Response of artificial human skin to irritants: cytokine and prostaglandin release

W. Bowers, Jr., M. Blaha, A. Alkhyyat
and J. Walker*

U.S. Army Research Institute of Environmental
Medicine, Natick, MA 01760-5007, *U.S. Army Natick
Research, Development and Engineering Center

ABSTRACT

Cytokines have been implicated in aspects of vesicant injury/repair. This study describes responses of artificial human skin (Skin² and EpiDerm) to chloroethyl ethyl sulfide (CEES), defined by interleukin-1α (IL-1α), tumor necrosis factor-α (TNF-α) and prostaglandin E₂ (PGE₂) release. Skin² and EpiDerm in Millicells of 6 well Costar trays containing 1ml of assay media/well were exposed to CEES (2.0mg/L, flow rate 1L/min for 2hr) in humidified air. Control tissues were exposed without CEES. Millicells containing Skin² or EpiDerm (12/group) were transferred to fresh assay media and incubated for 22 hr. Tissues (6/group) were used for MTT tests. Media from each well were stored in liquid N₂. IL-1α (RIA or ELISA), PGE₂ (RIA or EIA), and TNF-α (EIA) were measured in thawed specimens. CEES significantly increased release of IL-1α (192pg/ml ± 34.9, control 55pg/ml ± 16.6) and PGE₂ (3,977pg/0.1ml ± 1,197, control 2,541pg/0.1ml ± 570) from Skin², but not TNF-α levels, with viability (MTT) 3%. Neither IL-1α nor TNF-α were elevated by CEES-exposed EpiDerm, although PGE₂ was elevated (258pg/0.1ml ± 71 vs 184 ± 79), viability 46%. We conclude pro-inflammatory mediators, IL-1α and PGE₂, could play significant roles in CEES injury and that either fibroblasts are critical to the process, or EpiDerm, which lacks fibroblasts, is somehow more resistant.
Response of artificial human skin to irritants: cytokine and prostaglandin release

Bowers, W., Jr., M. Blaha, A. Alkhyyat, and J. Walker

U.S. Army Research Institute of Environmental Medicine
Natick MA 01760-5007

Cytokines have been implicated in aspects of vesicant injury/repair. This study describes responses of artificial human skin (Skin² and EpiDerm) to chloroethyl ethyl sulfide (CEES), defined by interleukin-1α (IL-1α), tumor necrosis factor-α (TNF-α) and prostaglandin E₂ (PGE₂) release. Skin² and EpiDerm in Millicells of 6 well Costar trays containing 1ml of assay media/well were exposed to CEES (2.0mg/L, flow rate 1L/min for 2hr) in humidified air. Control tissues were exposed without CEES. Millicells containing Skin² or EpiDerm (12/group) were transferred to fresh assay media and incubated for 22 hr. Tissues (6/group) were used for MTT tests. Media from each well were stored in liquid N₂. IL-1α (RIA or ELISA), PGE₂ (RIA or EIA), and TNF-α (EIA) were measured in thawed specimens. CEES significantly increased release of IL-1α (192pg/ml ± 34.9, control 55pg/ml ± 16.6) and PGE₂ (3.977pg/0.1ml ± 1.197, control 2.541pg/0.1ml ± 570) from Skin², but not TNF-α levels, with viability (MTT) 3%. Neither IL-1α nor TNF-α were elevated by CEES-exposed EpiDerm, although PGE₂ was elevated (258pg/0.1ml ± 71 vs 184 ± 79), viability 46%. We conclude pro-inflammatory mediators, IL-1α and PGE₂, could play significant roles in CEES injury and that either fibroblasts are critical to the process, or EpiDerm, which lacks fibroblasts, is somehow more resistant.

Artificial Skin, Vesicant, CEES, IL-1α, TNF-α, PGE₂

NSN 7540-01-280-5500