Three to four decades ago, the chronic hypoestrogenemia of menopause was considered a pathologic state. Our sophisticated evidence-based clinical trials and basic science evaluation of estrogen receptor function are giving us an amazing understanding of the role of eu-estrogenemia.2,3

A large number of menopausal women are following the recommendation of “lowest dose for the shortest duration,” to treat vasomotor instability and urogenital atrophy. Also, millions of women abruptly stopped HRT in 2002 on the recommendation of Jacques Rossouw, the head of Women’s Health Initiative (WHI) at the National Institutes of Health (NIH). We have named this epidemiologic phenomenon, Rossouw’s cohort.1 As clinical gynecologists and fellow ophthalmologists, we have another three decades in which we will be observing our patients’ health, well-being, and quality of life. We warily consider what suboptimal retinal blood flow will mean for our patients who are chronically hypoestrogenemic.

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Author Response: Eu-estrogenemia and Retinal Blood Flow

We thank Drs. Turner and Kerber for their supportive letter in the importance of the findings of our study published in the May issue of the journal, “Postmenopausal Hormone Therapy Increases Retinal Blood Flow and Protects the Retinal Nerve Fiber Layer.”1 This study was designed to bring to light the significant beneficial role that estrogens play by increasing retinal blood flow and protecting the retinal nerve fiber layer in women. There is a large body of evidence indicating that estrogens have beneficial vasomotor effects in several vascular beds, and there is a growing body of evidence that they have protective and trophic effects on the neurons in the brain. However, our understanding of the role of estrogens in the retina and optic nerve is limited, and we are just seeing the tip of the iceberg.

We are pleased that Drs. Turner and Kerber have called gynecologists’ and ophthalmologists’ attention to the visual function of women who are chronically hypoestrogenemic. Particularly, we believe that this hypoestrogenic state could be important in women who experience early menopause onset, premature ovarian failure caused by chemotherapy and radiotherapy, genetic disorders, and hypopituitarism,2 and in women undergoing aromatase inhibitor or selective estrogen receptor modulator therapy used for treating or preventing the recurrence of breast cancer.3 Women who are chronically hypoestrogenemic may be susceptible to impaired ocular blood flow, which is hypothesized to be a contributing factor in the etiology and progression of age-related macular degeneration4 and glaucoma5 to the thinning of the retinal nerve fiber layer, which is a clinical feature of glaucoma.

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Problems with Monotherapy for Bacterial Keratitis

I read with interest the article by Kaye et al.1 in the January issue, “Bacterial Susceptibility to Topical Antimicrobials and Clinical Outcome in Bacterial Keratitis.” The authors found a fairly high rate of failure of monotherapy for bacterial keratitis with either ciprofloxacin or ofloxacin (5%), particularly due to resistance from Streptococcus pneumoniae and other Streptococcus species. Based on my October 1998 publication in the journal,2 I was not surprised. What did surprise me is that the authors did not add topical fortified gentamicin when faced with a clinical failure due to Streptococcus sp. My experimental data and my anecdotal clinical experience suggest that this treatment would have been beneficial.

The authors are to be commended, however, for showing the lack of correlation between the MICs (minimum inhibitory concentrations) of fluoroquinolones and the clinical response of streptococcal keratitis. This finding is important because the newer fluoroquinolones (e.g., moxifloxacin, gatifloxacin) have been said to have improved efficacy in the Gram-positive spec-

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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*. Naturally, 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 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.
2. 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)...”.

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...