Final Report

Pulmonary Deposition of Aerosols in Microgravity
NAGW-4372

University of California, San Diego
Principal Investigator
G. Kim Prisk, Ph.D.

October 24, 1997

Abstract

The intrapulmonary deposition of airborne particles (aerosol) in the size range of 0.5 to 5 microns is primarily due to gravitational sedimentation. In the microgravity (μG) environment, sedimentation is no longer active, and thus there should be marked changes in the amount and site of the deposition of these aerosol. We propose to study the total intrapulmonary deposition of aerosol spanning the range 0.5 to 5μm in the KC-135 at both μG and at 1.8-G. This will be followed by using boli of 1.0μ aerosol, inhaled at different points in a breath to study aerosol dispersion and deposition as a function of inspired depth. The results of these studies will have application in better understanding of pulmonary diseases related to inhaled particles (pneumoconioses), in studying drugs delivered by inhalation, and in understanding the consequence of long-term exposure to respirable aerosols in long-duration space flight.

Relevance

This program seeks to obtain a better understanding of the processes of deposition of inhaled particles in the human lung. Inhaled particles deposit on the walls of the airways and gas exchange regions of the lung by three mechanisms: impaction of large particles, sedimentation of medium sized particles, and movement by diffusion of the smallest particles. Particle deposition is important in many diseases that result from working in dusty environments, e.g., silicosis and asbestosis among many. Further, the deposition of particles in the lung is very important in the delivery of many therapeutic agents e.g. the metered dose inhalers used by asthmatics. In these cases, the site and efficiency of deposition of the medium sized particles is critically important for the efficacy of the drug therapy. Since sedimentation is a gravitational process, by studying the changes in deposition of test particles in the absence of gravity, we hope to gain a better understanding of the entire process of deposition. This can then be fed back to provide better aerosol generation, targeting more specific sites in the lung. The process of deposition in the weightless environment is also clearly important for the people that will be continuously exposed to suspended particles in the Space Station environment.

Our data to date suggest that alveolar deposition of small particles may in fact be much higher than originally anticipated. Since the alveoli are highly susceptible to damage by inhaled substances, this may have a fundamental bearing on the development of some environmentally based pulmonary diseases. For example, it is now believed that much of the rise in asthma prevalence may be due to the inhalation of small (< 2.5 micron) particles, and new federal standards are being proposed to control the levels of these particles. The recent findings in our studies of total deposition emphasize the need for direct measurements of regional deposition and

dispersion, studies using inhaled boluses of particles. We have already completed these measurements as part of this program.

Progress

For administrative reasons this program was split into two separate grants, NAGW-4372, and NAG-53742. Thus this final report **covers only the first two of the originally proposed three years**. Under the follow-on grant we will complete the analysis and reporting of the experimental work performed under NAGW-4372.

In FY 1997 we performed the bolus dispersion and deposition studies planned in our original proposal. The total deposition system developed for the previous studies was modified to include pneumatically operated sliding valves that allowed for the breathing path of the subject to be switched under computer control at precisely defined points in a test breath. Subjects were asked to perform a standardized respiratory maneuver in which they exhaled to RV, inhaled at ~0.4 l/sec to a volume approximately 1 liter above the FRC in 1G, and then exhale at ~0.4 l/sec to RV. This maneuver was performed in both the microgravity and hypergravity portions of the KC-135 flight profile. During the controlled inspiration, the pneumatically operated valves were triggered to deliver a 70ml bolus of particle laden air at a given point in the inspiration. The point was set at a number of predefined penetration volumes. For example, if the valves were triggered very late in the inspiration, then only a small volume of particle free air would follow the bolus and the resulting lung penetration volume was very small, with particles staying mostly in the central airways. In contrast, if the valves were triggered early in the inspiration, the resulting lung penetration volume of the bolus was large and the particles were delivered to the small airways and alveolar regions of the lung. Several penetration volumes between 150 ml and 1500 ml were chosen and studied.

We had originally planned to perform bolus studies using 1 micron particles. In March 1997 we flew the bolus system for the first time and achieved excellent results. During this set of flights it became apparent that we were in fact able to perform our tests at closer intervals than we had originally anticipated, and as a consequence during the subsequent flights in July and August 1997 succeeded in completely mapping the regional intrapulmonary deposition of 0.5, 1 and 2 micron particles in normal gravity, microgravity and hypergravity. This is a significant increase in the amount of scientific data we were able to collect beyond that originally proposed.

In FY 1997 we completed the manuscript reporting the total deposition studies performed in FY 1996 and submitted this to the *Journal of Applied Physiology*. The paper received a favorable review and has been accepted for publication. The enhanced deposition reported in that paper, which we attributed to enhanced diffusion, has sparked a considerable degree of interest, especially from the group of Dr. James P. Butler at the Harvard School of Public Health. Butler and Tsuda have recently published a report of a novel new mechanism of convective mixing in the lung periphery they refer to as "Stretching and Folding". We intend to pursue the idea that stretching and folding is responsible for our unexpected results. The microgravity environment of the KC-135 provides us with a unique opportunity to do this as in the absence of gravity we can examine the behavior of the aerosol particles without the confounding effects of gravitational sedimentation.

At this point we have completed the experimental phase of the proposed research with approximately 200% of the data we intended to collect. We will spend much of the next FY analyzing and interpreting the results. We intend to pursue some modeling studies to shed light on the results under the follow-on grant NAG-53742.

Publications Arising

Darquenne, C., M. Paiva, J.B. West, and G.K. Prisk. Deposition of aerosols in the human lung at different gravity levels. Am. J. Respir. And Crit. Care Med. 155:A955, 1997. (Abstract)

Darquenne, C., M. Paiva, J.B. West, and G.K. Prisk. Intrapulmonary aerosol deposition in micro- and hypergravity: Evidence for enhanced alveolar deposition. J. Aerosol Med. 10:252, 1997. (Abstract)

Darquenne, C., M. Paiva, J.B. West, and G.K. Prisk. Effect of microgravity and hypergravity on deposition of 0.5 to 3 μm-diameter aerosol in the human lung. J. Appl. Physiol. In Press, 1997.