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The cutaneous immune response becomes insensitive to oxazolone stimulation following chronic application of 0.1% and 0.5% oxazolone. Lei Zhang, Brenda Abrigo, Sally S. Tinkle. CDC/NIOSH. Morgantown, WV 26508. SPON: M.I. Luster

Many studies have documented that, in cutaneous hypersensitivity (CHS), 0.5% - 3% oxazolone (OXA) induces keratinocyte hyperplasia, cell infiltration into the dermis, Th1/Th2 cytokines and lymph node cell proliferation. To evaluate these parameters in a chronic, low dose exposure paradigm, B6,129 mice were sensitized and challenged with 0.5%, 0.1% or 0.05% OXA (week 1), and challenged 3 consecutive days each week for 5 weeks. Ear thickness increased significantly with application of 0.5% OXA only and declined toward baseline by week 6. Histological analysis of challenged ears revealed dose-dependent keratinocyte hyperplasia and inflammatory cell infiltration that peaked in weeks 2 and 3 and decreased in magnitude by week 5. An *in situ* apoptosis assay revealed significant increase in apoptotic cells in the dermis in week 3, compared to week 1. We measured dose-dependent increases in IL-1- β , IFN- γ and IL-4, however IFN- γ levels declined significantly in week 3, whereas IL-1- β and IL-4 remained elevated. 0.5% OXA, but not 0.1% or 0.05%, increased TNF- α significantly. OXA did not induce *in vitro* lymph node cell proliferation for any concentration of chemical after a single challenge dose (week 1) and no cell proliferation for 0.05% OXA at any time point. 0.5% OXA induced 4.8 and 10.5 fold increases in cell proliferation at weeks 2 and 3, but not at week 6. 0.1% OXA induced a 3 fold increase in proliferation at week 3. These data demonstrate that 0.5% and 0.1% OXA stimulate CHS for 2 to 4 weeks but that the cutaneous immune response to OXA becomes insensitive to OXA stimulation after 5 to 6 weeks of chronic, low dose chemical exposure. (Support by CDC/NIOSH)