A Simple Biologically-Based Dynamic Model for Beryllium Sensitization

Stefaniak, A B[*]; Virji, M[*]; Day, G[*]; Schuler, C[*]; Tinkle, S[†]

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*National Institute for Occupational Safety and Health, Morgantown, WV, USA; and, †National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA.

- Background:
- Objectives:
- Discussion:

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Background:

People exposed to beryllium compounds are at risk of developing immunologic sensitization to beryllium (SENS). Using inhalation exposure estimates derived from airborne sampling data, epidemiology studies have been unable to demonstrate a clear and consistent exposure-response relationship for SENS.

Objectives:

The purpose of this work is to present a novel, biologically based dynamic model that emphasizes the contribution of skin exposure in development of SENS and focuses on a few key steps in the progression from skin exposure to SENS. This model is part of a larger overall conceptual model that accounts for inhalation exposure. For at least a subset of the beryllium exposed population, skin exposure is the primary contributor to SENS (i.e., more immunologically sensitive organ than the lung).

Discussion:

Development of SENS is known to require exposure factors and involve immunologic and genetic factors; however, the mechanisms by which these factors interact to cause SENS remains poorly understood. In our model, exposure factors include contaminant distributions (mass, chemistry, and particle size, number, and surface area) and the rates at which materials are deposited, cleared, and made bioavailable in the skin. Immunologic factors include the rates at which bioavailable material is processed to form antigen; antigen is presented by Langerhans cells and recognized by beryllium-naïve T-lymphocyte cells (a genetic factor); and activated T-lymphocyte cells proliferate and differentiate into beryllium-specific memory CD4+ T-cells (i.e., development of SENS). We hypothesize that the rate-limiting exposure factor in the SENS process is the rate at which beryllium becomes bioavailable in the skin. As such, biologically relevant exposure metrics for SENS include beryllium dissolution rate characterized by chemistry, particle size and surface area and the exposure pattern (duration, amount, etc.). In summary, this model is potentially useful for selecting biologically relevant metrics of exposure for use in the development of job-exposure matrices for epidemiology studies of systemic sensitizers.