Management

Findings of the Endophthalmitis Vitrectomy Study (EVS) provide guidelines for management of Post-Operative Endophthalmitis

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ENDOPHTHALMITIS VITRECTOMY STUDY

Multicenter randomized trial carried out at 24 centres in U.S. (1990-1994)

Purpose : To determine

- The role of IV antibiotics in the management of POE
- Role of initial vitrectomy in management.

- **Patients :** N = 420 patients having clinical evidence of POE within 6 weeks of cataract surgery

ENDOPHTHALMITIS VITRECTOMY STUDY

Intervention

Random assignment to immediate vitrectomy (VIT) or vitreous biopsy (TAP). They were also randomly assigned to **treatment with IV** or no IV.

Medications :After initial VIT or TAP, all patients received intravitreal injection of amikacin (0.4 mg) + vancomycin (1 mg).

Vancomycin (25 mg in 0.5 ml), ceftazidime (100 mg in 0.5 ml), dexamethasone (6 mg in 0.25 ml) were administered subconjunctivally.

IV treatment: ceftazidime (2 g every 8 hrs) + amikacin (6mg/kg every 12 hrs) for 5-10 days

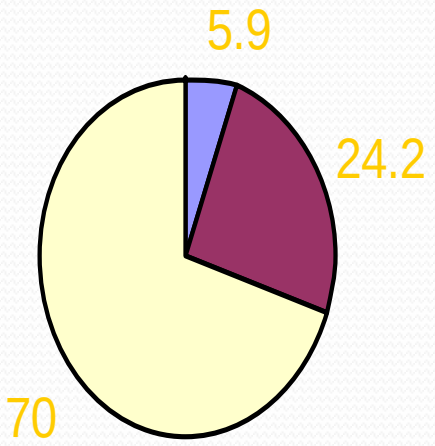
Main outcome measure

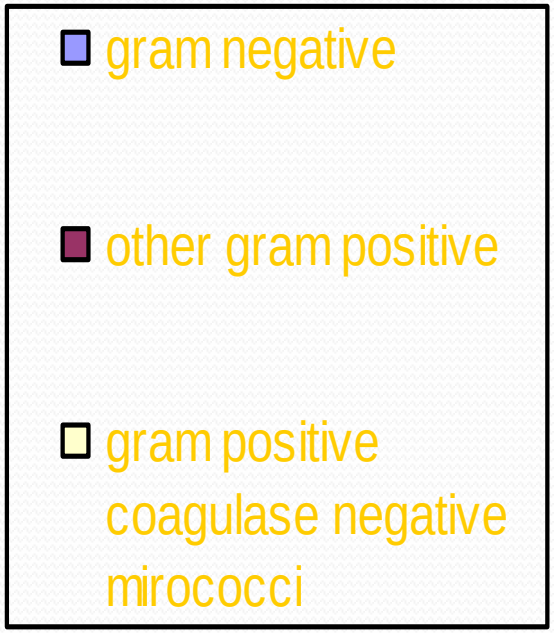
Evaluation of visual acuity and clarity of ocular media at 3, 9, 12 months

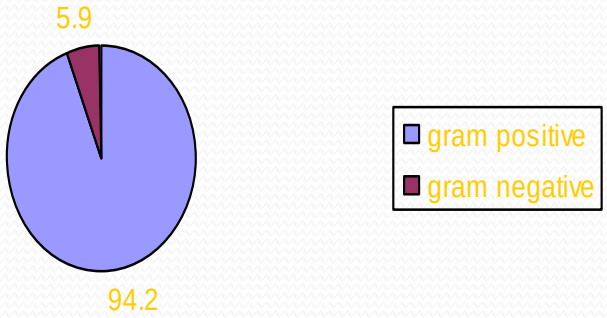
ENDOPHTHALMITIS VITRECTOMY STUDY - RESULT

- In established endophthalmitis, antibiotics when given oral or I.V. have poor penetration into the vitreous cavity.
- Hence, intravitreal injections are treatment of choice.
- Intravitreal injections rapidly achieves therapeutic levels at the sites of infection

SPECTRUM OF ISOLATES FROM EVS







For gram positive organisms

- **Because most cases are caused by gram positive** organisms, vancomycin- (broad-spectrum activity against most gram positive species) has become an agent of choice
- **Thus vancomycin 1 mg in (0.1 ml) is given intravitreally**
- Non toxic in recommended clinical dosage.

Arch Ophth 1999; 117: 1023-1027

RESULTS OF EVS

- Systemic antibiotics were of no benefit in this study
- Initial Vitrectomy was only beneficial for patients presenting with a very poor visual acuity.

For gram negative organisms

- **Gentamicin (0.4 mg) was used, but was found to be associated with retinal toxicity**
- **Amikacin was used (4 times less retinal toxicity than gentamicin as shown by animal studies)**
- Amikacin covers large number of gram negative organisms and those resistant to other aminoglycosides

Management - EVS study

- Etiology : 75% Gram + ve & 6% Gram - ve .
- 20% culture negative
  - Cataract surgery:
    - Entry related : Staphylococcus & Streptococcus
    - Infected phacoemulsifion: Psuedomonas
    - Infected viscoelastic : Bacillus
- Intervention:
  - > PL : AC Tap with intra-vitreal
  - ≤ PL : Core Vitrectomy + Intravitreal antibiotics

- Outcome: of immediate vitrectomy
  - In HM : no change
  - With ≤ PL :
    - 3 fold ↑ V/A of > 20/40
    - 2 fold ↑ V/A of > 20/100
    - 50% ↓incidence of severe visual loss
- Recommendation
  - Intravitreal antibiotics: Vancomycin + Ceftazidime to all eyes
  - Vitreous Tap: Presenting Vision > HM
  - Vitrectomy: Presenting Vision LP
  - Systemic antibiotics: No benefit of IV Amikacin, and Ceftazidime

Initial selection by smear report-

- Gram positive cocci : Cefazolin /Vancomycin
- Gram positive bacilli: Vancomycin
- Gram Negative bacilli/cocci : Amikacin / Ceftazidime
- Fungus: Amphotericin B

- Empirical therapy: for Bacteria
  - Vancomycin 1.0 mg/0.1 mL
  - Ceftazidime 2.25 mg/0.1 mL.
  - Amikacin 400 µg/0.1 mL exchange for ceftazidime
  - VRE : Linezolid 400µg/0.1ml

Empirical therapy: for Fungal

- Amphotericin B (0.005mg/0.1ml) 0.15 to 0.5%

***Vancomycin* combined with *amikacin or ceftazidime* appears to be best association in treatment of POE.**

Complete and Early Vitrectomy for Endophthalmitis

- Why perform vitrectomy: several advantages
  - Increases retinal oxygenation
  - Provides a large specimen
  - Definite treatment
  - Reduces the inflammatory debris
  - Reduces macular complications
  - Direct inspection of the retina
  - Better availability of pharmacological agents to the retina
  - Accelerating visual rehabilitation

Why Perform Early Vitrectomy?

- Early surgical intervention: advantageous
  - Allows immediate treatment
  - Prophylactic measure, preventing complications
  - Improved visibility : ↓ risk of surgery

Why Perform Complete Vitrectomy?

- Complete vitrectomy: advantageous
  - Removal of macular debris

Role of silicone oil

- Routine use of silicone oil: not recommended
- unique advantages:
  - Bacteria do not multiply in silicone oil
  - Silicone oil treats RRD
  - Better visualization in post-op

STEROIDS

- Based on experimental studies in rabbits, an intravitreal injection of 0.2-0.4 mg of dexamethasone was recommended within first 10 hrs after inoculation (except when fungal infection is suspected)

B J O 1997; 81: 1006-51

Confusion???

- How many IV
- When vit
- Topical and other meds
- When to stop

Intravitreal Antibiotics: modification based on -

- Organisms isolated
- Sensitivity pattern
- Clinical response

Repeat intravitreal injection

(Preferably single antibiotics)

- No/ inadequate response to 1st inj.
- Only if repeat culture is positive

Monitor clinical course every 4-6 hours

- Stable / improvement - continue medical therapy
- Worsening - vitrectomy

VITRECTOMY

- Absent fundus glow
- No response to medical treatment
- Suspected fungal infection
- To clear media opacity

VITRECTOMY

- General/ Local anesthesia
- Standard 3 port technique
- Collection of the vitreous specimen
- Limited core vitrectomy
- Intravit. inj. of antimicrobials $\pm$ steroids

POST OPERATIVE

- Close watch for improvement in symptoms (pain)
- Analgesics, if necessary
- Topical / systemic- antibiotics / antifungals/ steroids
- Topical cycloplegics, AGM
- Repeat AC tap & intravitreal injection if :
  - Persistent inflammation
  - Recurrent vitreous fibrin
  - Persistent media opacity

Prognostic factors

- Presenting visual acuity
- Culture positivity
- Type / virulence / sensitivity of organisms
- Duration of infection / precipitating factors
- Host response
- Associated RD / macular edema

ROLE OF PROPHYLACTIC ANTIBIOTICS

Studies have shown that prophylactic antibiotic reduces the number of conjunctival bacteria at the time of surgery

- Optimal choice of pre-operative topical antibiotic depends on spectrum of bacteria covered
  - Rapidity of killing
  - Duration of action
  - Penetration and toxicity of antibiotic
  - Antibiotic susceptibility pattern
  - Cost

Prophylaxis: 3 days pre-op

"What I am trying to accomplish with 3 days of preoperative antibiotics is 2-fold: first, to minimize the inoculum, have the fewest number of organisms on the field (including the conjunctiva, lids, and lashes); second, I try to get the maximum penetration into the eye so that in case any pathogens were inoculated at the time of surgery, there were bactericidal levels ready to kill them. With gatifloxacin, there is enough drug to treat both, beginning 3 days preop and continuing 1 week postop."

Dr. Calvin W. Roberts, MD

Professor, Dept. of Ophthalmology, Joan and Sanford T. Weill Medical College of Cornell University, New York

Prophylaxis: On day of surgery

"I don't start preoperative antibiotics until the patient arrives on the day of surgery. The drops are given 15 mins apart, starting 2 hrs prior to surgery. An antibiotic is administered immediately at the conclusion of surgery, every hour while the patient is awake for the first day, and then 4 times per day afterwards for a week. The reason I don't use several days of pre-operative antibiotics is the potential risk of propagating resistant bacteria, which may then cause problems, including endophthalmitis."

Dr. Francis S. Mah

Asst. Prof. Of Ophthalmology

Co-director of the Charles T. Campbell Ophthalmic Microbiology Laboratory

3 days vs 1 hr pre-op use of fluoroquinolones

Aim: To determine the efficacy of reducing conjunctival bacterial flora with topical fluoroquinolone (Ofloxacin) when given for 3 days compared to 1 hour before surgery.

Methods

89 patients (92 eyes)

Study group (44 eyes)

1 drop q.i.d for three days + 1 drop every 5 mins, 1 hour prior to surgery

Control group (48 eyes)

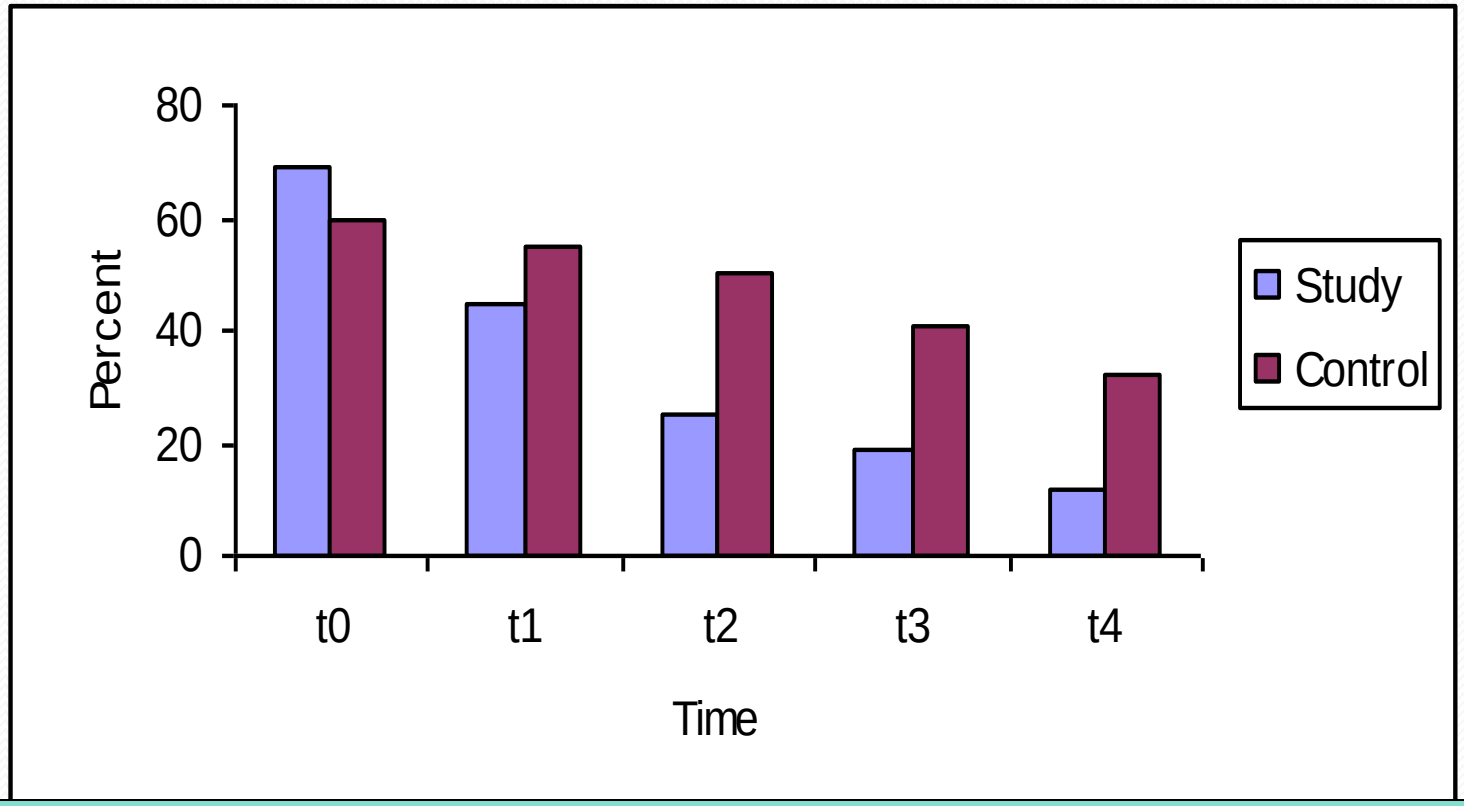
1 drop every 5 mins, 1 hour prior to surgery

All patients: a scrub of 5% povidone iodine for a minute + 2 drops of 5% povidone iodine

Conjunctival cultures obtained and inoculated

Ophthalmol 2002; 109: 2036-41

Percent of positive conjunctival culture

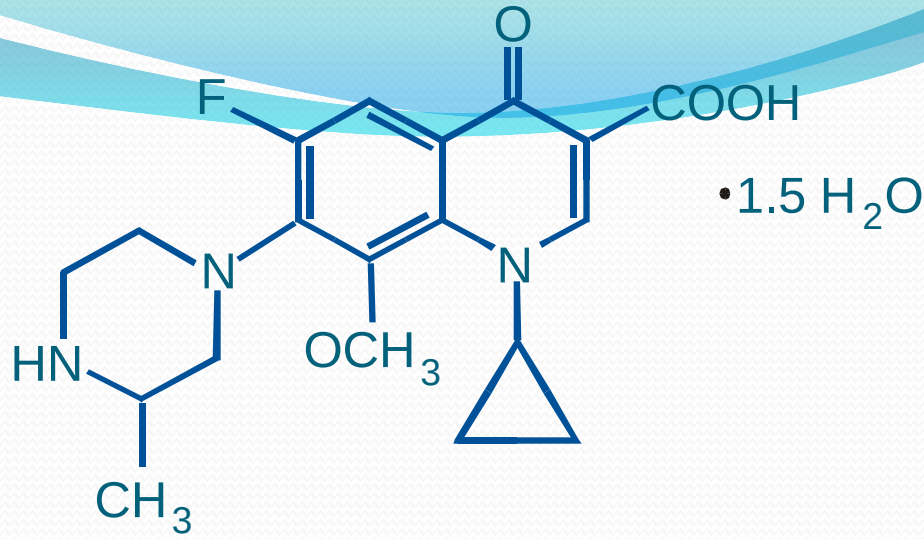


The application of topical fluoroquinolone for 3 days before surgery appears to be more effective in eliminating bacteria from conjunctiva than application 1 hour before surgery

3rd generation fluoroquinolones (Ciprofloxacin, Ofloxacin): widely used as prophylactic agents

Topical fluoroquinolones are commonly used prophylactic agents because of their broad spectrum of activity covering the majority of these pathogens found in endophthalmitis

A new generation to treat infection



- The fourth generation fluoroquinolones like gatifloxacin, moxifloxacin have enhanced activity against gram positive pathogens.
- Organisms resistant to earlier gen FQs are susceptible to fourth gen FQs
- Secondly they are less prone to encourage development of resistant strains

Surv Oph 2004,49 (2),S55-61

Potential role of 4th gen FQs

- In terms of forestalling the development of resistance, primary use of 4th gen FQs may actually be a better strategy than initial use of older FQs

- Conventional strategy of reserving the use of newer anti-microbial only when older anti-microbial fails may not be a wise strategy if applied to FQs

Dr. Francis S. Mah, MD

Asst. Prof. Of Ophthalmology

Co-director of the Charles T. Campbell Ophthalmic Microbiology Laboratory

"Use of these currently-available, weaker agents (i.e. ciprofloxacin, ofloxacin, and levofloxacin) will only facilitate the continued development of resistant strains. Immediate use of the fourth generation should eradicate the more resistant bacteria along with those that have yet to develop resistance."

Aim : To study *in vitro* potency of 2nd, 3rd, 4th generation fq's for: bacterial endophthalmitis isolates

Results	CIP	OFX	GAT	MOX	Potency by Rank (p=.05)
2nd Gen FQ-Res SA	64	64	3.5	1.75	mox>gat>cip =ofx
2nd Gen FQ-Sen SA	.32	.63	.11	.06	mox>gat>cip >ofx
CoagNeg Staph FQ	64	64	2.0	2.5	mox=gat>cip =ofx
CoagNeg. Staph FQ	.13	.38	.09	.05	mox>gat=cip > ofx
Strep. pneumoniae	.75	2.0	.22	.09	Mox>gat=cip >ofx
Gram-negatives	.06	.19	.06	.08	Cip=gat=mox > ofx

***In vitro* study suggests that the 4th generation FQ are more potent than the 2nd and 3rd generation FQ for gram-positives and equally as potent for gram-negatives.**

The 4th gen FQ appear to cover 2nd and 3rd generation FQ resistance

Am J Ophthalmol. 2002 Apr;133(4):463-6

INCREASING FLUOROQUINOLONE RESISTANCE

- A number of recent studies have reported emerging resistance to fq's among ocular isolates particularly among gram positive organisms
- In recent years, up to 30% or more of *S. aureus* strains are found to be fluoroquinolone resistant

Surv Ophth 2004; 49(2): 579-583

ESCRS guidelines for endophthalmitis 2013

The new ESCRS guidelines provide cataract surgeons with easy-to-follow, step by-step procedures that they can readily adapt to their daily practice.

Prophylaxis guidelines for endophthalmitis

- Consider using topical quinolone for 24to 48 hrs before surgery
- And apply topical quinolone (same type) to cornea or conjunctiva with one drop one hour prior to surgery and one drop prior to surgery.
- It is mandatory to apply one drop povidone iodine 5% or 10 ml povidone iodine 5% on a sponge pad , or aq. Chlorhexidine 0.05%, to the cornea and conjunctival sac for a minimum of 3 min. prior to surgery- Apply 10% povidone iodine Chlorhexidine 0.05%,to the periorbital area in the OT as skin antiseptics, and allow to spill over into the conjunctival sac.
- Surgeons washes hand with antiseptic soap solution (povidone iodine or Chlorhexidine)gowns up and wears sterile gloves and a mask.
- Check that theatre air flow is running and that doors are closed.
- Apply surgical drapes and taping of eyelids to remove eyelashes from the surgical field (do not cut eye lashes)

- Perform phacoemulsification surgery . Consider using foldable IOLs that can be inserted through a sterile injector.

- Apply 1 mg cefuroxime in 0.1ml saline (0.9%)by intra cameral injection at the end of surgery. This is unlicensed use of cefuroxime given at the surgeon's discretion .

- Use of vancomycin (or gentamycin) in the irrigation field or by intra cameral injection is not proven and is not encouraged.

- Reapply topical quinolone (same type) at the end of surgery as one drop stat. one drop 5 min later and one drop 5 min later again

Prophylaxis

- Pre-operative scrub -Povidone-iodine (5%) has
  - broad antibacterial, as well as antifungal & antiviral activity
  - It decreases conjunctival flora growth to 91%
  - Can destroy bacteria in 30 secs

DIAGNOSTIC GUIDELINES FOR ACUTE VIRULENT ENDOPHTHALMITIS

Observe patient for :

- Pain
- Blurring or loss of vision
- Swollen Lids
- Inflammed /edematous conjunctiva
- Discharge into conjunctiva
- Corneal edema (Infiltrates/ Ring abscess)
- Cloudy anterior chamber with cells/hypopyon/ fibrin clot
- Afferent pupillary defect
- Vitreous clouding (Vitritis) from inflammation precluding view of retinal vs
- Involvement of posterior segment – retinitis/ retinal periphlebitis/ retinal edema/papillary edema
- Absent red reflex

Check B-scan ultrasonography – vitritis/retinal detachment
Especially useful in eye with opaque media

MAKE A CLINICAL DIAGNOSIS OF ENDOPHTHALMITIS
(with photography if possible)

BEWARE OF DELAYING THE DIAGNOSIS WITH A TRIAL OF CORTICOSTEROID DROPS

THIS IS A MEDICAL EMERGENCY

PERFORM AN INTRAVITREAL TAP WITHIN ONE HOUR

Pefrorm vitreous tap in OT using the vitrector/ portable vitrector (BD Visitech in OPD clinic)

TREATMENT GIUDELINES FOR ACUTE VIRULENT ENDOPHTHALMITIS (Presumed and not proven)

- Make clinical diagnosis of Endophthalmitis
- Pefrorm aqueous and vitreous tap/or vitrectomy (pars plana approach), to collect samples for Gram stain/culture/PCR
- Inject antibiotics emperically into vitreous using a combination of either Vancomycin 1 mg/ 0.1 ml & ceftazidime 2 mg /0.1 ml (First Choice) or Amikacin 250 mcg /0.1 mland ceftazidime 2 mg /0.1 ml (second choice)
- USE A SEPARATE SYRINGE & 30G NEEDLE FOR EACH DRUG AND DO NOT MIX DRUGS TOGETHER IN THE SAME SYRINGE.
- DO NOT point the needle towards the retina but forwards instead and inject very slowly into mid-vitreous.

- Inject dexamethasone 400 mcg (preservative free)/0.1 ml into the vitreous at the same time
- For acute virulent endophthalmitis begin adjunctive systemic therapy with the same antibiotics as those used intrvitreally for 48 hrs to maintain higher levels in posterior segment.
- Consider beginning systemic therapy with corticosteroids (prednisolone 1 mg /kg/day)
- Consider referral to a vitreoretinal surgeon for an opinion on full vitrectomy

Diagnostic guidelines for chronic endophthalmitis

Observe patient for

- Pain
- Blurring or lossof vision
- Cloudy ant.chamber with cells
- Recurrent hypopyon uveitis that fails to respond to corticosteroids
- Plaque in the capsular bag (saccular or granulamatous endophthalmitis)
- Vitreous clouding (vitritis) from chronic inflammation reducing a view of retinal vessels

- Ckeck B-scan USG for vitritis and retinal detachment

- Make a clinical Diagnosis of Chronic Endophthalmitis

- Investigate for a Microbial Source
  - Pefrom an Anterior Chamber Tap (Gram stain/Culture / PCR)
  - Perform a vitreous tap , if vitriis (Gram stain/Culture / PCR)
  - If a decision is made to remove the IOL , then collect and send the capsule fragments to the microbiologist and to histopathologist for paraffin-section based Gram stained films .Also collect sample into glutraldehyde to perform electron microscopy (identify intra-cellular bacteria)

TREATMENT OF CHRONIC ENDOPHTHTHALMITIS

- Delayed-onset (or indolent) endophthalmitis - *Propionibacterium acnes* (which often has a granulomatous inflammation and capsular plaque) or fungal pathogens.

- Initial treatment - with vitreous tap and injection of intravitreal antibiotics

- *P. acnes* infection - intravitreal & in the bag vancomycin /
  - vitrectomy with IOL explant and complete capsulectomy.

- Bleb-associated infections
  - Grade 1 (infection limited to bleb) and grade 2 (involvement of anterior chamber) blebitis can be initially managed with **intense topical treatment (either topical fluoroquinolone every two hours or hourly fortified vancomycin and tobramycin) and oral moxifloxacin.**
  - Grade 3 (involve vitreous cavity) are treated as any other postoperative infection.

INTRAVITREAL DRUGS

- **ALWAYS** have a chosen empirical regime of antibiotics ready in advance for intravitreal use in a clinic or OT setting.

- Have instructions prepared for making-up correct dilutions and have necessary sterile equipment (bottles and syringes) available within the operating theatre

DILUTION OF INTRAVITREAL DRUG

NAME OF DRUGS	DILUTE	METHOD OF DILUTION	STEPS OF DILUTION IN 1 ML SYRINGE
AMPHOTERICIN –B (50 mg) Intravit dosage 5 mcg	10 ml (only distill water)	**Double dilution**	
AMIKACIN (250 MG) Intravit dosage 250 mcg	-	**Double dilution** if decadron second dilution with decadron	
VANCOMYCIN (500 mg) Intravit dosage 1 mg	5 ml	**Single Dilution**	
FORTUM (1 g) (Ceftazidime) Intravit dosage 2.25 mg	4 ml	**Single Dilution** If decadron directly dilute with decadron	
VORICONAZOLE (200 mg) Intravit dosage 50 mcg	19 ml	**One & Half Dilution**	
GENTAMYCIN (80 mg) Intravit dose 80 mcg		**Double Dilution**	
CIPLOX (200 mg) Intravit Dosage		**No Dilution**	Take 0.1 ml and inject

PORTABLE VITRECTOR

PORTABLE VITRECTORS

Office-based vitrectomy and can run on battery power.

The first vitrector designed for office use was the Visitrec (Beaver Visitec, Waltham, MA), designed by Robert Josephberg and introduced in 1994.

This concept gradually transformed into the now commercially available Intrector (Insight Instruments, Inc., Stuart, FL).

The Intrector is a 1,200-cuts-per-minute (CPM) guillotine-style vitrector with dual-lumen 23-gauge probe.

The probe contains a central infusion channel and peripheral aspiration/cutter channel connected to a 3-mL syringe for manual aspiration

How to prevent medico-legal in aspects in post-operative endophthalmitis

- The main pre-operative medico-legal issues are ;

- **Patient assessment**
  - Detailed documentation of medical & ophthalmic history, and consultations or referrals in medical record.
  - Pre-existing medical conditions (diabetes / hypertention)
  - Ophthalmic conditions (Blocked tear duct)
  - Visual acuity assessment
  - Careful & complete ocular examination (Blepharitis/ Retinal detachment)
  - Determination of correct intraocular lens

- **Informed Consent** – explained risks/hazards / complications of surgical procedure

- Post-operative issues
  - Properly inform pts of complications in post-opertive or post-discharge period specifically about clinical signs & symptoms that require immedaite assessment.
  - Arrange adequate follow-up care for patients after surgery

- Discharge card

  It is an important documentatry evidence against the doctor so due importance should be given in writing the discharge summary.

  It should always include
  - instructions to be followed by the patient after his discharge
  - instructions about the follow-up visits
  - Situations the patient report to doctor immediately.

Thank You