Meniscus formation during tracheal installation of surfactant

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Espinosa, F. F., and R. D. Kamm. Meniscus formation during tracheal installation of surfactant. J. Appl. Physiol. 85(1): 266–272, 1998.—The method of surfactant installation into the lungs for treatment of neonatal respiratory distress syndrome is an important attribute of delivery, and it may determine the overall efficacy of treatment. Previous studies primarily focused on the rate at which the bolus is instilled. These findings show that rapid injections lead to a more homogeneous distribution, whereas slow infusions drain into the dependent lung with respect to gravity, resulting in a heterogeneous deposition. These results suggest that it is beneficial to form a meniscus, from which a more homogeneous dispersal can proceed. The objective of the present study was to develop a functional criterion for meniscus formation during bolus injection. An in vitro experiment was used to examine the clinical setting of surfactant instillation. The physical variables examined were the bolus viscosity (μ) and density (ρ), gravity (g), injection rate (Q), orientation of the trachea with respect to gravity (θ), tracheal size (D), surface tension (σ), and catheter size (d). All quantities were varied, except gravity and catheter size. Experimental results show that a meniscus will form when $N_{St} > 0.004Re^3$, where $N_{St}$ is Stokes number and Re is Reynolds number, $N_{St} = \mu Q/D^3g sin\theta$, a ratio of viscous effects to gravitational effects, and $Re = \rho QD^2/\mu$, a ratio of inertial effects to viscous effects. Rapid injections, high viscosity, and small inclination with respect to gravity promote meniscus formation. These results can be used to refine the guidelines for administration of surfactant replacement therapy.

Acute respiratory distress syndrome; respiratory distress syndrome; surfactant bolus; surfactant replacement therapy

SURFACANT REPLACEMENT THERAPY (SRT) is generally effective, yet 33% of those treated show only a transient response or no response (2). In an attempt to reduce this significant failure rate, a variety of factors related to treatment have been studied. Areas under investigation range from pretreatment ventilation strategies, where it has been hypothesized that large tidal volumes before treatment increase protein leaks into the alveoli, leading to surfactant inactivation (5), to variation of the volume of the instillate; larger volumes have been found to produce a more uniform distribution of surfactant, improving the response to treatment (4, 13). Recent investigations have focused on the method of instillation; they have addressed whether surfactant should be rapidly injected or slowly infused into the lungs (11, 12) and demonstrated that the method of instillation may determine the overall efficacy of treatment. Each of these studies has focused on a single aspect of SRT without an appreciation of the overall surfactant dispersal process. The functional relationships between administration rate, bolus properties, geometry, and lung orientation and the initial deposition or subsequent dispersal of the bolus have not been systematically studied.

The most common procedure for administration of surfactant starts with the neonate removed from the ventilator and placed in one of four positions: head-down, left or right lateral or head-up, or left or right lateral position. The first quarter-dose aliquot is then rapidly injected over 2–3 s into the trachea via a 5-Fr catheter threaded down the endotracheal tube. The neonate is then hand ventilated for 30 s at 30–60 breaths/min before being repositioned, and the next aliquot is injected. This procedure is repeated until all four aliquots have been administered. For example, a 1-kg neonate receives a total of 100 mg of phospholipid suspended in 4 ml of saline, with each quarter-dose being 1 ml (9). This procedure has been found to provide a homogeneous distribution, with some transient effects of cyanosis, bradycardia, and increased $P_{CO_2}$ (14). Alternative instillation strategies have recently been reported that explore the effects of instillation rate (11, 12), multiple instillations (8, 12), lung orientation with respect to gravity (1), and positive end-expiratory pressure (PEEP) (6) on surfactant dispersal and treatment efficacy.

In general, a wide range of instillation rates can be envisioned, ranging from a slow infusion to a rapid injection. On the basis of prior practice we classify delivery as 1) slow infusion, i.e., instillation of 1–10 ml of surfactant over ~1–45 min, or 2) rapid injection, i.e., delivery of the same volume over 2–15 s (1, 8, 11, 12). Segerer et al. (11) and Ueda et al. (12) reported that rapid injection was associated with a relatively uniform distribution and favorable response, in contrast to slow infusion, which resulted in a highly nonuniform distribution and poor response. Additionally, Ueda et al. found that with slow infusion a second dose entered into the same lung units as the first, with little increase in $P_{O_2}$ after the second-dose. In a similar experiment, Ploit et al. (8) demonstrated that with slow infusion of surfactant the second-dose deposits in the same lung as the first dose, but additionally they found that some surfactant was delivered to surfactant-deficient alveoli. However, distribution remained grossly nonuniform. In contrast to the findings of Ueda et al., an increase in $P_{O_2}$ was observed after the second dose, signifying that some additional recruitment had occurred. In both studies the second dose was delivered 2 h after the first. The difference might lie in anatomic differences in the animal models: Ueda et al. used preterm lambs, whereas Ploit et al. employed a rabbit model.

Broadbent et al. (1) demonstrated that surfactant accumulation occurring with the infusion mode of
instillation was influenced by chest orientation, i.e., deposition favoring the dependent lung with respect to gravity. No redistribution was observed when the rabbit was repositioned after treatment. Recently, Merritt et al. (6) investigated whether keeping the airways inflated with PEEP during rapid bolus injection rather than removing the subject from ventilation during instillation would influence surfactant distribution or reduce adverse transient effects such as decreased oxygenation. The use of PEEP during instillation resulted in a more uniform distribution through the lungs with a smaller drop in O2 saturation. However, no significant physiological differences were noted between the two instillation techniques after 12 h.

These studies suggest that the initial placement of the bolus may determine the ultimate distribution of surfactant within the lungs. The question as to why rapid injections result in more uniform distributions and, therefore, better therapeutic response (11, 12) has not been carefully studied. As will be shown, rapid injections help ensure meniscus formation in the trachea and main stem bronchi, from which a more uniform dispersal process can proceed. The first inspiration after instillation will drive the meniscus down all parallel pathways, coating the airways with surfactant, with immediate deposition of some fraction of the bolus in the periphery. Subsequently, delivery of surfactant to initially untreated air spaces can continue via surface tension gradients (3). In this manner, the surfactant is distributed more uniformly throughout both lungs rather than simply flowing into the dependent lung according to gravity, as observed with slow infusion (11, 12).

Our aim is to identify the critical parameters of surfactant instillation and their influence on the initial deposition of an instilled surfactant bolus. In particular, we seek to identify the conditions under which a meniscus will form in the trachea. In this in vitro experiment we considered the effects of bolus viscosity, injection rate, orientation of the trachea with respect to gravity, surface tension, and tracheal size. This study provides a framework for examining present instillation techniques and for exploring alternative strategies.

METHODS

Assumptions. Some assumptions and simplifications have been made to focus on the fundamental physical factors influencing the injection process. Clinical practice involves surfactant administration by syringe through a 5-Fr catheter slipped through the endotracheal tube or via a side-port adapter atop the endotracheal tube. The former technique is shown schematically in Fig. 1. To capture both methods in a single experimental setup, we considered the case where the injected fluid from the catheter or the infused surfactant from the side-port adapter flows along the tracheal wall or down the endotracheal tube by placing the catheter near the model airway wall. The results are extrapolated to conditions where the catheter does not lie along the side of the trachea and are addressed in DISCUSSION.

Bench-top experiments. The conditions under which a meniscus plug formed in the trachea was examined by using a simple bench-top model of the trachea-and-catheter combination (Fig. 2). The trachea was modeled by a 20-cm-long glass capillary tube. This length was used to avoid any end effects on meniscus formation. For accurate placement, the flexible catheter was replaced by an 18-gauge syringe needle (~1 mm ID) with a blunt tip and mounted on a positioning rail. The needle was connected by tubing to a 30-ml syringe mounted on a syringe pump (model 944, Harvard Apparatus, Natick, MA). The needle and capillary components were rigidly secured to a Plexiglas base that could be rotated in the vertical plane. We examined how fluid viscosity, capillary diameter, orientation, surface tension, and injection flow rate influenced meniscus formation.

Water-glycerol mixtures of different ratios were used to examine the effect of viscosity. Values of viscosity ranged from 0.01 to 0.8 g·s⁻¹·cm⁻¹ and were measured using a Cannon-Fenske-Ostwald bulb viscometer (model 200, International Research Glassware, Kenilworth, NJ). Additionally, the density depended on the water-glycerol content, ranging from 1 g/ml when viscosity was 0.01 g·s⁻¹·cm⁻¹ to 1.22 g/ml when viscosity was 0.8 g·s⁻¹·cm⁻¹. Surface tension was reduced to 25–35 dyn/cm with use of a detergent in the water-glycerol solution and was measured by a ring tensiometer (model 70535 du Nouy tensiometer, Cenco Instruments, Chicago, IL). The entire test sequence was repeated without detergent (surface tension ~50–60 dyn/cm) to examine the influence of surface tension. These values were selected to mimic the possible range of surface tensions of a surfactant bolus.

Three capillary internal diameters of 0.23, 0.35, and 0.4 cm were selected to coincide with the range of neonatal tracheal diameters. For example, for a 1-kg neonate, an endotracheal tube with an internal diameter of 0.25 cm (Dr. T. Berger, personal communication) is typically used; it is fit into a trachea with an internal diameter of 0.35–0.4 cm. Orientations of 0, 5, 10, and 20° from horizontal approximated positions in which an infant might lie during treatment (9). We chose injection flow rates between 0.1 and 0.7 ml/s, a range that encompasses rates encountered when a catheter is used to administer surfactant (e.g., 1 ml injected over 2–3 s results in flow rates of 0.5 and 0.3 ml/s, respectively). These experimental values are compiled and summarized in Table 1.

Before an experiment was initiated, the glass capillary tube was bathed in a 50:50 aqueous-Micro cleaner solution (International Products, Trenton, N J) at 50°C for 1 h. After the tube was cleaned, it was rinsed with distilled water to remove residual cleaner. This treatment left the glass highly wettable, allowing a thin film of water to coat the interior surface. After each experiment the capillary tube was thoroughly flushed with distilled water and reused without retreatment if a thin film of water could be maintained. Having the capillary lined with water was critical, because it not only mimicked conditions in the trachea, but it provided a perfectly wetting interface to the incoming bolus. Effects
arising from a nonzero contact angle formed against unwetted glass gave different results.

A series of experiments were conducted for a given viscosity, capillary diameter, and orientation while the flow rate was varied. Before a set of experiments was carried out, the capillary was mounted and the position of the needle within the capillary was adjusted to be approximately flush with the bottom of the glass tube (Fig. 2). The capillary was then removed, its internal surface was coated with a thin layer of water, and it was returned to its mount. (In a separate maneuver, in which the capillary was weighed before and after it was coated with water, the thickness of the water layer was estimated to be \(10^{-3}\) cm). The syringe pump, set at a predetermined flow rate, was immediately switched on to reduce the time available for pooling of the water lining the capillary tube. The injected liquid flowed along the length of the initially empty pressure tubing to allow the pump to reach a steady flow rate, thereby providing a steady flow rate before the solution issued forth from the needle into the capillary. Whether a meniscus formed was noted, and the syringe pump was turned off. The experiments were timed and videotaped to determine the volume required for meniscus formation.

Analysis. To identify the parameters that determine whether a meniscus forms, a simple analysis is given before we present the experimental results. Figure 3 shows a bolus being injected into a capillary oriented at an angle \(\theta\) and accumulating at some downstream position. As a first approximation, the meniscus-forming process can be considered as one in which the liquid cannot drain away from the injection site as fast as it is introduced. If the liquid accumulates to some critical depth, surface tension forces eventually dominate, drawing the liquid around the circumference to form a meniscus that occludes the tube. The effects of gravity, viscosity, and jet momentum are considered in this analysis.

The following scaling analysis is based on the observation that a liquid meniscus forms when a sufficient volume of liquid accumulates near the tip of the infusion catheter. Our experiments (see Results) show this volume to be \(1.6D^3\), where \(D\) is the diameter of the airway. By analogy to studies of airway closure due to an axisymmetric liquid layer lining the wall of an airway (7), we anticipate that the formation of a meniscus will be primarily dependent on the accumulated liquid volume, although surface tension will influence the rate at which a meniscus forms once a sufficient amount of liquid is present, as long as surface tension does not approach zero, its value will have relatively little effect on the stability condition and, therefore, on meniscus formation. As shown in Fig. 3B, liquid is supplied via the catheter and is acted on by the forces of gravity and viscous shear stress. The rate at which surfactant solution accumulates locally is determined by an interaction between the momentum of the liquid issuing from the catheter tip and gravity, both acting to propel the liquid into the lung, and the viscous shear stress that acts at the wall of the trachea, tending to impede its motion. For the purpose of this approximate scaling analysis, consider the control volume shown in Fig. 3B. We take a volume of liquid extending some length \(L\) in the axial direction, corresponding to the region where liquid tends to accumulate and potentially attain a depth sufficient to become unstable and form a meniscus, obstructing the airway, as described above. The first of the three terms in this balance is the momentum of the liquid jet

\[
\rho U^2 A \sim \rho Q^2 / d^2
\]

where \(\rho\) is the density of the liquid, \(V\) is the velocity of liquid issuing from the catheter of diameter \(d\), \(A\) is area, and \(Q\) is injection flow rate. The second term is the viscous retarding force (viscous stress times surface area) that scales as

\[
\mu U D L / h
\]

where \(U\) is a measure of the velocity within the liquid pool \((U h D \sim Q)\) and \(h\) approximates the pool depth. Third, the gravitational force scales as

\[
\rho g h D L \sin \theta
\]

where \(g\) is gravity. The viscous force retards the flow of liquid away from the site of deposition, whereas momentum and gravity augment it. If gravity or jet momentum dominates viscous forces, the liquid has sufficient momentum to flow away from the deposition site. Thus two ratios are of interest: one represents the relative importance of the viscous
force to gravity, and one represents the ratio of jet momentum to viscous effects. The first of these is the Stokes number ($N_{St}$) and can be written

$$N_{St} = \frac{\mu Q}{(Dh)^3 \rho g \sin \theta}$$

Our interest lies in the situation when $h, D$, since that is when surface tension has the potential to produce a meniscus. Making this substitution, we arrive at an expression for the Stokes number that is relevant to the present situation

$$N_{St} = \frac{\mu Q}{D^4 \rho g \sin \theta}$$

The second parameter, representing the ratio of jet momentum to viscous force in the liquid pool, has the form of a Reynolds number ($Re$)

$$Re = \frac{\rho Q h^2}{(\mu)^2 L}$$

where we have once again taken $h \sim D$. In addition, we wish to consider the case in which the axial extent of the accumulating liquid is sufficient for meniscus formation. As mentioned above, our experiments show that a volume of $\approx 1.6D^3$ is required. Setting this equal to the liquid volume in Fig. 3B, hDL, and letting $h \sim D$ again, we find that $L \sim D$ at the critical instant. By substitution, the critical $Re$ becomes

$$Re = \frac{\mu Q D}{(\mu)^2}$$

From the physical arguments above, we expect that a meniscus will fail to form if the Stokes number is sufficiently small or the Reynolds number is sufficiently large. In either case, liquid will leave via the right side of the control volume in Fig. 3B at a rate sufficient to prevent meniscus formation (the imbalance between viscous forces, on one hand, and jet momentum and gravity, on the other, instills the exiting liquid with momentum, thereby increasing the rate at which liquid flows away to the right).

We use this analysis to motivate the choice of parameters to use in plotting the experimental results. When the conditions for meniscus formation are mapped onto a plot of the Reynolds number vs. the Stokes number (see RESULTS), a clear separation is obtained.

**RESULTS**

The purpose of these experiments was to obtain a criterion for the circumstances under which a meniscus would form. The approximate analysis in METHODS suggests that if the experimental conditions are mapped onto a plot of Stokes number vs. Reynolds number, it should be possible to distinguish a region of meniscus formation. This was done for a wide range of experimental conditions (Table 1) leading to $10^{-3} < N_{St} < 1$ and $10 < Re < 10^3$, with the results plotted in Fig. 4. A well-defined boundary is observed that separates conditions leading to meniscus formation from those that do not. Experiments with $\theta = 0$ are not plotted here, but all horizontal cases examined led to meniscus formation. All experiments were performed with and without surfactant; no difference was observed in terms of whether a meniscus formed.

The separation boundary shows a weak Reynolds number dependence and is approximately described by a power law relation of

$$N_{St} \approx 0.004 Re^{1/3}$$

which is shown by the solid line in Fig. 4. Therefore, for $N_{St} > 0.004Re^{1/3}$, a meniscus will occlude the airways, provided a sufficient volume of liquid is injected.

The volume requirement was determined from examining recordings of the experiments. With knowledge of the time elapsed from when the bolus first emerged from the needle until a meniscus formed and the flow rate, the volume injected was determined. This gave rise to the additional constraint that a volume $>1.6D^3$
is required for a meniscus to form. This relationship was confirmed with a smaller series of tests (n = 20) without surfactant.

Two examples are presented to illustrate how the physical variables interact to influence meniscus formation. Consider, for example, the effect of orientation with respect to gravity, as characterized by the term $\sin \theta$. To see this effect, one starts at a point within the no-meniscus region (e.g., $N_{st} = 0.005$, $Re = 40$, Fig. 4A) and holds $Re$ constant while varying $\sin \theta$. Increasing the inclination angle increases the influence of gravity (decreases Stokes number) and moves one further from the meniscus criterion. The bolus drains away more rapidly because of an increased contribution of gravity, and no meniscus forms. In contrast, when the inclination angle increases the influence of gravity and holds $Re$ constant while varying $\sin \theta$, the bolus Reynolds number, a ratio of inertial to viscous effects. These take into account the effects of orientation with respect to gravity, viscosity, flow rate, airway size, and momentum.

Animal experiments in the literature indicate that a more homogenous distribution and favorable response occur when the bolus is given as a rapid injection than when it is administered by slow infusion (11). From our results, we observe that a rapid injection promotes meniscus formation, filling the trachea and bronchi with the bolus. A meniscus effectively collects the injected liquid, preventing it from flowing downstream dependent airways. On the next inspiration the bolus could presumably be drawn into the lungs in proportion to regional lung expansion, producing a distribution more uniform than would be achieved by gravity. This study provides a basis for understanding how the bolus is initially situated after instillation, before it is dispersed through the lungs.

Current protocol calls for positioning the infant in different orientations for each quarter-dose administered (9). Table 2 lists some variations that might exist during treatment (Fig. 4). Cases A–D examine how changes in flow rate and viscosity could alter the final distribution of surfactant.

We have identified the governing parameters and determined functional relationships that describe the initial fate of a bolus injected into the trachea. This process is the first phase of SRT and, according to previous animal studies, may determine the overall surfactant distribution and ultimate efficacy of treatment (8, 11, 12). The results from our in vitro experiments indicate that the instilled bolus accumulates locally to form a meniscus or drains away toward the dependent airways with respect to gravity. This behavior is characterized by two parameters: 1) Stokes number, a ratio of viscous to gravitational effects, and 2) the bolus Reynolds number, a ratio of inertial to viscous effects. These take into account the effects of orientation with respect to gravity, viscosity, flow rate, airway size, and momentum.

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### Table 2. Possible conditions during surfactant administration and corresponding parameter values from this study

<table>
<thead>
<tr>
<th>Case</th>
<th>$\theta$, degrees</th>
<th>$\mu$, g·s$^{-1}$·cm$^{-1}$</th>
<th>$Q$, ml/s</th>
<th>$Re^*$</th>
<th>$N_{st^*}$</th>
<th>Meniscus</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>20</td>
<td>0.2</td>
<td>0.2</td>
<td>40</td>
<td>0.005</td>
<td>N</td>
</tr>
<tr>
<td>B</td>
<td>20</td>
<td>0.2</td>
<td>0.5</td>
<td>100</td>
<td>0.012</td>
<td>?</td>
</tr>
<tr>
<td>C</td>
<td>20</td>
<td>0.5</td>
<td>0.2</td>
<td>16</td>
<td>0.012</td>
<td>?</td>
</tr>
<tr>
<td>D</td>
<td>20</td>
<td>0.2</td>
<td>0.5</td>
<td>40</td>
<td>0.029</td>
<td>Y</td>
</tr>
<tr>
<td>E</td>
<td>5</td>
<td>0.2</td>
<td>0.5</td>
<td>100</td>
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<td>Y</td>
</tr>
<tr>
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<td>0.2</td>
<td>0.01</td>
<td>2</td>
<td>0.0002</td>
<td>N</td>
</tr>
</tbody>
</table>

Values for Reynolds ($Re$) and Stokes numbers ($N_{st}$) were calculated using $D = 0.4$ cm, $d = 0.1$ cm, liquid density ($\rho$) = 1 g/ml, and gravity ($g$) = 981 cm/s$^2$. Y, yes; N, no. *For comparison with instillation times given in Survanta insert (9), injection times for a 1-ml bolus injected at $Q = 0.5$ and 0.2 ml/s are 2 and 5 s, respectively.
deposition process at a fixed orientation of 20°. For example, for administration of Survana (Ross Laboratories) to a 1-kg neonate, it is recommended that a quarter-dose of 1 ml be given over 2–3 s, corresponding to an injection flow rate of 0.5–0.3 ml/s. Even greater rates of 1 ml/s have been used in animal experiments (11). The injected volume of 1 ml is more than adequate to satisfy the constraint that volume is >1.6D^3; therefore, Fig. 4 can be used to determine whether a meniscus forms. Beginning with case A, we start out at a location in Fig. 4 where no meniscus forms and the liquid flows freely to the dependent region of the lung. Increasing the flow rate (case B) or increasing the viscosity (case C) leads to more accumulation of surfactant in the trachea, producing situations near the boundary of the two regions, suggesting that the outcome would be inconsistent, sometimes leading to meniscus formation and other times not. The combination of rapid injection and high viscosity (case D) or a shallow angle of inclination (case E) results in a meniscus being formed. An alternative approach to rapid injection is administration of surfactant by slow infusion to reduce transient side effects (6). This condition (case F) clearly results in no meniscus being formed.

In light of the scenarios just presented, how might the instillation process be better controlled? Those parameters under clinician control are the flow rate, orientation, and to some degree the catheter diameter; the other variables are fixed by physiology or are physical properties of the liquid. Equation 9, derived from the criterion for meniscus formation (N_st > 0.004 Re^4), provides the functional relationship and sensitivity of each variable on the instillation flow rate. This criterion is strongly influenced by the size of the trachea or endotracheal tube (depending on the location of the catheter) and moderately affected by liquid density and viscosity, orientation, and catheter size. Equation 9 provides a lower limit for flow rate if a meniscus is to be achieved. Conversely, it can be viewed as an estimate of the maximum flow rate that can be used without producing airway obstruction. For example, inclination of 5°, airway diameter of 0.4 cm, catheter diameter of 0.1 cm, liquid density of 1 g/cm^3, and gravity of 981 cm/s^2 reduce Eq. 9 to Q_{crit} = (5.2 \times 10^{-3} ) \mu^2 \text{g/ml cm s}^{-1} \text{cm}^2 \text{for viscosity expressed in grams per second per centimeter and } Q_{crit} \text{ in milliliters per second. With viscosity of 0.2 g·s}^{-1}·\text{cm}^{-1} \text{(case E in Table 2), } Q_{crit} = 0.18 \text{ ml/s (i.e., for a 1-ml aliquot; injection time is } \sim 5.5 \text{ s). The bolus will occlude the airway for larger flow rates but would likely drain along the airway for smaller administration rates encountered during treatment.}

To locate where current treatment lies, in Fig. 4 we obtained unused portions of Survana (lot no. 16 916 Z7) and measured its viscosity using a Cannon-Fenske-Ostwalt-type bulb viscometer (models 200 and 350, International Research Glassware). At 25 and 37°C the viscosity was 100 and 75 g·s}^{-1}·\text{cm}^{-1}, respectively. For injection flow rates of 0.2 and 0.5 ml/s, this places one above and to the left of points C and D in Fig. 4, for inclination of 20°, airway diameter of 0.4 cm, catheter diameter of 0.1 cm, liquid density of 1 g/cm^3, and gravity of 981 cm/s^2. Thus, in a clinical setting under these physical conditions and for this surfactant preparation, it is likely that a meniscus forms unless the injection time is >5 s (Q \leq 0.2 ml/s).

It is appropriate to comment on the extent to which these results are valid and can be applied with confidence in different situations. The catheter position plays an important role in determining whether the bolus forms a meniscus in the trachea or drains into a main stem bronchus. The results presented here were obtained with the catheter positioned at the wall (Fig. 2). A meniscus will form if the criterion is met (N_st > 0.004 Re^4), and the liquid will drain away toward a main stem bronchus if the criterion is not met. In the instance when the catheter is located away from the wall and directed along the axis of the trachea, however, the liquid can leave the catheter as a stream, landing at a point downstream from the tip of the catheter. If the meniscus criterion is satisfied, a liquid plug will still form, but at the more distal location. As the bolus is more rapidly injected or the catheter is placed further within the trachea, the bolus may directly enter a main stem bronchus. With all other parameters fixed, the smaller diameter of the bronchus promotes meniscus formation because of the strong dependence of the Stokes number (N_st \sim D^{-4}) and volume requirement (V \sim D^3) on diameter. With a daughter-to-parent diameter ratio of 2:3 for the bronchus and trachea bifurcation, the Stokes number for the bronchus is approximately five times greater than the tracheal value with a decrease in the Reynolds number by two-thirds of the tracheal value. The volume requirement also drops to 30% of the volume needed in the trachea. For example, a case where the Stokes number is 10^{-2} and the Reynolds number is 20 on the basis of tracheal diameter produces conditions near the border between the meniscus and no-meniscus regions (Fig. 4). However, if the bolus streams into the bronchus, the Stokes number increases to 0.05, moving well within the region where a meniscus would form.

Is it possible to form a meniscus in an adult lung? For a given set of bolus properties and fixed orientation, an adult tracheal diameter of \sim 2 cm reduces the Stokes number by a factor of 625 with respect to the value obtained for a neonate with a capillary diameter of 0.4 cm. From Fig. 4, clearly no meniscus will form in the trachea of the adult by this method, nor will a meniscus form in the adult main stem bronchus, where the Stokes number is 123 times smaller than in the neonatal trachea. Drastic measures such as increasing the viscosity 1,000-fold to offset the geometric size is neither realistic nor desirable, suggesting that meniscus formation may not be practical in the adult.

It may seem strange that surface tension was not found to play an important role in this process and was not included in our scaling analysis. The reason for omitting surface tension effects comes from several observations. First, as shown by Otis et al. (7), although surface tension affects the rate at which a meniscus
forms from an initially uniform liquid layer on the wall, it does not alter the conditions (e.g., thickness of the liquid layer) necessary to produce meniscus formation. Second, the effects of surface tension gradients that might arise during injection to redistribute the liquid are likely to be small. This statement is based on the observation that in the present experiments in which the surface tension difference between the endogenous liquid (pure water) and exogenous liquid was maximized, there was little evidence that flows driven by surface tension gradients were affecting meniscus formation, at least on the time scales of injection. Finally, these heuristic arguments gain support from the observation that surface tension had no discernible influence on the experimental outcome.

Once the meniscus is formed, the bolus no longer preferentially drains to dependent regions of the lung with respect to gravity. The bolus volume can fill the major bronchi and part of the trachea. With the bolus in place, the surfactant can be delivered throughout the lungs as it is advanced distally on the next inspiration.

Samples of Survanta for the viscosity measurements were kindly provided by Richard Slavin (Neonatal Respiratory Therapy, Brigham and Women’s Hospital, Boston, MA). The contributions of Drs. Mary Ellen Avery and Jeffrey J. Fredberg in providing a clear perspective of the clinical setting and Dr. Ascher Shapiro in offering helpful suggestions during the experiments are gratefully acknowledged, as is the help provided by S. Godding in conducting the experiments. This study was supported by National Heart, Lung, and Blood Institute Grant HL-33009 and the Freeman Foundation.

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Received 29 January 1997; accepted in final form 26 February 1998.

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