Guidelines for Performing Intravitreal Therapy
1. Purpose and scope (Please include this heading)

The aim of this document is to provide ophthalmologists with a practical set of guidelines that will enable them to safely perform intravitreal injection therapy. Intravitreal injections may be safely performed in either an office (rooms) environment or an operating theatre environment.

This document aims to provide the ophthalmologist with guidance to prepare the patient and safely perform intravitreal therapy, regardless of the environment in which treatment is performed. The location used for procedures should comply with relevant national healthcare standards1.

There are some important post-operative principles that need to be followed, but the specific follow-up details depend on the drug that has been injected, and are beyond the scope of this document.

2. Intravitreal Therapy Technique – A Step-by-Step Guide

2.1 Pre-treatment counselling and consent

It is essential to obtain informed consent for intravitreal therapy, and such informed consent must contain a clear explanation of the potential vision threatening complications of an intravitreal injection. Specifically, the patient needs to be informed of the risk of endophthalmitis, retinal detachment, traumatic cataract and significant vitreous haemorrhage. In patients receiving intravitreal triamcinolone, the risk of a steroid induced intraocular pressure rise, and increased cataract formation, must be discussed. The use of a printed information sheet may be a useful adjunct for informed consent, and a sample document is included in these guidelines (Appendix A).

Informed consent should be re-confirmed with the patient under certain circumstances:

(a) The clinician becomes aware of new or latent complications or adverse reactions which were not necessarily known at the time the procedure was first offered to the patient, and therefore not discussed as part of the original consent process

(b) Changes in the patient’s ophthalmic and general clinical condition, which may result in a change in the benefits and / or risk of the treatment

(c) Availability of alternative therapies to the one for which the patient has originally consented

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1 In Australia: Australian Commission on Safety and Quality in Health Care (ACSQHC) (September 2011), National Safety and Quality Health Service Standards, ACSQHC, Sydney
It is also essential that the patient understands how to contact the ophthalmologist or clinic where the intravitreal injection was performed, if they have a problem following treatment. A sample instruction sheet is attached (Appendix B).

2.2 Pre-injection assessment

Active ocular surface infection should be controlled and treated prior to the use of the intravitreal therapy. Many patients take anti-platelet agents or anticoagulants. It is not necessary to cease these medications prior to the intravitreal therapy. Such patients may be warned that they are more likely to sustain subconjunctival haemorrhage following intravitreal injection.

There is some controversy regarding the use of intravitreal steroids in patients who are steroid responders. It is beyond the scope of these guidelines to provide specific information in this area, and ophthalmologists need to make an individualised decision regarding the safety of intravitreal steroids in patients who are steroid responders and in those who have pre-existing glaucoma. Patients with a history of herpetic keratitis need careful assessment as it is recognised that intraocular steroids may be contraindicated in patients with active herpetic keratitis.

2.3 Consent and correct patient / site confirmation

Intravitreal injection is an invasive procedure, and standard precautions to confirm consent and correct patient and site should be taken, regardless of location of the injection (clinic rooms or operating theatre)

- Written informed consent documentation should be checked. Many patients undergoing intravitreal therapy will require an ongoing course of treatment, and this may be indicated on the consent form.

- The eye due to undergo intravitreal therapy should be clearly marked (eg with a marking pen on the forehead above the correct eye) and this should be confirmed with the patient’s medical record / consent form as the correct eye (“Time Out”). The drug to be injected into the eye should also be confirmed.

2.4 Pre-injection preparation

Table 1 lists the basic equipment necessary to perform intravitreal injections. The instruments may be supplied as a pre-prepared sterilised pack for convenience.

- At a minimum, topical anaesthetic is necessary for intravitreal therapy. However, many ophthalmologists additionally use gel or subconjunctival anaesthetic at the proposed site of intravitreal injection.
• A critical step prior to injection is to use topical antiseptic to irrigate the ocular surface and conjunctival sac. The usual preferred antiseptic is povidone-iodine 5%. Despite adequate topical anaesthesia, this may cause significant ocular surface irritation, and it is recommended that residual povidone-iodine be irrigated from the ocular surface at the conclusion of the injection. Some patients are extremely sensitive to povidone-iodine (true allergy is rare), and aqueous chlorhexidine 0.1% may be used as an alternative topical antiseptic. It is essential that alcoholic chlorhexidine, which is highly toxic to the cornea, is not used on or around the eye.

• The eyelashes and margins of the eyelid must not contaminate the needle during injection. The most reliable way to ensure this is the use of a lid speculum.

• Sterile gloves should be worn. The use of a sterile drape is left to the individual ophthalmologist’s discretion.

• There is some evidence that wearing a mask and/or minimising talking during intravitreal injections may reduce the incidence of endophthalmitis following intravitreal injection. It has also been noted that the microbiological spectrum of post-injection endophthalmitis differs from that following cataract surgery, with oral/respiratory flora (especially Streptococcus species) in a higher proportion of patients. As it may be impractical or unsafe for the ophthalmologist to avoid talking altogether during intravitreal injections, it is recommended that the ophthalmologist wear a mask, and the patient avoid talking / coughing during the procedure. If other staff (nurse, orthoptist etc) or family members are present in the room, they too should wear a mask or avoid talking.

2.5 Injection technique

A sterile syringe and needle are used to give the intravitreal injection. A 27 gauge needle is required to inject triamcinolone given its particulate nature, while a 30 gauge (or smaller) needle can be used for other drugs. The injection should be given 3-4mm from the limbus in a pseudophakic eye and 4mm from the limbus in a phakic eye.

If the needle touches eyelashes or anything else that is potentially non-sterile before entering the eye, the needle should be discarded and replaced with a fresh one. This will mean that a lower dose of drug will be injected because of loss of volume in the dead space of the needle.

2.6 Post injection management

(a) The intraocular pressure is increased for several minutes following an intravitreal injection, and the degree of elevation depends on a number of factors, principally the
volume injected. There may be non-perfusion of the central retinal artery for several minutes following injection, though this is uncommon with the standard 0.05mL dose used for anti-VEGF therapy. Non-perfusion is typically accompanied by significant visual loss or total loss of vision in the injected eye. In the vast majority of patients, vision returns within 5 minutes as the intraocular pressure lowers. It is seldom necessary to perform an anterior chamber paracentesis when the volume injected is less than 0.1 ml.

(b) Although post injection topical antibiotics following have been used in most large clinical trials of intravitreal therapy, there is no evidence that such antibiotic use lowers the rate of postoperative endophthalmitis. Resistance to topical antibiotics develops rapidly, and may select out more virulent strains of bacteria. The vitreous penetration of topical antibiotics is also questionable. Pre-injection antibiotics have been shown to confer little benefit over topical povidone-iodine 5% alone. For these reasons, antibiotics are not routinely recommended either pre- or post-injection. Predisposing lid abnormalities/infections should always be treated however, and if necessary injection should be deferred until there is no active infection.

(c) It is critically important that the patient is aware that severe pain, worsening of vision, new floaters or increasing diffuse conjunctival injection require urgent re-assessment by the ophthalmologist. A mechanism must be in place to allow the patient to contact the treating ophthalmologist or a facility with ophthalmic staff after hours. Endophthalmitis typically occurs within five days of the injection. The presentation may be atypical, particularly if steroids have been injected intravitreally. The precise follow-up regimen following intravitreal therapy needs to be individualised dependent upon the medication that has been injected, and full details are beyond the scope of this document.

(d) Some drugs, particularly intravitreal triamcinolone, have additionally been associated with a sterile non-infectious form of severe intraocular inflammation sometimes termed “sterile endophthalmitis” or “pseudo-endophthalmitis”. The differentiation between infectious and non-infectious post-injection inflammation in eyes following intravitreal injection may be impossible, and whenever there is doubt, the eye should be managed as if it has infective endophthalmitis, using standard treatment. Such management typically involves vitreous and aqueous taps for microbiology, followed by intravitreal broad spectrum antibiotics. Prompt treatment of suspected endophthalmitis is essential. Clinics performing intravitreal therapy should consider having available an “endophthalmitis kit” (Appendix C), depending on their proximity to facilities capable of urgently treating endophthalmitis. Full treatment guidelines for endophthalmitis are beyond the scope of this document.

2.7 Bilateral same day injections

It has become increasingly common for patients to undergo bilateral intravitreal therapy. Some patients will specifically request bilateral same-day treatment to reduce the burden of treatment visits, or because of the need to travel long...
distances for treatment. Although same-day bilateral treatment has not been studied in randomised controlled trials, it has become an accepted practice performed by retinal specialists worldwide. It is essential that intravitreal treatment of each eye be considered as a separate sterile procedure, conducted according to the above guidelines. Although there is generally very low level systemic absorption of intravitreally injected medications, there may be safety concerns with intravitreal anti-VEGF agents in certain patients. Bilateral same-day injection will increase the potential systemic absorption of intravitreal medications, and this must be considered in patients where there are potential systemic safety concerns.

Summary of standard guidelines for intravitreal injections

1. Safe to give intravitreal therapy in clinic or operating theatre setting
2. Informed consent and correct site procedures (“time out”) essential
3. Surgeon to wear mask, others to minimise talking
4. Topical antiseptic pre injection
5. Topical +/- gel or subconjunctival anaesthesia
6. Lid / lash control (eg speculum), sterile gloves +/- sterile drape
7. Follow up regimen depends on drug injected
8. Mechanism to contact Ophthalmologist urgently post injection
9. Post-injection endophthalmitis must be treated as an emergency

Table 1: Pack for intravitreal therapy

Sterile dressing tray
5% povidone iodine
Topical +/- subconjunctival anaesthetic
Syringes, needles
Sterile lid speculum
Sterile gloves +/- sterile drape

Appendices:

Appendix A: Information Sheet and Consent Form
Appendix B: Instructions for Patients following Intravitreal Injection
Appendix C: Intravitreal antibiotic preparation / injection
Appendix A

Intravitreal Injections
Information Sheet and Consent Form

What is an intravitreal Injection?

An intravitreal injection is an injection into the vitreous which is the jelly like substance inside your eye. It is performed to place medicines inside the eye, near the retina.

Why is an intravitreal injection performed?

Intravitreal injections are used to deliver drugs to the retina and other structures in the back of the eye. Common conditions treated with intravitreal injections include diabetic retinopathy, macular degeneration, retinal vascular diseases and ocular inflammation. These conditions often require a course of repeated intravitreal injections.

What is the intravitreal injection procedure?

We will lie you in a comfortable position. Anaesthetic (numbing) drops will be placed in your eye, and your eye will be cleaned with an antiseptic solution. This may initially cause a stinging feeling. The eye is usually held open with an instrument (speculum). The medicine is then injected into your vitreous: you may feel slight pressure and a momentary sharp feeling on the eye when this is done. After the injection procedure, the doctor will check your eye and your eye may be covered with an eye pad.

What are the side effects?

After the injection you may have a gritty feeling in the eye, and the eye may look bloodshot. This will usually resolve over a few days. You may see floaters which will become smaller and disappear over one to two weeks. Sometimes you may see round floaters which are tiny bubbles of air - these are harmless, and will be absorbed by the eye within 1-2 days.

Are there any risks?

Injecting any medication into the eye may result in increased pressure within the eye, inflammation, or more serious side effects such as cataract formation, bleeding within the eye, damage to the retina (retinal detachment or tear) or other eye structures. These side effects are rare, estimated at less than 1 per 1000 injections. It is possible that you may get an infection within your eye (endophthalmitis) as a result of the intravitreal injection. The chance of an infection is low (estimated at less than 1 per 1000 injections). An infection may lead to vision loss or, in rare cases, loss of the eye.
Preparation for the injection

It is very important for you to tell us about any health conditions that you have, all the medications that you are taking, and especially any allergies to medications that you have had in the past. You will be asked to sign this form on the day of your appointment.
CONSENT TO INTRAVITREAL INJECTION

I, _____________________________________ have read, or have had read to me, the above information concerning the procedure of intravitreal injection and understand it to my satisfaction. I consent to the procedure being performed.

I understand that repeated injections are required, and I consent to a course of continued injections. I may decide to discontinue treatment and withdraw this consent at any time.

(Delete above paragraph where applicable)

Signature of patient _____________________________ Date: / / 
Witness _____________________________ Date: / /
Appendix B

Instructions for patients following intravitreal injection

Name: ........................................................................................................

Date: / /

You have had an injection of .................................................................

- If you have an eye pad on your eye, please try to keep your eye closed.
  You may remove the eye pad two hours after the injection.

- If you have been given eye drops, please use them  times a day

- Paracetamol or a simple pain tablet may be taken if necessary.

You may notice any of the following over the next two days:

- Grittiness / feeling of something in the eye: this can be quite severe in the first few hours after the treatment, but should settle down after that

- Redness of the eye, especially in the area where the injection was given. Occasionally there will be a large red spot on the white of the eye. This should be painless and the vision will not be affected. It will gradually disappear.

- Blurry vision

- Floaters or “blobs” in your vision: these will become smaller and disappear over a few days. If you have had an injection of triamcinolone, the floaters may persist for a longer time. Check this with your doctor.

You will be given an appointment for your next checkup, and next injection if necessary, at the reception desk before leaving.

You must report if you have any of the following

- Severe pain
- Marked worsening of vision or loss of vision
- Floaters/clouds in the vision which are new or increasing in the days after injection

In case of emergency call ******, or go to the Emergency Department at ******
Appendix C

Endophthalmitis pack

Keep this page inside pack (plastic bag) containing all of following
Check expiry every 6 months and replenish after use.

Pack contents

Xylocaine 2% (with or without adrenaline 1 in 100,000)
Vancomycin – 1 ampoule 500mg
Ceftazidime (Fortum) – 1 ampoule 1g
Sterile lid speculum
Sterile toothed forceps
Intravitreal injection pack (if needed)
Sterile gloves
Povidone-iodine 5%
Syringes (with spares) – 10ml x2, 5ml x 4, 2ml x3, 1ml x 4
Needles (with spares) – 30 gauge x5, 18G drawing up x 3, 23 gauge x 2
Normal saline (10ml) for injection – 5 ampoules
Local pathology request form and specimen bag

Technique

1. Prepare antibiotics before tap and inject procedure.
   (a) Dilute vancomycin 500mg ampoule in 5mls of normal saline in the vial (=100mg/ml).
   Further dilute (in 5ml syringe) 1ml of this solution in 4mls of saline to give 5mls of
   20mg/ml solution. Draw up 0.1ml of this in 1ml syringe (2mg in 0.1ml) ready for injection
   into the eye (30 G needle).
   (b) Dilute Ceftazidime 1g in 5mls of saline in the vial (= 200mg/ml). Further dilute 1ml of
   this with 8mls of saline to give 10mls of 20mg/ml solution. Draw up in 1ml syringe 0.1ml
   of this solution (2mg in 0.1ml) ready for injection into the eye (30 G needle).

2. Inject subconjunctival local anaesthetic in the area of tap and inject then apply
   topical betadine. Once anaesthetic is active, place eyelid speculum.

3. With 23 gauge needle on 1 or 2ml syringe, insert needle through pars plana into mid
   vitreous cavity, and aspirate tap sample (~0.3 ml).

4. Inject vancomycin 0.1ml (2mg) through pars plana (toothed forceps often required to
   stabilize the eye which is now softer after the tap).

5. Inject ceftazidime 0.1ml (2mg) as above.

6. Send specimen for urgent microscopy / culture / sensitivity

7. Commence intensive topical steroids and topical antibiotics +/- oral antibiotics +/- oral
   steroids.
Bibliography


