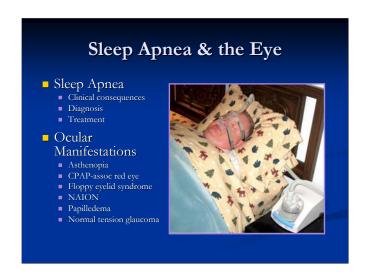


SLEEP APNEA IS A NEWLY DISCOVERED DISEASE (1966)

- Still learning about it, including it's effects on the eyes

THE MOST COMMON "MEDICAL" SLEEP DISORDER

- excluding shift-work and self-induced sleepiness (late night partying)
- Most prevalent disease discovered in the 20^{th} century 20% of adult population in Western countries
- Prevalence is growing b/c primary risk factor for developing OSA is obesity

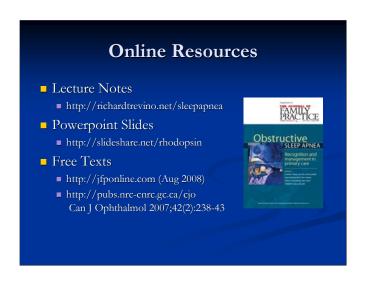


1. NECK

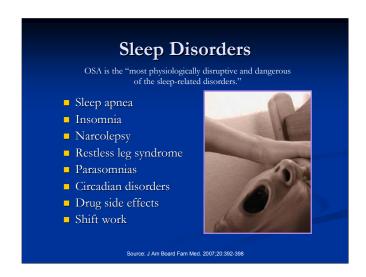
- larger on outside, smaller on the inside
- Pickwickian: Obese male, 30-60yo, always sleepy, snores loudly

2. CPAP

- mask may leak into the eyes
- noncompliance



Can J Ophthalmol April 2007



OSA is the most common medical sleep disorder

- prevalence growing in parallel with prevalence of obesity

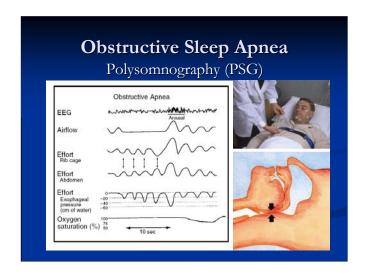
IT IS NOT ONLY THE MOST COMMON SLEEP DISORDER, BUT ALSO THE MOST PHYSIOLOGICALLY DISRUPTIVE AND DANGEROUS SLEEP DISORDER

- Life threatening disease:
 - Having OSA places pts at risk of developing MI and CVA
- A recently published longitudinal study found pts with severe OSA had 3-4x the death rate of persons without OSA.
- Wide spread effects throughout the body As we shall see, not even the somewhat remote and esoteric world of eye care is immune from the influences of this devastating disease

OSA is the most physiologically disruptive and dangerous of the sleep-related disorders

- OSA predisposes to MI and CVA
- higher mortality rate

To understand why, we must look at exactly what happens in OSA



What happens is this:

- 1. The airway closes shutting down airflow, and the patient continues to attempt to breath
- 2. The oxygen levels of the blood drop and eventually this triggers a sympathetic "fight or flight" response that arouses the pt from sleep and restores airflow

Three major pathophysiologic processes:

HYPOXIA/HYPERCAPNIA

- oxidative stress and chronic inflammation
- CNS effects: vasodilation leading to increased intracranial pressure

SYMPATHETIC ACTIVATION

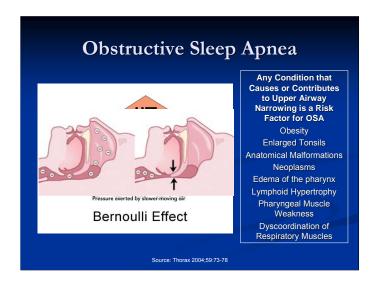
- Sleep is normally dominated by parasympathetic activity which helps support "rest and repose"
- bursts of sympathetic activity is response to cessation of respiration
- Sympathetic activation causes arousal, and restores airflow, but also causes: increases heart rate, increases blood pressure

SLEEP FRAGMENTATION

- disruption of the normal sleep cycle
- leads to the principle symptom of OSA: sleepiness

SUMMARY

Airway closure -> Apnea -> hypoxia -> sympathetic activation -> arousal -> sleep fragmentation



Upper airway collapse is the primary event that causes OSA

WHY DOES THE AIRWAY CLOSE?

To understand why the airway closes, we have to understand the Bernoulli effect.

Lower pressure caused by rapidly moving air in the pharynx draws the walls of the airway inward

Pharynx is by nature very floppy. Unlike the trachea, which has cartilaginous rings to keep it open, the pharynx relies upon dilator muscles to counter the Bernoulli effect

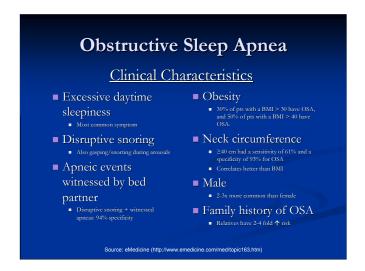
When inhale, dilator muscles in the pharnyx contract to keep the airway open

When asleep dilator muscles relax and their activity is relatively suppressed. Hence, there is a greater tendency for the pharnyx to narrow during inspiration

THE KEY VARIABLE IN WHETHER OR NOT AIRWAY CLOSURE WILL OCCUR IS THE INITIAL SIZE OF THE PHARNYX.

Anything that narrows the pharynx will predispose to OSA

The most common contributory factor by far is obesity



TOP 3 SYMPTOMS:

- 1. Sleepiness:
- Most common presenting symptom
- Described more often as tiredness, lack of energy, fatigue
- Most pts not aware that they have a sleep problem.

2. Snoring:

- extremely loud, disturbing the bed partner, the entire household, and even neighbors
- Due to upper airway resistance

3. Witnessed events:

- Cessation of breathing reported by the bed partner is usually a source of great anxiety because of fear that breathing may not resume.

OBESITY:

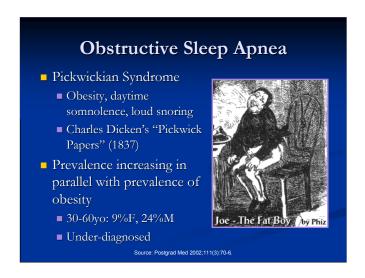
- By far the most significant medical association with OSA is the reciprocal relationship between OSA and obesity
- Obesity narrows the airway and predisposes to closure; OSA causes fatigue and neurohormonal changes that predisposes to obesity
- 30% OSA pts are not obese

Neck circumference: The bigger the neck is on the outside, the smaller it is on the inside

SEX:

- fat distribution: more central in men (thicker necks)
- hormonal: more OSA in postmenopausal women. HRT provides some protection

FAMILY HX: craniofacial structure



PICKWICKIAN SYNDROME

- Meaning has changed over time (ie: dyslexia)
- Recently refers to "Obesity Hypoventilation Syndrome" == OSA + COPD
- Classically refers to the typical OSA presentation: sleepy obese male who snores loudly
- Personified in the character Joe from Charles Dicken's "Pickwick Papers" (1837)

PREVALENCE FIGURES:

The most prevalent dx to be discovered in the 20th century

Prevalence increases with age, and peaks in 50-60yo age group.

- increasing tissue laxity
- prevalence may plateau after 65 years (survivor effect)
- OSA can occur in any age group, incl children

Obstructive Sleep Apnea Clinical Consequences Cognitive and Emotional Cardiovascular Disease ■ HTN, CAD/MI, CHF, ■ Impaired mental functioning Arrhythmia ■ Depression Stroke ■ Mood alteration Obesity Effects on bed partners Metabolic Syndrome ■ Disruptive snoring Other Diseases Accidents ■ Morning headache, Eye, ■ Drowsy driving Liver, Kidney, others ■ Workplace Source: How Stuff Works (http://healthguide.howstuffworks.com/sleep-apnea-in-depth.htm)

This is by no means an exhaustive list of the many effects that OSA has on the patient.

THE BIG THREE

CARDIOVASC DX

- OSA is #1 cause of secondary HTN
- Strength of relationship between OSA and HTN is second only to the relationship between OSA and obesity
- Dose-response relationship: increased severity of OSA -> increased risk of HTN
- Sympathetic activation: nocturnal spikes in BP
- OSA assoc with increased risk of MI

STROKE

- any degree of OSA almost doubles the risk of stroke
- moderate OSA are 3 times more likely to have a stroke than are members of the general population

OBESITY

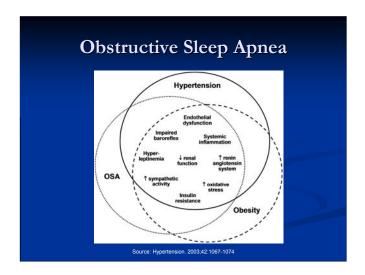
- Obesity remains the single most significant risk factor for OSA
- Reciprocal relationship: Obesity is both a cause and a consequence of OSA
- Daytime sleepiness + decreased physical activity + neuroendocrine chgs (LEPTIN RESISTANCE)
- CPAP tx -> weight loss
- increased obesity -> worsen OSA

COGNITIVE

- the purpose of sleep is to refresh and restore the brain.
- diminished cognitive function stems from hypoxic brain injury, reduced alertness, or both

PUBLIC HEALTH

- In 2000, 1400 highway deaths attributable to OSA



Relationship between OSA, HTN, and Obesity and metabolic syndrome

- each exacerbates one another, and all contribute to metabolic syndrome
- a combination of physiologic changes that gives rise to diabetes, heart disease, and CVA

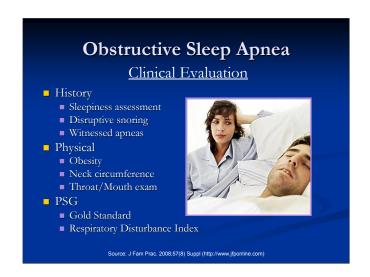
OSA may contribute, at least in part, to some of the pathological processes traditionally ascribed to obesity alone,

- most notably sympathetic overactivity and humoral, metabolic, and neuroendocrine abnormalities.

Compelling data support the association of OSA with hypertension.

OSA probably contributes to or exacerbates the obesity-related hypertension.

Sleep apnea is at the top of the list of causes of secondary hypertension



HOW TO SCREEN FOR OSA

- 1. Ask about fatigue
- Epworth sleepiness scale: fast validated office assessment
- 2. Ask about snoring problem
- 3. Ask bed partner about witnessed apneas
- 4. OSA Habitus (Pickwickian syndrome)

Obesity

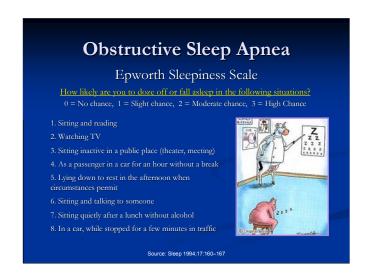
- most common, but not only cause of airway crowding
- 30% OSA pts are not obese
- mouth and throat exam essential for r/o other causes
- 5. Overnight sleep study
- Sleep specialist or pulmnologist

RDI:

5-15

15-30

>30

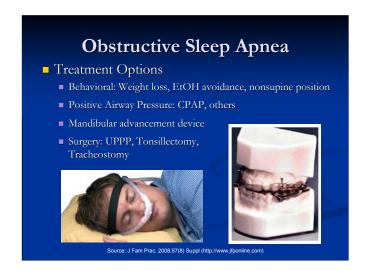


ESS: Best tool for the office assessment of sleepiness

a validated method of assessing the likelihood of falling asleep in a variety of situations

simple to use and interpret and takes less than 2 minutes to complete

SCORE ≥ 10 INDICATIVE OF EXCESSIVE SLEEPINESS



BEHAVIORAL

- Augment other therapies

CPAP

- Mainstay therapy for most pts with OSA
- air splint
- Major limitation of CPAP: achieving acceptable compliance
- Complications: dry nose, Nasal congestion, skin irritation, eye irritation (from air leaks around the mask).

ORAL APPLIANCES:

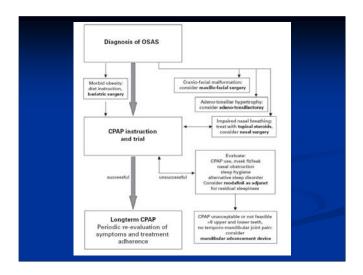
- unable or unwilling to use CPAP, less efficacious than CPAP

SURGERY

- craniofacial or other structural abnormalities that can be corrected with surgery (2% of OSA cases)
- surgical intervention is not as effective in OSA as CPAP (except tracheostomy)

UPPP: Uvulopalatopharyngoplasty

- most commonly performed surgical procedure for OSA
- removal of part of the soft palate and uvula
- success rate of 39% (defined as a 50% reduction in AHI score leading to an AHI ≤20)



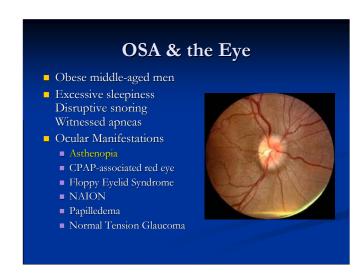
Overview of management of OSA

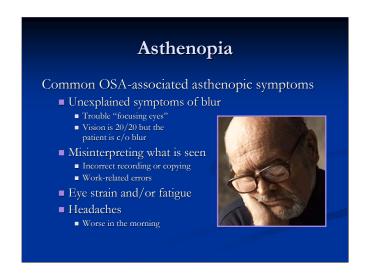
Inadequate CPAP

 apneas can occur despite CPAP if pressure too low, mouth breathing, nasal obstructions, etc

RESIDUAL SLEEPINESS

- Up to half of patients with OSA have residual sleepiness,
- possibly due to irreversible hypoxic injury to wake-active neurons
- Modafinil is a wakefulness-promoting agent (?use may decrease compliance with CPAP)





IF OSA IS IN THE MED HX

- be on the lookout for sxs of fatigue
- possibly due to poor compliance or residual fatigue

IF OSA NOT IN THE MED HX

- high index of suspicion for OSA whenever cc is fatigue or asthenopia
- esp if habitus is pickwickian
- screen for sleepiness

If the pt is dx with OSA and presents with these sxs

- compliance?
- residual fatigue

If pt is not dx with OSA

- pickwickian?
- sleepiness screening
- question bed partner

Asthenopia

- If OSA is in the medical history
 - Be on the lookout for sxs of fatigue
 - Possibly due to poor compliance or residual fatigue
 - Offer supportive management
- If OSA is not in the medical history
 - High index of suspicion whenever the chief complaint is fatigue or asthenopia
 - Especially if habitus is Pickwickian
 - Be prepared to screen for sleepiness



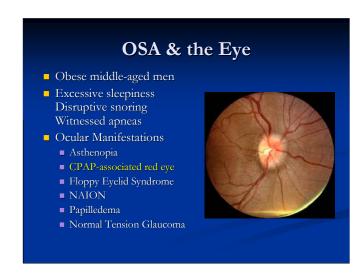
CPAP compliance stats

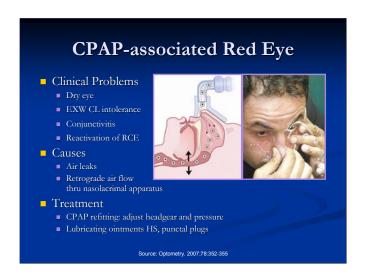
- 46% use regularly (4 hrs/night at least 5 nights/week)
- 50% drop out 1st year

Weight and OSA

- loss of 10% of body weight -> 26% reduction in risk of having OSA
- 10% gain in weight -> 6x increase in odds of getting OSA

EDUCATE PTS THAT OSA CAN CAUSE PERMANENT EYE DAMAGE





A variety of common ocular problems have been associated with CPAP use

As a reminder, CPAP delivers air under pressure to the nose.

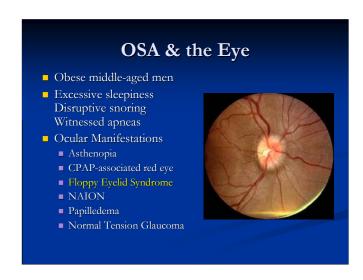
- during the night, air may escape from around the mask and blow onto the eyes resulting in morning sxs of dry, irritated eyes
- alternatively air may find its way up through the naso-lac duct, and cause similar problems

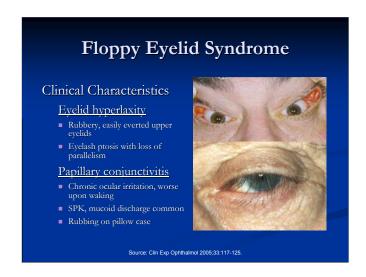
There are a series of valves that inhibit retrograde flow up the duct, but in many people these vales are not totally effective in preventing retrograde flow.

- many of these people learn as children that they can perform cool schoolyard tricks to impress their classmates such as blowing their lunch milk out of their eye

INCLUDE CPAP-USE IN THE DIFFERENTIAL DIAGNOSIS OF THESE COMMON EYE PROBLEMS

It is important that OSA be included in our history forms because most pts will not necessarily associate eye problems with it





FES is the classic ocular manifestation of sleep apnea

- the first ocular condition to be associated with the disease
- originally described in 1981, the same year that CPAP was introduced as a tx for OSA

FES = hyperlaxity + conjunctivitis/keratitis

- clinically, many asymptomatic pts with floppy lids encountered who do not have conjunctivitis
- others will simply have complaints of dry eye

Degree of floppiness may vary

- no grading or quantification system exists
- subjective impression of how easily the lid self-everts

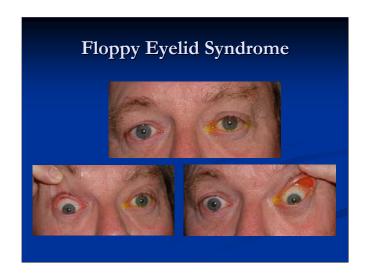


Conspicuous finding that may be the presenting sign of OSA

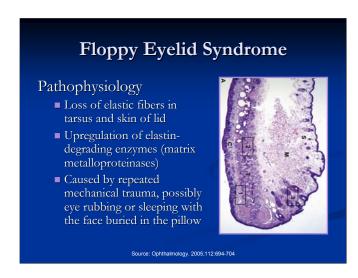
Eyelash ptosis may also be age-related

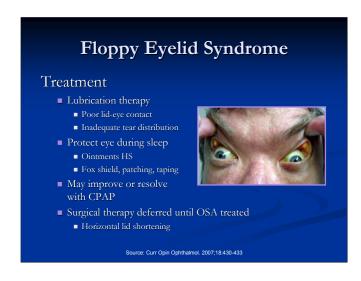
- not associated with floppy lids

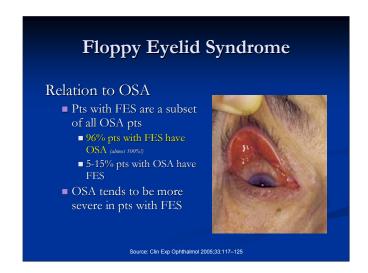
When a pt with down-pointing lashes are encountered, pull the lid upward to assess whether the lid will self-evert



May be Unilateral or bilateral – presumable based upon what side the pt usually sleeps on







Almost all pts with FES have OSA

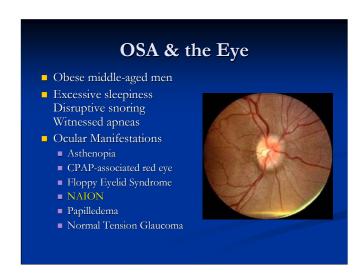
But only a small number of pts with OSA have FES

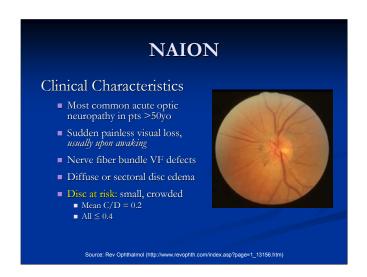
- A pattern we will see repeated with other ocular manifestations of the disease

FES associated with more severe OSA

- More severe OSA associated with higher mortality rates (3-4x normal)

FES PTS HAVE OSA UNTIL PROVEN OTHERWISE!





Hayreh (1997): 50% upon awakening 25% early morning 25% other times

- suggests that a nocturnal events play a role in the disease process

Disc-at-risk

- bjo 2006 osa/naion study
- 27 consecutive naion cases

NAION Pathophysiology Idiopathic ischemic process Disorder of posterior ciliary artery circulation Transient poor circulation in the ONH Trigger Event: Fall in blood pressure below a critical level? There is no actual blockage of the posterior ciliary arteries Cascade Effect Mechanical crowding caused by small crowded disc Ischemia → Swelling → Compression → Ischemia

Trigger event

- precipitating event that triggers onset in predisposed individuals
- nocturnal arterial hypotension suspected

NAION Treatment Aspirin Decreases incidence in fellow eye at 2 years, but not at 5 years Control of predisposing systemic disease May slow progression or reduce incidence in fellow eye Hypertension, Diabetes, Hyperlipidemia, OSA Avoid phosphodiesterase 5 inhibitors (Viagra, Levitra, Cialis) May increase risk of NAION in fellow eye

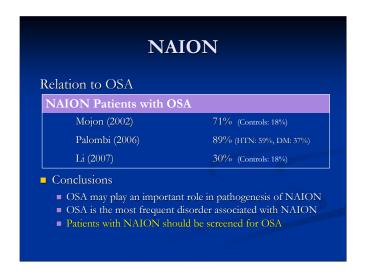
Vasculopathic risk factors

Erectile dysfunction drugs (EDD)

- *Medicolegal obligation to inform them of risk to fellow eye*
- lawsuits against Pfizer

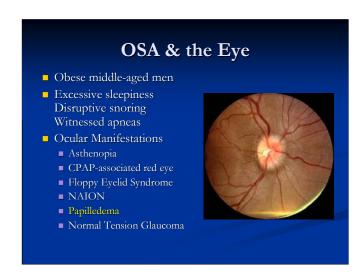
Viagra

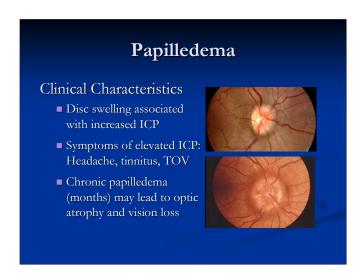
- cause/effect unclear, may impair autoregulation (increased nitric oxide levels)
- onset of NAION within 24hrs of using Viagra
- Avoid if: disc-at-risk, TVL, MI, NAION



How to screen?

- Sleepiness assessment (ESS)







Lumbar puncture

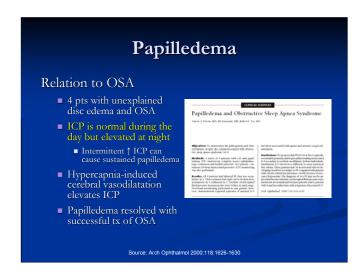
- measure CSF pressure
- collect sample of CSF for biochemical, microbiological, and cytological analysis
- inflammation, infection, evidence of intracranial bleed, tumor cells

If after neuroimaging and CSF analysis a cause for the elevated ICP is not found, the pt is said to have IIH

COPD and OSA -> Increase CO2 levels -> vasodilation -> Increase ICP

Vitamin A toxicity -> brain edema -> Increase ICP

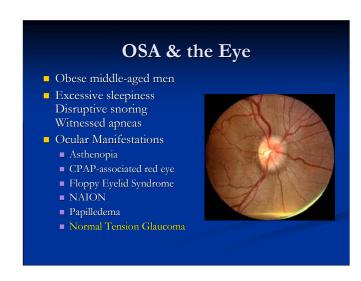
Diamox 250mg po QID – suppresses CSF production, lowering ICP, and helping to speed resolution of papilledema $\,$

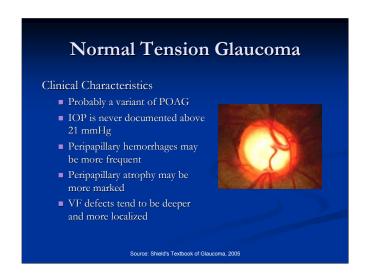


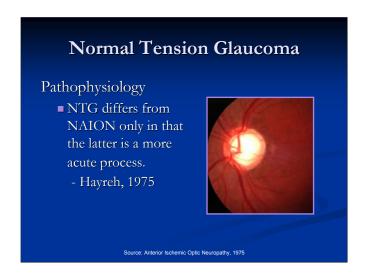
Elevated ICP in OSA

- Cerebral vasodilation: Primary cause is cerebral vasodilation secondary to decreased oxygen and increased CO2
- contributing factors may be elevated central venous pressure due to forced expiration against a closed glottis and arterial hypertension

pressure elevation during sleep ranging from 50 to 750 mm H2O (normal < 220 mm H2O)

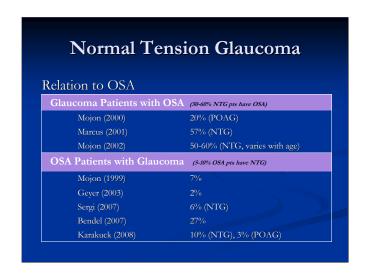






Collaborative Normal-Tension Glaucoma Study

Low-Pressure Glaucoma Treatment Study



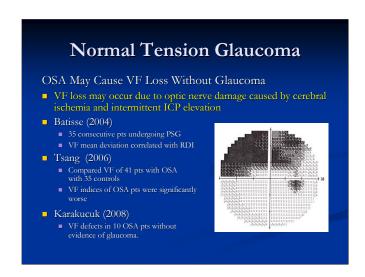
This question has received lots of research attention: 8 studies

Incidence of OSA in general population: 10-20% Incidence of glc in general population: 1.5-3%

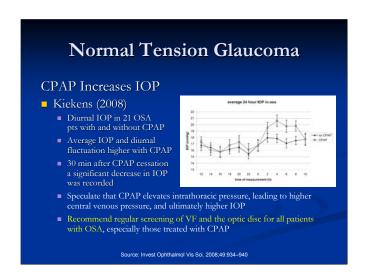
Very few (<10%) OSA pts have glaucoma (but perhaps higher than general pop) Many (perhaps most) NTG pts have OSA

Similar to situation with FES!

Big range (2% - 27%) may reflect difficulty deciding what constitutes glaucoma



OSA may cause VF defects independent of glaucoma secondary to intermittent ICP elevation



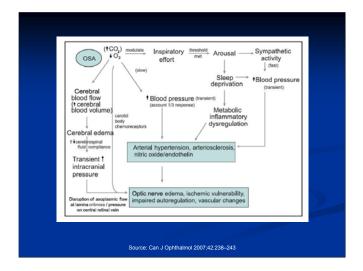
Pts may appear to have NTG, but IOP is elevated nocturnally due to CPAP

First session: Dx with OSA but not yet started on CPAP

During the second session, the CPAP mask remained applied during the overnight measurements.

Immediately after CPAP cessation in the morning, the patients were asked to remain supine.

Thirty minutes later, IOP was measured to evaluate the effect of acute CPAP withdrawal.



The immediate physiological effects of OSA involve hypoxia, hypercapnia, and inspiratory effort.

Hypoxia and hypercapnia

- •Large fluctuations in vascular oxygen and carbon dioxide function as metabolic stresses that may overwhelm the autoregulatory capacity of the optic nerve head and retina.
- •hypoxia-induced cerebral vasodilatation impedes cerebral perfusion pressure, which may ultimately hinder autoregulation.
- •The effect of hypercapnia during sleep is circumvented because chemoreceptor sensitivity is decreased nocturnally and also because of the body's high buffering capacity.
- •Hypoxia, detected by carotid chemoreceptors, leads to increases in blood pressure and hemodynamic changes.

Inspiratory effort

- •activates the sympathetic system and creates sleep disturbance.
- •Since the optic nerve is not innervated by the autonomic nervous system, direct effects of sympathetic arousal are unlikely.
- •Decreased intrathoracic pressure created by inspiratory effort leads to increased stroke volume and cardiac output. This results in transient elevations in blood pressure and a number of hemodynamic changes.

