ENDOPHTHALMITIS AFTER INTRAVITREAL INJECTION

The Importance of Viridans Streptococci

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Purpose: To determine the rate of postinjection endophthalmitis and compare microbial etiology and outcomes in office-based injection-related endophthalmitis versus those acquired after operating room procedures.

Methods: Retrospective, observational case series. Consecutive cases of endophthalmitis seen at Retina Consultants of Houston between July 2000 and July 2010 were classified as postsurgical or post-intravitreal injection. Cases secondary to glaucoma surgery, trauma, and endogenous sources were excluded. Main study measures were incidence of endophthalmitis, microbiology results, and visual outcomes.

Results: In all, 109 cases of endophthalmitis were identified: 88 postsurgical and 21 post-intravitreal injection (3 from clinical trials and 5 from outside ophthalmologists). A total of 33,580 intravitreal injections were performed at Retina Consultants of Houston (endophthalmitis rate = 0.04%, 13 of 33,580; 95% confidence interval, 0.02–0.07%). The most common organisms isolated overall were coagulase-negative staphylococci, while viridans streptococci, a component of human oral flora, was identified over three times more often in the postinjection group compared with the postsurgical group. Compared with all other culture-positive cases related to intravitreal injection, postinjection endophthalmitis secondary to viridans streptococci presented much more rapidly (P < 0.001) and final visual outcomes were much worse (P = 0.004).

Conclusion: Although the overall risk of postinjection endophthalmitis is low, viridans streptococci were identified over three times more frequently in postinjection cases compared with postsurgical cases and these cases had much worse clinical outcomes. The office-based setting for intravitreal injections may lead to a higher risk for infection from oral pathogens.

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Over the past 10 years, the use of intravitreal injections has increased exponentially in retina offices as new therapeutic agents and expanding indications have been introduced that have supplanted surgical and laser-based therapies for many retinal diseases.1 Along with the increased number of injections has come an increase in the number of complications, with infectious endophthalmitis being the most common adverse event leading to a poor visual outcome.2,3 The reported incidence of infectious endophthalmitis after intravitreal injection varies from 0.009% to 0.87% in retrospective trials4,5 to 0% to 0.2% in prospective trials.6,7 The purpose of this study is to report the incidence and visual outcomes of infectious endophthalmitis after office-based intravitreal injections seen at a single tertiary care retina practice over the last 10 years and to compare microbial differences between these cases versus infection secondary to anterior segment surgery.

Methods

This study was a retrospective observational consecutive case series performed after obtaining approval of the study protocol by the Institutional Review Board of The Methodist Hospital in Houston,
TX. Billing records of all patients seen at Retina Consultants of Houston between July 2000 and July 2010 were reviewed in a consecutive manner to obtain a total number of endophthalmitis cases seen and the total number of intravitreal injections performed. We identified individual cases of endophthalmitis by screening for the International Classification of Diseases, Ninth Revision, codes 360.01 (acute endophthalmitis) and 360.03 (chronic endophthalmitis). Patient records were classified by etiology and reviewed for age, gender, affected eye, preinjection pinhole visual acuity (if an injection-related infection), date of presentation and pinhole visual acuity, treatment (vitreous and/or anterior chamber paracentesis vs. pars plana vitrectomy), final visit date and pinhole visual acuity, and culture results. Cases included in this review were those that were postsurgical or post-intravitreal injection, with postsurgical cases including endophthalmitis after cataract surgery, secondary lens implantation, or corneal transplant. We excluded cases potentially acquired in the community setting, including all cases of bleb-associated endophthalmitis, endogenous endophthalmitis, and infection secondary to trauma and corneal ulcer. Intravitreal injections included in this study were triamcinolone acetonide (4 mg/0.1 mL), pegaptanib sodium (0.3 mg/0.1 mL; Macugen; Eyetech, Inc, Palm Beach Gardens, FL), bevacizumab (1.25 mg/0.05 mL; Avastin; Genentech, Inc, South San Francisco, CA), ranibizumab (0.5 mg/0.05 mL; Lucentis; Genentech, Inc), preservative-free triamcinolone (4 mg/0.1 mL; Triences suspension; Alcon Labs, Fort Worth, TX), and dexamethasone intravitreal implant (0.7 mg; Ozurdex; Allergan, Inc, Irvine, CA). Indications for injection consisted of macular edema secondary to but not limited to diabetes, cataract surgery, retinal vein occlusion, uveitis, and choroidal neovascularization secondary to age-related macular degeneration or other various etiologies.

Although there are variations between intravitreal injection techniques between the different physicians at our practice, standard protocol involves both preinjection and postinjection antibiotics (typically a topical fourth-generation fluoroquinolone such as gatifloxacin [Zymar; Allergan, Inc] or moxifloxacin [Vigamox; Alcon Labs] or the generic aminoglycoside tobramycin ophthalmic solution) ranging from 1 day to 3 days before to 1 day to 3 days after injection. After written informed consent and discussion of the risks, benefits, and alternatives of the planned injection, patients receive topical anesthesia by Proparacaine followed by a surgeon-dependent choice of TetraVisc 0.5% solution (OCuSOFT, Inc, Rosenberg, TX), subconjunctival injection of 2% lidocaine, or a 4% lidocaine hydrochloride–soaked pledget. After a minimum of 3 minutes, drops of either 5% or 10% povidone–iodine solution are used to disinfect the ocular surface, and some surgeons use 10% povidone–iodine–soaked cotton tip applicators to cleanse the eyelid skin and adnexa. A sterile lid speculum is used to hold the eye open, and calipers are used to mark the injection site 3.5 mm to 4 mm posterior to the limbus. After the injection, retinal artery perfusion is confirmed by visual acuity and the patient is educated about the signs and symptoms of possible endophthalmitis and instructed to continue postinjection antibiotics. Per practice protocol, patients return for a “safety check” 1 week after their first intravitreal injection primarily for educational purposes to reinforce the signs and symptoms of acute postinjection endophthalmitis.

The objectives of this study were to identify the risk per injection for endophthalmitis, to compare the culture results of these cases with those seen after other anterior segment surgery–related endophthalmitis, and to investigate clinical outcomes of postinjection cases. Endophthalmitis was a clinical diagnosis based on typical symptoms and signs including pain, decreased visual acuity, conjunctival erythema, anterior chamber reaction, hypopyon, and vitritis. All patients underwent vitreous tap, and anterior chamber tap was performed at the discretion of the treating physician. All specimen testing (Gram stain, fungal stain, and aerobic, anaerobic, and fungal cultures of anterior chamber and vitreous tap samples) was performed at the microbiology department of The Methodist Hospital, Houston, TX. Pinhole Snellen visual acuities were converted to logarithm of the minimal angle of resolution for statistical analysis. The following conversion to logarithm of the minimum angle of resolution was used for vision worse than 20/400: counting fingers = 1.6, hand motion = 2.0, light perception = 2.5, and no light perception = 3.0. Statistical comparisons were performed using chi-square, Student’s t, and exact tests where appropriate. The 95% confidence intervals (95% CIs) for rates were calculated assuming binomial distribution. We assumed statistical independence for each injection event, and all analyses were performed using SAS 9.1.3 (Cary, NC) or Stata (College Station, TX).

Results

Between July 2000 and July 2010, a total of 33,580 intravitreal injections were performed: 3,515 of 4 mg of triamcinolone acetonide, 984 of 0.3 mg of pegaptanib...
sodium, 6,675 of 1.25 mg of bevacizumab, 22,336 of 0.5 mg of ranibizumab, 60 of 4 mg of preservative-free triamcinolone, and 10 of 0.7 mg of dexamethasone implant (Table 1). Of the 21 total cases of postinjection endophthalmitis identified (Table 2), there were 6 men and 15 women, with an average age of 76 years (range, 30–91 years). The duration of follow-up for each patient averaged 16 months, with a range from 1 month to >5 years. The mean number of days from injection to presentation was 4 days (range, 1–9 days), except for the 3 patients with viridans streptococcal endophthalmitis who all presented on postinjection Day 1 ($P < 0.001$).

The original indications for intravitreal injection of the patients with post-intravitreal injection endophthalmitis were exudative macular degeneration ($n = 16$), diabetic macular edema (2), central retinal vein occlusion (1), macular edema secondary to a retinal arterial macroaneurysm (1), and choroidal neovascularization secondary to myopic degeneration (1).

Five cases referred in after intravitreal injections performed by outside ophthalmologists and three cases that occurred in our clinical research practice were excluded in calculations of the risk of infection per injection as we could not accurately determine the total number of injections involved that produced these eight cases. The overall rate of intravitreal injection–related endophthalmitis in our clinical practice was therefore 13 infections out of 33,580 injections, or 0.04% (95% CI, 0.02–0.07%). Of the 13 cases from our clinical practice, 2 followed triamcinolone acetonide injection (rate = 2/3,515, or 0.06%, 95% CI, 0.01–0.2%), 3 followed bevacizumab injection (rate = 3/6,675, or 0.05%, 95% CI, 0.01–0.13%), and 8 followed ranibizumab injection (rate = 8/22,336, or 0.04%, 95% CI, 0.02–0.07%); there was no difference among these 3 rates ($P = 0.91$).

Positive cultures were obtained in 58 of 88 (66%) postsurgical cases and 12 of 21 (57%) postinjection cases (Table 3). The most common organisms isolated in both groups were coagulase-negative staphylococci (38 of 88 and 9 of 21, respectively). In the postinjection group, the other 3 positive cultures were all viridans streptococcal pathogens: 1 *Streptococcus mitis*, 1 *Streptococcus salivarius*, and 1 with *S. mitis* from the anterior chamber and *Streptococcus sanguinis* from the vitreous tap. The prevalence of viridans streptococcal species in the postinjection group (3 of 21, 14.3%) was >3 times greater than that seen in the postsurgery group (4 of 88, 4.5%), with the difference trending toward statistical significance ($P = 0.13$).

There was no relationship between the injecting physicians and the infection cases, as the 13 cases from the clinical practice were spread evenly between 7 physicians and the 3 cases of viridans streptococci
Table 2. Cases of Postinjection Endophthalmitis

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (Years)</th>
<th>Gender</th>
<th>Agent</th>
<th>Indication</th>
<th>Days to Presentation</th>
<th>Preinjection VA</th>
<th>Presentation VA</th>
<th>Final VA</th>
<th>Culture</th>
<th>Follow-up (Months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>79</td>
<td>F</td>
<td>IVTA</td>
<td>AMD</td>
<td>2</td>
<td>20/70</td>
<td>CF</td>
<td>20/400</td>
<td>No growth</td>
<td>63</td>
</tr>
<tr>
<td>2</td>
<td>91</td>
<td>F</td>
<td>IVL</td>
<td>AMD</td>
<td>7</td>
<td>CF</td>
<td>HM</td>
<td>CF</td>
<td>No growth</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>86</td>
<td>F</td>
<td>IVL</td>
<td>AMD</td>
<td>5</td>
<td>20/60</td>
<td>CF</td>
<td>20/70</td>
<td>Coagulase-negative staphylococci</td>
<td>45</td>
</tr>
<tr>
<td>4</td>
<td>77</td>
<td>F</td>
<td>IVL</td>
<td>AMD</td>
<td>2</td>
<td>20/30</td>
<td>20/400</td>
<td>20/30</td>
<td>Coagulase-negative staphylococci</td>
<td>36</td>
</tr>
<tr>
<td>5</td>
<td>84</td>
<td>M</td>
<td>IVL</td>
<td>AMD</td>
<td>3</td>
<td>20/60</td>
<td>CF</td>
<td>20/200</td>
<td>Coagulase-negative staphylococci</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>87</td>
<td>M</td>
<td>IVL</td>
<td>AMD</td>
<td>3</td>
<td>20/200</td>
<td>CF</td>
<td>20/200</td>
<td>No growth</td>
<td>28</td>
</tr>
<tr>
<td>7</td>
<td>82</td>
<td>F</td>
<td>IVL</td>
<td>AMD</td>
<td>1</td>
<td>20/200</td>
<td>HM</td>
<td>LP</td>
<td>Streptococcus salivarius</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>90</td>
<td>F</td>
<td>IVL</td>
<td>AMD</td>
<td>5</td>
<td>CF</td>
<td>HM</td>
<td>20/400</td>
<td>Coagulase-negative staphylococci</td>
<td>19</td>
</tr>
<tr>
<td>9</td>
<td>65</td>
<td>F</td>
<td>IVL</td>
<td>AMD</td>
<td>9</td>
<td>20/40</td>
<td>CF</td>
<td>20/30</td>
<td>No growth</td>
<td>21</td>
</tr>
<tr>
<td>10</td>
<td>85</td>
<td>M</td>
<td>IVL</td>
<td>AMD</td>
<td>3</td>
<td>20/60</td>
<td>HM</td>
<td>20/100</td>
<td>Coagulase-negative staphylococci</td>
<td>16</td>
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<tr>
<td>11</td>
<td>73</td>
<td>F</td>
<td>IVA</td>
<td>AMD</td>
<td>7</td>
<td>20/50</td>
<td>20/200</td>
<td>20/30</td>
<td>Coagulase-negative staphylococci</td>
<td>14</td>
</tr>
<tr>
<td>12</td>
<td>79</td>
<td>F</td>
<td>IVL</td>
<td>AMD</td>
<td>5</td>
<td>20/40</td>
<td>20/400</td>
<td>20/40</td>
<td>Coagulase-negative staphylococci</td>
<td>14</td>
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<tr>
<td>13</td>
<td>62</td>
<td>M</td>
<td>IVL</td>
<td>DME</td>
<td>7</td>
<td>20/40</td>
<td>HM</td>
<td>NLP</td>
<td>Coagulase-negative staphylococci</td>
<td>14</td>
</tr>
<tr>
<td>14</td>
<td>82</td>
<td>F</td>
<td>IVL</td>
<td>AMD</td>
<td>1</td>
<td>20/30</td>
<td>HM</td>
<td>LP</td>
<td>Streptococcus mitis (AC),</td>
<td>14</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>sanguinis (vit)</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>82</td>
<td>F</td>
<td>IVL</td>
<td>AMD</td>
<td>3</td>
<td>20/30</td>
<td>HM</td>
<td>20/60</td>
<td>Coagulase-negative staphylococci</td>
<td>12</td>
</tr>
<tr>
<td>16</td>
<td>30</td>
<td>F</td>
<td>IVA</td>
<td>Myopic CNVM</td>
<td>1</td>
<td>20/50</td>
<td>HM</td>
<td>HM</td>
<td>Streptococcus mitis</td>
<td>10</td>
</tr>
<tr>
<td>17</td>
<td>45</td>
<td>M</td>
<td>IVL</td>
<td>CRVO</td>
<td>3</td>
<td>20/200</td>
<td>20/200</td>
<td>20/400</td>
<td>Coagulase-negative staphylococci</td>
<td>1</td>
</tr>
<tr>
<td>18</td>
<td>82</td>
<td>F</td>
<td>IVTA</td>
<td>ME/RAM</td>
<td>1</td>
<td>20/100</td>
<td>CF</td>
<td>CF</td>
<td>No growth</td>
<td>7</td>
</tr>
<tr>
<td>19</td>
<td>78</td>
<td>M</td>
<td>IVL</td>
<td>AMD</td>
<td>3</td>
<td>20/30</td>
<td>HM</td>
<td>20/50</td>
<td>Coagulase-negative staphylococci</td>
<td>6</td>
</tr>
<tr>
<td>20</td>
<td>77</td>
<td>F</td>
<td>IVA</td>
<td>DME</td>
<td>1</td>
<td>20/40</td>
<td>HM</td>
<td>20/40</td>
<td>No growth</td>
<td>4</td>
</tr>
<tr>
<td>21</td>
<td>78</td>
<td>F</td>
<td>IVL</td>
<td>AMD</td>
<td>3</td>
<td>20/40</td>
<td>CF</td>
<td>20/200</td>
<td>No growth*</td>
<td>1</td>
</tr>
</tbody>
</table>

*Gram stain with gram-positive cocci in pairs but culture negative.

AMD, age-related macular degeneration; CF, count fingers; CNVM, choroidal neovascular membrane; CRVO, central retinal vein occlusion; DME, diabetic macular edema; F, female; HM, hand motion; IVA, intravitreal bevacizumab; IVL, intravitreal ranibizumab; IVTA, intravitreal triamcinolone acetonide; LP, light perception; M, male; NLP, no light perception; RAM, retinal arterial macroaneurysm; VA, visual acuity.
came from 3 different physicians. All 21 patients initially had intravitreal tap and injection performed on presentation, and 6 of the patients in this series underwent vitrectomy at some point in their clinical course. Ten of 21 patients had final visual acuities that returned to within 1 line of preinjection visual acuity, while 4 patients had final outcomes of hand motion, light perception, and light perception. Three of these 4 patients were culture positive for viridans streptococcal species and their final visual outcomes were hand motion, light perception, and no light perception (Snellen equivalent 20/4,309), while the 18 patients with coagulase-negative staphylococci or negative cultures had a mean final visual acuity of 20/162 ($P = 0.004$).

All three patients who had postinjection endophthalmitis secondary to viridans streptococci presented with a more aggressive and devastating clinical outcome. Two occurred after intravitreal ranibizumab and 1 followed bevacizumab injection. In addition to presenting on Day 1, all 3 of these cases (Patients 7, 14, and 16) lost significant vision (from initial visual acuities of 20/200, 20/30, and 20/50 to final visual outcomes of light perception, light perception, and hand motion). Although there was not any antibiotic resistance (to intravitreal injection of vancomycin or ceftazidime or to antibiotic treatment with fortified vancomycin, fortified tobramycin, or topical moxifloxacin ophthalmic) and despite successful anatomical surgical repair, all three patients lost vision because of retinal necrosis and the development of retinal detachment.

**Discussion**

In this study, we reviewed consecutive cases of endophthalmitis seen at a single tertiary referral retinal practice over 10 years and found an overall incidence of post-intravitreal injection infection rate of 0.04%. The most common pathogens identified were coagulase-negative staphylococci, followed by viridans streptococci. There were over three times higher rates of viridans streptococci in the post-intravitreal injection infections compared with the postsurgical infection cases; of statistical significance, the viridans streptococci patients presented much earlier and had significantly worse final visual outcomes.

As the use of intravitreal injections has multiplied with modern retinal pharmacotherapy, postinjection endophthalmitis has become a more commonly seen complication, but reports of its incidence vary significantly. Prospective trials investigating ranibizumab, triamcinolone acetonide, and pegaptanib have reported a wide range of endophthalmitis rates per injection from 0% to 0.2%, while multiple other retrospective case series have reported a cumulative rate of 0.047% (51 of 109,104) with a range of 0.009% to 0.87%. The 2 largest published retrospective studies were both multicenter studies and reported an incidence of 0.022% after 26,905 injections of intravitreal bevacizumab and ranibizumab and 0.049% after 30,736 injections of anti–vascular endothelial growth factor agents (intravitreal pegaptanib, bevacizumab, and ranibizumab). The cumulative rate of 0.047% after intravitreal injection appears to be slightly higher than that reported (0.04%) in a large case series of endophthalmitis after cataract surgery.

In our report, one of the largest series of consecutive intravitreal injections performed at a single practice, there was an overall per injection risk of endophthalmitis of 0.04% (95% CI, 0.02–0.07%), which falls within the range of risks described in previous reports. This endophthalmitis rate includes 6 different therapeutic

### Table 3. Organisms Cultured by Type of Endophthalmitis

<table>
<thead>
<tr>
<th></th>
<th>Postsurgical</th>
<th>Post-intravitreal injection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Total cases of endophthalmitis</td>
<td>88 (100)</td>
<td>21 (100)</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci, n (%)</td>
<td>38 (43)</td>
<td>9 (43)</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>4 (5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Viridans streptococci</td>
<td>4 (5)</td>
<td>3 (14)</td>
</tr>
<tr>
<td>Beta-hemolytic streptococci</td>
<td>1 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Streptococci, unspecified</td>
<td>1 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Enterococcus spp.</td>
<td>1 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><em>Propionibacterium acnes</em></td>
<td>4 (5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Actinomyces spp.</td>
<td>1 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><em>Serratia</em> spp.</td>
<td>2 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>2 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Culture negative</td>
<td>30 (34)</td>
<td>9 (43)</td>
</tr>
</tbody>
</table>
agents used in intravitreal injections over the last 10 years, including the “off-label” use of triamcinolone acetonide and bevacizumab. While there have been multiple reports of noninfectious endophthalmitis after intravitreal triamcinolone\(^{39-41}\) and severe intraocular inflammation after intravitreal bevacizumab,\(^{42,43}\) in this series the rate of infectious endophthalmitis after these agents did not appear to be statistically higher than that seen after ranibizumab.

The success rate in obtaining positive cultures was consistent between the different endophthalmitis study groups (between 57 and 66%). Similar to results seen in the Endophthalmitis Vitrectomy Study, which reported that 70% of all responsible isolates were coagulase-negative staphylococci, in this study the most common organisms cultured in both groups were also coagulase-negative staphylococci. Most cases of postsurgical endophthalmitis are attributed to seeding from the patient’s conjunctiva and adnexa,\(^{44,45}\) and normal conjunctival flora consists of the same bacteria typically found on the skin or in the upper respiratory tract; the majority are gram-positive bacteria including staphylococcus and corynebacterium, while gram-negative organisms can also be found.\(^{56-58}\) Several recent publications have described conjunctival flora in patients undergoing intravitreal injection and have documented coagulase-negative streptococci as the predominant conjunctival organism. Moss et al\(^{49}\) found 65 positive cultures with 71 bacterial strains in 136 injections performed in 85 patients; 59 of 71 strains (83%) were identified as coagulase-negative streptococci. Kim et al\(^{50}\) found 57 isolates from 48 eyes in 24 patients, with coagulase-negative streptococci being 27 of 57 isolates (47%).

In the current reported series, other than the cases with coagulase-negative staphylococci, the remaining three culture-positive cases identified in the post-injection group were all viridans streptococcus species. *Streptococcus* species are classified based on hemolysis patterns as alpha-, beta-, or nonhemolytic, with the alpha-hemolytic streptococci divided into pneumococci and viridans. Viridans streptococci are a diverse group of bacteria that are a part of the normal human microbiologic flora, found in the upper respiratory tract and alimentary tract, in these groups may be in part attributable to the procedure itself. Anterior segment surgery is done in the operating room under sterile conditions, and in the United States and Canada, the surgeon and all operating room personnel are typically gowned, gloved, and wearing surgical facemasks. There are no prospective studies of surgical facemask use and subsequent rates of postoperative infectious endophthalmitis in the setting of cataract surgery\(^{54}\); several retrospective studies\(^{55,56}\) have recommended the use of these masks, with one demonstrating increased bacterial cell counts on the patient during cataract surgery performed without masks.\(^{56}\) Intravitreal injections are most often performed in the office setting, and while some surgeons use sterile gloves, the majority do not use surgical facemasks and the prepping for the procedure only creates a semi-sterile environment. Previous reports\(^{57,58}\) have confirmed contamination of needle points with conjunctival bacteria after intravitreal injection by direct inoculation, but as viridans streptococci are rarely found as normal conjunctival commensals, we postulate that during the procedure itself, talking between the patient, surgeon, and other staff may also provide for contamination of the needle or the patient’s conjunctiva with viridans streptococcus organisms.

While there have been several reports about the rates of endophthalmitis after intravitreal injection, less data exist regarding outcomes. A few small series\(^{22,25}\) have suggested that patients typically do well with a return to baseline vision, although the largest published retrospective series\(^{23}\) of 15 cases of endophthalmitis after
anti–vascular endothelial growth factor injections reported that only 2 of 3 of patients returned to baseline vision, with 20% having "very poor outcomes"—defined as hand motion vision or worse. In this series, 10 of the 21 patients had a return to within 1 line of baseline vision, while 4 patients had final outcomes of hand motion vision or worse. Three of these 4 patients with poor final outcomes had endophthalmitis with cultures positive for viridans streptococcus. All 3 of these patients presented within 1 day of injection with hand motion vision but experienced a rapid and further decline in their clinical condition, with all 3 experiencing total retinal detachments requiring pars plana vitrectomy; 2 of these patients ended up with light perception vision and 1 with hand motion vision. The rapidity of the onset of infection after injection and the poor visual outcomes were both statistically significant in comparison with the 18 postinjection patients who had coagulase-negative staphylococcus identified or negative cultures; of these 18, only 3 underwent pars plana vitrectomy and none of them developed a retinal detachment at any point during their follow-up. One had a poor final outcome with no light perception vision, but the mean visual outcome for this set of patients was 20/162.

Viridans streptococci have not been frequently described in the literature as being either a causative or a virulent organism in postinjection endophthalmitis. However, a reexamination of previously published studies demonstrates that viridans streptococci are an underrecognized pathogen that may lead to poor outcomes. Chen et al described a case of S. mitis after pegaptanib injection with initial vision of 20/50 and a final visual outcome of hand motion after irreparable retinal detachment; Fintak et al reported 6 cases of postinjection endophthalmitis, and 3 were culture positive for viridans streptococci, with final visual outcomes of light perception, hand motion, and count fingers from initial acuities of 20/40, count fingers, and 20/80; Klein et al reported 15 cases, with 2 positive for viridans streptococci and final visions of 5/200 and hand motion from initial acuities of 10/200 and 20/30. In addition, immediately preceding the presentation of our data at the American Society of Retinal Specialists meeting in Vancouver, British Columbia, Canada (August 2010), McCannel discussed a metaanalysis of cases of postinjection endophthalmitis and a higher incidence of Streptococcal isolates.

This study was a retrospective analysis of postinjection infections at a single tertiary referral clinical retina practice and has inherent weaknesses including the possibility of geographical variation or bias in the causative organisms seen in infectious endophthalmitis and the potential of patient nonreporting or dropout, although the practice protocol of having patients return 1 week after their first intravitreal injection for a "safety check" allows for further patient reeducation and counseling on warning symptoms of any potential infection. As using billing codes for infection surveillance is not as good as the prospective and active surveillance of infection, this study may not fully capture all cases of endophthalmitis; another limitation is the variable follow-up time, with some patients seen for only 1 month after the onset of infection. While the absolute number of cases is still small, these data imply that the intravitreal injection technique and setting may expose eyes to poor prognosis infections.

Viridans streptococcal species are a potentially underrecognized organism in postinjection endophthalmitis that can lead to rapid infection and very poor final visual outcomes. As oral bacterial commensals are rarely found in normal conjunctival flora, we propose that the most likely source of contamination of the needle or the patient’s conjunctival surface is either from the medical staff or the patient and occurs immediately preceding the injection procedure. Overall, there were only 3 cases of viridans streptococci out of >33,000 injections, and in most instances it may not be feasible to perform intravitreal injections in a sterile environment with a surgical facemask for the retinal surgeons, the office staff, and the patient. However, in all circumstances, physicians must adhere to antiseptic techniques to decrease the risk of infection. In addition, we suggest that the physician may consider keeping the injection needle capped as long as possible, minimizing talking between the surgeon and patient during the procedure, and holding one’s breath during the actual injection to eliminate any possible sources of contamination from oral pathogens. Future prospective studies could investigate the role of wearing a surgical facemask during the intravitreal injection procedure, although the number of patients required to power such a study could be prohibitive.

Key words: alpha-hemolytic streptococcus, bevacizumab, endophthalmitis, intravitreal injection, ranibizumab, triamcinolone acetonide, viridans streptococci.

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