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REGIONAL AEROSOL DEPOSITION IN HUMAN UPPER AIRWAYS

Progress Report
for Period March 1, 1992 - February 28, 1993

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Technical Progress Report

Project Title: Regional Aerosol Deposition in Human Upper Airways
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Abstract

During the report period, laboratory experimental studies were carried out to investigate the factors influencing the deposition of aerosols ranging in size from 1 nm to 10 μm in the human nasal, oral, pharyngeal and laryngeal airways. These experimental studies were performed in replicate upper airway physical models and in human volunteer subjects. New replicate models of the oral passage of an infant, the oral passage of an adult at two openings and the combined nasal and oral airways of an adult were constructed during the period, adding to the existing models of adult, child and infant nasal and oral airways models.

Deposition studies in the adult oral and adult nasal models were performed under simulated cyclic flow conditions with 1 nm particles to compare with previously measured constant flow studies. Similar studies with inertial particles (1-10 μm diameter) were performed with the adult nasal model; in both instances, results with cyclic flow were similar to constant flow results using a simple average flow rate based on inspiratory volume and time of inspiration. Human subject studies were performed with particle sizes 5-20 nm for nasal inspiration; preliminary analysis shows good agreement with model studies at several representative flow rates. Nasal inspiratory inertial deposition of 1-4 μm diameter particles was measured in several adults as a function of airway dimensions; dimensional changes of the valve area by decongestion did not produce concomitant deposition changes.

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Replicate Model Construction

Several new models of the adult and child nasal and oral passages have been constructed in the report period. These models did not employ magnetic resonance images as with past replicates, but were constructed from a combination of post mortem and in vivo negative casts. Two new adult mouth casts were constructed; these extended from the lips to the mid-trachea and represented two degrees of open oral passage corresponding to medium and heavy exercise. The passage from epiglottis to mid-trachea was similar to the original oral mouth model, made from a post-mortem negative cast. The anterior oral passage was copied from dental alginate impressions made in vivo from uncured alginate boluses. The oropharynx was sculpted as a wax negative to blend with the two other sections and correspond to anatomic figures. Each hollow airway replicate of transparent polyester plastic was cast about the wax negative which was removed by boiling water. These models were characterized by the tongue-palate separation and the airway distance cross-sectional area relationship.

An infant oral passage replicate airway model was also constructed. As above, the region from epiglottis to mid-trachea was produced from an infant post-mortem negative cast. The oral region from lips to epiglottis was derived from a commercial model infant mouth used for intubation training. As with the adult oral model, the cast polyester hollow airway was formed around the wax negative which was then removed.

A combined oral-nasal adult airway replicate model has also been produced in the report period. This model combine a mouth model at low exercise conditions with a full, two sided nasal passage. With this model, the behavior of aerosols during oral-nasal breathing simulation can be studied. Although the model airways are rigid, methods for adjusting the relative flow rates between the oral and nasal passage are being investigated.

The construction of these models considerably extends the range of conditions possible to study with aerosols of interest. This is consistent with the overall aims of the project, i.e., to study the effect of age, airway dimension and flow on the deposition of aerosols of appropriate size regimes.

<u>Constant Flow Results with Replicate Models</u>

Adult oral passage models M,N and O (representing three levels of open airway) have been studied with unattached progeny particles (1 nm diameter) of Po^{218} at inspiratory flow rates ranging from 4-30 l min^{-1}. The average deposition percent for these conditions was 50-60% with no significant trend observed for the degree of oral opening. The results are consistent with other oral measurement made in models earlier in this research program, but differ significantly with the assumption of zero deposition percent made prior to this research program.

Both nasal and oral adult models were studied during the report period with particles of size 1-10 μm at constant flow from 7-45 $lmin^{-1}$. Significant differences between the three oral models were noted, and these were all less efficient than nasal deposition for the same conditions. In all cases, flow and size dependence could be expressed for inertial size particles by the scaling parameter d_p^2Q where d_p is particle diameter and Q is flow rate.

Replicate child nasal passage models were studied with ultrafine aerosol particles ranging from 1-200 nm diameter. These studies were performed at ITRI using casts prepared at Johns Hopkins. The results of these studies are similar to adult nasal passage results with similar particle sizes in that the deposition percent was from 80-90% at 1 nm and decreased to 5% at 0.2 μm. At any given particle size, the child nasal passage was slightly more efficient at removing particles than the adult nasal passage.

Cyclic Flow Measurements in Replicate Airway Models

Measurements of aerosol deposition percent during inspiratory cyclic flow in adult oral and nasal replicate airway models were performed during the report period with ultrafine and inertial size particles. Measurements of unattached radon progeny (Po^{218}) during cyclic inspiratory flow in an adult nasal and an adult oral model were performed at Harwell Laboratory, UK. A tidal volume of 750 cm^3 was used for both sets of measurements with breathing frequency varying from 10-25 min^{-1}. The results of these experiments showed that equivalent constant flows give similar results for overall deposition percent. In these experiments, sinusoidal flow was established by a standard eccentric piston pump.

Measurements of overall aerosol deposition in nasal replicate casts of inertial size particles (1-10 μm diameter) with cyclic flow were made in the Aerosol Research Laboratory (JHU). The cyclic inspiratory flow was produced by a cam driven piston pump which gave a more physiologically appropriate flow pattern. Average flow rates ranging from 7-45 $lmin^{-1}$ were studied. The results plotted in terms of the inertial parameter d_p^2Q gives a single sigmoidal relationship, similar to that obtained from constant flow studies. The cyclic flow plot was essentially identical to the constant flow plot for an equivalent flow equal to the inspiratory volume divided by the inspiratory time.

Human Subject Ultrafine Aerosol Studies

Studies of the nasal passage deposition of unattached progeny aerosols (1 nm diameter) were performed at Harwell. The results of these experiments at flow rates from 5-20 $lmin^{-1}$ compared well with replicate airway studies. Deposition percentage ranged from 94-98%, somewhat higher than replicate studies at the same conditions. The studies were carried out with three normal adult subjects.

A human deposition apparatus for particles in the 5-200 μm size range has been constructed and employed for one subject. The studies are performed with nasal passage exposure at constant flow; the aerosol is passively carried into the nose and out the mouth. The results of the initial studies are still being analyzed, but appear to give similar trends to those of casts. The aerosol employed is elemental silver.

Human Deposition Studies of Inertial Particles

Deposition of 1-4 μm diameter aerosols has been measured in six adult human subjects. The aerosols were produced by a spinning top generator detuned to yield a polydisperse distribution of spherical DEHS particles. The studies consisted of nasal dimensional measurements with acoustic rhinometry (AR) followed by deposition measurements. The dimensions were altered by topical administration of decongestant and congestant, which produced marked changes in the cross sectional area at the nasal valve area. Despite these changes, the deposition, in general, did not undergo significant change. However, when the entrance flow geometry was altered by "circularizing" the nostril, there was a marked reduction in deposition percent. These phenomenon are being investigated further to better understand the factors which influence nasal deposition.

Research Proposal Summary

In the next period of studies, it is proposed to continue the experimental measurements of ultrafine deposition in human subject, covering both the unattached progeny (1 nm) and the size range from 5-200 nm. A range of flow rates will be used with several additional subjects to obtain information about subject variability and the dependence upon flow rate and particle size.

Studies of inertial particle deposition will also continue to further elucidate the mechanism of impactive deposition and its relation to nasal passage shape and size. Local deposition of aerosols will be investigated using Tc^{99m} as a site of initial deposition indicator.

Replicate model studies will be focussed on local deposition of ultrafine and inertial aerosols in both nasal and oral models. The site of deposition will be related, for the nose, to the region of rapid mucociliary clearance. It has been hypothesized that most inertial aerosol deposits in the non-ciliated anterior zone. Little data on the local deposition of ultrafine aerosols exist, either in models or in human subjects. Studies are needed to predict the average lifetime of deposited radon progeny aerosol and other environmental aerosols, based on local deposition and clearance mechanisms.

Replicate models which simulate the surface characteristics of in vivo airways are needed to confirm existing hypotheses on the possible growth of ultrafine and inertial size aerosols. At present, the models are without a mucus simulant and at room temperature. For unattached and attached radon progeny, it has been assumed that little growth occurs in the moist, heated airways, and limited data appears to support this. However, this is not the case for other energy related aerosols, and the replicate casts are ideal to investigate this phenomenon when suitably modified.

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