

Clinical perspective



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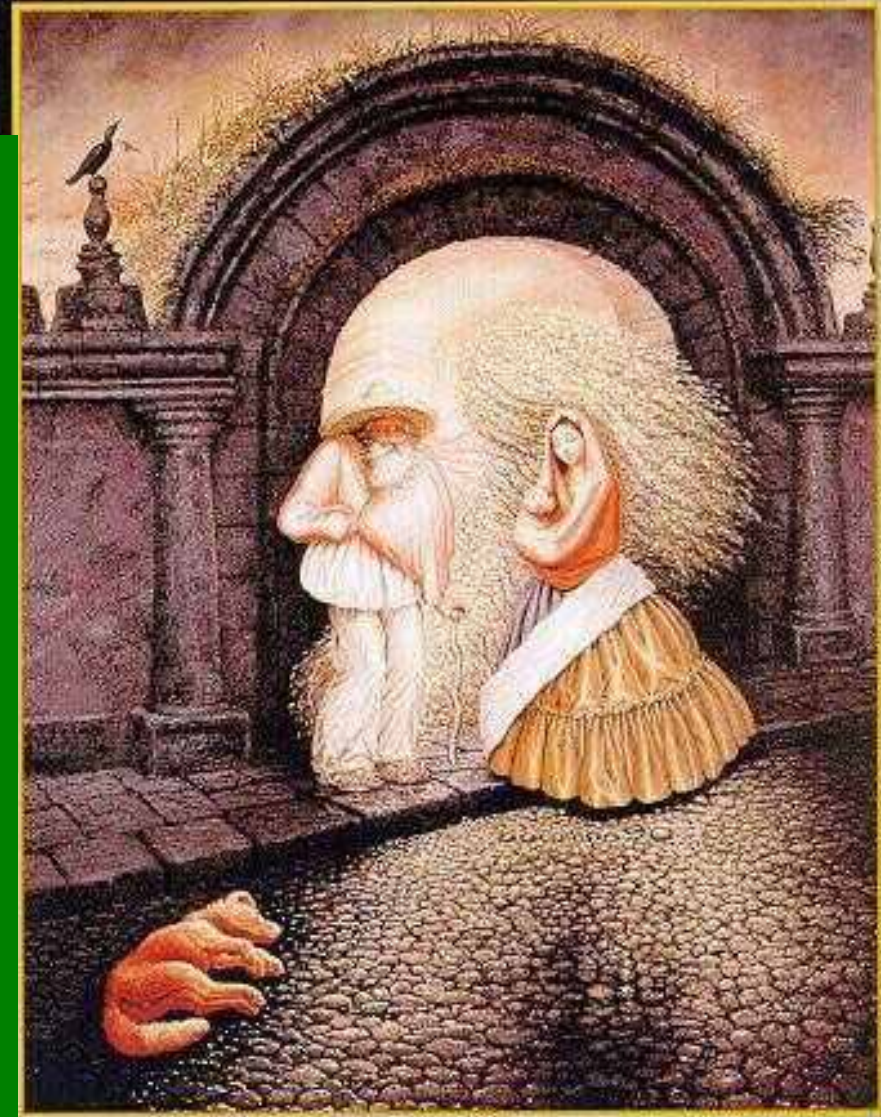
4g FG

- Difference between gati and Moxi
- 4G FQ usage in clinical practice

4th G FQ certainly seem
to offer several advantages over
3g FQ

There are some differences between
Gati and Moxi

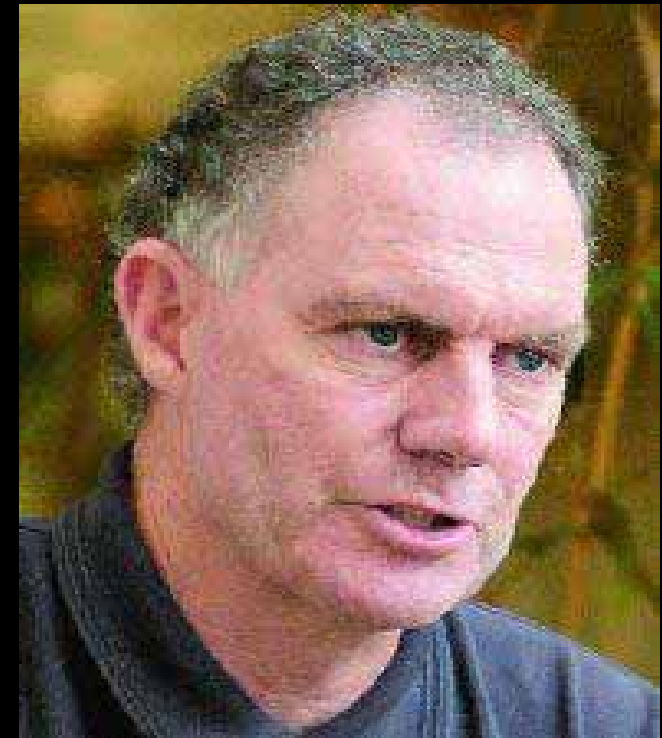
Is it clinically relevant?





Gatiflox or
Moxiflox

Is one superior than
the other?



Preservative Vs Unpreserved

- Play a key role in maintaining the sterility of topical antibiotics (Ab)
- Protect from bacterial, fungal and protozoan contamination
- Prevent decomposition of the drug in room or higher temp
- Increases the overall effect of the Ab

Preservatives

- Toxicity to the delicate ocular surface
- Diffuse punctate keratitis to epi erosions
- Chronic use can lead to chronic conj inflammation and scarring
- Effect worse in dry eye patients

BAK

- Most commonly used
- Low concentration in gatiflox (0.005%)
- Ofloxacin, lumigan (0.005%)
- Xalatan(0.020%)



Gatiflox

☞ gatiflox killed all strains of filamentous fungi and yeasts to a greater extent than Moxiflox

Reeves and Rupp – Allergan Micro Lab

ARVO – April 2004

- Reduces the potential for contamination

Moxifloxacin

- Significant potency of the drug - self preserved
- No ocular surface damage
- Implication in frequent dosing and pre LASIK

Moxiflox

- Preservative efficacy test
- FDA approves after USP tests
- Over 50 USP preservative efficacy tests over 3 years --- meets and exceeds all FDA requirements and USP standards without the need for BAK

Moxi

- Challenges with Pseudomonas, staph aureous, acanthamoeba , nocardia- showed acceptable killing
- Schlech et al , Micro lag, Alcon
- Poster in ARVO April 2004

Gati Vs Moxi

- How long can a bottle be used in a tropical country
- More studies required
- Not to forget the advantage of the preserved and unpreserved molecule
- **BEST TO JUDGE** on individual case basis.

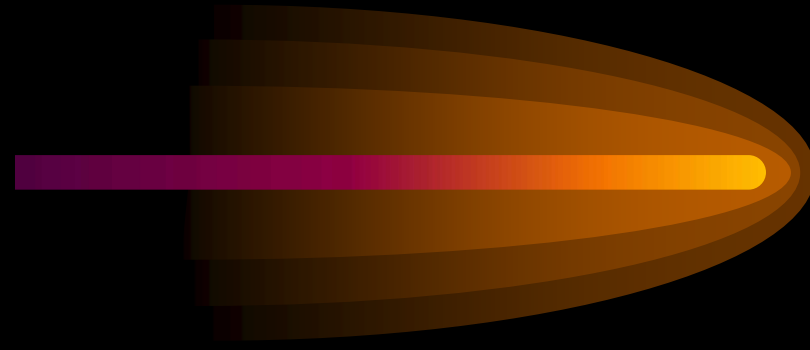
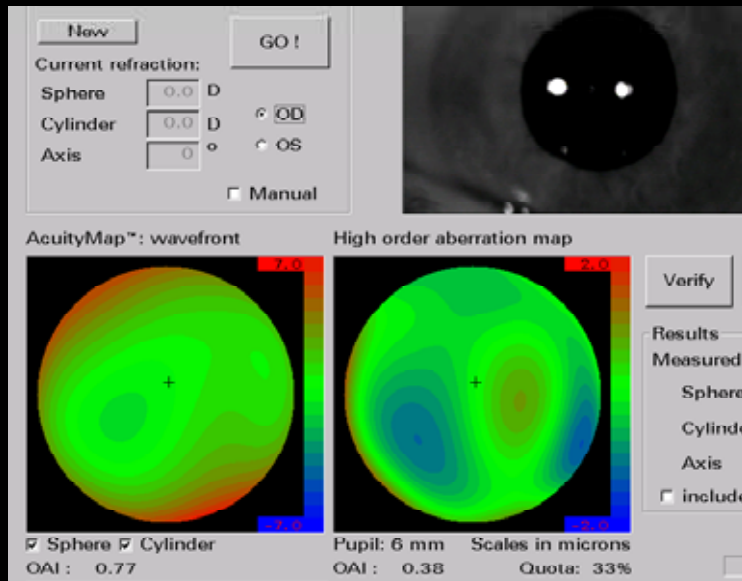
Tolerability and drug toxicity

- Gatiflox showed greater tolerability
- *Donnefeld et al* Current medical research and opinion vol 20, 2004: 1753-58
 - * less conjunctival hyperemia, stinging and burning
 - * moxi showed pupil miosis

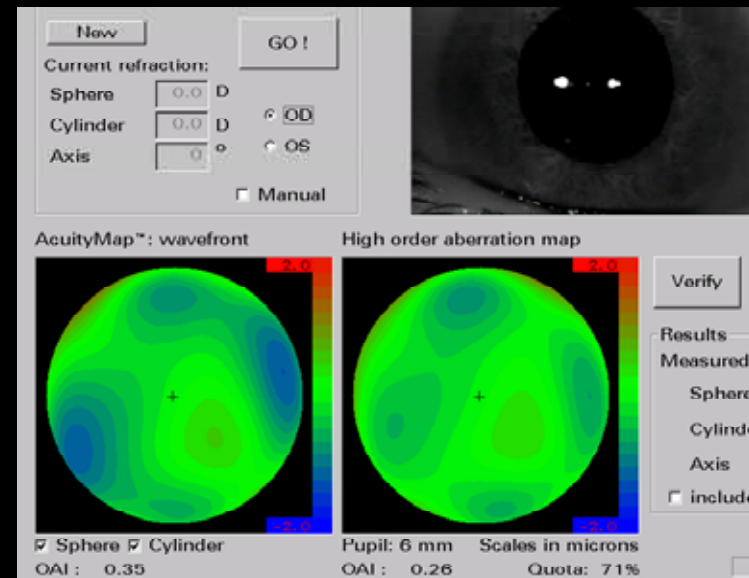
Toxicity

- ?? Moxi released prostaglandins due to higher concentration (0.5% vs 0.3%)
- Miosis IF TRUE = bad news
- Problem in cataract surgery
- Concentration issue in LASIK
- Altered wave front measurement

Pre-Op Patient 2



Post-Op 1 Week Patient 2



Toxicity

- *Nguyen et al – ARVO 2004*
- Poster : 10 subjects
- No difference between the 2

Durrie and Tratter Jour Ocular Pharm and Ther June 2005 , 21: 236-41

No difference for LASIK and LASEK for 1 week

Gati Vs Moxi

- ARVO 2003 : moxi was used for new born Conjunctivitis from 0 days 27 days
- Both are tolerated well
- Await more studies to see whether miosis indeed happens
- Our personal experience should help in months to come

MIC₉₀

- Kowalski Am J Ophthalmol 2003 sep
- MIC s for 177 bacterial isolates
- Gati showed lower MIC for G- ve
- Moxi showed for G+ ve
- 4gFQ showed significant lower MIC than 2
- *Ciproflox showed lowest MIC for gram - ve*

Aqueous penetration

- Levine J cataract Refract Surg 2004 oct 30:2177
- In 2004 rabbit study – no difference
- Solomon et al ophthalmology 2005 march
- 52 eyes during cataract sx, double masked prospective study
- Moxi penetrated significantly higher

Aqueous penetration

- Kim et al current research and opinion
2005;1:93-94
- Prospective, randomized double masked 25
pts each gp
- Moxi had significant penetration



AC

- Higher concentration of moxi is likely to be the reason
- In either case both have AC concn more than required

0.3% vs 0.5 %

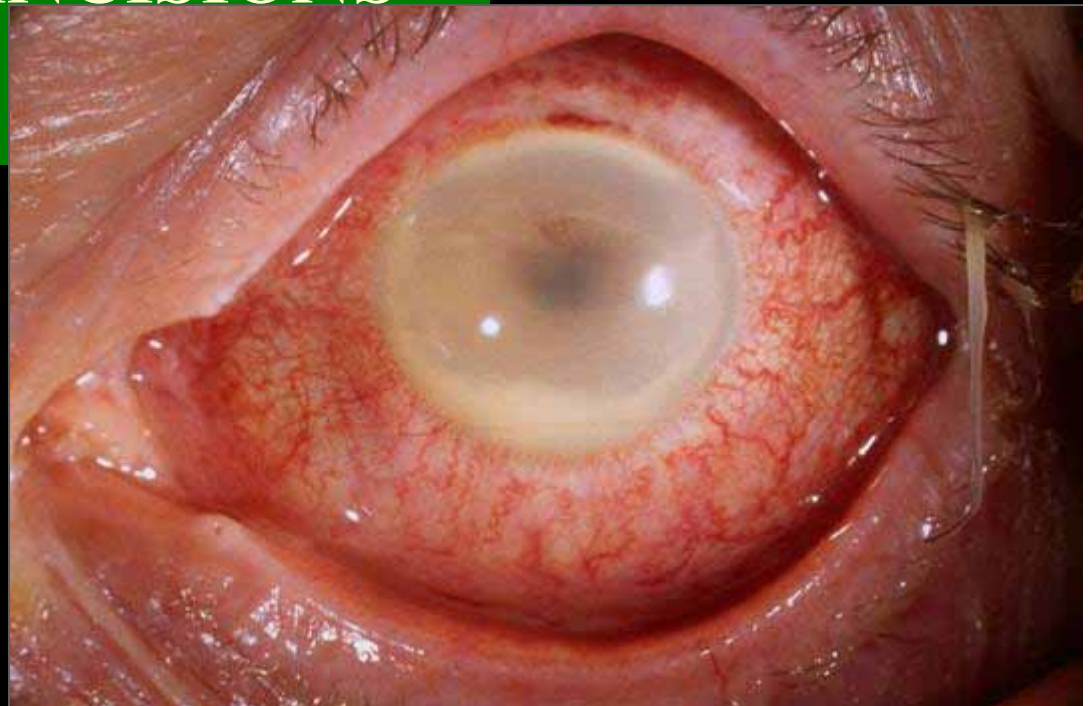
- Most preparations are 0.3%
- Higher concentration- more potency, more toxicity
- Good solubility – allows to make high concentration
- Implications
- Both seem to work

Clinical perspective

- *DO WE need to ROUTINELY USE 4gFQ in our clinical practice for prophylaxis?*

- Endophthalmitis is the devastating complication
- IT HAS INCREASED IN THE LAST DECADE
- CLEAR CORNEAL INCISIONS – RISK FACTOR

surgery



ENDOPH

- Taben et al. Arch Ophthalmol May 2005
- 1963- 2003
- 3 140650 sx, 215 studies chosen
- Overall data 0.128%
- 0.265% 2000-2003
- 0.087% 1990s
- 0.158% 1980s

endophth

- Clear corneal – 0.189%
- 0.074% - scleral incision
- 0.062% - limbal incision

- Endophth has increased in last 10 years
- More with CC incisions

endophth

- McDonnell et al Ophthalmol april 2004
- Dynamic morphology of the CC incisions were studied
- Lab study
- Indian ink on cadaver eyes
- Poor wound apposition with low IOP
- Allowed fluid to enter the eye

CCI

- Increased CCI – learning curve
- Changing Ab resistance
- Recent emphasis on speed
- Less attention to detail, compromised tech
- *Shingleton JCRS 2001- 27:524-27*
- 20% IOP less than 10mm Hg

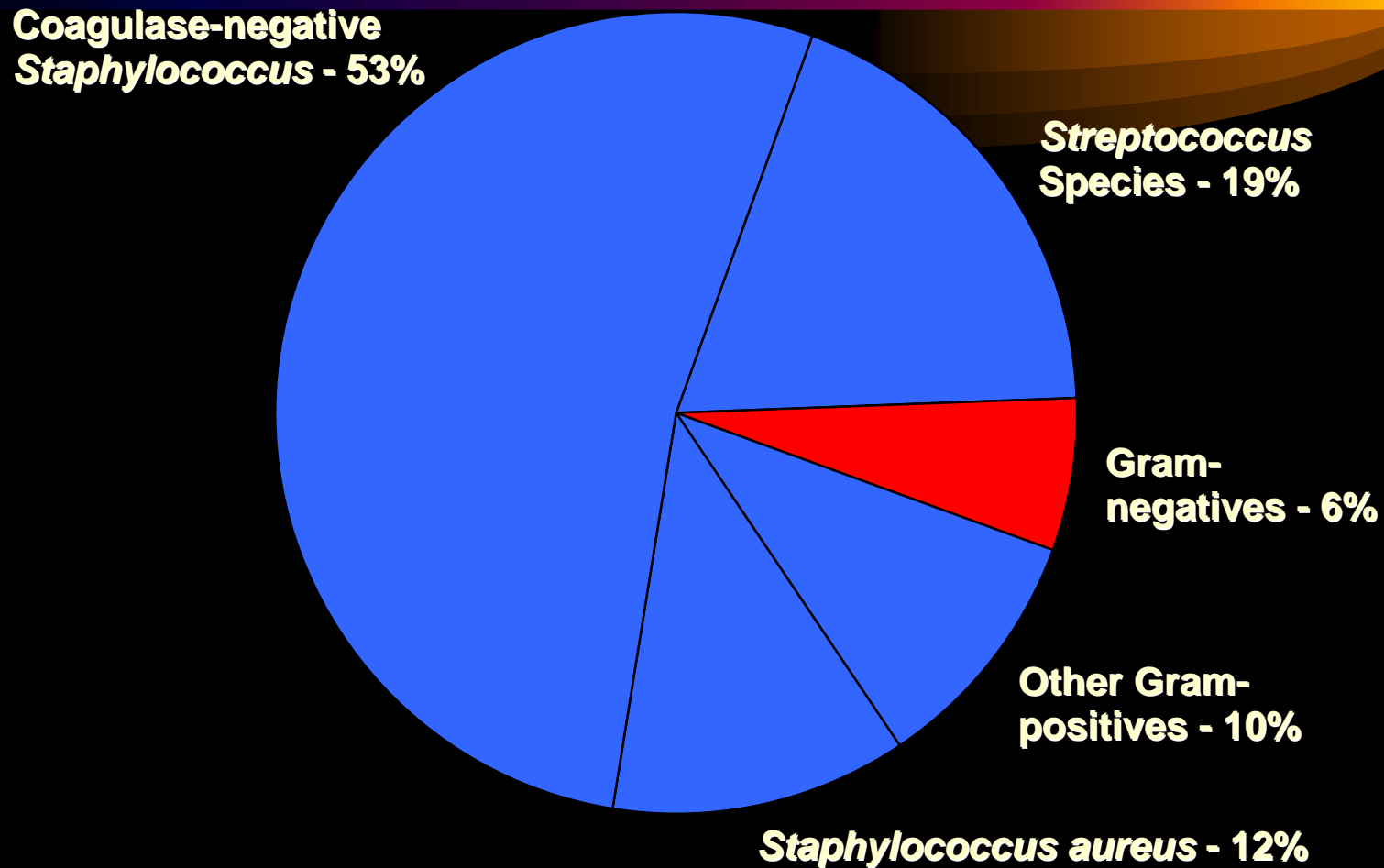
prophylaxis

- Treat pre existing blepharitis
- Pre op drops
- Povidone iodine 5% pre op
- Post op drops
- Intra cameral - cefuroxime
- Sub conj
- oral

Povidone iodine

- 10% skin prep
- 5% conj sac
- Bactericidal, fungicidal, viricidal
- PI and FG work better
- *Serratia* and *Bacillus* PI did not work

*Distribution of Bacteria Isolated From
Endophthalmitis
(1993-2001) (N = 294)*



Role of 4g FQ

- G +ve
- Broad spectrum
- Low MIC
- Faster kill
- Very good AC penetration



prophylaxis



Both gatifloxacin n moxi achieve AC levels in
More than required Concentration

Systemic 4g FQ

- Both achieve excellent concentration in vitreous after oral admin.
- Logical to use for endophthalmitis
- Prophylaxis – not recommended
- Resistance, cost, side effects
- Probably for high risk cases

caution

- Prolong QT interval in ECG
- Hypokalemia
- Anti arrhythmic drugs
- Prolonged QT interval
- Children
- Pregnancy/lactation

?4g FG for prophylaxis

- Rapidly becoming the std of care
- Rarity of resistance
- ? Evidence based
- ?Medico legal implication

Resistance

- Bacterial DNA- super coiled state
- Multiplication- uncoiling, duplication and division
- DNA gyrase – essential for SC and uncoiling
- Topoisomerase IV- breaking duplicated DNA

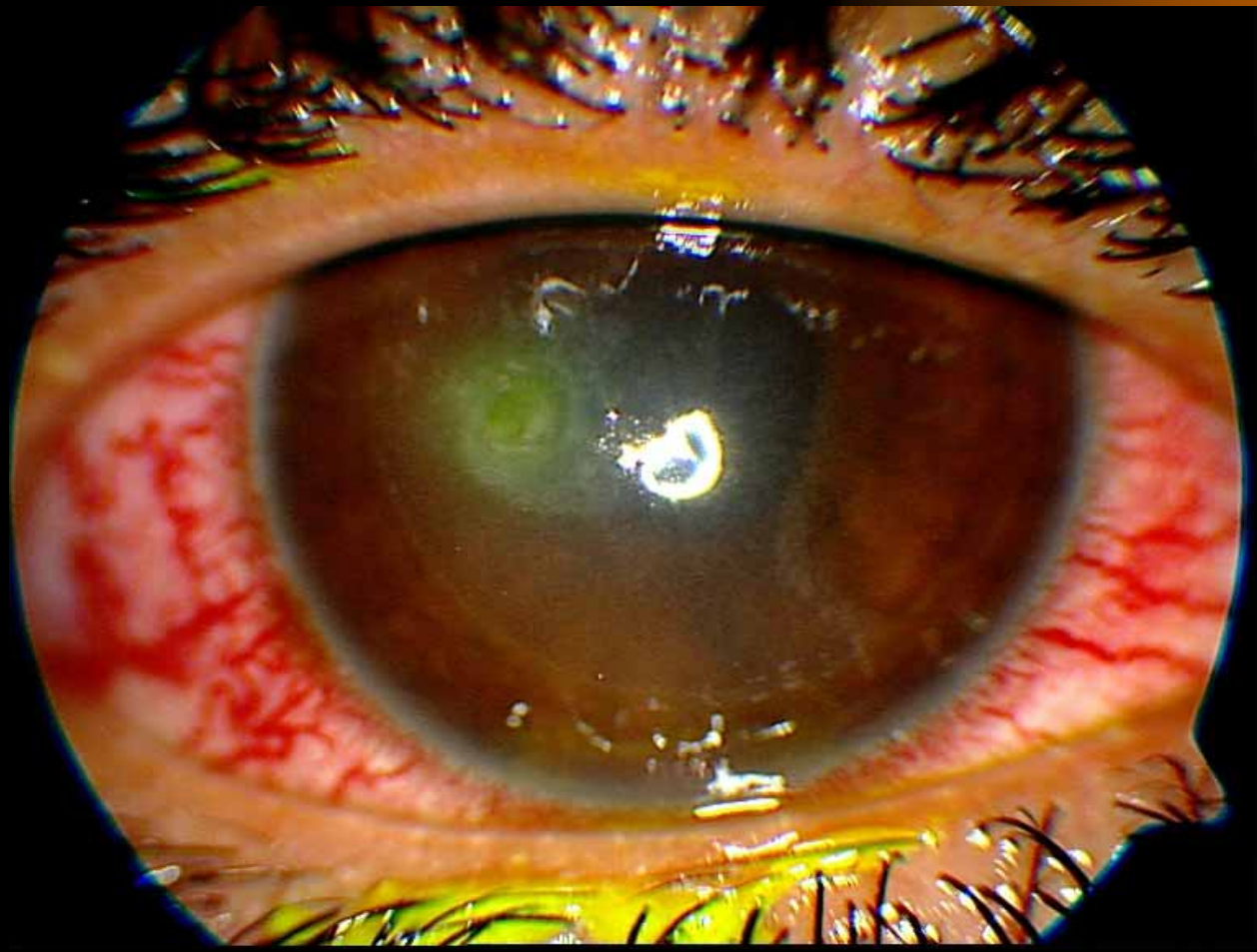
resistance

- Change in target enzyme
- Change in permeability of the organism
- Efflux pump
- Gene conferring resistance

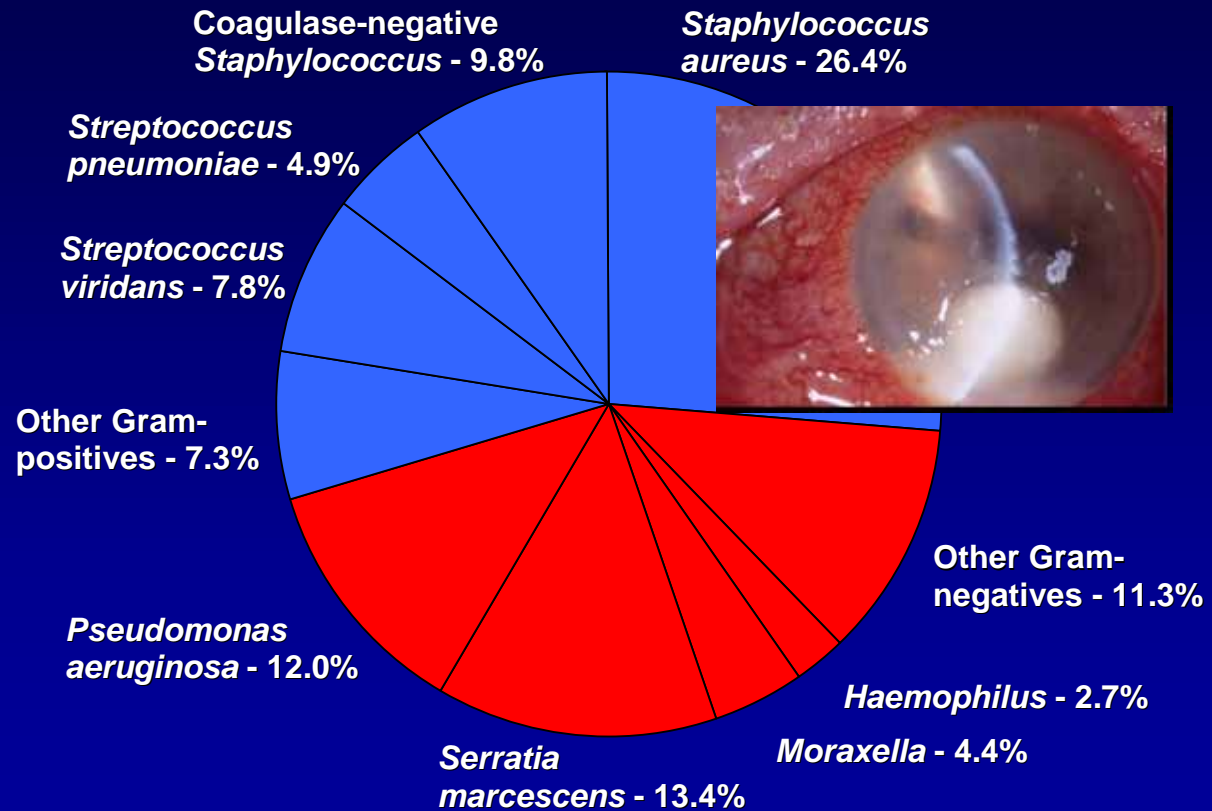
- For 4g FQ 2 mutations required due to 2 target enzymes

Infection

- *Can it be used as empirical mono therapy for ocular surface infections?*
- ?still consider a combination of fortified Abs



Distribution of Bacterial Keratitis (1993-2001) (N = 841)



Kowalski, et al. *Am J Ophthalmol.* 2003. In press.

monotherapy

- Previous \Abs were limited to either +ve or – ve coverage
- Oflox somewhat came closer
- Stept pneumonia was not covered
- Resistance to 3gFQs

Bacterial keratitis

- In vitro supports a broad spectrum including MRSA, ATM, nocardia, strpt pneumonia, PSA

Kowalskii et al Am J Ophthalmol 2003 sep

MIC of 177 isolates

Gatii, moxi, cipro, oflo and levo

Bact Keratitis

- MIC of gati- G -ve better
- MIC for Moxi G +ve
- Cipro demonstrated lowest MIC for G-ve
- Rhee et al Am J Ophthal aug 2004
- In vitro susceptibility for Cipro resistant Pseudomonas
Cipro did well

Bact keratitis

- More clinical studies are required
- Do not forget scrape
- Gram stains and culture
- Probably moxi for +ve
- Gati for – ve
- Cipro still drug of choice for PSA

LASIK

- Can we use 4g FQ as pre & post prophylaxis for LASIK



NTM

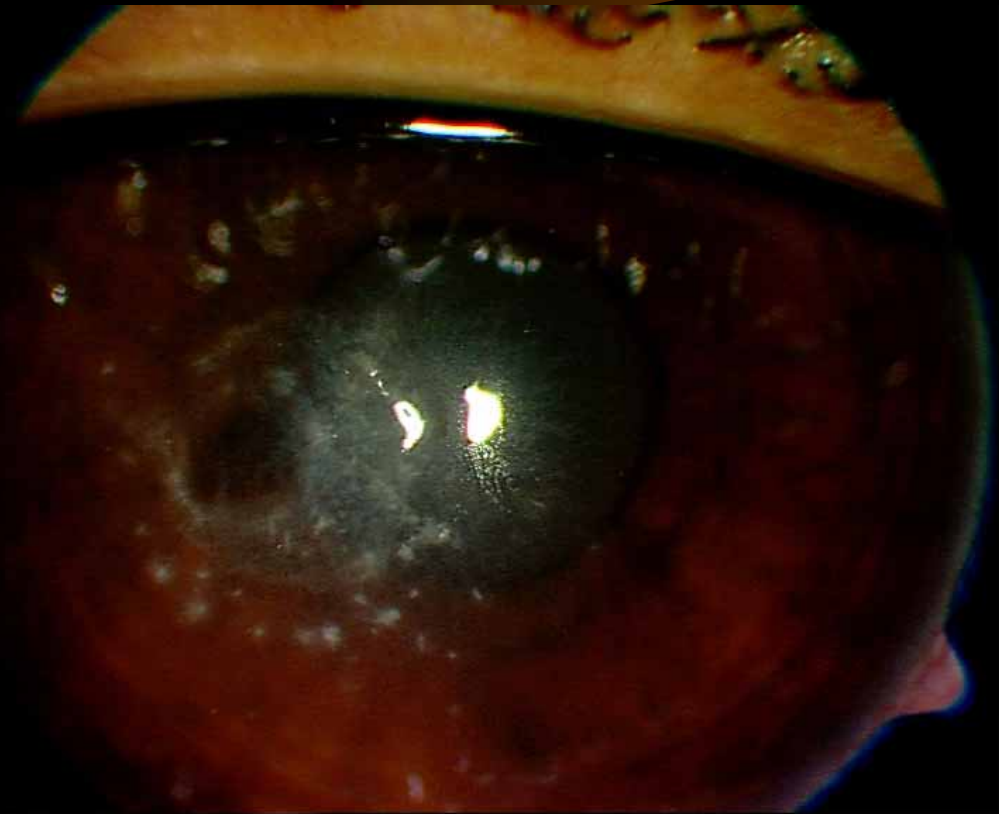
Thomas and velotta

NTM current status

Cornea April 2005

24: 245-55

Medline, culture proven



NTM

- 94 cases
- NTM 53 % all post LASIK infections
- 64% of bacterial infection
- 50 cases
- 14% bilateral
- 3days- 6 months

NTM



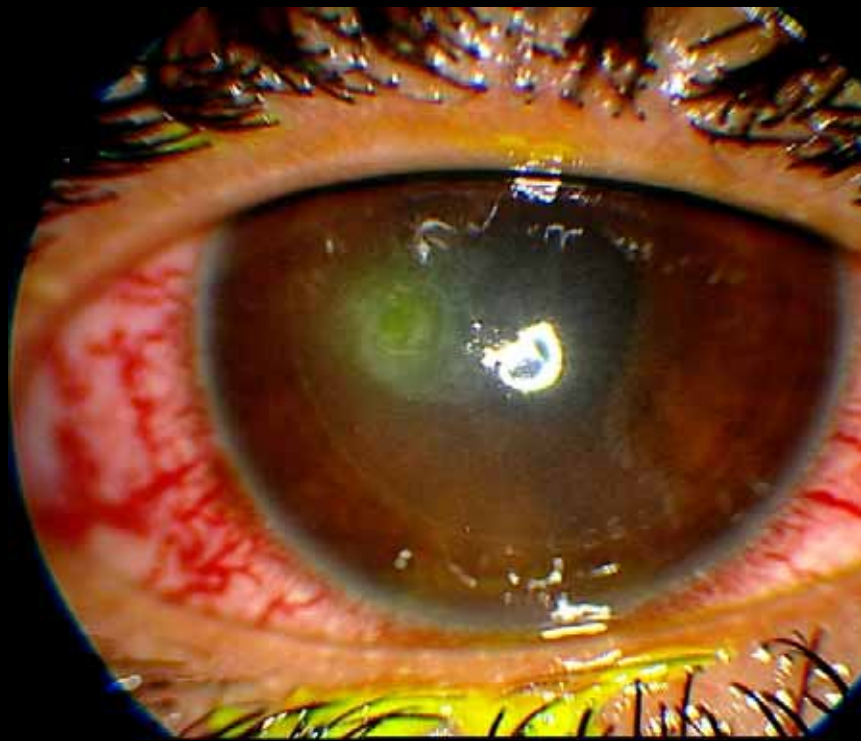
- 86% no predisposing factors
- Trauma
- Flap enhancement
- Prior RK

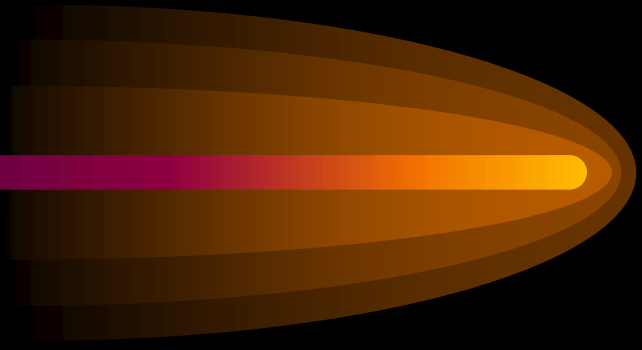
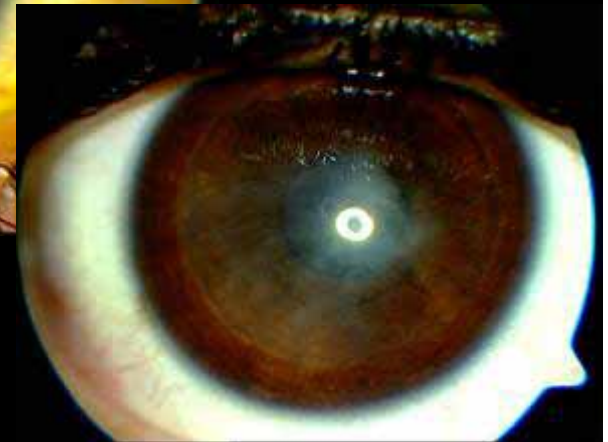
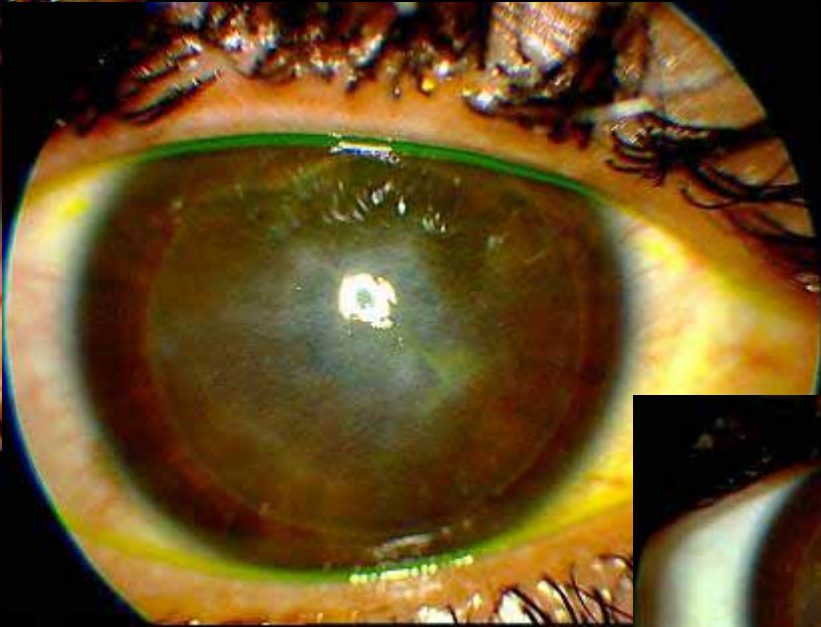
NTM

- No endophthalmitis
- 4 required PKP
- 20/20-20/40 = 54%
- 20/200 = 14%

NTM

- Treatment
- 3 Ab s were used in 50%
- 2 drugs in 24%
- 4 drugs inn 21%





DRUGS IN NTM

- Amikacin
- Clarithromycin
- Ciproflox
- Gati/moxi
- Flap removal

NTM

In vitro studies justify
the use of 4g FQs

Ciproflox still very good
for LASIK prophylaxis

But await clinical results
with these newer agents



SUMMARY

4g FQ definitely better
than 3gFQ

The difference between
Gati and **MOXi** does not
appear to be relevant
clinically

We are probably right
in most of the situation



Thank
you



Good news you
have a definite
case against the
surgeon that did
your LASIK
operation..

Indeed the
Drug has
Penetrated
Well!!