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NEW METHODS FOR EVALUATING SKIN INJURY FROM SULFUR MUSTARD IN THE HAIRLESS GUINEA PIG

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ABSTRACT

We have reported (Proceedings of the 1991 Medical Defense Bioscience Review) the use of a reflectance color meter for the quantification of erythema and a high frequency ultrasound system for the evaluation of edema by measuring skin thickness. This report compares these two techniques with several new methods including laser Doppler flowmetry (LDF) to measure microcirculation, skin elasticity measurements made both parallel (Dermal Torque Meter, DTM) and perpendicular (Cutometer) to the skin surface, and capacitance measurements for evaluating the skin hydration state. The skin of anesthetized hairless guinea pigs was exposed to saturated HD vapor (1.4mg/ml) at 4 sites for 3, 5, 7, or 9 minutes. Lesions were evaluated by each of the analytical methods at various times up to 24 hours post-exposure. Results have demonstrated a dose-response relationship between HD vapor exposure and erythema (reflectance color meter), edema (high frequency ultrasound), cutaneous microcirculation (LDF), and skin elasticity measured perpendicular to the skin surface (Cutometer). HD vapor cutaneous exposure had only a marginal effect on skin elasticity parallel (DTM) to the skin and on moisture content. These preliminary results suggest that reflectance color meter, high frequency ultrasound, LDF, and skin elasticity measurements may be useful for determining the efficacy of candidate antivesicant therapies.

OBJECTIVE

The objective of this project was the evaluation of new bioengineering techniques including reflectance colorimetry, high resolution ultrasound imaging, laser Doppler flowmetry, skin elasticity measurements, and skin capacitance measurements to determine their utility for the quantitative assessment of skin damage following cutaneous exposure to HD vapor.

EXPERIMENTAL METHODS

Each hairless guinea pig (HGP) was exposed to saturated HD vapor (1.4 mg/L) using 30 mm vapor cups, for 3, 5, 7, and 9 min. The 4 exposure sites were rotated to account for any variability due to anatomical location. A negative control site on the lower back was also used on each animal.

Skin lesions were evaluated by 6 bioengineering techniques. including a reflectance color meter (Minolta Chroma Meter, model CR-300) for erythema, high frequency ultrasound imaging (Cortex Technology, model Dermascan C) for edema (skin thickness), Laser Doppler Flowmeter (Perimed, model PF3) for cutaneous microvascular perfusion, Dermal Phase Meter (Nova Technology Corp., model DPM 9003) for skin hydration state, a Dermal Torque Meter (Dia Stron Limited, model DTM) for skin elasticity parallel to the surface, and a Cutometer (Courage and Khazaka, model SEM 474) for skin elasticity perpendicular to the surface.

Measurements were taken before exposure and at 6, 12, 18, and 24 hours post exposure (except that skin elasticity measurements were only taken before exposure and at 24-hours post exposure).

RESULTS

The results from each analytical technique are summarized in Figures 1-5. No data is presented for the skin hydration state because a correlation between HD dose and lesion response was not observed.

DISCUSSION

Erythema (Fig 1) reached a maximum by the first observation time (6 hrs) for all exposure doses. Previous work has demonstrated that the first indication of erythema occurs as early as 2 hours post exposure and reaches a maximum 4-6 hr post exposure. For all doses, erythema decreases slightly at observation times greater than 6 hr post exposure. The degree of erythema was essentially the same for the 5, 7, and 9 min doses. Previous work with the HGP demonstrated that the degree of erythema increased with a linear dose-response curve for HD vapor doses of 2 to 4 min. This current study confirms that observation.

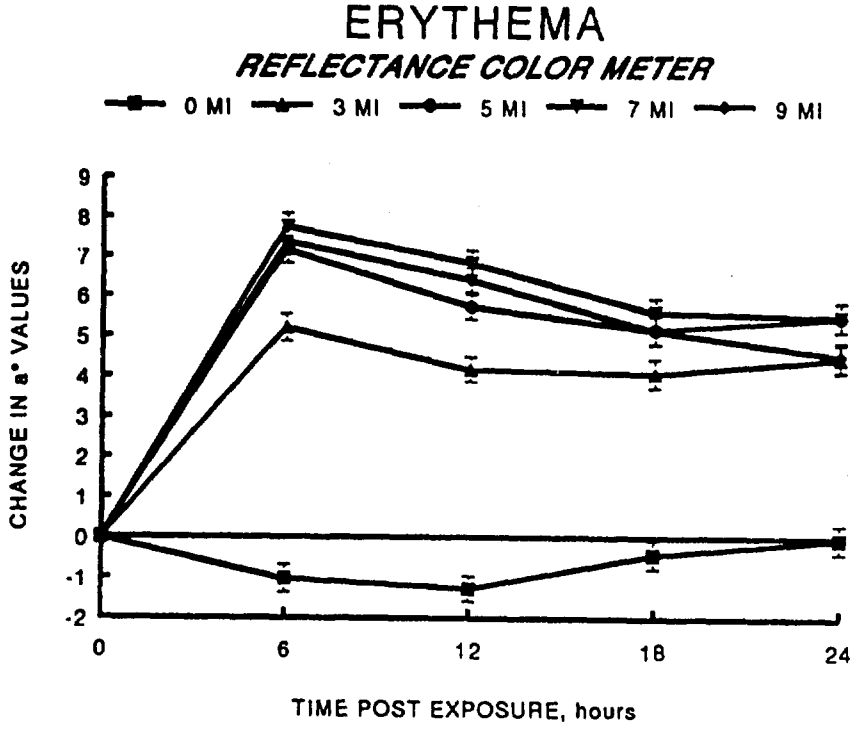

Fig 1. Erythema following HD vapor exposures of 0-9 min in HGP. Mean (± SEM) increase in reflectance color meter a* chromaticity values at various observation times (n = 28).

Edema (Fig 2) for all doses demonstrated a significant increase at the 6 hr post exposure observation, reached a maximum at the 12-hr observation, and then remained unchanged through the 24-hr observation. The edema response in the HGP was delayed relative to the erythema response. This is consistent with other animal models including man. At all observation times a dose-response relationship was observed.

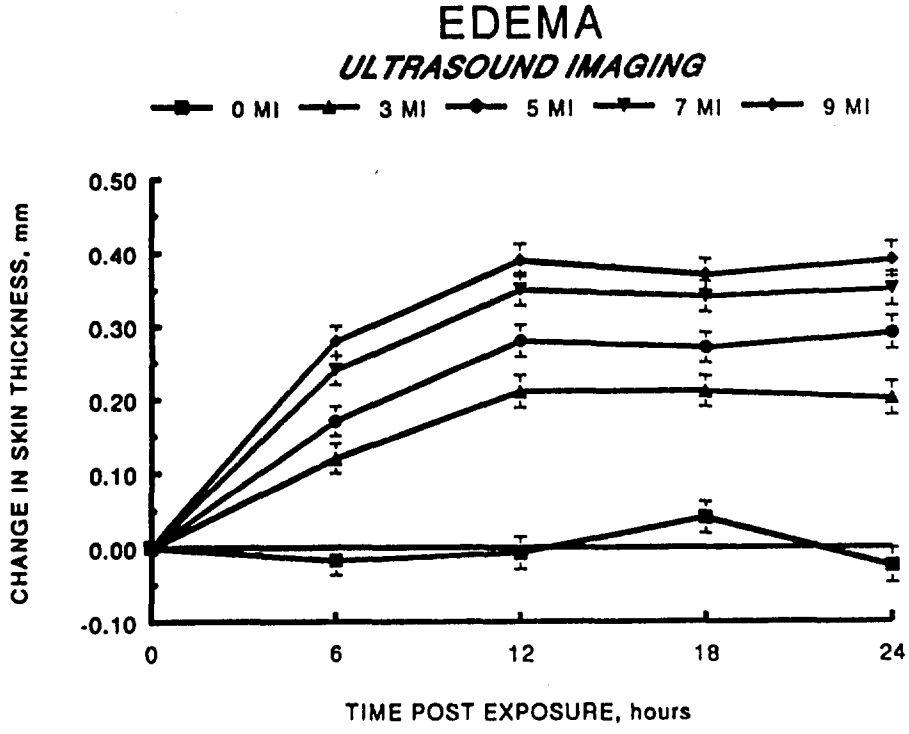

Fig 2. Edema following HD vapor exposures of 0-9 min in HGP. Mean (± SEM) increase in full skin thickness as measured by high frequency ultrasound imaging at various observation times (n = 28).

The microvascular perfusion (Fig 3) reached a maximum at the 6-hr post exposure observation and then remained unchanged through the 24-hr reading. The perfusion level reached a maximum with a 5-min exposure time. There was a close correlation between the erythema and microvascular perfusion data because both measured the same basic inflammatory response.

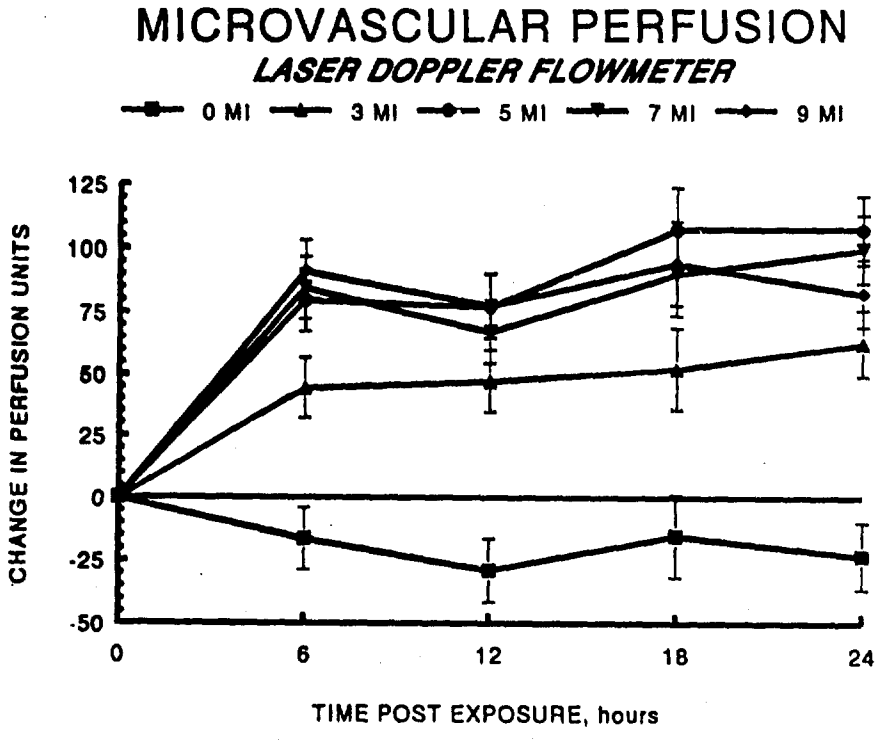

Fig 3. Microvascular perfusion following HD vapor exposures of 0-9 min in HGP. Mean (± SEM) increase in perfusion units as measured by the laser Doppler flowmeter at various observation times (n = 16).

Both measurements of the skin elasticity DTM (Fig 4) and Cutometer (Fig 5) showed a significant dose-response to HD exposure time but the Cutometer had a much greater dynamic range. The best interpretation for the observed decrease in skin elasticity with increasing HD dose at 24 hr post exposure is that significant edema (see Fig 2) caused the skin to be pre-stretched so that additional stretching was difficult.

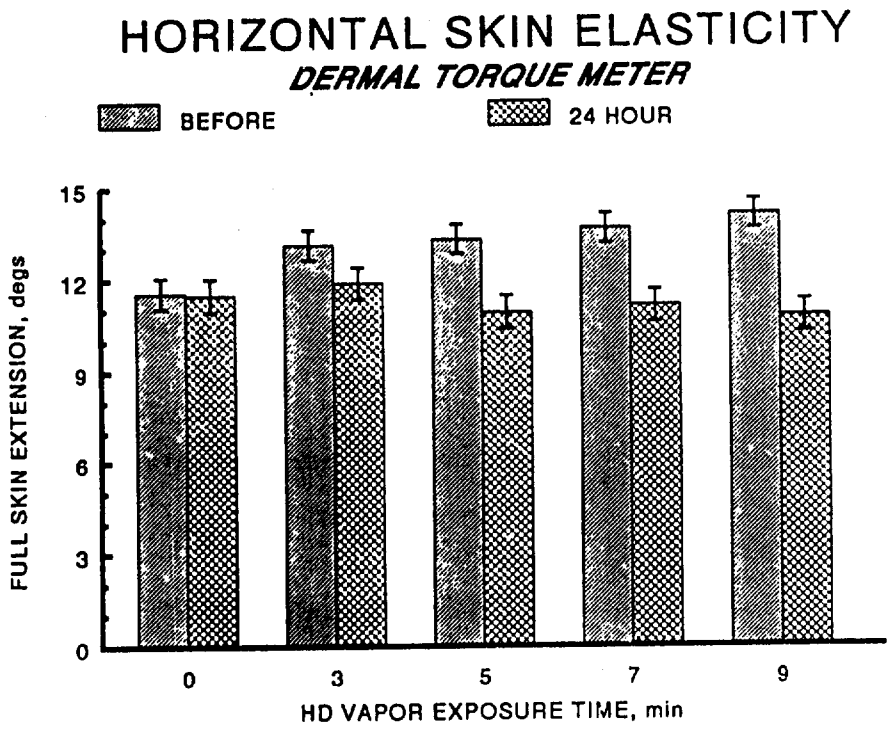

Fig 4. Skin Elasticity horizontal to surface following HD vapor exposures of 0-9 min in HGP. Mean (± SEM) full skin extension as measured by the dermal torque meter at various observation times (n = 28). Torque applied was 8 mNm.

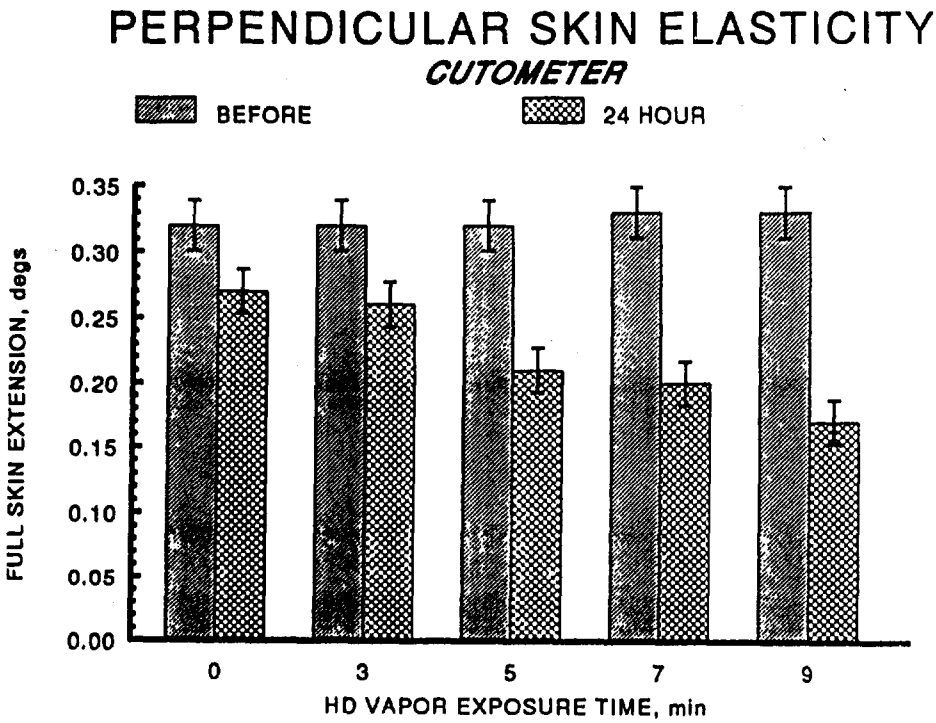

Fig 5. Skin Elasticity perpendicular to surface following HD vapor exposures of 0-9 min in HGP. Mean (± SEM) full skin extension as measured by the cutometer at various observation times (n = 28). Vacuum applied was 500 mbar.

CONCLUSIONS

Bioengineering techniques provide an objective, quantitative, and reproducible assessment of cutaneous injury following HD vapor exposure.

In the HGP, we have demonstrated a dose-response relationship between HD vapor exposure and erythema (reflectance color meter), edema (ultrasound imaging), microvascular perfusion (LDF), and skin elasticity (DTM and Cutometer).

All these instrumental methods provide an assessment of the inflammatory response following HD exposure.

These bioengineering techniques can be used for determining the efficacy of candidate antivesicant therapies.