

1996 Medical Defense Bioscience Review

May 12-16, 1996



**U.S. Army Medical Research
and Materiel Command**



19960705 058

DTIC QUALITY INSPECTED 1

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-1 α (IL-1 α), 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-1 α (RIA or ELISA), PGE₂ (RIA or EIA), and TNF- α (EIA) were measured in thawed specimens. CEES significantly increased release of IL-1 α (192pg/ml \pm 34.9, control 55pg/ml \pm 16.6) and PGE₂ (3,977pg/0.1ml \pm 1,197, control 2,541pg/0.1ml \pm 570) from Skin², but not TNF- α levels, with viability (MTT) 3%. Neither IL-1 α nor TNF- α were elevated by CEES-exposed EpiDerm, although PGE₂ was elevated (258pg/0.1ml \pm 71 vs 184 \pm 79), viability 46%. We conclude pro-inflammatory mediators, IL-1 α 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.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE 5 June 1996	3. REPORT TYPE AND DATES COVERED Abstract	
4. TITLE AND SUBTITLE Response of artificial human skin to irritants: cytokine and prostaglandin release			5. FUNDING NUMBERS	
6. AUTHOR(S) Bowers, W., Jr., M. Blaha, A. Alkhyyat, and J. Walker				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) U.S. Army Research Institute of Environmental Medicine Natick MA 01760-5007			8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) Same as 7.			10. SPONSORING/MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION/AVAILABILITY STATEMENT Approved for public release; distribution is unlimited.			12b. DISTRIBUTION CODE	
13. ABSTRACT (Maximum 200 words) <p>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 \pm 34.9, control 55pg/ml \pm 16.6) and PGE₂ (3,977pg/0.1ml \pm 1,197, control 2,541pg/0.1ml \pm 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 \pm 71 vs 184 \pm 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.</p>				
14. SUBJECT TERMS Artificial Skin, Vesicant, CEES, IL-1 α , TNF- α , PGE ₂			15. NUMBER OF PAGES	
			16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT	