

# Contaminated Artificial Tears: Observations From the Front Lines

In February, the FDA warned eye-drop users to stop buying EzriCare Artificial Tears and to toss their already purchased eyedrop bottles due to potential bacterial contamination with an uncommon strain of *Pseudomonas aeruginosa*.<sup>1</sup> The FDA and the CDC, along with state and local health officials, reported a 12-state outbreak of the multidrug-resistant strain of the bacteria, which was linked to a Global Pharma manufacturing plant in India. The FDA also noted “associated adverse events” including “hospitalization, one death with bloodstream infection, and permanent vision loss from eye infections.” (At time of press, the outbreak had spread to 16 states, and more than 68 cases had been documented.)

In a series of *JAMA Ophthalmology* reports, ophthalmologists across the country detailed cases and their approaches to diagnosis and treatment. Several authors spoke with *EyeNet* about the eye infections and the associated new strain, called carbapenem-resistant *P. aeruginosa* with Verona integron-mediated metallo- $\beta$ -lactamase and Guiana extended-spectrum- $\beta$ -lactamase.<sup>2</sup>

## Sample Cases

“Many people have used these [EzriCare] drops, and, as we have seen in our patients, some of the consequences of contaminated eyedrops can be dev-

astating,” said Marissa K. Shoji, MD, at Bascom Palmer Eye Institute in Miami.

**Miami report.** In their report, Dr. Shoji and her Bascom Palmer colleagues describe the case of a 72-year-old man who presented in January with severe pain and hand motion vision in his right eye and 20/20 VA in his left. The patient’s IOP was 29 mm Hg in the right eye and 14 mm Hg in the left (see page 21). “When we examined him, he had a severe corneal infection of his right eye with a large central corneal ulcer and hypopyon,” said Dr. Shoji. They took a culture of the corneal ulcer, started the patient on fortified vancomycin and tobramycin drops, and followed him closely.

At his follow-up about two days later, his infection appeared to be worse despite consistent use of the antibiotics, said Dr. Shoji. Having seen an FDA warning about the EzriCare drops, the Bascom Palmer team asked the patient about artificial tear use and encouraged him to bring in his bottle, which they identified as the EzriCare brand and then sent off to be cultured. In their report, they describe the patient as having “severe multidrug-resistant *P. aeruginosa* keratitis after EzriCare artificial tear use, with cultures of the corneal infiltrate and the patient’s EzriCare drops identifying the same strain of multidrug-resistant *P. aeruginosa*.”<sup>3</sup>

The Bascom Palmer team has con-



**INITIAL EXAM.** Slit-lamp image of a large central corneal infiltrate with hypopyon.

tinued to follow the patient, adjusting his antibiotics based on the culture sensitivities of the bacterial strain and his clinical course. Dr. Shoji noted that it’s challenging to treat this strain given the resistance pattern. “It has been shown to be resistant to many antibiotics, including typically effective classes such as carbapenems, fortified aminoglycosides, and cephalosporins.”

Two months into treatment, the patient had improved, but his BCVA is now 20/400 due to residual corneal scarring, Dr. Shoji said.

**Miami update.** By early April, the Bascom Palmer physicians had seen seven patients with the same rare strain of multidrug-resistant *P. aeruginosa*. While only their initial patient had both his artificial tear drops and corneal infiltrate concomitantly cultured, Dr. Shoji stated that it is possible that the

number of cases linked to the contaminated drops may have been underreported, as several patients in the Bascom Palmer cohort presented with this corneal infection before the CDC warning. Careful evaluation of patients with such multidrug-resistant corneal infections is required.

It's impossible to know why some people are at higher risk for infection from the contaminated drops than others, said Guillermo Amescua, MD, also at Bascom Palmer. "We don't have any specific risk factors; the cohort of patients is small," he noted.

"A paper discussing our experiences with and outcomes of these seven multidrug-resistant cases is currently being prepared for publication," Dr. Shoji said.

## Observations and Treatments

**Treatment.** At Bascom Palmer, Dr. Amescua used rose bengal photodynamic antimicrobial therapy (RB-PDAT)<sup>4</sup> to treat a patient with infectious keratitis linked to the new strain of *P. aeruginosa*. He noted that RB-PDAT is still experimental and is currently undergoing NIH-funded clinical trials in India and Brazil.

In RB-PDAT, the green light (wavelength: 500-550 nm) of PDT activates the rose bengal dye to generate reactive oxygen species, which are toxic for the infectious organism, he said. "We've been very successful at killing *Pseudomonas* in our in-vitro experiments with RB-PDAT. We have been able to show 100% killing of the organism in multiple strains of *Pseudomonas*, and that's why we offered it for this patient," said Dr. Amescua.

The patient successfully underwent one 45-minute standard treatment, including a half hour of loading the rose bengal drops on the cornea followed by 15 minutes of light therapy, which resulted in clinical improvement and avoidance of therapeutic penetrating keratoplasty (TPK).

"Success metrics include avoidance of TPK. Secondary outcome measures include number of RB-PDAT treatments; time from first RB-PDAT treatment to clinical resolution, with clinical resolution defined as re-epithelization of the

epithelial defect with decreased pain and inflammation; and resolution of infiltrate," said Dr. Shoji.

Of the seven patients with the rare infection treated at Bascom Palmer, not all were as fortunate as his RB-PDAT patient, Dr. Amescua said. Three underwent a corneal transplant, and one of those patients later required evisceration.

**Systemic repercussions.** To date, three people who used the contaminated eyedrops have died, the CDC has reported.

"I don't know the details of the reported deaths associated with this organism," Dr. Amescua said. "Most likely, those patients were already very sick and in the ICU. I'm very skeptical that this was an infection that started in the cornea and killed the patient. I've been treating hundreds of ulcers per year for 13 years, and I've never seen a patient die from an infection that started in the cornea. It would be very unlikely, but we will have to get the details from the CDC to have better judgment." At Bascom Palmer, he added, "None of our patients required admission to the hospital due to the infection."

## Lessons Learned

In a related editorial, Christina R. Prescott, MD, PhD, and Kathryn A. Colby, MD, PhD, discussed the potential for rare and dangerous infections related to seemingly benign artificial tears.<sup>5</sup> They refer to the recent spate of infections as "a wake-up call" for ophthalmologists.

**Safety is not a given.** "This outbreak is a harsh reminder that all eyedrops, including artificial tears, are medications with potential adverse effects, most commonly ocular but potentially systemic," they wrote.

Patients are living longer, and more people are using preservative-free artificial tear eyedrops for dry eyes, said Dr. Prescott, at NYU Langone Health in New York City. As a result, it's increasingly important to remind patients of safety concerns.

"We don't necessarily think of over-the-counter drops as a medical treatment. We think, 'They're just artificial tears.' But we need to make sure these

drops are from a reputable company, that patients are handling them in a sterile manner, and that if an eyedrop doesn't have a preservative, then [safe] packaging is really important."

**Quality control is key.** Single dose, disposable vials are the safest bet because they're sterile. Unfortunately, Dr. Prescott pointed out, they are not ideal for the environment. To address this issue, some companies have developed proprietary bottles with valves that are designed to reduce the likelihood of contamination, she said.

"The current outbreak involved a preservative-free artificial tear, but it was just packaged in a normal reusable bottle that had no safety features to reduce contamination," Dr. Prescott said. She added that the bottle "never should have been used for a preservative-free medication."

Dr. Prescott also advised ophthalmologists to recommend that their patients avoid online ordering when purchasing eye medication. A traditional pharmacy is more likely to be selling products that have better safety and quality control standards, she said, though a well-known online pharmacy should be okay.

This outbreak is a reminder to always ask patients to bring their drops to the office so you can check to be sure it is made by an established company, said Dr. Prescott. "Sometimes people pull the bottle out of their handbag or whatever they are carrying, or even their pocket, and [the bottle is] dirty, the label is worn off, and you can't read the expiration date. In those cases, you can say 'Throw it out,'" she said.

Dr. Shoji encourages ophthalmologists to ask their patients to bring in recent contact lenses and contact solution bottles, in addition to their eyedrops, and consider culturing them in addition to the corneal infiltrate, especially if there is concern that these items may be associated with infection.

**Early detection is essential.** Dr. Shoji added that flagging infections early—especially those that are atypical—and treating them early and following patients very closely can be critical. "If an infection continues to go untreated or if appropriate antibiotics are not used, the

infection can rapidly worsen, potentially causing a corneal perforation or requiring an emergent TPK. Severe cases may even necessitate removal of the eye.”

Even when a corneal infection is appropriately treated, she said, it can still cause residual scarring that can limit vision. She added that such cases may require surgery for visual rehabilitation and may need substantial time postoperatively to recover vision. She noted that the seriousness of these cases underscores the importance of prevention, but if these infections do occur, prompt identification, close follow-up to monitor disease progression, and appropriate treatment are essential for the best chance at visual recovery.

### A Reminder to Report

Finally, it's crucial to report unusual cases to the FDA and the CDC. “Our field depends on the careful observation of treating ophthalmologists who then spread the word of their findings,” wrote Drs. Prescott and Colby. “We all need to be vigilant observing and reporting unexpected events.”

1 [www.fda.gov/drugs/drug-safety-and-availability/fda-warns-consumers-not-purchase-or-use-ezri-care-artificial-tears-due-potential-contamination](http://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-consumers-not-purchase-or-use-ezri-care-artificial-tears-due-potential-contamination). Accessed April 21, 2023.

2 <https://emergency.cdc.gov/han/2023/han00485.asp>. Accessed April 21, 2023.

3 Shoji MK et al. *JAMA Ophthalmol*. Published online March 23, 2023.

4 [aao.org/education/clinical-video/rose-bengal-photodynamic-antimicrobial-therapy-bas](http://aao.org/education/clinical-video/rose-bengal-photodynamic-antimicrobial-therapy-bas).

5 Prescott CR, Colby KA. *JAMA Ophthalmol*. Published online March 22, 2023.

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**Dr. Shoji** is a resident at Bascom Palmer Eye Institute in Miami and starts her fellowship at Shiley Eye Institute in San Diego this summer. *Relevant financial disclosures:* None.

For full disclosures, see this article at [aao.org/eyenet](http://aao.org/eyenet).

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<sup>1</sup>Sufficient anesthesia with IHEEZO lasted an average of 21.5 minutes in the clinical trial, while mean total surgical time was 13.9 minutes.<sup>2</sup>

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References: 1. Iheezo. Prescribing Information. Harrow IP, LLC; 2022. 2. Data on File. Harrow IP, LLC; 2023.

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