Glaucoma medical treatment & Cornea Graft survival

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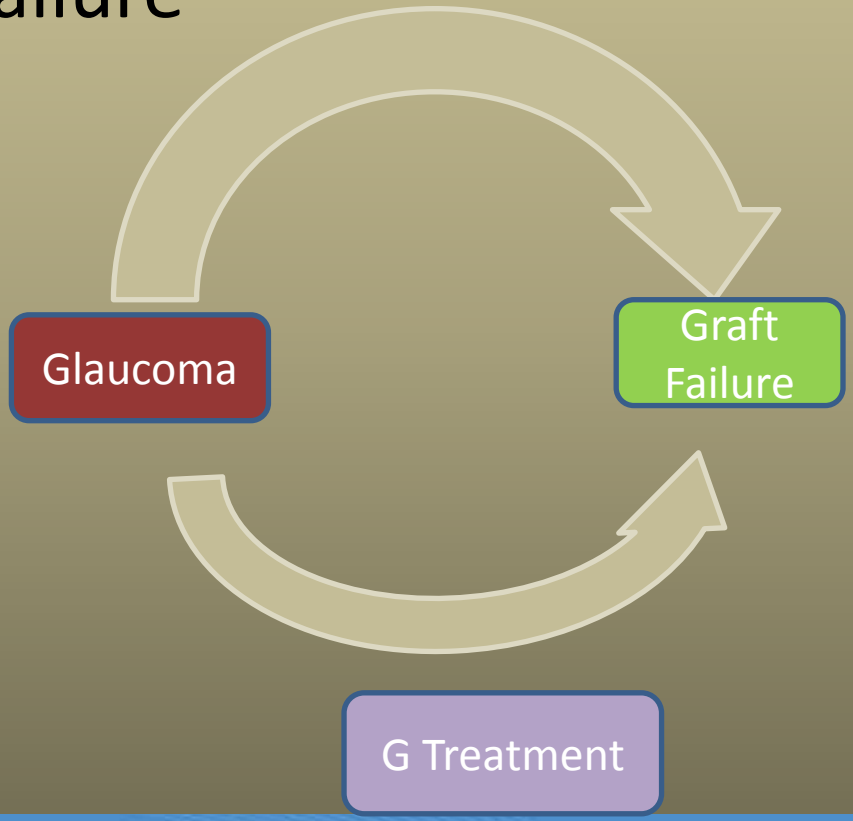
Medical Director
AthensVision Eye Institute

PKPG (PKP-Glaucoma)

- Uncontrolled IOP is a leading cause of graft failure
- aggressive treatment is usually necessary.

PKPG

- Even treated glaucoma has an increased risk of graft failure



Patient #1

A 38 yo WM underwent a 8.0mm penetrating IEK Keratoplasty for keratoconus in his right eye in Sept 2012

In May 2013 he requests my opinion for significant visual loss x2 weeks.

Eye Meds: Dexamethasone 0,1% qid

Vision: HM

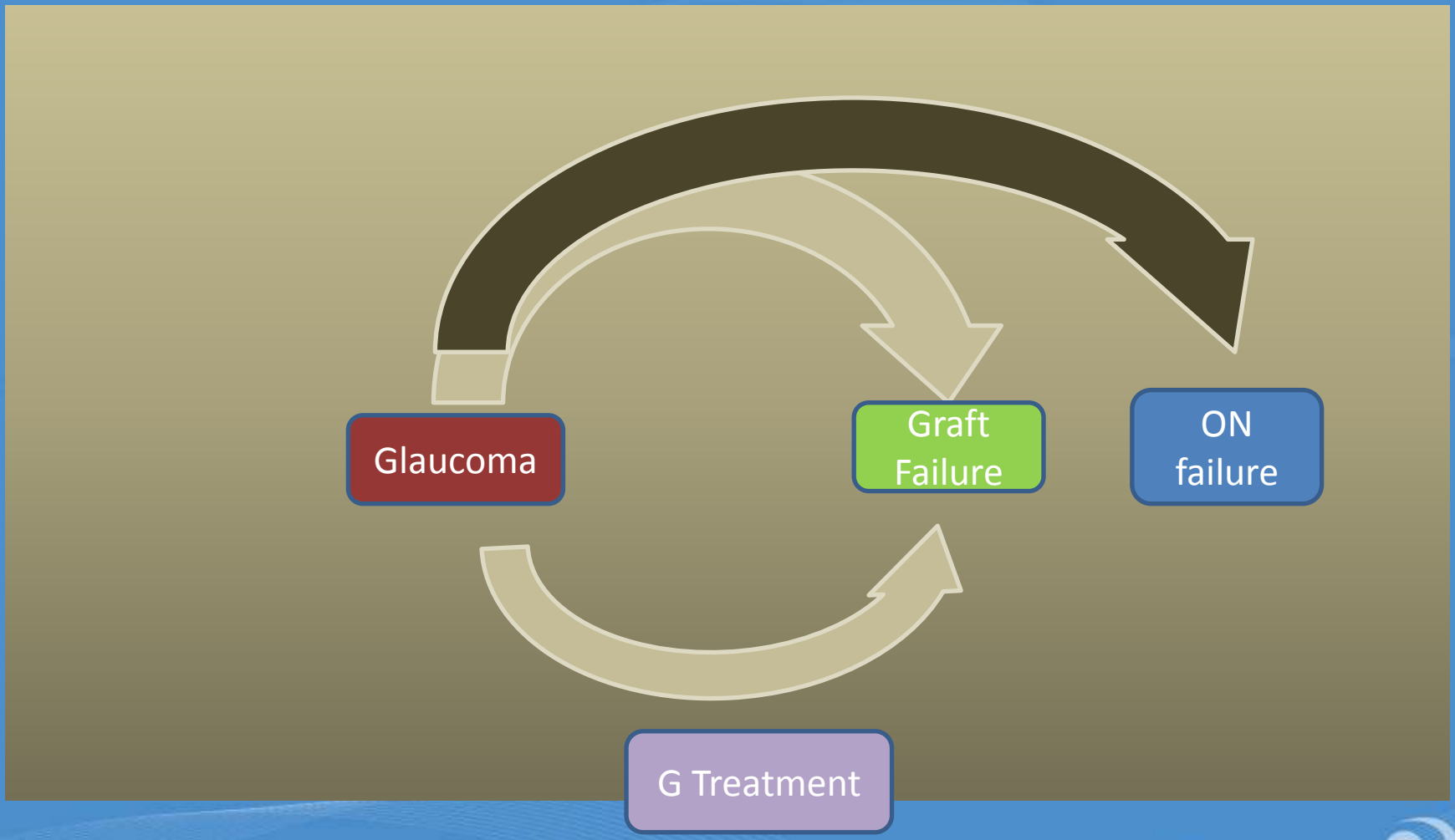
SLEX: Clear Graft

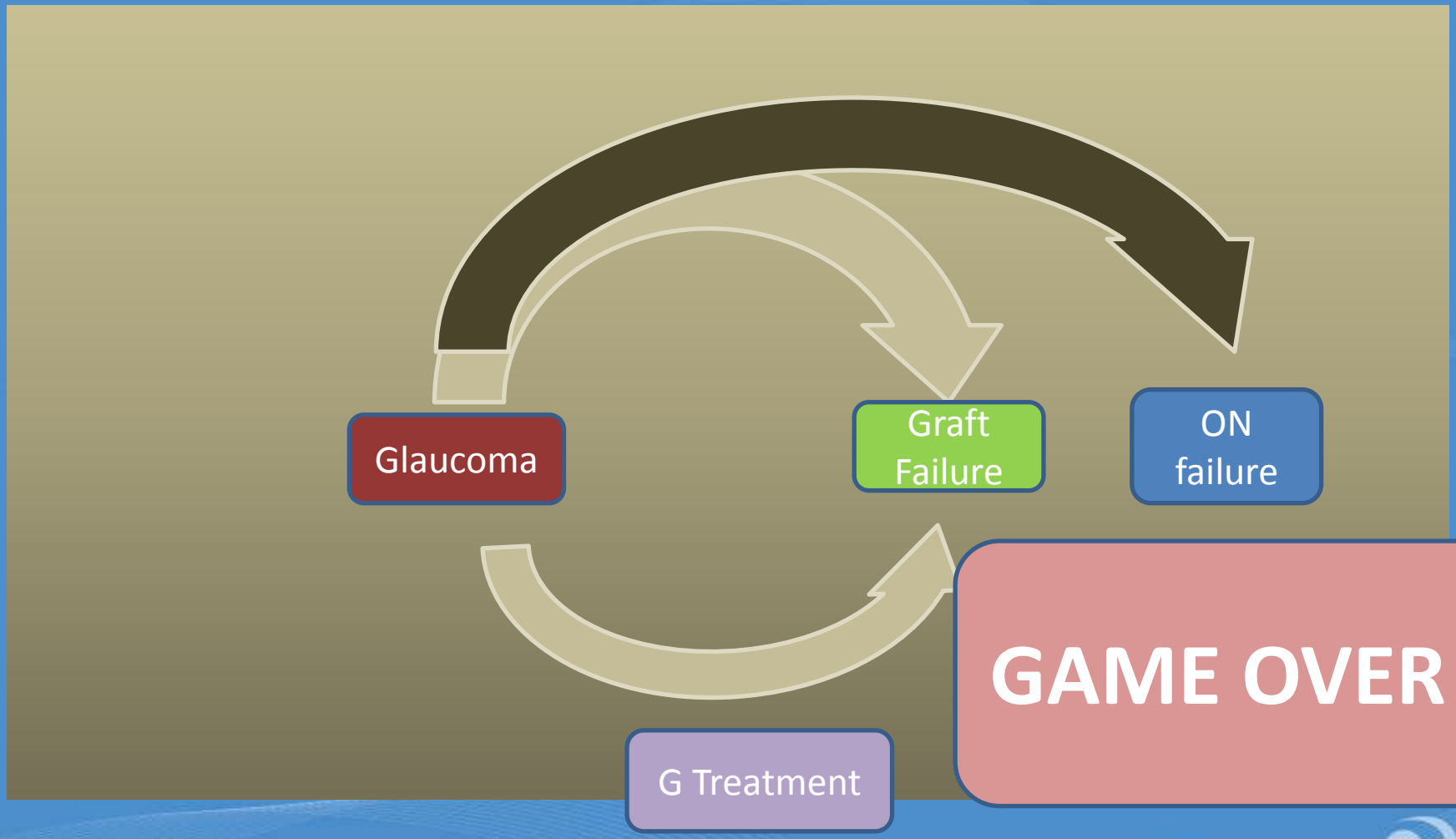
+++APD/ Cupped out ONH

T_{Gappl}: OD 44/48 (90 degrees apart)


Glaucoma
Graft Failure


Glaucoma
Graft Failure
G Treatment


Glaucoma
Graft Failure
ON failure
G Treatment


Glaucoma
Graft Failure
ON failure
GAME OVER !
G Treatment

Conclusion 1

- Uncontrolled IOP after PKP (PKPG) is one of the leading causes of graft failure **and visual loss**.
- **Aggressive treatment is mandatory**

⇧IOP>>Loss of Ganglion cells > Visual Loss

Patient #2

68 yo WM monocular with PBK referred for DSEK
POHx : Phaco, Trabx1, revisionx1
Meds: Xalatan qHs , Cosopt bid
(C/D 0,8) T appl 22mmHg
Pachym 734μ Va 20/400-

Action: Ahmed Valve in the Sulcus, T appl 14 no meds, Pachym 625μ , surgery deferred for >2 years so far…

Va 20/50-

Conclusion 2

- Controlling uncontrolled IOP before keratoplasty may even improve Corneal Longevity
- **Aggressive treatment is mandatory**

⇧IOP>>Loss of Endothelial cells > Visual Loss

Patient #3

67 yo WM monocular Patient with failed graft referred for DSEK

POHx : Phaco, PKP x2

Meds: Xalatan qHs , Cosopt bid, Alphagan bid

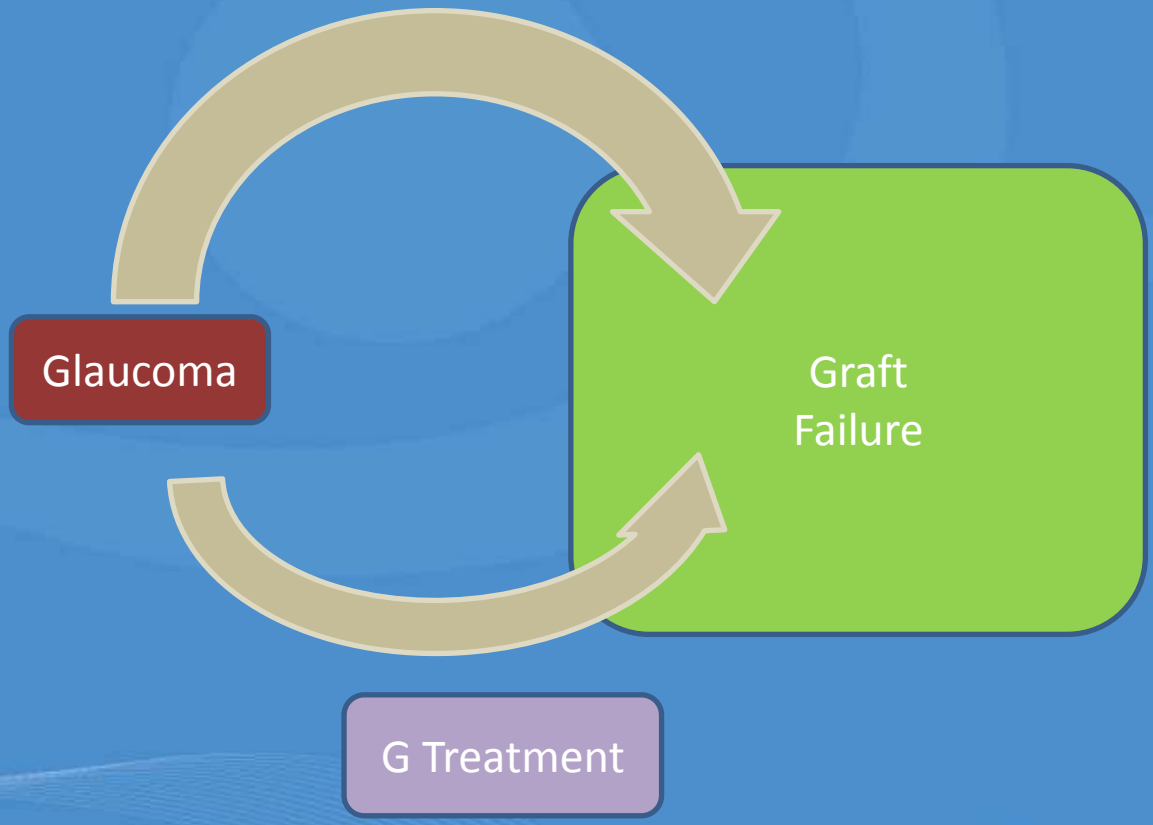
C/D ?? T appl 22mmHg

Pachym 674µ Va HM / **NO NASAL PROJECTION**

Dx

Conclusion 3

- **You may restore vision after a failed graft but NO ONE, ANYWHERE in the WORLD can restore vision in a eye with a cupped out ON**


Glaucoma
Graft
Failure
G Treatment

10+ Keratoplasty “Failure” Reasons

- **Graft Rejection**
- **Late Endothelial Failure**

• **“wrong” indication**	eg central fusion disruption syndrome
• **Refractive Failure**	anisometropia
• **Ocular Surface Disease**	HOA, Infection, Inflammation, Toxicity
• **Recurrent Disease**	Dystrophies, Herpes, keratoconus
• **Concurrent Disease**	Glaucoma, ARMD
• **Complication**	infection, hemorrhage, expulsion, RD….
• **Eye Failure**	Glaucoma, Endophthalmitis, RD…..
• **Patient Failure**	Topical & Systemic Immunomodulation

- **All Aspects of Graft Failure May Be Associated with Glaucoma/ and its management**

Corneal Graft Survival/Failure

- Which Graft?
- Which Recipient?
- Which Indication?
- Which Surgical Procedure?

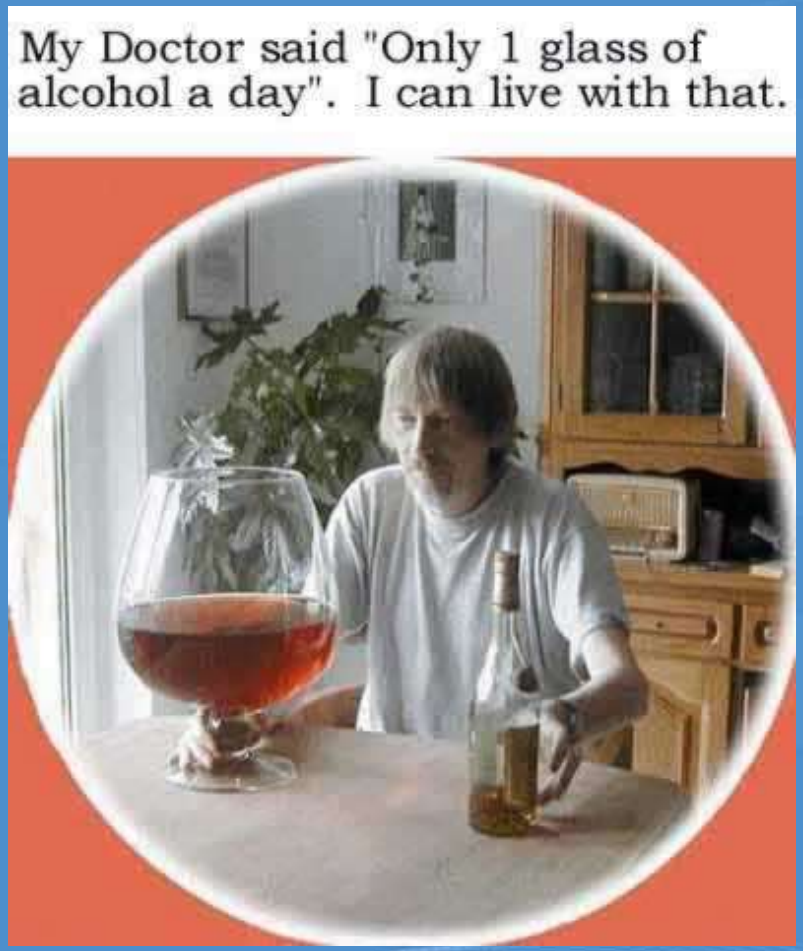
Which Graft?

ΔΗΜΟΚΡΙΤΟΣ
ΕΘΝΙΚΟ ΚΕΝΤΡΟ ΕΡΕΥΝΑΣ ΦΥΣΙΚΩΝ ΕΠΙΣΤΗΜΩΝ

IB-A

- Death to Preservation Time
- Endothelial count/ morphology
- Death to Transplantation Time
- Organ Culture vs Hypothermic Storage
- Which medium?
- Donor Age
- Donor History
- Procurement Protocol
- HLA Matching
- ABO typing
- Unescorted Flight >12 h

Which Recipient?



- Compliance with Tx
  - Worse with poor vision
- Age and Glaucoma Risk

Which indication?

- Keratoconus
- Corneal Dystrophy
- Fuchs
- PBK/ABK
- Trauma
- Infection
- Chemical Burn
- Aniridia
- OCP/ SJS
- Silicone Keratopathy
- ……

Which Keratoplasty Surgery?

- **PKP <8,5**
- PKP >8,5
- DALK
- AD-DALK (9.0)
- TILK (10+)
- DSEK <9.0
- DSEK >9.0
- DMEK
- Boston Kpro
- OOKP

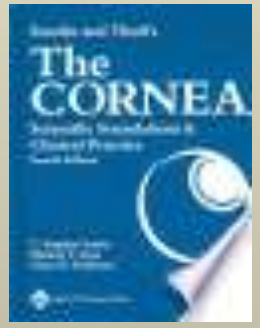
- **Combined with ECCE, phaco, Trab, Valve, MIGS iridoplasty, artificial iris implant…IOL sutured, Glued, Iris Claw……**

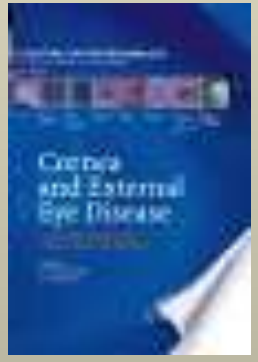
(Which Surgeon?.....)

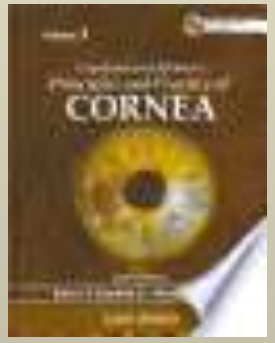
Cornea Graft Survival:
What we (usually) tell our patients

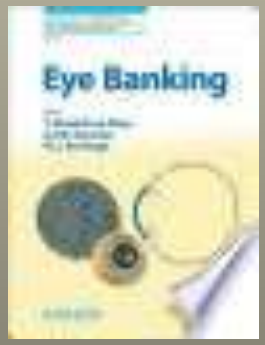
- **Cornea transplantation is the most successful transplantation in Medicine. No systemic medication is needed**
- Most first grafts for keratoconus will survive at least 5-10 years (~95% to 90-%). Other indications have somewhat lower success rates.
- At least ¼ of grafts will experience a rejection episode but 90% of them are reversible and should receive prompt attention & Rx

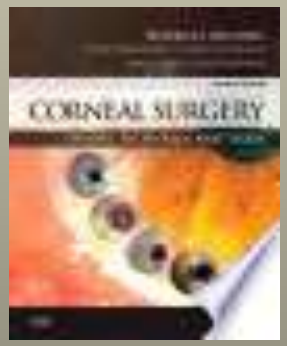
“the most successful transplant in Medicine”





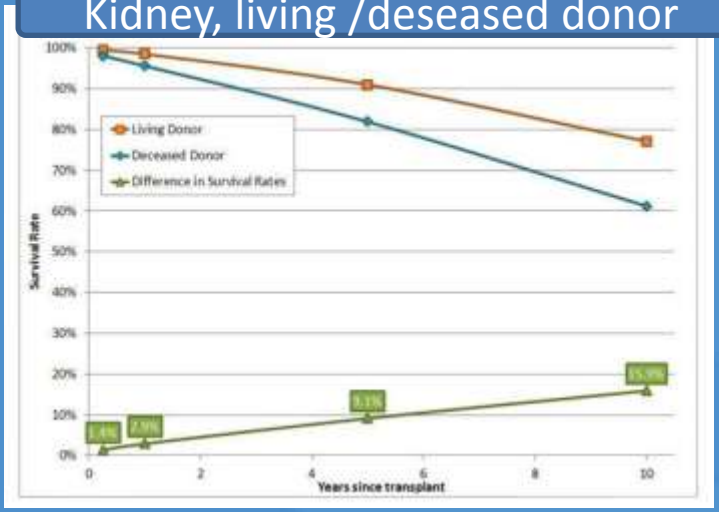




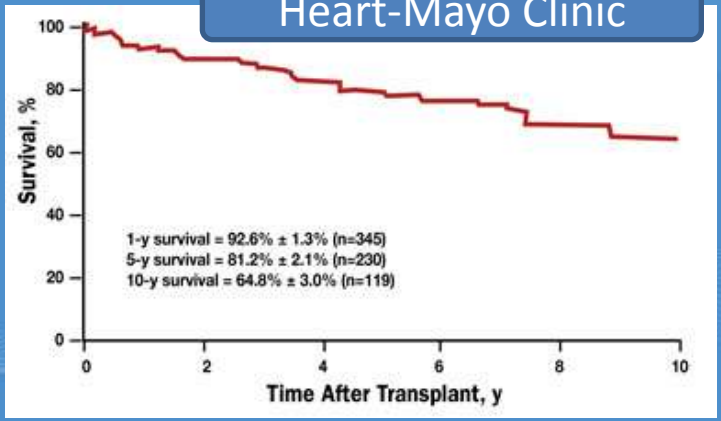


Graft Survival - failure

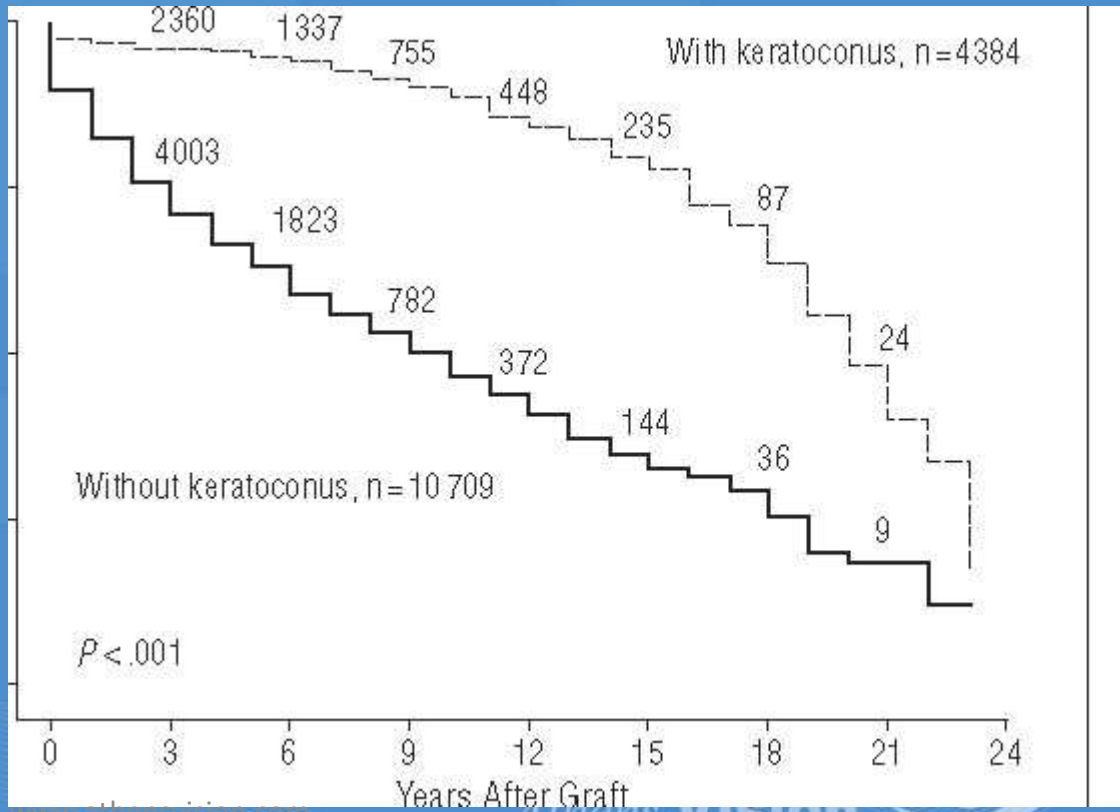
Kidney, living /deseased donor



Heart-Mayo Clinic



Austr Graft Registry



Transplantation in the 21st Century

- **Molecular based Tissue Matching**
- **"3rd generation" immunosuppression**
- **Living related donor Organ Grafts**

These improvements are not applicable to cornea transplantation…

but breakthrough technology may soon be applicable

eg Genetherapy in the EyeBank setting

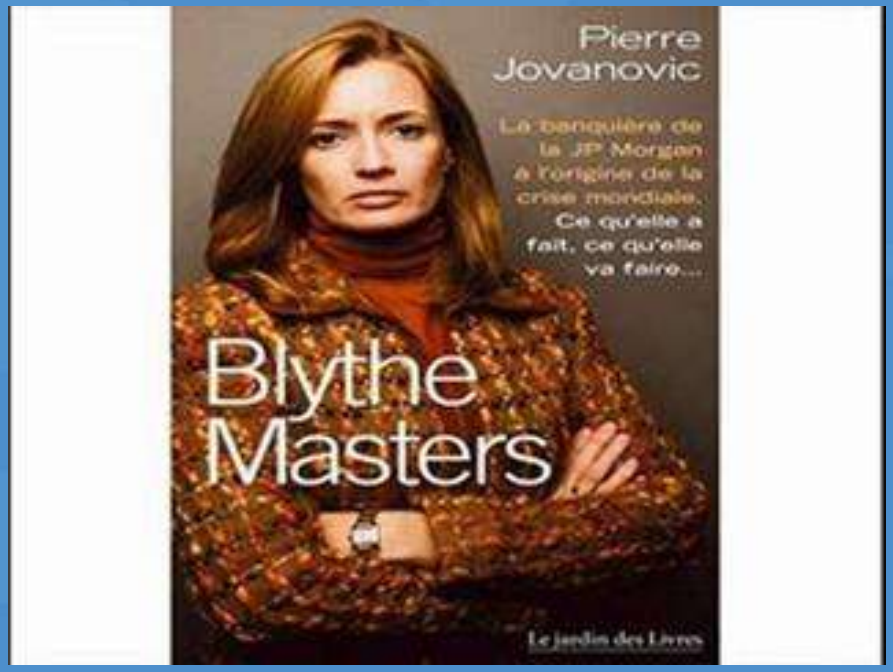
OxfordBioMedica

ENCORSTAT

Athens Vision

What do you know about CDS?

“Credit Default Swap”



(Blythe Masters- JP Morgan 1994)

National Eye Institute
NATIONAL INSTITUTES OF HEALTH

Cornea Donor Study (CDS) Investigator Group

Ophth 2008

5 year Report: ECD

1/median 824 Group A (69% loss)

2/ median 654 Group B (75% lossEndothelial loss afterPKP)

Ophth 2013

Only 14%of grafts have a ECD of >1000cells/mm at 10 years

median cell loss over 75% (median ECD 628 !)

JAMA Ophthalmol 2013 Apr;13 (5): 601-608
Ophthalmology 2008; 115:627-632
Ophthalmology 2013 Dec;120(12):2428-35

http://cds.jaeb.org/

- 1. Beck RW, Gal RL, Mannis MJ, Holland EJ, Cavanagh HD, Foulks GN, Heck EL, Lindquist T, Macsai MS, Smith RE, Stark WJ, Stulting RD, Sugar J. **Is donor age an important determinant of graft survival?.** Cornea 1999; 18(5):503-510 (Published).
(*Manuscript*) | View Publication 2. Cornea Donor Study Group. **An evaluation of image quality and accuracy of eye bank measurement of donor cornea endothelial cell density in the Specular Microscopy Ancillary Study.** Ophthalmology 2005; 112:431-440 (Published).
(*Manuscript*) | View Publication 3. Cornea Donor Study Group. **Baseline donor characteristics in the Cornea Donor Study (CDS).** Cornea 2005; 24(4):389-396. (Published).
(*Manuscript*) | View Publication 4. Cornea Donor Study Group. **Clinical profile and early surgical complications in the Cornea Donor Study (CDS).** Cornea 2006; 25(2):164-170 (Published).
(*Manuscript*) | View Publication 5. Benetz BA, Gal RL, Ruedy KJ, Rice C, Beck RW, Lass JL for the Cornea Donor Study Group. **Specular microscopy ancillary study methods for donor endothelial cell density determination of Cornea Donor Study images.** Current Eye Research 2006; 31:319-327 (Published).
(*Manuscript*) | View Publication 6. Cornea Donor Study Investigator Group. **Donor age and corneal endothelial cell loss five years after successful corneal transplantation: specular microscopy ancillary study results.** Ophthalmology 2008; 115:627-632 (Published).
(*Manuscript*) | View Publication 7. Cornea Donor Study Investigator Group. **The effect of donor age on corneal transplantation outcome: results of the cornea donor study.** Ophthalmology 2008; 115:620-626 (Published).
(*Manuscript*) | View Publication 8. Dunn SP, Stark WJ, Stulting RD, Lass JH, Sugar A, Pavilack MA, Smith PW, Tanner JP, Dontchev M, Gal RL, Beck RW, Kollman C, Mannis MJ, Holland EJ on behalf of the Cornea Donor Study Investigator Group. **The effect of ABO blood incompatibility on corneal transplant failure in conditions with low risk of graft rejection.** American Journal of Ophthalmology 2009; 147: 432-438 (Published).
(*Manuscript*) | View Publication 9. Sugar A, Tanner JP, Dontchev M, Tennant B, Schultze RL, Dunn SP, Lindquist TD, Gal RL, Beck RW, Kollman C, Mannis M, Holland E, for the Cornea Donor Study Investigator Group. **Recipient risk factors for graft failure in the Cornea Donor Study.** Ophthalmology 2009; 116: 1023-1028 (Published).
(*Manuscript*) | View Publication 10. Powe A, Gal RL, Beck RW, Mannis MJ, Holland EJ on behalf of the Cornea Donor Study Investigator Group. **The Cornea Donor Study.** Vision Pan-America 2009; 8:134-137 (Published).
(*Manuscript*) 11. Sugar J, Montoya M, Dontchev M, Tanner JP, Beck RW, Gal RL, Gallagher S, Gaster R, Heck E, Holland EJ, Kollman C, Malling J, Mannis MJ, Woody J for the Cornea Donor Study Investigator Group. **Donor risk factors for graft failure in the Cornea Donor Study.** Cornea 2009; 28: 981-985 (Published).
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(*Manuscript*) | View Publication 13. Lass JH, Beck RW, Benetz BA, Dontchev M, Gal RL, Holland EJ, Kollman C, Mannis MJ, Price F, Raber I, Stark WJ, Stulting RD, Sugar A for the Cornea Donor Study Investigator Group. **Baseline factors related to endothelial cell loss following penetrating keratoplasty.** Archives of Ophthalmology 2011; 129: 1149-1154 (Published).
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(*Manuscript*) 15. Sugar A, Montoya M, Beck RW, Cowden JW, Dontchev M, Gal RL, Kollman C, Malling J, Mannis MJ, Tennant B for the Cornea Donor Study Investigator Group. **Impact of the Cornea Donor Study (CDS) on Acceptance of Corneas from Older Donors.** Cornea (Accepted).
(*Manuscript*)

Important CDS Outcomes

- Evaluated over 1000 patients with endothelial dysfunction (Fuchs-ABK-PBK)
- Donor age up to 75, and other factors(retrieval-processing-preservation-utilization) ABO incompatibility: no effect on graft survival for at least 5 years
- Risk of graft failure 4x greater for PBK/ABK then Fuchs (27-7%)
- Prior Glaucoma Surgery or preoperative Glaucoma medication use also increased graft failure
- Pearls: phakic status vs pseudophakia or triples and female increased risk for failure in Fuchs
- Sharp decrease of ECD within the first 6mos (mean 24% vs 10% normal) is a predictor for later graft failure within 5 years

Cornea Graft Survival:
What we (usually) do not tell our patients

- Graft survival “for other” indication approaches ~80% at 5 years for medium risk and less then 50% for the high risk.
- Graft Survival continues to drop after 10-15 years for at least 10 more years.
- **Few grafts actually have 4-dig endothelium numbers after 5 years**
- The chance of rejection in the second graft doubles.
- There is a real risk of traumatic wound dehiscence with expulsion hemorrhage.
- **A failed graft is oftentimes worse then the original disease!**
- **There is a frank risk of developing *blinding* Glaucoma**

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Leading clinical and laboratory ophthalmology and vision research

Laser scanning in vivo confocal microscopy highlights **profound reductions in cell density at every level** of the transplanted cornea and alterations to the subbasal plexus that are still apparent up to 40 years after penetrating keratoplasty.

RL Niederer et al, Corneal Innervation and Cellular Changes after Corneal Transplantation: An In Vivo Confocal Microscopy Study, Feb 2007,28,(2), 621-626

Incidence of Glaucoma after PKP

37% of phakic eyes and 88% of aphakic eyes have an IOP of more then 25

Irvine AR, Kaufman HE Intraocular pressure following penetrating keratoplasty. Am J Ophthalmol 1969; 68 (5): 835-844

- **Incidence of glaucoma varies with the indication, phakic status, Hx of prior glaucoma, Regrafting, combined surgery with cat (triple), Presence of PAS**
  - Expect less then 5% incidence in Keratoconus patients
  - expect 1/3 to ½ of patients with PBK to develop glaucoma
  - Prior controlled glaucoma: 4X higher risk to progress
  - Regrafts: 2X higher risk

Kirkness CM et al,Cornea 1992;11(5) 427-432
Simmons RB et al Trans Am Ophthalmol Soc 1989;87:79-91
Sihota R et al, Aust N Z J Ophthalmol 1998;26(4):305-309

Glaucoma and Graft Failure

	3 year Graft Failure Rate with Glaucoma	3 year Graft Failure Rate without Glaucoma
CCTSRG	47%	30%
ACGR	40.7 - 43.4%	15.3%

Table 3. Adjusted RRs for Factors Impacting Various Causes of Initial Graft Failure*

Risk Factor	Failure Type: Any Type	Failure Type: Rejection	Failure Type: Endothelial	Failure Type: Surface
Preoperative glaucoma medication				
RR (95% CI)	2.1 (1.6-2.7)	2.2 (1.3-3.6)	1.8 (1.1-3.0)	2.8 (1.5-5.2)
P value	<.001	.002	.02	.002
Peripheral anterior synechiae				
RR (95% CI)	2.0 (1.5-2.7)	1.7 (0.9-3.2)	2.9 (1.7-4.9)	1.1 (0.5-2.8)
P value	<.001	.08	<.001	.76
Deep stromal vascularization				
RR (95% CI)	1.9 (1.3-2.6)	2.7 (1.6-4.8)	1.1 (0.5-2.3)	1.6 (0.7-3.8)
P value	<.001	<.001	.82	.29
Diabetes mellitus				
RR (95% CI)	1.3 (1.0-1.8)	1.3 (0.7-2.3)	2.3 (1.4-3.8)	1.2 (0.6-2.5)
P value	.08	.46	.002	.69
Recipient race				
RR (95% CI)	2.4 (1.5-3.8)	2.2 (0.9-5.2)	3.6 (1.8-7.4)	0.6 (0.08-4.3)
P value	<.001	.07	<.001	.59
Recipient bed ≤7 mm				
RR (95% CI)	2.6 (1.7-4.0)	3.2 (1.5-6.7)	4.8 (2.4-9.5)	2.0 (0.6-6.5)
P value	<.001	.003	<.001	.23

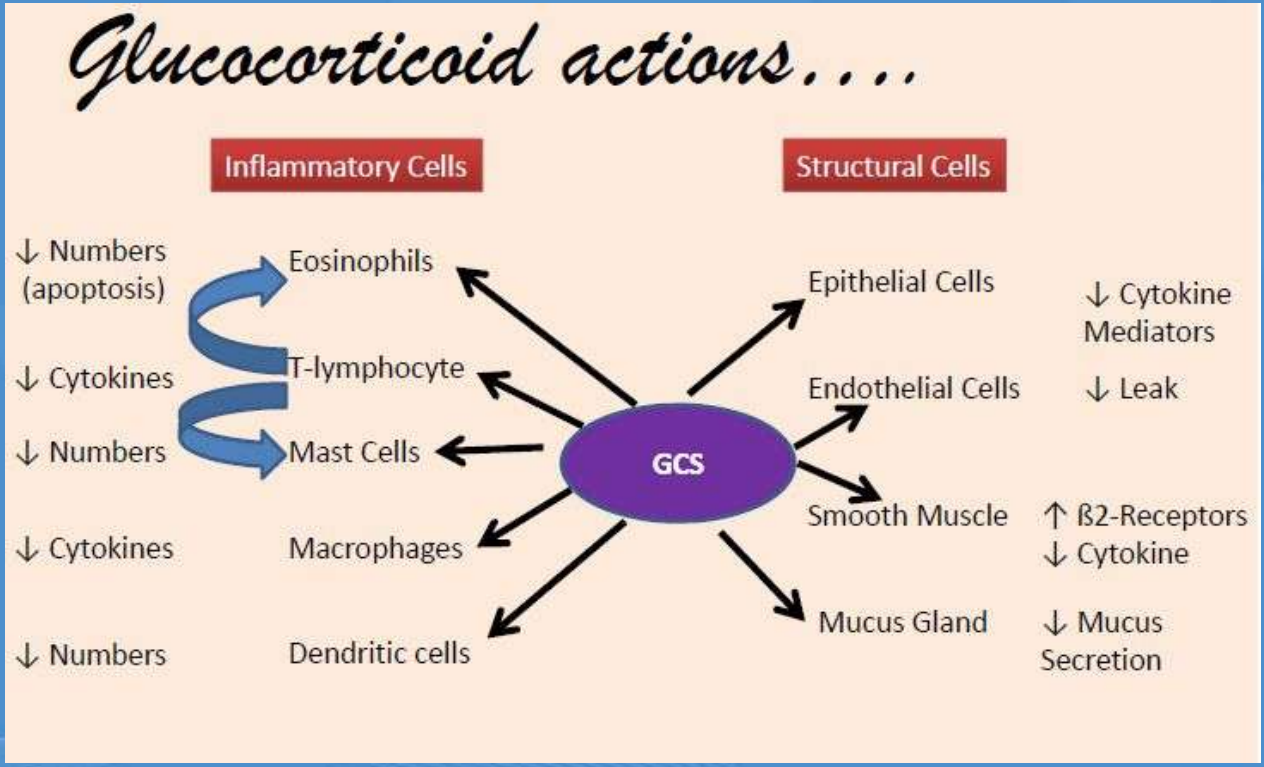
Abbreviations: CI, confidence interval; RR, relative risk.
*The RRs and *P* values were determined by Cox proportional hazards regression modeling. *P*<.05 was considered significant.

Price MO et al. Arch Ophthamol 2003; 121:1087-92
CCTSRG. Cornea 1993; 12:93-103
ACGR 1993; Aust N Z J Ophthalmol 1993; 21Suppl:1-48

A Edward Maumenee

- introduction of topical corticosteroids/ immunology of graft rejection

Steroids discourage the movement of effector cells into the graft… is the mainstay of our treatment strategy



D J Coster et al, 2010

Steroids- induced Glaucoma

M R Raxeghinejad, L Jay Katz, Ophthalmic Res 2012;47:66-80

"approximately one-third of individuals (and 90% of POAG's) experience a ***moderate increase*** in IOP after topical steroid use.....BUT LESS THEN 31"

"Mostly" reversible on stopping but NOT always!

GLC1A/ TIGR/ MYOC 1q21/ 1q31

Espildora J et al Cortisone-induced Glaucoma:a report on 44 affected eyes J Fr Ophthalmol 1981;4:503-508

Armaly MF, Becker B: Intraocular pressure response to topical corticosteroids. Fed Proc 1965; 24: 1274–1278.

Steroid induced glaucoma-mechanism

- **Decrease Outflow (Extracellular matrix deposition)**
  - Inhibition of glycosaminoglycans catabolism
  - Stabilization of lysosomal membranes, inhibiting release of enzymes which break down GAG's
  - Inhibition of phagocytosis of foreign material by trabecular endothelial cells, blocking outflow channels
  - Inhibition of PG E /F whose normal function is to increase outflow activity
  - Structure activity studies indicate direct relationship between anti-inflammatory potency to hypertensive effect

Steroid induced glaucoma after refractive surgery

- Tamburrelli C et al, Underestimate of tonometric readings after photorefractive keratectomy increases at higher intraocular pressure levels Invest Ophthalmol Vis Sci 2005;46:3208-3213
- Davidson Rs et al, Intraocular pressure-induced interlamellar keratitis after LASIK surgery , J Glaucoma 2003;12:23-26
- Hamilton et al. Steroid induced glaucoma after laser in situ keratimileusis associated with interface fluid, Ophthalmology 2002;109:659-665
- Samuelson T W Refractive Surgery in Glaucoma Curr Opin Ophthalmol 2004;15:112-118
- Yamaguchi T et al, Diagnosis of steroid-induced Glaucoma After Photorefractive Keratectomy J Refr Surg 2008;24:413-415
- Munger R, Changes in measured intraocular pressure after hyperopic photorefractive keratectomy m J Cat and Refr Surg 2001; 27:1254-1262

Low Risk keratoplasty

- Topical steroids (prednisolone) still universally used for routine postoperative management for at least 6 months

- 12-26% switch to Loteprednol for routine management

JB Randelman&RD Stulting. Cornea 2006;25 (3): 286-290

	Rise in IOP (mmHg)	Anti-inflammatory potency
Dexamethasone 0,1%	22+/-2.9	24
Prednisolone 1%	10 +/-1,7	23
Fluorometholone 0,1%	6,1+/-1,4	11
Hydrocortisone 0,5%	3,2+/-1.0	1
Tetrahydrotriamsinolone 0,25%	1,8+/-1,3	1,4
Medrysone 1,0%	1,0+/-1,3	1,7

Stewart et al Arch Ophthalmol 1979;97:2139-2140

- Difluprednate 0,05%
- Dexamethasone 0,1%
- Prednisolone acetate 1%
- Prednisolone phosphate 1%
- Rimexolone susp 1%
- Loteprednol 0,5%
- Fluorometholone 0,1%


BAUSCH+LOMB
LOTEMAX
loteprednol etabonate
ophthalmic gel 0.5%
Sterile
Rx Only
LOTEMAX.GEL
loteprednol etabonate
ophthalmic gel 0.5%


Lotemax
loteprednol etabonate
ophthalmic ointment 0.5%
Sterile
Rx only


Bausch & Lomb
Lotemax
15 mL


LOTEPREDNOL ETABONATE OPHTHALMIC SUSPENSION 0.5% w/v
L-Pred
5mL
Sterile
ALLERGAN


5ml
Rx
Loteprednol
Etabonate Ophthalmic
Suspension 0.5% w/v
Loteflam
Eye Drops
Cipla

Loteprednol: Ester Steroid
“soft drug” concept of Bodor:
predictable metabolism to inactive metabolites after exerting their therapeutic effect

- **IOP rise above 10 mmHg: expect it in 2% of patients treated (0,5% placido)**

  Ester based Steroid

Recommended in low risk Keratoplasty

Holland EJ et al Attenuation of ocular Hypertension with the use of topical loteprednol etabonate 0,5% in steroid responders after corneal transplantation, Cornea 2009;28:1139-1143

30 patients switched and IOP dropped without increase in rejection risk

Randelman et al Prevention and treatment of corneal graft rejection: Current practice patterns Cornea 2006;25:286-290

Erdmus et al Steroid induced intraocular pressure elevation or glaucomaafter penetrating keratoplasty in patients with keratoconus or Fuchs dystrophy Cornea 2009;28:759-764

Difluprednate

- Defluorinated Prednisolone emulsion
- Penetrates the epithelium rapidly
  - 3% IOP rise of more then 10mmHg

    Korenfeld MS et al, J Cataract Refract Surg 2009;35:26-34
  - 3,7% IOP rise of more then 10mmHg

    Smith et a, Clin Ophthalmol 2010;4:983-991
- Has been used successfully in normal risk keratoplasty J H Huang et al, IOVS 2011;52

Steroid sparing treatment

- Cyclosporin 0,5-2%
- Tacrolimus 0,03%

MOORFIELDS
PHARMACEUTICALS

cycloKAT®
cyclosporine 0.1%
Santen A Clear Vision For Life

LuxBio SCIENCES
LUMITECT

Steroid induced Glaucoma Tx

- **Medical treatment of Steroid Induced Glaucoma**
  - Beta Blockers, a2 Agonists, CAI's
  - Laser Trabeculoplasty
- **Surgery:**
  - **Expect further significant Steroid induce rise in IOP in 23%of eyes despite successful Trab**

    Thomas R, Arch Clin Exp Ophthalmol 1988;226:337-340
  - **Trabeculectomy**

    Jonas JB et al J Glaucoma 2004;137:758-760,

    Honjo M et al, J Glaucoma 2000;9:483-485

ERAPEUTICS

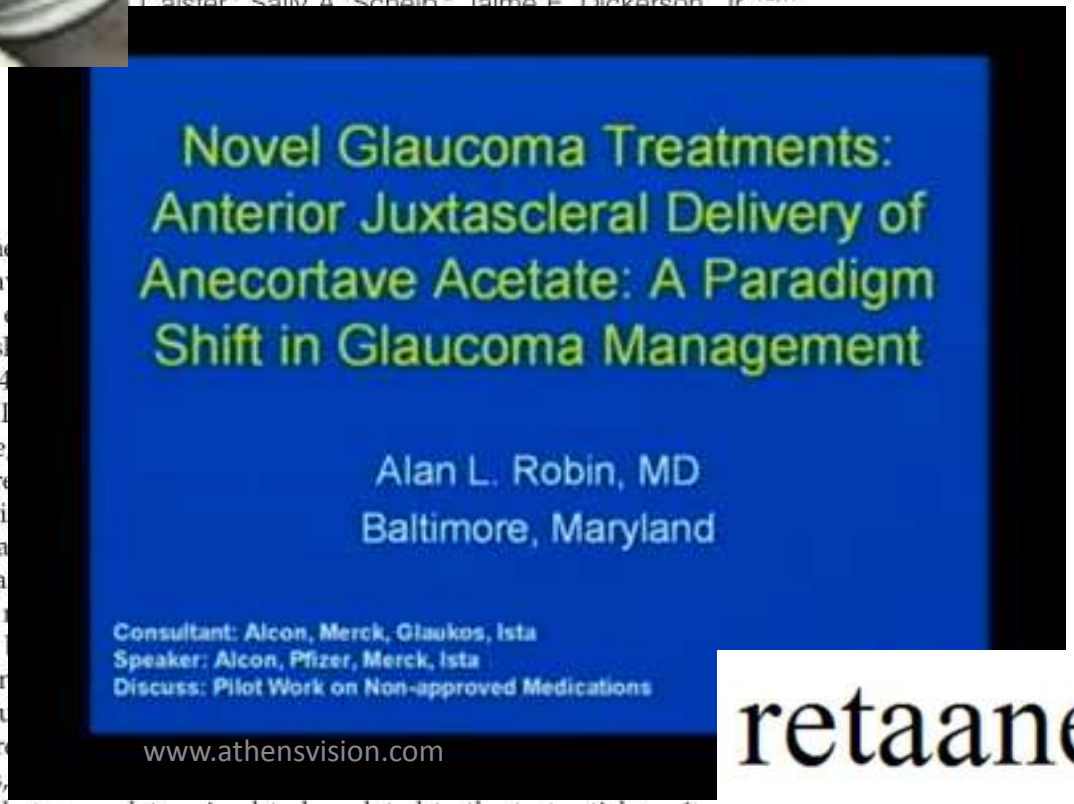
ORIGINAL ARTICLES

oid-Induced Elevated Intraocular
with Anecortave Acetate:
domized Clinical Trial

G. Callanan,[2,3] Monte S. Dirks,[4] Marlene R. Moster,[5,6]
Calster[1] Sally A. Scheib[9] Jaime E. Dickerson, Jr.[10,11]

Abstract

Purpose: The present study is th
(IOP)-lowering effect of anecorta
tascleral depot (AJD) in patients
Methods: This was a double-mas
patients had an IOP of at least 24
treatment with steroids. A target
of the 4 treatment groups: vehicle
the assigned treatment. Patients r
6. IOP was measured at each vi
responsiveness, slit lamp examina
a dilated fundus examination wa
Results: Seventy patients were
3.4 mmHg (9.1%) decrease from
groups (5.4 mmHg, 16.6%) were r
AA group at week 4 was redu
($P = 0.0487$). The mean time to tr
15 mg AA, and 30 mg AA groups,
were no serious adverse events that were determined to be related to the test article or its administration



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retaane

RSVP respondez s'il vous plait
Please Respond!

- Redness
- Sensitivity
- Vision
- Pain

*Surface keratopathy s/p PKP **

- Punctate Keratopathy, PED, Hurricane Keratopathy, (Vortex) Keratopathy, Rim Defects & Filamentary Keratopathy
  - 25% of graft failures attributed to surface problems **
  - Denervation/ Toxic medications/ abnormal lid-cornea/lack of hemidesmosomes/ abnormal curvature relationship/ increased permeability
  - Vortex Keratopathy 15-30-80%-confocal # (Medication/ Sutures/ Time)
  - Older Patients/ Preoperative lid disease / Use of Abx increased risk of PEK

*Bron AJ Vortex patterns of the corneal epithelium Trans Ophthalmol Soc UK 1973;93:455-472

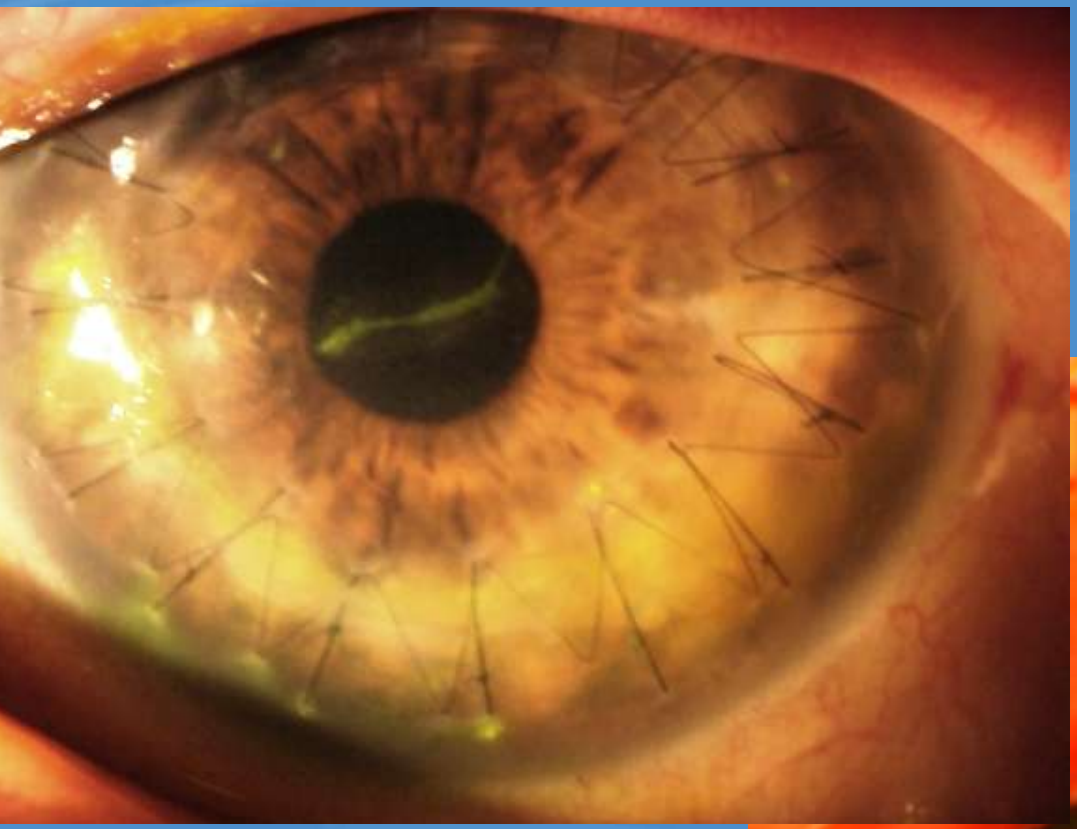
#Vahid Feiz et al Surface keratopathy after Penetrating Keratoplasty Tr Am Ophth Soc 2001;99:159-170

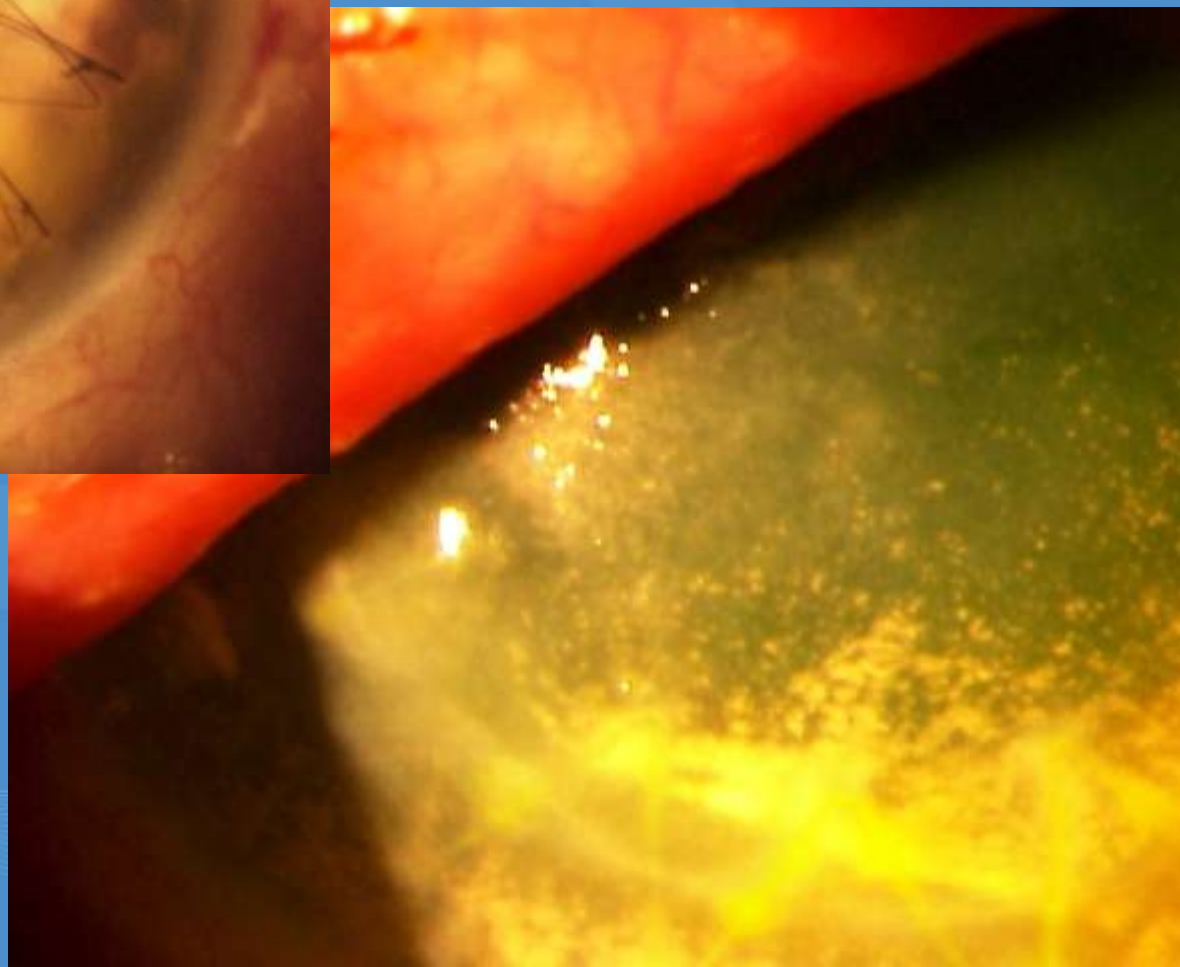
**Price FW et al Five year corneal graft survival: A large single center patient cohort Arch Opthalmol 1993;111:799-805

- Superficial Hypertrophic Dendritiform Epitheliopathy *

*Mannis MJ et al, Cornea 1998;17(3):257-61

** Akhtar S et al, Cornea, 2006;25(5):623-7





Treatment for PKPG

- (Ancillary) Medical Treatment

- Surgical
  - Trabeculectomy
  - Tube/Shunt
  - MIGS?
  - Cyclodestruction

….No Eye Can Withstand >2500$ worth of ocular Surgery

- **Laser ALT : 1 study Arch Ophthalmol** 1988; 106(2): 185-188
  - PAS induction and poor visability

NOT Recommended

- **Cyclodestruction**
  - Diode/ krypton/ Nd:YAG laser
    - Diode 72% success with single tx: Ocakoglu Curr Eye Res 2005; 30(7): 569-574
    - Equal to Trab MMC/ Shunt Ayyala et al, Ophthalmology 1998; 105(8):1550-56
  - Success (<21mmHg 63-97%)
  - Graft failure rates: 17-44%

Medical therapy of PKPG

- **Beta –adrenergic blocking agents**
  - Superficial punctate keratopathy, corneal anesthesia, impaired mucous layer and DES
- **Adrenergic Agents**
  - CME and decreased potency
- **Alpha2-adrenergic agonists**
  - Brimonidine 0,2%
  - Apraclonidine: niche AC bleeding
    - Association with ocular allergies and intraocular inflammation

Lass et al Timolol therapy in secondary angle closure glaucoma post penetrating keratoplasty. Ophthalmology 1979;86(1):51-9

Medical therapy of PKPG

- **Miotics**
  - Old fashioned and PAS, breakdown of blood-aqueous barrier
  - RD risk
- **Prostaglandin analogues**
  - Uveoscleral outflow mechanism
    - Caution with patients HSV keratits

Wand et al Latanoprost and herpes simplex keratitis Am J Ophthalmol 1998;126(4) 602-4

Prostaglandine analogs and OSD*

- Squamous metaplasia
- Stimulation of HLA-DR overexpression at the conjunctival surface
- Changes in the metalloproteinase/ tissue inhititor balance

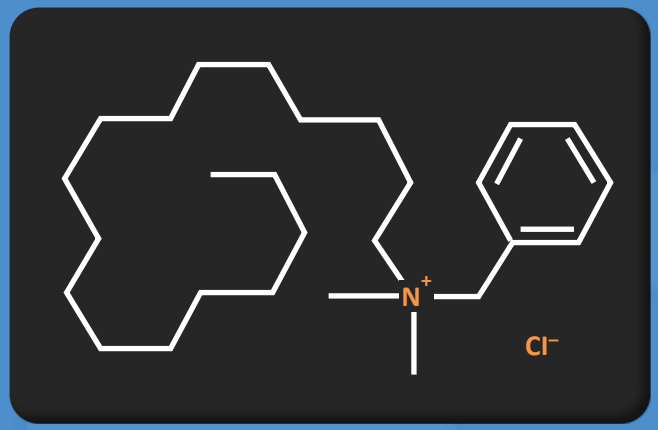
*Christophe Badouin et al, Ophthalmology 2008;115:109-115

Medical therapy of PKPG

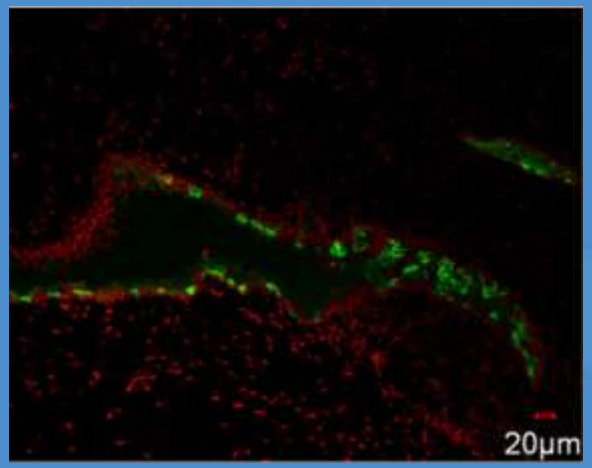
- **Topical carbonic anhydrase inhibitors**
  - Risk of decompensation
    - Konowa A et al. Irreversible corneal decomensation in patients treated with topical dorsolamide Am J Ophthalmol 1999;127 (4) 403-6
    - Cautious in history of patients with aphakia, uveitis: association with CME
- **Systemic CAI's**
  - Excellent for post op Spikes
  - Long Term use limited: Paresthesias, tinnitus, nausea, GI disturbances, fatique, depression, anorexia, weight loss

Glaucoma medication	Potential Problems in PKPG
Beta Blockers	SPK, corneal anesthesia, dry eye, subconj fibrosis
Alpha-adrenergic drugs	SPK, dry eyes, allergies
Miotics	Inflammation, graft rejection, RD, subconj fibrosis
Topical CAI's	Induce graft failure in borderline endothelial counts
Prostaglandindins	Uveitis, CME, rec HSV
Adrenergic agents	Epithelial toxicity and CME in aphakia and pseudophakia

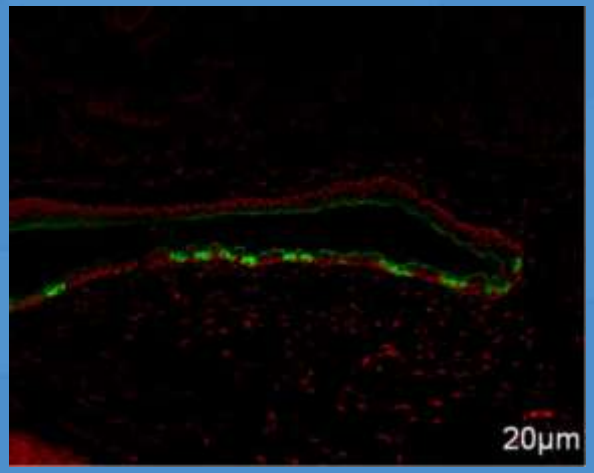
Konowal A et al. Am J Ophthalmol 1999; 127:403-6
Liu GS et al. J Ocul Pharmacol 5:329-42
Baudoin C et al. Curr Opin Ophthalmol 1996;25:15-30
Wand M et al. Am J Ophthalmol 1999;127:602-604
Perry HD et al. Cornea 1997;16:284-8
Dhaliwal JS et al. Cornea 2008;27:488-493



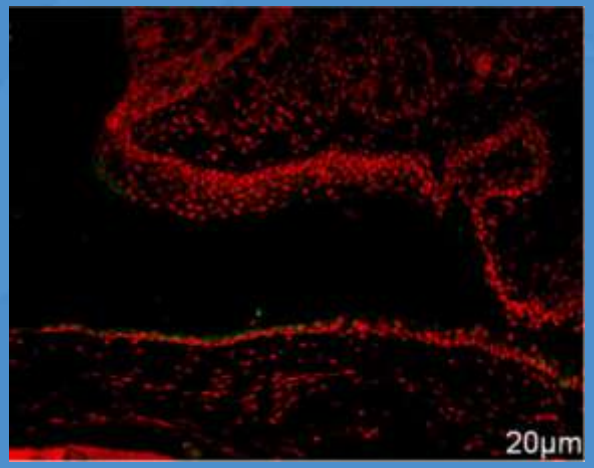
MUC5AC staining



Conjunctival fornix
Control



Conjunctival fornix
BAK



Bulbar conjunctiva
BAK

PKPG medication*

- **Acting Agent**
- **Profile of Side effects**

- **Presence of Preservatives**
- **pH level**
- **Free Radical Concentration**

D Lockington et al, Free radicals and the pH of topical glaucoma medications: a lifetime of ocular chemical injury? Eye(Lond) May 2012;26(5): 734-741

	TAS mmol/l	pH	preservative
Xalatan	0,00	6,8	BAK
Duotrav	0,00	5,5	BAK EDTA
Lumigan	0,89	7,4	BAK
Travatan	0,67	6,5	EDTA PQ-1
Combigan	0,25	6,8	BAK
Azarga	0,31	6,8	BAK EDTA
Betoptic	0,31	6,8	BAK EDTA
Cosopt Cosopt monodose	0,45 0,50	5,8 5,8	BAK none
Trusopt	0,58	5,8	BAK
Xalacom	0,61	6,1	BAK
Saflutan	0,70	5,3	(EDTA)
Azopt	0,74	6,8	BAK EDTA
Brimonidine	0,78	6,1	BAK
Ganfort	0,66	7,4	BAK
Iopidine	4,54	5,3	BAK

Conclusions: Keratoplasty and Glaucoma

- **Anticipate Glaucoma and treat it aggressively!**
  - Expect Steroid associated Glaucoma in up to 1/3 of PKP patients
  - according to the indication of Surgery the risk is up to 80%
- **Immaculate Surgical Keratoplasty technique**
    - Graft dimentions
    - Suturing technique
    - Peripheral Iridotomies
    - Complete removal of Viscoelastic
    - Treat postop inflammation
- **Identify increased IOP before and after Keratoplasty**
- **Identify Glaucoma before and after keratoplasty**
  - **ONH photos**
  - **Perimetry**
  - **SDOCT ONH**
- **Treat increased IOP**
  - **Steroids and steroid sparing Tx**
  - **Medical treatment in PKPG is ONLY ANCILLARY!**

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Thank you for your attention!