

Application of flow cytometric measurement of Th1/Th2 intracellular cytokines to epidemiology studies of children exposed to environmental toxicants.

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Studies of chemically induced toxicity in children have focused on neurotoxicity, genotoxicity, and carcinogenicity, with less emphasis on the immunotoxic effects. Yet, recent studies show that exposures to pesticides and air pollution are associated with immune-related disorders including immunosuppression, leukemia, and asthma. Cellular immunophenotyping, antibody production, and cytokine secretion are important indicators of immune function and thus potential immunological biomarkers. To evaluate the feasibility of using these markers in studies involving children, we conducted several validation experiments to assess the effects of subject age, blood sample volume, and timing of sample collection and processing on the variability and reproducibility of flow cytometric measurements of T-helper lymphocyte cytokine production (Th1/Th2), immunophenotyping of cell subpopulations, and IgE antibody production in adults and children. Inter- and intra- individual variability of these markers were evaluated over six months, in addition to the effect of a 24hr, 48hr, and 72hr delay in processing and analysis. T-helper lymphocyte percentage was found to be consistent in adults over the 6-month period and stable after delayed analyses. The Th1 and Th2 subpopulations were also stable over time. Young children on average produce 10-times less Th1 IFN- γ cytokine and IgE antibody than adults. Th1 cytokine levels were inversely and Th2 directly correlated with IgE production. These results are consistent with the current understanding of IFN- γ 's inhibitory role on IgE production. We plan to utilize these biomarkers to investigate whether prenatal and early childhood exposures to pesticides and air pollution alter the immune response, including subsequent development of immunosuppression and asthma.