

Endophthalmitis

Disclaimer: This Clinical Practice Guideline ('CPG') was written for use in The Royal Victorian Eye and Ear Hospital Emergency Department. It should be used under the guidance of an Ophthalmology or ENT registrar. If clinical advice is required, please contact the Eye and Ear Admitting Officer for assistance: EYE: +61 3 9929 8033; ENT: +61 3 9929 8032. Links to internal Eye and Ear documents cannot be accessed from the website CPG.

See also: Intravitreal Injection Procedure for the Treatment of Endophthalmitis in the Emergency Department, Appendix 1: Preparation and Reconstitution of Intravitreal Injections for the Treatment of Endophthalmitis

Description:

Endophthalmitis is inflammation involving both the anterior and posterior segments of the eye. It is most commonly infectious in origin. Infectious endophthalmitis can be exogenous, or less commonly, endogenous. Post-operative, infectious endophthalmitis following an intraocular procedure is classified as acute if diagnosed within 6 weeks of the procedure or chronic (delayed onset) if it occurs after six weeks. Non-infectious sterile endophthalmitis is rare.

IMPORTANT: target time from presentation to intravitreal tap and injection ('door to needle') is \leq 60 minutes.

Red Flags:

- Acute, infectious endophthalmitis is an **ophthalmic emergency** that requires immediate intervention. Suspect in any patient with pain, decreased vision, intraocular inflammation and a history of:
 - Recent intraocular ophthalmic procedure (eg. cataract surgery, intravitreal injection)
 - Ocular trauma
 - Previous glaucoma filtering surgery with bleb
- Consider endogenous endophthalmitis. Ask if there has been a current or recent history of fevers, sepsis, malaise, intravenous drug use or of a concurrent systemic infection.
- Non-infectious (sterile) endophthalmitis is a diagnosis of exclusion

How to Assess:

Aetiology:

- Infectious:
 - Exogenous: recent history of intraocular surgery (most commonly 3-7 days post-surgery, but can be earlier or later), intravitreal injection, penetrating ocular trauma, previous glaucoma filtering surgery.
 - Endogenous: immunosuppressed, diabetic, indwelling catheters (eg. urinary catheter or peripherally inserted central catheter (PICC) line), intravenous drug use
- Non-infectious (sterile):
 - Acute post-operative inflammatory reaction to non-infectious substances introduced to the anterior chamber during surgery: Toxic anterior segment syndrome (TASS). Typically presents within 24 hours of surgery with painless, limbus-to-limbus corneal oedema, marked anterior chamber inflammation +/- hypopyon, increased intraocular pressure, a dilated or irregular pupil and absent vitreous inflammation. TASS responds to intensive topical steroids.
- Differential Diagnosis:
 - Uveitis related to conditions such as sarcoidosis, Beçhet's, Herpetic disease
 - Masquerade syndromes such as: leukemia, intraocular lymphoma, etc

History:

- Symptoms: pain, decreased vision, redness and photophobia. Pain is more characteristic of endophthalmitis, whereas TASS is usually painless.

Examination:

- Eyelid oedema
- Conjunctival chemosis, injection
- Anterior segment:
 - Corneal oedema
 - Anterior chamber: cells, flare, fibrin, hypopyon
- Posterior segment:
 - Vitreous cells
 - Progressive vitritis
 - Presence of "string of pearls" (Candida spp.)
 - Retinitis and periphlebitis
 - **Note:** there may be no view of the retina if there is significant corneal oedema, anterior chamber fibrin or vitritis.

Investigations

- B-Scan ultrasound of the posterior segment to look for vitritis, if examination with a fundus lens or indirect ophthalmoscopy is not possible

Acute Management:

Note: target time from presentation to intravitreal tap and injection ('door to needle') is \leq 60 minutes

Post-operative/exogenous infective endophthalmitis suspected:

- Discuss with Admitting Officer (AO) +/- Vitreoretinal (VR) fellow to confirm need for tap and inject
- Complete consent form (MR45/MR159)
- Anterior chamber paracentesis and vitreous aspiration for microscopy, cultures and sensitivities, followed by intravitreal injections of ceftazidime (2 mg/0.1 ml), vancomycin (1 mg/0.1 ml) and dexamethasone (400 mcg/0.1 ml) (see Intravitreal Injection Procedure for the Treatment of Endophthalmitis – Emergency Department) Also see: Appendix 1: Preparation and Reconstitution of Intravitreal Injections for the Treatment of Endophthalmitis
- Be aware of risks of intravitreal injection for the treatment of endophthalmitis:
 - Retinal detachment
 - Acute IOP rise
 - Vitreous haemorrhage
- Admit the patient under the VR unit after discussion with the VR fellow
- Ongoing topical treatment
 - Prednefrin Forte® 1 drop every 1-2 hours while awake
 - Atropine 1% 1 drop bd,
 - Chloramphenicol 0.5% 1 drop qid
 - Substitute g.ofloxacin 0.3% hourly (day +/- night) for chloramphenicol if corneal/scleral wound, bleb/corneal infection is suspected
 - Oral ciprofloxacin 750 mg BD for 5-7 days. Reduce dose in renal impairment (Calculated Creatinine Clearance <50mL/min)

Endogenous endophthalmitis suspected:

- Discuss with AO and Medical Retina/Ocular Immunology fellow
- Immediate anterior chamber paracentesis and vitreous aspiration for microscopy, cultures and sensitivities. If viral aetiology suspected, viral PCR should also be requested.
- Intravitreal injections depending on suspected aetiology
 - Bacterial: intravitreal 2mg/0.1mL ceftazidime, 1mg/0.1mL vancomycin
 - Fungal endophthalmitis: intravitreal 100mcg/0.1mL voriconazole
 - Viral endophthalmitis: intravitreal 2.4mg/0.1mL foscarnet
- Consult Infectious Disease (ID) department at St Vincent's Hospital
 - Discuss appropriate empiric systemic antibiotic treatment depending on suspected aetiology, until culture results are available.
 - If sepsis/medically unwell, may require transfer to St Vincent's Hospital
- Systemic work-up based on clinical suspicion
 - Baseline FBE, UEC, LFTs and BSL
 - Consider cultures: blood, urine, indwelling catheter etc
- Admit Medical Retina/ Ocular immunology Unit

Appendices:

Appendix 1: [Preparation and Reconstitution of Intravitreal Injections for the Treatment of Endophthalmitis](#)

Appendix 2: [Equipment Required](#)

Appendix 3: [Procedure/ Method](#)

Appendix 4: [Aqueous and Intravitreal tap and intravitreal injection technique](#)

Appendix 5: [Principles of Management](#)

Please note: these procedure documents are written for use at the Royal Victorian Eye & Ear Hospital. Please modify the procedures according to local requirements.

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Evidence Table

Author(s)	Title	Source	Level of Evidence (I – VII)
Jackson, Timothy L.	Moorfields Manual of Ophthalmology.	Book	IV
Bruce, A., Loughnan, M.	Anterior Eye Disease and Therapeutics A-Z. Chatswood, NSW: Churchill Livingstone Elsevier, 2011.	Book	IV
Crock, C., Sandhu S., Miln L., et al.	Intravitreal Injection Procedure for the Treatment of Endophthalmitis – Emergency Department.	The Royal Victorian Eye and Ear Hospital CPG.	VI
Connell, P.P., O'Neill, E.C., Fabinyi, D., Islam, F.M.A., Buttery, R., McCombe, M., Essex, R.W., Roufail, E., Clark, B., Chiu, D., Campbell, W. & Allen, P	Endogenous endophthalmitis: 10-year experience at a tertiary referral centre	Journal (Eye)	IV

The Hierarchy of Evidence

The Hierarchy of evidence is based on summaries from the National Health and Medical Research Council (2009), the Oxford Centre for Evidence-based Medicine Levels of Evidence (2011) and Melynck and Fineout-Overholt (2011).

- I) Evidence obtained from a systematic review of all relevant randomised control trials.
- II) Evidence obtained from at least one well designed randomised control trial.
- III) Evidence obtained from well-designed controlled trials without randomisation.
- IV) Evidence obtained from well-designed cohort studies, case control studies, interrupted time series with a control group, historically controlled studies, interrupted time series without a control group or with case series.
- V) Evidence obtained from systematic reviews of descriptive and qualitative studies.
- VI) Evidence obtained from single descriptive and qualitative studies.
- VII) Expert opinion from clinician, authorities and/or reports of expert committees or based on physiology.

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Appendix 1: Preparation and Reconstitution of Intravitreal Injections for the Treatment of Endophthalmitis

Note: maintain asepsis, swab rubber port after removal of cap prior to introducing dilutions, and MIX WELL AFTER EACH DILUTION

USE PREFILLED CEFTAZIDIME 6mg/0.3mL & VANCOMYCIN 3mg/0.3mL SYRINGES IN ED OMNICELL FRIDGE

WHENEVER AVAILABLE:

Preparation steps for **CEFTAZIDIME** intravitreal injection dose = 2mg/0.1mL (Gram-negative coverage)^{3,4,5}

Step	Complete (please initial)
1. Add 9.4 mL of 'Sodium Chloride 0.9% for Injection' to the 1g vial of Ceftazidime (1g/10mL=100mg/mL=10mg/0.1mL)	<input type="radio"/>
2. Withdraw 0.2mL of the solution from the vial using a 1mL syringe (20mg/0.2mL)	<input type="radio"/>
3. Add 0.8mL of 'Sodium Chloride 0.9% for Injection' to this syringe (20mg/mL= 2mg/0.1mL)	<input type="radio"/>
4. Discard 0.9mL of solution leaving 0.1mL to inject intravitreally. Label syringe.	<input type="radio"/>

Preparation steps for **VANCOMYCIN** intravitreal injection dose = 1mg/0.1mL (Gram-positive coverage)^{4,5}

Step	Complete (please initial)
1. Add 10mL of 'Sodium Chloride 0.9% for Injection' to the 500mg vial of Vancomycin (500mg/10mL = 50mg/mL=5mg/0.1mL)	<input type="radio"/>
2. Withdraw 0.2mL of solution from the vial using a 1mL syringe (10mg/0.2mL)	<input type="radio"/>
3. Add 0.8mL of 'Sodium Chloride 0.9% for Injection' to this syringe (10mg/mL = 1mg/0.1mL)	<input type="radio"/>
4. Discard 0.9mL of solution leaving 0.1mL to inject intravitreally. Label syringe.	<input type="radio"/>

Preparation steps for **DEXAMETHASONE** intravitreal injection dose = 400mcg/0.1mL

Step	Complete (please initial)
1. Using a 1mL syringe withdraw 0.1mL of solution from the 4mg vial of Dexamethasone (4mg/1mL = 400mcg/0.1mL)	<input type="radio"/>
2. Label syringe ready to inject 0.1mL of this solution intravitreally.	<input type="radio"/>

Preparation steps for **FOSCARNET** intravitreal injection dose = 2.4mg/0.1mL (Anti-viral coverage)

Step	Complete (please initial)
1. Using a 1mL syringe withdraw 0.1mL of solution from the 250mL vial of Foscarnet (6g/250mL = 24mg/mL= 2.4mg/0.1mL)	<input type="radio"/>
2. Label syringe ready to inject 0.1mL of this solution intravitreally.	<input type="radio"/>

Preparation steps for **VORICONAZOLE** intravitreal injection dose = 100mcg/0.1mL (Anti-fungal coverage)^{5,6}

Step	Complete (please initial)
1. Add 19mL of 'Water for Injections' to 200mg vial of Voriconazole (200mg/20mL = 10mg/1mL = 1mg/0.1mL)	<input type="radio"/>
2. Withdraw 0.1mL of solution using a 1mL syringe (1mg/0.1mL)	<input type="radio"/>
3. Add 0.9mL of 'Water for Injections' to this syringe (1mg/1mL = 100mcg/0.1mL)	<input type="radio"/>
4. Discard 0.9mL of this solution leaving 0.1mL to inject intravitreally. Label syringe.	<input type="radio"/>

Appendix 2

Equipment Required:

- Procedure trolley
- Alcohol wipe
- Disposable yellow biohazard bag
- Sharps bin
- Sterile instruments: Sub-Tenon set (disposable) and calipers
- 1 inch Micropore™ surgical tape
- Intravitreal pack
 - Syringes:
 - A. 20mL x 1
 - B. 10mL x 3
 - C. 5mL x 1
 - D. 3mL x 1
 - E. 1mL x 8
 - Needles:
 - A. 18G x 3
 - B. 21G x 3
 - C. 23G x 1
 - D. 25G x 1
 - E. 30G x 8
 - Red (syringe) caps x 3
 - Betadine swab stick x1 or Chlorhexidine aqueous 0.1% irrigation solution if Betadine allergy
 - Eye Pad
 - Blue eye pack
 - Eye drape
 - Vannas scissors
 - Subtenon cannula
 - Sterile gown and shield mask
 - Sterile marker x1
 - Sterile gloves (Steriles)
 - Sodium chloride 0.9% 10mL polyamp x 5
 - Water for injection 10mL polyamp x 3
- Chloramphenicol eye ointment x1
- Lignocaine 2% plain polyamps x1
- Intravitreal drugs
- Parenteral labels

Anaphylaxis Kit/Resuscitation Equipment

- Should be available in the immediate vicinity

Treating Medical Officer/Assisting Nurse/Medical Officer

- Sterile gloves and gown
- Surgical Masks and eye protection

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Appendix 3:

Procedure/Method

Ensure Hand Hygiene is practiced as per Hand Hygiene Procedure

Aseptic Technique is employed to maximise and maintain asepsis

Check consent and ensure the patient's eye is marked for the correct site

Pharmacy procures and supplies ready to use (pre-filled) syringes of ceftazidime 6mg/0.3mL and vancomycin 3mg/0.3mL suitable for intravitreal injection. The pre-filled syringes are available in ED automated dispensing (Omniceil®) fridge. In the event that the pre-filled syringes are not available, ceftazidime and vancomycin intravitreal injections can be prepared following the instructions in the checklist in Appendix 1

Ensure preparation of other injections has been followed using the checklist in Appendix 1 and is ready on a sterile field and covered by a sterile drape.

Note: Once the patient enters the room the door to the Treatment Room is to remain closed until the procedure is completed. Failure to do so may compromise patient safety and increase the risk of complications. Traffic into the Treatment Room must be kept to a minimum whilst the procedure is in progress.

Patient Preparation:

- Insert an intravenous cannula in the patient
- Ensure the safe transfer of the patient to, and make as comfortable as possible on, the treatment trolley. Ensure there is clean linen on the patient trolley and place a crepe drape under patient's head. Ensure head of the bed trolley is positioned under the supply air vent.
- Re-explain procedure and reassure the patient. Reinforce the need for the patient to remain as still as possible throughout the procedure

Prior to procedure, the treating Medical Officer and the Assistant are to complete the written ***Intravitreal Tap and Injection for Endophthalmitis in the Emergency Department Safety Checklist, MR45/MR159 (IP)***, as recommended by the World Health Organization (W.H.O).

This includes:

- Confirmation of patient identity against patient name, date of birth, and address
- Confirmation of correct site and marking of site
- Confirmation of allergy status
- Confirmation of valid consent and signatures

Setup:

Assisting Nurse/Medical Officer to assist the treating Medical Officer to:

- Clean procedure trolley with alcohol wipe and set up equipment
- Provide sterile equipment to treating Medical Officer using sterile technique
(**Note:** Equipment not to be opened onto sterile field)

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Post procedure:

1. Ensure patient is comfortable before leaving
2. Discard any sharps appropriately off the sterile field
3. Discard used materials and equipment appropriately e.g. into yellow biohazard bag
4. Ensure room is cleaned and disinfected, including all surfaces and equipment e.g. trolley and slit lamp in room, if used
5. Ensure linen is changed on patient trolley
6. Restock equipment/consumables

Appendix 4: Aqueous and Intravitreal Tap and Intravitreal Injection Technique

1. Registered Nurse or Second Medical Officer to Contact **St Vincent's Pathology**, prior to procedure to inform that sample will require urgent pick-up and processing.
2. Perform Hand Hygiene.
3. Apply **oxybuprocaine drops (use minim)** topically to affected eye.
4. Inject 2% **lignocaine subconjunctivally** to the **superotemporal** quadrant of affected eye (25G needle) or other site if co-ocular condition. Allow minimum of **5 minutes** to uptake. Proceed to dissecting into the subtenon's space and injecting 2% lignocaine with a subtenon's needle, a total volume of 3-4 mls
5. Don mask.
6. Perform surgical hand wash (minimum of 5 minutes for initial case and 2 minutes for subsequent cases) or use Surgical Hand Rub as per manufacturer instructions. Don sterile gloves and gown.
7. Perform a **Betadine® prep** and apply a **sterile drape**.
8. Obtain an aqueous sample by inserting a 30-gauge needle on a 1ml syringe (loosen the plunger first) via clear cornea near the limbus (do not use original phaco incision). Withdraw approximately 0.05–0.10ml (**watch for volume in the dead-space**) of aqueous.
9. Apply a mark with callipers either **4/3.5mm from the limbus** depending on lens status (phakic/ pseudophakic) over the anaesthetised area and fixate the eye appropriately. It is preferable to obtain a sample superiorly.
10. Perform a vitreous biopsy via a **slow aspirated tap** with **25G needle** (1/2 inch needle aimed perpendicularly to three quarters depth).

Aim for **>0.3mL – watch for volume in the dead-space**. If a dry tap observed, do not attempt forceful aspiration, but move sequentially to **23G** or **21G** aspirated taps using a new syringe and needle.

Cap sample with red bung **and apply patient label**. If no sample obtained consider a one port cut biopsy. Ensure asepsis during sample collection and handling.
11. **Inject intravitreally 0.1mL** each of desired **antibiotic/antifungal/antiviral/steroid as per protocol**.
12. Inject **subconjunctival** vancomycin (25mg) and ceftazidime (100 mg) from the first dilution prepared as per Appendix 1.
13. Apply pad for 2 hours. Instruct patient to sit upright post-op to avoid precipitating antibiotics at fovea.
14. Perform hand hygiene
15. Complete operation sheet noting time of procedure.
16. Sign pathology form, add contact details and send sample to St Vincent's Hospital. Ensure both the pathology form and specimens are correctly labelled.

Appendix 5: Principles of Management

POST-SURGICAL ENDOPHTHALMITIS

Intravitreal ceftazidime, vancomycin, dexamethasone

Note: For patients hypersensitive to penicillin (clinician to confirm severity of hypersensitivity), treat with vancomycin and dexamethasone only

POST-TRAUMATIC ENDOPHTHALMITIS

Intravitreal ceftazidime/vancomycin.

Institute intravitreal/oral steroid only when sensitivities available

Note: In patients with a poorer prognosis post-operatively or post-trauma such as:

- Streptococcal infection/post traumatic bacillus species
- Perception of light visual acuity
- RAPD
- Early <2 days presentation
- > 50% hypopyon
- Corneal ring infiltrate
- Only eye with vision
- Possible involvement of sclera

Consider:

1. Primary pars plana vitrectomy (PPV) initially or
2. At 24 hours re-injection or PPV and re-inject

ENDOGENOUS ENDOPHTHALMITIS

Intravitreal ceftazidime/vancomycin + voriconazole is first line treatment for endogenous endophthalmitis.

These cases must be discussed with the VR/OIC consultant on call.

TOPICAL AND ORAL TREATMENT FOLLOWING TAP AND INJECTION

- **Evidence of wound infection/wound dehiscence/bleb infection** necessitates frequent application (hourly by day) of topical therapy:
 - Gutte ofloxacin or
 - Gutte ciprofloxacin or
 - Gutte vancomycin (only if gram positive organisms suspected)
- **No evidence of wound infection**
 - Gutte chloramphenicol QID
- **All patients receive the following topical applications**
 - Topical steroid eye drops 1-2 hourly by day
 - Gutte atropine 1% BD

ORAL OR INTRAVENOUS ANTIBIOTICS

No role in primary management if exogenous endophthalmitis

ORAL STEROID THERAPY

If initial VA is CF's, HM's or PL commence oral prednisolone and a PPI if medically fit and preliminary culture results known

Recommendations for Intravitreal Antibiotics

REPEAT INTRAVITREAL ANTIBIOTICS

- **Culture reveals coagulase negative Staphylococcus**

No repeat injection unless failure to improve or clinical deterioration such as:

1. Increased pain
2. Increased hypopyon
3. Corneal ring infiltrate
4. Increased media opacification

- **No growth**

If clinical improvement then NO repeat injection is required

No clinical change or deterioration

1. Re-biopsy and re-culture at 24 -48 hrs depending on severity of deterioration
2. Re-inject with antibiotics and steroid as per post-surgical endophthalmitis protocol

- **Culture other than coagulase negative Staphylococcus**

Repeat injection of antibiotic and steroid at 24-48 hrs depending on clinical picture

Other antibiotics may be used based on organisms and in vitro sensitivity (consult St Vincent's Infectious Disease and/or pharmacy if necessary)