THE RETINA CARE CENTER
An affiliate of PRISM Vision Group®
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Needles In The Eye

We are all well acquainted with the look of shock and terror when a patient first hears that the treatment of choice is to put a needle in their eye. “Isn’t there an eye drop that I can use instead!?” These days, many of our elderly patients, and even some of our diabetic patients, know of people who have had injections in their eyes. Most of our patients, however, have never heard of this procedure. (Figure 1)

Every once in a while, a patient wonders out loud, “Who came up with needles in the eye?” In fact, intravitreal injections have been used as far back as 1911 when injections of air were used to stabilize retinal detachments. After 1945, intravitreal injections were used more often as a drug delivery method to treat infectious processes like endophthalmitis and cytomegalovirus, as well as a treatment for inflammatory conditions. In the late 1990s, pharmaceuticals were being developed to target the signals that promoted neovascularization. After 2004, intravitreal Avastin revolutionized the field of vitreoretinal disease. Since that time, FDA approved medications that target vascular endothelial growth factor (VEGF) have reversed blinding disease in millions of people worldwide. (Figure 2)

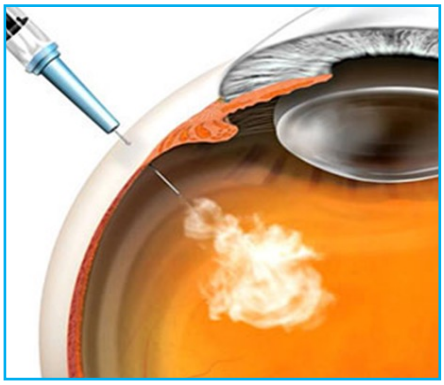

Figure 2

We have all witnessed the great success of this treatment for our patients with diabetes, exudative macular degeneration, and vein occlusions. When faced with fear of vision loss, the hope of a sight saving procedure motivates our patients to agree to their first intravitreal injection.

The number one concern for every patient is “Will I feel pain?” The number one concern for every retina specialist, however, is safety and efficacy. (Figure 3) Every physician is sympathetic to this misalignment in goals. But, as eye doctors, we are all aware of the potential risks with any invasive procedure. From time to time, however, injection patients will encounter post procedure problems. Sometimes, the first doctor they call might be their primary eye physician. It is worthwhile to review the potential negative outcomes of intravitreal injections so we can all work together to ensure that our patients receive superior care.

Figure 3

Throughout the years, certain standards of care have been identified as being critical for the safe delivery of intravitreal medications. Risk reduction measures currently include the use of topical betadine as an antiseptic. Betadine is applied to the injection site for a minimum of 30 seconds prior to the intravitreal injection. This practice has been shown to reduce the bacterial load on the surface of the conjunctiva reducing the risk of endophthalmitis. The bacterial load is high on the eye lashes and lid margin. Therefore, the eyelids are retracted away from the injection site during the procedure. (Figure 4) After the injection is complete, the eye is rinsed of the abrasive betadine. On occasion, however, there is some level of discomfort that our patients experience.

Figure 4

Surface irritation from betadine elicits the most complaints of pain. Retina specialists try to minimize this irritation, especially in patients who suffer from preexisting ocular surface disease. Clinical studies dictate, however, that we cannot forego this critical safety step. Some injection patients will contact their primary eyecare physician after they have had a particularly difficult injection day. It is common to hear “I have had so many injections, and this has NEVER happened to me before.” Any pain or blurred vision reported on the day of the injection is overwhelmingly related to the procedure itself, whether it be from the immediate aftereffects of betadine, subconjunctival hemorrhage from the anesthetic application or on occasion a corneal epithelial defect. These problems can usually be delt with over the phone with instructions for aggressive lubrication and overnight rest. If the symptoms have not improved by the next day, however, the patient should be examined to rule out a corneal abrasion (Figure 5) or other complication.

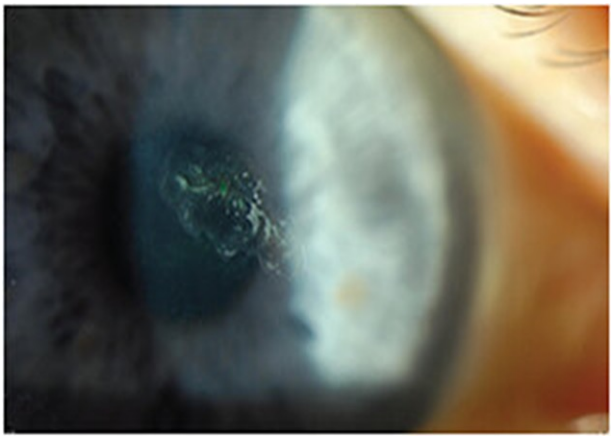

Figure 5

From time to time, patients will report a loss of vision starting on the day of the injection. This is sometimes related to intraocular vasculature being traumatized by the needle entering the eye, resulting in vitreous hemorrhage (Figure 6) or, rarely, a hyphema, both of which can be aggravated by ubiquitous anti-platelet and anti-coagulant medications. We measure 4 mm from the limbus for our injection sites, but occasionally intraocular vessels in the retina or ciliary body are disturbed with the needle. This is a situation that usually just requires reassurance that the hemorrhage will clear with time as the majority resolve spontaneously; rarely vitrectomy is required. It is important to check the INR for patients taking warfarin.

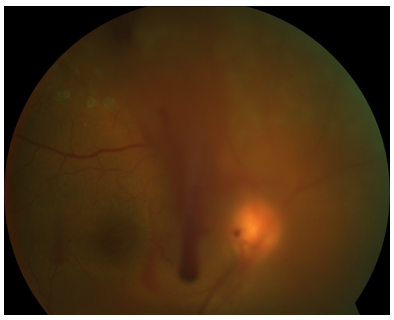

Figure 6

Similarly, and seemingly even more rare, is the occasional retinal hole, tear or detachment after an injection. (Figure 7) This is usually not directly related to the injection site itself, with the needle puncturing the retina, but rather by the changes to the structure of

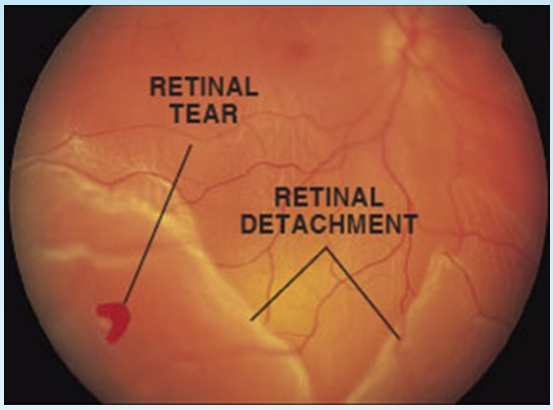

Figure 7

the vitreous gel. Changes in the physical construct of the gel can set off tractional forces that can tear the retina. Patients are advised that any new flashes of light, new floaters or loss of peripheral vision need to be reported immediately.

Subconjunctival hemorrhage is a common occurrence with intravitreal injections. (Figure 8) The incidence increases when a patient is on systemic anti- coagulation. It is also related, in part, to the anesthetic technique used. Options for anesthesia include topical drops, viscous gel, and subconjunctival injections. Subconjunctival hemorrhage is more common when a needle is used for local anesthesia, but this situation will occasionally occur with any injection technique. Although not worrisome to eye doctors, the unsightly appearance in the mirror will often result in a distress call from the patient.

Figure 8

Increasing discomfort, blurred vision, or new floaters reported within seven days after an injection is considered an emergency. The physicians at The Retina Care Center are on call around the clock for your patients and will examine a patient in the middle of the night if the clinical situation warrants emergent care. Endophthalmitis is always a statistical risk of intravitreal injections, even under the best of circumstances. (Figure 9) These events are rare, but they will never be an impossibility. A 2011 meta- analysis of more than 100,000 intravitreal injections of anti-VEGF medications described endophthalmitis in 0.049% of all cases. Staphylococcus epidermidis, Staphylococcus aureus, and Viridans group streptococci have all been found to be causative agents in injection related endophthalmitis. Treatment involves sampling the vitreous fluid for culture and injection of intravitreal antibiotics, namely vancomycin and ceftazidime. Topical steroids are used to dampen the inflammatory response, which can often be as damaging to the eye as the infection itself. The clinical course dictates selectively supplementing with intravitreal steroid or, at times, pars plana vitrectomy. The prognosis for visual recovery is dependent on the causative bacteria, as some bacteria are more virulent than others.

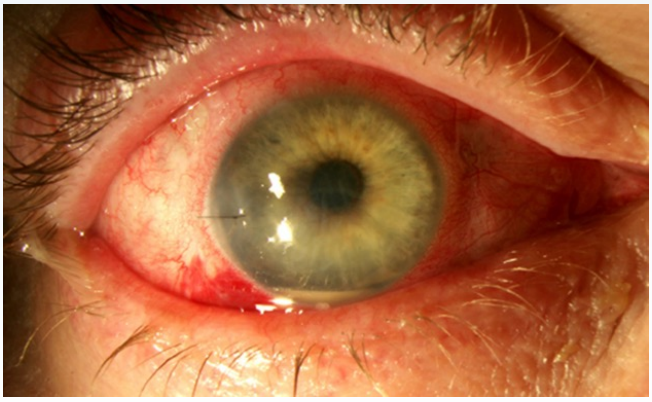

Figure 9

Your referral is the first step in establishing the trust of our injection patients. They are grateful for the opportunity to save their vision and, in many cases, successfully reverse vision loss. While intravitreal injections are a revolutionary, sight saving therapy, these injections are an ongoing treatment plan that increases a patient's risk of developing glaucoma and early cataract formation. Continuous correspondence with each patient's referring physician is the foundation for appropriate co-management of these patients.

References:

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McCannel CA. Meta-analysis of endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor agents: causative organisms and possible prevention strategies. Retina. 2011;31:654-661.

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At the forefront of clinical research

The Retina Care Center continuously conducts clinical trials at our Baltimore, MD office. Our clinical research coordinators will be happy to discuss the inclusion/exclusion criteria or any other aspect of these studies with you or your patients. If you have any questions, please feel free to contact:

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Enrolling Studies:

Dry AMD

Golden: A Phase 2, Randomized, Placebo-Controlled, Double-masked Study to Assess Safety and Efficacy of Multiple Doses of IONIS-FB-L, an Antisense Inhibitor of Complement Factor B in Patients with Geographic Atrophy Secondary to Age-related Macular Degeneration (AMD)

Gyroscope Therapeutics GT005-002 / Explore: A Phase 2, Outcomes assessor-Masked, Multicentre, Randomised Study to Evaluate the Safety and Efficacy of Two Doses Of GT005 Administered as a ASA Single Subretinal Injection in Subjects with Geographic Atrophy Secondary to Age-related Macular Degeneration

Horizon: A Phase II, Open-label, Outcomes-assessor Masked, Multicenter, Randomized, Controlled Study to Evaluate the Safety and Efficacy of Two Doses of GT005 Administered as a Single Subretinal Injection in Subjects with Geographic Atrophy Secondary to Dry Age-related Macular Degeneration

Gallego: A Phase II, multicenter, Randomized, Single-masked, Sham-controlled Study to Assess Safety, Tolerability, and Efficacy of Intravitreal Injections of FHTR2163 in Patients with Geographic Atrophy Secondary to Age-related Macular Degeneration (Gallego)

Wet AMD

Amgen: A Randomized, Double-masked, Phase 3 Study of ABP 938 Efficacy and Safety Compared to Aflibercept (Eylea) in Subjects with Neovascular Age-related Macular Degeneration

Opthea Shore: A Phase 3, Multi-centre, Double-masked, Randomized Study to Evaluate the Efficacy and Safety of Intravitreal OPT-302 in Combination with Ranibizumab, Compared with Ranibizumab Alone, in Participants with Neovascular Age-related Macular Degeneration (nAMD)

Soon to Enroll Studies:

Wet AMD:

- Belvedere- ML43000: A Phase III/IV, Multicenter, Open-Label, Single-Arm Study of The Efficacy and Safety of the Port Delivery System with Ranibizumab in Patients with Neovascular Age-related Macular Degeneration Previously Treated with Intravitreal Agents other than Ranibizumab

- RGX-314 Atmosphere: This Randomized, Partially Masked, Controlled, Phase 2b/3 Clinical Study will Evaluate the Efficacy and Safety of RGX-314 Gene Therapy in Participants with nAMD. The Study will Evaluate 2 Dose Levels of RGX-314 Relative to an Active Comparator. The Primary Endpoint of this Study is Mean Change in Best-corrected Visual Acuity (BCVA) of RGX-314 Relative to Ranibizumab. Approximately 300 Participants who Meet the Inclusion/Exclusion Criteria, will be Enrolled into One of 3 Arms.

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