Sleep Apnea
& the Eye

Rick Trevino, OD, FAAO
Rosenberg School of Optometry
University of the Incarnate Word

Online Resources

Lecture Notes

http://richardtrevino.net

Email me

rctrevin@uiwtx.edu

Disclosures

None

Sleep Apnea & the Eye

- **Sleep Apnea**
  - What it is
  - How it's diagnosed & treated
- **Ocular Manifestations**
  - Asthenopia
  - CPAP-assoc red eye
  - Floppy eyelid syndrome
  - Retinal Conditions
  - NAION
  - Papilledema
  - Normal tension glaucoma

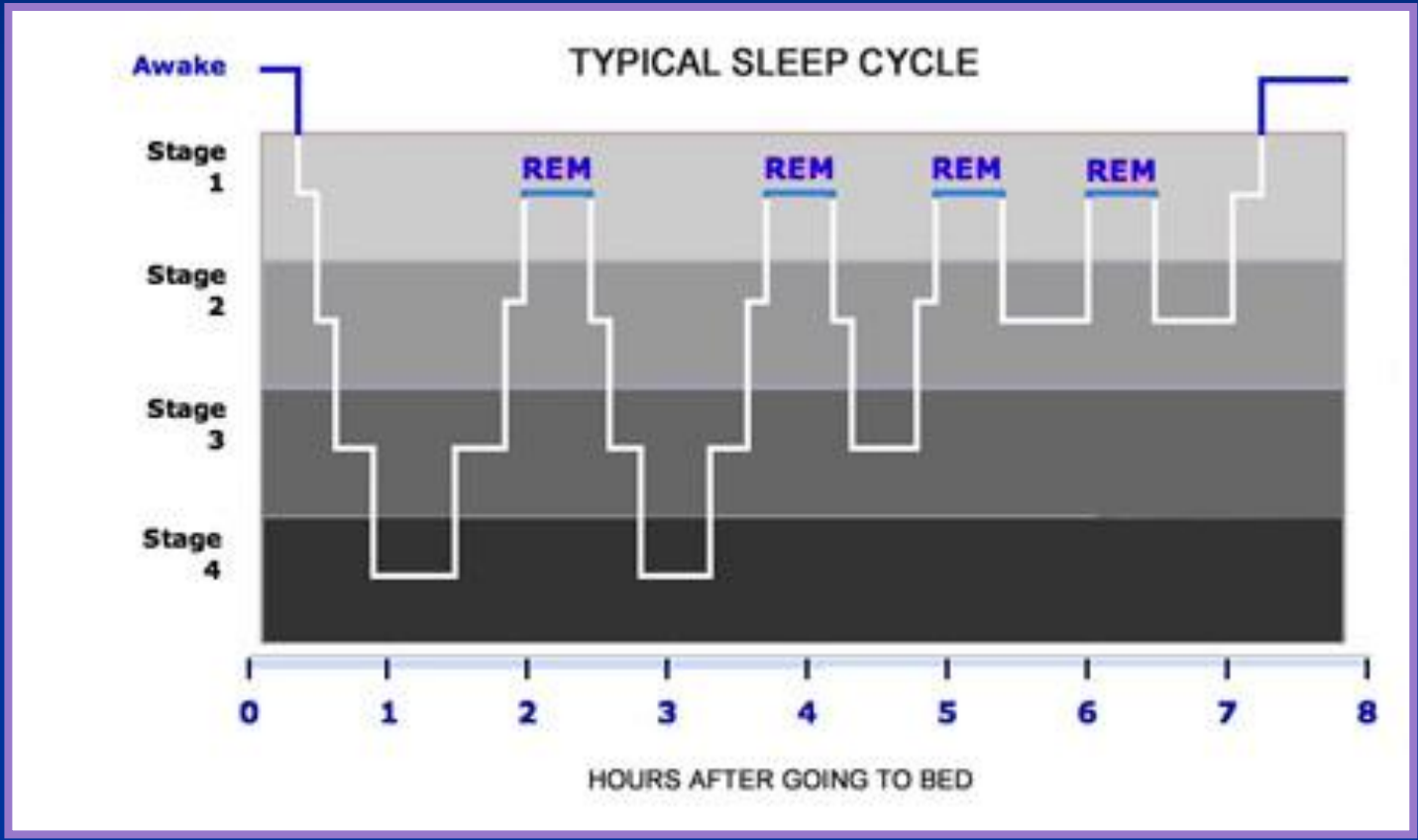
Sleep Disorders

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

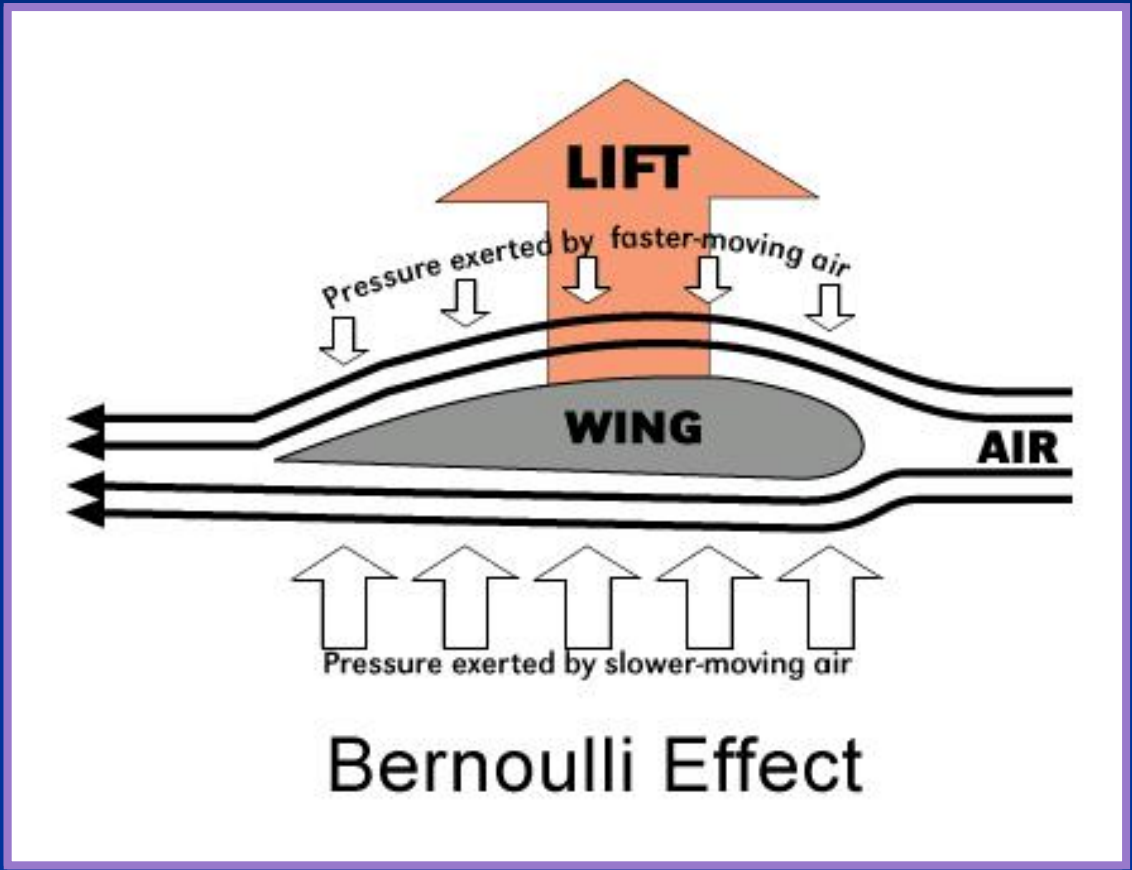
- Sleep apnea
- Insomnia
- Narcolepsy
- Restless leg syndrome
- Parasomnias
- Circadian disorders
- Drug side effects
- Shift work

PMID: 17615420

Sleep Architecture



Obstructive Sleep Apnea



Bernoulli Effect

Any Condition that Causes or Contributes to Upper Airway Narrowing is a Risk Factor for OSA

- Obesity
- Enlarged Tonsils
- Anatomical Malformations
- Neoplasms
- Edema of the pharynx
- Lymphoid Hypertrophy
- Pharyngeal Muscle Weakness
- Dyscoordination of Respiratory Muscles

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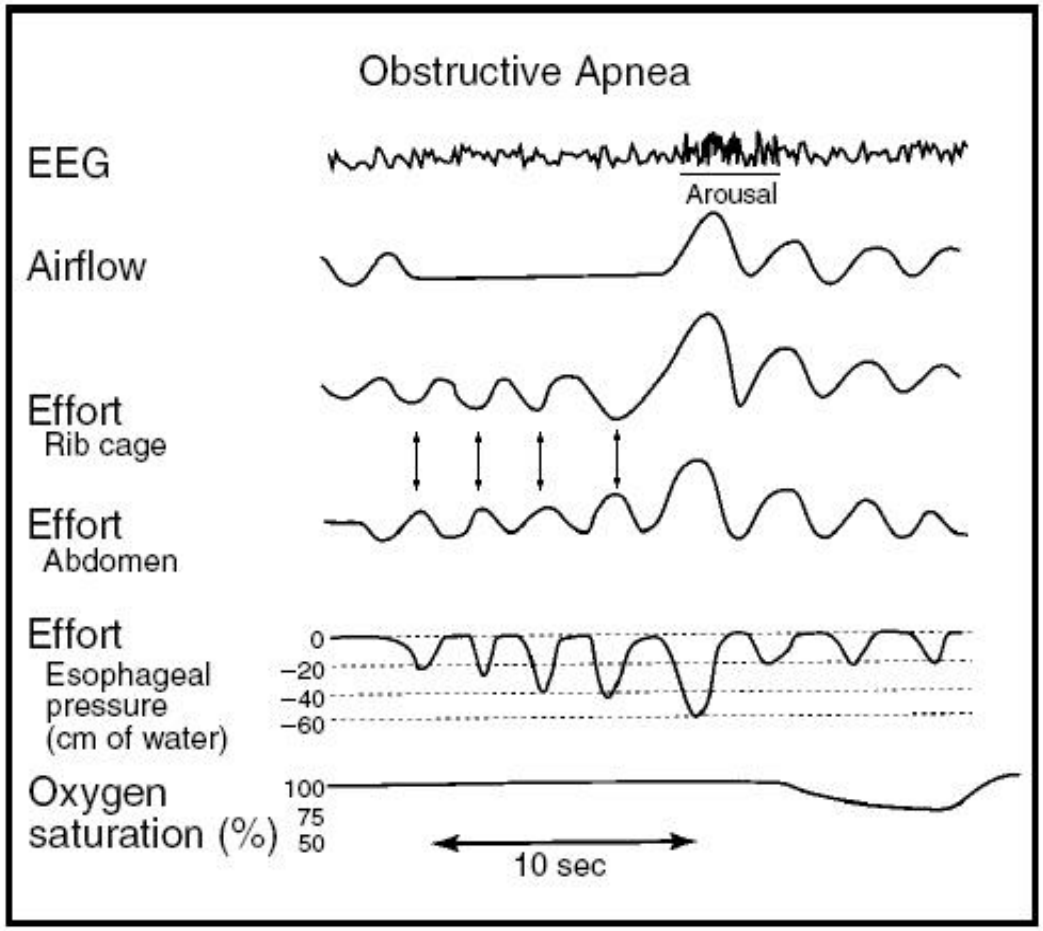
Obstructive Sleep Apnea

Polysomnography (PSG)

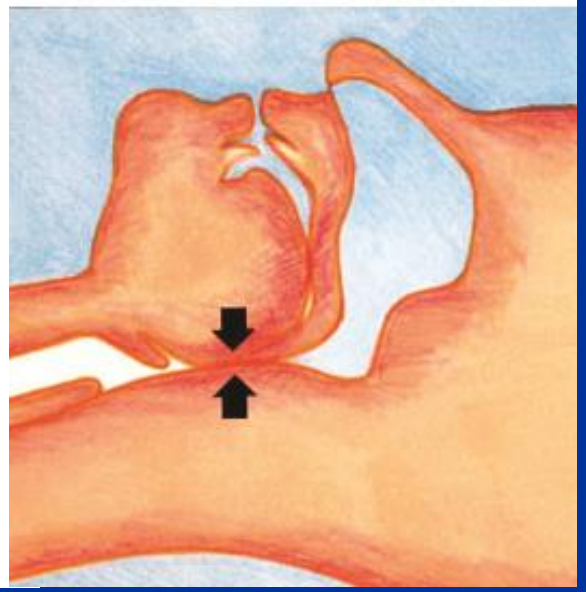


OSA Grading Scale

Mild: 5-15 episodes/hr

Mod: 15-30 episodes/hr

Severe: >30 episodes/hr



Obstructive Sleep Apnea

Clinical Characteristics

Excessive daytime sleepiness

- Most common symptom

Disruptive snoring

- *"Do you have a snoring problem?"*

Apneic events witnessed by bed partner

- Disruptive snoring + witnessed apneas: 94% specificity

Obesity

- 30% of pts with a BMI > 30 have OSA, and 50% of pts with a BMI > 40 have OSA.

Neck circumference

- ≥40 cm had a sensitivity of 61% and a specificity of 93% for OSA
- Correlates better than BMI

Male

- 2-3x more common than female

Family history of OSA

- Relatives have 2-4 fold ↑ risk

Obstructive Sleep Apnea

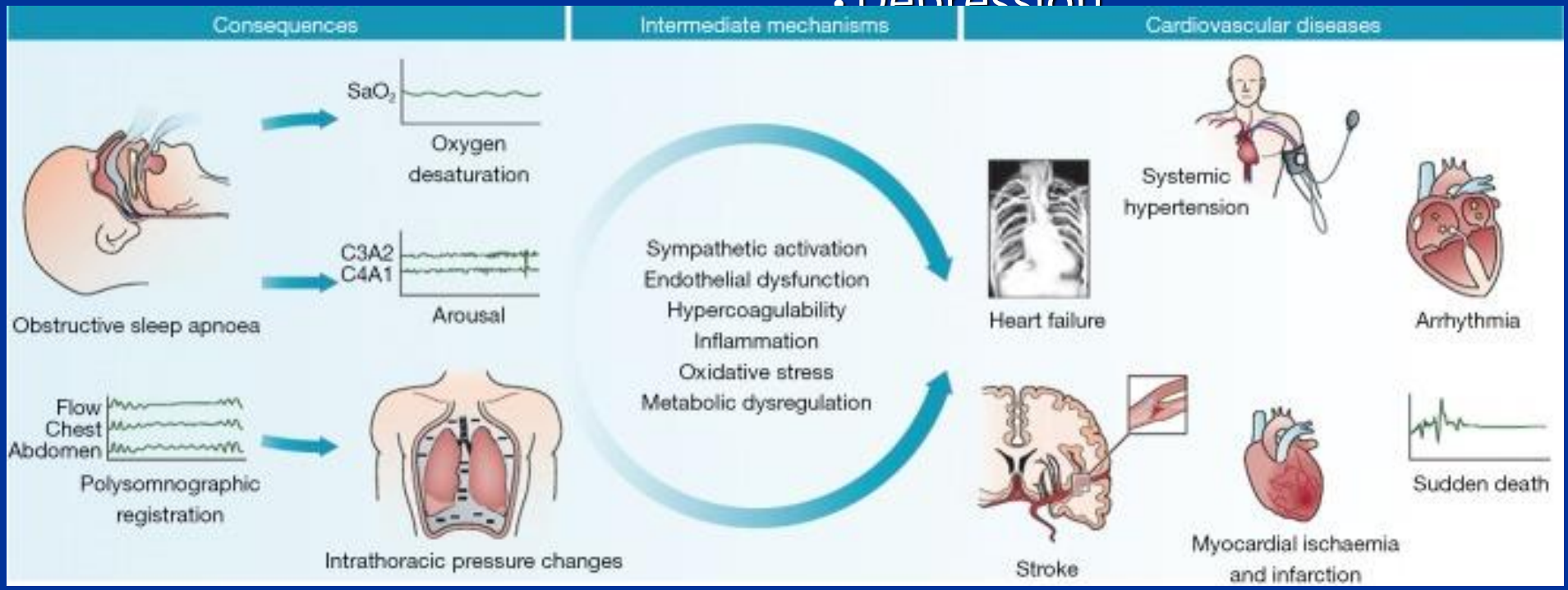
Clinical Consequences

Cardiovascular Disease

- HTN, CAD/MI, CHF, Arrhythmia

Cognitive and Emotional

- Impaired mental functioning
- Depression



AWAKE AT THE WHEEL

DROWSY DRIVERS are involved in an estimated **6% OF ALL CRASHES** and **21% OF FATAL CRASHES.**

An Average of **328k** Crashes Annually

109,000 CRASHES WITH INJURIES

6,400 FATAL CRASHES

DRIVERS ages 16-24 **are 80%** more likely to be in a **drowsy driving accident**

Males are **60% more likely** to be in a drowsy driving crash

OTHER RISK GROUPS:

- Shift workers (work the night shift or rotating shifts)
- Drivers with untreated sleep disorders such as sleep apnea
- Drivers who use sedating medications
- Drivers who do not get 7-9 hours of sleep

WARNING SIGNS OF

Obstructive Sleep Apnea

Clinical Evaluation

History

- Sleepiness assessment
- Disruptive snoring
- Witnessed apneas

Physical

- Obesity
- Neck circumference
- Throat/Mouth exam

PSG

- Gold Standard
- Respiratory Disturbance Index; Apnea/Hypopnea Index

PMID: 18687235

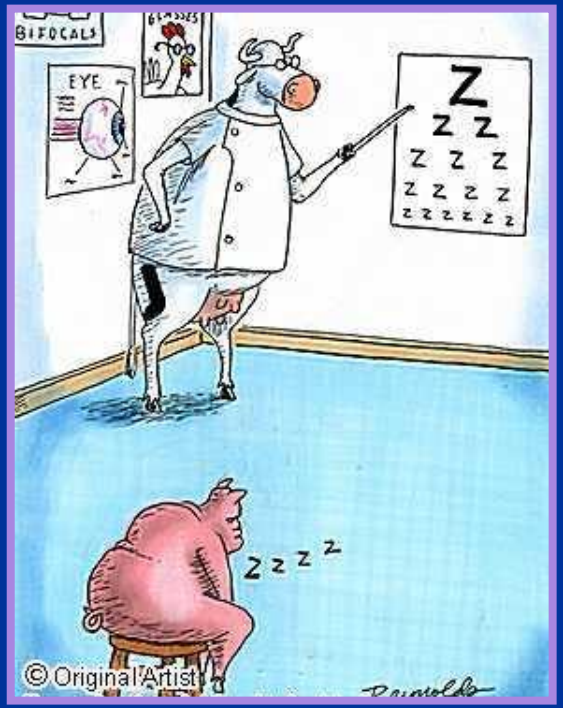
Obstructive Sleep Apnea

Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations?

0 = No chance, 1 = Slight chance, 2 = Moderate chance, 3 = High Chance

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



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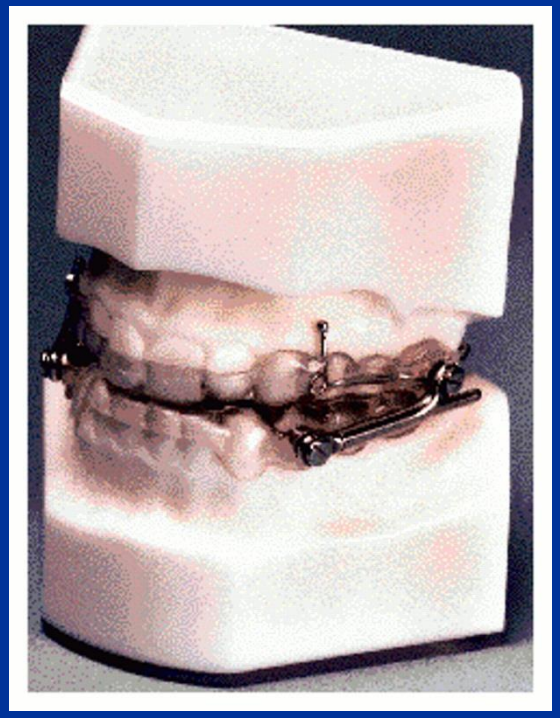
Obstructive Sleep Apnea

Treatment Options

- Behavioral: Weight loss, EtOH avoidance, nonsupine position
- Positive Airway Pressure: CPAP, Provent, others
- Mandibular advancement device
- Surgery: UPPP, Tonsillectomy, Tracheostomy



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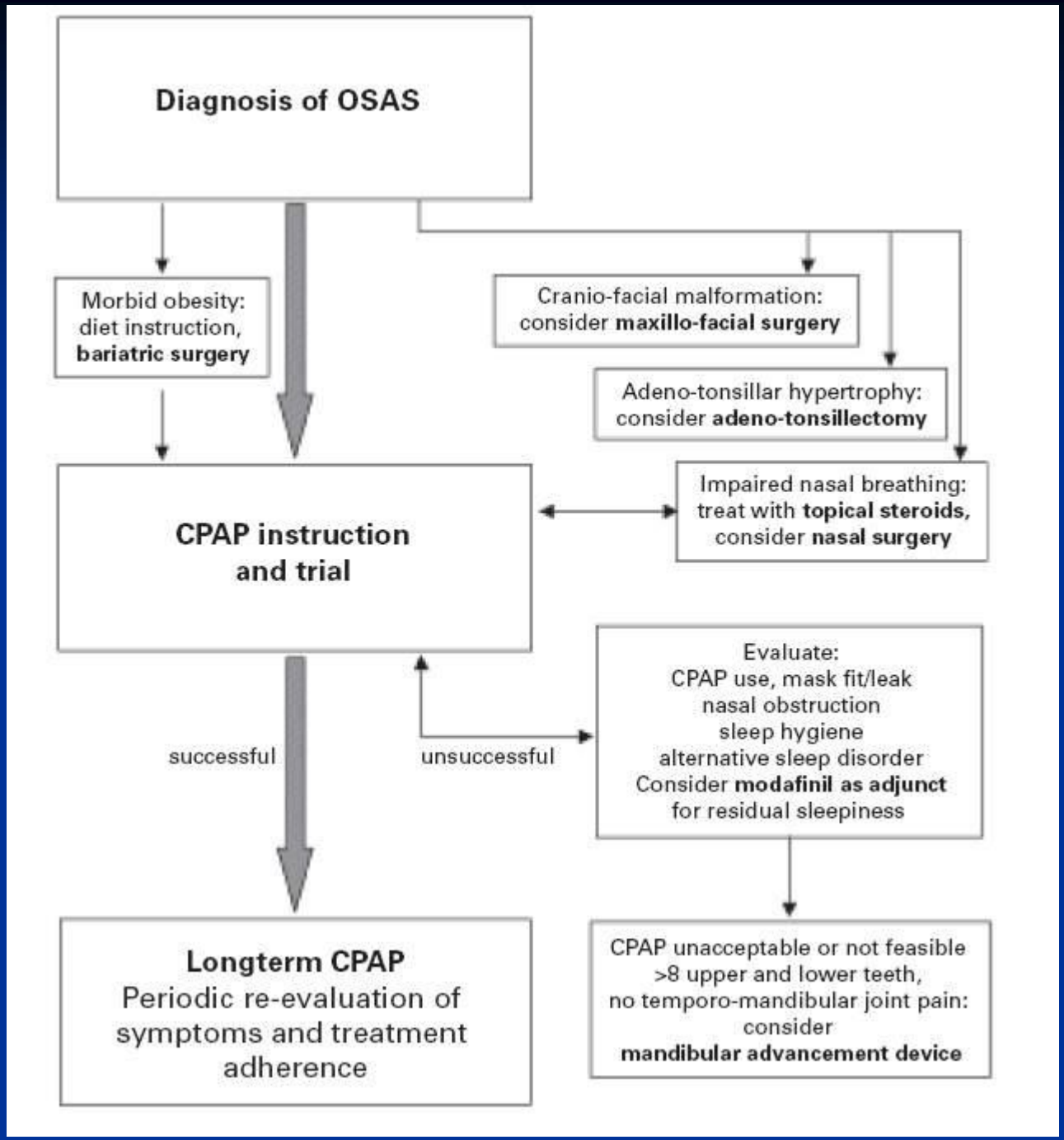
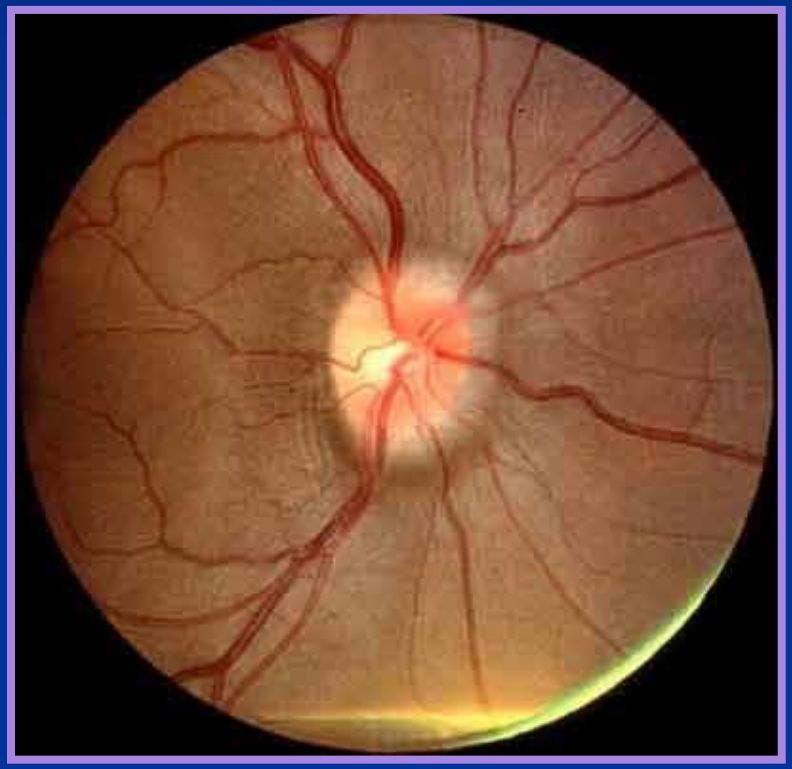

Diagnosis of OSAS
Morbid obesity: diet instruction, bariatric surgery
Cranio-facial malformation: consider maxillo-facial surgery
Adeno-tonsillar hypertrophy: consider adeno-tonsillectomy
Impaired nasal breathing: treat with topical steroids, consider nasal surgery
CPAP instruction and trial
successful
unsuccessful
Evaluate:
CPAP use, mask fit/leak
nasal obstruction
sleep hygiene
alternative sleep disorder
Consider modafinil as adjunct for residual sleepiness
Longterm CPAP
Periodic re-evaluation of symptoms and treatment adherence
CPAP unacceptable or not feasible
>8 upper and lower teeth,
no temporo-mandibular joint pain:
consider
mandibular advancement device

OSA & the Eye

Ocular Manifestations of Sleep Apnea

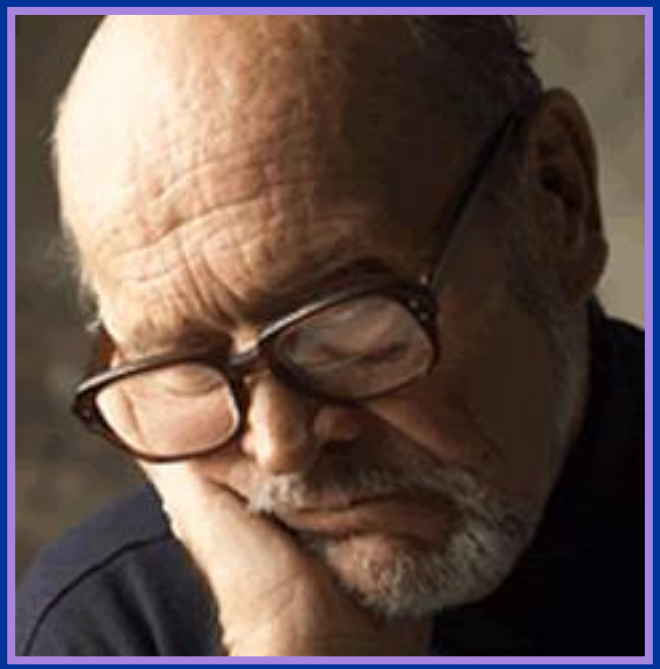
- Asthenopia
- CPAP-assoc Red Eye
- Floppy Eyelid Syndrome
- Diabetic Retinopathy
- NAION
- Papilledema
- Normal Tension Glaucoma



Asthenopia

Common OSA-associated asthenopic symptoms

- Unexplained symptoms of blur
  - Trouble "focusing eyes"
  - Vision is 20/20 but the patient is c/o blur
- Misinterpreting what is seen
  - Incorrect recording or copying
  - Work-related errors
- Eye strain and/or fatigue
- Headaches
  - Worse in the morning



Asthenopia

If OSA is in the medical history

- Ask about sleepiness or fatigue
- Possibly due to poor compliance or residual fatigue
- Offer supportive management (eg. CPAP compliance)

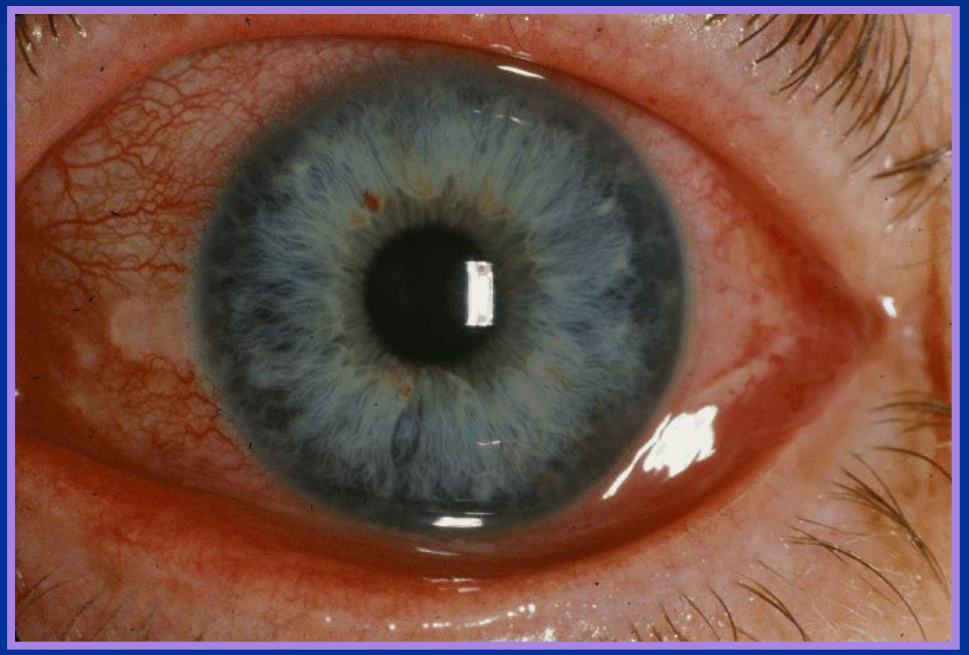
If OSA is not in the medical history

- High index of suspicion whenever the chief complaint is fatigue or asthenopia
- Especially if habitus is Pickwickian
- Be prepared to screen for sleepiness

CPAP-associated Red Eye

Clinical Problems

- Dry eye syndrome
- EXW CL intolerance
- Recurrent corneal erosion
- Infectious conjunctivitis



Causes

- Air leaks
- Retrograde air flow thru nasolacrimal apparatus (*Saline bubble test*)

Treatment

- Lubricating ointments HS, punctal plugs
- CPAP refitting: adjust headgear and pressure
- Intranasal surgery

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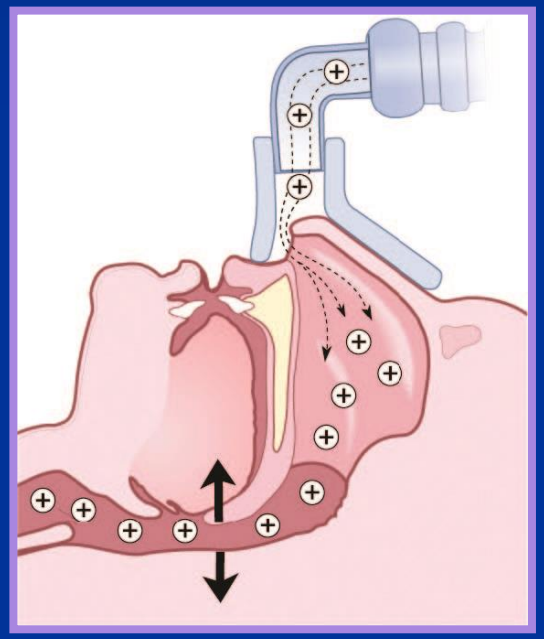
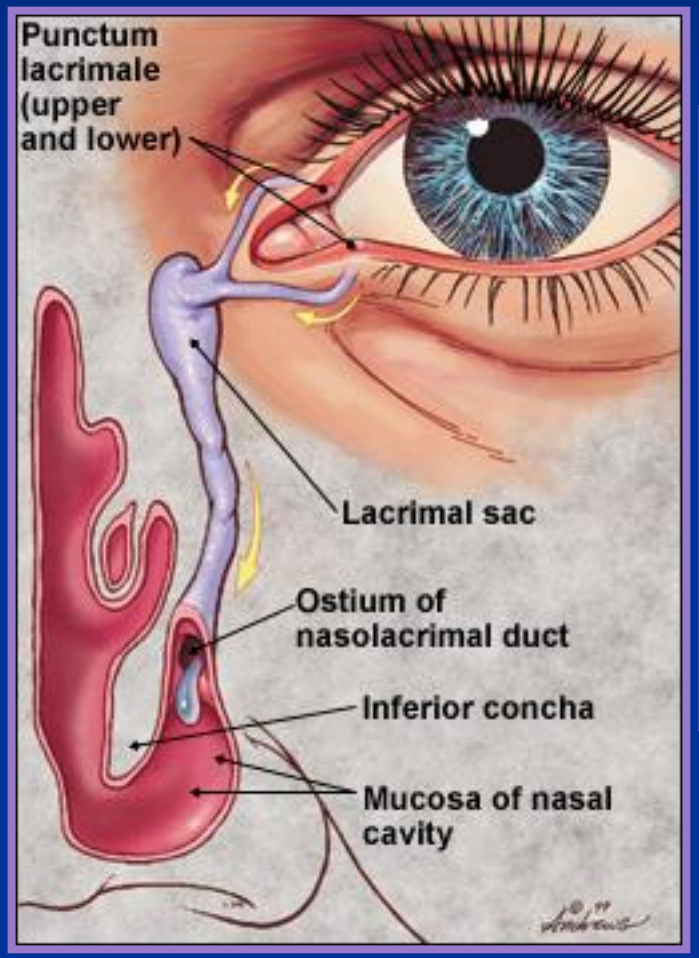
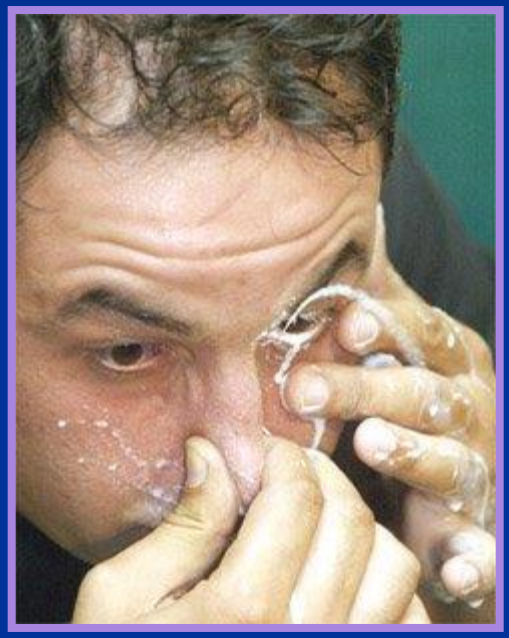
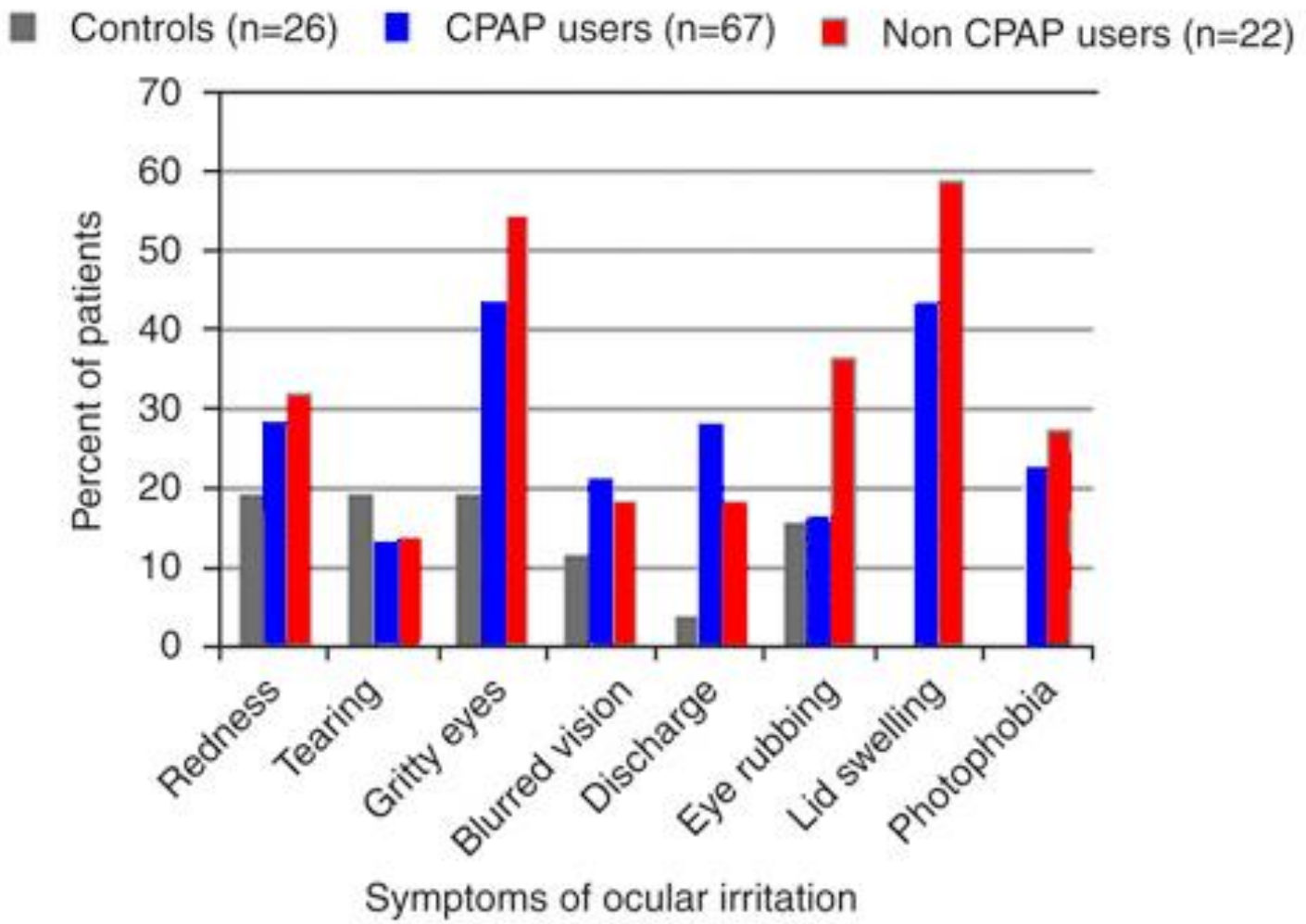
CPAP-associated Red Eye









Persons with OSA generally have greater ocular discomfort than controls, but is greatest among persons that are noncompliant with CPAP

PMID: 19680276

Floppy Eyelid Syndrome

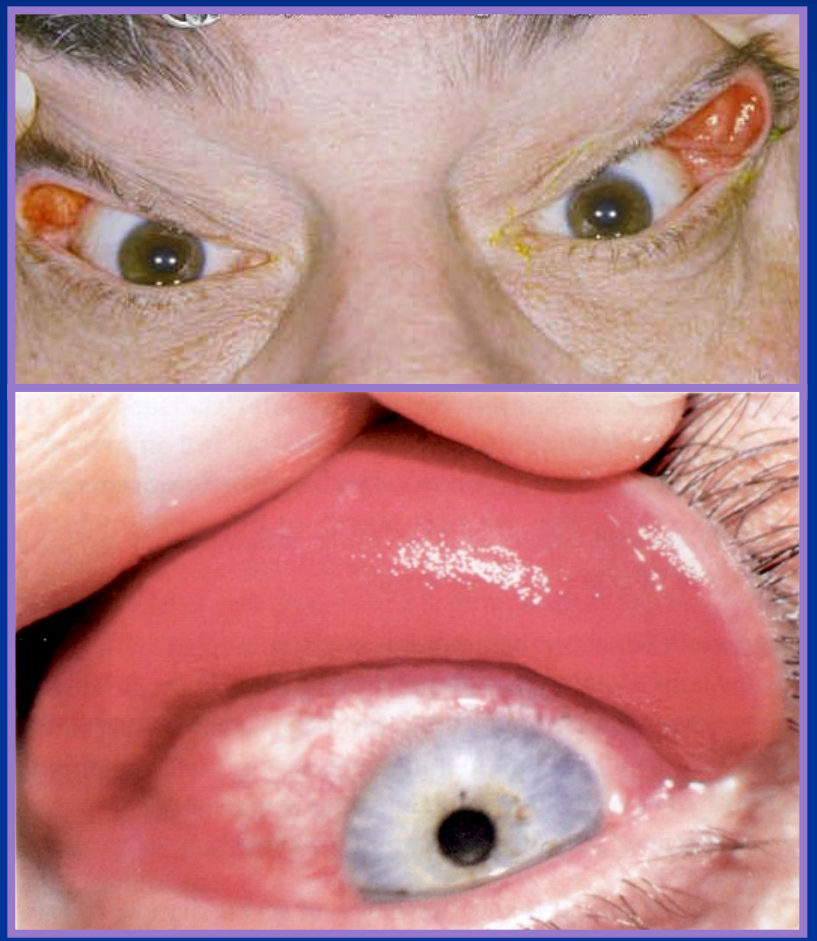
Clinical Characteristics

Eyelid hyperlaxity

- Rubbery, easily everted upper eyelids
- Eyelash ptosis with loss of parallelism

Papillary conjunctivitis

- Chronic ocular irritation, worse upon waking
- SPK, mucoid discharge common
- Rubbing on pillow case



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Floppy Eyelid Syndrome

Eyelash ptosis

- Downward displacement of eyelashes
- Lashes may point in various directions
- Loss of parallelism
- Pts may trim with scissors

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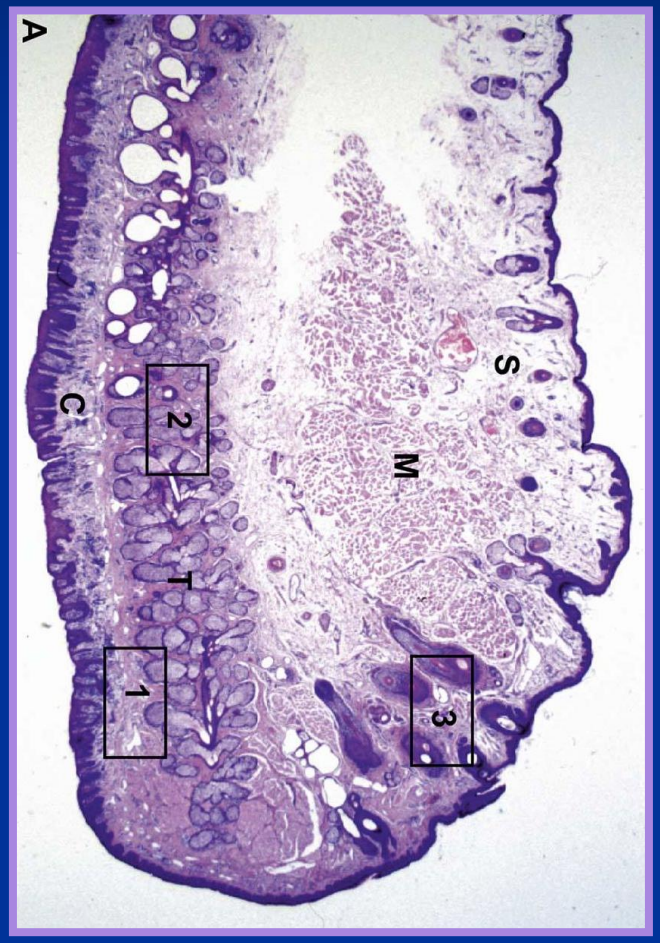
Floppy Eyelid Syndrome

Floppy Eyelid Syndrome

Pathogenesis

- Loss of elastic fibers in tarsus
- May be caused by repeated mechanical trauma, possibly eye rubbing or sleeping with the face buried in the pillow
- FES also highly associated with keratoconus, reinforcing suspected role of mechanical trauma
- Pedrotti (2018): OSA is 10-20x more common among pts with KCN



PMID: 24141141, 29319596

Floppy Eyelid Syndrome

Treatment

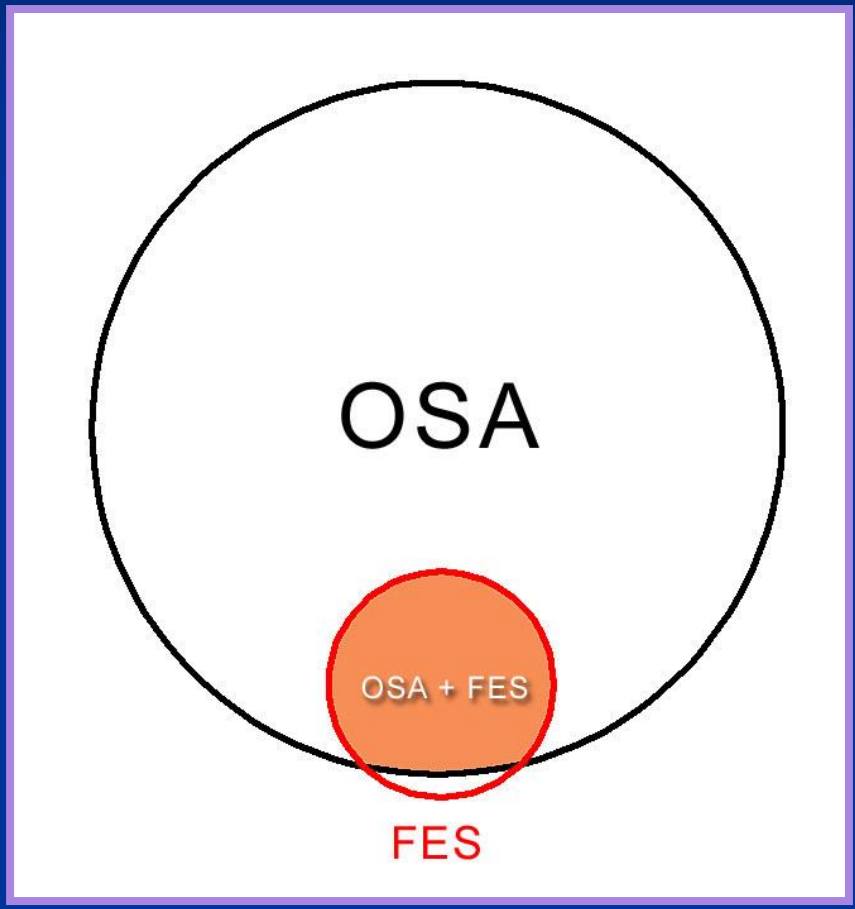
- CPAP therapy
  - Treatment of OSA can improve sxs
- Protect eye during sleep
  - Ointments HS
  - Patching, taping, sleep mask
- Surgery is considered the definitive treatment
  - 25-50% failure rate within 2yrs

PMID: 20097426

Floppy Eyelid Syndrome

Relation to OSA

- About 10-20% of OSA pts have FES
- 40% of pts with severe OSA have FES
- 96% pts with FES have OSA
- FES strongly associated with OSA even after adjusting for weight



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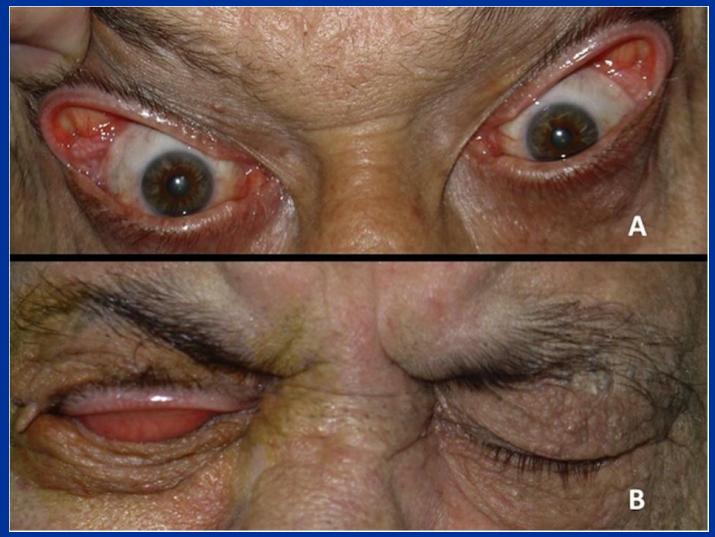
Floppy Eyelid Syndrome

Relation to Glaucoma

- FES and glaucoma are both associated with OSA
- FES may serve as a marker for those patients with OSA that also have glaucoma
- In a recent study, 5% of OSA pts without FES had glaucoma, compared 23% of those with FES



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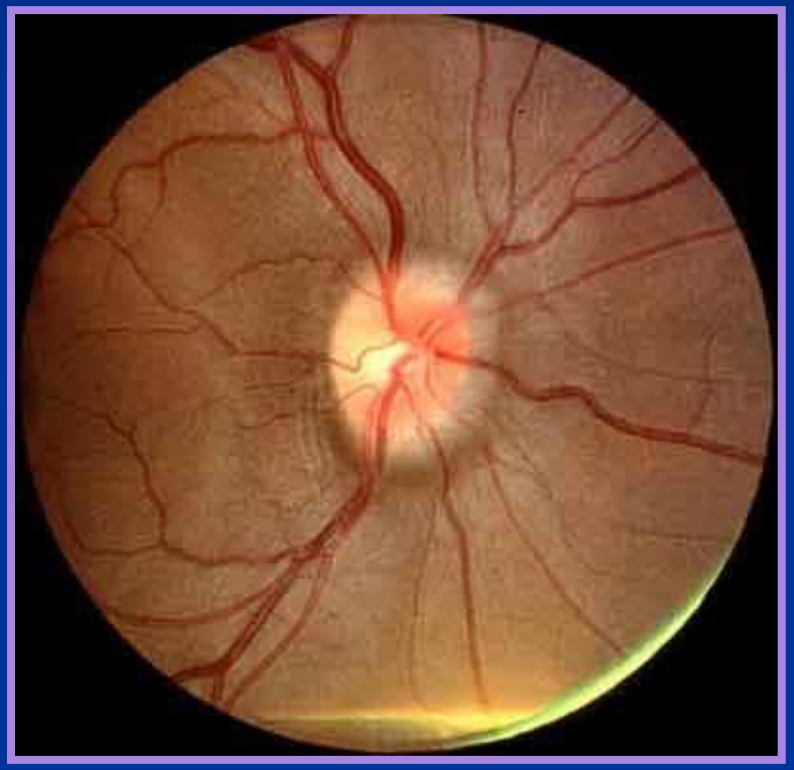
OSA & the Eye

Ocular Manifestations of Sleep Apnea

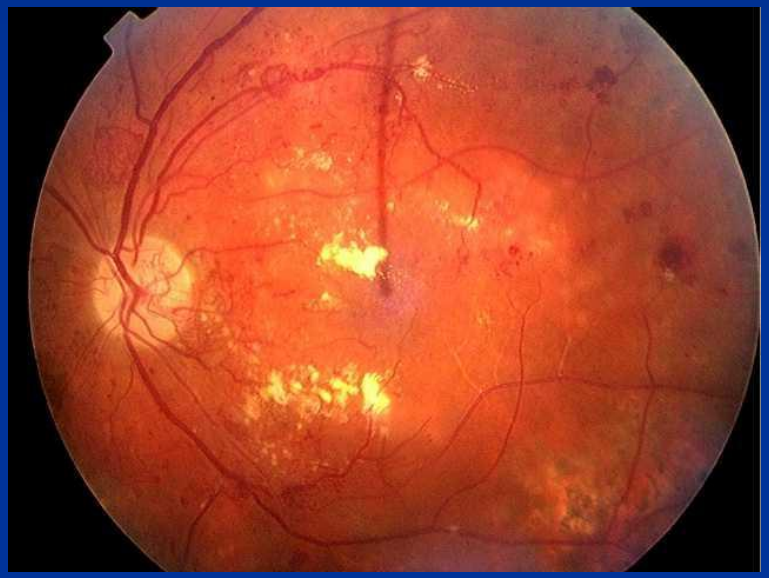
- Asthenopia
- CPAP-assoc Red Eye
- Floppy Eyelid Syndrome
- Retinal Conditions
- NAION
- Papilledema
- Normal Tension Glaucoma



Diabetic Retinopathy

OSA increases risk of progression of retinopathy

- Diabetic retinopathy is more common and severe in patients with OSA, independent of other risk factors
- Risk of progression associated with severity of OSA
- CPAP may slow progression of diabetic retinopathy by minimizing nocturnal hypoxia



- Diabetics with OSA should be screened for retinopathy and encouraged to be compliant with CPAP

PMID: 20381785, 28937527

Other Retinal Disorders Associated with OSA

Central Serous Chorioretinopathy

- OSA may be a risk factor for CSCR, and treatment of OSA has been reported to hasten recovery of CSCR

Central Retinal Vein Occlusion

- OSA may be a risk factor for CRVO, and has been associated with bilateral simultaneous CRVO

Anti-VEGF treatment failure

- OSA has been associated with Avastin treatment failure of AMD and diabetic macular edema

PMID: 31800457, 30188014, 26841211

NAION

Clinical Characteristics

- Most common acute optic neuropathy in pts >50yo
- Sudden painless visual loss, *usually upon awaking*
- Nerve fiber bundle VF defects
- Diffuse or sectoral disc edema
- Disc at risk: small, crowded
  - Mean C/D = 0.2
  - All ≤ 0.4

NAION

Pathophysiology

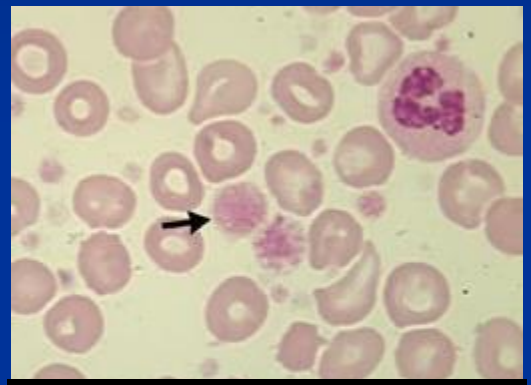
- Idiopathic ischemic process
  - Disorder of posterior ciliary artery circulation
  - Transient poor circulation in the ONH
  - ***Trigger Event***: Fall in blood pressure below a critical level?
  - There is no actual blockage of the posterior ciliary arteries
- Cascade Effect
  - Mechanical crowding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

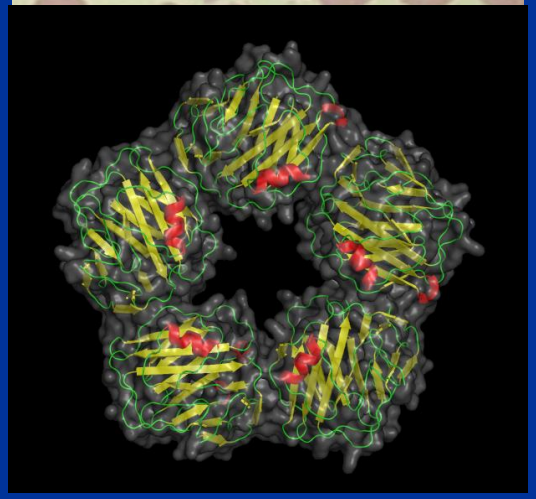
http://webeye.ophth.uiowa.edu/dept/AION/Index.htm

NAION

Diagnosis: Must exclude GCA in every case

- ESR
- C-Reactive Protein
  - Levels increase in presence of inflammation
  - Upper limit normal does not rise with age
- Platelets
  - Secondary thrombocytosis due to chronic inflammation





NAION

Treatment

- Aspirin
  - Decreases incidence in fellow eye at 2 yrs, but not at 5 yrs
- Surgical decompression
  - No benefit (Ischemic Optic Neuropathy Decompression Trial)
- Control of predisposing systemic disease
  - May slow progression or reduce incidence in fellow eye
  - Hypertension, Diabetes, Hyperlipidemia, OSA
- Avoid phosphodiesterase 5 inhibitors (Viagra, Cialis, etc)
  - May increase risk of NAION in fellow eye

NAION

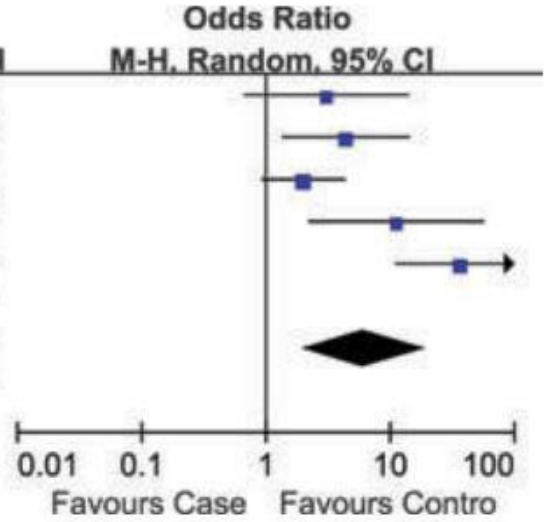
Relation to OSA

NAION Patients with OSA

Study or Subgroup	Case Events	Case Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Arda et al 2013	17	20	13	20	17.9%	3.05 [0.66, 14.14]
Bilgin et al 2013	15	27	6	27	20.7%	4.38 [1.34, 14.28]
Li et al 2007	22	73	13	73	23.7%	1.99 [0.91, 4.35]
Mojon et al 2002	12	17	3	17	17.2%	11.20 [2.20, 56.92]
Palombi et al 2006	24	27	1011	5615	20.5%	36.43 [10.95, 121.22]
Total (95% CI)		**164**		**5752**	**100.0%**	**6.18 [2.00, 19.11]**
Total events	90		1046			

Heterogeneity: $Tau^2 = 1.24$; $Chi^2 = 17.40$, df = 4 (P = 0.002); $I^2 = 77\%$

Test for overall effect: Z = 3.16 (P = 0.002)



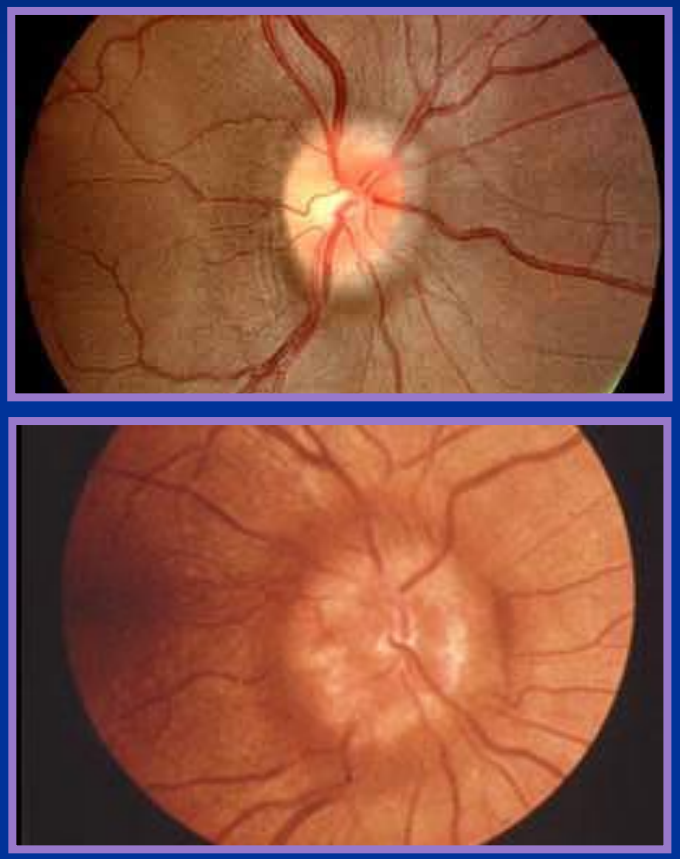
(Wu, 2015)

- OSA may be the systemic disorder most frequently associated with NAION – OSA pts have 6x higher risk
- Every patient newly diagnosed with NAION should be tested for OSA

Papilledema

Clinical Characteristics

- Disc swelling associated with increased ICP
- Symptoms of elevated ICP: Headache, tinnitus, TOV
- Chronic papilledema (months) may lead to optic atrophy and vision loss



Papilledema

Work-up

- Urgent MRI or CT scan
- Lumbar puncture if imaging normal

Idiopathic Intracranial Hypertension

- "Pseudotumor cerebri"
- Syndrome of elevated ICP, papilledema, normal MRI/CT, normal CSF
- Secondary pseudotumor cerebri syndromes with an identifiable cause (venous sinus thrombosis, vitamin A toxicity, COPD, OSA)
- Tx: Diamox 250mg po QID , Underlying cause if known

Papilledema

Relation to OSA

- Stein (2011)
  - Reviewed 2.3 million insurance company billing records
  - Persons with OSA have 30% to 100% increased risk of developing papilledema
- Parvin (2000)
  - 4 pts with unexplained papilledema that resolved with successful treatment of OSA
  - ICP may be normal during the day but elevated at night
  - Intermittent (nocturnal) ↑ ICP can cause sustained papilledema
  - Hypercapnia-induced cerebral vasodilatation elevates ICP

OSA & the Eye

Ocular Manifestations of Sleep Apnea

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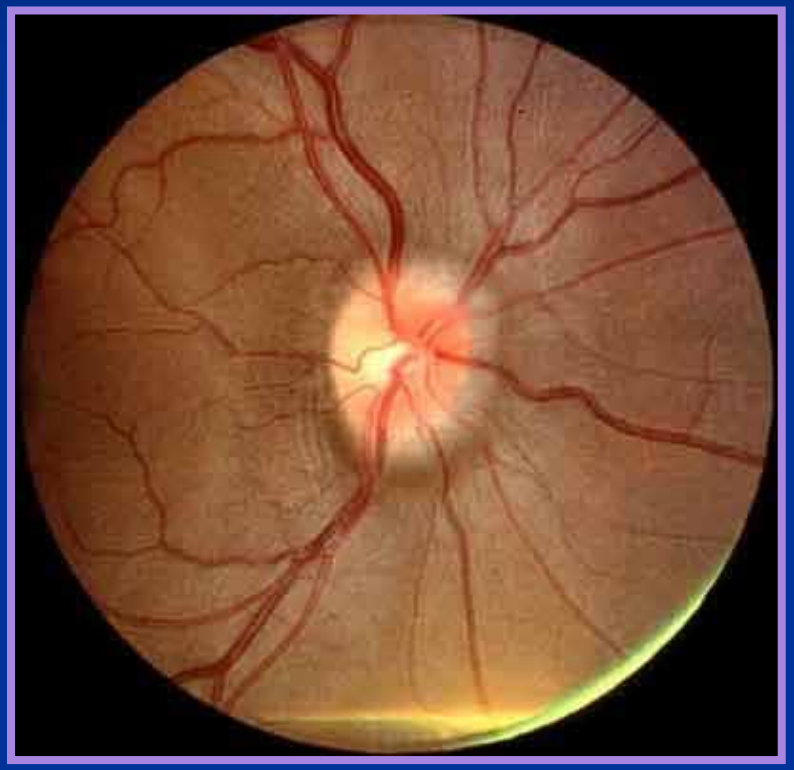
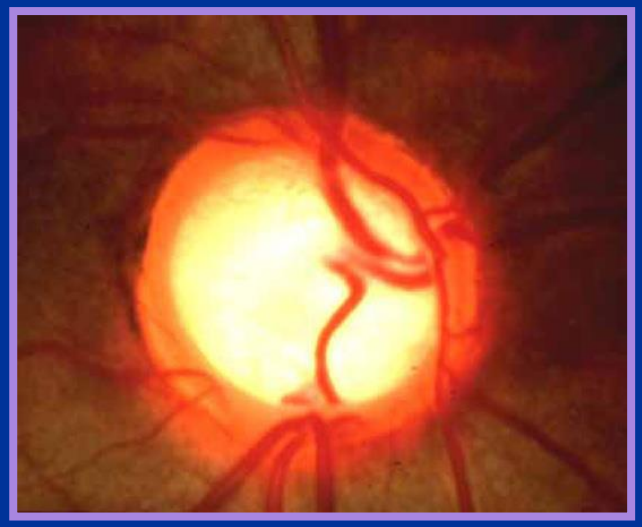


Normal Tension Glaucoma

Clinical Characteristics

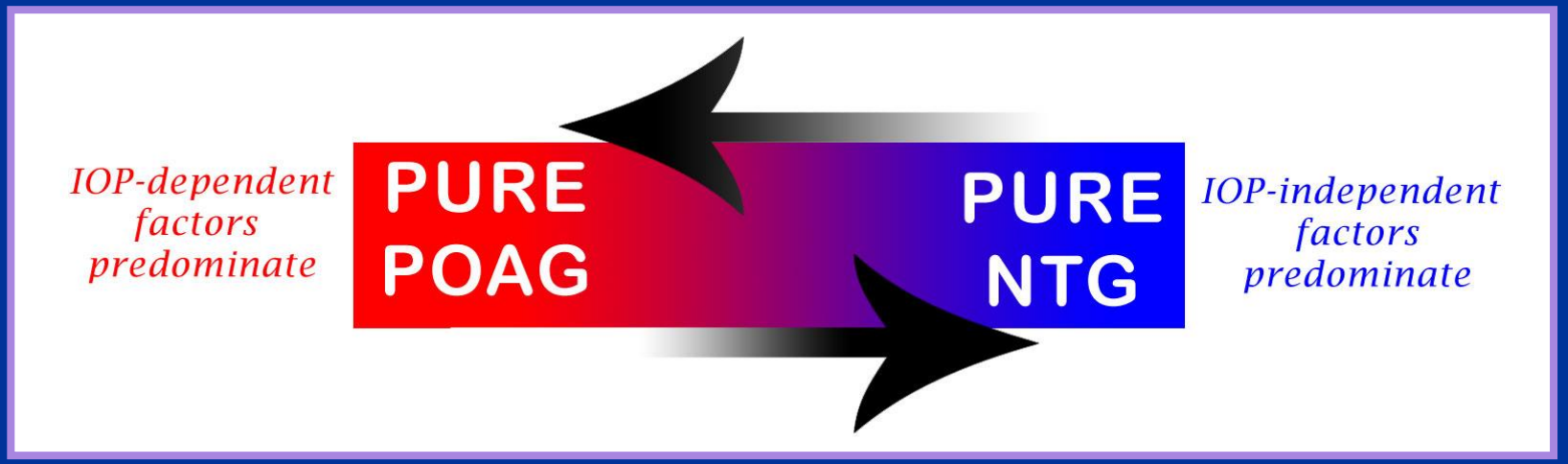
- Probably a variant of POAG
- IOP is never documented above 21 mmHg
- Peripapillary hemorrhages may be more frequent
- Peripapillary atrophy may be more marked
- VF defects tend to be deeper and more localized



Normal Tension Glaucoma

Pathophysiology

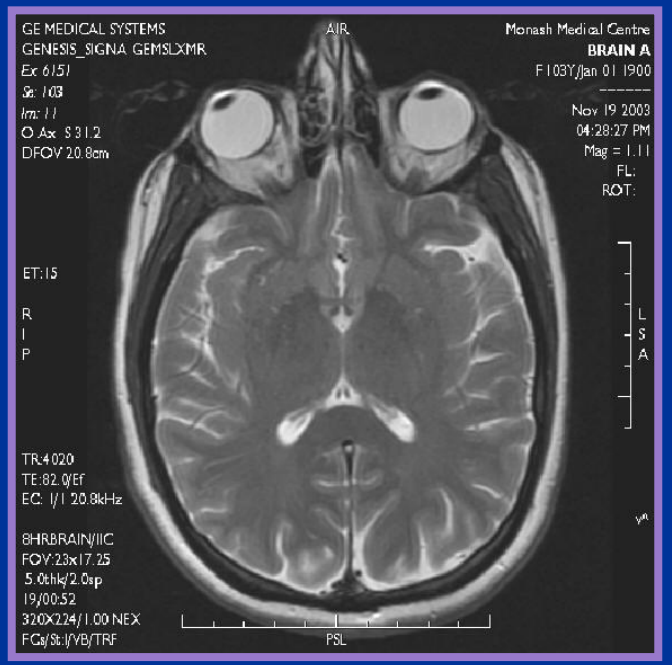
- IOP-independent factors predominate
  - Vascular insufficiency: CVD, HTN
  - Vasospasm: migraine, Raynaud's phenomenon
  - Translaminar pressure difference: low ICP



Normal Tension Glaucoma

Diagnosis

- R/O other glaucomas
  - POAG with diurnal IOP fluctuation
  - IOP normalization (Burnt-out glaucoma, steroids)
- R/O other optic neuropathies
  - NAION, space-occupying lesions, congenital anomalies
  - When to order neuroimaging:
    - Younger age (<50 yrs)
    - Reduced VA (< 20/40)
    - Vertically aligned VF defects
    - Neuroretinal rim pallor



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Normal Tension Glaucoma

Glaucoma Patients with OSA

POAG	Girkin (2006)	1%
POAG	Roberts (2009)	17%
POAG	Mojon (2000)	20%
NTG	Khandgave (2013)	23%
POAG	Balbay (2014)	33%
NTG	Bilgin (2014)	42%
POAG	Blumen (2010)	48%
NTG	Marcus (2001)	57%
NTG	Mojon (2002)	50-60% (varies with age)

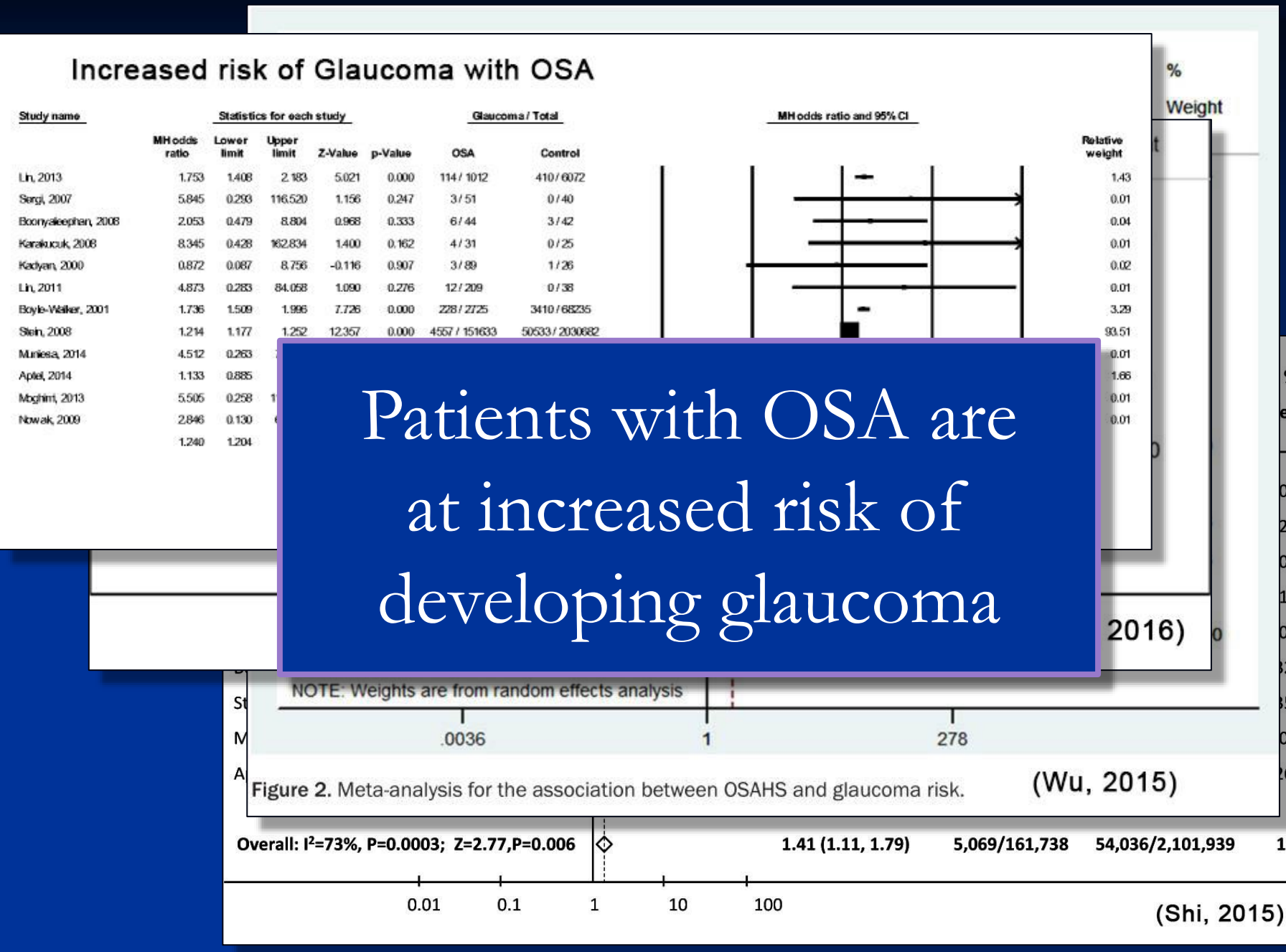
Greater than general pop estimate of 10-20%

OSA Patients with Glaucoma

		POAG	NTG
	Geyer (2003)	1%	1%
	Kadyan (2010)	2%	
	Karakuck (2008)	3%	10%
	Aptel (2014)	4%	
	Mojon (1999)	4%	3%
	Boonyaleephan (2008)	5%	9%
	Hashim (2014)	5%	15%
	Boyle-Walker (2011)	8%	
	Bendel (2008)	27%	
	Sergi (2007)		6%
	Lin (2010)		6%

NTG is at least as common as POAG in this patient population

Greater than general pop estimate of 1.5-3%

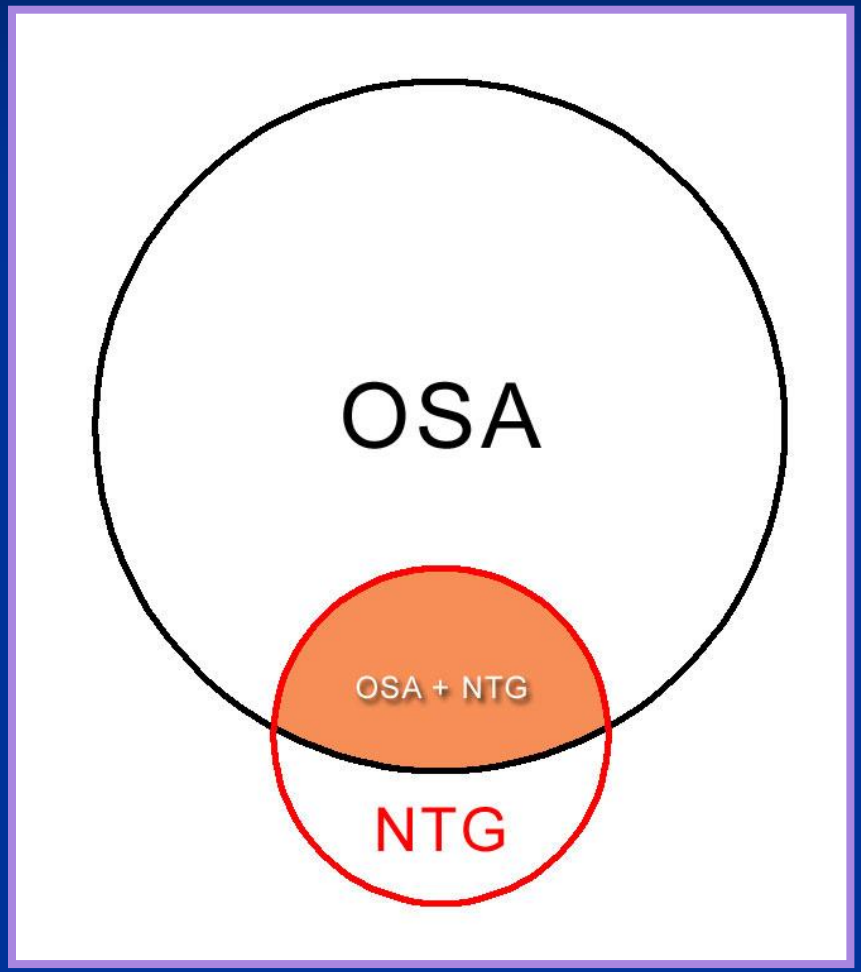


Patients with OSA are at increased risk of developing glaucoma

Normal Tension Glaucoma

Relation to OSA

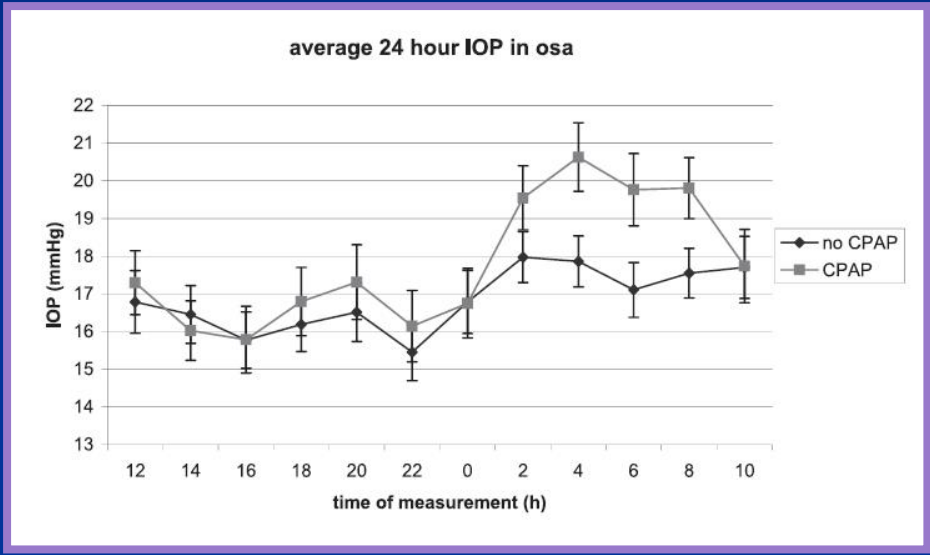
- 5%-10% of OSA patients have NTG *(<3% general pop)*
- Up to 50% of NTG patients have OSA
- Treatment of OSA may help stabilize NTG (Kremmer, 2003) and improve VF performance (Sebastian, 2006)



Normal Tension Glaucoma

CPAP Increases IOP

- **Kiekens (2008)**
  - Diurnal IOP measured with and without CPAP
  - Average IOP and diurnal fluctuation higher with CPAP
  - Speculate that CPAP elevates intrathoracic pressure, leading to higher central venous pressure, and ultimately higher IOP
  - Recommend regular screening of VF and the optic disc for all patients with OSA, especially those treated with CPAP



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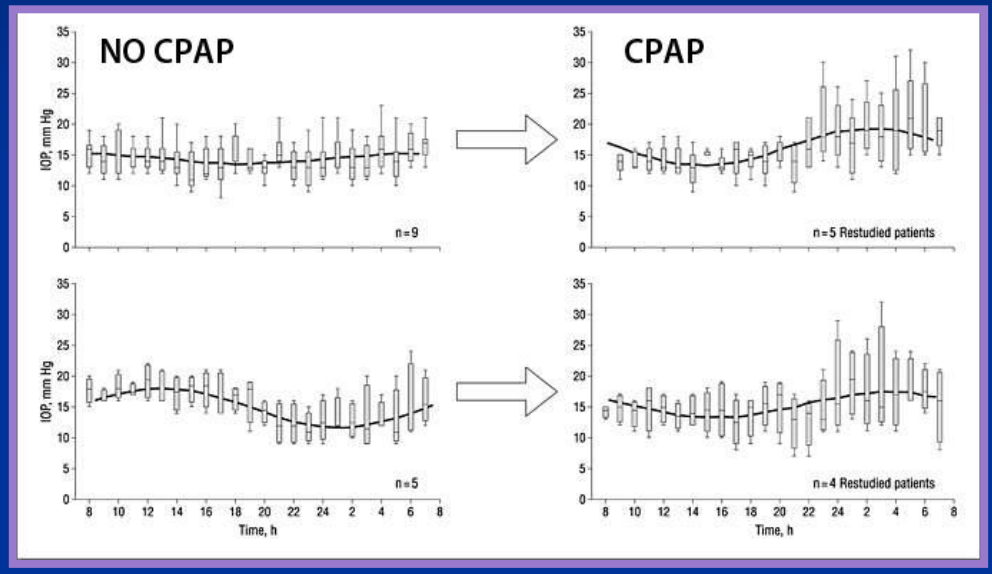
CPAP and IOP

CPAP Increases IOP

- **Pepin (2010)**
  - Diurnal IOP measured with and without CPAP
  - CPAP caused a significant increase in nocturnal IOP
  - Speculate that some effects of untreated OSA may result in decreased nocturnal IOP and these are normalized by use of CPAP
  - Concludes that IOP changes induced by CPAP are explained by restoring normal IOP rhythm rather than by a deleterious effect of the device



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CPAP and IOP

- **Cohen (2015)**
  - CPAP not associated with nocturnal rise in IOP
- **Ulusoy (2015)**
  - Compared glaucoma prevalence among OSA patients who did and did not use CPAP
  - No difference in glaucoma prevalence with CPAP use

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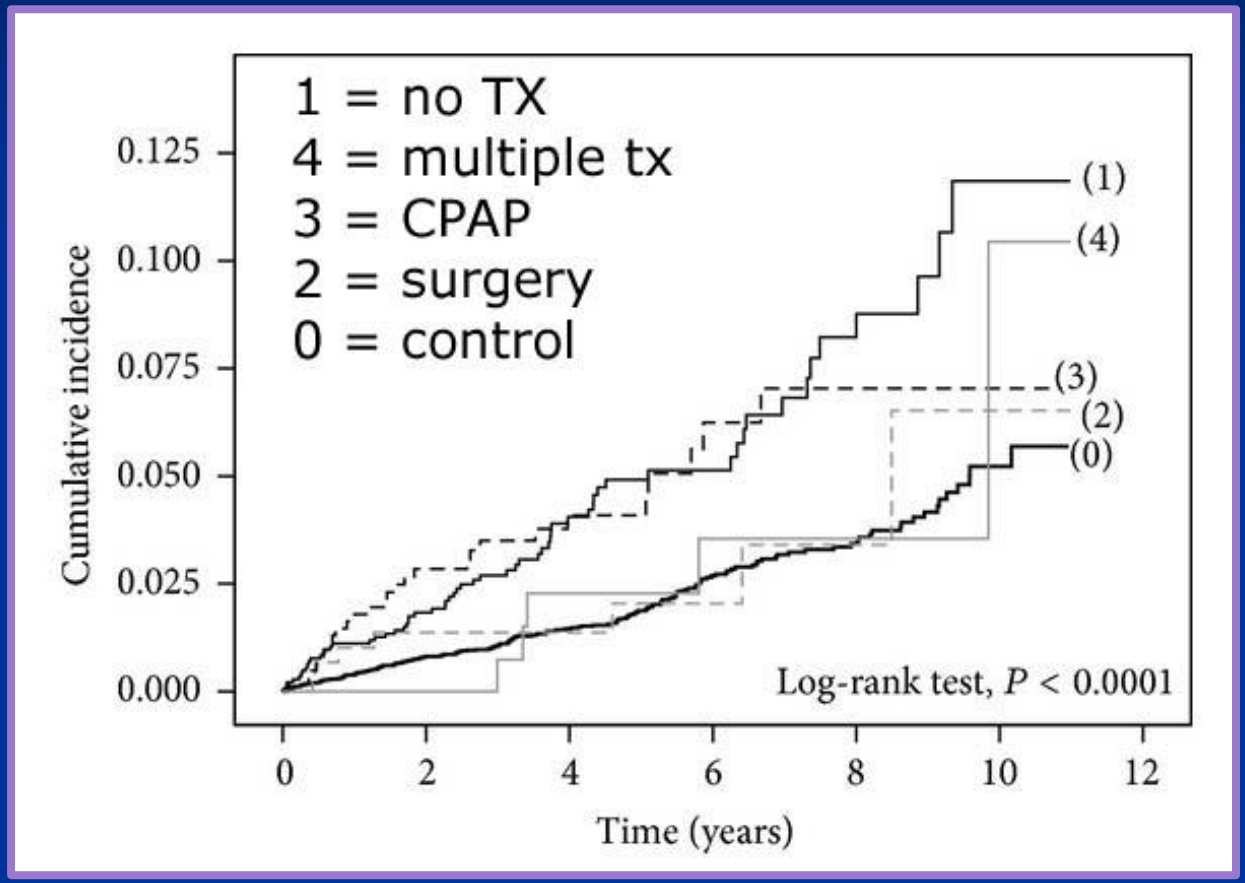
CPAP and IOP

Chen (2014): OSA treated with CPAP have higher rates of glaucoma than OSA treated with surgery



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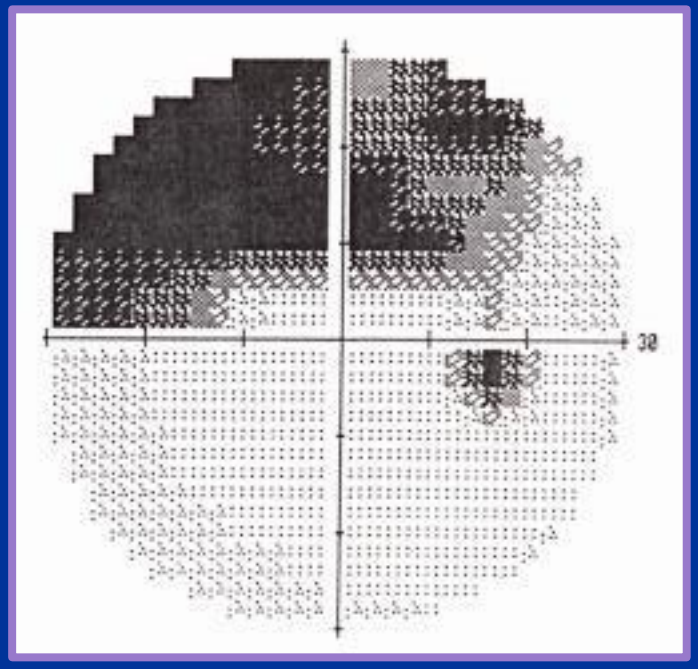
Normal Tension Glaucoma

OSA May Cause NFL Loss Without Glaucoma

- **NFL thinning may represent** preclinical NTG
- This "silent optic neuropathy" may evolve into NTG in some patients

OSA May Cause VF Loss Without Glaucoma

- VF loss may occur due to optic nerve damage caused by cerebral ischemia and intermittent ICP elevation



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Normal Tension Glaucoma

Conclusions & Recommendations

- Persons with OSA should be screened for glaucoma
  - Risk of glaucoma is correlated with severity of OSA
- Patients with NTG should be screened or at least questioned about OSA
  - Treatment of uncontrolled OSA may help stabilize glaucoma and improve VF performance
- Initiation of CPAP therapy may increase nocturnal IOP
  - The clinical significance of this is unknown

Key Points

- OSA is strongly associated with many ocular disorders
- Include OSA in your medical history
- FES is a marker for severe OSA and is a risk factor for glaucoma
- Screen for OSA in patients with NAION or NTG

Thank You!