16. The Role of Sensitization Routes in the Development of Type I Hypersensitivity to Natural Rubber Latex in Mice

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Latex allergy has become recognized internationally as a serious health hazard. The most concerning allergic response to natural rubber latex (NRL) products include asthmatic reactions and life threatening anaphylactic shock. While the prevalence of latex allergy in the general population has been estimated between 2.5% and 6.5%, increased risk has been associated with several occupations and medical conditions. It has been suggested that approximately 17% of the 5.5 million U.S. health care workers (HCW) are now allergic to NRL while even higher incidences of latex allergic spinda bifida patients have been reported (20%–70%). In addition to the varied prevalence rates, different allergen specific IgE profiles have been associated with HCW as compared to spina bifida patients. As HCW are thought to be primarily exposed to latex allergens dermally and by inhalation, and spina bifida children are additionally exposed subcutaneously to latex via numerous surgical procedures, a leading hypothesis is that the route of latex sensitization results in the varied IgE immune response. Preliminary studies were designed to demonstrate the ability of mice to mount IgE responses to NRL proteins. Female B6C3F1 mice were dosed intranasal with ~10μg of latex protein every fifth day over 5½ weeks (9 exposures total). ELISA determinations demonstrated total IgE levels for latex protein treated mice which were almost 4-fold higher than those of control mice (3,500 ng/ml vs. 900 ng/ml). In addition, spleens and lung associated lymph nodes from these mice were analyzed by flow cytometry and demonstrated increased expression in B220 (B-cells) and surface IgE. 73% of the B220(+) lymphocytes from latex treated mice stained positive for surface IgE while only 13.5% did so for vehicle exposed mice. Likewise, 43% of B220(+) splenocytes stained positive for IgE compared to 9% from vehicle mice. In subsequent studies, mice were injected subcutaneously once per week with doses of latex proteins ranging from 1.5μg–200μg. Mice were tail bled weekly and total IgE levels were monitored. Total IgE concentrations were significantly increased by day 14 following injections of only 12.5μg of latex protein and peaked above 10,000 ng/ml in one study and 5,000 ng/ml in another following 50μg injections. These experiments suggest that the mouse will serve as an acceptable test system to mimic latex exposure routes. Future studies will also examine the IgE, splenocyte, and draining lymph node responses following exposure to latex proteins by inhalation and topical application. IgE immunoblot profiles will be characterized to help support the hypothesis that the exposure route by which NRL sensitization occurs results in the varied NRL immune responses reported in the literature.

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