The Pharmacology of Glaucoma: NOT just IOP, Think DPP, OMG!

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EVIDENCE BASED MEDICINE

- Rational care requires a scientific approach to patient management
- Sound clinical research should be the basis for therapeutic decisions
- Know the Disease: Pathophysiology
- Know the patient: Histories
- Know the therapy: Pharmacology

The impact of clinical research on current glaucoma management

- Who we treat and who we watch
- Initial drug selection/ maximizing drug combinations / max medical therapy
- How we (most accurately) assess disease progression
- The relationship between IOP and BP in GLC patients
- Evaluating and resolving similar studies with differing outcomes (sponsor bias?)

I'm a clinician, so let's talk patients TWO Patients (a priest and a lawyer) with the same med HX walk into a bar

- 54 Y/O WT M presents for general exam/DM eye evaluation
- FM HX DM, HTN
- FM EYE HX-NEG
- Patient Med HX:

Type II DM X 5 Yrs-A1-C = 7

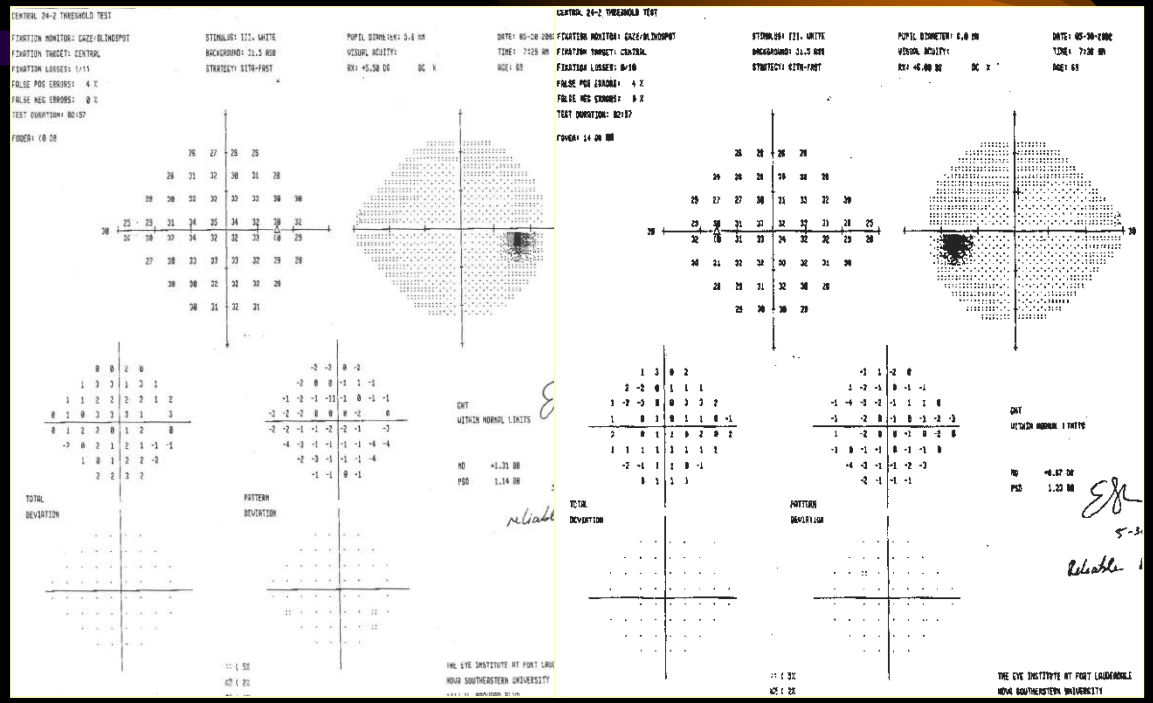
BP controlled with TX = 125/65

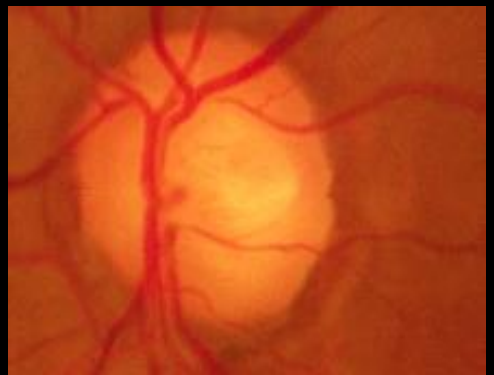
Lipitor for elevated lipids

- No allergies

Significant eye findings

- IOP's: 26/24@ 9AM
- C/D: 0.5/0.5 OU
- VF: 30-2





NML VF's & Discs c elevated IOP's.....TX??

Hold the thought

What is glaucoma?

Just one of many types of

Anterior Optic Neuropathy

Definition does not mention IOP-

IS IOP IMPORTANT?

“TOM” says that it is

The OHT Study - Goals

Evaluate the safety and efficacy of using topical ocular hypotensive medication(s) in preventing or delaying the development of POAG in individuals with elevated IOP

Identify baseline demographic and clinical factors that predict which individuals would develop POAG

OHTS – Study Design

- Patients randomly assigned to one of two groups
  - Treatment or Close Observation
  - Treatment goal to lower IOP at least 20%
- Management
  - Humphrey VF 30-2 every 6 months
  - Annual dilated exam & photos

OHTS Population

Entry Criteria	OHTS demographics
–Age 40 – 80 –Normal visual fields • Humphrey 30-2 FT –Normal optic discs –Untreated IOP • 24 to 32 mm Hg in qualifying eye • 21 to 32 mm Hg in fellow eye	–Enrollment complete in 10/96 –Last patient 5 yr. data 11/8/01 –1,636 subjects at 23 clinical centers –1,408 completed 5 yrs. –409 (25%) African American

OHTS Study Design

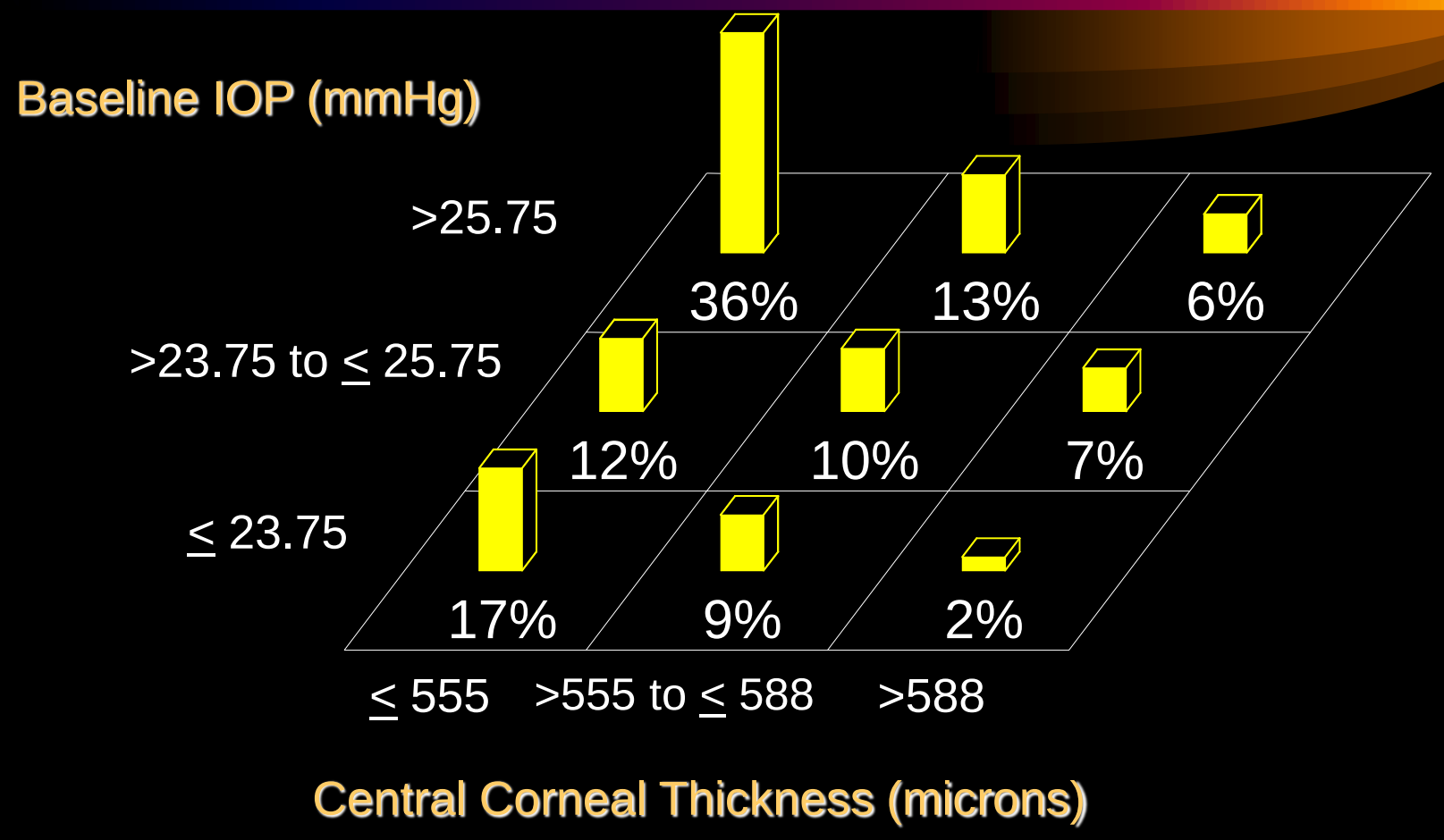
- 1,636 individuals randomized to Therapy (817) or Observation (819)

- Minimum life of study – 5 years
  - 7 years follow-up for some patients
  - Some individuals dropped out, medication started or withdrawn, died, or lost to follow-up
- 1,408 completed study
  - Observation (706) vs. Therapy (702)

Facts, Fiction and Statistics
KNOW YOUR OHT's (N = 1636)

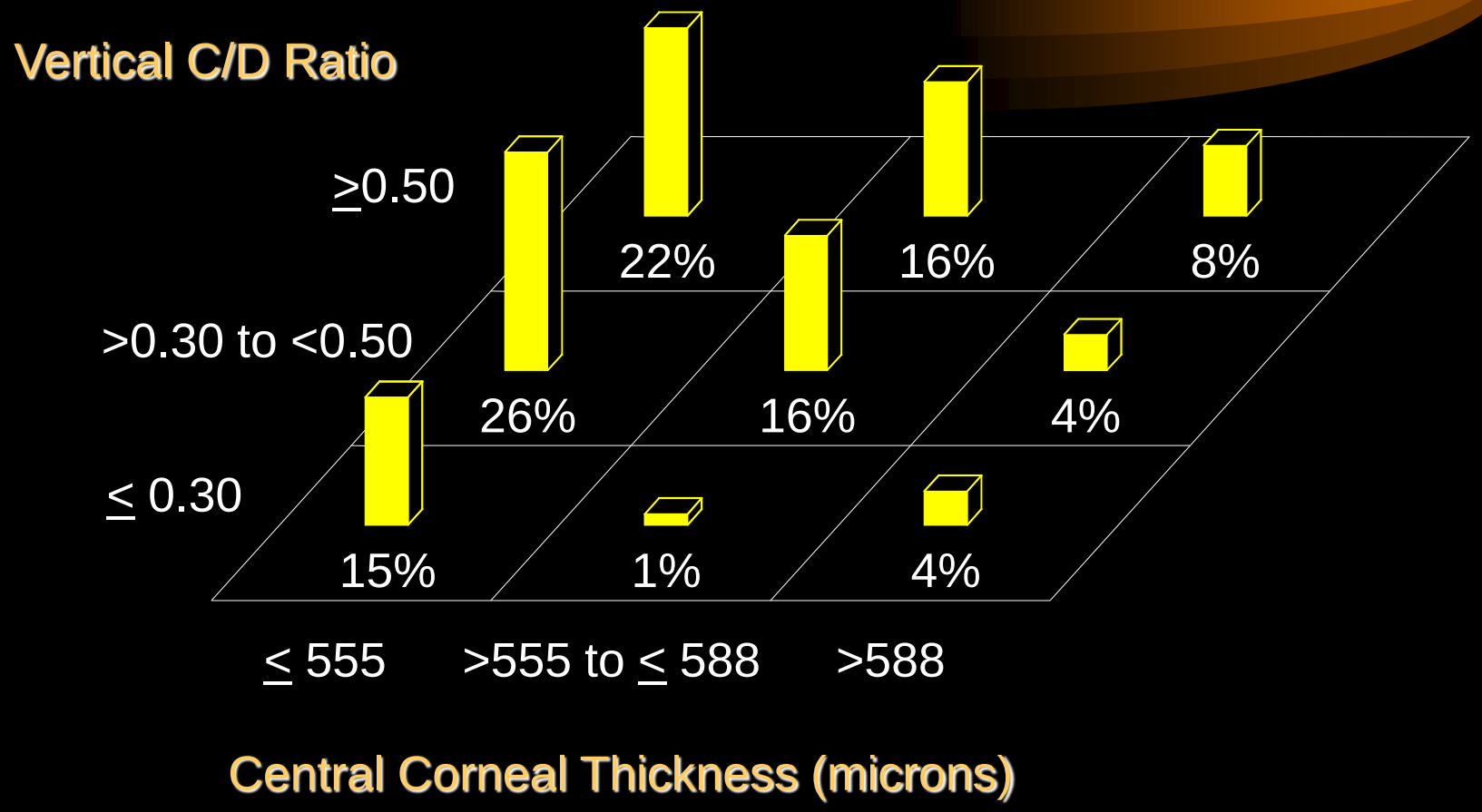
- Early TX of ocular hypertension reduced the risk of glaucoma by FIFTY PERCENT
- 9.5% VS 4.4%
- That means that over 90% of UNTREATED ocular hypertensives DO NOT GET GLAUCOMA
- Know your NNT-Number needed to TX
- Need to TX 20-42 to prevent 1 case of glc

POAG Endpoints by Central Corneal Thickness and Baseline IOP (mmHg) in Observation Group*



* through 8 Nov 2001

POAG Endpoints by Central Corneal Thickness and Baseline Vertical C/D Ratio in Observation Group*



* through 8 Nov 2001

The OHTS Lesson

- Treating all ocular hypertensives is not safe/effective or cost effective
- Pachymetry is important
- Conversion best determined by Optic Nerve (Nerve fiber layer) changes HOLD THAT THOUGHT
- TX is optional if risk is acceptable
- IF NFL changes or disc changes TX-DON'T wait for VF changes (thank Harry Quigley again)

Assessment

- Tonometry
- Optic nerve evaluation
- Visual fields
- Pachymetry
- NFL analysis

Optic Disc Hemorrhage (Drance Hemorrhage)

- Usually Superficial In NFL
- Present On Or Adjacent To The Disc
- 70% Located Infra-temporally
- Resolve In One To Three Months
- Often Recurrent

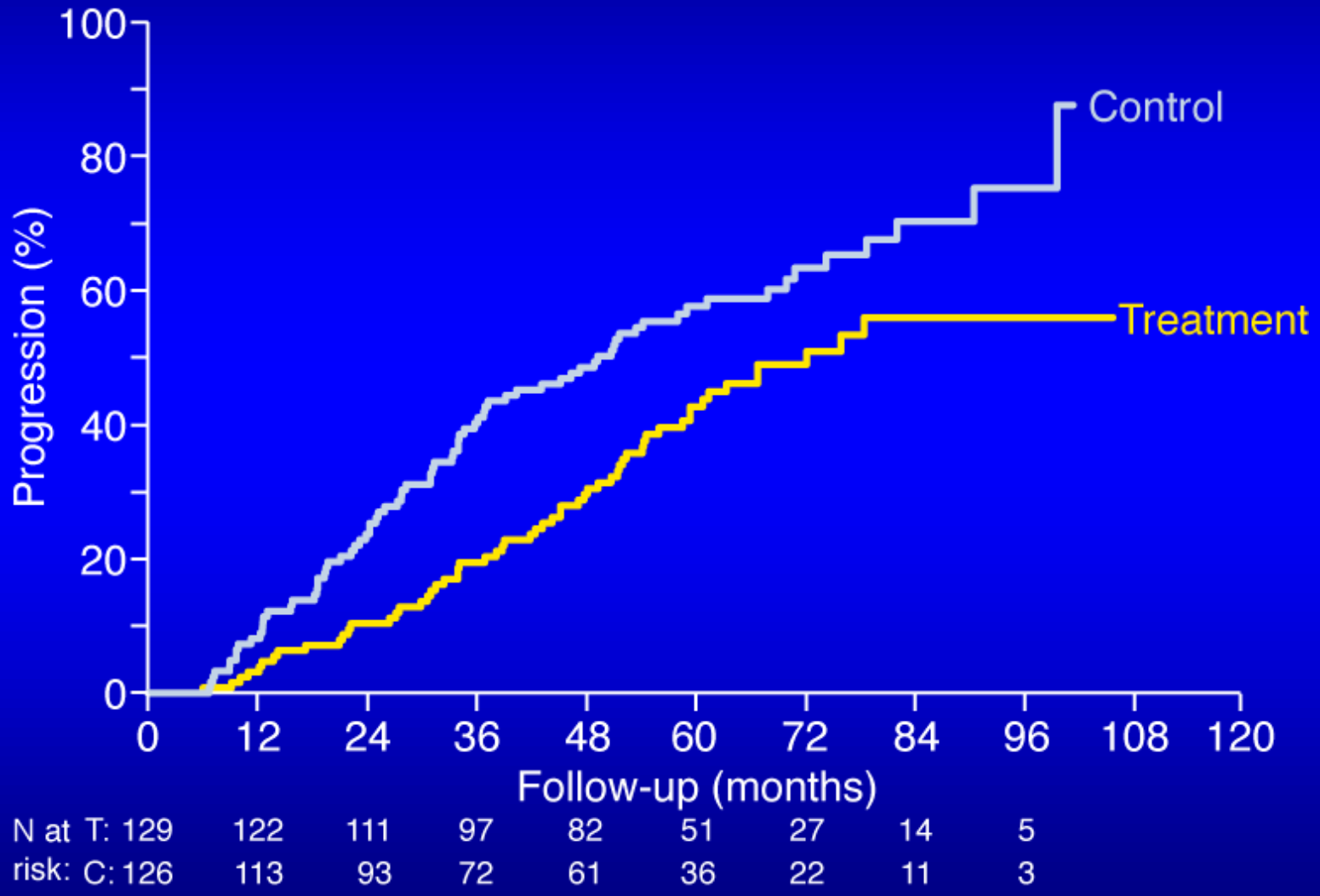
Optic Disc Hemorrhage (Drance Hemorrhage)

- Occurs In 2-23% Of Glaucoma Patients
- More Frequent - Normal Tension Than High Tension Glaucoma
- Indicator Of Early Or Progressive Nerve Damage
- May Precede Optic Nerve And Visual Field Changes
- Warrants Re-evaluation Of Current Treatment

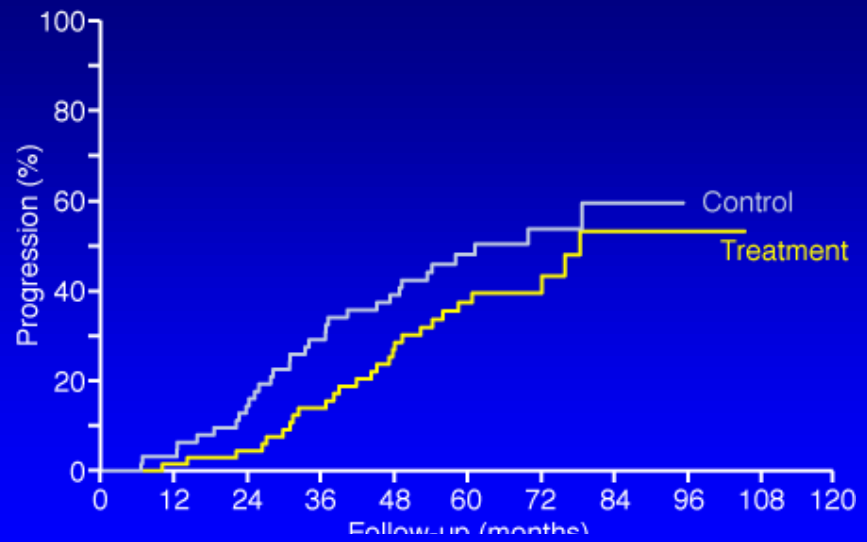
EMGT-Early Manifest Glc Trial (NEI and Swedish Res. Council-Anders Hiejl 2002)

- 6 year study of TX VS non-TX of early glc patients with IOP</= 30 and minimal VF defect N = 255 TX: Betaxolol and ALT-AVG 25% drop in IOP
- TX lowered risk of progression by 10%/mm drop in IOP-
- TX lowered early damage seen in control group
- Risk increased with higher IOP, greater field defects, exfoliation and recurrent disc heme
- First sign of progression VF-86%, Disc change 1%, Both 13% / NNT = 6

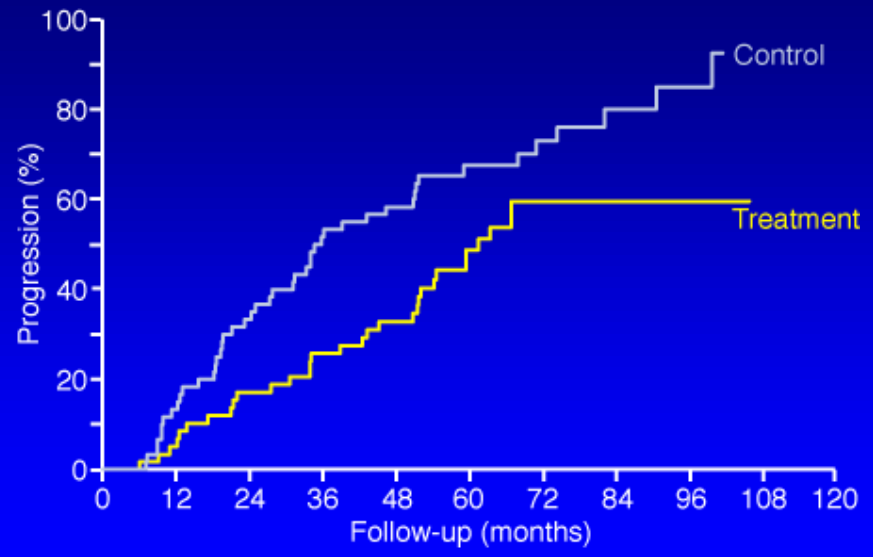
Progression of all patients



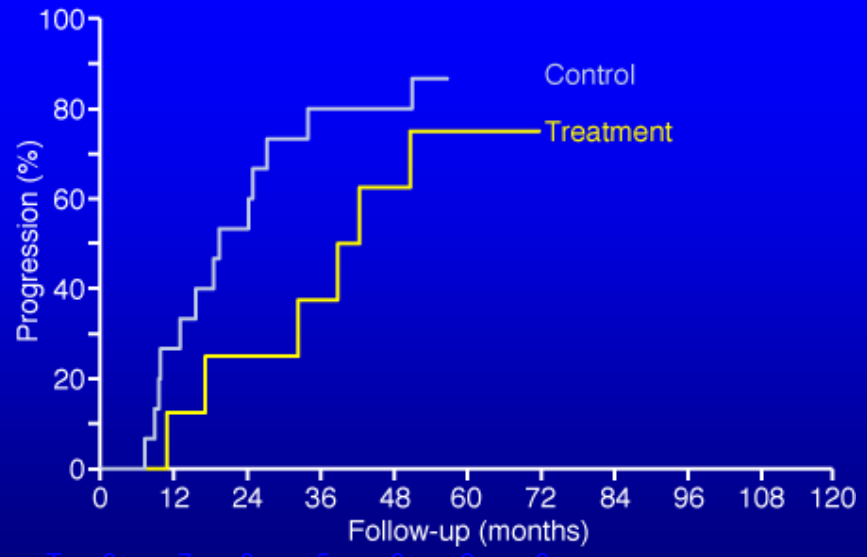
IOP <21 mmHg



IOP ≥21 mmHg

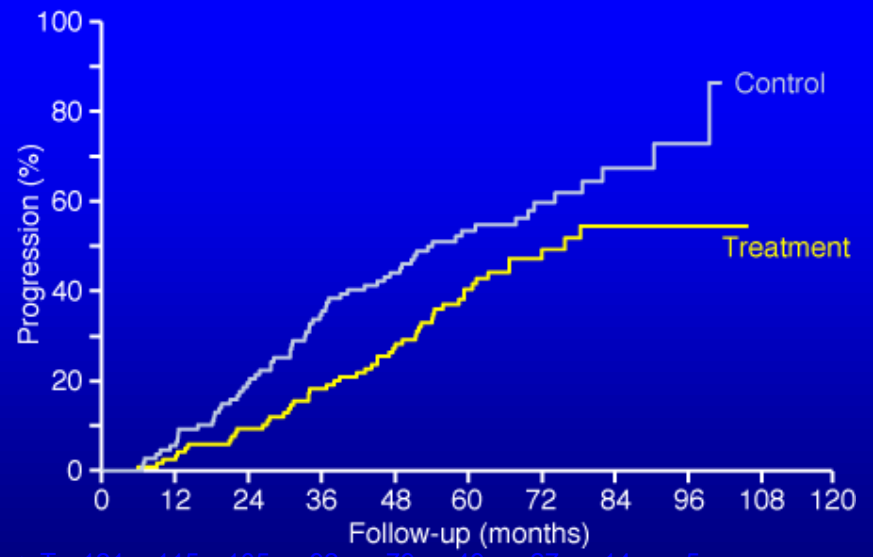


Exfoliation



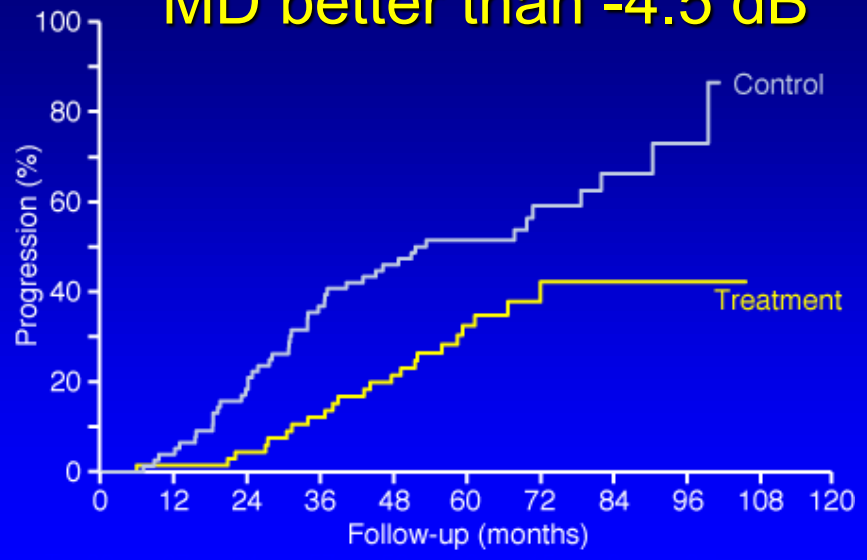
N at risk:	T:	8	7	6	5	3	2	0
	C:	15	11	7	3	3	0	0

No exfoliation

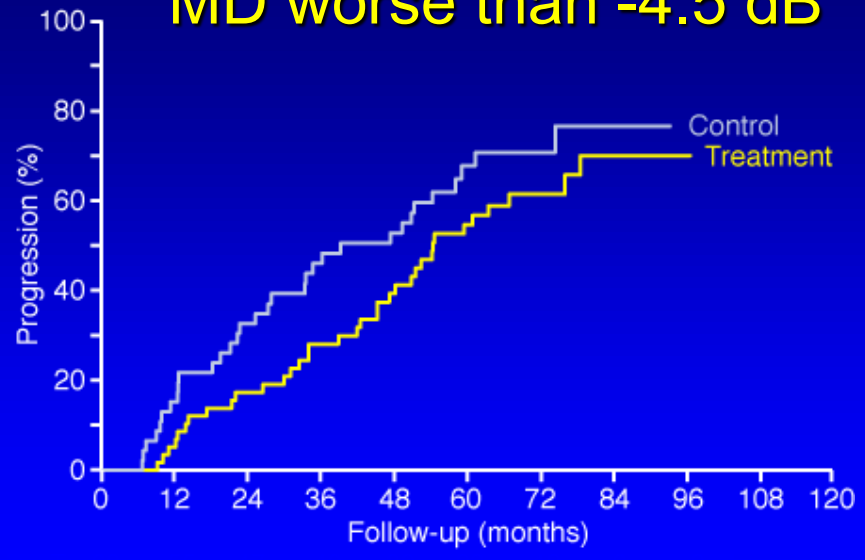


N at risk:	T:	121	115	105	92	79	49	27	14	5
	C:	111	102	86	69	58	36	22	11	3

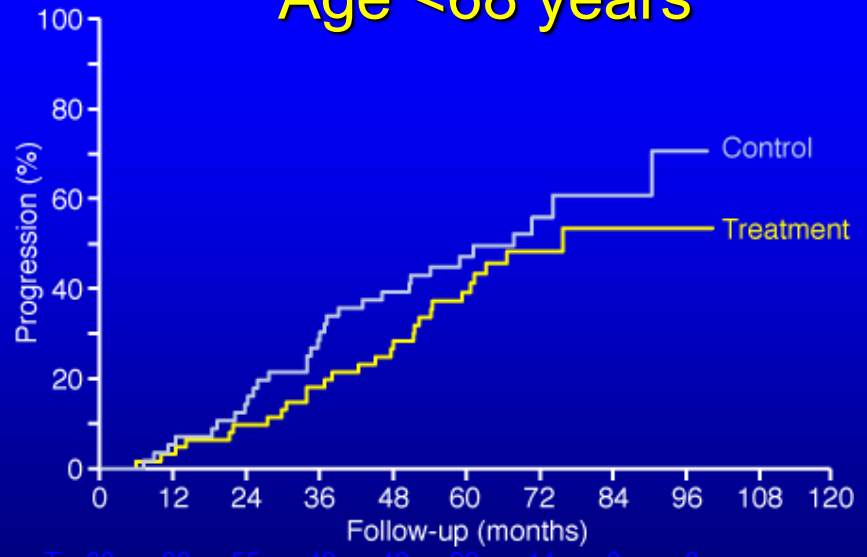
MD better than -4.5 dB



MD worse than -4.5 dB



Age <68 years



N at risk:									
T:	63	60	55	49	42	29	14	8	3
C:	57	53	48	40	33	22	12	8	1

Age ≥68 years

N at risk:									
T:	66	62	56	48	40	22	13	6	2
C:	69	60	45	32	28	14	10	3	2

EMGT (fast) Conclusions

1. EVERY 1 MM DROP IN IOP = 10% REDUCED RISK OF PROGRESSION

2. VF'S ARE THE BEST PREDICTOR OF GLAUCOMA PROGRESSION IN PATIENTS WITH DX'D GLC
3. TX INCREASED RISK OF CATARACT
4. DISC (DRANCE) HEMMORRHAGES PREDICT PROGRESSION

EMGT: Take Home Messages

- Reducing IOP 25% (about 5 mmHg) prevents the progression of early glaucomatous defects – halves the risk!
- Study about white Swedes with moderately elevated IOPs
- Observations regarding progression in lenticular opacification requires further study

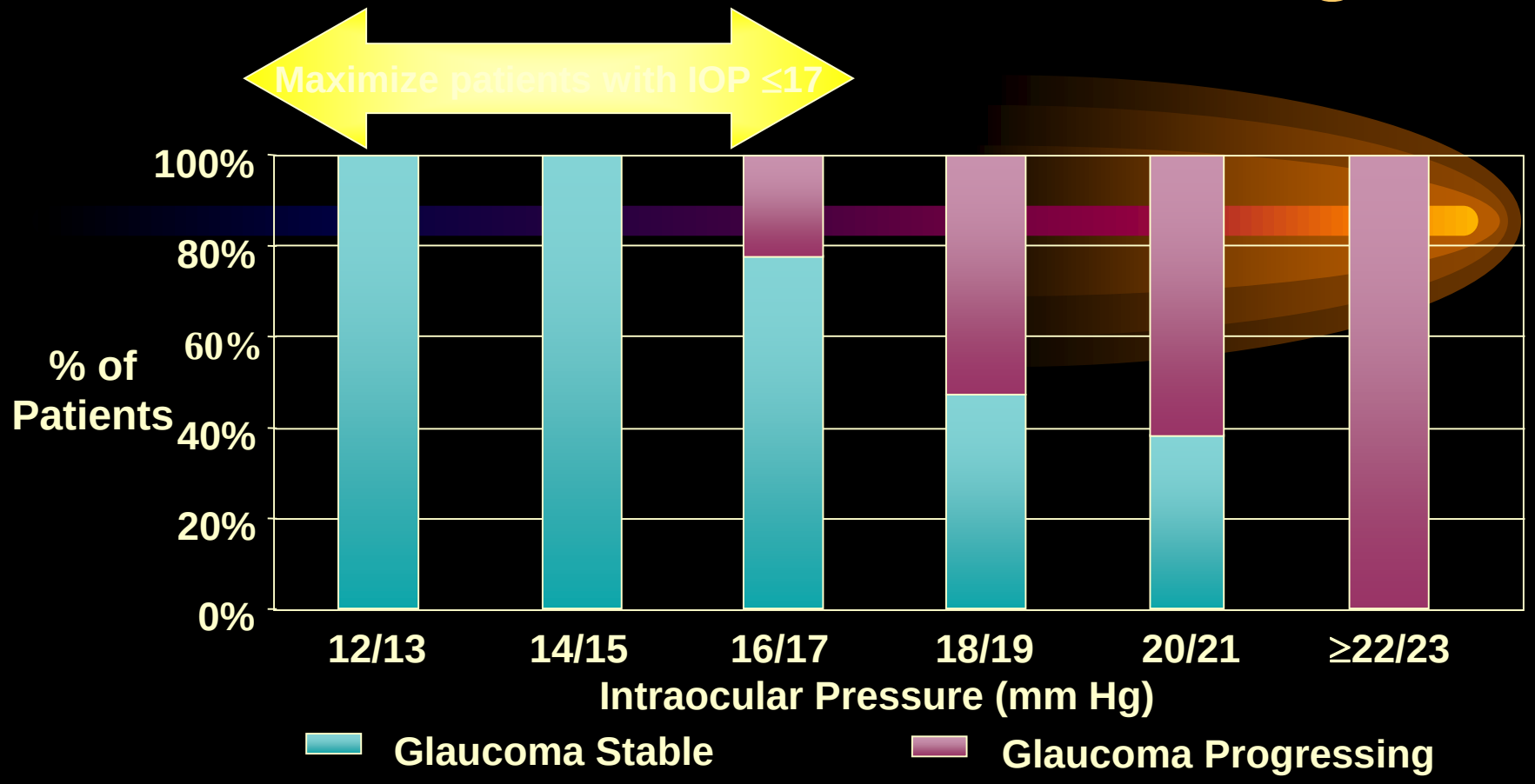
The real story of OHTS VS EMGT (thanks Harry Quigley)

- ON reserve VS ON decompensation
- Don’t wait for VF loss to TX Ocular

Hypertensives=save the reserve-monitor disc/NFL with OCT/GDX

- VF’s very sensitive in patient’s that have lost their reserve NFL
- Depend heavily on VF’s in dependable VF takers with pre-existing field loss

Lower IOP Stabilizes Glaucoma Progression



Additional Support (AGIS):

"The AGIS data support the suggestive evidence from earlier studies that achieving low levels of intraocular pressure slows the progression of glaucomatous optic neuropathy"

Adapted from: Mao LK, et al. Am J Ophthalmol 1991;111:51-55.
(AGIS):7 Amer Jrl Ophthalmol 2000;130(4):429-440

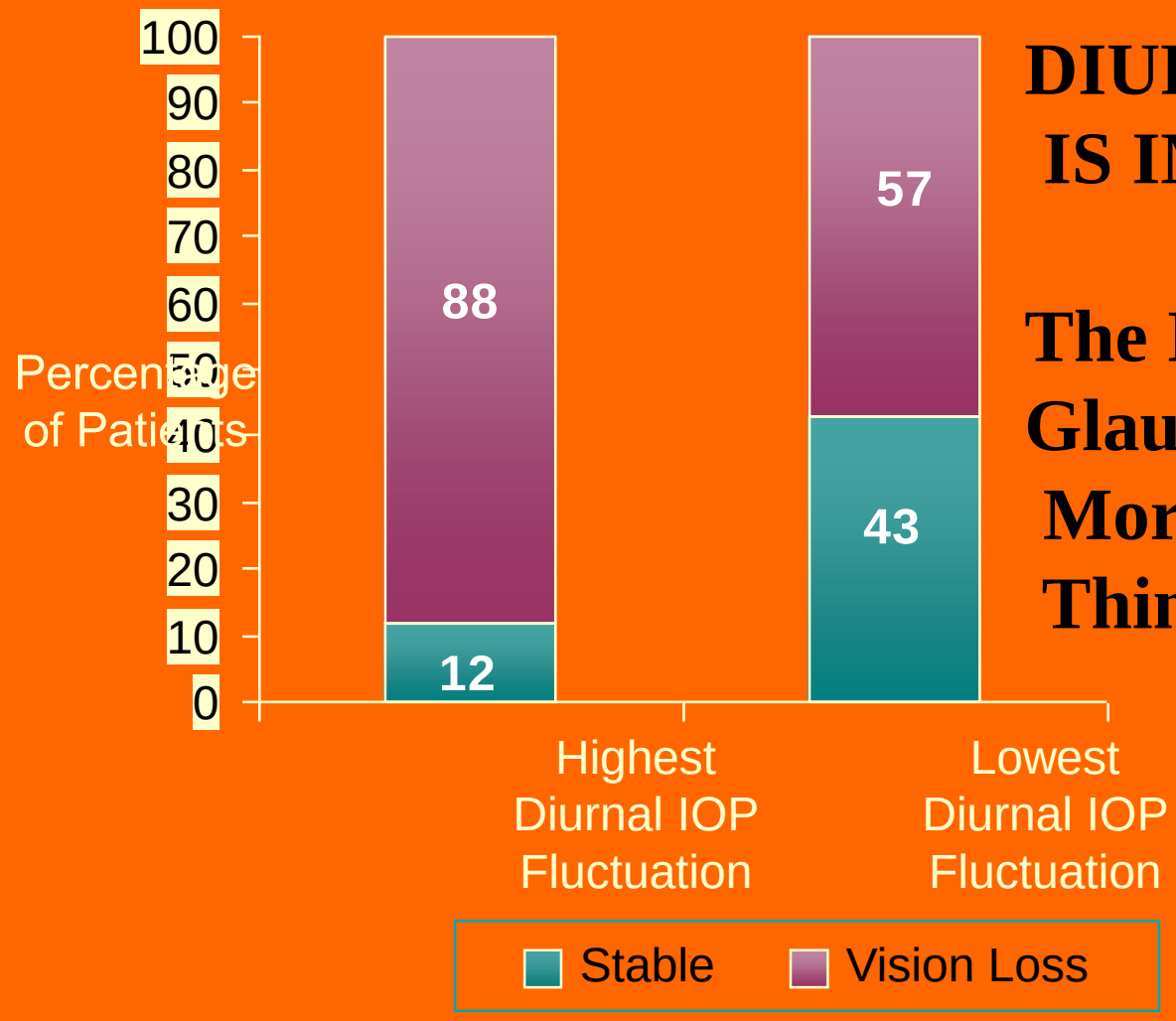
ASRANI: Get it low AND KEEP IT LOW ALL DAY

Low IOP during office hours is important, but 24 hour control is the key-Asrani study demonstrates importance of a flat diurnal curve

- Method:
- 64 patients (105 eyes)
- Self tonometry 5X / day X 5 days = 25 readings per patient
- Avg range 10 +/- 2.9mm Hg
- Risk of progression directly related to degree of fluctuation
- Caprioli AGIS data confirms importance of dirunal fluctuation as an independent risk factor

Low Pressures Should Be Maintained Over 24 Hours

Risk Associated With Diurnal IOP Variations



DIURNAL CHANG IS IMPORTANT

The IOP in Glaucoma Fluctuat More Than You Think

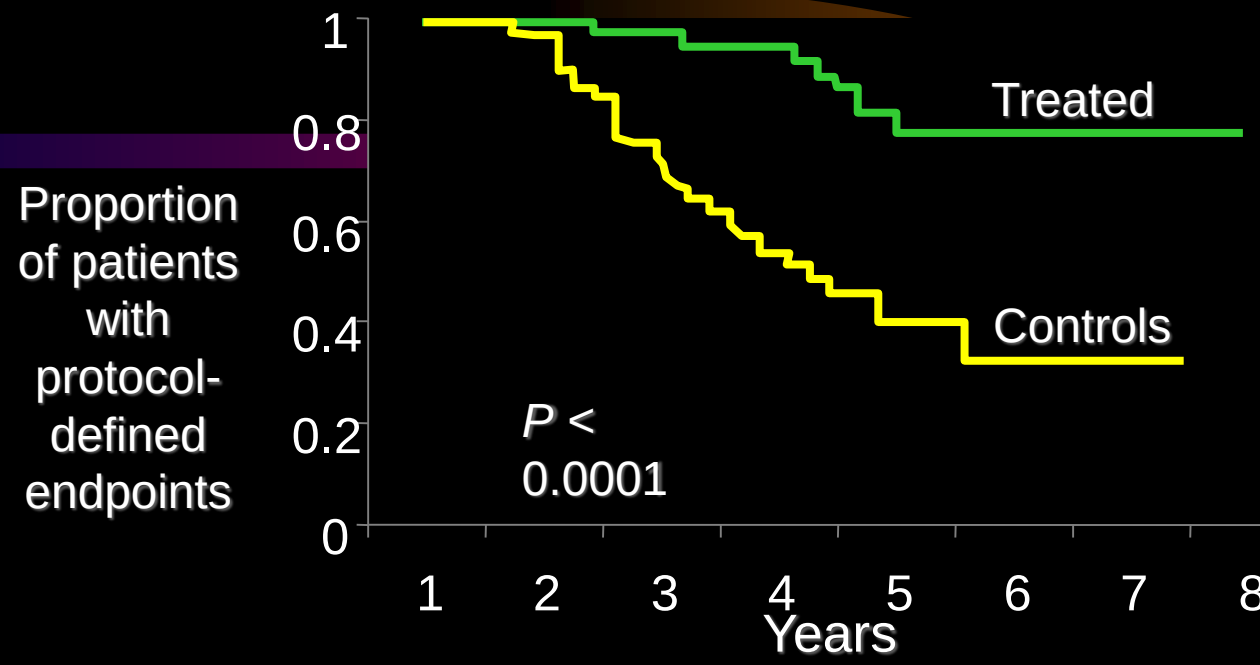
Asrani S, et al.. J Glaucoma. 2000;9(2):134–142.

Normal IOP Does Not Exclude Glaucoma

- The Baltimore Eye Survey:
- Up to 50% of the Patients Diagnosed With Glaucoma (Based on Optic Nerve and VF) Had an Initial IOP Reading Below 21Mm Hg
- Tonometry Is Not a Glaucoma Test
- Glaucoma Testing Is a Complete Eye Exam
- If You Are Not Diagnosing Glaucoma in Patients With Normal IOP, Then You Are Missing Cases of Glaucoma
- Lowering IOP is Beneficial for Patients with NTG

Collaborative NTG Treatment Trial

- CNTG Group. *Am J Ophthalmol.* 1998;126:487-497
- 30% IOP reduction limits VF progression by 2/3 @@@@@@
- 140 eyes



Beware of Pseudo NTG:

Diurnal fluctuation

Thin corneas

These studies indicate the need for at least three Baseline IOP Readings Before Starting Glaucoma Treatment

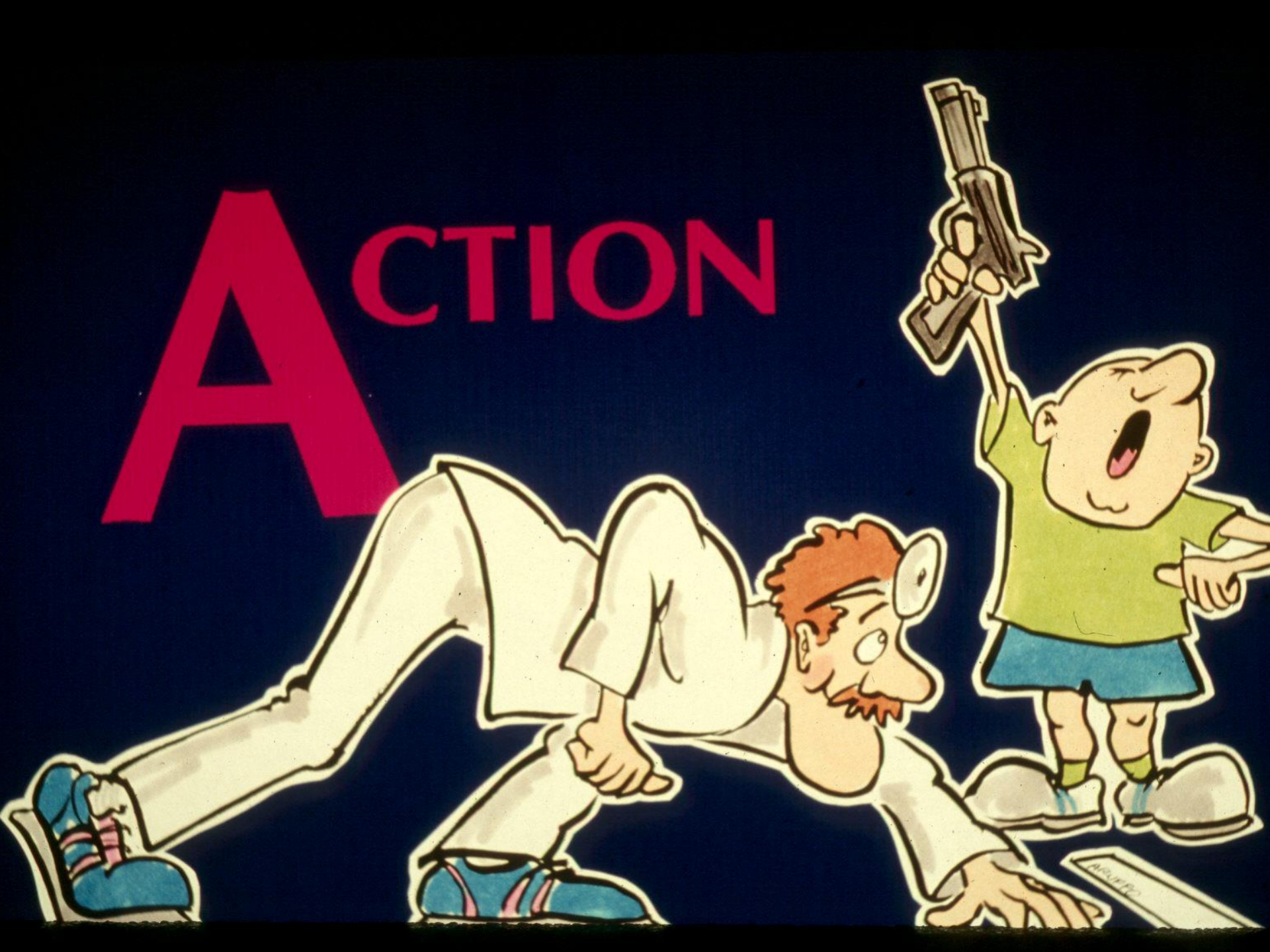
- Helps Uncover Diurnal Fluctuation
- Mix Two Morning Readings With One Afternoon
- Imperative for Setting Target Pressures
- Emphasize the Highest Reading when Setting the Target Pressure
- Allows for Determining the Effectivity of Medications
- A Diurnal study is imperative for NTG suspects
- Pachymetry is now standard of care

LALES Study
C/D Ratio as screening tool

- Los Angeles Latino Eye Study
- Comprehensive evaluation for predictors of eye disease in this population
- 6,357 latinos over 40Y/O
- Vertical C/D > 0.6 cutoff for glc screening
- 92.3% sensitive for glc
- 95.3% specificity for glc

The 3-A's of Glaucoma Management

- A- Assessment
- A- Action
- A- Adios


ACTION

Treatment goals

- Minimum 20%
- Below 18mm hg
- Minimize diurnal variation

KWIK KWIZ

- 67 Y/O AA female
- (+) Type II DM X 20 yrs
- (+) Systemic hypertension
- (+) 2nd degree heart block
- (+) atrial fibrilation
- (+) Hyperlipidemia
- (+) On renal transplant list – on dialysis
- (+) Lupus
- (+) Asthma

MED HX: Continued

DRUGS

- Lisinopril
- Lipitor
- Amiodarone
- Digoxin
- Insulin
- Steroid inhaler/oral pred as needed
- Frequent HX of hypoglycemic events

ALLERGIES

Thiazide Diuretics

Glyburide

Clonidine

Eye findings

- **BVA: OD 20/20**

OS 20/50

- **Pupils: 3mm (+) 3RX OU**

(-) APD

SLE: OU: NML

IOP: OD 26 OS 29

Gonios: TM visible in 2 quadrants OD and 3 OS

Pachymetry: 505/498

Discs: H/V

OD: 0.6/0.9

OS: 0.8/0.9

Available Treatments

Drug Class	Mechanism of Action
Cholinergic agonists	Ciliary muscle contraction (facilitating uveoscleral outflow and trabecular outflow)
β_2-Adrenergic agonists	Increasing trabecular outflow by a mechanism that is not completely understood
β_2-Adrenergic antagonists	Inhibition of aqueous production by the ciliary epithelium
α_2-Adrenergic agonists	Inhibition of aqueous production by the ciliary epithelium ± increasing uveoscleral outflow
Carbonic anhydrase inhibitors	Inhibition of aqueous production by the ciliary epithelium
Prostaglandin $F_{2\alpha}$ derivatives	Increased uveoscleral outflow

When combining drugs-go for synergism

- **Reduced Aqueous**
- **Beta-blockers**
- **Alphagan**
- **Propine/epi**
- **Azopt/Trusopt/ Diamox**

- **Increased outflow**
- **Pilo**
- **Prostaglandins**
- **Propine/epi**

Ocular Beta-Blockers

- 30 years of experience
- Known efficacy
- Known contraindications

Name 8 potentially fatal Beta-blocker Adverse Effects

- **Adverse Effects**

1. Asthma
2. Coronary insufficiency
3. Heart block/arrhythmia
4. Depression
5. Diabetics
6. Anaphylaxis reversal
7. Lipid abnormality in coronary artery disease
8. Impotence (just feel like you want to die)

Are You Short of Breath?@@@@@

- Peak flow testing is "IN"-standard of care-ONLY objective test of lung function
- Check pulse and BP
- AVOID B-BLOCKERS AND THE LAWYERS WILL HATE YOU

Is it safe to use beta blocker topicals and orals together?

- MAYBE
- Probably NOT a good idea
- LOWER EFFICACY-HIGHER SIDE-EFFECTS
- AVOID BETA-BLOCKERS at NIGHT, lower efficacy, reduced perfusion@@@@@

On-going patient evaluation is critical

- 10% of patients have obvious contraindications to beta-blockers
- 12% of “normals” will develop significant side-effects that will require discontinuation of TX
- Good VS Bad side-effects

Avoid beta-blockers at night?

- @@@@@@@@@@@@@
- Reduction of aqueous production during sleep
- Drop in BP during sleep
- Beta blockers reduce perfusion pressure by vasodilation and decreased cardiac output
- Increased risk of nocturnal hypotensive event

Topical CAI's -Wonder Drug or Wonder DUD

WHEN it works it works real good: Equivalent to BB: 15-25%

-Trusopt-

When it fails it fails real bad

Poor for monotherapy

Great with…..

Note: they are sulfonamides

The same/but different

Alphagan-Alpha-2 specificity makes for a better drug

- Alpha-2 Specific
- No tachyphylaxis
- Reduced allergy
- BID dosage if in combination-TID is more appropriate if used alone(diurnal drift)
- Beta blocker equivalent
- Good choice for pulmonary compromised patients
- Neuro-protective? Not in humans yet
- Perfusion pressure

Sympathomimetics

- Epinephrine/Propine
- No efficacy
- Red eyes
- Contraindicated in:
- High BP

Heart disease

Migraine patients

A DEAD (OBSOLETE) DRUG

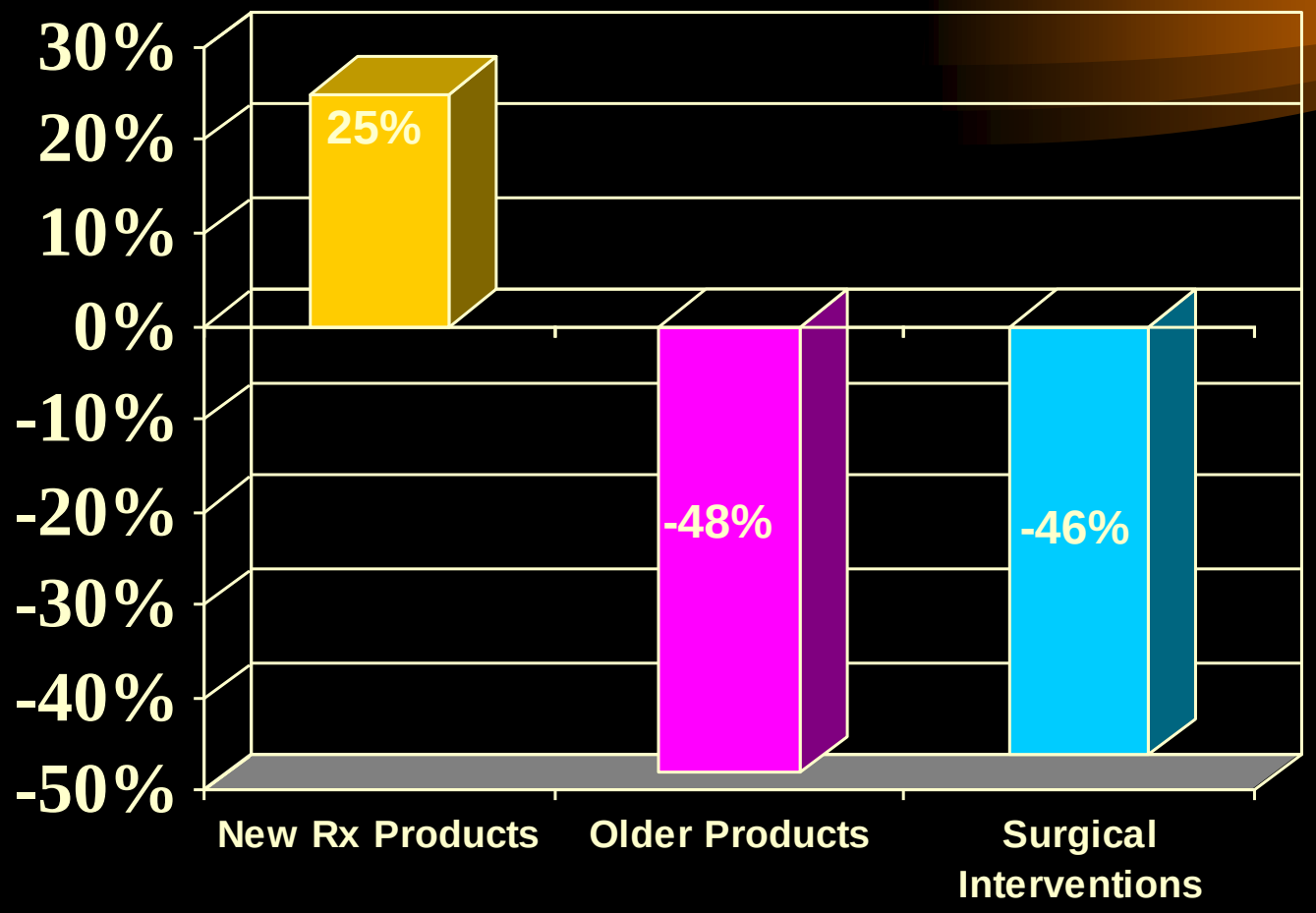
Prostaglandin Derivatives

QUESTION #1:Should prostaglandins be used as first line therapy

- 1. Incredible efficacy
- 2. Minimal systemic side-effects
- 3. Minimal diurnal fluctuation
- 4. Minimal tachyphylaxis
- DUHHHHHHHHHHHH

Glaucoma Surgery Trend 1994-1999

Use of newer, more expensive glaucoma agents increased, while surgeries decreased



*Source: Bateman 2002, **Walt 2002***

The “NEW” Prostaglandin

Latanoprostene bunod 0.024%

- **MOA:**
- **1. Increase in extra-trabecular outflow**
- **2. Bunod component donates nitric oxide which produces increased trabecular outflow**
-

JUPITER STUDY-Phase 1

- Single arm study with 130 POAG/OHTN Japanese patients
- Range of IOP = 15 – 30 mmHg
- Avg drop in IOP from 19.6mm down to 14.4 mmHg = 26.5%

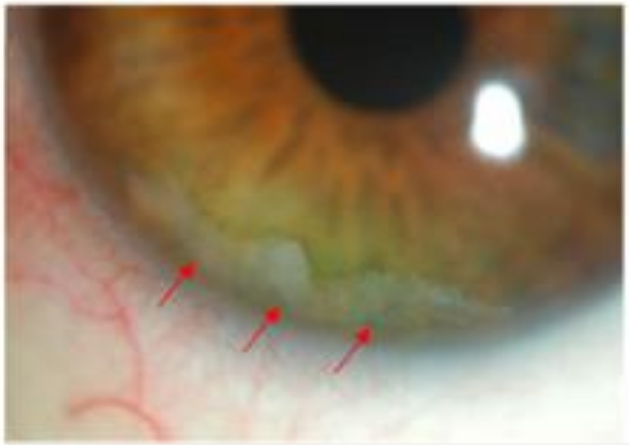
VOYAGER Phase 2

- Latanoprostene vs Latanoprost
- Compared latanoprost 0.005% = -7.77mmHg
- LBN: 0.006% = -7.81mmHg
- 0.012% = - 8.26 mmHg
- 0.024% = - 9.00 mmHg
- 0.040% = - 8.93 mmHg
- On avg: 1-1.5mm lower IOP = 29.8% vs 34.6%
- Hyperemia:
- LBN 7% Latanoprost 8.5%
- Cost: 5ml : $366- $392

- **Netarsudil 0.02%**
- **Rho-Kinase Inhibitor**
- **Inhibits both the enzyme rho-kinase and norepinephrine transporter = increased adrenergic activity**
- **MOA:**
- **1. Increased trabecular outflow**
- **2. Decreased episcleral venous pressure**
- **3. Decreased aqueous production**

In ROCKET1 and ROCKET2, somewhere between 5% and 15% of patients encountered one or more of the following side effects

Corneal deposits



Blurry vision

Conjunctival hemorrhage

Drug delivery

- Contact lenses
- Punctal Plugs
- Insertable
- Injectables

On the horizon: New topical ocular drug delivery systems

- Mystic Pharmaceuticals "nautilus" unit dose non-preserved microspray or drop dispenser-5-30uL adjustable

- Eyenovia: Electrostatic "pixel" size spray: Piezo-electrically "prints" 6uL dose onto surface of eye vs 50uL drop

- Ocular Therapeutix: Dextenza: Reabsorbable dexamethasone releasing lacrimal insert –Phase III , failed to reduce itching in allergic conjunctivitis-97% retained after 30 days- no IOP spikes?

Neuroprotection: Currently NONE, but in the Future

- Block excitotoxins: Produce cellular damage after ischemia or stress
- Glutamate
- Aspartate
- N methyl-d-aspartate (NMDA)
- Calcium channel blockade

Treatable Risk Factors For Glaucoma Progression And Their Relationship To Adjunctive Medications

- **Treatable**
  - **Intraocular pressure (IOP)**
    - **Elevated IOP**
    - **Variation in IOP**
      - **24 hours (diurnal and nocturnal)**
  - **Ocular Perfusion Pressure**

American Academy of Ophthalmology. Primary Open-Angle Glaucoma Suspect, Preferred Practice Pattern. San Francisco: American Academy of Ophthalmology, 2005. Available at: www.aao.org/ppp.

Ocular Perfusion Pressure and Glaucoma Progression

Low ocular perfusion pressure has been shown to be strongly associated with the prevalence of glaucoma progression in multiple population-based surveys

Tielsch JM, et al. *Arch Ophthalmol.* 1995.

Leske MC, et al. *Arch Ophthalmol.* 1995.

Leske MC, et al. *Arch Ophthalmol.* 2002.

Quigley HA, et al. *Arch Ophthalmol.* 2001.

Bonomi L, et al. *Ophthalmol.* 2000.

Leske et al.Ophthalmology 114 (11), November 2007

BP – IOP = Ocular Perfusion Pressure (OPP)

(BP is mean arterial pressure, diastolic BP, or systolic BP)

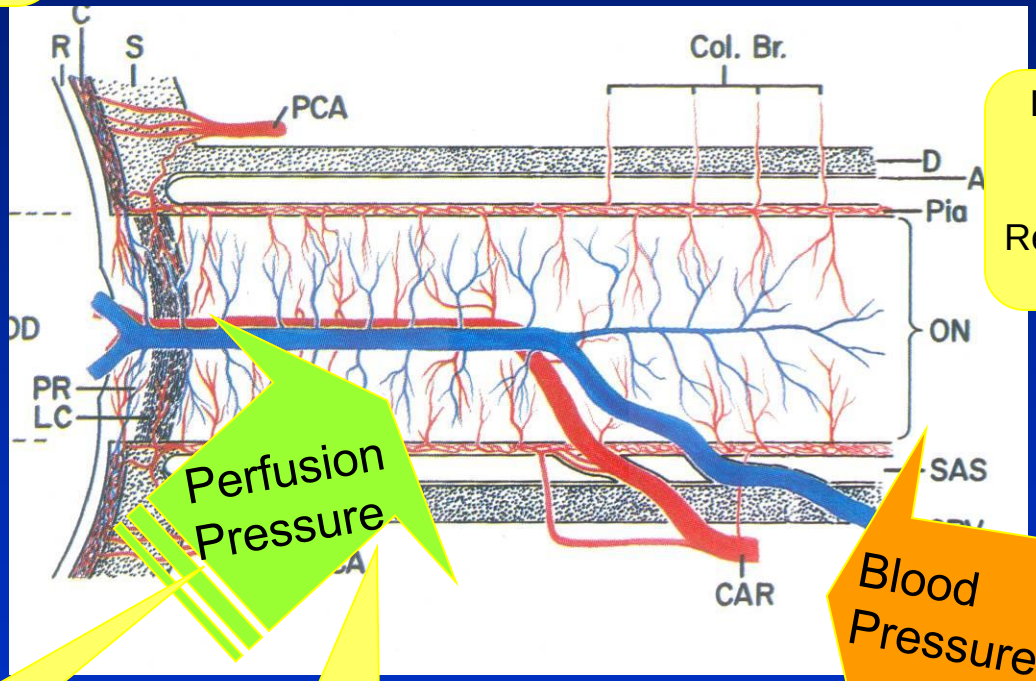
Perfusion Pressures

- Mean arterial pressure (MAP) = 2/3 diastolic + ½ systolic
- Mean Arterial OPP = MAP- IOP
- Systolic OPP = Systolic - IOP
- Diastolic OPP = Diastolic - IOP

Ocular Perfusion Pressure and Glaucoma Progression

Higher
IOP
Negatively Impacts
Perfusion Pressure

IOP



Perfusion Pressure

Lower Diastolic, Systolic, or Mean Pressure Reduces Perfusion Pressure

Blood Pressure

Lower
Perfusion Pressure
Is Associated with
Increased Risk for
Open Angle Glaucoma

Perfusion Pressure
Is a Result of
A Delicate Balance
Between IOP
and Blood Pressure

Leske MC, et al. Ophthalmology 2007; 114,: 1965-72
Leske MC, et al. Ophthalmology 2008;115, 65-93.
Hayreh SS. Trans Am Acad Ophthalmol 1974;78:240-54

OPP and Glaucoma Progression: Population Studies

- **Baltimore Eye Survey (AA and Caucasian)[1]**
  - **6x excess of POAG in subjects with lowest category of Ocular Perfusion Pressure (OPP)**
- **Egna-Numarkt Study (Caucasian)[2]**
  - **Lower Diastolic Ocular Perfusion Pressure (DOPP) associated with marked, progressive increase in frequency of POAG**
- **Barbados 4 yr Eye Study (African-Caribbean)[3]**
  - **4-year risk of developing glaucoma increased dramatically at lower perfusion pressure**
- **Proyecto Ver (Hispanic)[4]**
  - **Found lower Diastolic Perfusion Pressure (DPP) associated with increased risk of POAG**

1. Tielsch, Katz, Sommer, Quigley, Javitt. Arch Ophthalmol 1995;113:216-21
2. Bonomi L, Marchini G, Marraffa M et al. Ophthalmology 2000;107:1287-93
3. Leske MC, Wu S-Y, Nemesure B, et al. Arch Ophthalmol 2002;120:954-9.
4. Quigley HA, West SK, Rodriguez J, et al. Arch Ophthalmol. 2001;119:1819-26.

Ocular Perfusion Pressure and Glaucoma Progression: New Evidence

- Barbados Eye Study 9-year Risk Factor Study
- EMGT Predictors for Long-term Progression
- Thessaloniki Eye Study
- EGPS Inter-current Risk Factors

OPP: Barbados 9-year

- **Cohort study of African-Caribbeans residing in Barbados, West Indies**
- **9-year risk of developing glaucoma increased dramatically at lower perfusion pressure**

Leske MC, Wu S-Y, Nemesure B, et al. Arch Ophthalmol 2002;120:954-9.

POAG Risk Factors 9-year BES

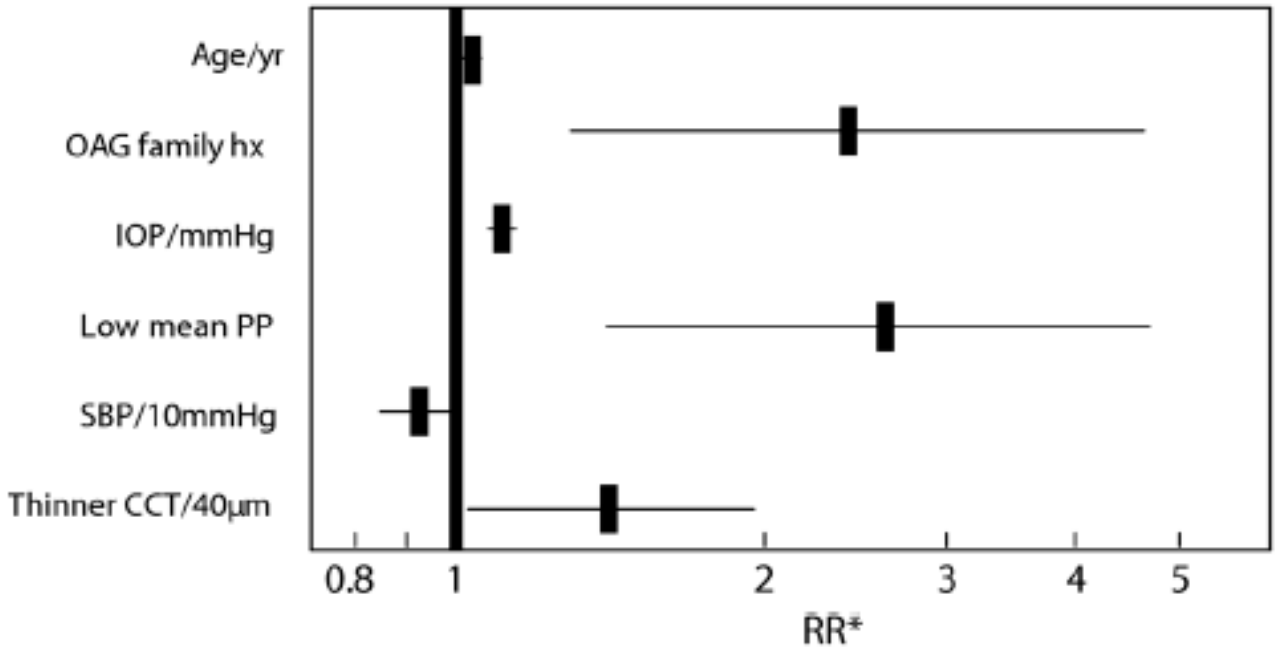


Figure 1. Risk factors for definite open-angle glaucoma (OAG; n = 3222). hx = history; PP = perfusion pressure; RR = risk ratio; SBP = systolic blood pressure. *Based on Cox regression models, adjusting for age, gender, intraocular pressure (IOP), and IOP- and blood pressure–lowering treatment; central corneal thickness (CCT) is presented as an odds ratio, based on logistic regression model in a subsample (n = 1023).

Leske MC, Wu S-Y, Nemesure B, et al. *Ophthalmol* 2008;115:85-93.

Barbados Eye Study Conclusions

- Correlates indicating increased risk of GLC progression (in order of significance)

Low mean perfusion pressure

Family HX of GLC

Corneal thickness

Elevated IOP

Age

Increased Systolic BP was a protective

Thessaloniki Eye Study

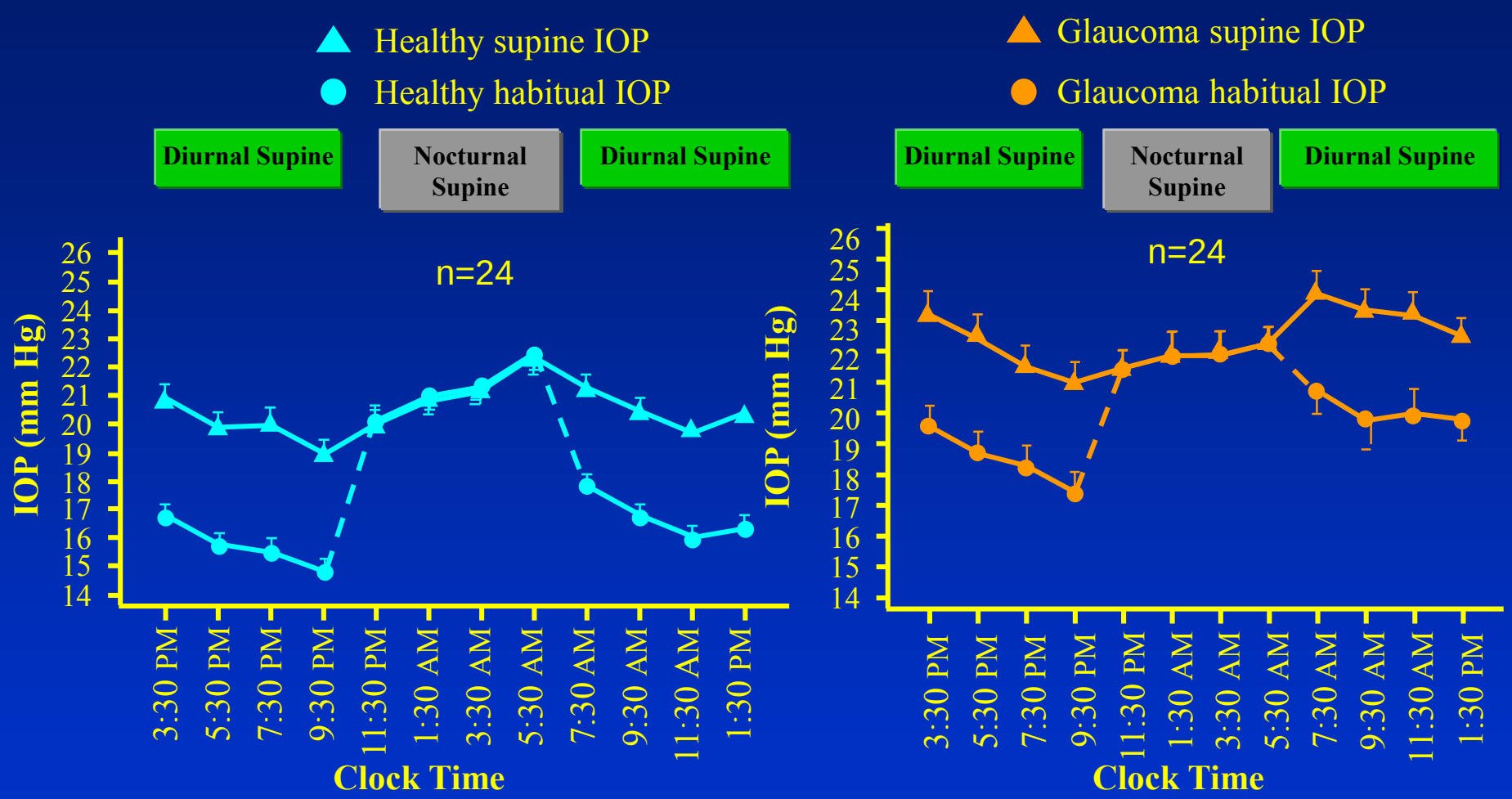
- Performed HRT in 263 subjects
- Excluded those subsequently identified with glaucoma
- Patients with DBP < 90 as a result of systemic anti-HTN treatment had larger C:D ratios and cup areas on HRT compared to normals with DBP < 90 and HTN patients with BP ≥ 90

Topouzis et al. Am J Opthalmol 2006;142:60-67

FINALLY, how does perfusion pressure data effect drug selection and treatment methods?

- What's happening to IOP at night?
- What drugs work well on a 24 hour? cycle (particularly during sleep)?
- Which drugs maximize 24 hour IOP control with minimal effect on BP?
- First, the LIU studies from Weinrebs GLC lab

IOP Is Higher at Night



- Both healthy eyes and eyes with glaucomatous changes showed higher nocturnal supine IOP than diurnal sitting IOP
- Supine IOP is higher than sitting IOP, regardless of time of day

Liu et al. *Invest Ophthalmol Vis Sci*. 2003;44:1586-1590.

Glaucoma Medications and their effects on Ocular Perfusion Pressure (OPP)

- 27 Patients treated with BID timolol 0.5%, BID brimonidine 0.2%, TID dorzolamide 2% or QHS latanoprost 0.005% for six weeks, followed by a 4-week washout period between different treatments

- 24-hour IOP monitoring in habitual position
- 24-hour systemic blood pressure monitoring

GOAL: Based upon drug effect on IOP and BP find the best mono therapeutic agent and best drug combination

Quaranta L et al. *Invest Ophthalmol Vis Sci.* 2006;47:2917-2923.

IOP Results

	Baseline	Timolol	Brimonidine	Dorzolamide	Latanoprost
Mean 24-Hour IOP (mm Hg)[1]	22.69	17.73	18.32	17.37	16.62

1. **Quaranta L et al. *Invest Ophthalmol Vis Sci.* 2006;47:2917-2923.**

Diastolic Ocular Perfusion Pressure (DOPP) Results

	Baseline	Timolol	Brimonidine	Dorzolamide	Latanoprost
Mean 24-Hour Diastolic Ocular Perfusion Pressure (mm Hg)[1]	50.7	53.0	46.2 Significant reduction in DOPP ($p < 0.0001$)	55.9 Significant improvement in DOPP ($p < 0.0001$)	56.4 Significant improvement in DOPP vs. baseline ($p < 0.0001$)

*** Reduction in DOPP is a risk factor for glaucoma progression[2]**

1. Quaranta L et al. *Invest Ophthalmol Vis Sci.* 2006;47:2917-2923.
2. Quigley HA, West SK, Rodriguez J, et al. Arch Ophthalmol. 2001;119:1819-26

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Brimonidine 46.2 Significant reduction in DOPP (p < 0.0001)

* Reduction in DOPP is a risk factor for glaucoma progression[2]

1. Quaranta L et al. *Invest Ophthalmol Vis Sci.* 2006;47:2917-2923.
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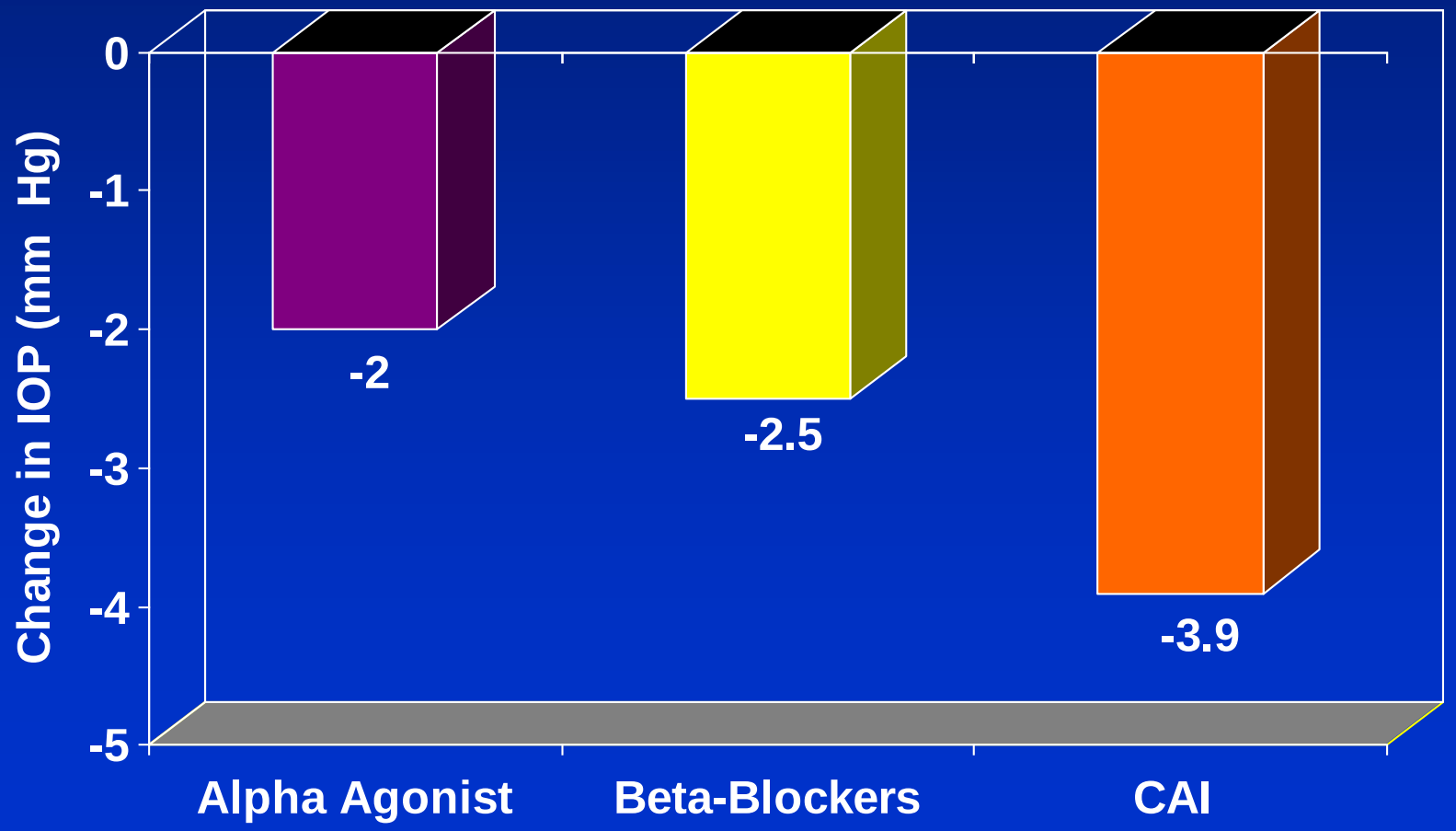
Additive effect on IOP of prostaglandin TX PLUS:



Source: Bateman 2002, Walt 2002

Study Conclusions

- PGA and CAI significantly increased DPP at all time points@@@
- Beta-blocker significantly increased DPP from 4AM to 4PM but had no effect at other times
- Alpha agonist significantly reduced DPP at multiple time points, primarily due to significant decrease in systemic BP@@@

Quaranta L, Gandolfo F, Turano R, et al. Invest Ophthalmol Vis Sci 2006; 47: 2917-23.

BEST Combinations

- Prostaglandin (+) Topical CAI
- Avoid Alpha agonist (decreases PP) ie lowers BP and least effective agent at night

Relationship between Nocturnal Hypotension and OPP

- Low BP at night, coupled with high IOP in supine position, compromise OPP
- Use systemic BP meds in the AM to minimize nocturnal hypotention
- Use IOP lowering drugs that lower IOP during BOTH the diurnal and nocturnal period (CAI's and prostaglandins)
- Avoid IOP meds that lower systemic BP at night (beta blockers, alpha agonists)

Graham, Drance. Surv Ophthalmol. 1999;43(suppl 1):S10-16
Hayreh, Zimmerman, Podhajsky. Am J Ophthalmol. 1994;117:603-624
Colligan, Dewe, Guillaume, Colligan-Brach. Int Ophthalmol 1998;22:19-25

Think holistically

- Consider measuring perfusion pressures
- Monitor those at greatest risk-low BP/over-aggressive BP control
- Nocturnal hypotension can produce NA-ION
- Talk with PCP

REASONS FOR TREATMENT FAILURE

- Adverse drug effects/ contraindications
- Too many drugs
- Efficacy
- Compliance

Compliance sucks