Rabbit Conjunctiva as a Target for Ocular Injury Induced by Sulfur Mustard

Author Block: L. B. Joseph[1], G. Wahler[1], C. R. Croutch[2], J. Kang[1], M. K. Gordon[1], D. E. Heck[3], and J. D. Laskin[1]. *[1]Rutgers, The State University of New Jersey, Piscataway, NJ; [2]MRIGlobal, Kansas City, MO; and [3]New York Medical College, Valhalla, NY.*

Sulfur mustard (SM; bis(2-chloroethyl) sulfide) is a bifunctional alkylating agent that has been used in chemical warfare. SM can induce ocular irritation, tearing, pain, photosensitivity, and short-term blindness depending on the dose and duration of exposure. In the present studies, we examined the effects of neat SM (0.4 microliters applied to the central cornea) on the conjunctiva of New Zealand white male rabbits. Twenty-eight days post-SM exposure rabbits were euthanized, eyelids removed and prepared for histology and immunohistochemistry. Following SM exposure, H&E staining revealed erosions in the epithelial surface of the conjunctiva, squamous metaplasia, engorged lymph nodes and an inflammatory cell infiltrate in the adjacent dermis, while Gomori's trichrome staining showed compacted dermal collagen. In control tissue, proliferating cell nuclear antigen (PCNA), a marker of cellular proliferation, was expressed in conjunctiva cell nuclei surrounding goblet cells; this was continuous throughout the basal layer. In SM-exposed rabbit eyelids PCNA was upregulated in the nuclei of cells in the hyperplastic conjunctiva, in cells surrounding goblet cells, and in cells in the basal epithelium. SM-induced PCNA expression was also expressed in the nuclei of cells in the dermal inflammatory cell infiltrate, and in nuclei of cells in the conjunctival-dermal associated appendages including lymph nodes and accessory lacrimal gland acini. pH2.AX, a marker of DNA double-strand breaks, was also expressed in PCNA expressing lymph nodes of SM-exposed rabbit eyelids. Keratin 17, a marker of epithelial cell wound repair, was constitutively expressed in basal cells of the conjunctiva in control eyelids while it was upregulated throughout the hyperplastic conjunctiva, in the accessory lacrimal glands, at the transition zone of the junction between the conjunctiva, and in the cornified epithelium. These data indicate that SM injury to the conjunctiva may in part modify epithelial cell function leading to impaired ocular barrier integrity. *Supported by NIH grants AR055073 and ES005022.*