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Neutrophils and Corneal Ulceration

C. Stephen Foster, MD

Although corneal epithelium, conjunctival epithelium, and corneal fibroblasts are all capable of producing matrix metalloproteinases, including classical collagenase, abundant evidence indicates that the preeminent source of degradative enzymes which produce corneal stromal destruction in cases of corneal ulceration are delivered to the site of the corneal ulceration by neutrophils. Routine histopathologic studies and ultrastructural studies show that, regardless of the initiating stimulus for corneal ulceration, neutrophils are routinely present, in abundant numbers, and they all exhibit the ultrastructural characteristics of "activated" neutrophils. By contrast, the origin of these neutrophils, similarly, is generally underappreciated: the preocular tear film.

The neutrophils have access to the damaged cornea primarily through the tears, and exclusion of the tears from the area of corneal degradation instantly arrests the ulcerative process. This was shown nearly 20 years ago in various experiments employing glued on hard contact lenses and the use of surgical adhesive itself, which provides its benefits to the ulcerating corneal not because of some sort of structural support, but rather because of a mechanical barrier to neutrophils from the preocular tear film. Indeed, histopathologic studies of such glued corneas shows essentially an acellular stroma in the affected stromal regions, whether the problem has been created by alkali burning, infectious keratopathy, an autoimmune process, or thermal burns.

We showed, additionally, in 1982, in both an alkali burn model and an immunogenic corneal ulceration model, that generalized immunosuppression with Cyclophosphamide reduced the ulceration rate from 86% in control eyes to 16% in treated animals (Archives of Ophthalmology, Vol. 100 page 1820, 1982). Additionally, selected neutrophil suppression by intravenous administration of a highly specific anti-guinea pig neutrophil serum also suppressed the development of corneal ulceration (25%). T lymphocyte or monocyte modifications with similar monospecific antisera had no effects on the rate of corneal ulceration. Clearly, neutrophil depletion after the onset of ulceration halted progression of the corneal ulcers.