Deposition and dispersion of 1-µm aerosol boluses in the human lung: effect of micro- and hypergravity

CHANTAL DARQUENNE, JOHN B. WEST, AND G. KIM PRISK
Department of Medicine, University of California, San Diego, La Jolla, California 92093-0931

Deposition and dispersion of 1-µm aerosol boluses in the human lung: effect of micro- and hypergravity. J. Appl. Physiol. 85(4): 1252-1259, 1998.—We performed bolus inhalations of 1-µm particles in four subjects on the ground (1 G) and during parabolic flights both in microgravity (µG) and in ~1.6 G. Boluses of ~70 ml were inhaled at different points in an inspiration from residual volume to 1 liter above functional residual capacity. The volume of air inhaled after the bolus (the penetration volume \( V_p \)) ranged from 200 to 1,500 ml. Aerosol concentration and flow rate were continuously measured at the mouth. The deposition, dispersion, and position of the bolus in the expired gas were calculated from these data. For \( V_p \approx 400 \) ml, both deposition and dispersion increased with \( V_p \) and were strongly gravity dependent, with the greatest deposition and dispersion occurring for the largest G level. At \( V_p = 800 \) ml, deposition and dispersion increased from 33.9% and 319 ml in µG to 56.9% and 573 ml at ~1.6 G, respectively (\( P < 0.05 \)). At each G level, the bolus was expired at a smaller volume than \( V_p \), and this volume became smaller with increasing \( V_p \). Although dispersion was lower in µG than in 1 G and ~1.6 G, it still increased steadily with increasing \( V_p \), showing that nongravitational ventilatory inhomogeneity is partly responsible for dispersion in the human lung.

There is a need to better understand the penetration and dispersion of aerosols in the lung as well as their ultimate deposition, whether the exposure occurs because of atmospheric pollution, occupational factors, or respiratory therapy. Aerosol dispersion results from mixing in the lung, and its measurement is a means of studying this process. Indeed, aerosols may be considered as a “nondiffusing gas” and may, therefore, be used to study the convective mixing occurring in the distal airways of the lungs without the confounding effect of diffusion always present in gas studies. The technique of aerosol bolus inhalation has been widely used to estimate aerosol dispersion in the respiratory tract (1, 4, 5, 11, 20). Particles deviate from the flow of the carrier gas by three mechanisms: diffusion, sedimentation, and inertia. Of these mechanisms, only sedimentation is a gravity (G)-dependent process. Because the lung distorts under its own weight, G force is also responsible for differences in regional ventilation (10, 14). Changes in the G level are, therefore, expected to affect the distribution of ventilation and the dispersion and deposition of aerosols, both because of changes in sedimentation and because of changes in regional ventilation.

To date, only two experimental studies have been reported on the effects of G on aerosol deposition. Hoffman and Billingham (12) collected deposition data with 2-µm-diameter particles in three subjects aboard a National Aeronautics and Space Administration (NASA) research aircraft. They found an almost linear increase in deposition with increasing G in the range of 0–2 G. More recently, Darquenne et al. (8) measured deposition of 0.5-, 1-, 2-, and 3-µm-diameter particles in four subjects on the ground and aboard the NASA research aircraft both in microgravity (µG) and at ~1.6 G. For 2- and 3-µm particles, their results were similar to those of Hoffman and Billingham (12) in that they found a nearly linear increase in deposition as a function of the G level. However, for 0.5- and 1-µm particles, deposition increased less between µG and 1 G than between 1 G and ~1.6 G. Thus deposition of the small particles in µG was higher than that predicted based on the hypergravity results and also based on existing models of aerosol deposition in the human lung. These results might be explained by two factors: first, a larger deposition by diffusion because of a higher alveolar concentration of aerosol in µG, since sedimentation is absent, and, second, the nonreversibility of the flow in the small airways, causing additional mixing of the aerosols.

In the present study, we performed aerosol bolus inhalations in normal subjects using 1-µm-diameter particles. We chose 1-µm particles because this was the size that showed the greatest discrepancy between predicted and actual deposition in µG in our previous study (8). Data were collected on the ground (in 1 G) and aboard the NASA Microgravity Research Aircraft in the weightless phase (µG) and in the ~1.6-G pullout phase. This paper reports the first results of bolus tests performed at different G levels in the human lung. The 1-G data were compared with previous studies (4, 7). The comparison of data obtained in µG and ~1.6 G with data obtained in 1 G helps to elucidate the effect of G on deposition and dispersion processes.

**METHODS**

Equipment. Aerosol bolus data were collected by using the equipment shown in Fig. 1. One position of the sliding valve SV1 allowed the subject to breathe air from the room through a two-way non-rebreathing valve equipped with filters. In the other position of the valve, the subject inspired the aerosol bolus located between the sliding valves SV2 and SV3, providing a bolus volume of ~70 ml. The measurement of the aerosol concentration and the flow rate were provided by a photometer (model 993000, PAR) (24) and a Validyne differ-
The aerosol generation. The bolus tube was filled with aerosol-containing monodisperse polystyrene latex particles (Duke Scientific). The particles were supplied in suspension (water), and the concentrate was diluted and dispensed via two Acorn II nebulizers (Marquest Medical Products). Before entering the bolus tube, the aerosol flows through a heated hose and a diffusion dryer to remove water droplets. The size of the spherical particles as specified by the manufacturer was 6.07 ± 0.014 (SD) µm. The aerosol concentration in the bolus tube was ~10^4 particles/ml air.

The aerosol generated by the nebulizers was checked with a particle sizer (PCS-2000 Special, PALAS). The size analysis confirmed the size of the particles given by the manufacturer and shows that the amount of doublets in the aerosol was <5%. Tests using conductive tubing showed no significant effect from possible electrostatic charges on the particles.

Data recording and analysis. A personal computer (IBM ThinkPad 360 CSE) equipped with a 12-bit analog-to-digital card (National Instrument, DAQ700) was used for data acquisition. Signals from the photometer, a G sensor, a barometric pressure transducer, and the pneumotachograph were sampled at 100 Hz. Custom software was developed for the data acquisition using National Instruments Lab WinCVI.

Data were collected on the ground and aboard the NASA Microgravity Research Aircraft. A typical flight consisted of a climb to an altitude of ~10,000 m, with the cabin pressurized to ~600 Torr. A "roller coaster" flight profile was then performed. The aircraft was pitched up at ~1.6 head-to-foot acceleration to a 45° nose-high attitude. Then the nose was lowered to abolish wing lift, and thrust was reduced to balance drag (thus maintaining µG). A ballistic flight profile resulted and was maintained until the aircraft nose was 45° below the horizon. In this manner, µG was maintained for ~27 s. A pullout averaging ~1.6 head-to-foot acceleration was maintained for ~40 s, causing the nose to pitch up to a 45° nose-high attitude, and allowed the cycle to be repeated. For convenience, the ~1.6-G hypergravity phase will be referred to as 1.6-G in the text.

Subjects and protocol. Four healthy subjects participated in the study. These were the same four subjects that participated in the previous study (8), and we retained their subject number for comparison purposes. Their relevant anthropometric data are listed in Table 1. After a few normal breaths, the subject exhaled to residual volume (RV) to ensure a known lung volume starting point. As functional residual capacity (FRC) varies significantly with G level (9, 17), we chose to use the more stable RV as the starting point for the test breath. Although there is some small change in RV in µG (9), the effect on our measurements is small. The test breath consisted of an inspiration from RV to FRC + 1 liter at a flow rate of ~0.45 l/s, immediately followed by an expiration to RV, also at a flow rate of ~0.45 l/s. A flowmeter provided visual feedback to the subject. FRC refers to the seated 1-G FRC of the subject, and it was fixed for all experiments on that subject. During the inspiration, an aerosol bolus of ~70 ml was introduced at different penetration volumes (Vp) ranging from 200 to 1,500 ml. The Vp was defined as the volume of air inhaled from the mode of the aerosol bolus to the end of the inhalation.

The protocol was repeated four times for each Vp, both in µG and in 1.6 G. Before the flight, a set of data was also collected on the ground (1 G) with the same protocol. The protocol was approved both by the Committee on Investigations Involving Human Subjects at the University of California.

Table 1. Anthropometric data

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Sex</th>
<th>Age, yr</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>FVC, %pred</th>
<th>FEV1/FVC, %pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>30</td>
<td>164</td>
<td>62</td>
<td>108</td>
<td>97</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>27</td>
<td>163</td>
<td>67</td>
<td>114</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>46</td>
<td>191</td>
<td>95</td>
<td>121</td>
<td>98</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>40</td>
<td>185</td>
<td>108</td>
<td>104</td>
<td>108</td>
</tr>
</tbody>
</table>

F, female; M, male; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 s; %pred, %predicted.
nia, San Diego, and by the Institutional Review Board at the Johnson Space Center, Houston, TX.

Data analysis. For each bolus test, three different parameters were calculated. They were the aerosol deposition, the aerosol dispersion, and the mode shift (MS). Deposition (DE) was calculated by using the following equation

\[ DE = 1 - \frac{N_{ex}}{N_{in}} \]  

(1)

where \( N_{in} \) and \( N_{ex} \) are the number of particles in the inspired and expired bolus, respectively. \( N_{in} \) and \( N_{ex} \) were calculated from the integration of the aerosol concentration as a function of the inspired and expired air. The integration was only done when the concentration exceeded 5% of the maximal expired concentration to reduce error due to the noise of the signal. An original tracing is shown in Fig. 2 for a bolus inhaled at a \( V_p \) of 500 ml. The shaded areas represent the portion of the inhaled and expired bolus, respectively.

On a graph of aerosol concentration as a function of the respired volume, the half-width is defined as the bolus width which concentration values are considered.

Dispersion. Figure 4A shows the dispersion as a function of \( V_p \) for each G level. Data were averaged over the four subjects (means ± SD). For \( V_p \geq 400 \) ml, dispersion was strongly G dependent, with the greatest dispersion occurring for the largest G level. For \( V_p = \) (ml) between the two points of one-half the maximum concentration of the bolus (Fig. 2). The change in half-width (H) reflecting the aerosol dispersion was obtained by the following equation

\[ H = (H_n^2 - H_{in}^2)^{0.5} \]

(2)

where \( H_n \) and \( H_{in} \) are the half-widths of the inspired and expired boluses, respectively. Only the volumes at one-half the maximum concentration of the bolus are required to compute \( H_n \) and \( H_{in} \). Therefore, their computation is not influenced by the 5% cutoff of the signal used in the deposition calculation.

The MS was defined as the difference between the position of the peak of the expired bolus (\( M_{ex} \)) and the volume penetration of the inspired bolus (Fig. 2)

\[ MS = M_{ex} - V_p \]

(3)

A negative value of MS indicates that the position of the mode of the expired bolus has shifted to a smaller lung volume than the location of the inspired bolus, i.e., that the bolus has moved toward the mouth.

Statistical analysis was performed by using Systat V5.0 (Systat, Evanston, IL). Measurements performed for the same experimental conditions with the same subject were not averaged before the statistical analysis was performed. Data were grouped in different categorical variables such as G level (µG, 1 G, and 1.6 G), \( V_p \) (200, 400, 600, 800, 1,000, 1,200, and 1,500 ml), and subject number. A two-way analysis of variance was performed to test for differences between the chosen categorical variables. Post hoc testing using Bonferroni adjustment was performed for tests showing significant F-ratios. Significant differences were accepted at the \( P < 0.05 \) level.

RESULTS

Bolus inhalations were performed on four healthy subjects for all \( V_p \) values ranging from 200 to 1,500 ml. However, at 1.6 G, because of high deposition, the expired bolus tracings we recorded for \( V_p > 800 \) ml had too high a noise-to-signal ratio and the data were discarded.

Deposition. The effect of G level on the deposition of the aerosol bolus is displayed in Fig. 2. The deposition averaged over the four subjects (means ± SD). The data were not significantly different from one G level to the other for \( V_p = 200 \) ml and were significantly different for \( V_p > 200 \) ml (\( P < 0.05 \)), with lower deposition being present at lower G levels. At \( V_p = 400 \) and 600 ml, significant differences were found between data in µG and 1.6 G and between data in 1 G and 1.6 G but not between data in µG and 1 G. At each G level, deposition increases with increasing \( V_p \). In µG, deposition varies from 18% at \( V_p = 200 \) ml to 50% at \( V_p = 1,500 \) ml. In 1 G, it varies from 14% at \( V_p = 200 \) ml to 69% at \( V_p = 1,500 \) ml; and at 1.6 G, it varies from 14% at \( V_p = 200 \) ml to 57% at \( V_p = 800 \) ml. The slope of the regression lines of deposition as a function of \( V_p \) is displayed in Fig. 2B (means ± SD). They are 0.023, 0.046, and 0.075%/ml in µG, 1 G, and 1.6 G, respectively.

Dispersion. Figure 4A shows the dispersion as a function of \( V_p \) for each G level. Data were averaged over the four subjects (means ± SD). For \( V_p > 400 \) ml, dispersion was strongly G dependent, with the greatest dispersion occurring for the largest G level. For \( V_p = \)
200 ml, there was a significant difference in dispersion values between µG and 1.6 G but not between µG and 1 G and between 1 G and 1.6 G. For each G level, dispersion was an approximately linear function of Vp. The slope of the linear regressions between dispersion and Vp are displayed in Fig. 4B (means ± SD). They are 0.19, 0.53, and 0.65 ml/ml in µG, 1 G, and 1.6 G, respectively.

MS. Figure 5 shows the effect of the G level on the MS. The MS is plotted on Fig. 5A as a function of Vp. At each G level, deposition increases with Vp as the aerosol bolus probes more distal airways (Fig. 3A). This can be referred to as the “penetration effect.” The increase in deposition may also be attributed to a “time effect.” By increasing the Vp, the bolus enters the respiratory tract earlier in the inspiration and, therefore, more time is available to the particles to deposit. Both effects con-

**DISCUSSION**

Deposition. This study reports the effect of G level on the deposition and dispersion of 1-µm aerosol boluses inhaled to various volumetric depths within the lung. Figure 3 illustrates the deposition of aerosol as a function of the Vp. Deposition increases with increasing Vp for each G level. Deposition is usually attributed to three main mechanisms: inertial impaction, gravitational sedimentation, and Brownian diffusion. For 1-µm-diameter particles, gravitational sedimentation is the mechanism that affects the most deposition in 1 G. The settling velocity of the spherical particles is ~33 µm/s in 1 G, whereas the Brownian displacement in 1 s is only ~13 µm (3). Inertial impaction is negligible for this particle size. In a previous study by our group (8), we computed the contribution of these three deposition mechanisms for a full inspiration of 1-µm-diameter particles with a one-dimensional model of the aerosol transport and deposition in the human lung. In 1 G, we found that deposition by impaction, sedimentation, and Brownian diffusion was 2.2, 78.6, and 19.2% of total deposition, respectively.

Gravitational sedimentation takes place primarily in the distal part of the lung where residence time in airways is high and airway dimensions are small. At each G level, deposition increases with Vp as the aerosol bolus probes more distal airways (Fig. 3A). This can be referred to as the “penetration effect.” The increase in deposition may also be attributed to a “time effect.” By increasing the Vp, the bolus enters the respiratory tract earlier in the inspiration and, therefore, more time is available to the particles to deposit. Both effects con-

**Fig. 3.** Deposition of aerosol bolus. A: data are means ± SD, averaged over the 4 subjects as a function of Vp. ○, Microgravity (µG); ■, 1 G; △, 1.6 G. *Significantly different compared with 1-G data, P < 0.05. B: slope of the regression lines between deposition and Vp for different gravity levels.

**Fig. 4.** Aerosol bolus dispersion. A: data are means ± SD, averaged over the 4 subjects as a function of Vp. ○, µG; ■, 1 G; △, 1.6 G. *Significantly different compared with 1-G data, P < 0.05. B: slope of the regression lines between dispersion and Vp for different gravity levels.
sured in µG. Indeed, for Vp itself does not explain the deposition values we measured in these experiments.

For a given Vp, deposition increases with G level. Of the three mechanisms of deposition, sedimentation is the only G-dependent process. Sedimentation is, therefore, the mechanism to account for the increased deposition in 1.6 G compared with 1 G. For Vp <400 ml, deposition was, however, not significantly different from one G level to the other, confirming that deposition by sedimentation is a process that takes place primarily in the periphery of the lung.

In µG, as inertia is negligible, deposition can only be attributed to diffusion. However, Brownian diffusion by itself does not explain the deposition values we measured in µG. Indeed, for Vp >400 ml where significant differences were found between G levels, deposition in µG is more than one-half the deposition in 1 G, which would imply that Brownian diffusion is the predominant mechanism of transfer of particles to the lung. This is in contradiction with the difference between the settling and diffusive velocity of these particles.

In a previous study (8), we observed a higher intrapulmonary deposition for small particles in µG than predicted by numerical models. The higher deposition was then explained by the nonreversibility of the flow and by a larger deposition by diffusion due to a higher alveolar concentration of aerosol in the absence of G. The nonreversibility of the flow was mainly explained by the asymmetry in the velocity profiles between inspiration and expiration. Very recently, Otani et al. (16) studied low-Reynolds-number cyclic flows in an alveolus model. They showed that these flows are irreversible, despite the low Reynolds number, causing substantial convective mixing in the periphery of the lung. The nonreversibility of the flow results in an additional mixing effect that moves the particles in the direction of the alveoli, increasing the apparent contribution of diffusional loss of particles in the lung. This increase in diffusional loss might explain the high deposition values we measured in µG in the present study.

Aerosol dispersion. Figure 4 illustrates the dispersion of aerosol as a function of the Vp. Dispersion is attributed to Brownian diffusion and convective mixing. As defined by Heyder et al. (11), convective mixing refers to all the mechanisms, except Brownian diffusion, which transport particles from tidal to residual gas. Convective mixing causes dispersion of aerosol boluses, depending on factors such as velocity patterns, airflow and alveolar geometries, asymmetries between inspiratory and expiratory flows, inhomogeneous ventilation of the lung, and cardiogenic mixing.

Velocity profiles in the airways are not uniform and allow particles at different radial positions in the airways to travel at different speed (21). The branching structure of the bronchial tree also imparts a directional asymmetry to the flow field, manifested by a difference in the shape of the velocity profile during inspiration and expiration. During inspiration, airflow is most rapid at the center of the airways, so that the aerosol bolus entering the lung is surrounded by a sheath of residual gas that is largely particle-free. Thus particles in the center of the airways travel more distal generations of the respiratory tract than do particles located near the walls of the airways, where velocities are smaller. During expiration, the velocity profile is more blunted, and particles in the center of the airways travel at a slower rate than during inspiration, whereas particles near the walls travel faster, preventing the bolus from recovering its original shape.

Ventilation inhomogeneities may be described by two mechanisms: convection-dependent ventilatory inhomogeneities (15) and diffusive processes. Whereas diffusive processes are responsible for ~30% of inhomogeneities of gas concentrations in 1 G (6), this mechanism is negligible for particles of 1 µm in size, as their diffusion coefficient is more than an order of magnitude lower than that of gases. Prisk et al. (18) showed in a study on ventilatory inhomogeneities determined from multiple-breath washouts during sustained µG that there was a reduction in the contribution of convection-dependent ventilatory inhomogeneities to overall ventilatory inhomogeneity. They concluded, however, that a considerable proportion of the inhomogeneity of ventilation present in the upright lung at 1 G during tidal breathing is nongravitational in origin. These ventilatory inhomogeneities also increase dispersion.
Rosenthal (19) showed in a theoretical study that ventilatory inhomogeneities should increase dispersion. Indirect experimental evidence of this statement can be found in a study by Anderson et al. (2) in which bolus aerosol dispersion was measured in normal subjects and in patients with cystic fibrosis (CF). CF is an obstructive disease that is known to increase inhomogeneities of ventilation. According to this paper, studies of pulmonary mechanics in patients with CF have shown an increase in the inhomogeneities of ventilation distribution. Anderson et al. showed that patients with CF exhaled boluses that were broader than those exhaled by normal subjects at all Vp values they examined (Vp = 100–700 ml). These authors believed that the increased bolus spreading in patients with CF was partly due to the increased inhomogeneities in ventilation distribution, compared with normal subjects. In our study, we modified the level of ventilatory inhomogeneities in healthy subjects by performing the test in µG where ventilatory inhomogeneities are still present (18, 23) but reduced, compared with normal G. We obtained lower dispersion values in µG than in 1 G.

Particles sediment during their transport in the airways and, therefore, do not follow the air streamlines. This effect is negligible in the first generations of the lung where bulk velocity is an order of magnitude larger than the settling velocity of the 1-µm-diameter particles. In the distal part of the lung, the radial position of the particles may significantly change while flowing through airways. However, according to Schulz et al. (22), who studied the convective and diffusive gas transport in canine intrapulmonary airways, the sedimentation rate does not affect significantly aerosol dispersion. They performed aerosol bolus inhalations in 1 G with 0.86 and 2.38-µm-diameter particles (a 7.7 times difference in settling velocity) and yet found no systematic differences between the dispersion of the smaller and the larger particles.

The convective mixing occurring over a single breathing cycle is the phenomenon assessed by aerosol bolus dispersion. The data we collected in this study highlight the effect of G on this phenomenon. As shown in Fig. 4A, for each G level, dispersion increases continuously with increasing Vp, indicating that each subsequent airway generation of the lung contributes to convective mixing. In the studied range of Vp values, this increase is approximately linear and is shown in the slope of the regression lines of dispersion as a function of Vp (Fig. 4B). For a given Vp, dispersion increases with G level: likely factors include the uneven distribution of ventilation and the asynchrony in regional filling and emptying of the lung, both of which increase with G.

However, while dispersion is lower in µG than in 1 G, it still increased steadily with increasing Vp, showing that nongravitational ventilatory inhomogeneity is partly responsible for dispersion. Although total ventilation inhomogeneity is reduced in µG, G-independent ventilatory inhomogeneities are still present and contribute to aerosol dispersion, as do cardiogenic oscillations, differences in velocity patterns between inspiration and expiration, the effect of secondary flow mixing at bifurcations, and laryngeal jetting. Although all these mechanisms may contribute to aerosol dispersion, the continuing presence of ventilatory inhomogeneities in µG (18, 23) suggests that aerosol dispersion in µG is largely due to nongravitational ventilatory inhomogeneities.

The relative contribution of G to dispersion also increases with Vp (Fig. 4). At Vp = 200 ml, no significant differences were found between dispersion at different G levels, whereas at Vp = 1,500 ml, dispersion in µG is only 51% of dispersion in 1 G. Based on the slope of the regression lines (Fig. 4B), dispersion due to G-independent factors is 36% of overall dispersion in 1 G and 30% of overall dispersion in 1.6 G. According to Verbanck et al. (23), the G-independent ventilatory inhomogeneities are at least as large as the G-dependent ventilatory inhomogeneities for gases. Our data show a lower contribution of the G-independent inhomogeneities to the overall dispersion than would be expected from the study by Verbanck et al. This might be explained by the absence of diffusion inhomogeneities in the aerosol experiments, which reduces the G-independent ventilation inhomogeneities.

MS. MS is displayed in Fig. 5. This parameter assesses the symmetry and reversibility of ventilation. Little or no difference between the Vp and the mode of the expired bolus (Vp = Mexp) indicates that the lung generally ventilates according to the first-in and last-out principle. A large difference (Vp < Mexp) suggests that ventilation is inhomogeneous and nonreversible. At each G level, the MS becomes more negative with increasing Vp. Up to a Vp of 600 ml, no significant differences were found among G levels. For larger Vp, the MS is more and more negative with increasing G and, therefore, with increasing ventilatory inhomogeneity. The increase in the MS may also be explained by a higher deposition at higher G levels. The particles that penetrate deeper into the lung deposit more, eroding the distal tail of the bolus and, therefore, shifting the mode of the expired bolus proximally. In µG, both deposition and ventilatory inhomogeneities are reduced, and the MS is greatly reduced.

Comparison with previous 1-G studies. The deposition, the dispersion, and the MS at 1 G were compared with data previously obtained by Brand et al. (4) and Darquenne et al. (7). Brand et al. (4) studied 79 healthy subjects and used Vp values ranging from 20 to 800 ml. Darquenne et al. (7) performed the bolus tests in 10 healthy subjects with Vp values ranging from 200 to 1,500 ml. The two previous studies used 0.87-µm-diameter particles and a flow rate of 0.25 l/s, compared with 1-µm-diameter particles and a flow rate of 0.45 l/s in our experiments. The three sets of data (means ± SD) for deposition, dispersion, and MS are displayed in Fig. 6, A–C, respectively. Given the differences in the protocols, our small subject population, and the inter-subject and intra-subject variabilities, we found the values for all three parameters similar to those of other investigators. The deposition data shown in Fig. 6A are, however, higher than deposition obtained by Ander-
we were able to collect data at 1 G and compare the measurements with those obtained on the ground in the same subject. The data are displayed in Fig. 7 for subject 2 used as an example. The comparison shows that the results obtained in both environments are similar, with no statistical differences between aircraft and ground data. This means that there were no

**Fig. 6.** Comparison of our 1-G data (●) with bolus studies of Brand et al. (4) (○) and Darquenne et al. (7) (△). Data are means ± SD. In our study, particle size ($d_p$) is 1 µm and flow rate ($Q$) is 0.45 l/s. In Brand et al. (4) and Darquenne et al. (7) studies, $d_p$ is 0.87 µm and $Q$ is 0.25 l/s. A: deposition, B: dispersion, C: mode shift.

**Fig. 7.** Comparison between data obtained for subject 2 on the ground (○, mean ± SD) and aboard the aircraft at 1 G (●). A: deposition, B: dispersion, C: mode shift.

son et al. (2) and Kim et al. (13) for 1-µm-diameter particles.

Effect of changes in gas density caused by altitude. Several flights were performed to collect all the data. During each flight, before the start of the first parabola,
systematic differences in our data introduced by the lower barometric pressure in the aircraft cabin and that we may, therefore, reliably compare aircraft and ground data. Similar comparisons were made for the three other subjects, and the results were the same. In summary, aerosol bolus inhalations were performed with 1-µm-diameter particles in four subjects on the ground and aboard the KC-135 aircraft during both weightlessness and the hypergravity phases. The boluses were inhaled at different Vp values ranging from 200 to 1,500 ml. The data showed that both bolus dispersion and deposition increased with Vp and that they were strongly G dependent, with the largest dispersion and deposition occurring for the largest G level. Even if dispersion was reduced in µG, it still increased steadily with Vp. The dispersion observed in µG can be explained by G-independent ventilatory inhomogeneities, the nonreversibility of the flows between inspiration, and expiration and cardiogenic mixing.

The authors acknowledge the collaboration of Janelle Fine, Jeff Struthers, Bob Williams, and Noel Skinner and the administrative assistance of Mary Murrell and Marsha Dodds. We also thank Manuel Paiva, Christa Roth, and Joachim Heyder for their scientific and technical support and Sylvie Verbanck from the Vrije Universiteit van Brussel (Belgium) where the size analysis of the aerosol was performed.

This work was supported by the National Aeronautics and Space Administration Grant NAGW-4372.

Address for reprint requests: C. Darquenne, Physiology/NASA Laboratory 0931, Dept. of Medicine, UCSD, 9500 Gilman Dr., La Jolla, CA 92039-0931 (E-mail: cddarquenne@ucsd.edu).

Received 16 January 1998; accepted in final form 10 June 1998.

REFERENCES