Airborne contaminants, such as toxic or irritating gases and particles, typically make first contact with the body on the inner surfaces of the nasal passages. The effects of exposure to such pollutants depend strongly on the patterns in which the contaminants are absorbed or deposited in the nasal passages, and the efficiency of their transport to the rest of the body through the bloodstream. Knowing where absorption or deposition is likely to occur is important to assessing the nature of risks posed by exposures to airborne contaminants. How far into the respiratory tract are they drawn? Where in the respiratory system are the gases absorbed or the particles deposited? Scientists who conduct “dosimetry” research aim to answer these and other questions that are vital to understanding how the level of a pollutant in the atmosphere translates into the amount of that pollutant present in sensitive tissues.

Currently, most human risk assessments of inhaled chemicals are based on extrapolations from studies of laboratory animals. These extrapolations introduce uncertainty, because the anatomy and airflow patterns of the human nasal cavity are quite different from those of rats and other laboratory animals. As shown in the figure, gases absorbed in one area of the upper respiratory tract in rats may be absorbed in a different area in humans. Furthermore, the physical structure of human nasal cavities varies across age groups, sexes, and ethnicities. Even individuals within the same group have different nasal cavity structures.

Approximately one third of the U.S. Environmental Protection Agency’s (EPA) inhalation reference concentrations (RfCs)—estimates of the level of continuous exposure to a chemical likely to carry no risk of adverse health effects during a person’s lifetime—are based on nasal effects. EPA and several other organizations, nationally and internationally, use these RfCs as inputs to decisions to protect health. The current RfCs for nasal toxicants rely on relatively crude estimates of nasal dose and absorption. Using dosimetry research to improve the science underlying these estimates will lead to more accurate assessments of potential health risks associated with inhalation exposure to hazardous air pollutants (“air toxics”), particulate matter, and chemicals found in occupational settings.

Three-dimensional computer models of the upper respiratory tract are a promising method for characterizing the differences between the nasal anatomies of laboratory animals and humans. The research described here, performed by Dr. Julia Kimbell and colleagues and sponsored by the Long-Range Research Initiative (LRI), involves the development of sophisticated models that can reduce the uncertainty associated with differences in nasal dose delivery and absorption between laboratory animals and humans. The models also are being used to help study factors that affect uptake of pollutants in the nasal cavity, enabling researchers to improve characterization of differences in nasal uptake between different groups of individuals, such as children and adults.

Different Noses, Different Doses

These diagrams show the simulated rate of delivery of formaldehyde to the wall of nasal cavities of a rat and a human based on a constant air flow.*

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The Long-Range Research Initiative (LRI), a program of the American Chemistry Council, sponsors research that increases scientific knowledge of the potential impacts that chemicals may have on human health, wildlife, and the environment. Results are publicly available. This LRI Perspective is one in a series of documents that summarize LRI-sponsored research. See www.USLRI.org.
Dr. Kimbell and her colleagues developed computational fluid dynamics models of rat and human nasal cavities based on computer reconstructions of the nasal passages of both species. The data for these reconstructions came from cross-sections of rat nasal passages and magnetic resonance imaging (MRI) scans of humans. The resulting models provide anatomically accurate, three-dimensional “meshes” that can be used to simulate airflow and the transport of inhaled gases through the nasal airways.

The researchers built a range of airflow rates into the model in order to simulate differences in the speed and flow of air through the upper respiratory tract that occur between a resting individual and an active one. The models also can account for changes in the route of breathing (such as from nose to mouth during heavy exertion) and even differences between a congested nasal passage (modeled using MRI scans of a congested nose) and one that is dilated.

Finally, the models incorporate the physical characteristics of the airborne contaminants being tested, such as the absorption characteristics of gases and the size and shape of particles. The models simulate the inhalation and transport of airborne contaminants using the major mechanisms of gas transport, taking into account anatomical features such as the presence of mucus lining in the nasal cavity and its effect on the absorption of gases.

Recently, Dr. Kimbell’s group began using the models to create plastic nasal molds, which can be used to confirm the predictions of the computer models.

The models developed in this research reveal significant differences between humans and rats in the uptake of gases and deposition of particles in the nasal cavity (see the graphic on page 1). By providing a detailed representation of the areas where absorption or deposition occur, these models facilitate the analysis of how physical differences between species and among individuals of the same species affect sensitivity to exposure. The improved understanding helps increase the accuracy of predictions of uptake and absorption that are used to support the derivation of RfCs and other toxicological criteria for protecting human health.

A good example of the relevance of Dr. Kimbell’s research to the protection of human health is provided by the group’s investigation of differences in nasal uptake between adults and children. In addition to developing four nasal models of human adults, the team is creating a model that simulates the behavior of airborne pollutants in the nasal cavity of a four-and-a-half-year-old child. This model can be used to estimate levels of exposures in children more realistically than the frequent current practice of using generic adult models to estimate children’s doses. Identifying and assessing potential risks to children’s health is an important priority for U.S. regulatory agencies, as directed by President Bush in April 2003, when he extended Executive Order 13045 requiring Federal agencies to conduct children’s health risk assessments for regulations that have significant economic consequences or potential disproportionate effects on children’s health.

Increasing the accuracy of risk assessments can increase the confidence of regulators and the public that sensitive populations—including children—are adequately protected, while helping ensure that costs associated with regulating air pollutants are commensurate with risk and with the degree of health protection that is achieved. EPA currently is evaluating how biologically based models, such as those developed by Dr. Kimbell, can be used to improve risk assessments. Among other benefits, the models can be used to perform experiments that replace some costly and animal-intensive laboratory studies.

Dr. Kimbell’s work has generated a surge of interest among other researchers in the field of nasal dosimetry, and has made a major contribution to improving the quality of human health risk assessments for airborne contaminants. This work also has important implications for the study of respiratory disease, allergy, and comparative physiology.


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