

News in Review

COMMENTARY AND PERSPECTIVE

This month, News in Review highlights selected papers from the original papers sessions at AAO 2022. Each was chosen by the session chairs prior to the meeting because it presents important news or illustrates a trend in the field. Only three subspecialties are included here; papers sessions also were held in six other fields.

CATARACT

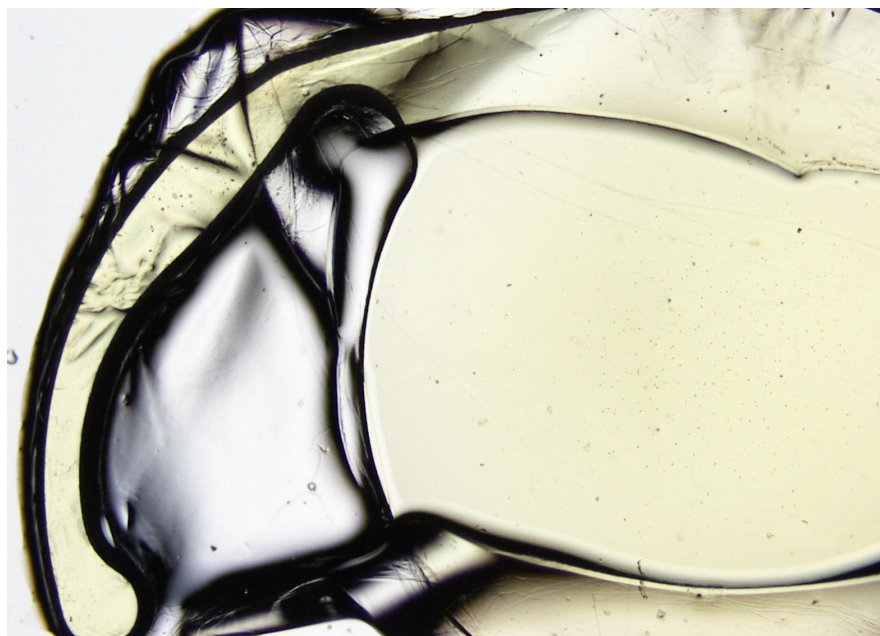
Illuminating Dead Bag Syndrome

SOME TWO DECADES AGO, SAMUEL Masket, MD, began to describe cases of late postoperative IOL dislocation in which the capsular bag appeared diaphanous and floppy and was unable to support the IOL within it. These cases shared some—but not all—characteristics with other conditions that lead to post-op in-the-bag IOL dislocation.

Now, researchers from the University of Utah are reporting clinical features and histopathological findings of the condition that has become known as “dead bag syndrome.”¹⁻³

How often does it occur? “In terms of prevalence, it is not that common,” said Liliana Werner, MD, PhD, at the John A. Moran Eye Center in Salt Lake City. She noted that surgeons who are aware of it may see five cases per year, and those in specialty practices may see one a month or more. Even so, there has been a recent uptick in cases, said Nick Mamalis, MD, also at the Moran Eye Center.

Under the microscope. “What is im-



EXAMPLE. This image shows an in-the-bag dislocated IOL in a patient with dead bag syndrome. The capsular bag is very clear, without fibrotic changes or proliferative material.

portant about this study is that we were able to evaluate the capsular bag from these patients and assess the pathologic findings for the first time,” Dr. Mamalis said.

The Utah case series involved 10 patients with suspected dead bag syndrome, from whom eight IOLs and seven capsular bags were removed because of subluxation or dislocation. No signs of zonular instability, a hallmark of IOL dislocation in many cases of pseudoexfoliation, were noted during the initial uneventful implantation surgeries, which occurred a mean of 10.6 years before explantation.

Histopathological examination of the seven capsular bags showed capsular thinning and/or splitting. Lens epithelial cells (LECs), believed to contribute to the health and structural integrity of the lens capsule, either were rarely seen or completely absent from the inner surface of the capsule.

In addition, there was no association between any particular IOL design or material (either three-piece silicone or single-piece hydrophobic acrylic) and dead bag syndrome.

A distinct entity. While the etiology of dead bag syndrome is unknown, the researchers hypothesize that late postoperative zonular failure is related to capsule splitting and delamination that occurs at the level of zonular attachments.

And even though dead bag syndrome shares some features with other late postoperative conditions that predispose to in-the-bag IOL dislocation, it is a distinct entity, the researchers said. For instance, although patients with pseudoexfoliation may show signs of zonular instability during cataract surgery with IOL implantation, these signs are usually absent in dead bag syndrome. Moreover, there is no capsular splitting in pseudoexfoliation—and no

evidence of pseudoexfoliation in dead bag syndrome.

True exfoliation manifests with capsular splitting and delamination, but it is not commonly associated with zonular weakness. In addition, exfoliation patients typically are in their 70s and 80s, and they often have been exposed to high heat or infrared radiation. However, in this study, patients with dead bag syndrome were younger (mean age, 66 years), with no known exposure to heat or radiation.

Unanswered questions. The results, particularly those regarding scarcity of LECs, have had some surgeons questioning whether capsular polishing during cataract surgery may trigger the syndrome. However, no established association between polishing and dead bag syndrome has been found to date.

“So where does the problem start? In the LECs, or in the capsule itself?” wondered Dr. Werner. “We need further study to understand the relationship between LECs and capsular strength. There are many unanswered questions, not only about the etiology of this syndrome but also about its manifestations.” —*Miriam Karmel*

1 Culp C et al. *J Cataract Refract Surg.* 2022;48:177-184.

2 Mamalis N et al. Clinical and histopathological findings in the dead bag syndrome. Paper presented at: AAO 2022; Oct. 1, 2022; Chicago.

3 Werner L. “The Dead Bag Syndrome.” Best-of-show video presented at: AAO 2022; Sept. 30-Oct. 3, 2022; Chicago.

Relevant financial disclosures—Drs. Mamalis and Werner: None.

GLAUCOMA

Checking IOP: Comparing iCare and GAT Results

THE COVID-19 PANDEMIC SPARKED A re-evaluation of the iCare tonometer, a handheld portable device that measures IOP without topical anesthetic and minimizes eye surface contact. In light of the possibility that iCare might also minimize viral transmission, researchers at Wills Eye Hospital

in Philadelphia evaluated the tonometer’s accuracy by comparing it to the gold standard, Goldmann applanation tonometry (GAT).¹

The researchers “did this study to investigate if iCare is an accurate method to measure IOP in the midst of COVID-19—and if it truly could be a substitute for GAT,” said Shreya Swaminathan, BS, at Sidney Kimmel Medical College. Both devices touch the surface of the eye, although iCare’s diameter is smaller.

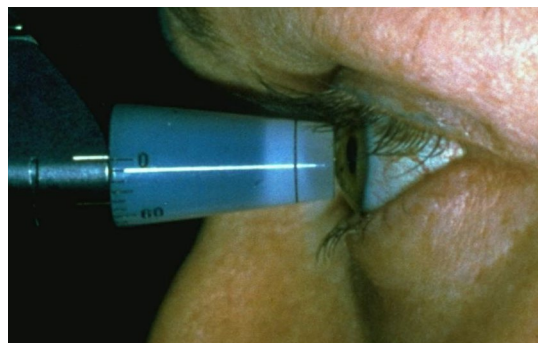
A retrospective assessment. For this retrospective cohort study, the researchers considered clinical data from 350 patients (700 eyes) seen between March 2020 and March 2021. They chose 350 right eyes for final analysis, repeating the analysis in the left eye for verification.

Initially, IOP was measured by ophthalmic technicians using iCare. Repeat measurements were performed within 90 minutes by a glaucoma specialist using GAT. Primary outcome measures included the correlation between iCare and GAT IOP readings and factors influencing the differences in those readings.

IOP correlation. IOP readings from both tonometers showed high levels of correlation, with an intraclass correlation coefficient (ICC) of .899. Bland-Altman plots indicated a 95% limit of agreement between -5.8 to 5.5 mm Hg, suggesting the devices are not interchangeable for measuring IOP. This trend was consistent in eyes with IOPs both above and below 21 mm Hg.

Additional results. Other findings included the following:

- Greater central corneal thickness (CCT) was significantly associated with increased divergence in IOP measurements obtained with the two approaches.
- For each decade of increase in age, the IOP reading was .4 mm Hg lower with iCare than with GAT.
- Greater variation between the two tonometers was noted at higher IOP ranges. Specifically, there were signifi-



IN PURSUIT OF ACCURACY. How should IOP be measured? Although GAT (shown here) is considered the gold standard, the iCare tonometer may also be used.

cantly more patients with an IOP difference greater than 3 mm Hg among those with IOP ≥ 21 mm Hg than among those with IOP ≤ 21 mm Hg.

- Factors not associated with differences in IOP measurements achieved with the two approaches included prior glaucoma surgery, mean retinal nerve fiber layer thickness, axial length, and factors involving the technicians (i.e., years of practice and level of certification).

A caution: not interchangeable. Despite the high intraclass correlation between the two devices, they cannot be used interchangeably, Ms. Swaminathan said. “The fact that more than 20% of patients had a difference of IOP readings greater than 3 mm Hg is striking and indicates that although iCare is close most of the time, it may not be an appropriate substitute for all patients,” she commented.

What’s next? Ms. Swaminathan stressed that further research needs to be done to find a method of measuring IOP that is both accurate and carries a low risk for viral transmission. “While iCare may not be completely accurate when it comes to IOP measurement, it may provide a clinical picture in an environment in which virus transmission is a large concern.” —*Miriam Karmel*

1 Swaminathan S et al. A comparison of iCare and Goldmann applanation tonometry measurements during the COVID-19 pandemic: a retrospective study. Paper presented at: AAO 2022; Oct. 3, 2022; Chicago.

Relevant financial disclosures—Ms. Swaminathan: None.

Gene Tx for DR

INTERIM RESULTS FROM THE PHASE 2 ALTITUDE study indicate that gene therapy has potential for the treatment of diabetic retinopathy (DR). In the initial cohort of patients treated with a single injection of the investigational therapy RGX-314 (Regenxbio), one-third had improved by 2 or more steps in disease severity at three months, and nearly half had improved by 2 or more steps at the six-month mark.

RGX-314, which is designed to deliver a transgene that encodes for an anti-VEGF fab protein similar to ranibizumab, offers the promise of reducing the burden of treatment for DR. For this study, the agent was delivered via suprachoroidal injection in the office setting.

“DR is a global problem—and while we have FDA-approved anti-VEGF drugs for nonproliferative disease, patients require frequent injections,” noted Arshad Khanani, MD, at Sierra Eye Associates in Reno, Nevada. “Gene therapy is a promising alternative.”

Study overview. ALTITUDE is a phase 2 randomized dose-escalation study. The primary outcome is the proportion of patients with an improvement of 2 or more steps in severity on the Diabetic Retinopathy Severity Scale (DRSS) at the one-year mark. Secondary outcomes include safety and tolerability of RGX-314, the development of any DR-related ocular complications, and the need for any additional interventions, including anti-VEGF injections.

Participants. All told, 60 participants have been enrolled at 18 study sites across the United States. Inclusion criteria include being 25 to 89 years of age and having DR secondary to type 1 or type 2 diabetes, no center-involving diabetic macular edema, and VA of 20/40 or better.

The interim results are from cohort 1, which comprises 20 patients. Of these, 15 have received RGX-314, and five are serving as observational con-



POTENTIAL. Researchers hope that gene therapy can reduce the treatment burden faced by patients with DR.

trols. A higher dose of RGX-314 will be evaluated in cohorts 2 and 3, which include 20 patients each.

Initial results. Results to date indicate that RGX-314 is well tolerated. Of the 15 treated patients in cohort 1, 47% demonstrated a 2-step or greater improvement in DRSS score from baseline at six months, compared to 0% in the observation group. One treated patient experienced a 4-step improvement during the six months. “This is pretty remarkable for one-time injections,” Dr. Khanani said.

Two incidences of adverse effects were noted; however, neither was drug-related. One case of mild episcleritis was reported two weeks after the patient received RGX-314, and the condition resolved with topical corticosteroids. No cases of intraocular inflammation were observed. (Of note, no prophylactic corticosteroids are being administered during the study.)

Looking ahead. Complete data will be presented next year, when one-year primary results for all cohorts will be available, Dr. Khanani said. And, he cautioned, “Compared to historical trials, the number of patients in this study is small, and we will have to look at long-term efficacy.” —Jean Shaw

1 Khanani A et al. Suprachoroidal delivery of RGX-314 gene therapy for diabetic retinopathy: the phase 2 ALTITUDE study. Paper presented at: AAO 2022; Oct. 2, 2022; Chicago.

Relevant financial disclosures—Dr. Khanani: Regenxbio: C,S.



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