Notes from the Field

Multistate Outbreak of Postprocedural Fungal Endophthalmitis Associated with a Single Compounding Pharmacy — United States, March–April 2012

On March 5, 2012, the California Department of Public Health was notified of nine cases of clinically diagnosed fungal endophthalmitis at a single California ambulatory surgical center. The initial investigation, led by the Los Angeles County Department of Public Health, determined that in all cases patients had undergone vitrectomy with epiretinal membrane peeling using a dye called Brilliant Blue-G (BBG) from Franck's Compounding Lab, Ocala, Florida. This investigation has since expanded to involve intravitreal injection of triamcinolone-containing products from Franck's, an overall total of 33 cases in seven states, and collaboration between state and local health departments, CDC, and the Food and Drug Administration (FDA). This report describes the current investigative findings. Clinicians should be aware of the ongoing investigation and should avoid use of compounded products labeled as sterile from Franck's during this ongoing investigation.

A probable case is defined as ophthalmologist-diagnosed fungal endophthalmitis occurring in a patient who underwent an invasive ophthalmic procedure, including but not limited to vitrectomy, corneal surgery, or intravitreal injections on or after August 23, 2011, the production date of the contaminated BBG lot. Confirmed cases meet criteria for probable infection and also have fungi identified from the affected eye by culture, genetic sequencing, or histopathology. Active case-finding in this investigation has included calls for cases through Epi-X postings, FDA MedWatch alerts, ClinMicroNet microbiology laboratories, e-mails sent to all members of two professional ophthalmology societies, and state and local health alerts.

As of April 30, a total of 33 confirmed and probable cases have been identified, with earliest onset of symptoms in November 2011. Of these, 20 cases (13 probable and seven confirmed) are associated with BBG dye use, and 13 (two probable and 11 confirmed) are associated with triamcinolone use. All BBG or triamcinolone products administered to patients reportedly were purchased from Franck's. All available isolates from the seven confirmed cases associated with BBG dye use were identified by culture or genetic sequencing as the mold *Fusarium incarnatum-equiseti* species complex. All available isolates from the 11 confirmed cases that occurred following intravitreal injection of triamcinolone-containing products have been identified as the mold *Bipolaris hawaiiensis*. Both *Fusarium* and *Bipolaris* are ubiquitous molds present in air, soil, and water. Among the 30 patients for whom data are available, 23 (77%) have suffered some degree of vision loss, ranging from partial to severe, or worsened vision because of infection; 24 (80%) have required repeat ophthalmic surgery.

Culture of unopened bottles and intact (unused, pharmacy-prepared) syringes of BBG dye collected by FDA yielded multiple bacterial and fungal species, including *F. incarnatum-equiseti* species complex, *Rhodotorula*, *Bullera*, *Pseudomonas*, and *Enterobacter* species. Microbiologic testing of triamcinolone-containing products from Franck's is ongoing. On March 9, Franck's recalled all BBG dye lots; on March 31, a single lot of triamcinolone was recalled. The investigation to identify the root cause of product contamination is ongoing. The pharmacy has not recalled or halted production of other sterile compounded products, which, in addition to ophthalmic preparations, include chemotherapy and numerous other medications administered by injection (including intrathecal and epidural), inhalation, and intranasal routes.

Postprocedural endophthalmitis is uncommon, complicating 0.04% of either intravitreal injections or pars plana vitrectomies (*1,2*). The majority of these infections are bacterial; fungal infection is rare and often is diagnosed only after a patient has failed empiric antibacterial therapy. Clinicians are encouraged to be vigilant for postprocedure adverse events, particularly among patients who have received a product labeled as sterile from Franck's, and should consider methods to confirm and treat possible fungal infection.

Compounding pharmacies, which combine or alter medications from standard preparations, provide needed formulations that often are not available from pharmaceutical companies. Compounded sterile preparations must be prepared according to aseptic practices recommended by organizations such as the United States Pharmacopeia, as stated in *United States Pharmacopeia-National Formulary* (*3*). However, contamination of compounded sterile preparations has caused outbreaks. Since 1990, FDA has learned of approximately 200 adverse events associated with 71 compounded products (*4*). A recent outbreak of bacterial endophthalmitis following intravitreal injection of contaminated bevacizumab occurred after breaches in aseptic technique at a different compounding pharmacy (*5*).

Because of the seriousness of endophthalmitis and because the full extent of the outbreak and root cause of contamination remain unknown, CDC recommends that, at this time, clinicians avoid use of compounded products labeled as sterile from Franck's. Health-care providers should maintain a heightened suspicion for infections among patients who

received compounded products labeled as sterile from Franck's and should report suspected infections to their local and state health departments for further investigation. Patients also should avoid use of compounded products labeled as sterile from Franck's and report adverse events or suspected infections promptly to their physician.

Reported by

Suber Huang, MD, Pravin Dugel, MD, American Society of Retina Specialists, Chicago, Illinois. George Williams, MD, American Academy of Ophthalmology. Moon Kim, MD, Kelsey Oyong, MPH, Clara Tyson, MSN, Laurene Mascola, MD, Los Angeles County Dept of Public Health. Kavita K. Trivedi, MD, California Dept of Public Health. Julie Duran, MPH, Colorado Dept of Public Health and Environment. Shannon Millay, MPH, Indiana State Dept of Health. Stephanie Black, MD, Chicago Dept of Public Health; Judith Conway, Illinois Dept of Public Health. Susanne Straif-Bourgeois, PhD, Louisiana Office of Public Health. Rick Sowadsky, MSPH, Nevada State Health Div. Ellen H. Lee, MD, New York City Dept of Health and Mental Hygiene. Tom Török, MD, Benjamin Sun, DVM, Career Epidemiology Field Officer Program, Office of Public Health Preparedness and Response; Shawn Lockhart, PhD, Julie Harris, PhD, Benjamin J. Park, MD, Div of Foodborne, Waterborne, and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases; Rachel Smith, MD, Christina Mikosz, MD, Raymund Dantes, MD, Yoran Grant, PhD, EIS officers, CDC.
***Corresponding contributors**: Christina Mikosz, dex0@cdc.gov, 213-240-7941; Rachel Smith, vih9@cdc.gov, 404-639-7738.*

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