

were also included for vehicle and naive controls. Both DCC and EDC produced a clear dose-related increase in lymphocyte proliferation in draining auricular lymph nodes compared to vehicle controls and stimulation indices of  $\geq 3$  were obtained for all but the lowest concentrations tested for each compound. Therefore, the threshold for skin sensitization was between 0.01 and 0.03% for DCC and between 0.1 and 0.3% for EDC. DCC was equipotent to DNCB in this assay. The results of the study show that both DCC and EDC have the potential to induce contact hypersensitivity and the potency of DCC appears to be 10 times higher than EDC at equivalent concentrations. The guinea pig maximization test for these two compounds yielded parallel results.

#### 1480 COMPARISON OF MURINE MODELS FOR THE IDENTIFICATION OF POTENTIAL CHEMICAL SENSITIZERS.

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Efforts have been underway to develop a phenotypic analysis assay for the identification and differentiation of chemicals with the potential to induce irritation and IgE mediated and T cell mediated sensitization. The purpose of these studies was to compare results obtained with this assay to those obtained in the Mouse Ear Swelling Test (MEST) and the Local Lymph Node Assay (LLNA). The Irritancy/Phenotypic analysis assay utilizes the endpoints of ear swelling for irritation and the expression of B220 and IgE on the lymph node cells draining the site of chemical exposure as an indicator of sensitization. By measuring the increase in ear swelling, the MEST evaluates the elicitation response of previously sensitized mice following chemical challenge. A mouse ear swelling irritancy assay is used to determine the minimal irritating concentration of each chemical to be used as the challenge concentration in the MEST. The LLNA utilizes [<sup>3</sup>H]-thymidine incorporation into draining lymph node cells as a measure of lymphocyte proliferation during the sensitization phase. Known human sensitizers, potassium dichromate (PDC) and 2,4-dinitrochlorobenzene (DNCB), and the irritant methyl salicylate (MSC) were used for the dose response comparison studies. Female BALB/c mice were exposed topically to the chemicals following the protocol for each assay (four consecutive daily exposures for both the irritancy/phenotypic analysis and LLNA and three days of induction followed by a single challenge eight days post initial exposure for the MEST). DNCB was identified as a sensitizer in all three assays at concentrations as low as 0.25%. MSC tested negative at all concentrations in the MEST, LLNA, and phenotypic analysis assay. PDC tested positive as a sensitizer in the LLNA at concentrations as low as 0.25%, while it tested positive only at the 0.5% concentration at the 48 hr measurement of the MEST. Results obtained in these studies from the Irritancy/Phenotypic analysis assay were comparable to those for the MEST and LLNA. (These studies were supported in part by the NIOSH/NIEHS interagency agreement #Y02ES10189.)

#### 1481 EFFECT OF VEHICLE ON POTENCY ASSESSMENT IN THE LOCAL LYMPH NODE ASSAY.

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The murine local lymph node assay (LLNA) has been validated for the identification of skin sensitization hazards. Contact allergens are identified as a function of proliferative responses induced in draining lymph nodes and this provides the opportunity also of assessing relative potency by reference to dose response analyses. In the current investigations, the known skin sensitizer 1,4-dihydroquinone has been tested in 7 vehicle systems in each of two independent laboratories. The results from the two laboratories were almost identical. The dose response data from the pairs of LLNAs were interpolated using a statistical model to derive the estimated concentration of 1,4-hydroquinone necessary to cause a 3-fold stimulation of proliferation, the EC3 value. The vehicles and mean EC3 values obtained were as follows: methylethylketone 0.07%; acetone 0.08%; acetone/olive oil (80/20 v/v) 0.15%; dimethylformamide 0.22%; dimethylsulfoxide 0.4%; propylene glycol and acetone/saline (50/50 v/v) vehicles both yielded negative results. Thus the results demonstrate that the apparent potency of a contact allergen can depend critically on the vehicle in which it is presented. These data reveal that the vehicle in which a chemical is encountered in the skin can have a significant impact upon skin sensitization potency. The implication is that accurate assessment of risk to humans will require an appreciation of the likely condition of exposure.

#### 1482 SEROPREVALENCE OF NATURAL RUBBER LATEX-SPECIFIC IgE ANTIBODY IN NON-HEALTHCARE WORKERS.

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Serological assays for latex (LAT)-specific IgE antibody are extensively used in the diagnosis of LAT allergy. We present the results of testing sera with two FDA 510K cleared, LAT IgE kits (CAP System and ALA/STAT Microplate [ALA]). Total IgE levels were also measured. The sera were obtained from 381 workers employed in numerous, non-healthcare industries over the last ten years and stored frozen. Twenty-six sera gave positive (pos) results using the ALA assay (6.82%), while 24 yielded pos results (6.30%), using the CAP assay (pos cutoff =  $\geq 0.35$  kIU<sub>AY</sub>/L). The assays agreed on the pos or negative (neg) status of 349 samples (91.6%). Discordant results (ALA pos, CAP neg) occurred in 17 sera (4.46%), while ALA neg, CAP pos results occurred in 15 sera (3.94%). Both assays agreed on the pos status of 9 sera (2.36%). The mean total IgE of all sera (N=374) was  $144.19 \pm 284.00$  kU/L ( $\pm$  SD). There were no significant differences (P=NS) between the mean ALA and CAP assays' measurements of LAT antibodies for all 381 participants, yielding  $0.28 \pm 0.19$  and  $0.34 \pm 0.59$  kIU<sub>AY</sub>/L, respectively. CAP and ALA results were significantly correlated, ( $0.271$ ,  $P < 0.01$ ). When sera with only pos LAT IgE antibodies were evaluated, CAP yielded significantly higher results than ALA ( $1.71 \pm 1.93$  (N=24) vs.  $0.75 \pm 0.55$  kIU<sub>AY</sub>/L (N=26), ( $P < 0.05$ ). Pearson correlation analyses of all sera indicated significant, albeit low, associations between total IgE levels and LAT specific IgE levels (ALA=0.117,  $P < 0.05$ ; CAP=0.411,  $P < 0.01$ ). These data indicate that both the CAP and ALA LAT specific antibody kits essentially agree on the seroprevalence of LAT IgE in non-healthcare workers (6.30% vs. 6.82%), respectively, and also agree with the seroprevalence (ALA, 6.4%) reported in 1000 blood donors (Ownby, 1996). The CAP assay gave significantly higher mean levels of LAT specific antibody in pos individuals than the ALA assay. However, both assays identify different individuals as being "pos", most probably since these assays detect different subsets of antibodies, presumably to different LAT allergen epitopes present in the kits.

#### 1483 MURINE IMMUNE RESPONSES TO NATURAL RUBBER LATEX PROTEINS.

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It has been estimated that up to 17% of the 5.5 million U.S. health care workers (HCW) demonstrate IgE antibodies to natural rubber latex (NRL) products; an even higher prevalence of latex allergic spina bifida patients have been reported (as high as 70%). Furthermore, different allergen specific IgE profiles have been associated with HCW as compared to spina bifida patients. Although the exposure routes which elicit allergic responses are identifiable, the route(s) by which NRL sensitization occurs remains unclear. Our objective is to develop murine models representative of different routes of exposure to better understand latex sensitization and for testing intervention methodologies. Female BALB/c mice were treated for ~2 months subcutaneously (sc) or topically (abraded or intact skin sites) with latex proteins ranging from 1.5µg - 200µg per exposure. Following sc exposure, total IgE levels were elevated in a dose response fashion beginning at day 14 and peaked near 12,000ng/ml following 8 weekly injections of 200µg. Likewise, IgE levels were increased 9-fold after two weeks of daily applications to abraded skin sites using 150µg of latex protein diluted in acetone. Fifty µg applications to abraded skin sites also resulted in greater than a 4 fold elevation in total IgE by day 16 whereas intact skin exposure produced no increases until day 37. By day 53, total IgE concentrations following 50µg topical exposures were comparable between "abraded" and "intact" mice. Antigen specificity was demonstrated when *in vitro* stimulation of splenocytes (sc exposed mice) with 20µg/ml latex proteins caused a 500% increase in <sup>3</sup>H-thymidine uptake. Immunoblots identified IgE specific for all of the major latex allergens (Hev b1-7) following either sc or topical latex exposure. Functional, latex specific IgE was demonstrated in a murine Active Cutaneous Anaphylaxis assay within 5 minutes of intradermal latex protein challenge (~10µg) in the ear. These results indicate that BALB/c mice should serve as an acceptable model to study hypersensitivity to NRL. (This project is supported in part by NIOSH/NIEHS Interagency Agreement #Y02ES10189.)

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# Preface

**This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster / discussion, workshop, roundtable, and poster sessions of the 38<sup>th</sup> Annual Meeting of the Society of Toxicology, held at the Ernest N. Morial Convention Center, New Orleans, Louisiana, March 14-18, 1999.**

**An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 419.**

**The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 444.**

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