

What's New and Exciting from the ASRS Meeting in San Diego

The ASRS (American Society of Retina Specialists) is the new name for the Vitreous Society, the largest professional association of retina specialists, with 1600 members. Several hundred papers and posters were presented over four and a half days, and we have summarized some of the most significant presentations. There will be more summaries in the next issue.

New data was presented from the AREDS (Age-Related Eye Disease Study) which showed that dietary intake of the carotenoids lutein and zeaxanthin seems to be protective against the development of advanced ARMD. Also from the AREDS trial, it seems that higher intake of omega-3 LCPUFA (long chain polyunsaturated fatty acid), which is contained in fish, was associated with reduced risk of neovascular ARMD. This corresponded with a self-reported intake of greater than 2 servings of fish per week. This association cannot be translated into a treatment or dietary recommendation, since we do not know if changing the diet at a later age will alter the risk. Future studies may answer this.

A fascinating new device known as Preferential Hyperacuity Perimeter was presented, which assesses functional macular changes specifically due to RPE elevation. By using a signal briefly flashed on a screen, it maps out relative paracentral scotomas. It has a high correlation with the presence of angiographic CNV

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Flashes and Floaters: How concerned should we be?

One of the most common presentations to optometrists and ophthalmologists is the complaint of "flashes and floaters". When we hear of such a complaint, we think of posterior vitreous detachments (PVDs), retinal tears, and, at times, a retinal detachment (RD). How concerned should one be of these complaints, and how soon does one need to see the patient? During the ophthalmic examination, we can take advantage of evidence-based clues that raises our suspicion of identifying retinal pathology.

What produces flashes? The most accepted theory on photopsias (proposed by Dr. Moor in 1940) is vitreous traction corresponding to the location of a retinal break. Dr. Verhoeff, a founding forefather of ophthalmology, has theorized (in 1956) that during ocular movements, a detached vitreous could hit the retina, the impact of which causes light flashes.

How about floaters? Release of pigment from the retinal pigment epithelium (RPE) or red blood cells from avulsed retinal vessels can cause floaters. In addition, intravitreous opacities associated with vitreous lique-

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Intravitreal Injection of Triamcinolone For Exudative AMD

Age-related macular degeneration (AMD) is the leading cause of severe vision loss among the elderly in the western world. There are two main manifestations of AMD: exudative and atrophic AMD. Approximately 10 to 20% of patients with AMD develop the exudative form of this disease. Exudative AMD is usually characterized by the presence of a choroidal neovascularization (CNV) which is associated with subretinal fluid, exudation, and hemorrhages. Without treatment, a CNV eventually develops into a macular disciform scar with loss of central vision

Currently the only treatments for CNV that have proved effective are laser photocoagulation and photodynamic therapy (PDT). The Macular Photocoagulation Study Group has proven the efficacy of laser photocoagulation in the treatments of extrafoveal, juxtafoveal, and subfoveal CNV. Unfortunately, in order for patients with subfoveal CNV to benefit from the treatment, the lesion needs to be small and classic or well-defined. Thus, the majority of patients with subfoveal CNV from AMD were not eligible for laser photocoagulation. Although laser treatment was effective in reducing or delaying severe vision loss in certain patients, it was associated with an acute laser-induced loss of central vision in the case of subfoveal CNV. Furthermore, it usually did not allow the patients to maintain enough vision required for driving or reading. Since its approval, PDT has largely supplanted laser photocoagulation as the most recommended treatment for patients with subfoveal CNV. The results from the Treatment of Age-related Macular Degeneration With Photodynamic Therapy (TAP) Study and the Verteporfin in Photodynamic Therapy (VIP) Study suggest that patients may benefit from PDT if subfoveal CNV is predominantly classic with evidence of recent vision loss, especially if the lesion is small or if the visual acuity is worse than 20/50. In contrast to the classic type of subfoveal neovascularization, for which PDT has been shown to stabilize or increase visual acuity, PDT has been less successful for the treatment of occult or minimally classic subfoveal neovascularization, but it is still worthwhile in select patients.

Increasing prevalence of exudative AMD and lack of a treatment option resulting in improved vision for the majority of patients have prompted the search for alternative treatment modalities for subfoveal CNV. There are converging lines of evidence to suggest corticosteroids may have a beneficial effect in patients with CNV. Eyes with CNV have histopathologic evidence of inflammation, and neovascularization is a frequent component of inflammatory processes. Histopathologic examination of choroidal neovascularization complexes has shown the presence of inflammatory cells. In surgically excised choroidal neovascular complexes, the amount

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faction and collagen fiber aggregation may also cause floaters.

How common are acute PVDs? What is the incidence of retinal pathology associated with PVDS? PVDs occur in approximately 63% of patients over 69 years of age. The ophthalmic literature estimates that 10-34% of eyes with flashes and floaters are found to have retinal breaks. These symptomatic breaks may progress to detachment in 33-46% of cases if left untreated. Therefore, careful vitreous and retinal exams are warranted to avoid overlooking these potential retinal breaks. As retinal breaks are not easy to find, a simple means to identify various signs in the clinical exam would be valuable in <u>stratifying high-risk</u> patients for retinal tears. A review of the literature provides an evidence-based approach to important factors of the clinical exam.



Figure 1

In 1983, Boldrey *et al* evaluated 589 patients with photopsia, vitreous floaters, or both in a prospective study designed to identify those at <u>high risk</u> for retinal tears. The study found, by computer analysis, that retinal tears had the strongest association with grossly visible vitreous or preretinal heme (91%), followed by 10-30 pigmented vitreous cells (65%) and visual symptoms of "dots" (51.7%). The density of the cells in the anterior vitreous was graded using a 1 X 9mm vertical slit-lamp beam. Boldrey found that a retinal tear was seen in 53% of patients who had one of the three above signs compared to 3.9% who had other signs.

In 1994, Hikichi *et al* conducted a large study (902 symptomatic eyes) to ascertain the relationship between floaters, light flashes, or both, & complications of PVDs. This study found the prevalence of PVDs to be 89% in patients complaining of flashes and floaters, 67% when seeing only flashes, and 40% when seeing only floaters. Of these patients, 13% complaining of flashes and floaters were found to have a retinal break compared to 12% with flashes and 5% with floaters alone.

As the association with flashes and floaters with retinal pathology is very significant, a thorough ophthalmic examination is warranted.

Sharma *et al*, in 1999, studied the importance of a qualitative vitreous examination in patients with an acute PVD. 59 patients with acute PVDs were evaluated for the presence of pigmented vitreous granules (Shafer's sign) and to determine if these patients have a higher likelihood of retinal tears than those with normal vitreous exam findings. This study concluded that retinal tears, in the setting of an acute PVD, were associated with pigmented vitreous granules 54% of the time. The same study found that patients with a PVD and with pigmented vitreous granules were 52 times more likely to have a retinal tear, based on an odds ratio model.

Tanner *et al*, in 2000, studied the predictive value of vitreous pigment in 200 eyes of patients with acute symptomatic PVDs and found that 92% of patients with a retinal break had a positive Shafer's sign, while 96.5% presenting with an RD had a positive Shafer's sign. Because of sensitivity to finding retinal pathology with Shafer's sign, this article recommended prompt referral to a retinal specialist.

What if pigmented vitreous cells are not identified during the examination, when should the patient be seen again? Van Overdam *et al*, in 2001, answered this very question by examining 250 consecutive patients with isolated acute PVDs. He re-examined patients in 6 weeks if no pigmented vitreous granules were noted and

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in 2 weeks if vitreous heme was found. On re-examination, retinal breaks were noted in an additional 5% of patients. This article provides a reasonable guideline as to when to see patients back after acute symptomatic PVDs.

The clinical approach to patients with flashes, floaters, or both, is to document the best corrected visual acuity along with performing a detailed slit lamp and indirect examination with skilled scleral depression.



The presence of pigmented anterior vitreous cells (figure 1) should highly raise your suspicion of a retinal tear (figures 2 & 3) and warrants a very careful retinal exam. If no such vitreous cells are noted, it is reasonable to re-examine the patient in 6 weeks, but the patient should be reevaluated immediately if symptoms of flashes and floaters arise.



How about developing a PVD in the fellow eye? Recently, in September 2004, Hikichi *et al* published the only prospective study which showed that a PVD developed in 65% of fellow eyes within 2 years, and 90% within 3 years, after development in the first eye.

By taking advantage of evidence-based associations of flashes, floaters, PVDs and retinal tears, we can hone in our skills by looking for clues in the history and clinic exam to make us more effective observers and better clinicians.

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of vascular endothelial growth factor (VEGF), the major cytokine involved in initiating angiogenesis, has been shown to be proportional to the amount of inflammatory cells present. In addition to anti-inflammatory effects, corticosteroids have direct antiangiogenic properties. Intravitreal injection of triamcinolone does not seem to cause direct ocular damage, and the drug persists in the vitreous cavity for several months.

Intravitreal triamcinolone has been used in pilot studies for the treatment of exudative AMD with an apparent beneficial effect. Penfold *et al* and Challa *et al* reported case series, and Danis *et al* later reported a small randomized trial showing improvement in treated patients as compared with controls. Treated patients appeared to demonstrate a favorable effect in terms of visual acuity and the fundus appearance. The improvement in visual acuity was significant for the examinations performed up to 3 months after the injection. About 4 to 5 months after the injection, visual acuity declined so that measurements obtained at the end of the follow-up period for that study did not differ significantly from the baseline values. In a recent study by Jonas *et al*, the authors concluded that reinjection of triamcinolone about 3 to 5 months after an initial injection may be beneficial if the first is associated with an increase in visual acuity.

Our Physicians

Michael S. Jacobson, M.D. Scott I. Lampert, M.D. Jay B. Stallman, M.D. Mark J. Rivellese, M.D. Atul Sharma, M.D. Sean Koh, M.D. The main side effect of intravitreal triamcinolone acetonide observed in these studies was an elevation of intraocular pressure. About forty percent of the eyes developed maximal intraocular pressure measurements higher than 21 mmHg during the follow up period, but the secondary ocular hypertension could usually be treated by topical antiglaucomatous medication without the development of glaucomatous optic nerve damage.

In conclusion, the data of the recent studies suggest that the intravitreal injection of triamcinolone can be a useful treatment alternative in AMD patients especially with large occult or minimally classic CNV.

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(choroidal neovascularization) and may be a useful monitoring tool.

At least five papers were presented on the use of intravitreal Kenalog (triamcinolone acetonide) in combination with PDT (photodynamic therapy) for the treatment of occult CNV. The rationale for this is that while PDT induces thrombosis to close neovascular vessels, it also up-regulates VEGF (vascular endothelial growth factor) which is angiogenic. The concomitant use of Kenalog may help to suppress this. The optimum timing of the injection relative to the PDT is unknown, and this has not been studied in large clinical trials. Kenalog is also being used intravitreally for macular edema associated with central retinal vein occlusion, branch retinal vein occlusion, diabetic retinopathy, and pseudophakic CME (cystoid macular edema), among other conditions. In chronic CME, intravitreal Kenalog was shown to be superior to sub-Tenon's Kenalog in reduction of leakage and foveal thickening, as well as improvement of visual acuity.

An interesting paper showed that the PAM (potential acuity meter) test can be highly predictive of visual improvement after PDT. Patients who do not demonstrate PAM results better than their Snellen acuity may be unlikely to get improved vision after PDT.

A number of new technological improvements in instrumentation and equipment promise to make vitreoretinal surgery safer and more precise. As you may know, 25 gauge sutureless transconjunctival vitrectomy is becoming increasingly more popular. (Standard vitreous instruments are 20 gauge, which are considerably larger.) The 25 gauge system works through small punctures which are self-sealing and require no conjunctival incision. It has been limited by excessive flexibility in the shafts of the instruments and inadequate transmission of light into the eye through the narrow fiber. New brighter Xenon light sources and new light fiber technology are vastly improving this method, as are stiffer probes. We will be offering this technique to appropriate patients, with the goal of improving patient comfort and speeding visual recovery.

Of interest for future years is the development of robotic stabilization devices to counter human tremors or other inaccuracy of movement. Also, the application of military night vision equipment to vitreous surgery may allow surgery to take place in the intraocular darkness with an internal light fiber.

Two new intravitreal sustained release drug delivery devices were described which will be useful in the long-term delivery of steroids. One of these can be injected into the vitreous in the office, and is biodegradable so that removal is not needed.

A four-year update on the use of silicone retinal microchip for the treatment of patients blinded by retinitis pigmentosa was presented, showing that in 10 patients there had been some objective and subjective improvement in vision.

These times hold exciting possibilities for substantial improvement in the way we treat retinal disease.

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