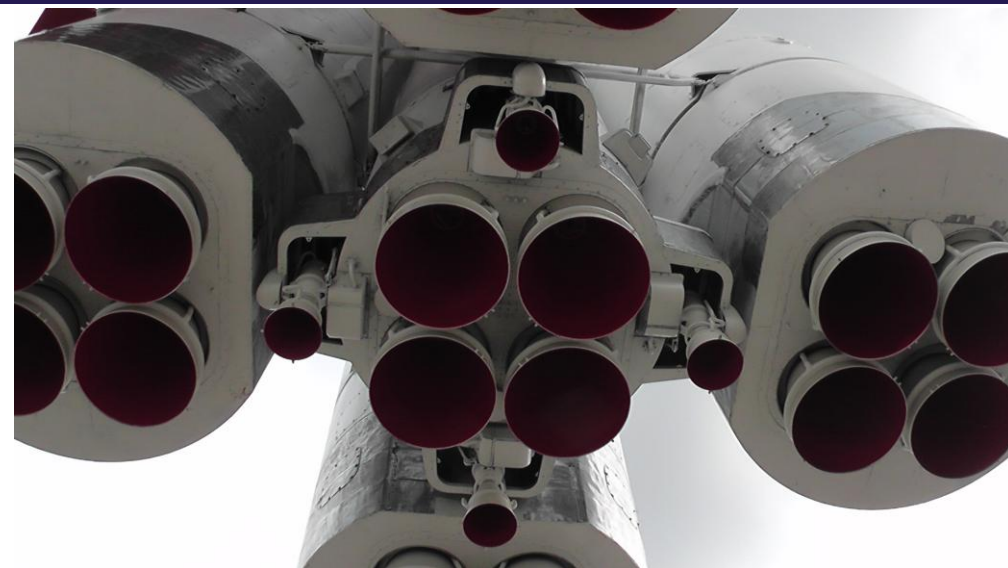


Sleep Update



Christopher R. Skinner MD, FRCPC, DABSM
Neurologist
Distinguished Teacher



Objectives

- **To review the different types of sleep disorders and how these effect daily life**
- **To review strategies to recognize and diagnose various sleep disorders**
- **To review treatments both pharmacological and non-pharmacological to treat sleep disorders**
- **What can I do to improve my sleep and the sleep of my bed partner?**
- **Questions**

Why do we sleep?

Sleep that knits up the raveled sleeve of care

The death of each day's life, sore labor's bath

Balm of hurt minds, great nature's second course

Chief nourisher in life's feast

Shakespeare MacBeth Act 2 Scene 2



Nightmare - Fuseli 1781

Sleep Definition

- A reversible behavioural state of perceptual disengagement from and unresponsiveness to the environment, is restorative and important for the proper functioning of an organism.

Common Sleep Disorders

- Obstructive Sleep Apnea
- Circadian Disorders
- Restless Legs
- Narcolepsy
- Parasomnias

THE IMPACT OF SLEEP DEPRIVATION



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- Challenger Disaster
- 3 Mile Island
- Chernobyl

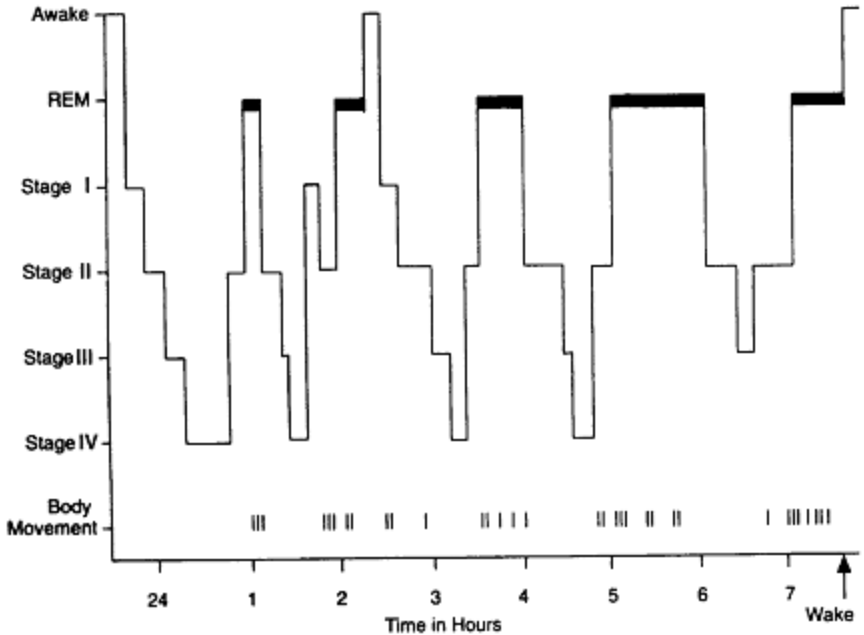
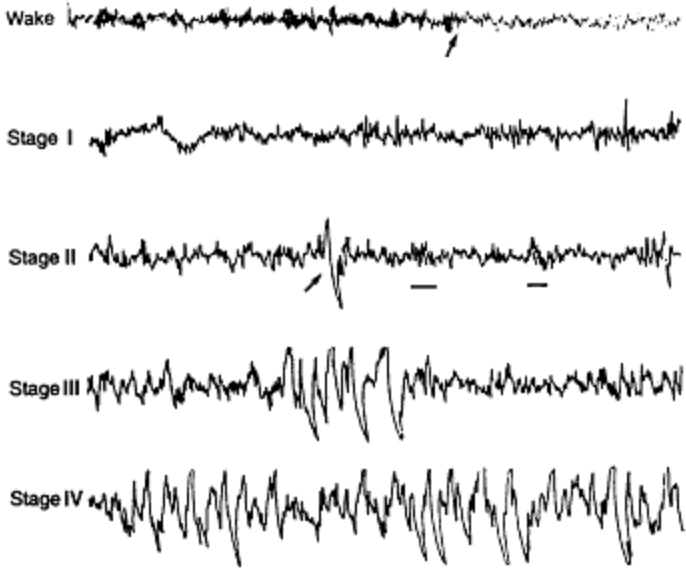


Sleep Stages

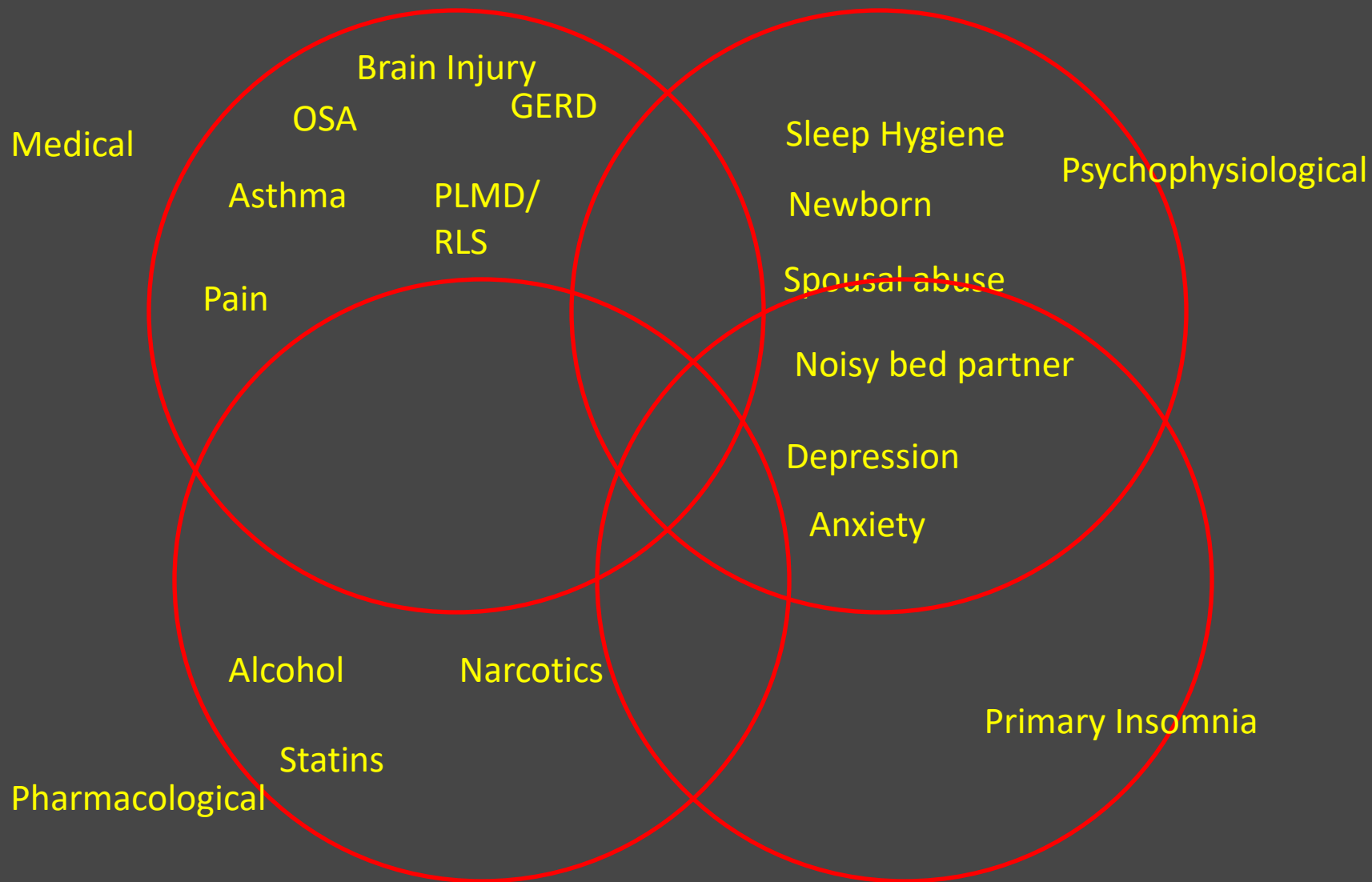


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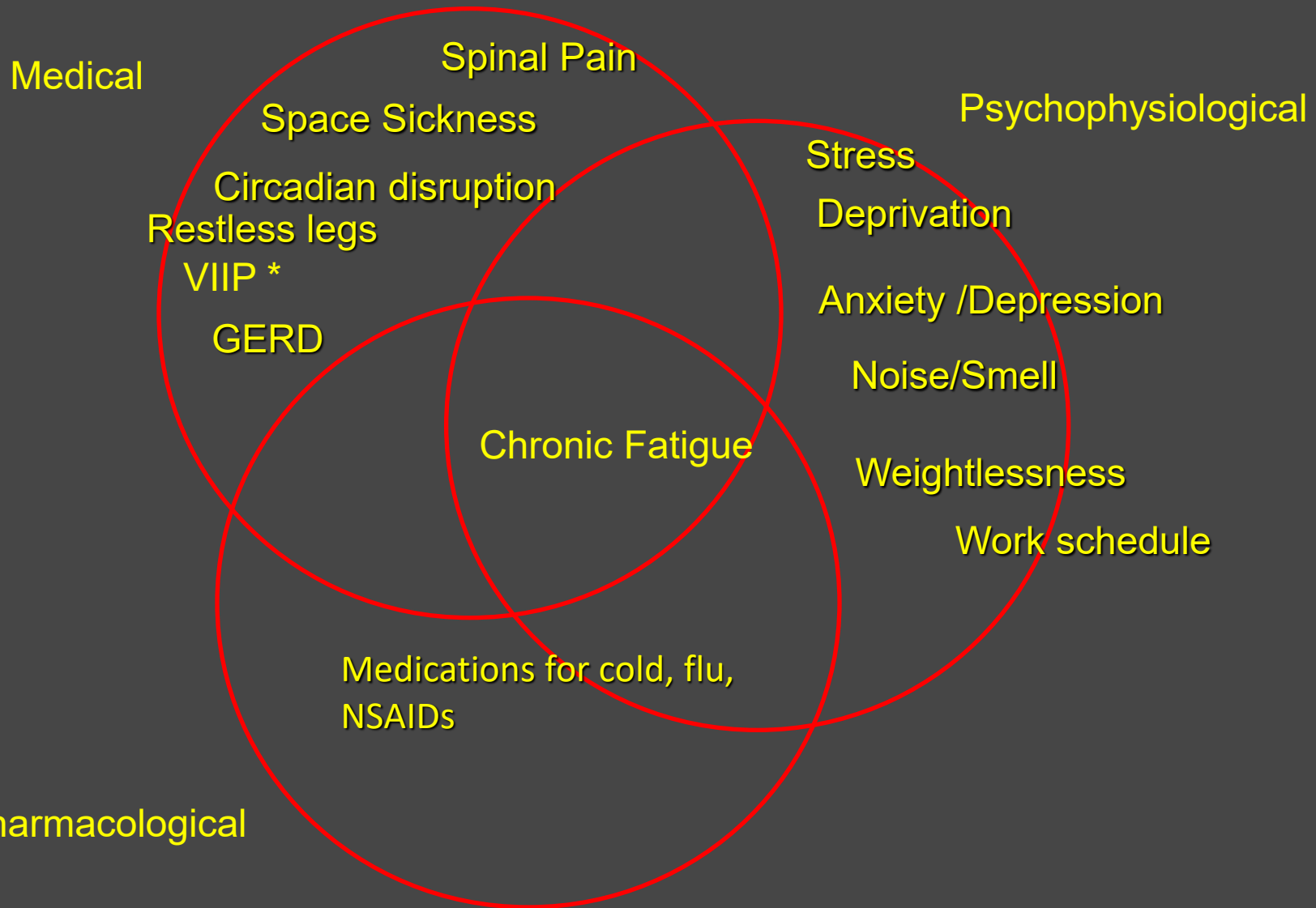
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Sleep Disruption Static Analysis



Sleep Disruption in Space Static Analysis

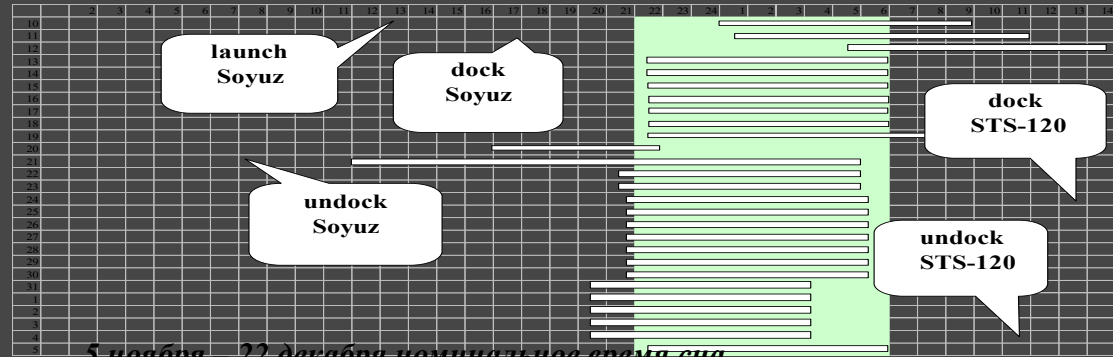


* Visual Impairment and Elevated Intracranial Pressure



Сдвиги сна в полете МКС-16

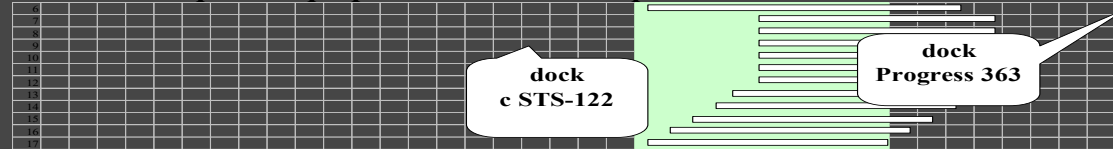
В.В.Богомолов, 2008



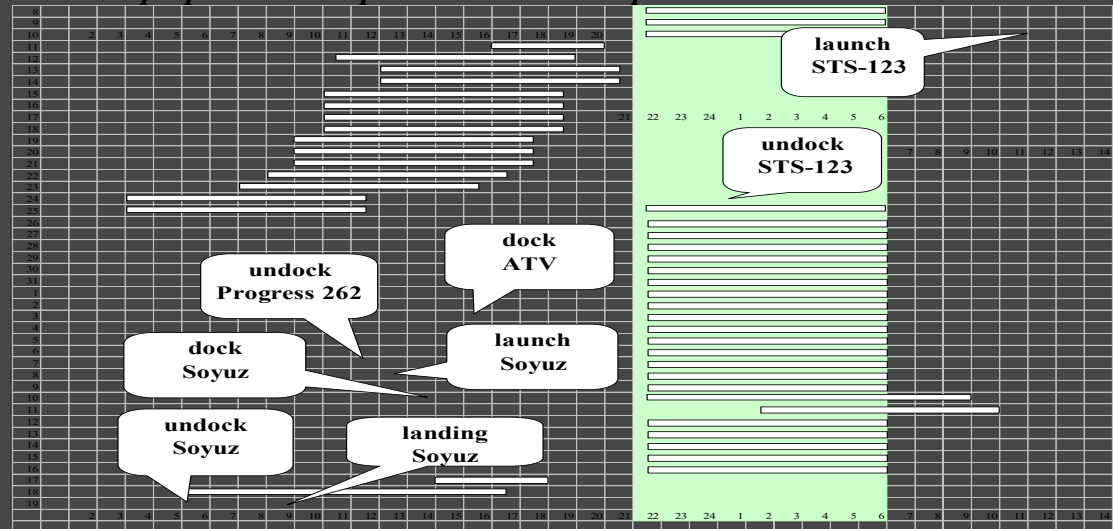
5 ноября – 22 декабря номинальное время сна



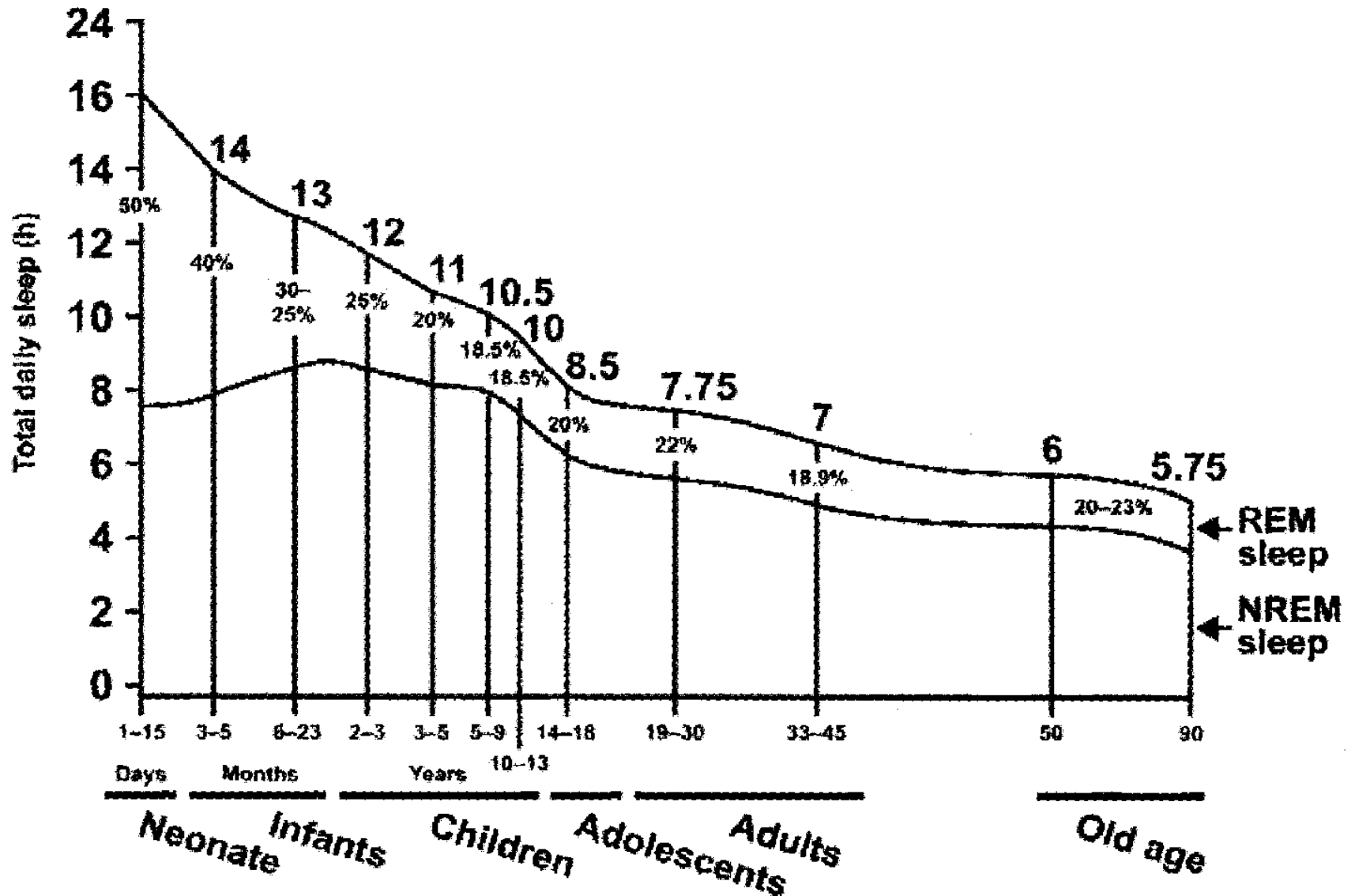
26 декабря – 02 февраля номинальное время сна



17 февраля – 10 марта номинальное время сна



Sleep Stages by Age



- 65-year-old man with obesity, excessive daytime sleepiness and memory difficulties, BP 150/95. BMI 33 kg/m²
- **Stop Bang Score 7**
 - Snoring
 - Tired
 - Observed
 - Elevated BP
 - BMI 33 kg/m²
 - Age 30
 - Male
 - Neck size > 17 inches
- **Aeromedical Safety Risk:**
 - Excessive daytime sleepiness with impairment of flight performance
 - Long-term risk of obesity, hypertension and metabolic syndrome

Stop Bang

<http://www.stopbang.ca/osa/screening.php>



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Yes No
Snooring ?
Do you **Snore Loudly** (loud enough to be heard through closed doors or your bed-partner elbows you for snoring at night)?

Yes No
Tired ?
Do you often feel **Tired, Fatigued, or Sleepy** during the daytime (such as falling asleep during driving or talking to someone)?

Yes No
Observed ?
Has anyone **Observed** you **Stop Breathing** or **Choking/Gasping** during your sleep ?

Yes No
Pressure ?
Do you have or are being treated for **High Blood Pressure** ?

Yes No
Body Mass Index more than 35 kg/m²?

Body Mass Index Calculator

cm / kg inches / lb

Height: Weight:

BMI:

Yes No
Age older than 50 ?

Yes No
Neck size large ? (Measured around Adams apple)
For male, is your shirt collar 17 inches / 43cm or larger?
For female, is your shirt collar 16 inches / 41cm or larger?

Yes No
Gender = Male ?

For general population

OSA - Low Risk : Yes to 0 - 2 questions

OSA - Intermediate Risk : Yes to 3 - 4 questions

OSA - High Risk : Yes to 5 - 8 questions

or Yes to 2 or more of 4 STOP questions + male gender

or Yes to 2 or more of 4 STOP questions + BMI > 35kg/m²

or Yes to 2 or more of 4 STOP questions + neck circumference 17 inches / 43cm in male or 16 inches / 41cm in female

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Modified from

Chung F et al. Anesthesiology 2008; 108: 812-821,

Chung F et al Br J Anaesth 2012; 108: 768-775,

Chung F et al J Clin Sleep Med Sept 2014.

What Happens at the Sleep Lab...



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STEPS:

- 1) → Referral
- 2) → Consultation with a Sleep Specialist
- 3) → Overnight Sleep Study
- 4) → Data is Analyzed by RPSGTs
- 5) → Results Appt with a Sleep Specialist

SLEEP
DISORDER
CLINIC



Rockwell

How Do We Measure Sleep in the uOttawa Laboratory?

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- EEG – brainwaves (Central & Occipital Leads)
- EOG – eye movements
- EMG – muscle tone
- EKG/ECG – heart
- Breathing:
 - 1) Airflow
 - & 2) Effort: Thoracic & Abdominal
- Blood oxygen saturation (SaO_2)
- Snore mic.
- Digital AV recording



VitalAire Ottawa
invites you to attend
CPAP CE
March 14th
9:00 to
1155 Lola
Ottawa





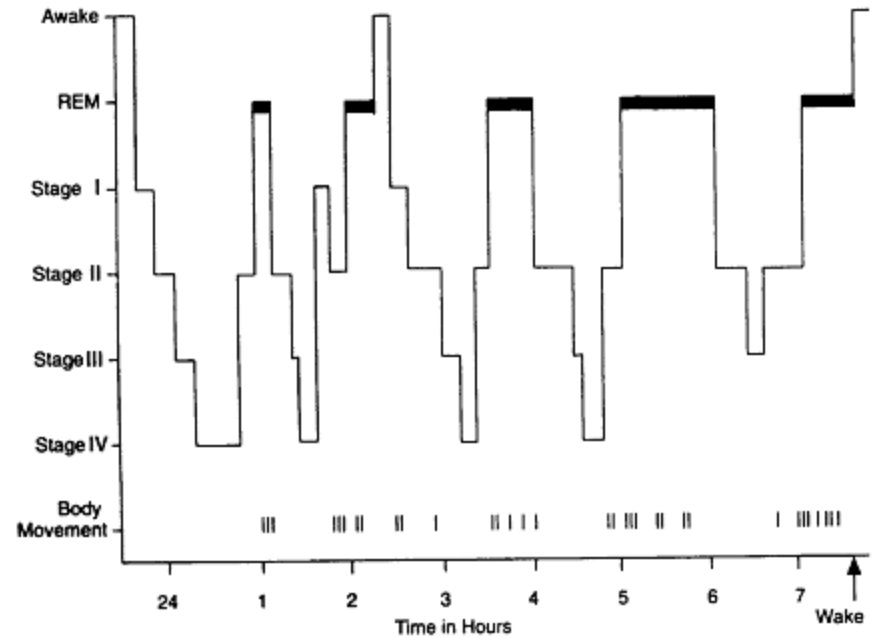
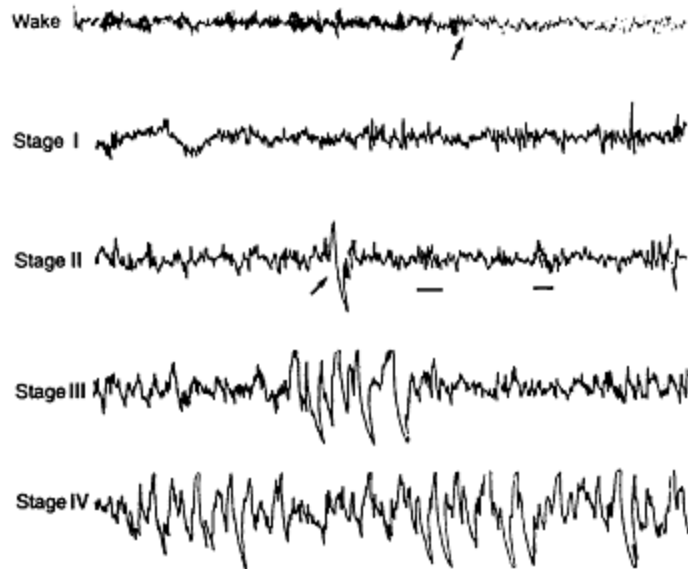


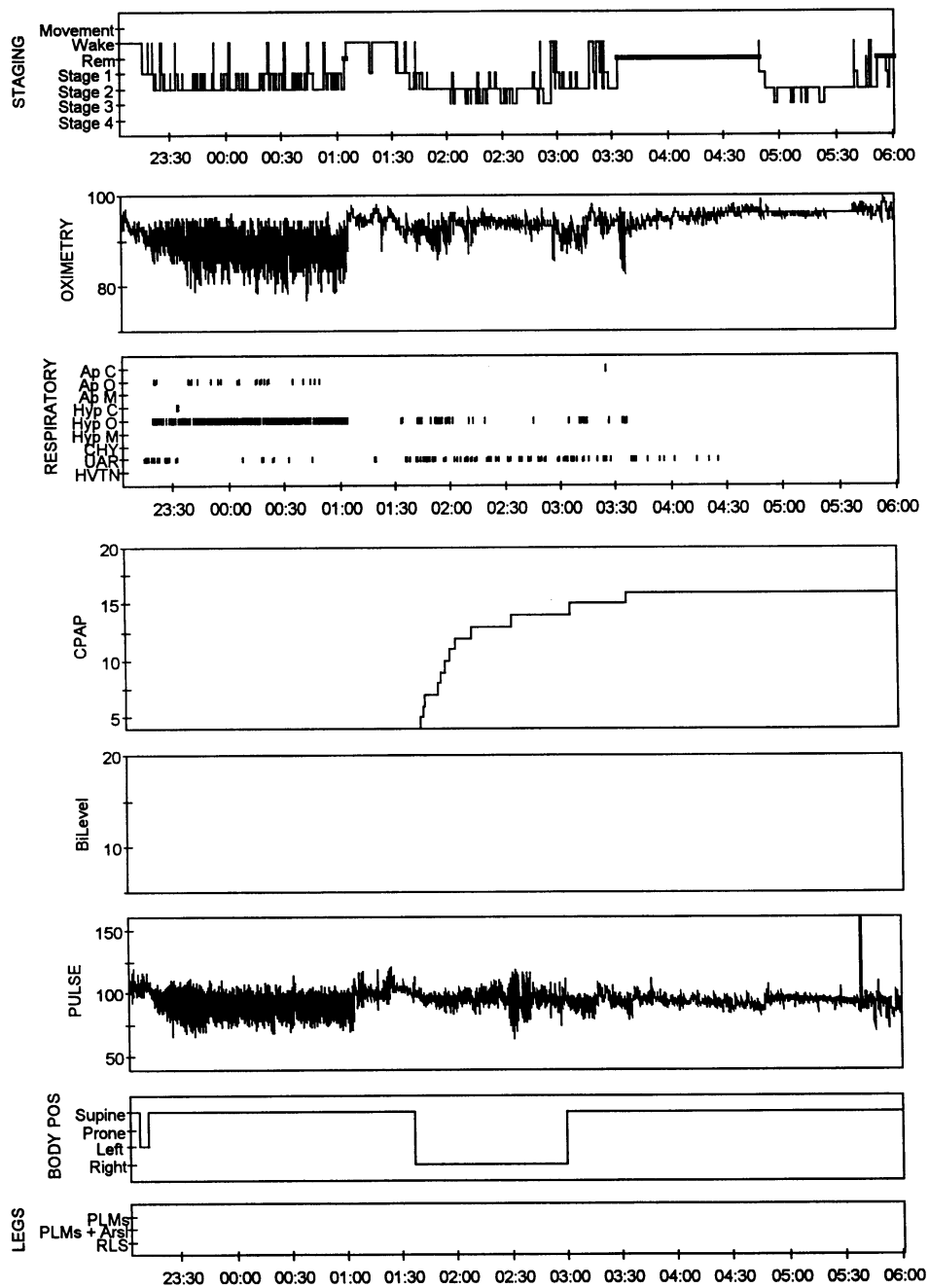
Sleep Stages



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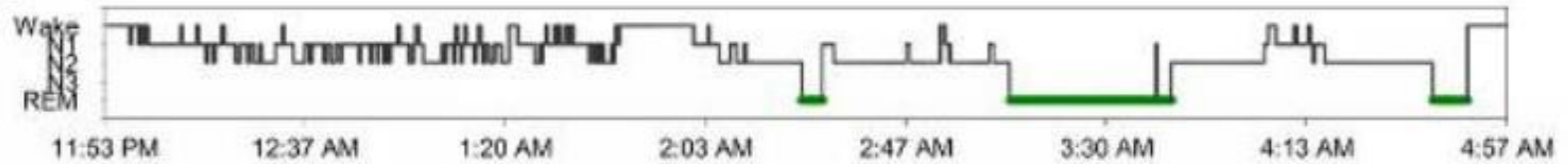
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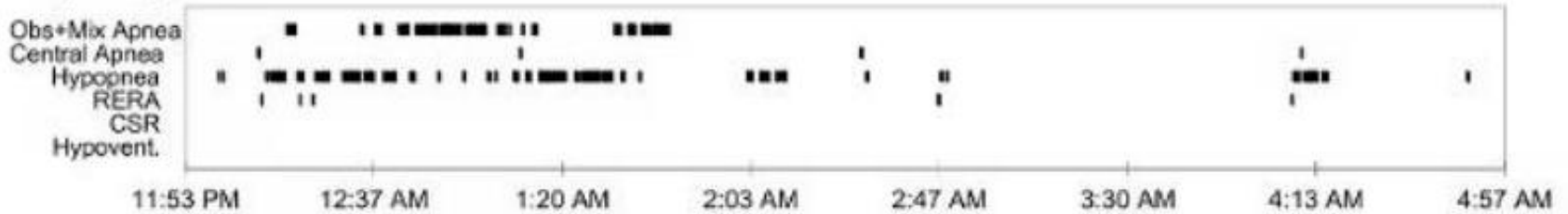


SPLIT NIGHT POLYSOMNOGRAPHY REPORT

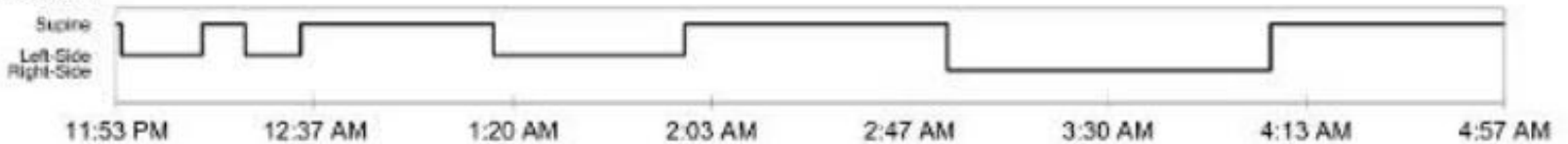
Hypnogram



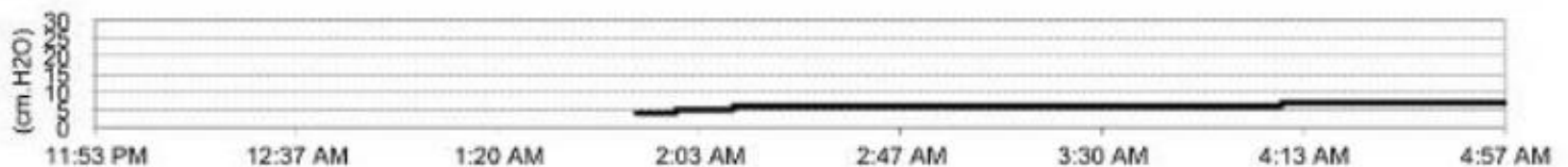
Respiratory Events



Body Position



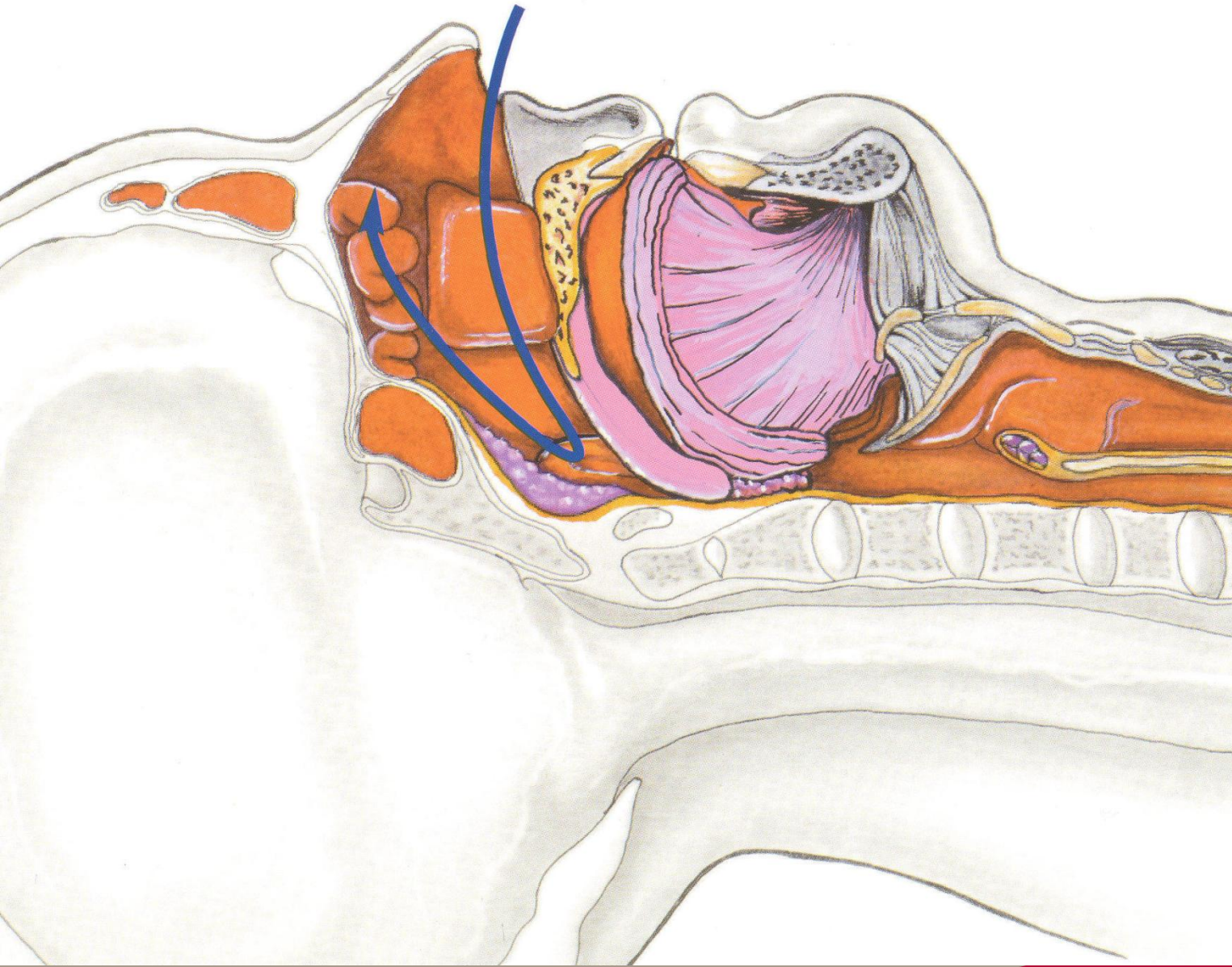
CPAP



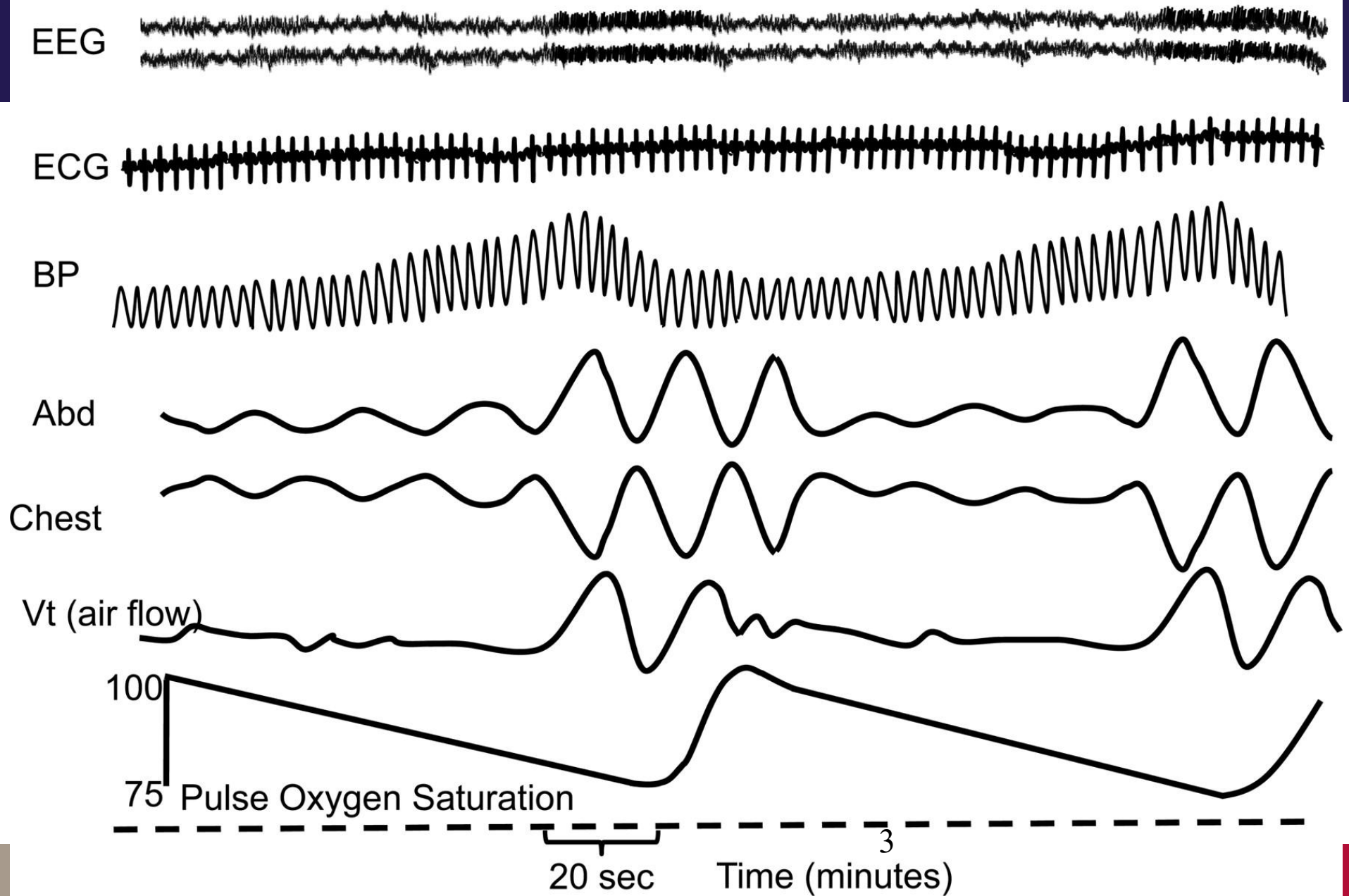
Blocked Airflow

Apnea

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Obstructive Sleep Apnea



The Sleep Apnea Syndromes

- Apnea defined as cessation of airflow at the nostrils and mouth lasting ten seconds or more
- Obstructive secondary to sleep induced airway obstruction
- Central apnea due to decrease activity of muscles of respiration
- Mixed apnea from a combination of both

Obesity

Micrognathia

Enlarged Tonsils and Adenoids

Enlarged Thyroid

Acromegaly (enlarges tongue)

Nasal Septal Defects

Myotonic Dystrophy

Miscellaneous:

Assoc'd With Narcolepsy-cataplexy (" -20%)

Relation to Sudden Infant Death Syndrome

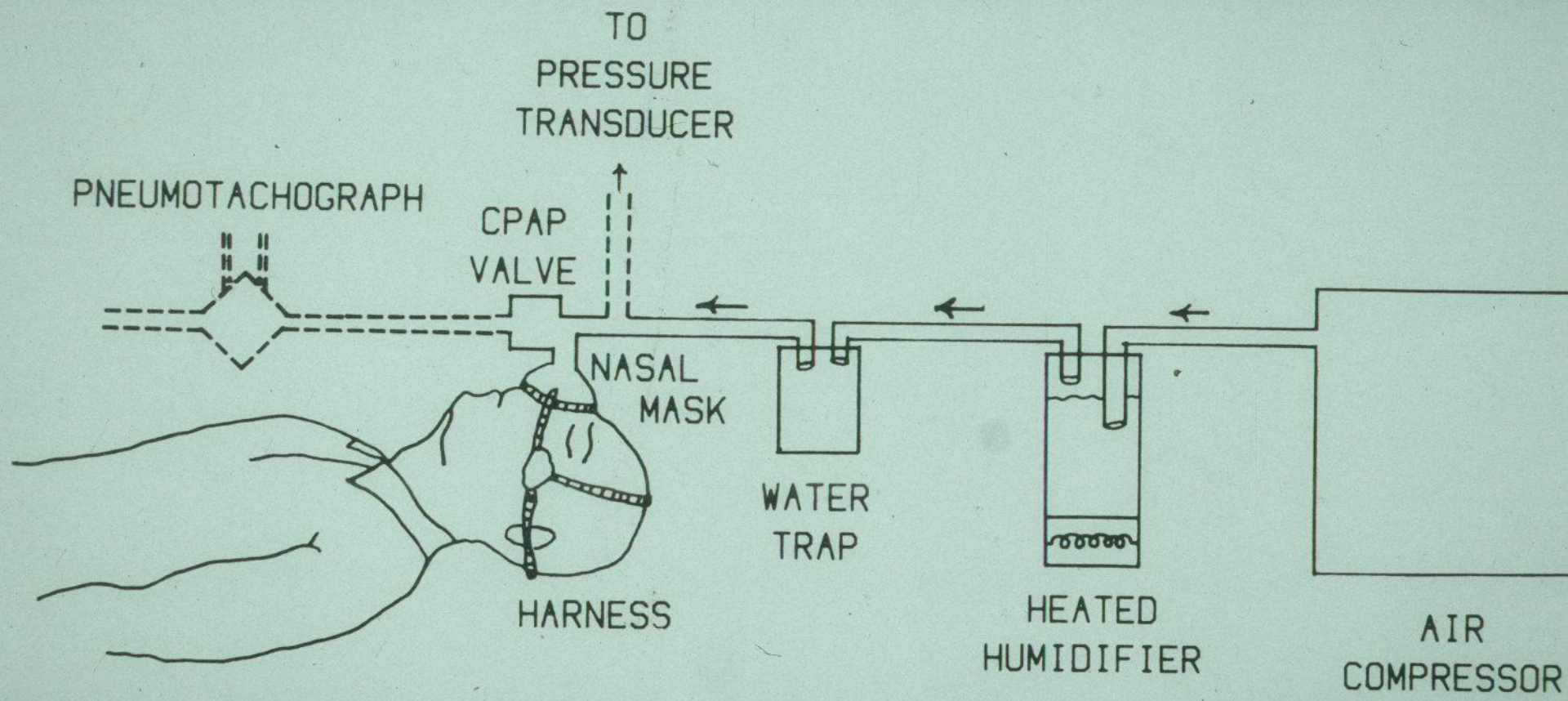




- Excessive Daytime Sleepiness
- Vigilance Impairment
- Cognitive Impairment
- Mood Disturbance
- Development of Neurodegenerative Disorders

- **Causal**
 - **Weight loss, weight loss, weight loss**
 - **Avoid sleeping in supine position**
 - **Dental appliances**
 - **Removal of T and A**
 - **Mandibular advancement surgery**
- **Relieve obstruction**
 - **Continuous nasal positive pressure in sleep (cpap)**
 - **Uvulo-palato-pharyngoplasty - UPPP**
 - **Tracheostomy**
- **Hypoglossal Nerve Stimulator**
 - **Requires surgery**
 - **May detach or become disconnected**
 - **\$\$\$**
- **Drugs**
 - **medroxyprogesterone - (pure Pickwickian)**

Abstinence from alcohol, hypnotics, sedatives





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Features

CPAP

Fixed pressure

Maximum 20 cm pressure

APAP

Pressure range 5 – 20 cm

Adjusts according pressure requirement

BiLevel

Pressure > 20 cm up to 30 cm

Adjusts according pressure requirement

Can enable minimum minute rate for CSA

Surgical Management UPPP



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Dental Apppliance



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■ History

- Excessive daytime sleepiness
- Snoring, witnessed apneas

■ Physical

- BMI
- Mallampati Index

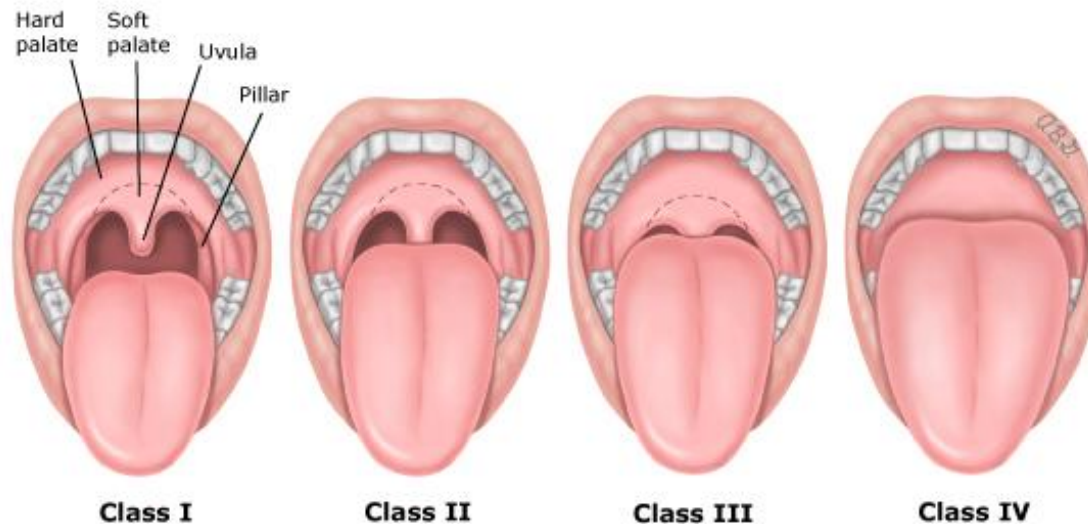
■ Tools

- Epworth (> 10 abnormal)
- Stop Bang (> 5 abnormal)

The modified Mallampati classification for difficult laryngoscopy and intubation

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Faculté de Médecine



The modified Mallampati classification^[1] is a simple scoring system that relates the amount of mouth opening to the size of the tongue and provides an estimate of space available for oral intubation by direct laryngoscopy. According to the Mallampati scale, class I is present when the soft palate, uvula, and pillars are visible; class II when the soft palate and the uvula are visible; class III when only the soft palate and base of the uvula are visible; and class IV when only the hard palate is visible.

Reference:

1. Samsoon GL, Young JR. Difficult tracheal intubation: a retrospective study. *Anaesthesia* 1987; 42:487.

UpToDate®

Epworth Sleepiness Scale

■ SITUATION

■ CHANCE OF DOZING

■ Time of Day

- Sitting and reading 3
- Watching TV 3
- Sitting inactive in a public place (e.g. a theater or a meeting) 3
- As a passenger in a car for an hour without a break 3
- Lying down to rest in the afternoon when circumstances permit 3
- Sitting and talking to someone 3
- Sitting quietly after a lunch without alcohol 3
- In a car, while stopped for a few minutes in traffic 3

Stop Bang

<http://www.stopbang.ca/osa/screening.php>



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Yes No
Snooring ?
Do you **Snore Loudly** (loud enough to be heard through closed doors or your bed-partner elbows you for snoring at night)?

Yes No
Tired ?
Do you often feel **Tired, Fatigued, or Sleepy** during the daytime (such as falling asleep during driving or talking to someone)?

Yes No
Observed ?
Has anyone **Observed** you **Stop Breathing** or **Choking/Gasping** during your sleep ?

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Chung F et al J Clin Sleep Med Sept 2014.

Cure?

- Can OSA be cured?

- Management of Risk Factors
 - Obesity
 - Bariatric surgery
 - GLP1 agonists
 - Obstruction
 - UPPP
 - Mandibular advancement surgery
- Most of moderate to severe OSA cases require CPAP indefinitely

- Requirement for monitoring of pilots and Class A truck drivers for 90 days per year while working
 - Adherence > 4 hours per night
 - AHI < 10/hour

- 50-year-old lady flies from Ottawa to Frankfurt for business
- The plane leaves at 20:00 and arrives at 07:00 local time after a six-hour flight
- She feels tired and irritable but needs to attend an important meeting that day
- What is her diagnosis

Circadian rhythm sleep disorders

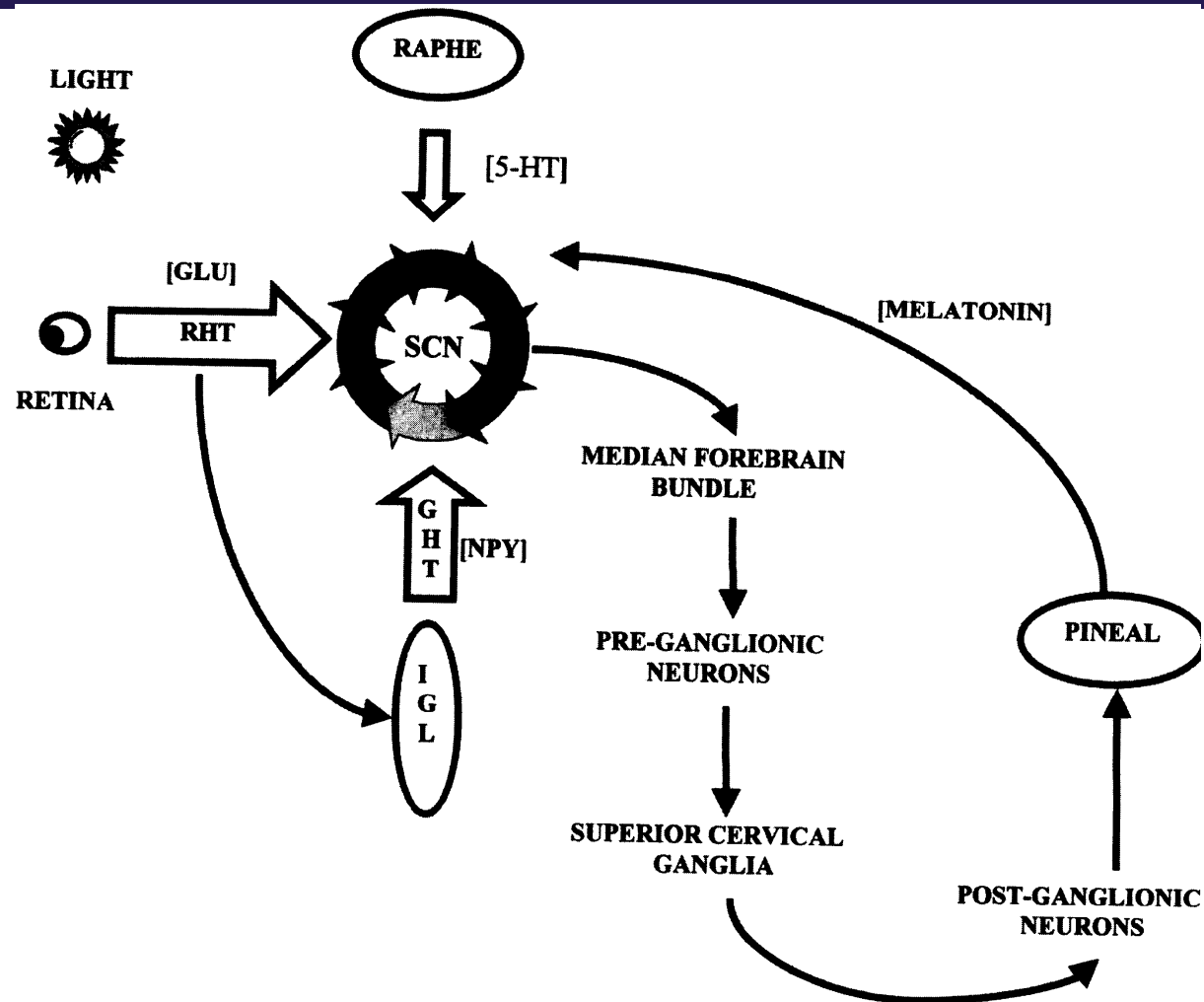
- Time zone change (jet lag) syndrome
- Shift work sleep disorder
- Irregular sleep-wake pattern
- Delayed sleep phase syndrome
- Advanced sleep phase syndrome
- Non—24-hour sleep—wake disorder
- Circadian rhythm sleep disorder NOS

Circadian System

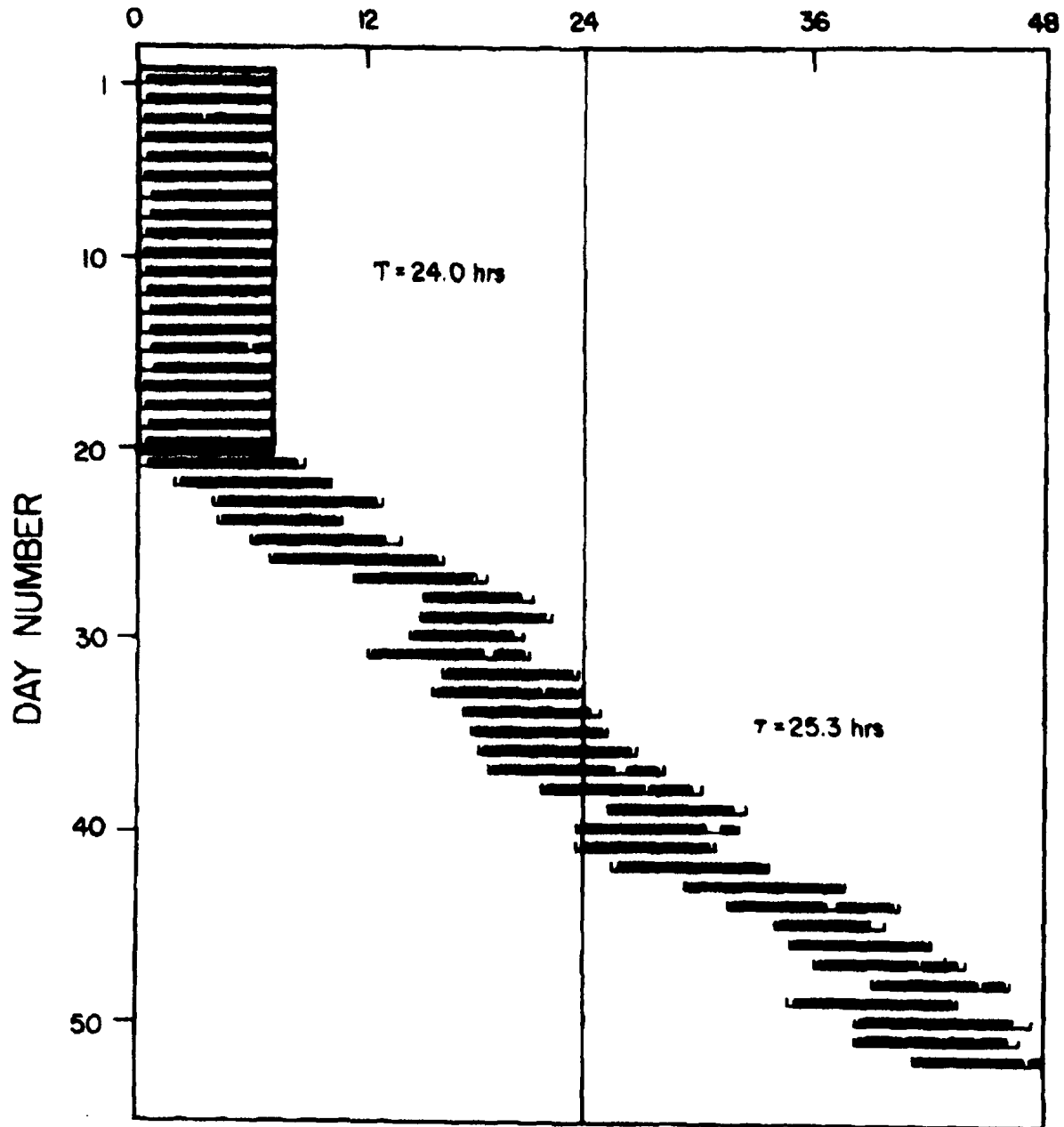


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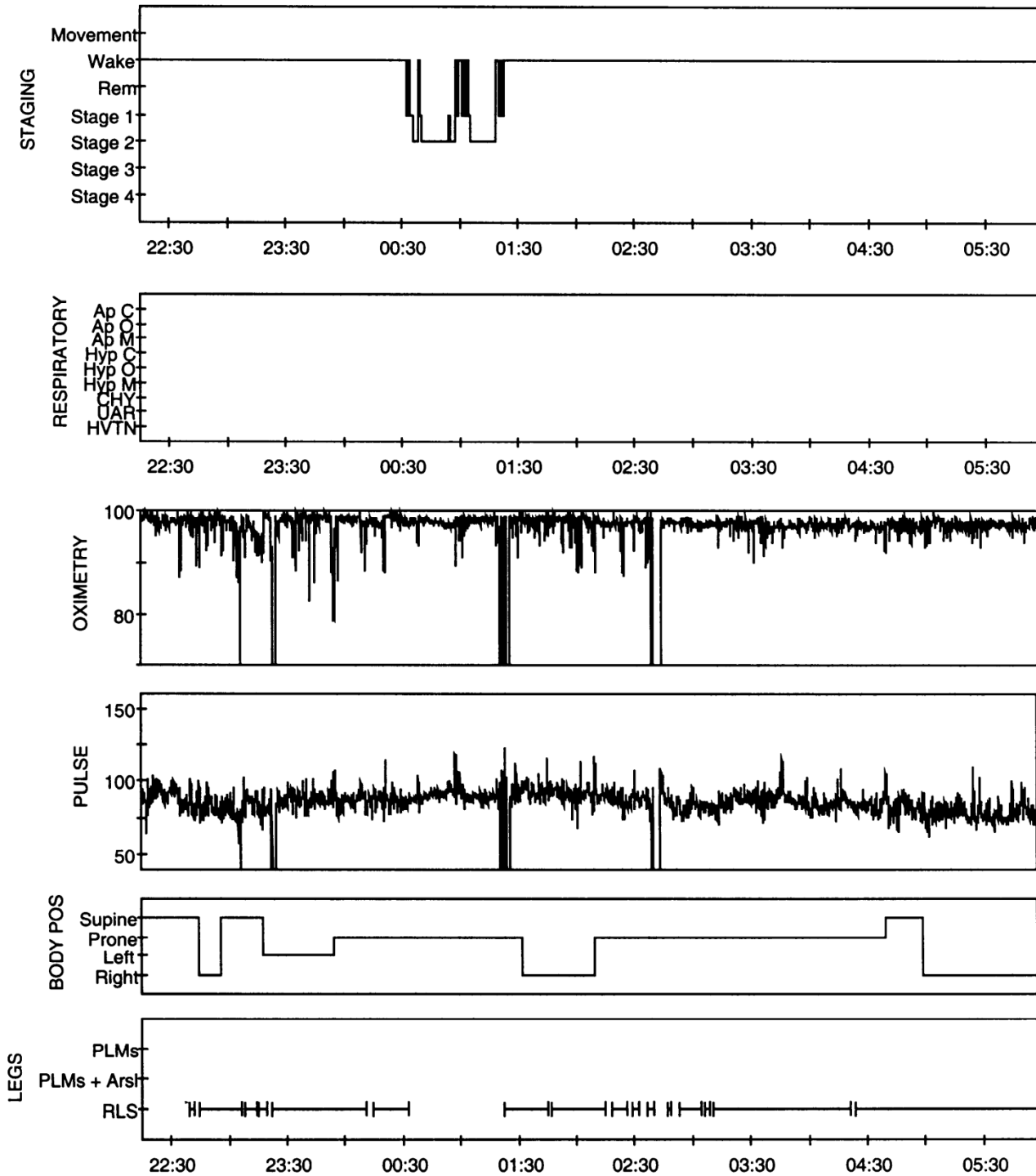


TIMING OF SLEEP (HOURS)



- **This 21-year-old right-handed university student**
- **Difficulty of sleep onset for the last six to seven years with witnessed apneas, when she sleeps over at other people's houses**
- **Currently she is a university student in psychology. She has evening classes but also is holding down two jobs, one that requires her to be up a 6:00 a.m.**
- **Often, she is not able to get to sleep until 4:00 a.m. and therefore she is sleepy at work.**

- ▣ **She is a nonsmoker and drinks only occasional alcohol. She is single without children.**
- ▣ **On examination, she is an overweight Afro-Canadian lady BMI 35 kg/m² with a blood pressure of 120/80, right arm sitting. Her heart rate was 84 and regular.**
- ▣ **She had normal heart sounds with no murmurs or bruits. Her chest was clear. Her throat was clear with normal tonsils for her age. Neurological examination was within normal limits.**



■ ?RLS

- Not aware
- Not circadian
- Poor sleep hygiene

- HGB 115
- MCV 73
- Target Cell, microcytic changes
- Sickledex – positive
- Ferritin 6

- Improved RLS and sleep on Fe, and BCP

- Most Restless Legs is not RLS
- Rule out
 - Low iron stores
 - Chronic pain
 - Neuropathy
 - Muscles disorders (statins)
- Medications
 - Cyclobenzaprine
 - Baclofen
 - Dopamine agonists – not capable with professional driving or flight operations

- Are disorders of arousal, partial arousal and sleep stage transition.
- General common features:
 - Mental confusion and disorientation
 - Automatic behaviour
 - Relative non reactivity to external stimuli
 - Poor response to efforts to provoke wakefulness

■ NREM

Sleepwalking (Somnambulism)

Sleep Terrors (aka Night Terrors)

Others examples: Sleep Related Eating Disorders,
Confusional Arousals, Somniloquy

■ REM

REM Behaviour Disorder (RBD)

Measured in the sleep lab with full EEG to rule out seizure activity

- Night Terrors



- 70-year-old man starts to hit his wife during the night causing a serious facial injury
- Similar events have happened over the last few years
- Good health – medication for blood pressure and cholesterol
- The daughter hears of this and calls the police for concerns about spousal abuse



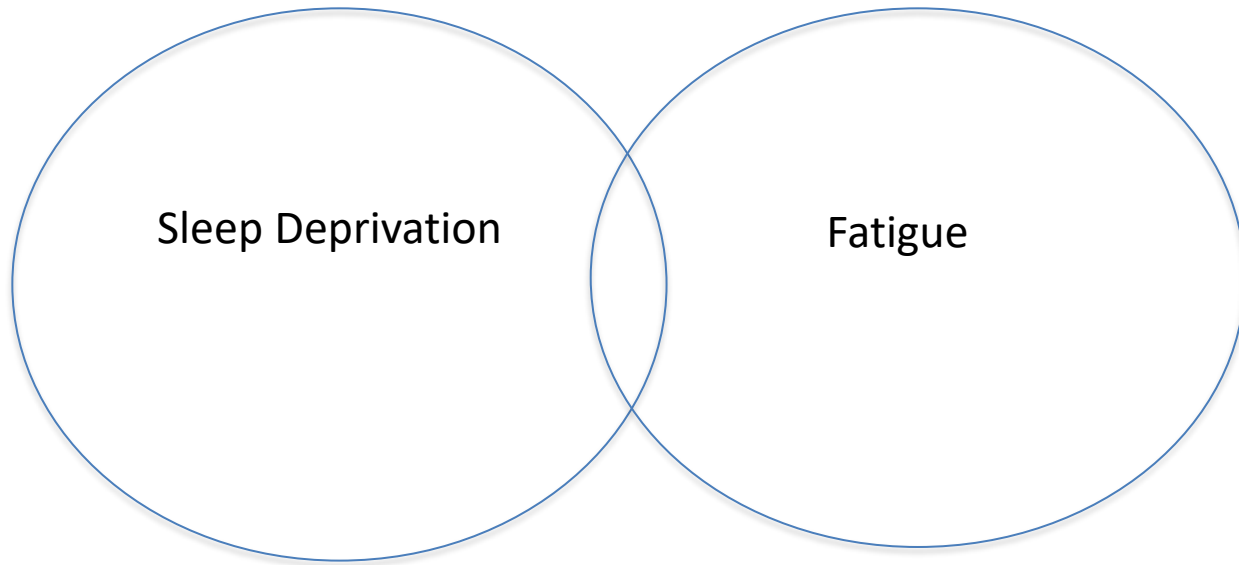
- 22 year old lady recently completed university starting a new job
- Excessive day time sleepiness
- Attacks of loss of muscle tone with emotion
- Recently bought her first car



- Recurrent periods of irrepressible need to sleep, $\geq 3x/wk$, ≥ 3 months
- Cataplexy*
- Hypocretin deficiency
(CSF Hcrt-1 $< 110\text{pg/mL}$)
- PSG – REM latency ≤ 15 min, or MSLT with SL ≤ 8 min and ≥ 2 SOREMPs

- **CNS Stimulants for EDS**
 - Methylphenidate
 - Amphetamines
- **CNS Alerting Drugs**
 - Modafinil
- **REM Suppressants (for e.g. Cataplexy)**
 - tricyclics
 - clomipramine
 - desipramine
 - Imipramine
 - SSRIs (“super selective REM inhibitors”)
 - MAO inhibitors
- **Sodium Oxybate [Xyrem]
(Sodium salt of Gamma Hydroxybutyrate (GHB))**
- **Experimental drugs – intranasal hypocretin**

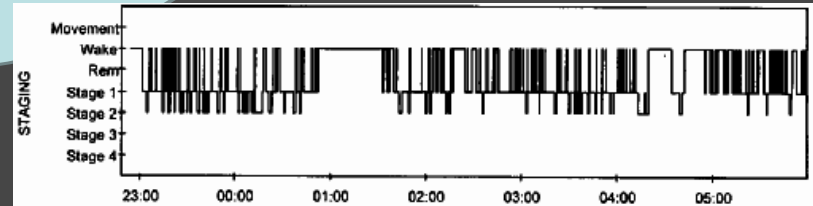
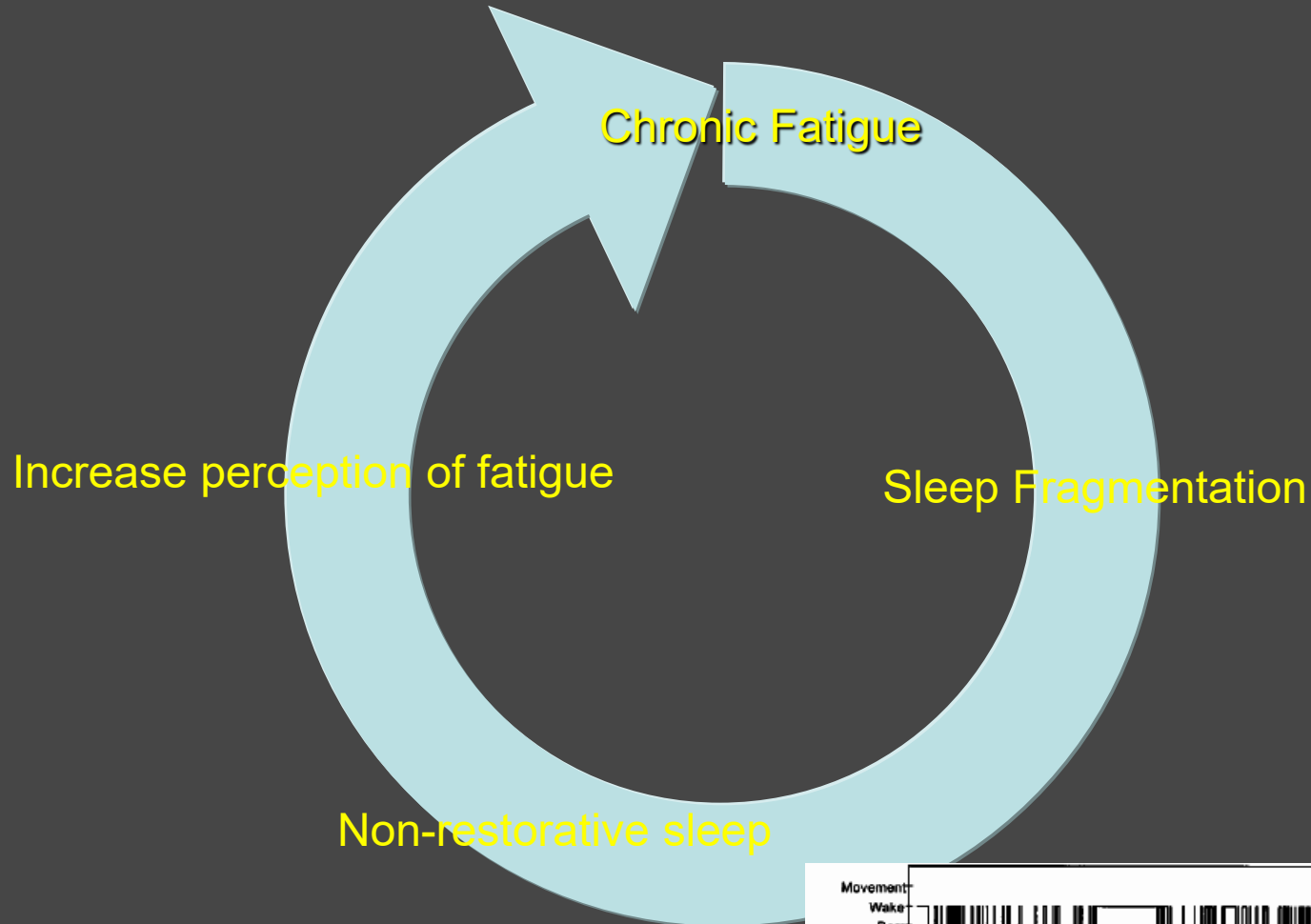
- weariness or exhaustion from labor, exertion, or stress
 - Not made better by sleep



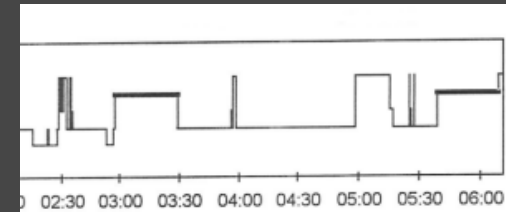
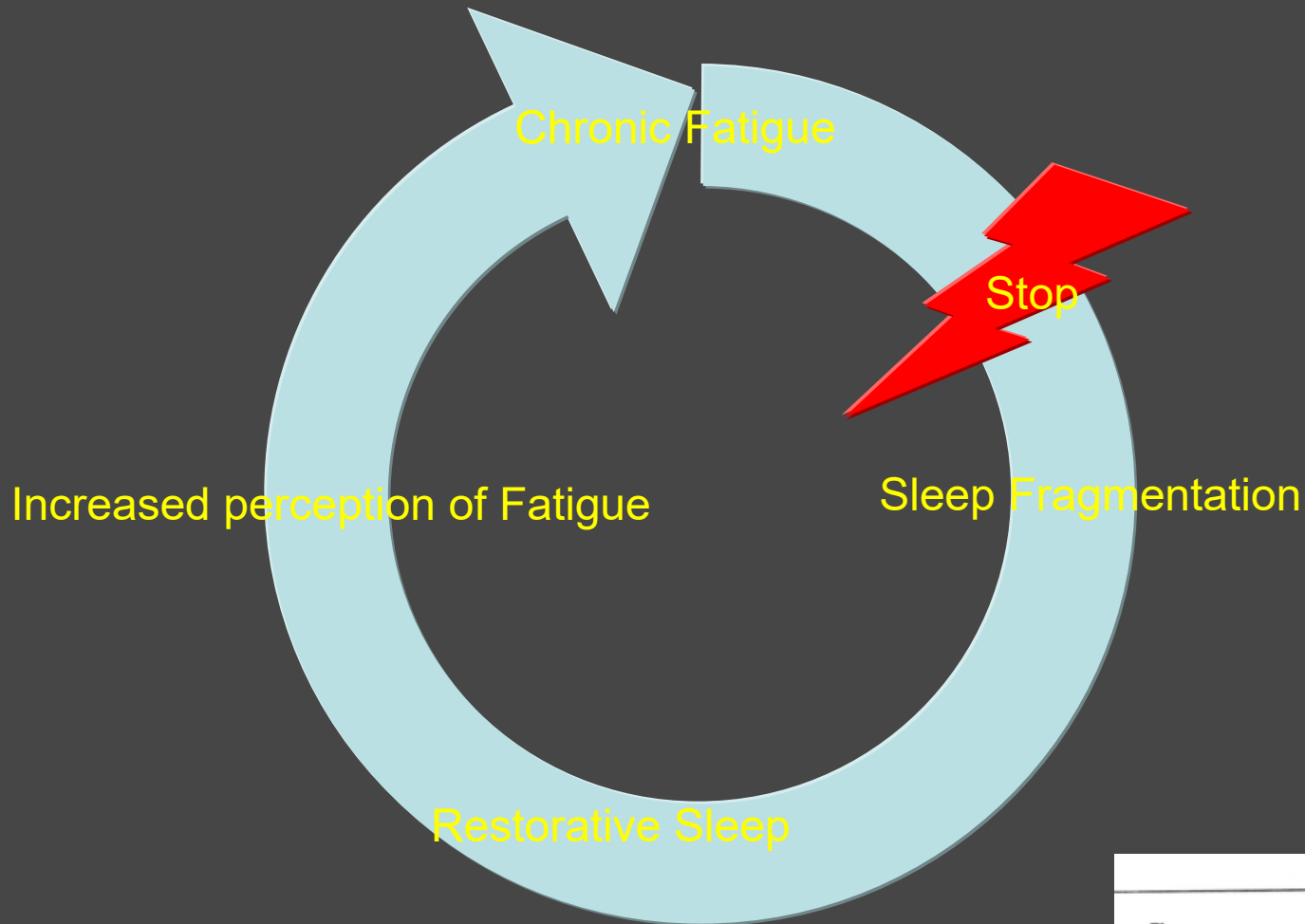
Sleep Deprivation

Fatigue

Vicious Circle



The Vicious Cycle





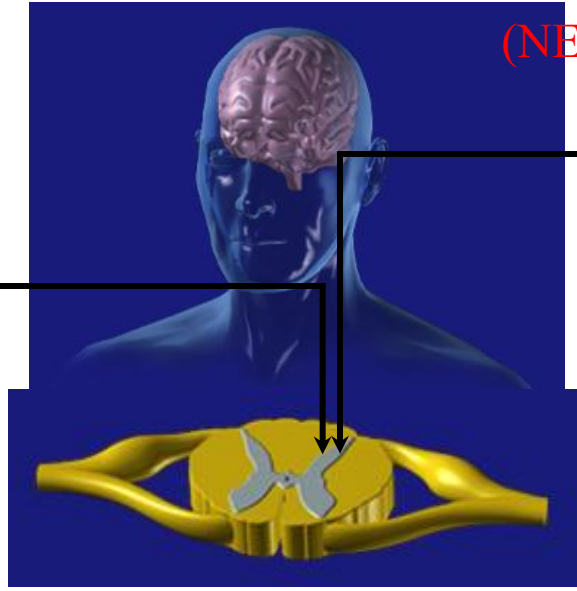
- Fatigue Avoidance Scheduling Tool (FAST) was developed by the United States Air Force in 2000–2001 to address the problem of aircrew fatigue in aircrew flight scheduling.
- Quantifies the effects of various work-rest schedules on human performance.
- The goal of the planner or scheduler is to keep performance effectiveness at or above 90% by manipulating the timing and lengths of work and rest periods.
- A work schedule is entered as red bands on the timeline.
- Sleep periods are entered as blue bands across the timeline, below the red bands.
- The calculated performance effectiveness represents composite human performance on a number of cognitive tasks, scaled from zero to 100%.
- The oscillating line in the graph represents expected group average performance on these tasks as determined by time of day, circadian rhythm, time spent awake, and amount of sleep, and various confidence limits around the average may be displayed.

Where to Target

- Sleep
 - Chloride via GABA A
 - Orexin
- Pain
 - Opioids
 - Sodium Channels
 - NMDA
- Spasticity
 - GABA B
- Both
 - NE/5HT
 - Ca via Alpha2 Delta1

Central sensitization

- Ca²⁺**
 - Gabapentin
 - Lamotrigine
 - Levetiracetam
 - Oxcarbazepine
 - Pregabalin
- NMDA**
 - Dextromethorphan
 - Ketamine
 - Methadone
 - Memantine
- GABA**
 - Benzodiazepines/
Agonists
 - Baclofen
- Dopamine Agonist**
 - Pramipexole
 - Ropinirole



Descending inhibitory pathways (NE/5HT, opioid receptors)

- Alpha adrenergic agents
- Opioids
- SNRIs
- SSRIs
- Duloxetine
- Tramadol
- TTCAs
- Tizanidine

Circadian Agents

- Melatonin
- Ramelton
- Circadin
- Orexin Antagonist**
 - Suvorexant
 - Lemborexant
 - Daridorexant

Peripheral mechanisms

- Carbamazepine
- Lamotrigine
- Lidocaine/Mexiletine
- Oxcarbazepine
- Topiramate
- TTCAs

First Line Agents

Agent	Starting dose and titration	Usual maintenance dose	Adverse effects	Comments
Tricyclic antidepressants				
Amitriptyline Nortriptyline Desipramine Imipramine	10–25 mg/day; increase weekly by 10 mg/day	50–150 mg/day	Drowsiness, confusion, orthostatic hypotension, dry mouth, constipation, urinary retention, weight gain, arrhythmia	Amitriptyline more likely to produce drowsiness and anticholinergic side effects; contraindicated in patients with glaucoma, symptomatic prostatism and significant cardiovascular disease
Anticonvulsants				
Gabapentin	300 mg/day; increase weekly by 300 mg/day	300–1200 mg three times daily	Drowsiness, dizziness, peripheral edema, visual blurring	Dosage adjustments required in renal failure
Pregabalin	75–150 mg/day; increase weekly by 50–150 mg/day	150–300 mg twice daily	Drowsiness, dizziness, peripheral edema, visual blurring	Similar adjustments in renal failure

Second Line Agents



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Agent	Starting dose and titration	Usual maintenance dose	Adverse effects	Comments
Serotonin noradrenaline reuptake inhibitors				
Venlafaxine	37.5 mg/day; increase weekly by 37.5 mg/day	150–225 mg/day	Nausea, dizziness, drowsiness, hyperhidrosis, hypertension, constipation	Dosage adjustments required in renal failure
Duloxetine	60 mg/day	60–120 mg/day	Sedation, nausea, constipation, ataxia, dry mouth	Contraindicated in patients with glaucoma
Others				
Lidocaine		5% patches or gel applied to painful areas for 12 h in a 24 h period		Most useful for postherpetic neuralgia; has virtually no systemic side effects; lidocaine patches not available in Canada

Benzodiazepines					
Estazolam, generic	15-60 min	10-24 h	Intermediate	1-2 mg	0.5-1 mg
Flurazepam, generic	30-60 min	50-100 h	Long	15-30 mg	15 mg
Quazepam, generic	30 min	25-41 h	Long	15 mg	7.5 mg
Temazepam, generic	45-60 min	10-17 h	Intermediate	15-30 mg	7.5-15 mg
Triazolam, generic	15-30 min	1.5-5.5 h	Short	0.125-0.25 mg	0.125 mg
Histamine Receptor Antagonist					
Doxepin (Silenor)	30 min	31-51 h	Long	3-6 mg	3 mg
Melatonin Receptor Agonist					
Ramelteon (Rozerem)	15-30 min	1-2.6 h	Short	8 mg	8 mg

Source: References 5-11, 13-17, 23, 43.

Benzodiazepine Receptor Agonists

Eszopiclone (Lunesta, generic)	15-30 min	6 h	Intermediate	1-3 mg	1-2 mg
Zaleplon (Sonata, generic)	<30 min	1 h	Ultrashort	10-20 mg	5 mg
Zolpidem (Ambien, generic)	30 min	2.5 h	Short	Female: 5-10 mg; male: 5 mg	5 mg
Zolpidem extended-release (Ambien CR, generic)	30 min	2.8 h	Short	Female: 6.25 mg; male: 6.25-12.5 mg	6.25 mg
Zolpidem solution (ZolpiMist)	30 min	1.7-8.4 h	Short	Female: 5 mg; male: 5-10 mg	5 mg
Zolpidem sublingual tablet (Edluar)	30 min	2.75 h	Short	Female: 5 mg; male: 5-10 mg	5 mg
Zolpidem sublingual tablet (Intermezzo)	30 min	2.5 h	Short	Female: 1.75 mg; male: 3.5 mg	1.75 mg

Summary of FDA-Approved Orexin Receptor Antagonists

	Suvorexant	DayVigo Lemborexant	Quvivig Daridorexant
Dosage form and strength	Tablets: 5 mg, 10 mg, 15 mg, 20 mg	Tablets: 5 mg, 10 mg	Tablets: 25 mg, 50 mg
Metabolism	Hepatic: CYP3A4 (major), CYP2C19 (minor)	Hepatic: CYP3A4/5	Hepatic: CYP3A4
Onset	30 min	<30 min	<30 min
T _{max}	2 h; delayed by high-fat meal	1-3 h; delayed by high-fat meal	1-2 h; delayed by high-fat meal
Excretion	Feces: 66%; urine: 23%	Feces: 57.4%; urine: 29.1%	Feces: 57%; urine: 28%
Half-life	12 h	5 mg: 17 h; 10 mg: 19 h	8 h
Initial dose	10-20 mg	5-10 mg	25-50 mg
Dose in elderly	10-20 mg	5-10 mg	25-50 mg

T_{max}: time to reach maximum concentration.

Source: References 5-11, 13-17, 23, 43.

Stop shortchanging your sleep

Listen to your bed partner

Snoring

Witnessed apneas

Daytime sleepiness

Postural Therapy

Weight management

Avoid alcohol in the evening hours

Consult your physician

Stop Bang

Epworth Scale

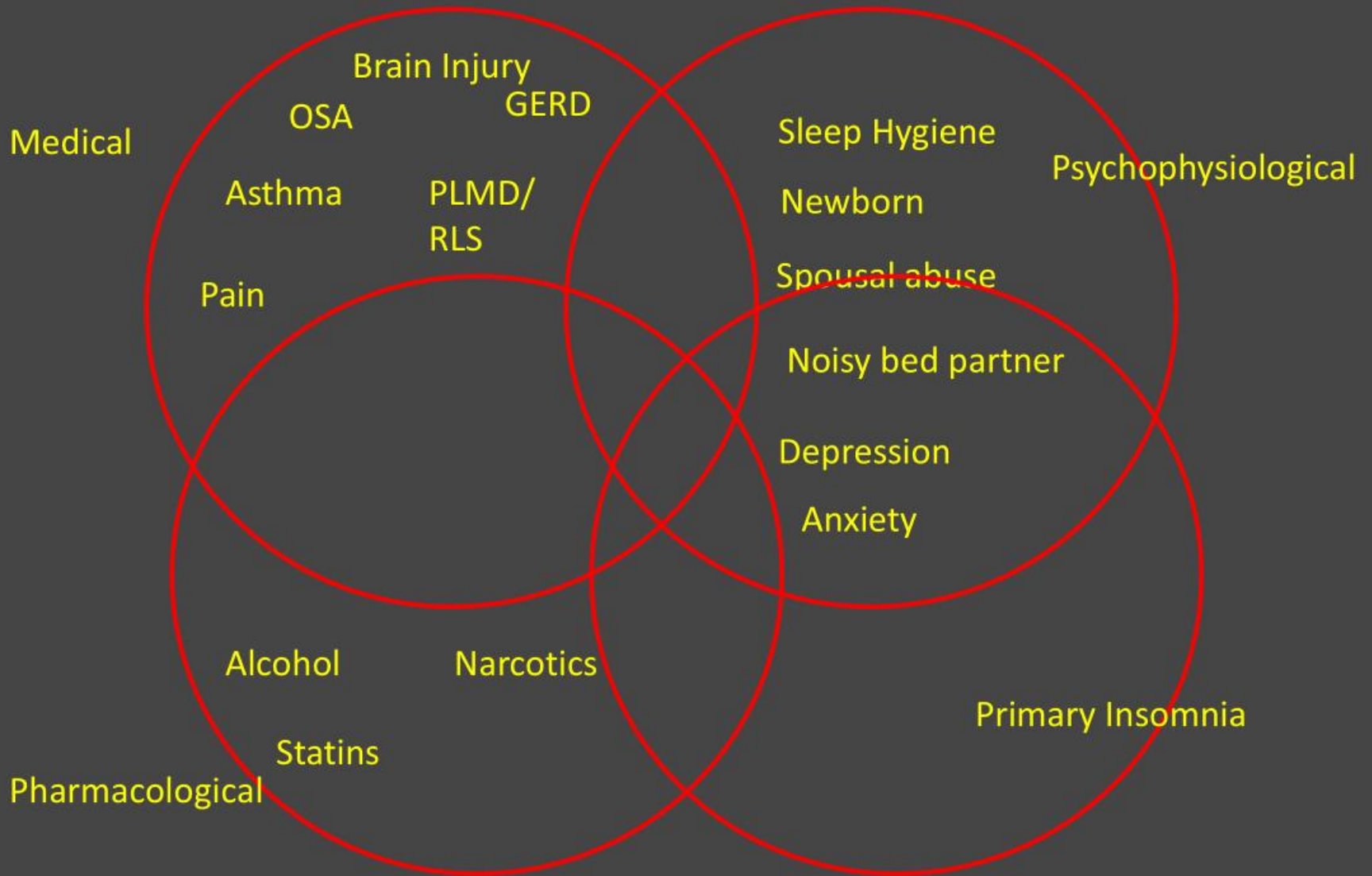
BMI

Examine the throat

Refer for sleep medicine assessment

- Best test
- More History especially from bed partner

Sleep Disruption Static Analysis



■ Questions