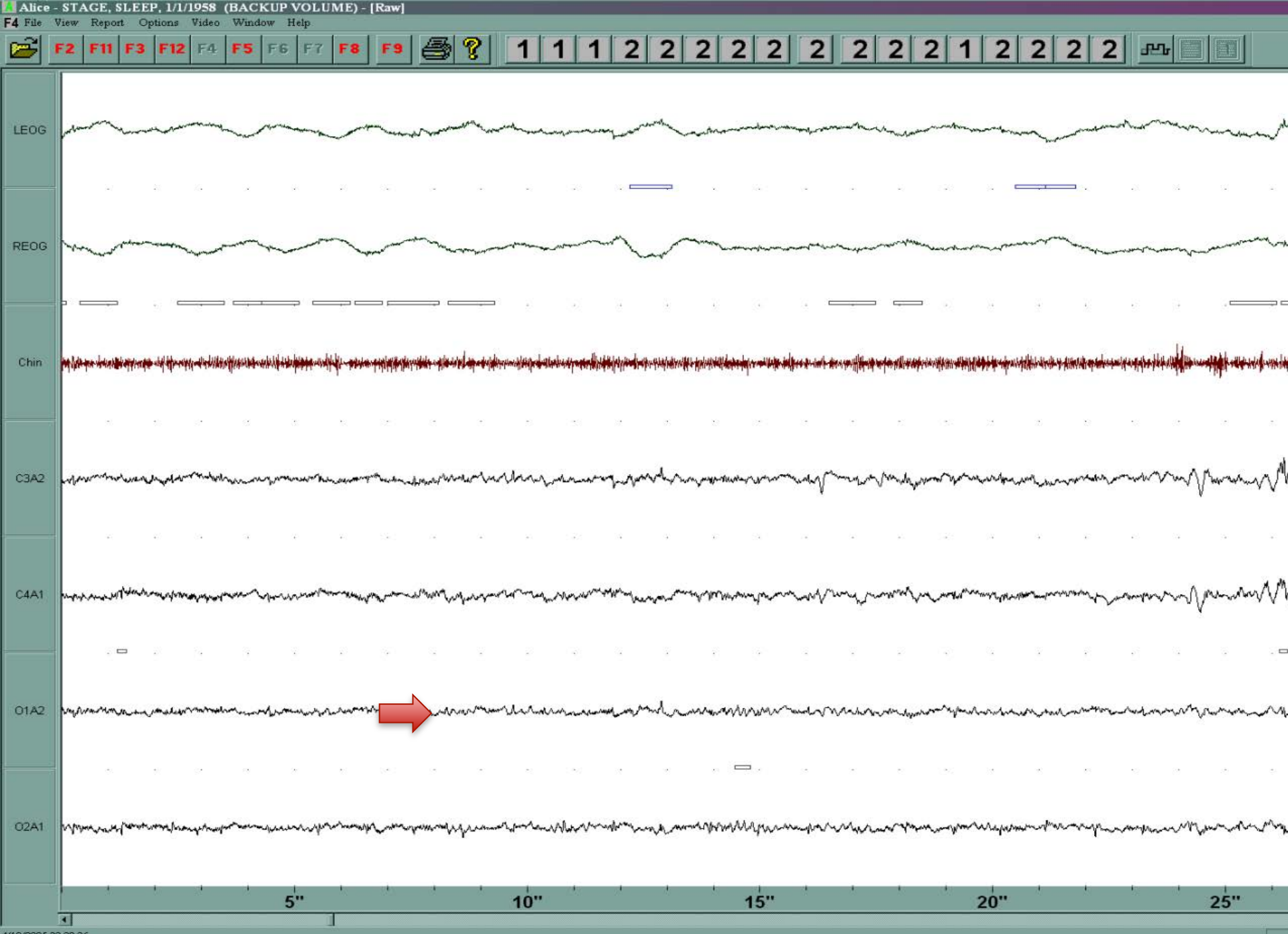
PSG data are divided into 30-second time periods or epoch

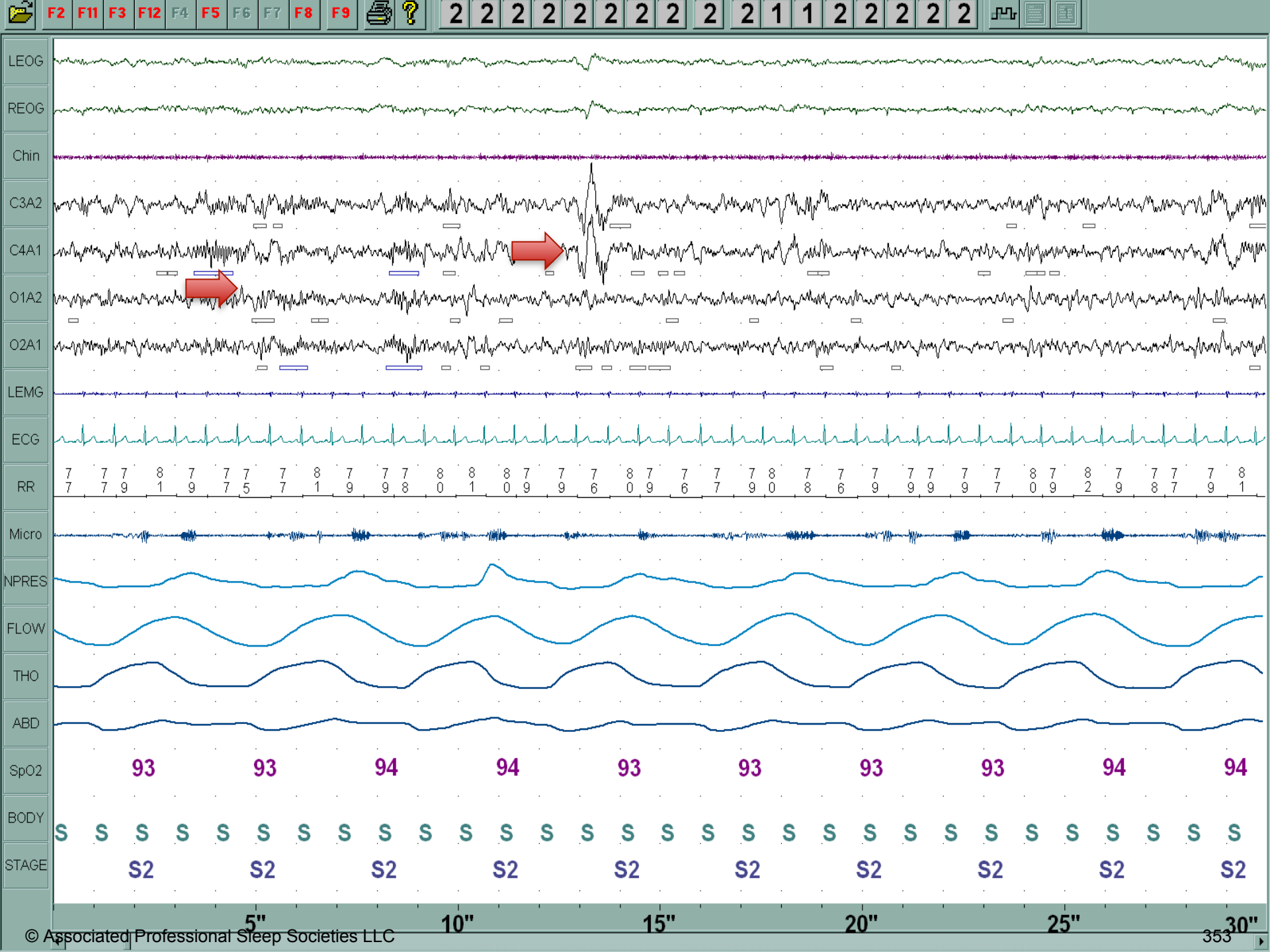
Each epoch is assigned a sleep stage that comprises the greatest percentage of the epoch

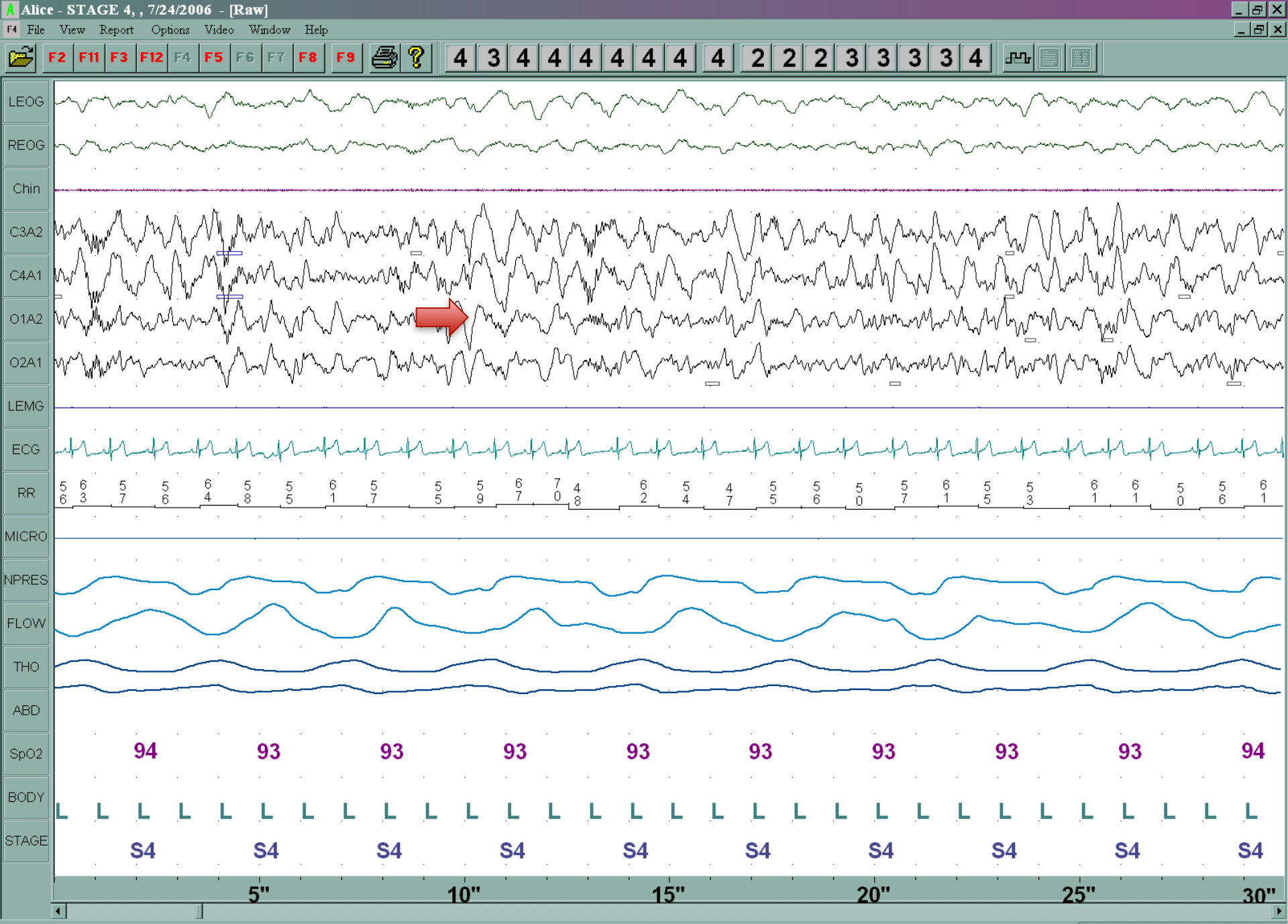
Scoring adult sleep stages

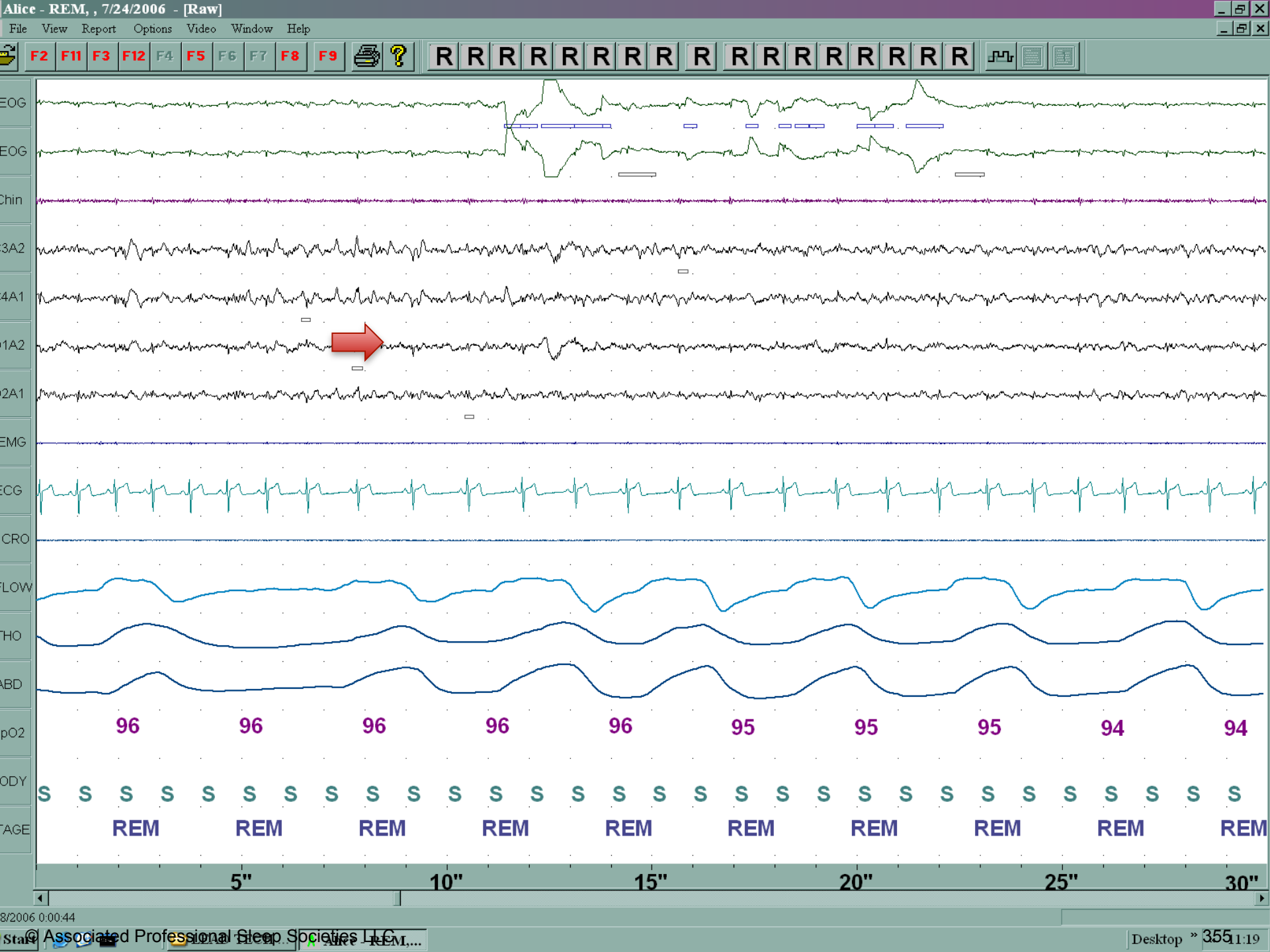
Stage W	> 50% of epoch contains alpha waves
Stage N1	> 50% of the epoch contains theta waves; no K complexes, sleep spindles or rapid eye movements
Stage N2	K complexes and sleep spindles
Stage N3	≥ 20% of epoch contains high-amplitude delta waves
Stage R	Theta waves, rapid eye movements, low chin EMG tone











Lee-Chiong's 4 Steps to Sleep Scoring

Step 1 Look for alpha waves	> 50% of epoch contains alpha waves = stage W < 50% of epoch contains alpha waves = Go to 2.
Step 2 Look for delta waves	≥ 20% of epoch contains delta waves = N3 < 20% of epoch contains delta waves = Go to 3.

Lee-Chiong's 4 Steps to Sleep Scoring

Step 3

Look for K complexes and sleep spindles

Present = N2

Absent = Go to 4.

Step 4

Look for REMs, low chin EMG tone, theta waves

Present = REM sleep

Absent = N1

Percentage of adult sleep stages

N1 (5%)
N2 (45%)
N3 (25%)
REM (25%)

50%-50% rule

Percentage of adult sleep stages

50% for N1, N2

50% for N3, R

N1 (5%)
N2 (45%)
N3 (25%)
REM (25%)

	Adult	Children
W	> 50% of epoch contains alpha waves	> 50% of epoch contains dominant posterior EEG rhythm
N1	> 50% of the epoch contains theta waves; no K complexes, sleep spindles or rapid eye movements	> 50% of the epoch contains theta waves
N2, N3, R	Same scoring rules	

Scoring sleep in newborn infants

	Active (REM) sleep	Quiet sleep
Behavior	Eyes closed, visible movements	Eyes closed and few movements
Breathing	Irregular	Regular
EEG	Low-voltage irregular or mixed	High-voltage slow, trace alternant or sleep spindles

Scoring sleep in newborn infants

	Active (REM) sleep	Quiet sleep
EOG	REMs	No movement
EMG	Low	Higher

Measuring airflow

Oronasal thermal sensor
recommended technique for identifying apneas

Nasal pressure transducer
recommended technique for identifying hypopneas

Measuring airflow

Oronasal thermal sensor

recommended technique for identifying apneas

Nasal pressure transducer

recommended technique for identifying hypopneas

Inspiratory flow signal

Obstructive events ⇒ plateau (flattening)

Central events ⇒ reduced but rounded

Recommended sensors

Respiratory effort	Inductance plethysmography Esophageal manometry
Oxygen saturation	Pulse oximetry
Alveolar hypoventilation	$PtcCO_2$ or $PetCO_2$

Scoring apneas

Decrease in peak thermal sensor amplitude by > 90% of baseline for

Adult	≥ 10 seconds
Pediatric	≥ 2 missed breaths (OSA)

Obstructive

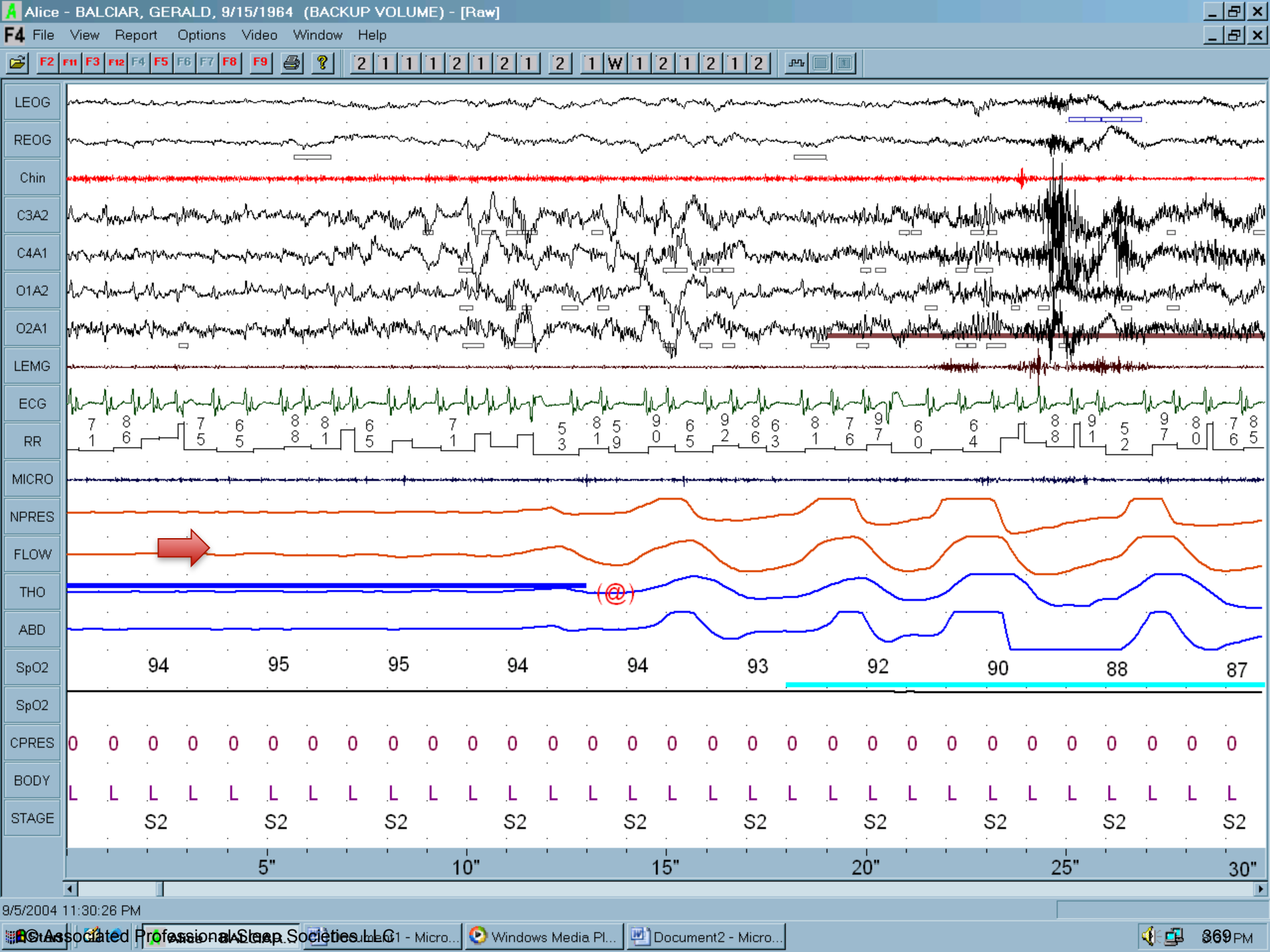
Inspiratory effort is present throughout the entire event

Central

Inspiratory effort is absent throughout the entire event

Mixed

Central event followed by an obstructive event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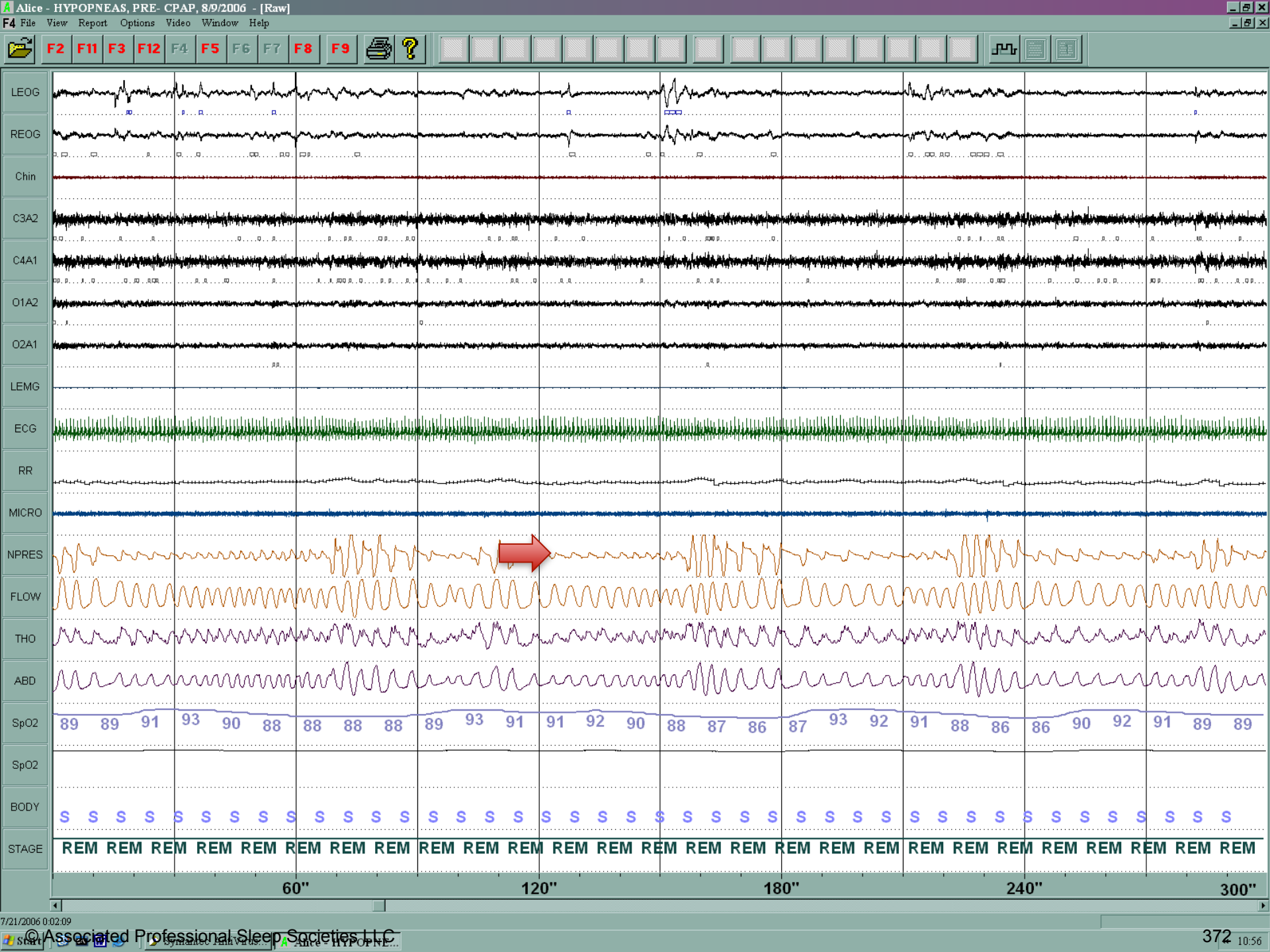
Scoring hypopneas

Decrease in nasal pressure amplitude

Adult	≥ 30% of baseline for ≥ 10 seconds *plus* ≥ 3% O2 desaturation
Pediatric	≥ 30% of baseline for ≥ 2 missed breaths *plus* arousal or ≥ 3% O2 desaturation



Scoring hypoventilation

Increase in $PaCO_2$, $PtcCO_2$ or $PetCO_2$

Adult	> 55 mmHg for ≥ 10 minutes, or ≥ 10 mmHg from wake value to > 50 mmHg for ≥ 10 minutes
Pediatric	> 50 mmHg for > 25% of TST

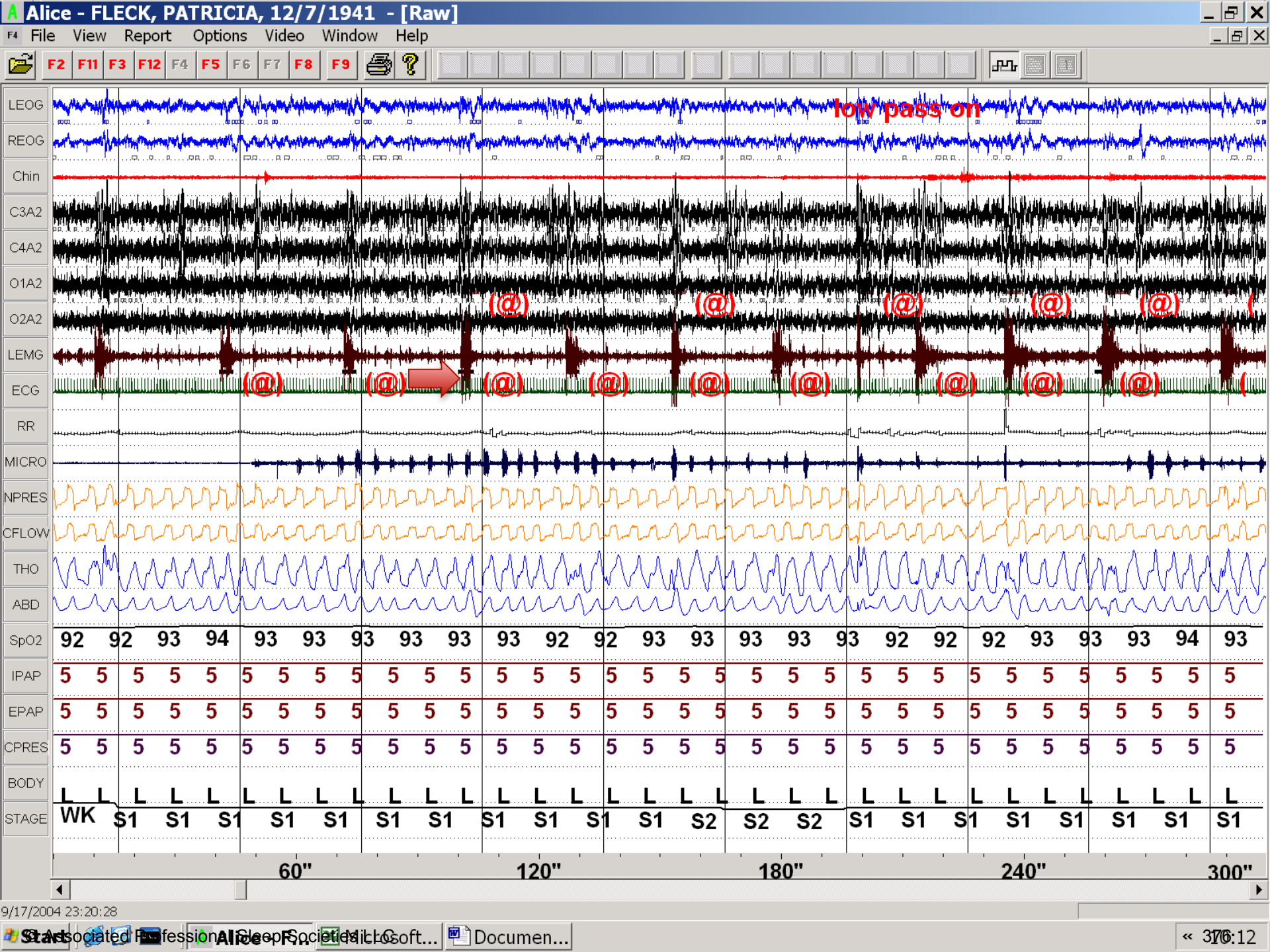
Scoring PLMS

≥ 4	Consecutive leg movements
0.5-10 secs	Duration for each event
≥ 8 μV	Amplitude above resting EMG
5-90 secs	Between onsets of consecutive movements

Scoring PLMS

Leg movements on different legs are counted as 1 movement if separated by < 5 seconds

Do not score LMs that are within 0.5 seconds of a SDB event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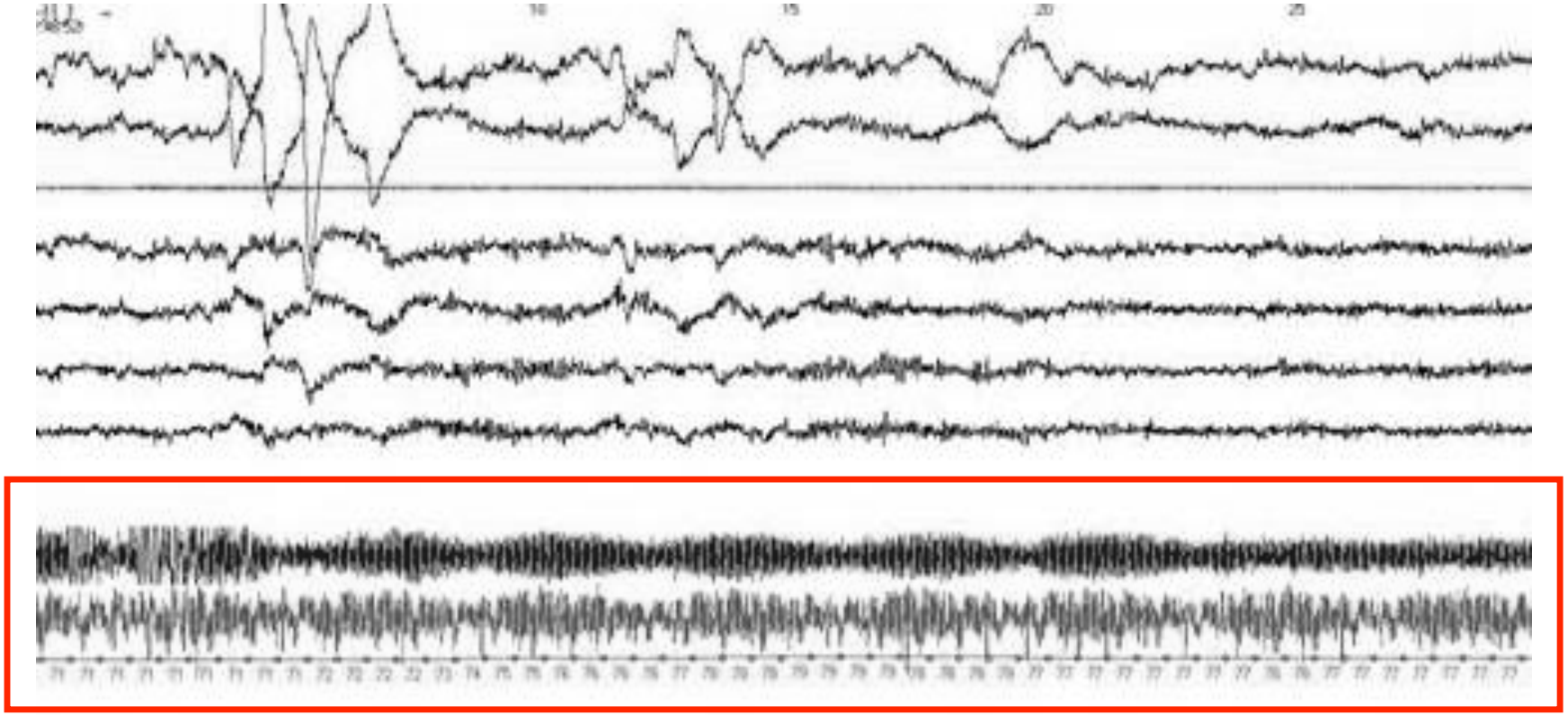
Scoring arousals

NREM arousals	Require changes in EEG only
REM arousals	Require changes in EEG and EMG
EEG changes	Abrupt EEG frequency shift (alpha, theta or > 16 Hz, but not spindles) ≥ 3 seconds and preceded by ≥ 10 seconds of stable sleep
EMG changes	Increase in chin EMG ≥ 1 second

60 Hz interference

Dense, square-shaped
EEG tracing

Due to
Interference by 60 Hz electrical activity from power lines
High and unequal electrode impedance
Lead failure



60 Hz interference

Dense, square-shaped EEG tracing

Corrective measure/s

Fix electrode placement or change leads

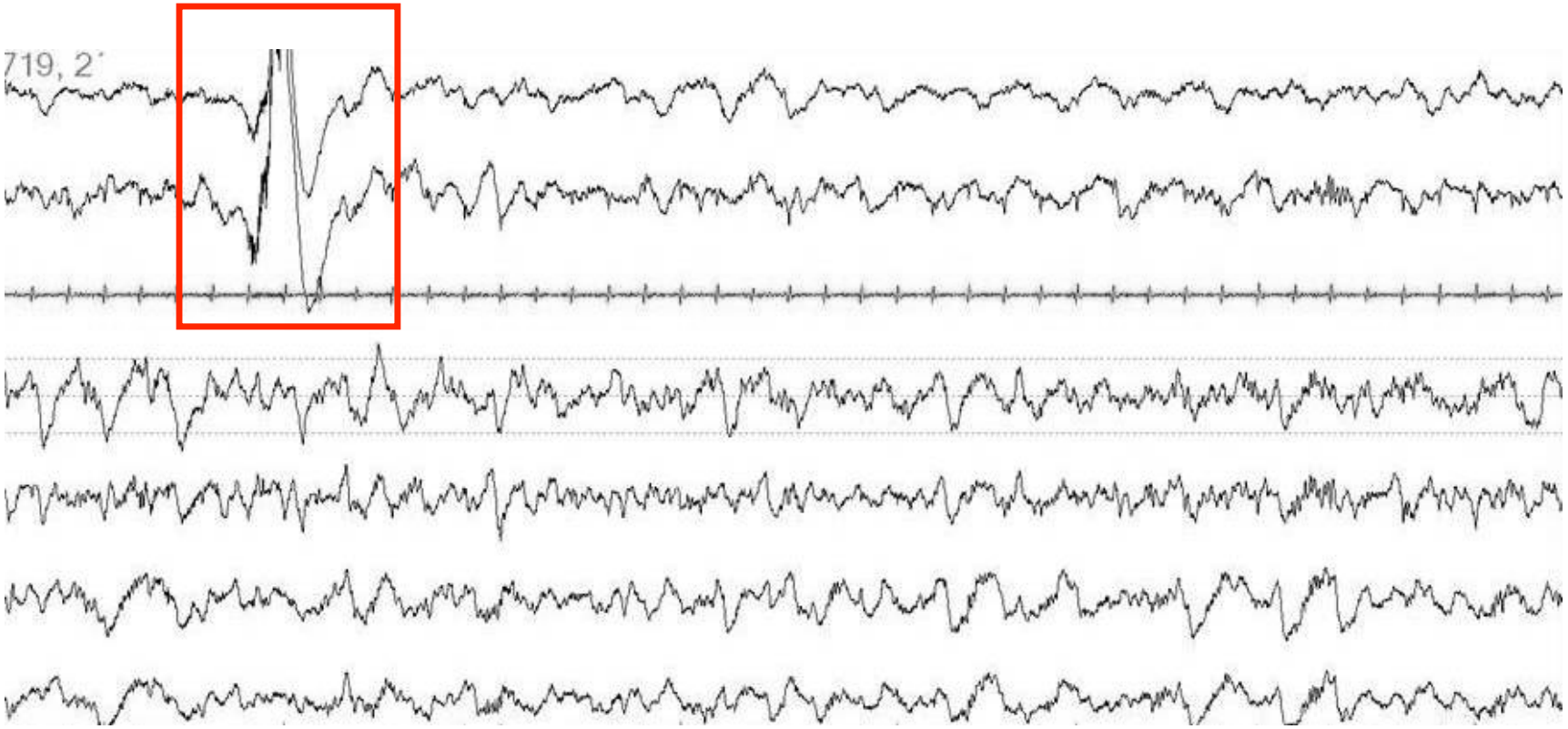
Use 60 Hz filter as a last resort

Electrode popping

Sudden, sharp, high-amplitude deflections

Due to

- Pulling of electrode leads away from the skin
- Patient lying on the electrode
- Faulty electrode placement
- Drying out of electrode gel



Electrode popping

Sudden, sharp, high-amplitude deflections

Corrective measure/s

Fix electrode placement or change lead

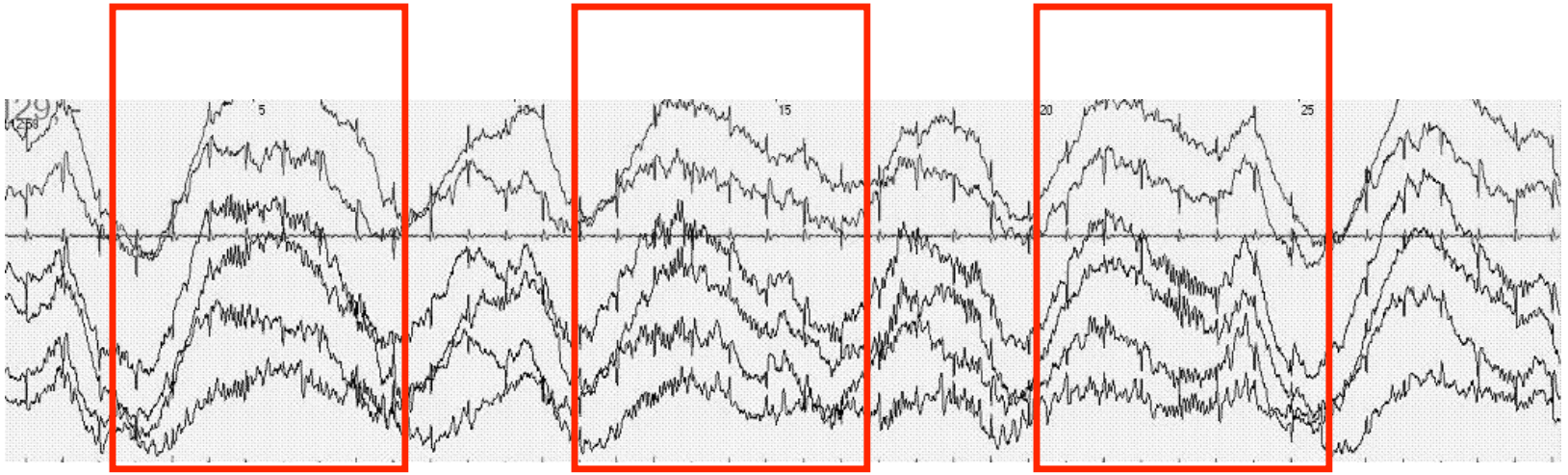
Apply more electrode gel

Sweat artifact

Slow undulating movements that are synchronous with respiration

Due to

Alterations in electrode potentials by salt in sweat



Sweat artifact

Slow undulating movements that are synchronous with respiration

Corrective measure/s

Decrease room temperature

Patterns of sleep architecture

High sleep input pattern

Low sleep input pattern

Circadian rhythm sleep patterns

Patterns of sleep architecture

High sleep input pattern

↓ SOL ↑ SE ↑ TST ↓ WASO

Low sleep input pattern

Sleep deprivation

Circadian rhythm sleep patterns

Disorders with EDS

Sedating medications

Patterns of sleep architecture

High sleep input pattern

↑ SOL ↓ SE ↓ TST ↑ WASO

Low sleep input pattern

Disorders with insomnia
Stimulant medications

Circadian rhythm sleep patterns

Patterns of sleep architecture

High sleep input pattern	Normal during habitual sleep schedule
Low sleep input pattern	During conventional sleep schedule:
Circadian rhythm sleep patterns	DSPS ↑ SOL and ↓ TST ASPS ↓ or normal SOL, ↓ TST, and early wake time

	MSLT	MWT
Measures	Tendency to fall asleep in quiet situations	Ability to remain awake in quiet situations
PSG prior to test	Required	Not required
Nap opportunities	4-5 naps at 2 hour intervals	4 naps at 2-hour intervals
Nap duration	20 minutes	40 minutes

	MSLT	MWT
Protocol	Lie down in a comfortable position in a dark, quiet room	Sit in bed in a semi-reclined position and in a dark, quiet room
Instructions	Close eyes and try to fall asleep	Try to stay awake

	MSLT	MWT
Termination of study	No sleep after 20 minutes 15 minutes after onset of sleep	3 consecutive epochs of N1 sleep 1 epoch of any other sleep stage No sleep after 40 minutes
Standard leads	EEG, EOG, chin EMG and ECG	EEG, EOG and chin EMG

Medications and sleep

↓ N3 and ↓ R	BZ receptor agonists Stimulants Opioids
↓ R, ↑ N3 and ↑ REM SL	Antidepressants

Benzodiazepines

Increase both spindle (12-14 Hz) and "pseudo-spindles" (14-18 Hz) density

SSRI

Can cause slow eye movements during NREM sleep ("Prozac eyes")

Can induce RBD

Antidepressants

Can induce or worsen RLS or PLMD (think: mirtazapine)

Exception: Bupropion

Biphasic effect

Alcohol

Stimulating – At low doses and on the rising phase of alcohol levels

Sedating – At high doses and on the falling phase of alcohol levels

Biphasic effect

Alcohol

Stimulating – At low doses and on the rising phase of alcohol levels

Visualize an animated person having fun at a bar

Sedating – At high doses and on the falling phase of alcohol levels

Visualize a drowsy person driving home after leaving the bar

Acute alcohol ingestion

Alcohol

PSG features

First part of the sleep period = ↓ SOL, ↓ WASO, ↑ N3, ↑ REM SL and ↓ R

Second part of the sleep period = ↑ WASO, ↓ N3 and ↑ R

Hypersomnolence

D' causes of sleepiness

Deprivation (sleep)
Disorder (sleep)
Disease
Depression
Delirium
Delayed sleep phase
Drugs (medications)
Dope (illicit substance)
Drinking (ETOH use)
Drama (malingering)

Narcolepsy

Cataplexy
Hallucinations
Insomnia (sleep disturbance)
Paralysis
Sleepiness

Think orexin
(appetite) ⇒ chips

	Narcolepsy	Idiopathic hypersomnia
Cataplexy	May be present	Absent
Daytime napping	Transiently refreshing	Not refreshing
Nighttime sleep	Sleep disturbance common, ↓ SOL, ↓ REM SL	May be normal or prolonged in duration
Response to stimulant therapy	More predictable improvement	Less predictable improvement

	Narcolepsy	Idiopathic hypersomnia
MSLT	↓ SOL, SOREMPs present	↓ SOL, SOREMPs may be present
HLA typing	DQB1*0602	CW2
CSF hypocretin	Low levels (narcolepsy with cataplexy) Normal levels (in some narcolepsy without cataplexy)	Normal levels

Kleine-Levin syndrome

Sleepiness
Eating
Xtacy
Young men

Kleine-Levin syndrome

Severity of hypersomnia may decrease over time

Diencephalic hypoperfusion on SPECT scan

Sleepiness

Narcolepsy

Most common cataplexy trigger	Laughter and anger
Most commonly affected in cataplexy	Leg and jaw weakness
Mechanism	Loss of hypothalamic hypocretin neurons
MSLT	Mean SOL < 8 minutes; ≥ 2 SOREMPs
CSF Hypocretin 1	< 110 pg/mL, or < 1/3 of mean normal control values
Wrong answer	HLA typing

Therapy for EDS disorders

Always the right answer	Sleep extension
Napping	Napping + caffeine is better
Single therapy for EDS, cataplexy and insomnia	γ-hydroxybutyrate
When using modafinil	Add a 2nd form of contraception to birth control pills
Development of liver failure	Ask about pemolione use
Development of rash	Stop modafinil
Suspect Klein Levin syndrome	Consider lithium therapy

Insomnia

Trust
the
National Inquirer

In 1966 she yawned... and her nightmare began

WOMAN HASN'T SLEPT IN 30 YEARS!

By ROSE GRADY
Weekly World News

Thirty years ago, Joan Moore yawned — and hasn't slept another wink since!

Now this woman, whose incredible ordeal has made medical history, prays for death, when she will at last be able to close her eyes in restful eternal sleep.

Gaunt and fragile from the ravages of her nightmare, the 57-year-old insomniac spends each night in a chair, dressed in a nightgown and waiting for the dawn.

"In the silence and emptiness, I feel as though I am the only person alive in the world," the Manchester, N.H., woman told *Weekly World News*.

"God has given me a cross to bear.

"Oh, how I wish I could remember what sleep was like."

Her sleepless Hell on Earth began one night 30 long years ago when then 27-year-old Joan, exhausted after a grueling day teaching elementary school, came back to her house and made a deep yawn.

"I remember it so well," she said.

"I got a very strange feeling in my head. I thought little of it when it happened, but I haven't been able to go to sleep since that time."

The country's top neurosurgeons have studied Joan's case for years, and several medical papers have been written on her condition.

"After months of tests, I came to the conclusion that she is suffering from the extremely rare condition of chronic celestitus," said one physician.

"This impaired the sleep section of her brain and produced total insomnia."

He explained that sleeplessness doesn't damage health because the body can function with little or no sleep.

But life for Joan is an unholy torment of waiting and praying for her nightmare to end.

During the day, she busies herself visiting with neighbors who stop by. But after they go home, she faces another long night without sleep.

"I just sit in my room with my rosary, praying to my dear God for mercy. I say, 'Oh, my beloved Jesus. Free me from prison. Please! Lift the cross that has burdened me for so many years.'

"Someday — maybe soon — I know that I will close my eyes in eternal sleep. My nightmare will be over. It will be a blessing I will embrace with all my heart."

'I just sit in my room and pray to God for mercy...'

BREEDER TURNS 2-POUND PUPS INTO KILLER GUARD DOGS

MEXICO CITY — Dog breeder Juan Reyes has developed the most effective crime-stopping canine yet: The killer Chihuahua!

You heard right. Reyes' vicious two-pound attack dogs are now the third most popular animal on the home protection market, just behind German shepherds and Dobermans. They resemble normal Chihuahuas, but their jaws are wider and stronger. They're specially bred to attack without mercy.

"Of course, just one won't do the job," says Reyes, 36. "They're too small. The idea is to buy eight or nine. When intruders break in, the dogs attack en masse and tear them apart.

"An armed burglar can stop a Doberman with a single shot. But when nine speedy Chihuahuas are flying at him at once, even if he gets two, the other seven will rip him to shreds."

FORMER schoolteacher Joan Moore dresses for bed each night, but she hasn't been able to get any sleep since 1966.

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FORMER schoolteacher Joan Moore dresses for bed each night, but she hasn't been able to get any sleep since 1966.

Risk factors
for insomnia

Old, poor, unemployed, divorced, frail, sick woman

Pathophysiologic model of insomnia

Predisposing factors	Physiologic or psychological hyperarousal Decreased homeostatic sleep drive
Precipitating factors	Changes in sleep environment or sleep-wake schedule Acute stressful life events
Perpetuating factors	Poor sleep hygiene Maladaptive behaviors related to sleep

Causes of insomnia: clues

Acute stressor	Adjustment insomnia
Lifelong insomnia	Idiopathic insomnia
Bad habits	Inadequate sleep hygiene
Very minimal/no sleep for several days	Paradoxical insomnia
Rumination and intrusive thoughts	Psychophysiologic insomnia

Insomnia: Cognitive behavioral treatments

Short-term benefits are comparable to pharmacologic therapy

Long-term follow-up, CBT is more effective than pharmacotherapy

Insomnia: Cognitive behavioral treatments

= drugs	Short-term benefits are comparable to pharmacologic therapy
> drugs	Long-term follow-up, CBT is more effective than pharmacotherapy

Insomnia: Cognitive behavioral treatments

Combined drug and CBT acutely (6 weeks) followed by CBT alone (6 months)

Best Long-term outcome

Insomnia: Cognitive Behavioral Treatments

↓ SOL (> effective than pharmacotherapy)

↑ TST (< effective than pharmacotherapy)

Most effective therapies

Stimulus control

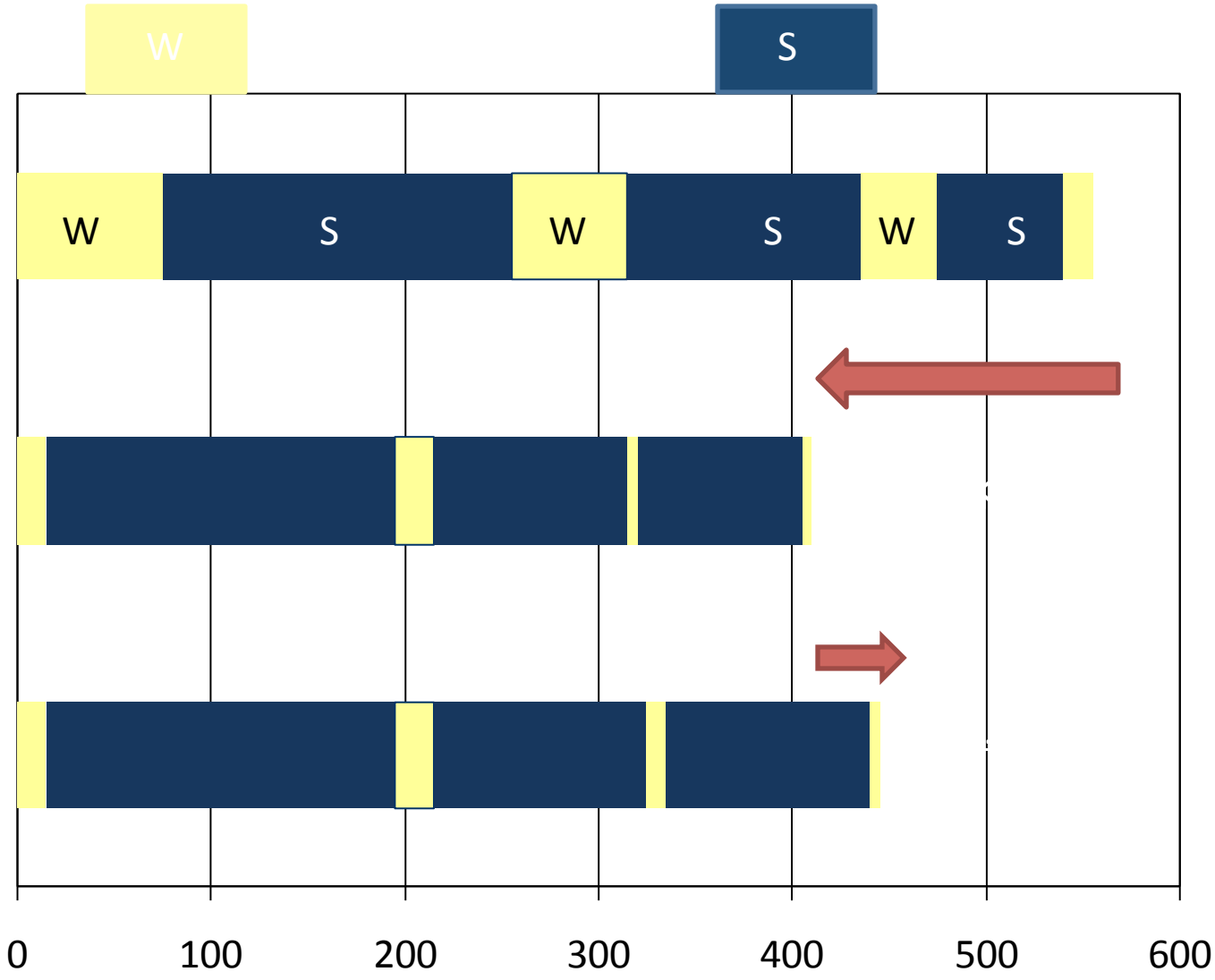
Sleep restriction

Cognitive therapy

Paradoxical intention	Decreases performance anxiety associated with efforts to fall asleep
Cognitive therapy	Addresses dysfunctional beliefs
Relaxation techniques	Decreases somatic and cognitive arousal
Stimulus control	Associates the bedroom/time to a conditioned response for sleep
Sleep restriction	Increases homeostatic sleep drive by reducing time in bed

CBT-I: what to tell your patient

Paradoxical intention	"Stay awake (if you can)."
Cognitive therapy	"Many of the things you know about your insomnia *might be* wrong."
Relaxation techniques	"Just chill."
Stimulus control	"Do not multi-task in bed."
Sleep restriction	"Less bedtime for more sleep time."



CBT-I: what to tell your child

Repetitive stalling or refusal to go to sleep at an *appropriate* time when requested to do so (Limit setting sleep disorder)	Go to bed. Enforce limits.
Inability to fall asleep unless certain desired conditions (e.g., favorite toy or presence of a caregiver) are present at bedtime. (Sleep-onset association disorder)	Go to bed. Extinction techniques.

Insomnia: pharmacotherapy

Patient is	
Female or adult requesting zolpidem	Start at lower dose
Taking ramelteon	Do not give fluvoxamine and avoid in hepatic impairment
Blind	Consider tasimelteon
Narcoleptic	Do not give surorexant
Complaining of priapism	Stop trazodone
Sleeping poorly at altitude	Consider acetazolamide

Insomnia: pharmacotherapy

Patient is	
Complaining of rebound insomnia	Slow drug taper and start CBT-I
Reporting a scaly rash	Inquire about use of kava
Suffering from hepatotoxicity	Stop valerian and kava
Having sleep maintenance insomnia	Choose longer acting agent
Sleepy the next day	Choose shorter acting agent

Parasomnias and restless legs syndrome

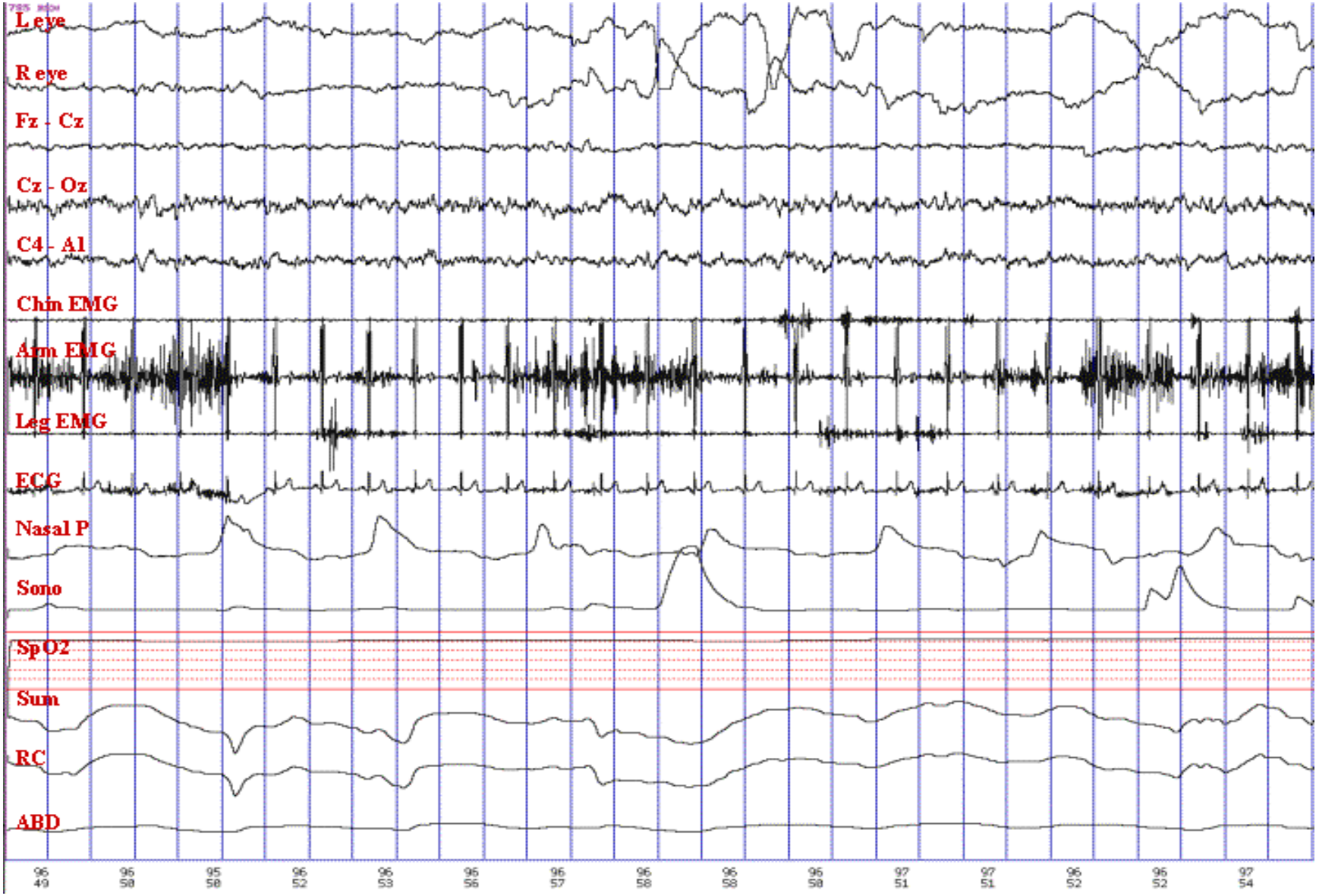
Physical or experiential phenomena that occur during sleep

Parasomnia

Parasomnia

Occurring during NREM sleep	Occurring during REM sleep
Confusional arousals	Nightmares
Sleep terrors	REM sleep behavior disorder
Sleepwalking	

	Nightmares	Sleep terrors	RBD
Time of night	Latter half of the night	First half of the night	Latter half of the night
Sleep stage	REM sleep	N3 sleep	REM sleep
Level of consciousness	Awake and alert	Confused and disoriented	Asleep
Memory of episode	Full recall	Partial or complete amnesia	Variable
Subsequent return to sleep	Delayed	Rapid	



Treating parasomnias

- Avoid sleep deprivation
- Trial of sleep extension
- Scheduled awakening for sleep terrors
- Image rehearsal for nightmares
- Prasozin for PTSD nightmares
- Stop zolpidem for sleep-eating

Managing RBD

- Low-dose clonazepam
- Melatonin
- Environmental precautions

Restless legs syndrome

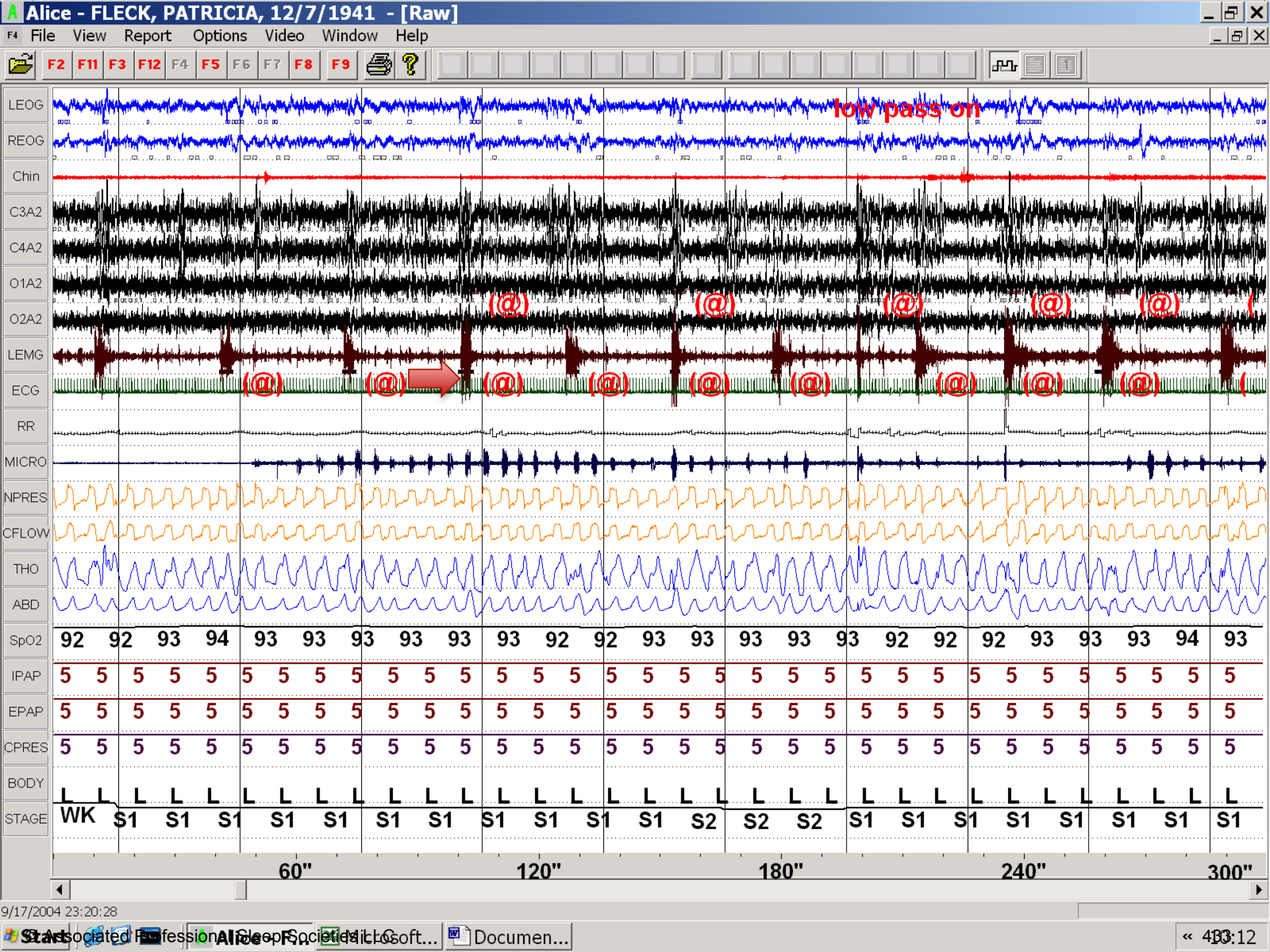
Inactivity
Discomfort
Limbs
Evening

Are relieved transiently by movement

Restless legs syndrome

Increased prevalence with anemia, uremia, pregnancy, aging and antidepressants (mirtazapine)

70%-90% of persons have PLMS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BODY
STAGE
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120"
180"
240"
300"
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Start
Alice - Fl...
Documen...
4:33:12

Treating RLS and PLMD

Diagnosing RLS	Select history; no PSG
Diagnosing PLMD	Choose PSG
Stop risk factors	Ask about antidepressants
If serum ferritin < 50 µg/L	Give iron
RLS in renal failure	Select ropirinole
Augmentation	Stop levodopa; decrease dose
Cardiac valve fibrosis	Stop pergolide
Impulse control disorder	Stop pramipexole and ropirinole
Asymptomatic PLMs	Do not treat

Circadian rhythm sleep-wake disorders

Actigraphy

Better at identifying sleep duration than SOL

Detects less TST than PSG

Actigraphy

Higher degree of correlation with PSG among normal sleepers than in patients with insomnia

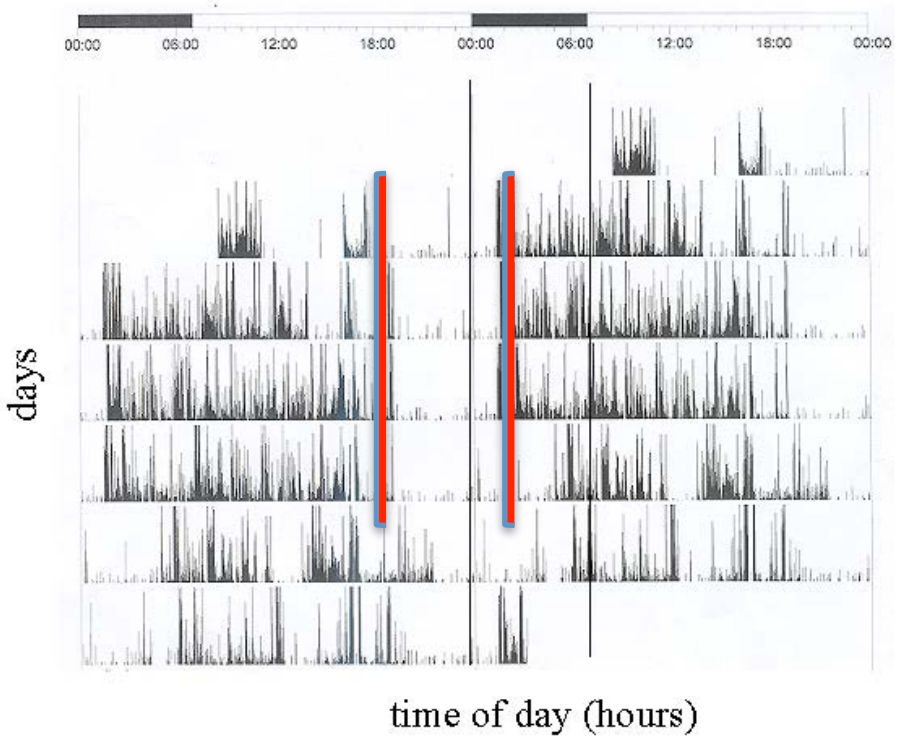
Circadian rhythm sleep-wake disorders

- Recurrent or persistent misalignment between the desired sleep schedule and the circadian sleep-wake rhythm
- Present with insomnia or sleepiness (or both)

Advanced sleep phase

Morning lark
≥ Middle age
r/o depression

Therapy:
PM light
(before CT_{min})

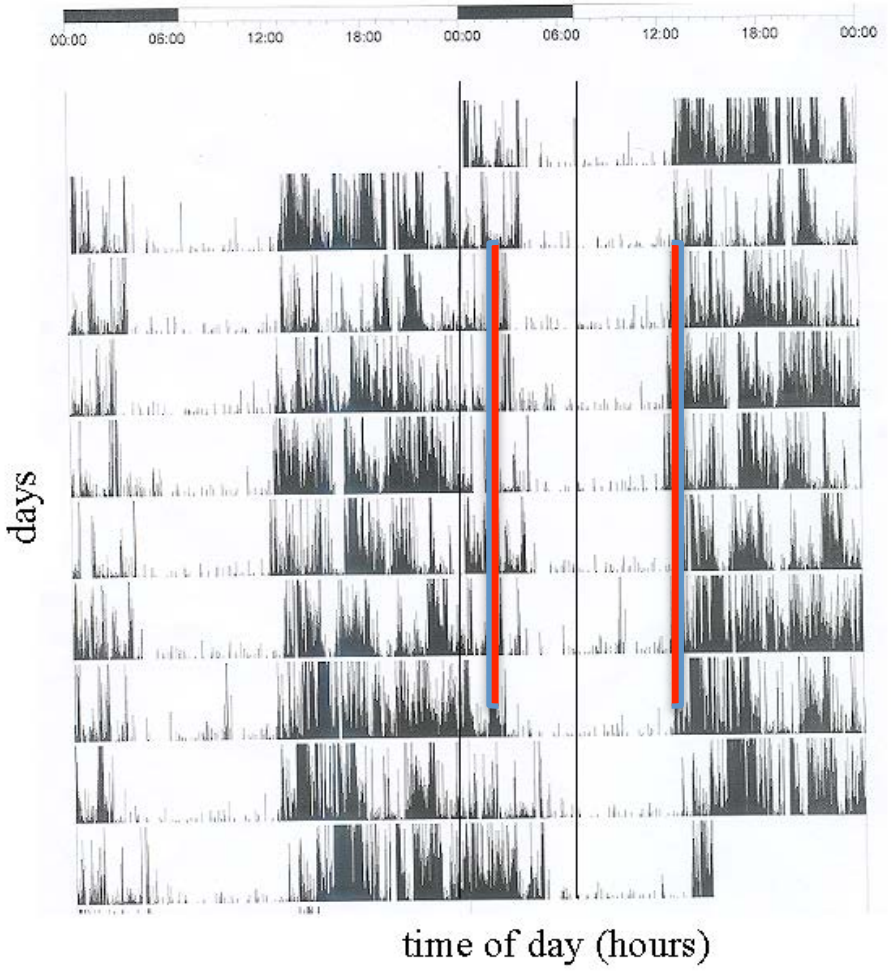


Moore R et al. Sleep: A comprehensive handbook. Wiley 2006

Delayed sleep phase

Night owl
Sleep inertia
Adolescence

Therapy:
AM light
(after CT_{min})
PM melatonin



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Delayed sleep phase

There was once a young boy
from Liverpool,
Who couldn't wake up early
to go to school.
He stayed up all night,
But he stood upright,
when given day light.
Since then, a regular sleep-
wake time has been the
rule.

Non-24 hour

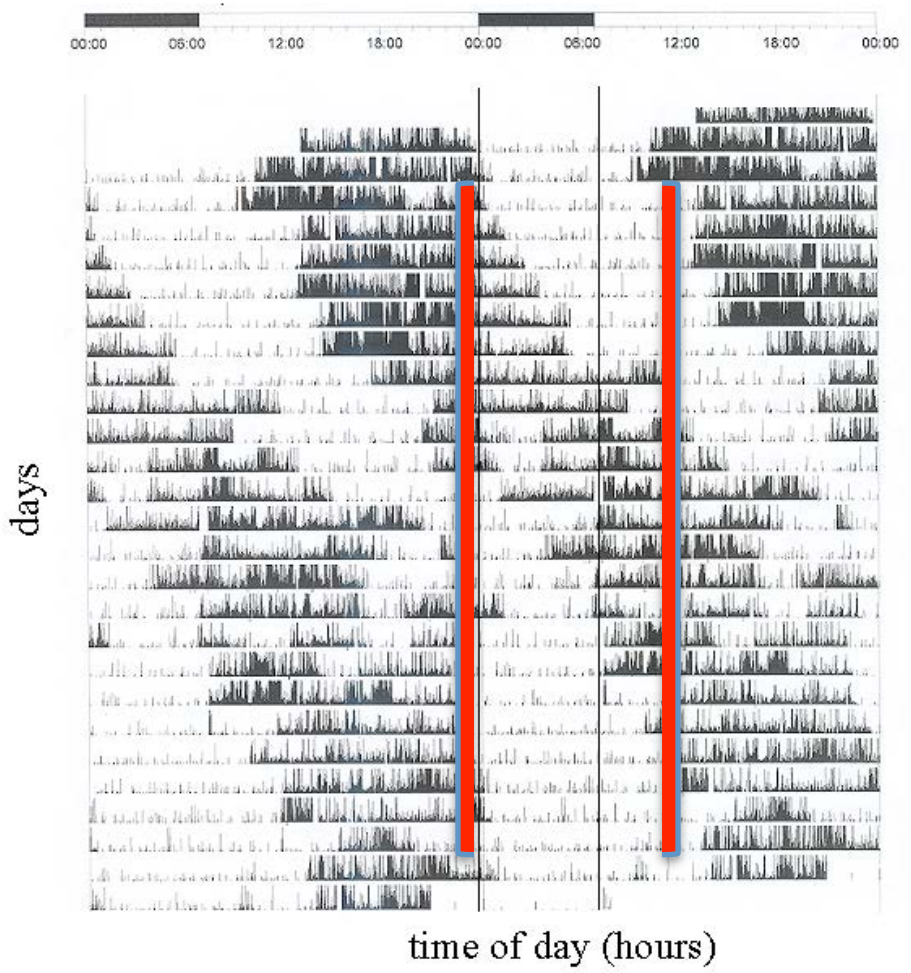
Progressive delay in sleep-wake times

Recurring EDS or insomnia

Blind person

Therapy:

PM melatonin



Moore R et al. Sleep: A comprehensive handbook. Wiley 2006

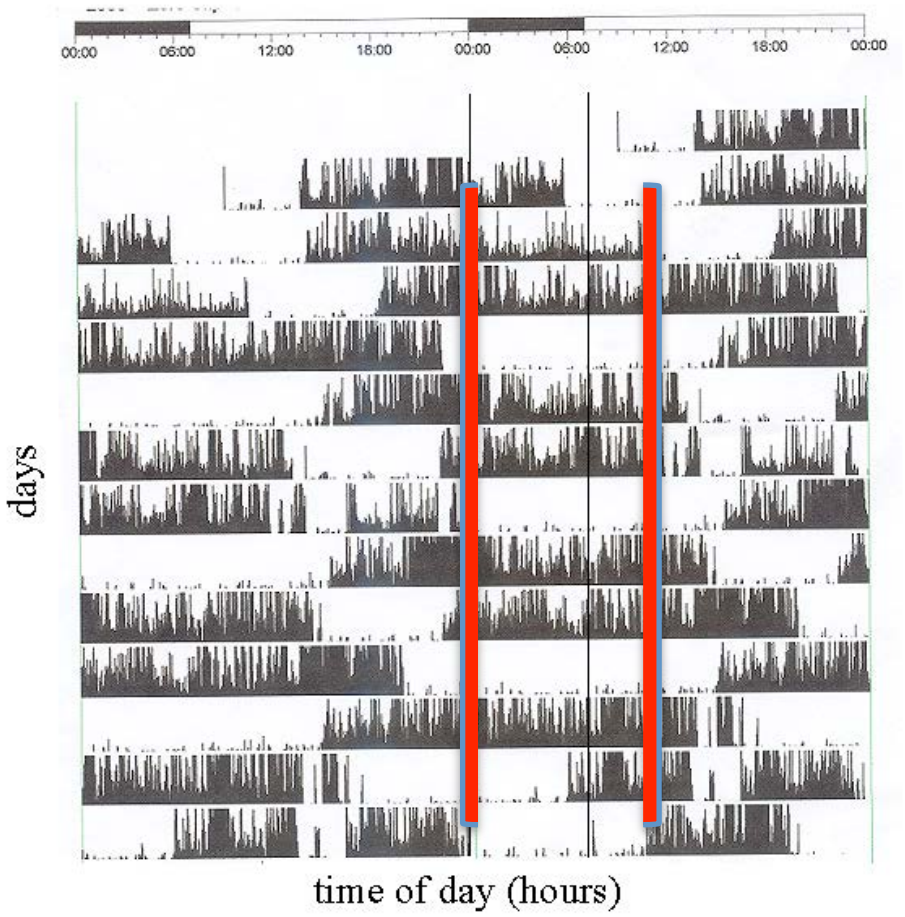
Non-24 hr circadian disorder

Three blind mice
three blind mice
See how they free-run

Irregular sleep-wake rhythm

No stable sleep-wake patterns
Dementia
r/o poor sleep hygiene

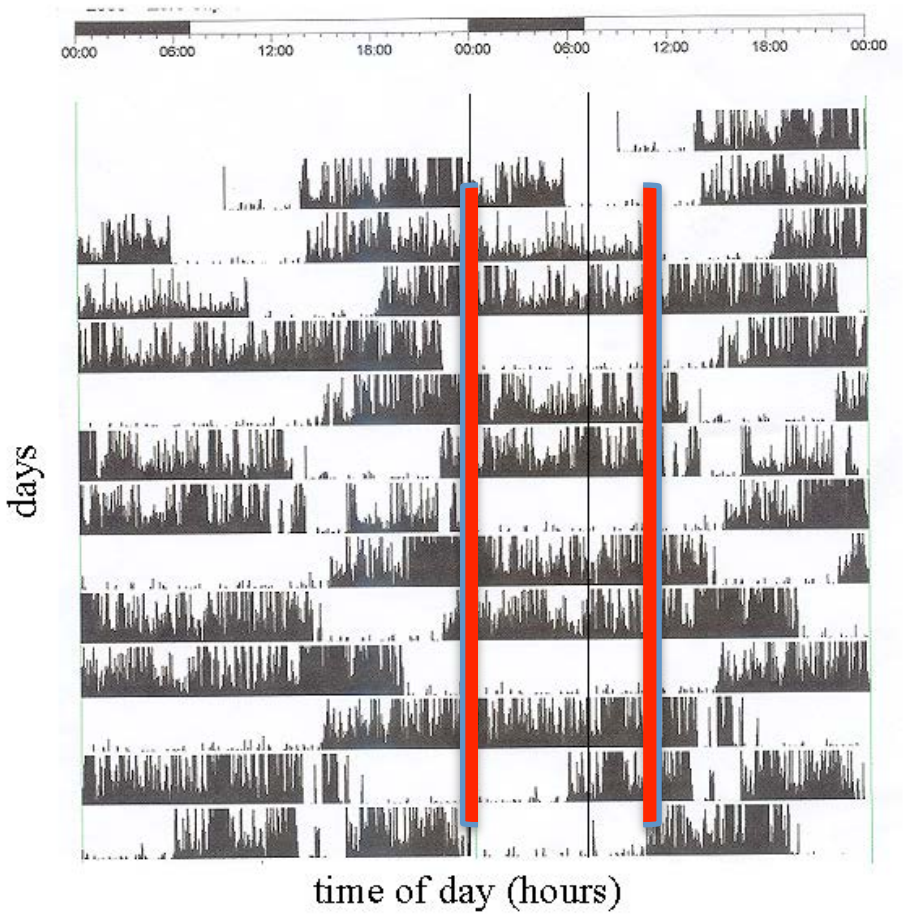
Therapy:
Evening melatonin



Moore R et al. Sleep: A comprehensive handbook. Wiley 2006

Irregular sleep-wake rhythm

Atrial fibrillation of circadian rhythms - irregularly irregular rhythm



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Shift work disorder

Workplace light exposure	To increase nighttime alertness
Wake-promoting agents	
Napping	

Shift work disorder

Workplace light exposure

Wake-promoting agents

Napping

To increase nighttime alertness

To improve daytime sleep

Allow sufficient time for sleep

Use of hypnotic agents

Jet lag

Transient insomnia and/or EDS due to rapid eastward or westward air travel across multiple time zones

Jet lag

Worse symptoms with:

Aging

Eastward travel

More time zones crossed

Jet lag

Less jet lag:

Worse symptoms with:
Aging
Eastward travel
More time zones crossed

"Go west, young man."

Jet lag

Less jet lag:

Worse symptoms with:
Aging
Eastward travel
More time zones crossed

"Go west, young man."
"But not too far."

Jet lag

Westward travelers are phase-advanced

Early evening sleepiness

Early morning waking

Jet lag

Westward travelers are phase-advanced

Early evening sleepiness

Early morning waking

Eastward travelers are phase-delayed

Difficulty falling asleep

Difficulty awakening the next day

In every exam, all travelers fly from New York to Paris

from New York
to Paris

Avoid light in the morning.
Increase light exposure in the afternoon.

from New York
to Paris

Symptoms remit within one day for every time zone change

Evaluation of CRSD

Sleep log or diary
Actigraphy
PSG is not routinely indicated

CRSD Therapy

Planned napping - SWD
Phototherapy – DSPS, ASPS, FRD, ISWR, SWD, JL
Melatonin – DSPS, FRD, ISWR, SWD, JL
Stimulants and hypnotics – SWD, JL

Genes

Familial insomnia	GAC to AAC mutation at codon 178 of chromosome 20 Cosegregates with a methionine polymorphism at codon 129
ASPS	hPer2 (human Period 2)
CCHS	PHOX2B gene
SUNDS	SCN5A mutation

Medical and neurologic disorders

Cause of nighttime hypoxia in COPD	Hypoventilation
Best predictor of nighttime hypoxia in COPD	Daytime SaO2
Diagnosing nocturnal asthma	Day vs. night PFT or peak flow
Sleep-related GER	Longer acid contact time
Polycystic ovarian syndrome	Greater risk of OSA
Nocturnal seizures	Frontal > temporal > parietal > occipital