trum, solely on the basis of in vitro results. The results of Kaye et al. suggest that these newer antibiotics, despite the claims, may not offer improved in vivo results against *Streptococcus* species. Because of this possibility, caution seems advisable when using monotherapy for any serious bacterial corneal ulcer. Instead, I prefer a topical fluoroquinolone (whichever agent) plus topical fortified gentamicin (13.6 mg/mL).

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Author Response: Problems with Monotherapy for Bacterial Keratitis

We thank Dr. Guzek for his comments on our paper published in the January issue of the journal. There may have been some misunderstanding of our methods and findings. It should be noted that we analyzed separately those patients who received monotherapy and whose corneal ulcers healed and those who either received combination therapy or whose ulcers did not heal.

In the combination group, a variety of combinations of agents were used including gentamicin and a fluoroquinolone. What we showed was the lack of an association between healing and minimum inhibitory concentration (MIC) when fluoroquinolone was used against streptococci, and in this group, we included only those patients with healed ulcers who had had monotherapy with a fluoroquinolone.

There are clearly many other factors that determine outcome in *Streptococcus*-associated keratitis, regardless of the antimicrobial used. For example, of the patients included with *Streptococcus pneumoniae* keratitis, one whose ulcer did not heal and who lost an eye had received combination treatment with ciprofloxacin (MIC, 0.75 mg/L) and teicoplanin (MIC, 0.032 mg/L). The MIC for gentamicin was 8 mg/L. Conversely, in a patient who received combination treatment with fluoroquinolone (MIC 0.75 mg/L) and gentamicin (MIC 24 mg/L) and second-line treatment with cefuroxime (MIC, 0.016 mg/L), the ulcer healed after 20 days, which was longer than the mean of 11.38 days (SD 6.54) in the pneumococcal group. Except for gentamicin, the expected corneal concentration (either chemical or bioassay) of the antimicrobials used in these two cases—ciprofloxacin, teicoplanin, and cefuroxime—was many times higher than the measured MICs for the isolated *S. pneumoniae*. It is therefore important to demonstrate a relationship between healing and the MIC for gentamicin or other antimicrobial combinations before a particular antimicrobial such as fortified gentamicin is advocated on the basis of in vitro MIC.

Before an additional or combination antimicrobial can be advocated for streptococcal keratitis, it is necessary to demonstrate either additivity or synergy or at least absence of inhibition for that particular combination, as we have shown for *Staphylococcus aureus* and *Pseudomonas aeruginosa*. nally, although the use of fortified gentamicin has been well recognized, so has its toxicity to the corneal epithelium.

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The Effect of Bevacizumab on Human Tenon Fibroblasts in Ocular Wound Healing

We have read the paper “Antifibrotic Activity of Bevacizumab of Human Tenon’s Fibroblasts In Vitro” of O’Neill et al. (published in Recently Accepted Papers on June 23, 2010) with great interest. We would like to thank the authors for their interesting work and for referring to our paper.

Unfortunately, our work has been erroneously cited with regard to the following points:

In the discussion of their paper (page 13, 2nd paragraph) the authors mention:

*Li et al.* found a single dose of 0.75 mg bevacizumab (0.03 mL of 25 mg/mL) given immediately after surgery significantly reduced the density of blood vessels and the number of inflammatory cells during the early stages of wound healing and reduced the collagen deposition in the later stages.

1. We injected a total volume of 300 μL (0.3 mL) instead of 0.03 mL; therefore, the dose and volume should be changed to: “... a single dose of 7.5 mg bevacizumab (0.3 mL of 25 mg/mL) ...

2. We never observed (or reported) an effect of inflammation after a single injection of bevacizumab; therefore, the phrase “... and the number of inflammatory cells...” should be removed.

Therefore, we feel that this statement should be changed as follows:

*Li et al.* found that a single dose of 7.5 mg bevacizumab (0.3 mL of 25 mg/mL) given immediately after surgery...
significantly reduced the density of blood vessels during the early stages of wound healing and reduced the collagen deposition in the later stages.

Once again, we are delighted that the authors cited our work, but we would greatly appreciate having these corrections conveyed to the readers.

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Author Response: The Effect of Bevacizumab on Human Tenon Fibroblasts in Ocular Wound Healing

I would like to thank Drs. Van Bergen and Stalmans for their recent letter regarding our manuscript published online June 23, 2010, “Antifibrotic Activity of Bevacizumab on Human Tenon’s Fibroblasts In Vitro.”

On behalf of my co-authors, I apologize for the inadvertent error made when quoting her work and would like to assure her that the same was amended before publication of the article, so that the sentence in the uncorrected proof that read:

"Li et al. found a single dose of 7.5 mg bevacizumab (0.03 mL of 25 mg/mL) given immediately after surgery significantly reduced the density of blood vessels and the number of inflammatory cells during the early stages of wound healing and reduced the collagen deposition in the later stages.

was changed to:

"Li et al. found a single dose of 7.5 mg bevacizumab (0.03 mL of 25 mg/mL) given immediately after surgery significantly reduced the density of blood vessels during the early stages of wound healing and reduced the collagen deposition in the later stages.

Again, thanks to Drs. van Bergen and Stalmans for their letter and for bringing the error to our attention.

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Genetic Testing and Clinical Characterization of Patients with Cone–Rod Dystrophy

With interest we read the article by Littink et al., which was published online June 16, 2010, on genetic screening of 126 probands with cone–rod dystrophy (CRD) for mutations in the ABCA4 gene and mutations in homozygous regions by single-nucleotide polymorphism (SNP) array analysis. The authors found that 31 of 90 patients had mutations detected by APEX (arrayed primer extension) ABCA4 microarray, and eight probands revealed pathogenic mutations in six different genes after sequencing. An additional ophthalmic work-up of these eight patients showed that two (25%) of the eight did not have CRD.

The authors excluded these patients from their final calculations and concluded that 27% of the CRD patients had mutations in ABCA4, 1% in PROM1, 2% in CERKL, and 1% in EYS. The authors claimed that the revisions in diagnosis illustrate the complexity of diagnosing retinal dystrophies and the power and utility of molecular genetic testing.

We question the accuracy of the gene frequencies provided by the authors. First, the diagnosis of the CRD patients who did not receive the additional clinical work-up is uncertain. If two (25%) of eight of the patients who were thoroughly examined after genetic screening did not have CRD, it could mean that the diagnosis in the remaining 118 probands was false in up to 30 persons. The initial CRD diagnosis was made by different ophthalmologists who sent DNA to the laboratory at various stages of the diagnostic process. The laboratory was ignorant of the stage. Some ophthalmologists had drawn blood at the patient’s first visit when tests such as ERG, color vision, and other psychophysical tests still had to be performed; others had obtained a blood sample after a definitive diagnosis was established. The great uncertainty in diagnosis does not justify the calculation of gene frequencies in this study group, and the frequencies are not representative of CRD.

Second, the methodology of genetic testing was not identical in the entire study group. Of the initial probands, 90 (71%) were tested for ABCA4 mutations by APEX microarray, and 95 (75%) were evaluated by one of two SNP arrays (250 K and 6.0; Affymetrix, Santa Clara, CA). Although the SNP arrays enabled detection of ABCA4 mutations in the six largest homozygous regions, homozygous mutations in smaller regions as well as compound heterozygous ABCA4 mutations could never have been detected. Therefore, the authors should have used 90 as the denominator in their frequency calculations of ABCA4. Likewise, frequency calculations of PROM1, CERKL, and EYS should be limited to the group of patients who were screened for these genes.

To gain insight into the disease pathogenesis, to help guide the diagnostic process in the clinic, and to direct focus for research funding, good genetic epidemiologic data on this incapacitating eye disease are necessary. There is a clear need for unbiased research with uniform inclusion criteria using a gold standard for diagnosis, complete testing of the total study group, and proper statistical analysis. To make this research feasible, good collaboration between clinicians, molecular geneticists, and epidemiologists is warranted.

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