

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 PC6.3](#), 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 PC6.3](#)) 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

Appendix:

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

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 Ceftriaxone (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"/>