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DERMAL TOXICITY OF THE TROPICAL
CYANOBACTERIUM CYLINDROSPERMOPSIS
RACIBORSKII

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Skin rashes commonly occur after recreational or occupational exposure to fresh waters infested with toxic cyanobacterial blooms but there are few if any pathological reports of skin lesions due to these organisms or their toxins.

It was recently shown that application of a culture of *Cylindrospermopsis raciborskii* to the abdominal skin of Balb/c mice resulted within 24 hours of a skin lesion characterized by erythema, oedema and scab formation. A histological study was then made of the progress of this lesion over 14 days following a single 70 µl application to 1 cm² of shaved abdominal skin of 190 µg cylindrospermopsis (CYN), the toxin per ml in 70% ethanol.

Inflammatory changes were evident by 12 hours and maximal by 48 hours, and characterized by epidermal ulceration, acanthosis and dermal oedema, hyperaemia and mainly polymorphonuclear infiltration. The changes had mainly subsided by 7 days and the skin had returned to normal by 14 days. In a subsequent dose response study in which the effect of a single exposure of 70% ethanolic CYN was observed, the no effect level was about 2 µg/ml.

In order to investigate the possibility of delayed contact sensitivity due to CYN, the mouse ear swelling test (MEST) was used. In this test, 100 µl of 70% ethanolic CYN at 100 µg/ml was applied to the shaved, tape stripped abdominal skin on days, 0, 1, 3 and 5, and 20 µl of 50 µg CYN/ml applied to the pinna of one ear on day 10. Ear pinna swelling was measured with a micrometer 24 and 48 hours post application of toxin. Two out of nine mice tested were positive for delayed contact sensitivity.

The study confirms that CYN is cytotoxic for the skin and in some individual animals can cause delayed contact sensitivity. Even though the toxin exposure levels are higher than those likely to be encountered by humans exposed naturally, skin rashes suffered by persons bathing in water infested by *C. raciborskii* may well have been directly caused by the toxin of this organism.

846 ANTIOXIDANT DEFENSE AND TOXIC EFFECTS OF
OCCUPATIONAL CHEMICALS TO SKIN

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A variety of compounds used in industry, such as cumene hydroperoxide (Cum-OOH), phenol (PhOH), and metal working fluids (MWFs), are toxic to the skin and can result in inflammation, allergic and contact dermatitis, and/or cancer promotion. The mechanisms for this toxicity are largely unknown. We hypothesize that free radical production with the attendant loss of antioxidant protection and the development of oxidative stress are key contributors to dermal toxicity. In vivo experiments revealed the formation of α-phenyl-N-tert-butyl nitro spin-trapped radical adducts in the skin of mice exposed to PhOH or Cum-OOH. Depletion of glutathione (GSH; pretreatment with DL-buthionine sulfoximine) prior to phenol exposure resulted in the production of significantly more radicals than in animals exposed to phenol alone. Similar results were obtained from animals given a vitamin E deficient diet for 20 weeks prior to dermal exposure to Cum-OOH. Mice maintained on a diet deficient in vitamin E and exposed to Cum-OOH had significantly higher rates of radical formation compared to the mice given a diet with a sufficient amount of vitamin E. Exposure to PhOH, Cum-OOH, or MWFs also resulted in reduction of antioxidant defense (oxidation of GSH and protein thiols, and decreased levels of vitamin E and total antioxidant reserves) in the mouse skin. Histologic evaluation after exposure to PhOH, Cum-OOH, or MWF revealed increased dermal inflammation when the above chemicals were applied to the skin of mice with pre-existing oxidative stress. In conclusion, impairment of antioxidant skin defense contributed to increased inflammation indicating the essential role of the latter against free radical skin damage. Antioxidant status is an important factor in determining the susceptibility to skin damage resulting from exposure to occupational chemicals.

847 EVALUATION OF DIPHOTERINE FOR RINSING OF
ALKALI BURNS AT THE HOSPITAL

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Alkali eye burns cause serious injuries. Because of the potential serious outcomes, a comparison was made of two emergent eye decontamination solutions: normal saline and Diphoterine. Diphoterine is an amphoteric and hypertonic polyvalent agent for eye/skin chemical splash rinsing.

Before the study, in vitro and in vivo tests were performed in order to show the interest of the study. The clinical study was approved by the appropriate human subjects committee. All consecutive cases of alkali ocular burns treated at the University Hospital Center of Fort de France were prospectively collected during a 4-year period. Injuries were classified according to the Roper-Hall classification (Grades 1-4). Regardless of the decontamination product used, the remainder of the therapeutic protocol was standardized according to injury Grade.

In vitro tests showed that ammonia penetrates through a semi-permeable membrane when the concentration is 0.35N. In vivo tests showed an absence of edema with more preservation of endothelial cells and decrease of intraocular pH with Diphoterine rinsing. During the clinical study, there were 66 cases of ocular alkali burns. Of these, 28 of patients had a unilateral burn. 48 eyes were decontaminated with normal saline and 56 eyes with Diphoterine. For Grades 1 and 2, the elapsed time to reepithelialization was significantly shorter with Diphoterine decontamination. There were insufficient cases in Grades 3 and 4 for statistical comparison.

In this clinical study, the elapsed time to reepithelialization was shorter in Grade 1 and 2 burns when Diphoterine was the decontamination solution. These results are comparable to prior observational studies and with in vivo studies. Diphoterine should be considered as an alternative to normal saline or other decontamination solutions for chemical eye splashes.

848 BERYLLIUM EXPOSURE AND THE PREVALENCE OF
CHRONIC BERYLLIUM DISEASE AND BERYLLIUM
SENSITIZATION

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The current Occupational Exposure Limit (OEL) for beryllium was believed to be protective against chronic beryllium disease (CBD) until studies in the mid-1980s began using newer medical diagnostic techniques that identified beryllium sensitization (BeS) and subclinical disease in the absence of physical symptoms. The objective of this study was to review all available epidemiologic studies of beryllium workers to assess whether any patterns are observed for exposure indices, job categories, manufacturing processes, chemical forms of beryllium (e.g., beryllium oxide, metal, and alloy), and the prevalence of CBD and BeS. In addition, the influence of particle size and different exposure metrics on CBD and BeS was evaluated. Despite considerable variation in study findings, several patterns are apparent. First, the prevalence of CBD and BeS was greatest among workers involved with machining or grinding of beryllium oxide and metal. Second, no cases of CBD have been reported among workers with exclusive exposure to mining or processing of beryllium ore. Third, differences in the prevalence of CBD involving work with different chemical forms of beryllium appear to be dependent on the operation and generation of fine particulate. Fourth, frequency and magnitude of peak concentrations, as well as particle size, appear to be associated with the prevalence of CBD and BeS. In contrast, mean or median airborne concentrations of beryllium, cumulative dose, and exposure duration have not provided consistent dose-response associations. Fifth, CBD and BeS are observed among workers who are employed in areas where airborne beryllium concentrations are generally greater than 0.2 µg/m³. Based on what has been learned in recent years, increased risk of BeS and CBD is likely derived from a combination of factors, such as particle size, chemical form of beryllium, and peak exposure, which are important to consider when setting an OEL for beryllium.

849 BERYLLIUM SENSITIZATION AND CHRONIC
BERYLLIUM DISEASE IN A BERYLLIUM METAL
MACHINING PLANT: ANALYSIS OF BERYLLIUM
EXPOSURE AND IMPLICATIONS FOR AN
OCCUPATIONAL EXPOSURE LIMIT

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The current occupational exposure limit (OEL) for beryllium has been in place for more than 50 years and was believed to be protective until medical diagnostic techniques in the 1980s identified beryllium sensitization (BeS) and chronic beryllium disease (CBD) in the absence of physical symptoms. A major challenge in identifying a revised OEL for beryllium is that previous studies have used inconsistent sampling and exposure assessment methodologies and definitions for BeS and CBD. These differences have prevented direct comparisons between studies, as well as the identification of a clear exposure-response relationship. Industrial hygiene and health surveillance data from a beryllium metal machining facility were analyzed to assess whether this information provides insight into the exposure-disease relationship for BeS and CBD, which could be useful in identifying an OEL that is protective of worker health. Airborne beryllium concentrations for different job titles were evaluated, historical trends of personal and ambient beryllium levels were compared for pre- and post-engineering control measures (implemented in the