

478 IMMUNOTOXIC EFFECTS OF EXPOSURE TO UV: STUDIES IN HUMAN SUBJECTS AND ANIMAL MODELS. K D Cooper, Immunodermatology Unit, Dept. of Dermatology, Univ. of Michigan, Ann Arbor, MI

UVB radiation has both carcinogenic and immunotoxic effects both in *in vitro* and *in vivo* systems. Dose response relationships exist in animal models for immunosuppression, acute photo toxicity, susceptibility to skin cancers and infectious diseases, and for immunization capacity. Recently we have been performing experiments in humans to determine a) whether immunosuppression occurs in humans as it does in mice after UV exposure, and b) the dose response relationship. Humans were indeed susceptible to the immunotoxic effects of UV radiation, and a 50% immunosuppressive dose can be calculated. To determine the extent of the population at risk, studies were performed to determine whether males and females have equal susceptibility. To determine if people of various skin types were equally susceptible, and if not, to what degree susceptibility can be ascertained, subjects were divided into fair skin med types (skin type I - III) and people of color (skin types IV-V). To determine whether the major mitigating strategies for protection against UVB radiation are effective against immunotoxic UVB effects, studies of immune suppression following sunscreen usage during UV exposure have been initiated. Thus, the dose response relationship of immune suppression with UV exposure, and the population at risk can be determined.

479 IMMUNOTOXICITY OF OZONE: A COMPARISON OF EFFECTS IN ANIMAL MODELS AND HUMAN SUBJECTS. R.B. Devlin, J.M. Johnson, M.J. Selgrade, S. Becker, and H.S. Koren. Health Effects Research Laboratory, US EPA, RTP, NC.

It is important to be able to extrapolate from animal toxicological data to human health risk for many pollutants for which direct human exposure data is not available. To develop such an extrapolation model for immunotoxicity, humans and mice were exposed to roughly comparable concentrations of ozone, and alveolar macrophages removed and assayed for the ability to phagocytose *C. albicans*. Phagocytic assays were also performed on human and mouse alveolar macrophages which were exposed to identical concentrations of ozone *in vitro*. These *in vitro*-exposed cells from both humans and mice had virtually identical decrements in phagocytic capacity. In addition, macrophages removed from *in vivo*-exposed humans and mice both had significant decrements in phagocytic capability. These data suggest that *in vitro* exposure of human and animal cells to ozone, coupled with *in vivo* exposure of animals, may be predictive of human *in vivo* exposure. This approach may be useful in using animal data to extrapolate the effects of toxic gases for which direct human *in vivo* exposure data cannot be obtained. This abstract of a proposed presentation does not necessarily reflect EPA policy.

480 THE SCID MOUSE AS A TOOL TO BRIDGE THE GAP BETWEEN HUMAN AND ANIMAL RESPONSES. H van Loveren, C de Heer, National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands.

Severe combined immunodeficient (SCID) mice lack functional T and B lymphocytes, and sustain the differentiation of xenogeneic (human) lymphoid cells from fetal lymphoid xenografts (SCID-hu mice). SCID mice have also been populated with human peripheral blood leukocytes (hu-PBL-SCID mice). These two model systems have already been shown to be valuable for the study of the human immune responses and lymphohematopoietic disorders. Attempts have now been made to use these model systems to study the toxicology of the human immune system. Experiments were started in which the immunotoxic agent 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) will be studied using the SCID model. Adverse effects on human lymphoid cells and/or tissues transferred in SCID mice will be compared with animal data. Obviously, models as described here have certain restrictions. Yet, data yielded by these models will have implications for the process of human risk assessment.

481 PROBLEMS ASSOCIATED WITH ASSESSING IMMUNOTOXIC EFFECTS IN HUMAN POPULATIONS EXPOSED OCCUPATIONALLY. R. E. Biagini, E. M. Ward and R. Vogt CDC/NIOSH & CDC/NCEH, Cincinnati, OH and Atlanta, GA

Field studies in humans designed to detect immunomodulation from exposure to xenobiotics present challenging problems to epidemiologists and immunotoxicologists. Exposed and control groups must be carefully selected, exposure to the xenobiotic must be sufficiently high and well documented, and the control group should be as similar as possible to the exposed. Immune biomarkers/function tests in an individual may be influenced by sunlight exposure, medication, illness and use of recreational drugs; all of these potential "confounding factors" must be taken into account. Sample acquisition usually is performed at sites geographically distant from the controlled environment of an investigator's laboratory, yielding an assortment of new problems that would not occur in clinical or hospital situations. Regulations and guidelines concerning the transport of biological samples and potential HIV and HBV exposure to personnel must be adapted to field conditions. In addition to the above, test batteries used must be designed to eclectically detect modulation of the immune system. For example, in an investigation of ethical narcotics production workers, NIOSH investigators found both evidence of immunosuppression (significantly decreased percentages of T helper-inducer [CD4<sup>+</sup>] cells), evidence of opiate-class sensitization (lowered epicutaneous titration thresholds), elevated anti-morphine IgG, and an elevated prevalence of asthma. In a non-comprehensive design directed to detect only immunosuppression as an expected outcome, much significant information would have been left undetected.

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## Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster/discussion, and poster sessions of the 33rd Annual Meeting of the Society of Toxicology, held at the Loews Anatole Hotel, Dallas, Texas, March 13-17, 1994.

An alphabetical Author Index, cross-referencing the corresponding abstract number(s), begins on page 439.

The issue also contains a Keyword Index (by subject or chemical) to the titles of all the presentations, beginning on page 467.

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