Sleep Apnea: A to ZZZZs

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Disclosures

- No financial conflicts of interest

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Learning Objectives

- Describe the risk factors, and the signs and symptoms that would prompt an internist to consider the diagnosis of the sleep-related breathing disorders: obstructive sleep apnea and central sleep apnea.
- Describe the increase in mortality and morbidities associated with undiagnosed or untreated OSA.
- Describe the STOP-BANG questionnaire and how it helps to look for the diagnosis of sleep apnea. Understand its sensitivity and specificity for the diagnosis of OSA.
- Describe the apnea-hypopnea index and how it relates to the diagnosis of OSA. Understand the indications for different types of sleep studies including home sleep study, split-night polysomnography, and PAP titration studies.
- Describe the treatment strategies for OSA including lifestyle changes, positive airway pressure, and oral appliances. Know the indications for bariatric surgery in the treatment of OSA.

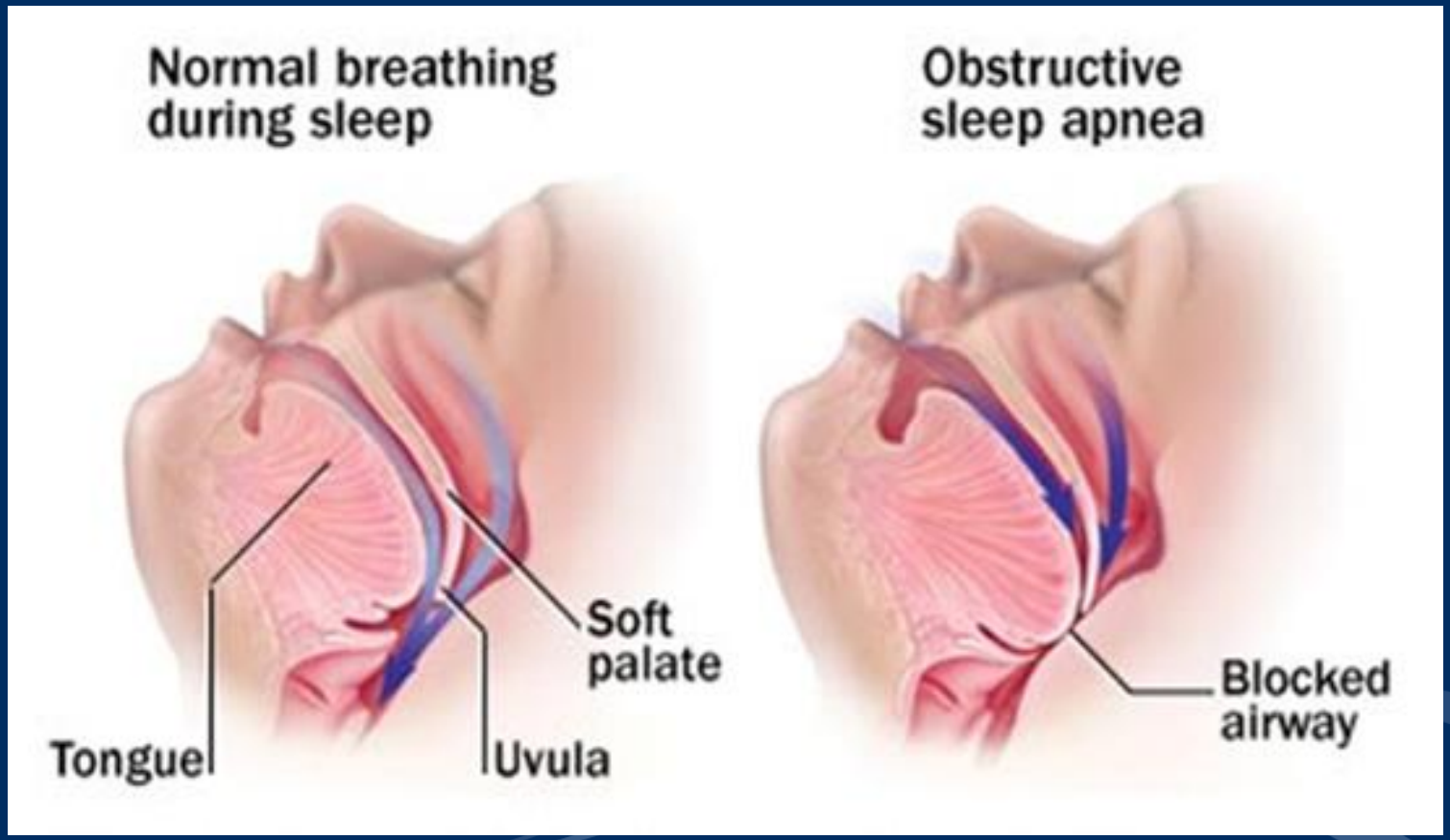
Sleep Related Breathing Disorders

- Obstructive Sleep Apnea
  - Common cause of excessive daytime sleepiness and sleep disruption
  - Most common sleep medicine referral
- Central Sleep Apnea
  - HFrEF and stroke patients
  - High dose opiates
- Hypoventilation Syndromes

What is OSA?

- Repetitive episodes of upper airway obstruction that occur during sleep
- Usually associated with a reduction in blood oxygen saturation
- Associated daytime dysfunction
  - daytime sleepiness
  - chronic fatigue

Pathophysiology of OSA



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Prevalence of OSA

- Wisconsin Sleep Cohort Study
  - Population based study: 602 working subjects, aged 30-60 years studied with PSG

	F	M
OSA	9%	24%

Prevalence for women increases post-menopausally

Young et al, NEJM 1993

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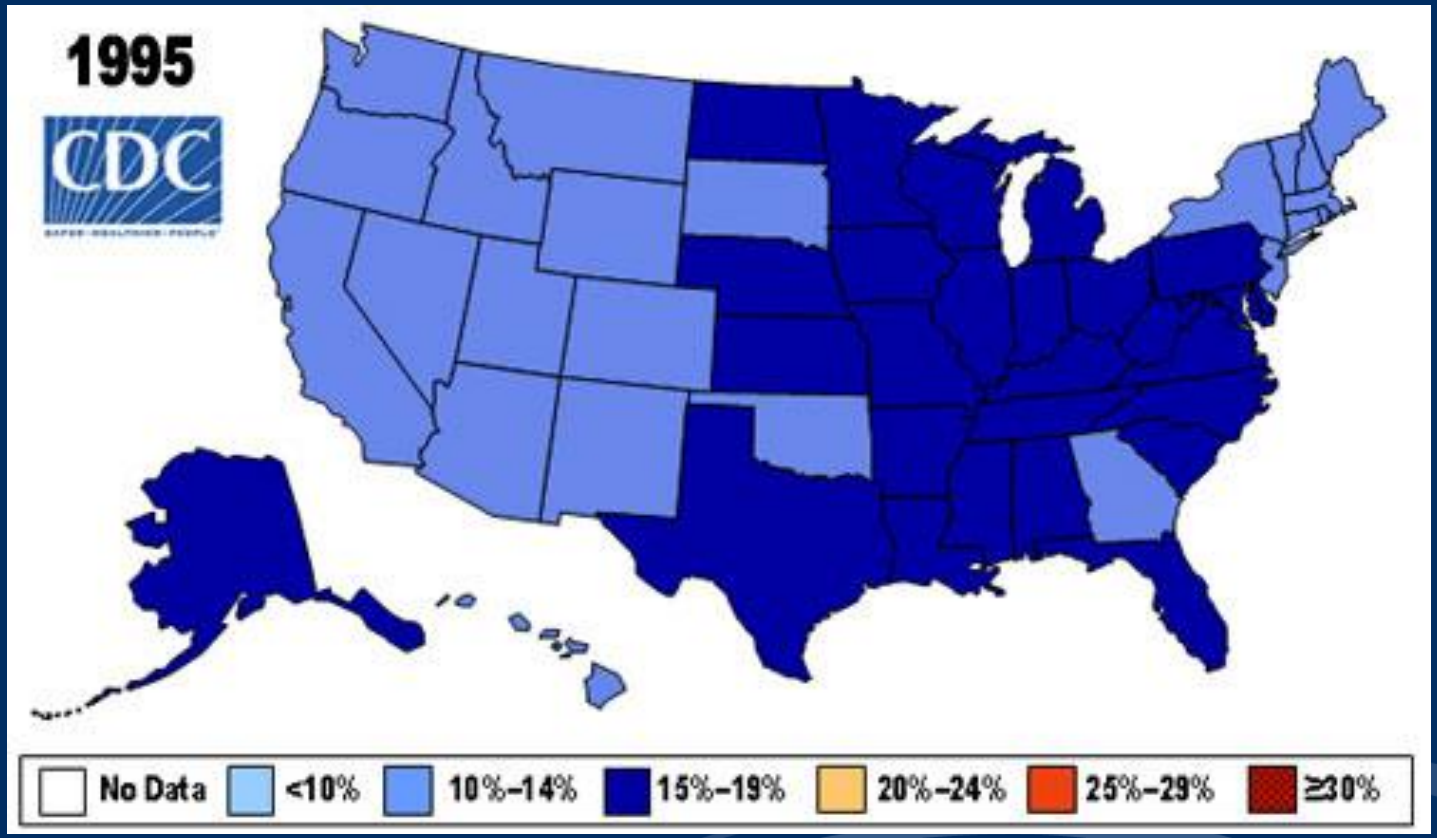
Prevalence of Obesity



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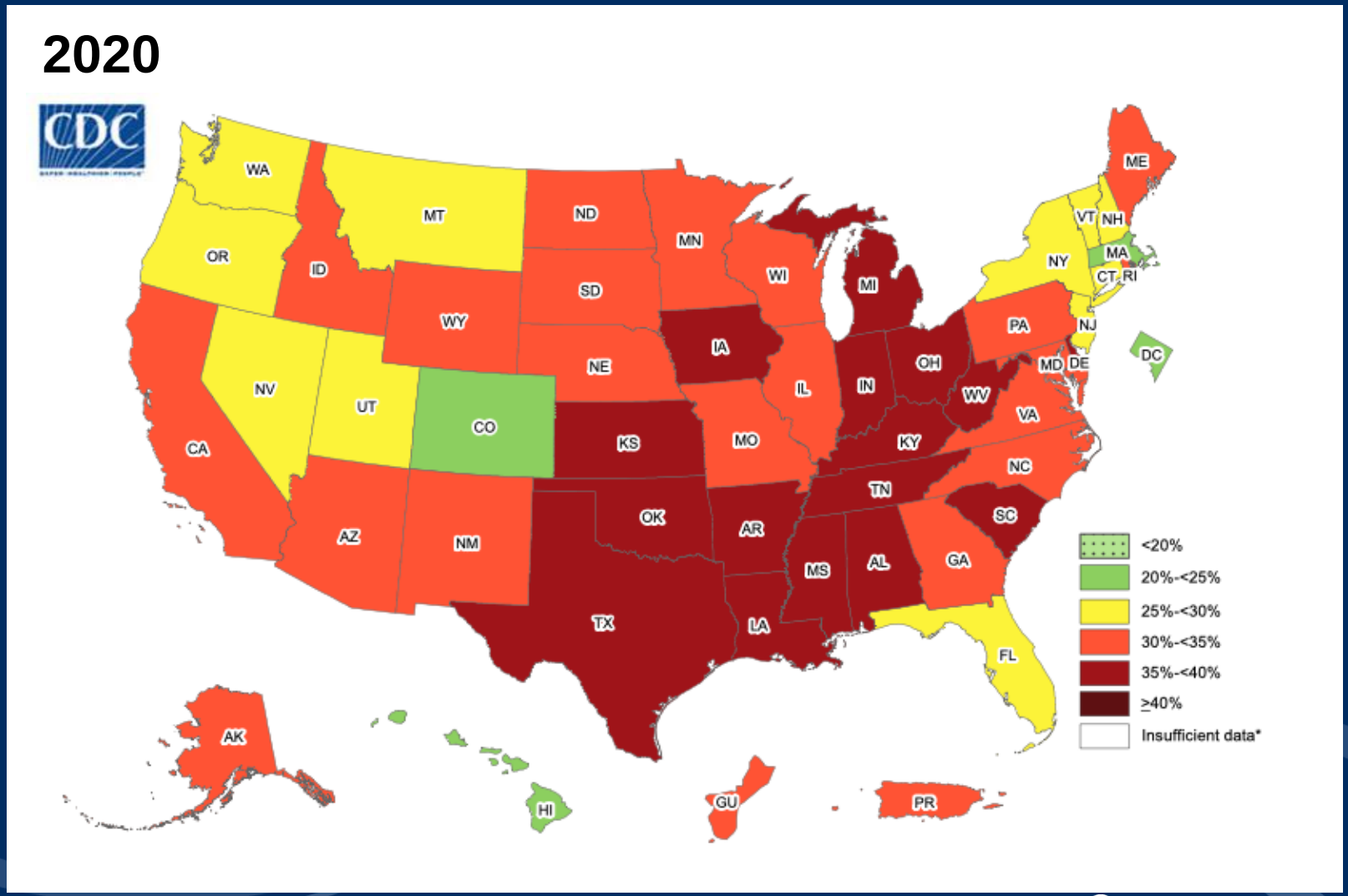
Prevalence of Obesity



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Risk Factors for OSA

- Sleep Heart Health Study: 5615 men and women
  - Male: 2.7x more likely
  - Age: Q10 year increase in odds by 24%
  - BMI
  - Neck girth
  - Snoring and witnessed breathing pauses
  - Each correlated with AHI >15

Young et al. Arch Int Med 2002

- Craniofacial abnormalities
  - Nasal obstruction
  - Enlarged uvula/tongue/tonsils
  - Low-lying soft palate
  - Retrognathia or micrognathia
  - Brachycephaly

Risk Factors for OSA

- Co-morbid illness
  - Obesity
  - Metabolic disorders (hypothyroidism, acromegaly)
  - Neurologic disorders (CVA, neuromuscular disorders)
- Genetic conditions
  - Trisomy 21 (Down syndrome)
- Medications and Substances
  - Sedatives: sleep aids
  - Testosterone replacement
  - Tobacco use
  - Alcohol use
- Family History
  - Increases risk of OSA 2 to 4 times

Symptoms/Signs of OSA

- Snoring
- Witnessed apneas
- Daytime sleepiness
- Sleep fragmentation
- Night sweats
- Nocturia
- Dry mouth/sore throat
- Leg kicking while sleeping
- Morning headaches
- Mood changes
- Decreased libido
- Memory problems
- Attention problems

- Obesity
- Associated diseases
  - Hypertension
  - Cardiac disease
  - Pulmonary hypertension
  - Stroke
  - Glucose intolerance

Case 1

- 65-year-old, non-obese, male presents to internal medicine clinic for hypertension follow up. His medications are as follows and he is strictly adherent.
  - Lisinopril 40 mg daily
  - Chlorthalidone 25 mg daily
  - Amlodipine 10 mg daily
- Blood pressure today is 164/92 mmHg.

Case 1 – Q1

What condition is most likely contributing to uncontrolled hypertension in this patient?

A. Renal artery stenosis

B. Obstructive sleep apnea

C. Pheochromocytoma

D. Cushing's disease

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Case 1 – Q1

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B. Obstructive sleep apnea

C. Pheochromocytoma

D. Cushing's disease

STOP-BANG Questionnaire

TABLE 2. STOP-BANG Questionnaire for identifying patients with obstructive sleep apnea (OSA)

SNORE	Do you snore loudly? (Snoring can be heard through closed door)
TIRED	Do you feel tired, sleepy, fatigued, during daytime?
OBSERVED	Has anyone seen you stop breathing during sleep?
BLOOD PRESSURE	Do you have or are you being treated for high blood pressure?
BMI	Is your BMI > 35kg/m2?
AGE	Are you older than 50?
NECK CIRCUMFERENCE	Is your neck circumference greater than 40 cm?
GENDER	Are you a male?

If the answer to three or more of these questions is "yes," a presumptive diagnosis of OSA can be made.

Modified from: Chung F, Elsaid H. Screening for obstructive sleep apnea before surgery: why is it important? *Current Op Anaesthesiol.* 2009;22: 405–411.

STOP-BANG Questionnaire

- Score of >= 3
  - Sensitivity 91.4% to identify moderate to severe OSA
  - False negative rate 8%
  - NPV 77% to exclude moderate to severe OSA
  - Specificity 28%

Pivetta B, Chen L, Nagappa M, et al. Use and Performance of the STOP-Bang Questionnaire for Obstructive Sleep Apnea Screening Across Geographic Regions: A Systematic Review and Meta-Analysis. *JAMA Netw Open.* 2021;4(3):e211009. doi:10.1001/jamanetworkopen.2021.1009

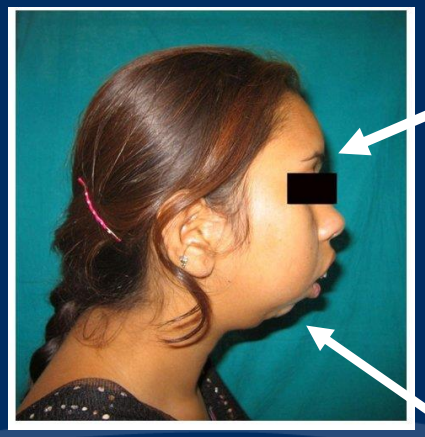
Clinical Examination

- Vital signs
  - Hypertensive
  - Arrhythmias
  - Requiring supplemental oxygen
- BMI >30 kg/m2
  - 40% of those with BMI >40 have OSAS and 50% of those with BMI >50 have OSA

    Kripke et al. Sleep 1997.
- Neck circumference
  - ≥40 cm associated with sensitivity of 61% and specificity of 93% for OSA
  - Men >17 inches, women >16 inches

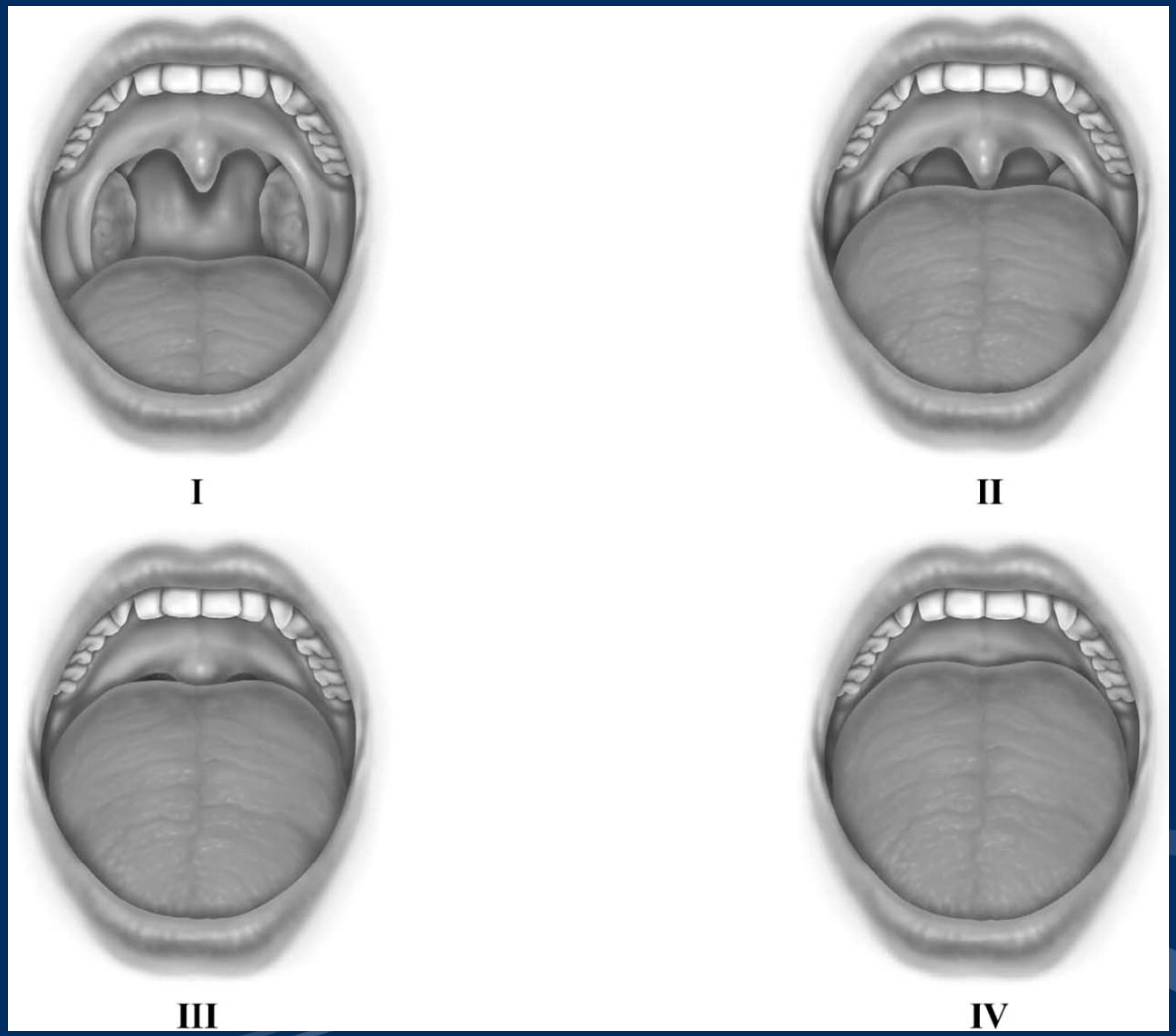
Clinical Examination

- Oral airway
  - Retrognathia (narrows the upper airway behind the base of the tongue)
  - Dental malocclusion and overlapping teeth (indicates small oral cavity)
  - Macroglossia
  - Edema and erythema of the uvula
  - Low-lying soft palate
  - Narrow high arched palate
  - Tonsillar hypertrophy
  - Lateral airway narrowing
- Nasal airway
  - Nasal valve collapse with sniff test
  - Small or asymmetric nares
  - Septal deviation
  - Enlarged inferior turbinates



Friedman Tongue Position

observed without protruding the tongue.



Friedman M et al. Otolaryngology -- Head and Neck Surgery 2006;134:187-196

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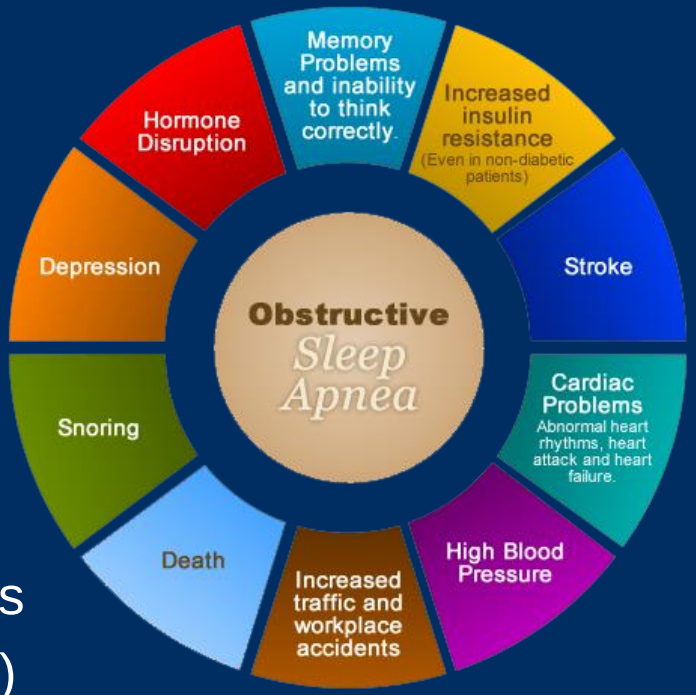
Consequences of OSA

- Coronary artery disease
- Heart failure
- Stroke
- Pulmonary HTN
- Cor Pulmonale
- Cardiac Arrhythmias (atrial fibrillation)
- GERD
- Increased frequency of seizures in epileptics
- Increased headache syndromes (migraines)
- Psychiatric/mood - depression, anxiety, irritability
- Social and sexual dysfunction
- Neurocognitive impairment/ Memory loss
- Increased risk of cancer (all types)



Shahar et al, AJRCCM 2001

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Case 2

52 yo M is evaluated for snoring noted by his wife and excessive daytime sleepiness. He often naps, unintentionally. ESS is 12. His past medical history is notable for seasonal allergies, obesity, and essential hypertension - controlled on lisinopril.

On physical exam, BP is 138/86 mm Hg, BMI is 32 kg/m^2. He has a low-lying soft palate, Friedman score III, and there is nasal congestion. The rest of the exam is normal.

Case 2 – Q1

What is the next appropriate step in management?

A. Prescribe methylphenidate
B. Start continuous positive airway pressure (CPAP)
C. Obtain sleep study
D. Prescribe nasal corticosteroids

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Home Sleep Test (HST)

- Used for most patients to diagnose OSA
- Less expensive, for patient and insurance
- More comfortable
- Faster than in-lab studies

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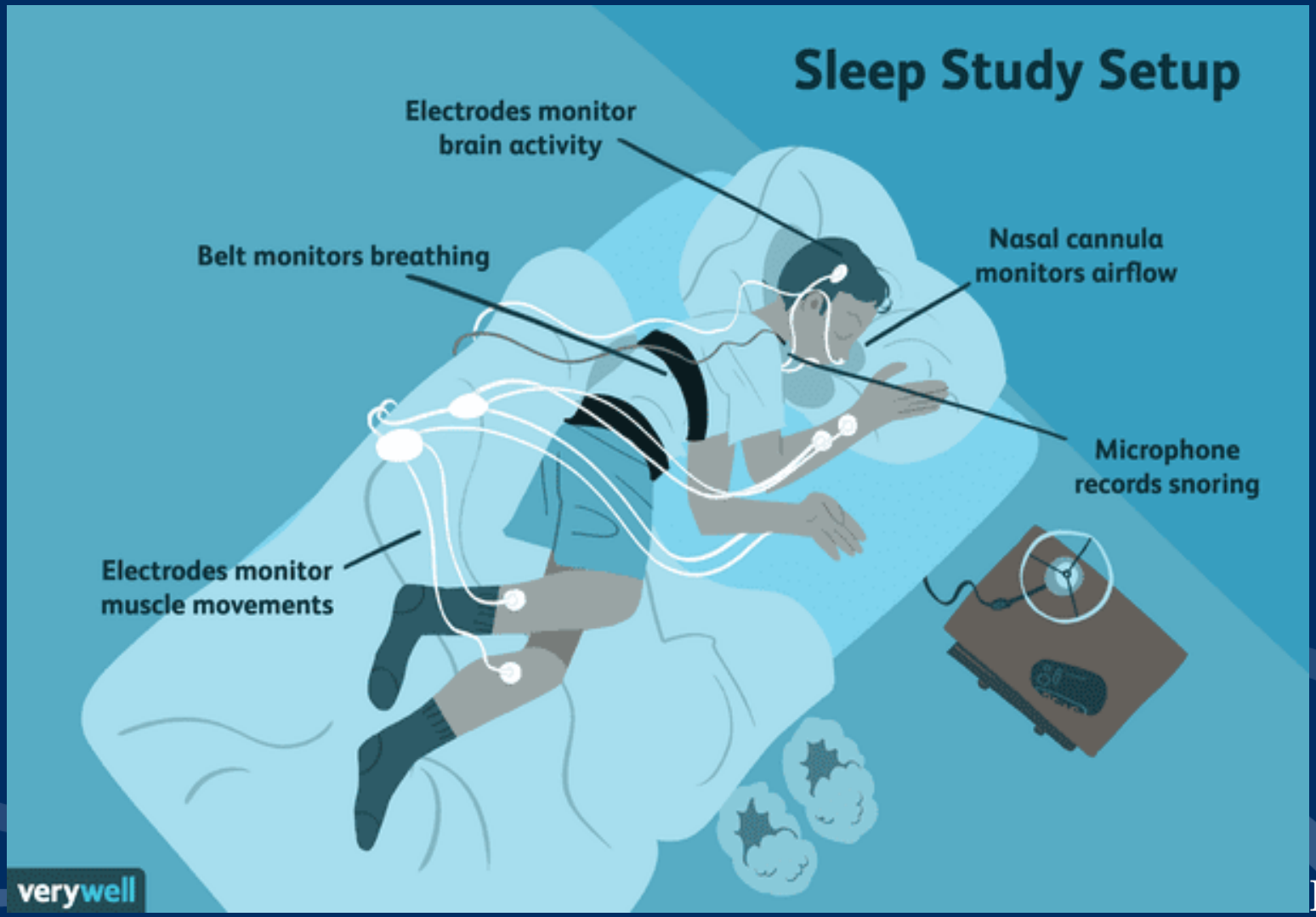
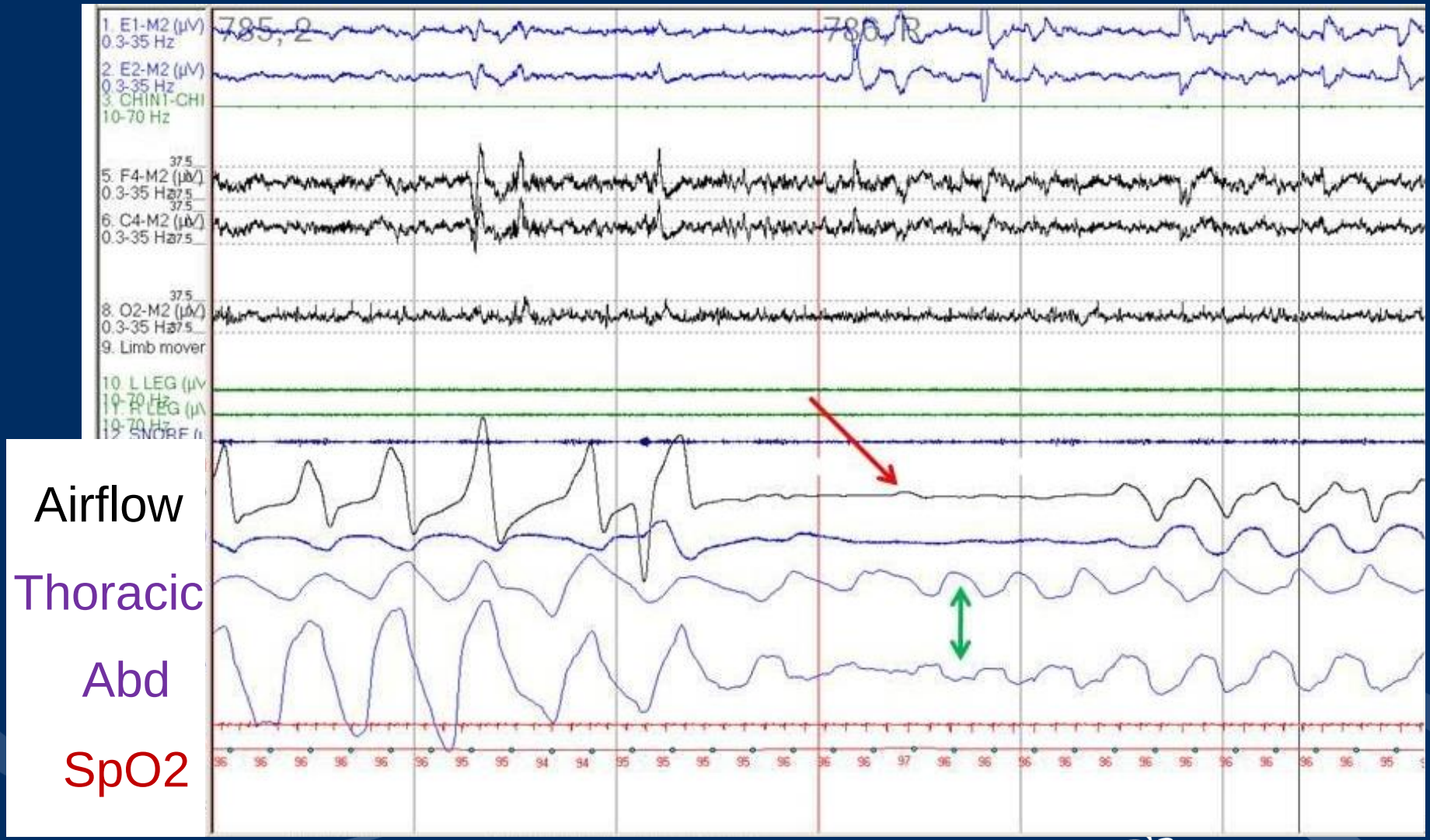
Reasons to Avoid HST

- Previous HST negative, indeterminate, or technically inadequate to make a diagnosis of OSA
- Suspected central sleep apnea
- Suspected parasomnia*
- 1 or more of the following comorbid medical conditions:
  - COPD with FEV1 < 60% predicted
  - Heart failure NYHA Class III or IV
  - BMI > 50 kg/m2
  - Confirmed obesity hypoventilation syndrome
  - Stroke in the last 90 days
  - Neuromuscular disease
  - Neurodegenerative disorder
  - Epilepsy

Diagnostic or Split-Night Polysomnogram

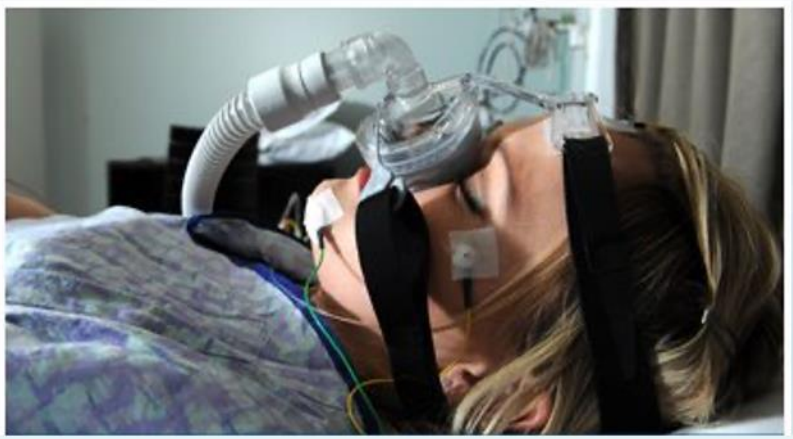


OSA – Example of a PSG



PAP Titration Indications

- Severe OSA on diagnostic study
  - No exact AHI for when to do PAP titration
- Significant hypoxia on diagnostic study
- Inadequate treatment on current PAP therapy
- Intolerance of current PAP therapy
- ***Need diagnostic study on file***



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OSA Severity

Measures of Sleep Apnea Frequency

- Apnea Index
  - # apneas per hour of sleep
- Apnea / Hypopnea Index (AHI)
  - # apneas + hypopneas per hour of sleep

Chart 2. Classification of the severity level of OSAHS according to the American Academy of Sleeping Medicine -1997.

APNEA/HYPOPNEA INDEX	LEVEL
<5	NORMAL
5-15	MILD
15-30	MODERATE
>30	SEVERE

AirView™

Age: 52

Diagnostic Report

Recording details 05/23/2019

Device			ApneaLink Air	Type:	III
Recording	Start:	10:43pm	End: 5:57am	Duration - hr:	7:14
Monitoring time (flow)	Start:	10:53pm	End: 5:55am	Duration - hr:	7:02
Oxygen saturation evaluation	Start:	10:53pm	End: 5:57am	Duration - hr:	7:04

Statistics

Events index	REI (AHI):	88.6	AI:	21.6	HI:	67.0
Supine			Time - hr	6:52	Percentage:	97.6
	REI (AHI):	89.0	AI:	22.1	HI:	66.9
Non-supine			Time - hr	0:09	Percentage:	2.4
	REI (AHI):	72.5	AI:	0.0	HI:	72.5
Upright			Time - hr	0:00	Percentage:	0.0
	REI (AHI):	0.0	AI:	0.0	HI:	0.0
Events totals			Apneas:	152	Hypopneas:	472
Apnea Index	Obstructive:	21.4	Central:	0.0	Mixed:	0.1	Unclassified:	0.0
Cheyne-Stokes respiration			Time - hr:	0:00	Percentage:	0
Oxygen desaturation			ODI:	87.0	Total:	615
Oxygen saturation %	Baseline:	92	Avg:	90	Lowest:	75
Oxygen saturation - eval time %	<=90%sat:	52	<=85%sat:	10	<=80%sat:	0
			<=88%sat:	31	<=88%Time - hr:	2:11
Breaths	Total:	5828	Avg/min:	13.8	Snores:	4281
Pulse - bpm	Min:	61	Avg:	93	Max:	114

Analysis guidelines: **AASM 2007, Manual scoring**

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Case 2 – Q2

What is the next appropriate step in management?

A. Send to an ENT surgeon
B. Advise weight loss
C. Start on oxygen therapy
D. Order an in-laboratory titration sleep study

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Gold Standard OSA Treatment

- Weight loss
- **PAP Therapy**
  - Produces a “pressurized” upper airway to maintain airway patency
  - Start therapy with PAP titration study vs Auto-PAP
  - CPAP before BiPAP

Patil et al, J Clin Sleep Med. 2019;15(2):335–343.

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Oral Appliances for OSA

- Relatively new therapy for OSA
- Two categories:
  - Mandibular Advancing Device
  - Tongue Retaining Devices
- Consider in patients with:
  - mild/moderate OSA
  - BMI < 35
- RCT suggest about equal efficacy to CPAP with better tolerance

Ramar et al, J Clin Sleep Med 2015;11(7):773–827.

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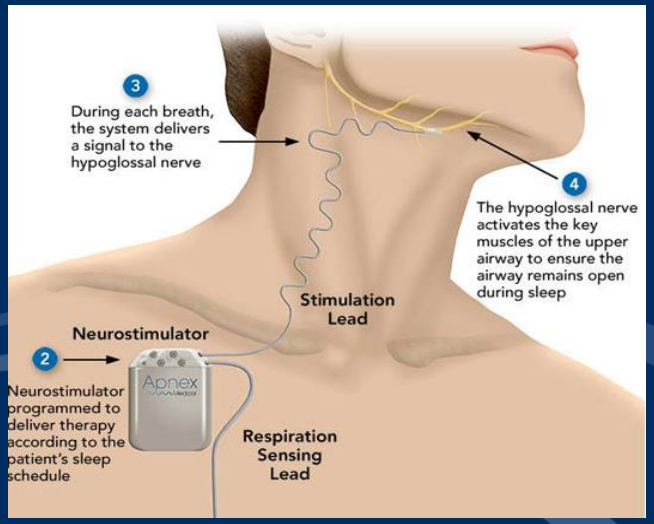
Alternative Treatments of OSA

- Provent nasal strips

- Positional therapy

- Hypoglossal nerve stimulator (INSPIRE)



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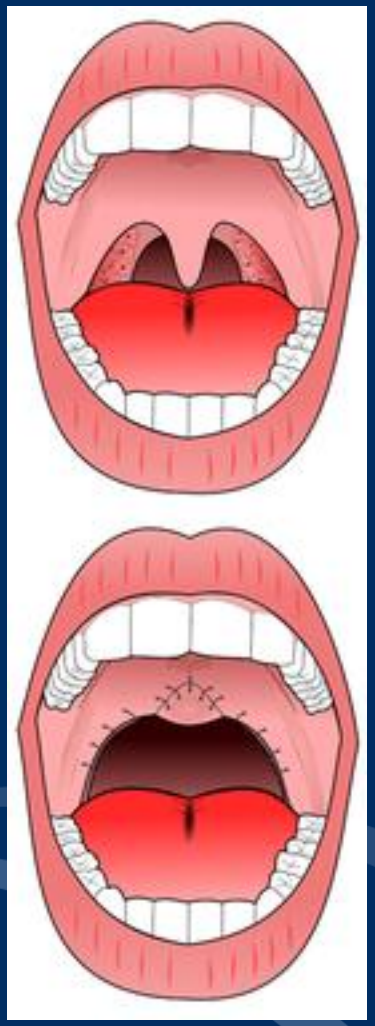
Surgical Treatment of OSA

- Numerous approaches have been tried
- Surgical data limited
- Procedures in general use:
  - Nasal surgery
  - Tonsillectomy +/- adenoidectomy
  - UPPP
  - Tongue reduction
  - Genioglossus advancement
  - Maxillomandibular Advancement (MMA)
  - Tracheotomy



Aurora et al, SLEEP 2010;33(10):1408-1413.

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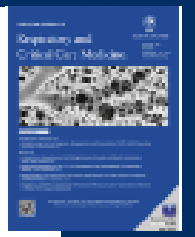
Treatment of OSA: Pharmacotherapy

- Limited success at this point in time

- Some efficacy may be present in the following situations:

Condition	Medication
OHV	Medroxyprogesterone
REM OSA	SSRIs, TCAs
Cheyne-Stokes	Theophylline

Am J Respir Crit Care Med. 2019 May 15;199(10):1267-1276. doi: 10.1164/rccm.201808-1493OC.



The Combination of Atomoxetine and Oxybutynin Greatly Reduces Obstructive Sleep Apnea Severity. A Randomized, Placebo-controlled, Double-Blind Crossover Trial.

Taranto-Montemurro L[1], Messineo L[1,2], Sands SA[1], Azarbarzin A[1], Marques M[1,3], Edwards BA[4,5], Eckert DJ[6], White DP[1], Wellman A[1].

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4 4 Sleep and Circadian Medicine Laboratory, Department of Physiology, and.

5 5 School of Psychological Sciences and Monash Institute of Cognitive and Clinical Neurosciences, Monash University, Melbourne, Victoria, Australia; and.

6 6 Neuroscience Research Australia and the University of New South Wales, Randwick, New South Wales, Australia.

Abstract

Rationale: There is currently no effective pharmacological treatment for obstructive sleep apnea (OSA). Recent investigations indicate that drugs with noradrenergic and antimuscarinic effects improve genioglossus muscle activity and upper airway patency during sleep. **Objectives:** We aimed to determine the effects of the combination of a norepinephrine reuptake inhibitor (atomoxetine) and an antimuscarinic (oxybutynin) on OSA severity (apnea-hypopnea index [AHI]; primary outcome) and genioglossus responsiveness (secondary outcome) in people with OSA. **Methods:** A total of 20 people completed a randomized, placebo-controlled, double-blind, crossover trial comparing 1 night of 80 mg atomoxetine plus 5 mg oxybutynin (ato-oxy) to placebo administered before sleep. The AHI and genioglossus muscle responsiveness to negative esophageal pressure swings were measured via in-laboratory polysomnography. In a subgroup of nine patients, the AHI was also measured when the drugs were administered separately. **Measurements and Main Results:** The participants' median (interquartile range) age was 53 (46-58) years and body mass index was 34.8 (30.0-40.2) kg/m^2. ato-oxy lowered AHI by 63% (34-86%), from 28.5 (10.9-51.6) events/h to 7.5 (2.4-18.6) events/h ($P < 0.001$). Of the 15/20 patients with OSA on placebo (AHI > 10 events/hr), AHI was lowered by 74% (62-88%) ($P < 0.001$) and all 15 patients exhibited a ≥50% reduction. Genioglossus responsiveness increased approximately threefold, from 2.2 (1.1-4.7)%/cm H_2O on placebo to 6.3 (3.0 to 18.3)%/cm H_2O on ato-oxy ($P < 0.001$). Neither atomoxetine nor oxybutynin reduced the AHI when administered separately. **Conclusions:** A combination of noradrenergic and antimuscarinic agents administered orally before bedtime on 1 night greatly reduced OSA severity. These findings open new possibilities for the pharmacologic treatment of OSA. Clinical trial registered with www.clinicaltrials.gov (NCT02908529).

Case 2 - PAP Titration Study

PAP TITRATION SUMMARY TABLE*

PAP Level	O2 Level	Time (min)	TST (min)	TST Supine (min)	REM (min)	Sleep Eff%	Apnea	Hypopnea	Central Apnea	Central Apnea Index	Supine REM AHI	AHI	Avg Spo2	Min SpO2
6	0	10.5	0	0	0	0%	0	0	0	0	0	0	95.1	
7	0	11.0	9.0		0	81.8%	0	2	0	0		13.3	93.0	91.0
9	0	15.5	14.5	6.0	0	93.5%	0	1	0	0	0	4.1	93.6	92.0
10	0	64.5	63.0	63.0	0	97.7%	0	2	0	0	0	1.9	93.4	92.0
11	0	33.5	33.5	33.5	2.5	100%	0	3	0	0	48.0	5.4	93.1	89.0
13	0	58.5	56.0	56.0	13.0	95.7%	0	3	0	0	9.2	3.2	93.5	90
14	0	311.5	299.0	299.0	73.0	96.0%	1	3	1	0.2	1.6	0.8	94.4	89.0

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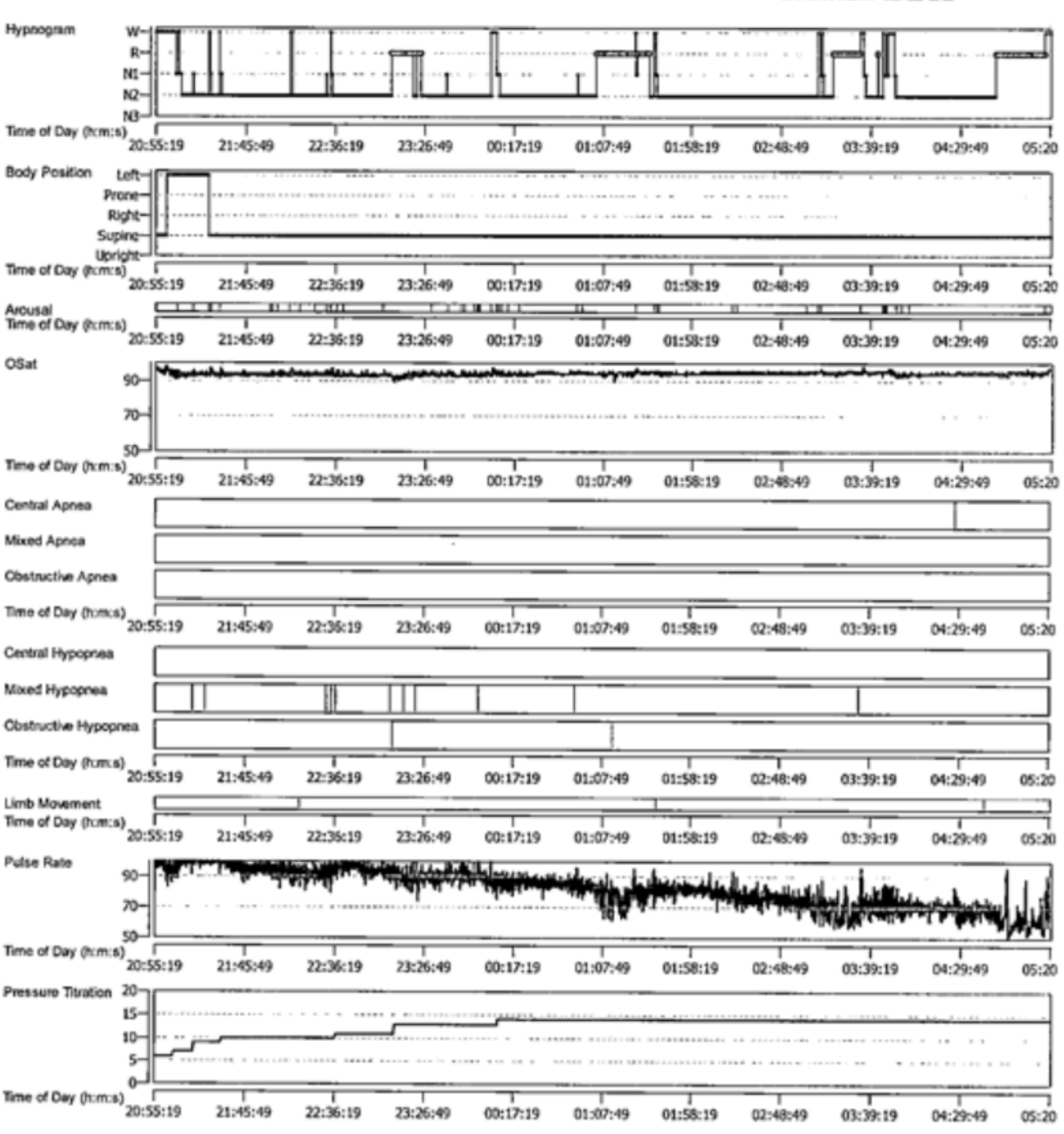
Hypnogram
W
R
N1
N2
N3
Time of Day (h:m:s)
20:55:19
21:45:49
22:36:19
23:26:49
00:17:19
01:07:49
01:58:19
02:48:49
03:39:19
04:29:49
05:20
Body Position
Left
Prone
Right
Supine
Upright
Arousal
OSat
90
70
50
Central Apnea
Mixed Apnea
Obstructive Apnea
Central Hypopnea
Mixed Hypopnea
Obstructive Hypopnea
Limb Movement
Pulse Rate
Pressure Titration
20
15
10
5
0

Case 2 – Q3

After 8 weeks of CPAP use, the patient notes some improvement in his sleep and energy. He continues to still feel drowsy and sleepy during the day. His ESS is a 9. There are no new changes to his PMH or his medications.

What is the next appropriate step in management?

A. Prescribed eszopiclone
B. Prescribe modafinil
C. Review data from the patient's CPAP device (compliance report)
D. Switch to Bilevel PAP therapy

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Compliance Report

Compliance

Payor	Standard

Usage

02/21/2018 - 03/22/2018

Usage days	**27/30 days (90%)**
>= 4 hours	**26 days (87%)**
< 4 hours	**1 days (3%)**
Usage hours	186 hours 5 minutes
Average usage (total days)	6 hours 12 minutes
Average usage (days used)	6 hours 54 minutes
Median usage (days used)	7 hours 4 minutes
Total used hours (value since last reset)	185 hours

AirSense 10 Elite

Serial number	23172245344
Mode	CPAP
Set pressure	14 cmH2O
EPR	Fulltime
EPR level	2

Therapy

Leaks - L/min	Median:	**0.1**	95th percentile:	**3.1**	Maximum:	**20.0**
Events per hour	AI:	**0.1**	HI:	**0.1**	AHI:	**0.2**
Apnea Index	Central:	**0.0**	Obstructive:	**0.0**	Unknown:	**0.0**
RERA Index						**0.8**
Cheyne-Stokes respiration (average duration per night)						**0 minutes (0%)**

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Compliance Report

Compliance

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RERA Index						**0.8**
Cheyne-Stokes respiration (average duration per night)						**0 minutes (0%)**

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Inpatient Insomnia: Causes

- Poor sleep hygiene!!
- Anxiety, depression, grief
- Pain
- Dyspnea/Cough
- Nocturia
- Restless legs syndrome
- Medications started or withdrawn
- Acute on chronic insomnia

Inpatient Insomnia: Management

- Environmental modification
  - Ear plugs, quiet sign, blinds open/closed
- Anxiety
  - Anxiolytic: benzo or benzo-RA
- Nocturia
  - Change in diuretic schedule
- Dyspnea
  - Head of bed elevation to 30 degrees
- Psychosis
  - Antipsychotic

Inpatient Insomnia: Management

- Melatonin 3-6 mg
  - Schedule it 2 hours before bedtime, not PRN
- Ambien
  - 5 mg for naïve patients, caution in elderly
- Mirtazapine <15 mg
  - Increased appetite
- Trazodone 50-100 mg
  - Not recommended as first line; morning grogginess
- Gabapentin 300-900 mg
  - 60 minutes before bedtime, Caution in AKI or ESRD
  - Helpful for pain control and/or restless legs syndrome
- Diphenhydramine 25-50 mg
  - Tolerance develops in days, avoid discharge on this medication
- Seroquel 25-100 mg
  - Comorbid psychiatric condition or psychosis

BUMC-P Sleep Medicine

- Clinic – Banner Lung Institute
  - Office phone: 602-521-3400
- Sleep lab – 755 E McDowell Road (green roof)
  - Scheduling phone: 480-412-3684
- We see everything – insomnia, OSA, CSA, narcolepsy, RBD, nocturnal epilepsy, etc
- Clinical rotations, Sleep fellowship
- Email me: kirstin.knobbe@bannerhealth.com

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