#### West Virginia University, ROBERT C. BYRD HEALTH SCIENCES CENTER OFFICE OF CONTINUING EDUCATION

The WVU School of Dentistry and Alumni Association Spring Conference Dr. Clarence C. and Maxine Davis Cottrill Endowed Lecture Presents

Practicing Sleep Medicine as a Dentist: What the Dentist and Team Need to Know April 27, 2018, Morgantown Marriott at Waterfront Place

> Presented By: Dennis R. Bailey, DDS

#### **Course Outline and Plan**

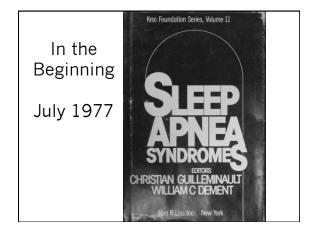
- Morning Session 8 AM to Noon Introduction to Sleep Medicine and Sleep Disorders Health Consequences of Sleep Disorders – Overview The Role of the Dentist – Importance of Nasal Airway
- Afternoon Session 1 to 4 PM
   Sleep Bruxism The Unknown Sleep Disorder
   Basics of Pediatric Sleep Disorders
   Oral Appliance Therapy Splints vs Oral Appliances

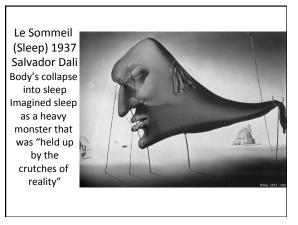
Introduction and Basics of Sleep Medicine Dennis R. Bailey, DDS, FAGD, D,ABDSM, FAAOP Private Practice: Denver, Colorado Co-Director: UCLA - Sleep Medicine Mini-Residency Past-President: Colorado Sleep Society Past Chair (2012-2016): Sleep Medicine

Committee – AAOP

#### Disclosures (non-financial)

<u>Consultant</u>: CareCore / MedSolutions Now: eviCore healthcare <u>Co-author:</u> Dental Management of Sleep Disorders <u>Consultant</u>: RhinoMed (Mute)



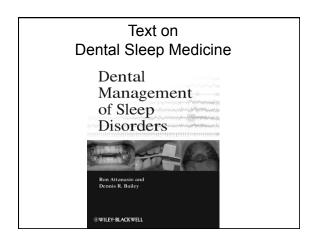


#### History and Sleep

- Based on "Wild Nights" by Benjamin Reiss professor of English Emory Univ.
- Sleep pre and post the Industrial Revolution around 1800
- Late 1800s the unions mandated 8 hours work, 8 hours rest and 8 hours for what you will
- Pre-Industrial Revolution sleep was not contiguous but was in four hour blocks

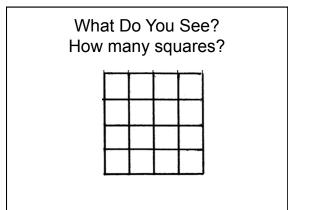
#### Roger Ekirch (Historian) Reports

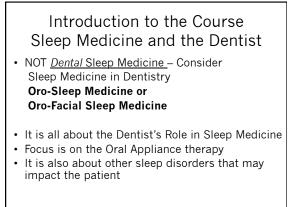
Prior to the Industrial Revolution we had "segmented" sleep – First four hours was "dead sleep" and second four hours "morning sleep" was separated by 1+ hours of quiet wakefullness called "the watching". This persisted into the early part of the 20<sup>th</sup> century in some cultures.

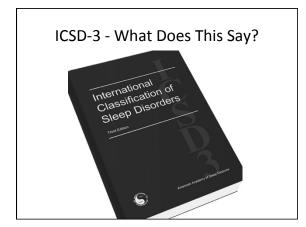


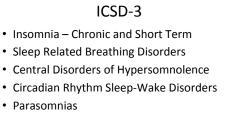
Aoccdrnig to rseaecrh at Hravard Uinervtisy, it deosn't mttaer waht oredr the ltteers in a wrod are, the olny iprmoatnt tihng is taht the frist and lsat ltteer be in the rghit pclae.

Tihs is bcuseae the huamn mnid deos not raed ervey lteter by istlef, but the wrod as a wlohe.









- Sleep Related Breathing Disorders
- Other Sleep Disorder
- Appendix: A & B

#### Earliest link between **Sleep and Performance**

Nathanial Kleitman in the 1930's Showed the link between sleep and performance

Sleep Deprivation negatively effects mood, ability to focus and our ability to access higher level cognitive function



## How Do We Define Performance? Related to Sleep and Sleep Deprivation

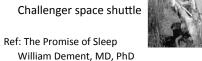
- Cognitively
- Functionally
- · Behaviorally
- Socially
- Athletically

#### **Insufficient Sleep and Accidents**

Examples of Sleep Deprivation:

Exxon Valdez Three Mile Island Chernobyl

Challenger space shuttle

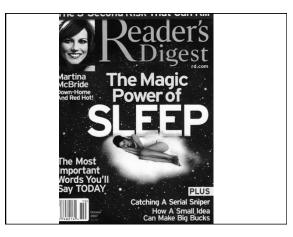


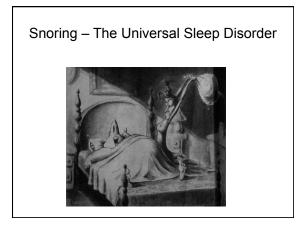
Sleep Medicine Alert, 1999

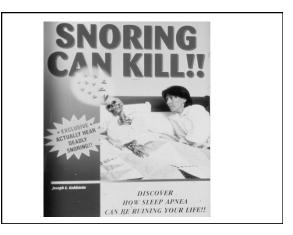
We Sleep 25% Less Than Our Forefathers

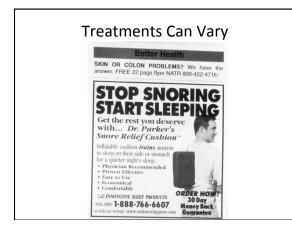
#### SUSTAINED WAKEFULLNESS

**17** Hours can Lead to a Decrease in Performance Equivalent to a Blood Alcohol Level of 0.05









## Sleep Disorders

25% of Americans Complain of Trouble Sleeping

25% of Americans Complain of Excessive Fatigue According to a Gallup Survey

Over 29% With Sleep Problems Use OTC Medications

# "Getting the Sleep You Need"

Average American Gets 243 Hours Less Sleep Per Year than they did in 1969

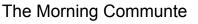
Sleep Research Institute "Getting the Sleep You Need" Washington, D.C. Feb/ March1999

13% of young adults Ages 18 - 29

complain of falling asleep at work

National Sleep Foundation's Sleep In America Poll

51% Report that Sleepiness Interferes with the Amount of Work They Get Done





# National Commission on Sleep Disorders, 1993

40 Million Americans have Some Type of Chronic Sleep Disturbance

20-30 Million have Intermittent Sleep Related Problem

## Falling Asleep On The Job

911 Operator Falls Asleep On A Call (Anne Arundel County, Maryland)

On July 24, 2004, a woman was startled awake She thought someone was breaking into her home She called 911 – as she described the situation the operator fell asleep to the point of snoring

## 100 Million

The Number of Americans Every Night Who Fail to Get a Good Night's Sleep

Estimated by the American Academy of Sleep Medicine

#### What Wives Like Least About Sleeping With Their Husbands

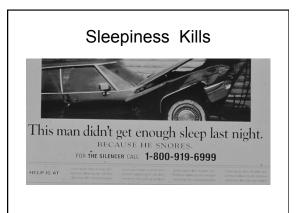
- 1. Snoring
- 2. Hog the Bed
- 3. Steal the Covers
- 4. Kick the Bed-Partner
- 5. Bruxism
  - From: USA Today, 1993

Sleep Disorders Sleep Deprivation Excessive Daytime Sleepiness

Add \$16 Billion to Healthcare Costs

Sleep Disorders Sleep Deprivation Excessive Daytime Sleepiness

> Result in \$50 Billion In Lost Productivity



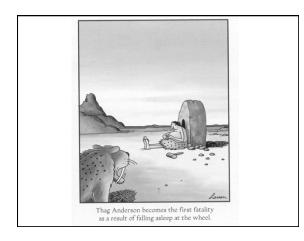
One In Five

Adult Americans Who Admit to Falling Asleep Behind the Wheel in the Last Year

From: National Sleep Foundation Study 2002

## Results of Drowsy Driving Annually

1,550 Deaths 76,000 Injuries 100,000 Police Reported Crashes \$12.5 Billion in Monetary Losses Source: National Highway Traffic Safety Administration



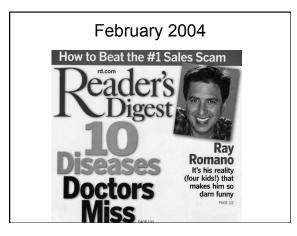
National Sleep Foundation Sleep in America Poll 2009

- 105 million (54%) have driven drowsy in the past year
- 54 million (28%) have driven drowsy at least once in the past month

## 2009 Sleep in America Poll

- 20 % report sleeping less than 6 Hrs on average - a decrease since 2001
- 27% have disturbed sleep a few nights a week in the past month
- 7 Hrs 24 mins optimum sleep usually get 6 Hrs 40 mins on typical workday

www.sleepfoundation.org (NSF)



## 10 Diseases Doctors Miss

- Celiac Disease
- Hypothyroidism
- Lyme Disease
- Lupus
- Sleep Apnea

### More Facts

- Sleep is just as important as diet and exercise
- The body NEVER adjusts to shift work
- Snoring is the primary cause of sleep disruption in 90 million adults (37 million on a regular basis)
- Do not sleep enough bigger appetite / more hungry (lower leptin level)
   Ref: National Sleep Foundation

## Random Facts About Sleep

- Man is the only mammal that willingly delays sleep
- Exercise regularly and sleep better
- 6 out of 10 health care providers feel they do not have adequate time to discuss Insomnia with patients
- Caffeine "most popular drug in the world" Coffee beans 2nd most traded commodity
- Naturally feel tired at 2PM and 2AM



## What is This Thing Called Sleep ?

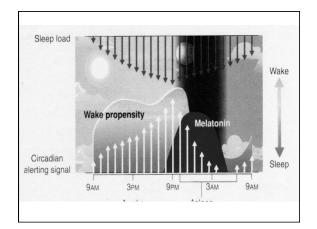
Overview of Sleep

Overview of Sleep Disordered Breathing (Snoring & Sleep Apnea)

## Length of Human Cycles

Circadian: About One Day (24.2 Hrs ["tau"]) Sleep / Wake Cycle - Temperature (present thru history – plants have a rhythm)

- Infradian: Greater than every 24 hour Longer than a Circadian Rhythm (Menstrual Cycle, Depression)
- Ultradian: Biologic Rhythms (variations) that occur more frequent every 24 hours - more than one time a day (heart rate, thermoregulation, nostril dilation)



Two Circadian Rhythms Independent of the Sleep-Wake Cycle

- Main Function: Promote
   Wakefullness
- Related to peaks in alertness late morning & early evening
- Related to troughs in alertness early morning & early afternoon

## Basics of Sleep & Circadian Rhythm

#### Zeitgeber

- Time Keeper
- Time ques light dark - noise - social interaction that allows people to

entrain to the 24 hour cycle

#### Entrainment

- Methods by which sleep / wake cycle is controlled
- Synchronization of a biologic rhythm

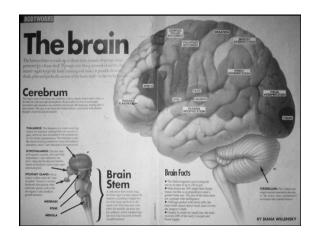
## Free Running Clock

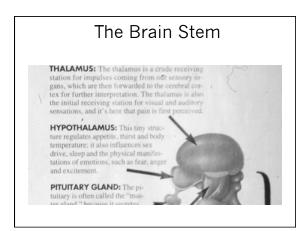
- No schedule
- Fluctuating sleep wake cycle
- Examples: Unemployed
  - Retired
  - Summer Break

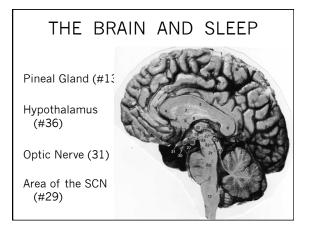
## Sleep Is Work !

Brain Activity shifts into New Areas

Brain Chemistry Changes The Brain Uses More Oxygen While Asleep Than Awake !







## Neurotransmitters and Wakefulness

- The Excited / Stimulated Awake circuitry Brainstem Monoamines Norepinephrine (NE) Serotonin (5HT) Dopamine (DA) Acetylcholine (Ach) Hypocretin (Orexin) Glutamate (CNS excitatory neurotransmitter)
- Calm / Quiet Wakefulness from Hypothalamus Histamine

## Additional Neurochemical Wake Promoting

Cortisol
 Wake promoting
 Increased in Insomnia

## Neurobiolgy of sleep

- Acetylcholine: REM sleep
   neurotransmitter (decreased in NREM)
- GABA: Main central nervous system neurotransmitter - CNS inhibitory neurotransmitter
- Adenosine: Sleep neurotransmitter (blocked by caffeine) accumulates as the day progresses
- Glycine: inhibitory neurotransmitter in the spinal cord (causes muscle atonia in REM)

## Also For Sleep

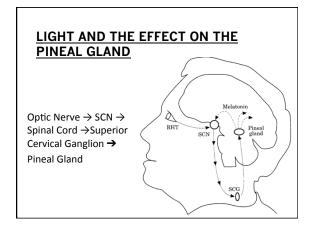
- Melatonin (a hormone)
- Entrainment of the Circadian cycle
- Initiate Sleep Derived from Tryptophan
- → Serotonin Released From Pineal Gland
- Potent Anti-inflammatory
- Levels altered by altered influence of light especially at night

#### Melatonin Study done with the Zebrafish

- More produced at night (regardless if animal nocturnal or diurnal)
- Production and effect related to a gene "aanat2"
- Action: "turns on Adenosine" thus regulates the homeostatic pathway

J Neuron March 5, 2015





#### Being Sleepy / Tired - 13.5% report related difficulties

- 23.2% have difficulty concentrating
- 18.2% have difficulty remembering things
- · Difficult to work on hobbies
- Hard to perform employment or volunteer work

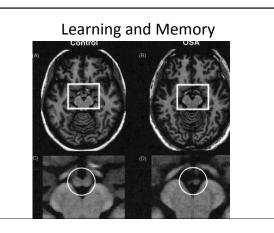
Ref: CDC:Weekly Morbidity & Mortality Report

## Sleep and Memory

- Sleep is involved in memory consolidation
- Process of changing new memory into more permanent form
- Begins with encoding represents stored experience in the brain

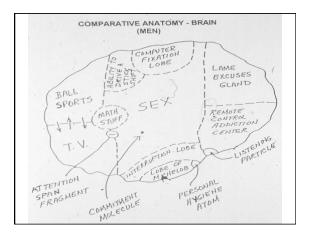
#### Memory Recall and Sleep Deprivation

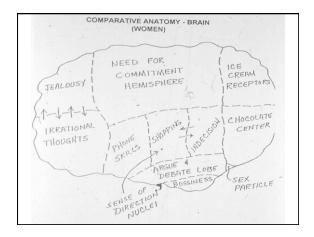
- Sleep Deprivation led to more difficulty with memory encoding performance (recall)
- Resulted in lower predictive ability of performance
- Sleep important both before learning and after helps with memory formation and encoding



## Mamillary Bodies

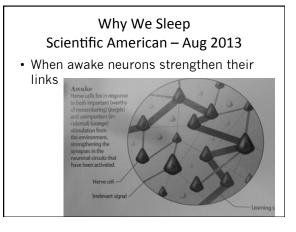
- Associated with memory
- Damage associated with memory loss
- Common in OSA may be related to hypoxia
- Associated with Thiamine (B1) deficiency similar to chronic alcoholism (Korsakoff's syndrome)







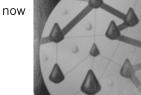




#### When asleep

 Weakens neuronal links – conserves energy

 Newly formed memories now "stick"



## Plasticity

- In humans the brain accounts for 20% of the body's energy budget
- Synaptic weakening during sleep restores brain circuitry to baseline – reduces excess energy use
- Sleep restores brain "to a state where it can learn and adapt while awake"

## Brain Chemistry

- Awake "soup of signaling chemicals" includes acetycholine, norepinephrine, dopamine, serotonin, histamine, hypocretin
- During NREM soup less concentrated
- Synapses weaken soup less concentrated
- Involves brain-derived neurotropic factor (BDNF) promotes synaptic strengthening and leads to memory acquisition – BDNF present during the awake state and lower during sleep

## Sleep Drives Metabolic Clearance from the Brain

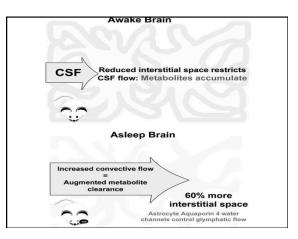
- Brain lacks a conventional lymphatic system

   instead CSF circulates through the brain –
   interchanges with interstitial fluid (ISF) and
   removes interstitial proteins (β-amyloid)
- CSF influx around arteries and ISF exists along veins
- Termed the glymphatic system →

# Sleep Drives Metabolic Clearance cont.

- Interstitial space during sleep is 60% greater thus an influx of CSF
- ISF increases removal of  $\beta\mbox{-amyloid}$  removal and other toxins
- Lack of sleep allows these toxins to accumulate
- Called the "dishwasher effect"

Science Vol 342 Oct 18, 2103



## Sleep Facilitates Clearance of Metabolites from the Brain: Glymphatic Function in Aging and Neurodegenerative Diseases

Rejuvenation Research AR Mendelson and JW Larrick Vol 16, No 6, 2013

#### Brain Glymphatic Transport A Rodent Study

- Transport controlled by the brain's arousal system during sleep
- Using MRI transport most effective in the lateral position not as effective in supine or prone position
- Lateral position has "evolved" to optimize waste removal
  - J of Neuroscience Aug 2015 35(31):11034-11044

## SirT3 (Sirtuin3) Protein

- Protects neurons in the Locus Coeruleus (related to alertness, attention, regulates sleep/wake cycle and cognition)
- Upregulates this protein when there is sleep loss for mitochondrial energy production – Reduces reactive oxidative species (ROS)
- Only related to short-term sleep loss
- Extended wakefullness = SirT3 missing results in cell death due to increased ROS
- J of Neuroscience March 2014 From: Univ of Penn

#### TREM2

Triggering Receptor Expressed on Myeloid 2

- Microglial surface receptor that triggers the intracellular protein tyrosine phosphorylation
- Deficiency augments the accumulation of beta amyloid

In: Cell 2015





## SLEEP DISORDERS

BASICS OF SLEEP MEDICINE

## Historical Review of Sleep

- 1913 Henri Peiron published "Le Probleme Physiologique du Sommeil" considered sleep from physiologic perspective – hypnotoxin theory
- 1929 Johannes Berger father of electroencephalography – described difference in brain activity during sleep and wakefullness

## More History

- 1936-1937 First continuous overnight sleep studies by Loomis and colleagues and gave rise to first sleep stage classification
- 1935 Bunning coined the term "biological clock"
- 1953 Asernisky & Kleitman revised sleep staging – mainly by finding REM sleep

## More Recently

 1972 – Robert Moore's work established circadian pacemaker in the SCN – soon after mapped the retinohypothalamic projection – linked light & darkness to sleep-wake circadian rhythm

## DEFINITION OF SLEEP

Mostly Described By What it is NOT

WHAT IS SLEEP ? Poorly Understood Effects Well Recognized

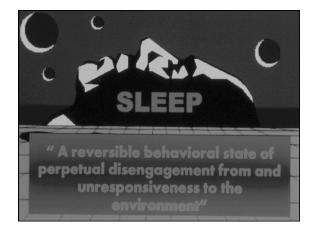
## <u>SLEEP</u>

Not An Altered State Of Consciousness

#### What Does it Mean To Be Awake

Wake State Instability is a Cognitive / Memory Manifestation of Sleepiness

Associated with Slow Wave Energy (SWE)



#### Another Definition

A complex reversible state characterized by behavioral quiescence, diminished responsiveness to external stimuli, and a stereotypical species-specific posture

Ancient Proverb

## Sleep is a Short-Short death Death is a Long-Long Sleep

## A Quiz

<u>Wide Awake</u> Low Energy Tired Drowsy ≌ (time) Asleep

## Partial Theory of Sleep

- Unlikely that Sleep has no Function
- Theories of Sleep Function Restorative and Somatic Growth Growth Hormone released at N3 sleep Metabolic theory Regulate body temperature
  - Energy conservation
  - Remove "toxins" generated while awake

## Partial Theories

- Survival Theory
   Protective / Adaptive Behavior
   Immune Defense Function
- Neural Growth & Processing Neuronal Plasticity Brain Development / Restoration Learning / Memory

# Short Sleep Duration and Obesity

- Decline in sleep duration over the past 50 years = 1.5 to 2 hr (Sleep in America poll 2005)
- Short sleep duration in children
   OR for obesity 1.89
- Short sleep duration in adults
   OR for obesity 1.55

Meta-Analysis of Short Sleep Duration and Obesity in Children and Adults SLEEP 2008;31(5):619-626

NORMAL SLEEP

Sleep Architecture

## **SLEEP ARCHITECTURE**

Sleep is an Active and Complex State.

 NREM Sleep
 Stage 1: Transitional Phase; 5% of Sleep Time

 Sleep
 Stage 2: Light Sleep; 50% of Sleep Time

 Delta Slow Wave Sleep (stages 3&4):
 Deep Sleep; 20% of Sleep Time

 REM Sleep
 Rapid-Eye-Movement Sleep:

 The Dream Stage; 25% of Sleep Time

Sleep Architecture

Stage 1 Transition 5%

Stage 2 Light Sleep 50%

Stage 3 & 4 Deep Sleep

Restorative Sleep

Slow Wave Sleep

REM Dream Sleep 25%

20%

Stage N1 (NREM 1) Stage N2 (NREM 2) Stage N3 (NREM 3&4) • REM

#### Stage R (REM)

Stage W (Wakefullness)

## REM Atonia

- Norepinephrine Serotonin Histamine shut down
- Leads to muscle atonia
- Two types of REM: Phasic and Tonic

## REM Sleep & Memory

- Effects Procedural and Spatial Memory
- **Procedural memory**: relates to everyday tasks – automatic retrieval like tying shoes
- **Spatial memory**: records information about the environment driving around and finding your way

## NREM & Memory

• Declaritive memory: Knowledge Facts Long term memory

## Physiology During Sleep

 Compared to awake levels: Sympathetic activity diminished Parasympathetic activity increased during NREM Sympathetic activity increases

phasic REM

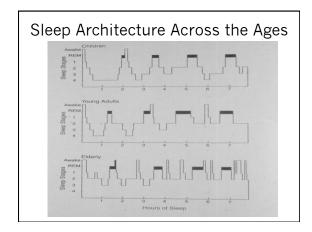
during

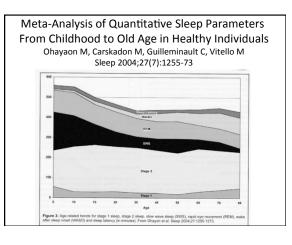
# CV System

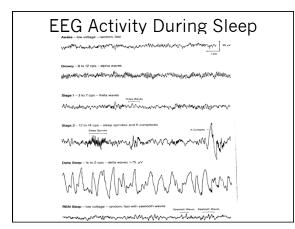
- Heart Rate, Cardiac output, Blood Pressure, systemic vascular resistance are lower during NREM
- All higher during phasic REM

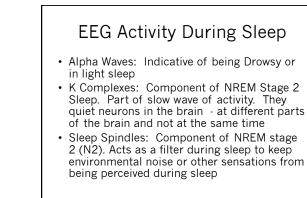
## Other Factors

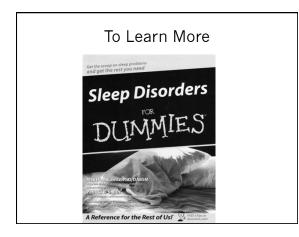
- Urine production less less glomerular filtration
- Gastric secretion at peak levels between 10PM and 2AM – least between 5AM and 11AM
- Endocrine system growth hormone increased in N3 sleep











# "Education is a progressive discovery of our ignorance"

James Howard Univ. of Washington - 1984

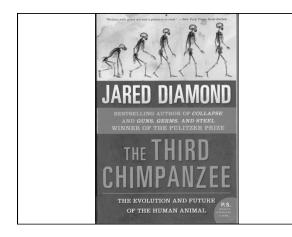
#### Sleep Related Breathing Disorders SRBD

It All Potentially Starts with Mouth Breathing Snoring Sleep Apnea (Obstructive Sleep Apnea Syndrome – OSAS) Hypopnea Upper Airway Resistance Syndrome – UARS

#### Evolution and Development of the Modern Airway, Speech Acquisition and Obstructive Sleep Apnea

The Great Leap Forward Hypothesis

Davidson TM, Sedgh J, Tran D, Stepnowsky CJ In: Sleep Med 2005;6(6):497-505



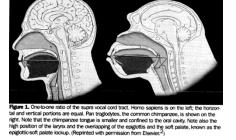
## The Great Leap Forward

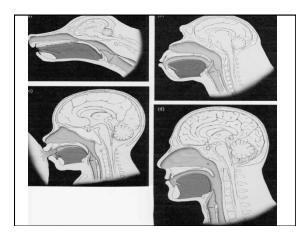
- Theory developed by Jared Diamond at UCLA in 1992
- Occurred about 40,000 years ago
- Predicated on the pressure to develop voice, speech and language
- "The third chimpanzee: the evolution and future of the human animal"

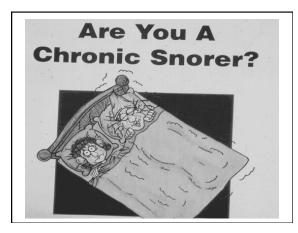
## Great Leap Forward

- Anatomic Changes to the Skull Evolved over Time to Facilitate Speech
- As a Result OSA Became More Severe
- The Maxillary & Mandibular Denture Bases were Altered
- The Nasal Airway Became Smaller
  The Tongue now Occupies the Oropharynx

## Evolution of Airway Obstruction and SRBD

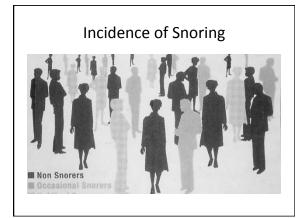


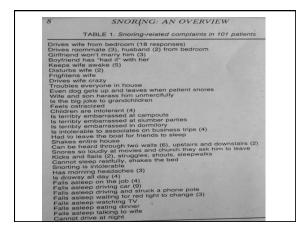


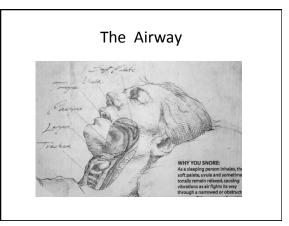


#### Noise Levels and Snoring In Decibels (dB)

- 30 dB = Whisper
- 40 dB threshold for heavy breathing vs snoring
- 60 dB = Normal Conversation
- 60 65 dB = Laughter
- 75 dB = Average radio Vacuum Cleaner
- 85 90 dB = Lawnmower
- 90 dB = OSHA limit Hearing damage if excessive exposure to levels above this
- 120 dB = Chain saw







#### Upper-Airway Inflammation Triggered by Vibration in a Rat Model of Snoring

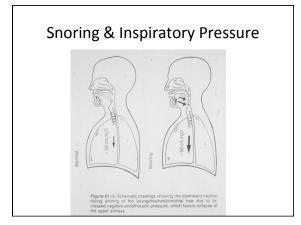
- Snoring is a source of upper airway injury, inflammation, loss of sensitivity, muscle and nerve dysfunction and sensory neuropathy
- Upper airway vibration triggers a local inflammatory process

Almendros I et al SLEEP, 2007:30(2);225-227

## Incidence of Snoring

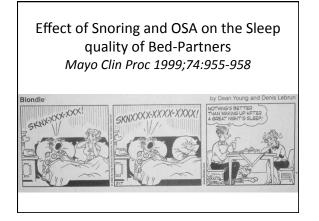
By the Age of 40 40% of Males 20% of Females

By the Age of 60 60% of Males 40% of Females



## Three Main Principals Related to Sleep Breathing Disorders

- Bernoulli Effect: as flow (velocity) increases so does negative pressure (paper straw)
- Venturi Effect: fluid flows through a tube less diameter – fluid speeds up (garden hose)
- Variable resistor: as flow (speed) increases so does resistance (seat belt)



#### How Likely is a Patient To Have Sleep Apnea ?

Chief Complaint	Odds Ratio
Non-Snorer	1
Snoring Alone	3
Snoring Plus Other	5
Signs of Sleep Apnea	

## Sleep Apnea is Common

- Prevalence: Men 25% Females 9%
- If Symptoms: Men 4% Females 2%
- N = 1200 Age 35-60
- From: Young NEJM 1993 Confirmed by Bixler AJRCCM 1997

## Sleep Breathing Disorder (SBD) and Prevalence

- Mild to severe sleep apnea (AHI>5) is 26%
- Prevalence when AHI >15 is 13% in men and 6% of women
- !4% of men and 5% of women: AHI >5 with daytime sleepiness (based on ESS)

Increased prevalence of Sleep-Disordered Breathing in Adults Peppard, Yopung, et al Am J Epidem April 2013

#### The Three Types of Apnea

- Obstructive: Absence of Airflow Despite Respiratory Effort (gasping)
- Central: Absence of Airflow and No Respiratory Effort
- Mixed: Combination of Obstructive & Central

#### APNEA DEFINED

- Apnea: Cessation of Breathing for 10 Seconds or Longer – 80-100% Decrease in Airflow & Thoracoabdominal Movement (now is defined as ≥90% in sensor signal that is ≥10 sec.)
- Hypopnea: Interruption of Breathing by 30% or More & Same Decrease in Thoracoabdominal Movement
- Both Associated with a 4% or More Fall in Oxygen Saturation

#### AASM scoring for Hypopnea as of Sept 2013

- (1A) At <u>></u>3% O<sub>2</sub> Desaturation:
- Peak signal drops by <u>></u>30%
- Duration <u>></u> 10 sec.
- And / or is associated with an arousal
- (1B) At <u>>4%</u> O<sub>2</sub> Desaturation:
- Peak signal drops by <u>></u>30%
- Duration is <a>>10sec</a>
- Arousals not included

#### Sleep Breathing Disorders Indices

- Apnea Index: The Average Number of Apneas per Hour of Sleep (AI)
- Apnea-Hypopnea Index: The Average Number of Apneas & Hypopneas per Hour of Sleep (AHI)
- Respiratory Disturbance Index: AHI + RERAs (RDI)

#### Severity

Mild OSA: AHI of 5 to 14

Moderate OSA: AHI of 15 to 29

Severe OSA: AHI of more than 30

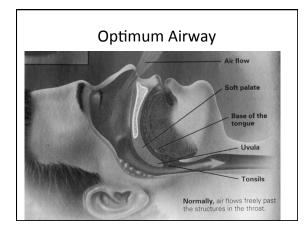
#### What About Oxygen Saturation

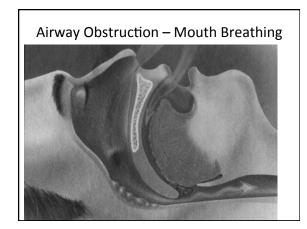
- Have to consider hypoxia (hypoxemia)
- Also Intermittent Hypoxia
- As well as Oxygen Desaturation Index (ODI)
- Oxygen desaturation hypoxia all lead to oxidative stress

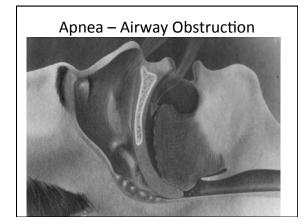
#### Factors other than AHI Hazard Ratio (HR)

- · Follow-up over median of 68 months
- Cohort of 1,172 people
- · Found to be more pathophysiologically relavent
- $O_2$  Saturation: <90% (9 mins vs 0 mins) HR = 1.5 Also need to consider desaturation index - ODI
- Sleep Time: 4.9 vs 6.4 Hrs. HR = 1.20
- Awakenings: 35 vs 18 HR = 1.06
- PLMs: 13 vs 0 HR = 1.05
- Heart Rate: 70 vs 56 beats per min. HR = 1.28
- Daytime Sleepiness: HR = 1.13

# AHI became non-significant after controlling for these other variables – particularly ODI and intermittent hypoxia These factors considered as "downstream" factors – more predictive of CV disease after controlling for known CV risk factors PLOS Medicine Feb 2014 Vol 11 Issue 2 Institute of Health Policy Univ of Toronto









#### Neurologic Basis of Sleep Disordered Breathing

- Some factors lead to small airway not all patients with small airways have OSA
- Maintain Airway Upper Airway reflex (UAR)
- Three Components:
  - 1. Propioception of upper airway tone
  - 2. Central nervous system processing
  - Reflex muscular changes
     Ref: NY Academy of Sciences 2008
     M. Broderick and C. Guilleminault

#### Neurogenic Polyneuropathy

- OSA patients have neurologic lesions in the pharyngeal musculature
- Abnormal increase of various nerve endings in the mucosal epithelium
- Also have sensory problems
- Friberg D et al 1998. Histological indications of a progressive snorers disease in an upper airway muscle. Am J Resp Crit Care Med 157:586-593.

## Is OSA a Systemic Disorder?

- · Inflammatory disorder
- · Oxidative stress disorder
- Atherosclerogenic disorder
- Pro-coagulant disorder
- · Metabolic disorder
- · Multi-system disorder
- · Societal disorder

#### Summary: Thoughts

Perhaps: Waking, REM sleep and NREM sleep are merely EEG representations of existence? Lee-Chiong in Sleep Medicine Clinics Vol 7 #3 2012

"Who you gonna believe Me or your own eyes"

Chico Marx

