**Letters**

**RESEARCH LETTER**

**Differences in Clinical Outcomes in Keratitis Due to Fungus and Bacteria**

Retrospective studies have suggested that, compared with bacterial keratitis, fungal keratitis has particularly poor outcomes. An unbiased analysis would ideally be performed in a prospective, standardized fashion. Herein, we compare clinical outcomes in ulcers due to bacteria and fungus using data collected from 2 similarly structured prospective clinical trials.

**Methods** | The National Eye Institute–funded Steroids for Corneal Ulcers Trial (SCUT) and the pilot study for the National Eye Institute–funded Mycotic Ulcer Treatment Trial (MUTT pilot) were concurrent, randomized controlled trials comparing outcomes in patients with bacterial (SCUT) and fungal (MUTT pilot) keratitis. Detailed methods have been previously reported.

Outcomes for both trials included best spectacle-corrected visual acuity and infiltrate or scar size at 3 months from enrollment, time to re-epithelialization, and corneal perforation. The 2 trials were conducted at the Aravind Eye Care System (Madurai, Pondicherry, Tirunelveli, and Coimbatore, India) by the same investigators; all measurements were made by the same graders according to identical protocols. Patients were enrolled during overlapping periods (September 2006 through February 2010 for SCUT; December 2007 through May 2008 for MUTT pilot). Institutional review board approval was obtained by the University of California, San Francisco Committee on Human Research and the Aravind Institutional Review Board, and written informed consent was obtained from each participant.

**Results** | Of 500 cases enrolled in SCUT and 120 cases enrolled in MUTT pilot, 485 cases in SCUT and 101 cases in MUTT pilot were culture positive, enrolled in India, and included in the analysis. Fungal keratitis cases were associated with approximately a 0.32-mm larger infiltrate or scar size compared with bacterial keratitis cases at 3 months, correcting for enrollment infiltrate size (P < .001) (Table). There was no difference in best spectacle-corrected visual acuity at 3 months in patients with fungal and bacterial keratitis (P = .12) (Table). Fungal keratitis cases re-epithelialized significantly more slowly than bacterial keratitis cases (median, 15 vs 7.5 days, respectively; P < .001). There were more perforations in the fungal keratitis group than in the bacterial keratitis group (16 of 101 [16%] vs 15 of 485 [3%], respectively; P < .001). Sensitivity analyses restricting the bacterial cases to only those enrolled during the same period as the fungal cases did not change the results.

**Discussion** | Fungal keratitis is frequently considered more difficult to treat than bacterial keratitis and is thought to have worse prognoses.

All culture-positive bacterial and fungal cases enrolled in India were included in the analysis. Three-month best spectacle-corrected visual acuity and infiltrate or scar size between fungus and bacteria were analyzed by linear regression controlling for baseline characteristics (enrollment best spectacle-corrected visual acuity or infiltrate or scar size). In patients who had undergone corneal transplantation prior to their 3-month visit, last observation carried forward or an assigned visual acuity of 1.7 was used, whichever was worse. For infiltrate or scar size, last observation carried forward was used in these patients. Time to re-epithelialization was analyzed with a Cox proportional hazards model controlling for baseline epithelial defect size. Perforation was assessed using Fisher exact test.

While there are inherent challenges in combining data from multiple clinical studies, these trials are a special case. The trials were conducted concurrently by the same investigators, outcomes were measured according to identical protocols, and the inclusion and exclusion criteria were nearly identical for both trials. For fungal ulcers, the epithelium was removed to enhance drug penetration, and approximately half of the cases received repeated scraping at 7 and 14 days because one of the
primary aims of the trial was to assess whether repeated scrap-
ing improved outcomes. The result of longer healing times in
fungal ulcers may be influenced by this. Re-epithelialization
is a difficult end point to measure, particularly in fungal kerat-
titis, so this result should be interpreted with some caution.
Other factors associated with fungal and bacterial keratitis
cases, such as geographic location of the patients, could act
as confounders in this study. Selection bias could occur be-
cause use of topical antibiotics prior to presentation is more
common than antifungal use, and culture-negative bacterial
ulcers may be milder. However, the results of this study sug-
uggest that fungal keratitis has a higher risk of perforation and
may have worse overall outcomes compared with bacterial
keratitis.

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Clinicalopathological Findings in Persistent Corneal Cowpox Infection
Cowpox viruses (CPXVs) belong to the genus Orthopoxvirus. 1 Increasingly,
CPXV infections have been reported in domestic cats, rats, and exotic zoo animals,
with humans potentially being infected through direct contact with these animals. 1 Typically, a
CPXV infection becomes apparent through the development of small skin lesions. Healing comes with scar formation and can take several weeks. Complications and severe courses have been reported in immunocompromised individuals. 2

Report of a Case | In February 2009, a 49-year-old woman presented to a local clinic with a swollen eyelid and phlyctenular changes of the cornea in her right eye. She received antibiotics and steroid eye drops for 2 weeks, but she developed a corneal infiltration and marginal ulceration and her best-corrected visual acuity (BCVA) decreased to 20/100. 3 Because of skin lesions on her shoulder that developed after direct contact with a rat suspected of being infected with CPXV, she was also tested for a CPXV infection. That was confirmed by real-time polymerase chain reaction from conjunctival and skin swab samples. The CPXV infection of the eye was probably caused by smear infection. Involvement of Staphylococcus aureus was shown by a swab, so she was given cefuroxime sodium and local antibiotics. Corneal infiltration then resolved, but limbal ulceration worsened. Four months after the initial infection, conjunctival swabs were negative for CPXV. From then on, she received steroid eye drops to control inflammation, ofloxacin eye drops because of subtotal erosion, and lubricants. From her general medical history, she solely reported a 22-year history of type 1 diabetes mellitus.

In March 2010, she presented at the University Eye Hospital Freiburg because of increasing corneal melting with persistent corneal erosion (Figure 1, A and B). Her BCVA was counting fingers. Penetrating limbokeratoplasty was performed. Postoperatively, her BCVA was 10/200 (Figure 1C) and she received immunosuppressive treatment with mycophenolate mofetil. 4 Three weeks later, the patient presented with scleritis, transplant erosion, and ocular hypotension. Her BCVA was