

# News in Review

COMMENTARY AND PERSPECTIVES

## IVT Injection Guidelines: 10-Year Update

Intravitreal (IVT) injection is the most common ophthalmic procedure performed in the United States today; the annual number will soon be double that of cataract surgeries. On the 10th anniversary of the 2004

publication of the original IVT injection guidelines,<sup>1</sup> an expert panel convened to update the guidelines on injection technique and monitoring. The complete 2014 guidelines are available in *Retina*.<sup>2</sup>

**Role of antibiotics.** The first significant change is a move away from the use of pre-, peri- and postinjection antibiotics intended to minimize endophthalmitis risk. A growing body of evidence has deemed such antibiotics unnecessary, and eliminating their use represents a huge cost savings and reduction in patient burden before and after the

procedure, according to Harry W. Flynn Jr., MD, the J. Donald M. Gass Chair of Ophthalmology and professor of ophthalmology at the Bascom Palmer Eye Institute in Miami.

**Contaminated droplets.** A major addition to the guidelines is an emphasis on limiting the spread of aerosolized droplets from the mouth of the patient or medical staff by using surgical masks or refraining from talking during the procedure. This change was prompted by a growing body of evidence implicating oral contaminants as a potential source of injection-



**INTRAVITREAL INJECTION.** The newly updated guidelines confirm the importance of povidone-iodine, seen in this eye, in providing effective antiseptics.

related endophthalmitis.

**Use of povidone-iodine.** In addition, consensus has grown even stronger regarding several recommendations that were included in the 2004 guidelines. Most notable are the importance of applying povidone-iodine to the site before the injection and the recognition that the eyelids are a major potential source of contamination.

“These aspects of IVT injection technique were universally agreed upon by the

panel and continue to be essential to proper technique,” said Emmett T. Cunningham Jr., MD, PhD, MPH, Director of the Uveitis Service at California Pacific Medical Center in San Francisco, adjunct clinical professor of ophthalmology at Stanford University School of Medicine, and research associate at the Francis I. Proctor Foundation, UCSF School of Medicine.

He added that povidone-iodine (5-10 percent) should be the last agent applied to

the intended injection site before injection. If a gel anesthetic is used, however, povidone-iodine should be applied both before and after the gel because, said Dr. Cunningham, “gel applied prior to povidone-iodine may prevent the povidone-iodine from contacting the conjunctival surface, thereby decreasing its effectiveness.”

**Other changes.** Dr. Flynn noted two other changes to

the guidelines that he considers particularly significant. First, there was concern in 2004 that the use of anticoagulation therapy may increase the risk of intraocular bleeding complications during or after an IVT injection. Clinical experience indicates no difference in the rate between patients using or not using systemic anticoagulants.

Second, past concerns about allergic reactions to

povidone-iodine were overblown. “Many patients will give a history of an allergy to shellfish or an iodine dye they may have received in the past. There has been no reported anaphylaxis after the use of topical ophthalmic povidone-iodine,” said Dr. Flynn. “Even though patients may occasionally have swelling or redness after the use of povidone-iodine, the benefit in terms of killing bacteria far outweighs

the localized swelling after the procedure.” Patients with previous anaphylactic reaction to iodine can be referred to an allergist, the guidelines advise.

—Gabrielle Weiner

1 Aiello LP et al. *Retina*. 2004; 24(5 suppl):S3-S19.

2 Avery RL et al. *Retina*. 2014; 34(12):S1-S18.

*Drs. Flynn and Cunningham report no related financial interests.*

## Autoimmunity & the Eye

# Can Treatment Prevent Thyroid Eye Disease?

A large longitudinal study has identified two treatment approaches that appear to reduce the risk of thyroid-associated ophthalmopathy (TAO) in patients with Graves disease. Surgical thyroidectomy and regular use of anticholesterol statin drugs were individually associated with significant risk reduction.<sup>1</sup>

Although these findings have not been confirmed, they could mark the beginning of a new clinical path, said senior author Raymond S. Douglas, MD, PhD, director of the Thyroid Eye Disease Center at the University of Michigan Kellogg Eye Center, in Ann Arbor.

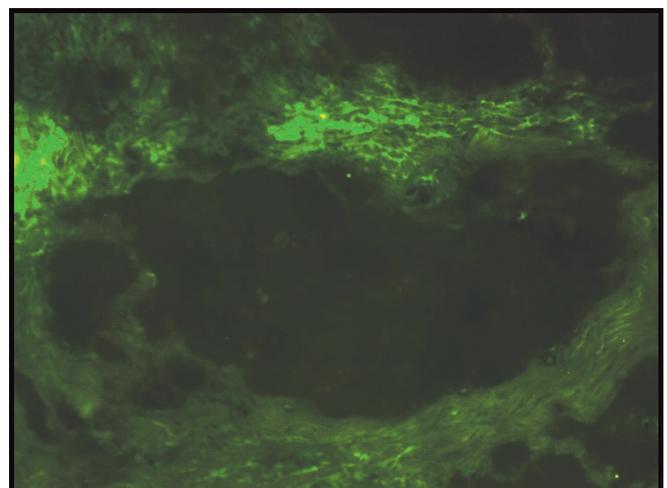
“Thyroid-associated autoimmunity, which encompasses thyroid eye disease, is the most common autoimmune disease. In fact, it affects 1 in 100 people. But all the studies up until now

have focused upon whether the treatment makes the eye disease better or worse,” Dr. Douglas said.

“Now, for the first time ever, we’re looking at interventions that actually can prevent the eye disease associated with Graves from happening—not just make it better, but prevent it.

“We currently have three ways to treat the underlying thyroid disease, and everyone believed they were about the same. But now this study suggests that, if you’re thinking about whether the patient will get the eye disease, the treatments really aren’t equivalent,” he said.

**Study details.** Dr. Douglas and colleagues examined nine years of data on all adults diagnosed with Graves disease within a large managed-care group. Of the 8,404 patients in the cohort, 740 (8.8 percent)



**TAO TRIGGERS.** Fibrocytes (labeled with green fluorescence) infiltrate the orbital tissue of patients with TAO and trigger inflammation and tissue remodeling. New research suggests that statin use may suppress that process and reduce the risk of TAO in Graves disease.

eventually developed TAO.

Because Graves is an autoimmune disorder that causes inflammation, the researchers looked for evidence that certain common drugs with anti-inflammatory properties might interfere with the still-unknown mechanisms by which thyroid dysfunction affects orbital tissues, Dr. Douglas said. Statins and cyclooxygenase 2 (COX-2) inhibitors were among the drugs investigated.

The following are key findings from the study:

- After the researchers controlled for confounding variables, the hazard ratio (HR) for TAO was 40 percent lower (adjusted HR, 0.60; 95% confidence interval [CI], 0.37-0.93) in Graves patients who took statins for 60 or more days per year compared with those who did not ( $p < .05$ ).
- Other cholesterol-lowering medications had no effect.
- Patients who had thyroidectomy had a 74 percent reduced risk of progressing to TAO compared with those treated with radioac-

tive iodine (adjusted HR, 0.26; 95% CI, 0.12-0.51).

- Radioiodine treatment and antithyroid medication, alone or in combination, did not reduce the TAO risk.
- COX-2 inhibitors had no effect on TAO risk.

**Potential applications.** Typically, there is a natural point in the course of

Graves disease at which preventive treatment might be initiated, Dr. Douglas noted.

“What we know now is that patients usually get the thyroid problem, and then we usually have a window of about six months until they get the eye disease,” he said. “Our study should prompt ophthalmologists to

make sure that the patient with Graves disease gets a thoughtful opinion on how to handle their thyroid issue, at an early stage.

“About 20 percent of the time the disease presents with eye issues first,” Dr. Douglas added. “So the ophthalmologist is a very important member of that

early-phase team, when all these treatment decisions are being made.”

—Linda Roach

1 Stein JD et al. *JAMA Ophthalmol*. Published online Dec. 11, 2014.

*Dr. Douglas reports no related financial interests.*

## Retina Report

# CATT Reports on Risk Factors for Growth of GA

The development of geographic atrophy (GA) has emerged as a potential long-term side effect of anti-vascular endothelial growth factor (anti-VEGF) therapy for neovascular age-related macular degeneration (AMD). A 2014 report from the Comparison of Age-related Macular Degeneration Treatments Trial (CATT) showed that the incidence of GA was approximately 18 percent in patients who were treated for two years with intravitreal anti-VEGF agents. Eyes treated with ranibizumab had a higher risk than those treated with bevacizumab, and eyes treated monthly had a higher risk than those treated pro re nata (PRN).<sup>1</sup>

More recently, CATT investigators looked at the growth rate of GA and found that GA associated with ranibizumab grew slightly faster than that associated with bevacizumab.<sup>2</sup>

**A surprising finding.** “The new CATT results show that although there

is a higher incidence of GA in the group receiving monthly injections, once GA develops there is no statistically significant difference in growth rate between monthly and PRN regimens,” said lead author Juan E. Grunwald, MD. Dr. Grunwald is professor of ophthalmology at the Hospital of the University of Pennsylvania and the Presbyterian Medical Center of Philadelphia, director of the Vivian S. Lasko Oculovascular Research Center at the Scheie Eye Institute, and principal investigator of the CATT Fundus Photography Reading Center.

This finding surprised investigators but is in line with recent research focused on genetic abnormalities that can affect the incidence of AMD pathologic features but do not necessarily affect the progression of these features,<sup>3</sup> he noted.

**Other risk factors.** The study identified other potential risk factors associated with faster GA growth in



**CHANGES OVER TIME.** At baseline (left), this eye has classic CNV; after the patient received two years of anti-VEGF therapy (right), GA lesions are apparent. Yellow arrow indicates GA associated with the total CNV lesion, and blue arrow indicates GA outside the area of total CNV lesion.

anti-VEGF-treated patients. These include greater distance from the fovea, extrafoveal location of choroidal neovascularization (CNV), predominantly classic CNV, GA in the fellow eye, and epiretinal membrane.

**For now, benefits trump risk.** Dr. Grunwald said that researchers don't know whether patients who receive anti-VEGF therapy have a higher risk of GA than those who receive no therapy because there is no natural history arm in CATT.

“Despite the risk of GA, patients' vision got better over the two years that we looked at GA,” Dr. Grunwald pointed out. “The reason is that most of the GA developed away from the center of the fovea and didn't interfere with central

vision very much. It takes a few years for the GA that develops in a location away from the fovea to reach the fovea and truly disrupt vision and quality of life.”

Though patients need to be followed for a longer period to see if the GA becomes a problem, “What we can say now, at two years, is that the anti-VEGF agents are absolutely worthwhile,” said Dr. Grunwald.

—Gabrielle Weiner

1 Grunwald JE et al; CATT Research Group. *Ophthalmology*. 2014;121(1):150-161.

2 Grunwald JE et al; CATT Research Group. *Ophthalmology*. Published online Dec. 24, 2014.

3 Caire J. *JAMA Ophthalmol*. 2014;132(5):528-534.

*Dr. Grunwald reports no related financial interests.*