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Mucociliary Transport in ICU Patients*

Franz Konrad, M.D.; Torsten Schreiber; Doris Brecht-Kraus, M.D.; and Michael Georgieff, M.D.

Objectives: The objectives of this study were to determine the bronchial mucus transport velocities in ventilated ICU patients and to study the possible role of impaired mucus transport in the development of retention of secretion and pneumonia.

Design: The patients were studied prospectively in a convenience sample trial.

Setting: The study took place at a university hospital.

Patients: Thirty-two ventilated patients in a surgical ICU were included in the study. The study was approved by the Ethics Committee of the University of Ulm.

Interventions: Bronchial mucus transport velocity (BTV) was measured with a small volume of technetium 99m-labeled albumin microspheres within the first 3 days of mechanical ventilation. The radiolabeled bolus was deposited at the distal end of the right and left main bronchus via flexible bronchoscopy. The movement of the microspheres toward the trachea was visualized and recorded using a scintillation camera. After determination of BTV, the patients were examined daily for 4 days to record pulmonary complications (defined as retention of secretion and nosocomial pneumonia).

Main measurements and results: The median BTV in the right primary bronchus was 0.8 mm/min and in the left it was 1.4 mm/min. In nine patients both radioactive drops remained at the application site. In 14 patients, a total of 19 pulmonary complications occurred (10 times retention of secretion, 9 times pneumonia). Patients with pulmonary complications had statistically significantly lower BTV compared with patients without pulmonary complications; in the left bronchus 0 (0 to 6.5) mm/min (median with range) vs 3.5 (0 to 10.5) mm/min (p<0.01) and in the right bronchus 0 (0 to 3.0) mm/min vs 4.7 (0 to 11.7) mm/min (p<0.01).

Conclusions: Ventilated patients in the ICU frequently have impaired mucus transport, which is associated with the development of retention of secretion and pneumonia.

(Chest 1994; 105:237-41)

BTV = bronchial transport velocity; MAA = macroaggregated albumin

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Mucociliary clearance depends on the complex interaction between ciliated columnar cells of the tracheobronchial tree and the special viscoelastic properties of the bronchial secretions. This system represents an important protective mechanism of the upper and lower respiratory tract whereby inhaled particles and microorganisms are removed from the tracheobronchial system. The potential consequences of impaired mucociliary clearance are portrayed by patients with primary ciliary dyskinesia who have absent or dyskinetic ciliary beating. At an early age, such patients are already affected by recurring retention of secretion, infections, and atelectasis. Patients in an ICU also have a tendency to retain secretions, particularly while receiving long-term mechanical ventilation. Of all hospitalized patients, they are the ones who are at most risk of contracting pneumonia. This suggests that mucociliary clearance is impaired in patients in the ICU. To date and to our knowledge, in intubated patients in the ICU, measurements of mucociliary clearance have not been reported in the literature. Hence, we determined the bronchial transport velocity (BTV) in patients in a surgical ICU and investigated the possible role of impaired mucus transport in the development of retention of secretion and pneumonia.

**Materials and Methods**

**Determination of BTV**

To measure BTV, we used a method based on that of Chopra et al who had determined the motion of a radioactive bolus in the trachea. The measurement of transport velocity in the trachea of intubated patients presents a problem, since the distance from the distal end of the trachea to the tip of the tube and thus the measuring distance can in some cases be very short. For this reason, we decided to measure the transport velocity in the right and left primary bronchus. The measurements were performed on patients lying in the supine position without elevating the upper part of their body. Bronchial transport velocity was determined with technetium 99m-labeled macroaggregated albumin (99mTc-MAA) with a particle diameter of 10 to 40 μm (Maascint, Medgenix, Brussels, Belgium). By means of a thin catheter (BC 9C, Olympus, Hamburg, Germany), 0.05 to 0.08 ml of 99mTc-MAA with an activity of 2 MBq was applied under visual control through the working channel of a flexible bronchoscope (BF 1 T 10, Olympus, Hamburg, Germany). The radiolabeled bolus was deposited onto the mucosa of the dorsal distal right and left primary bronchus (0.5 cm above the ostium of the superior segment of the lower lobe) in an atraumatic manner. The time required for visually controlled application of the radioactive bolus by bronchoscopy was on the average 2.5 min and at the most 3 min. For 30 min, this was followed by dynamic data acquisition with a scintillation camera (Starport system; collimator: low energy general purpose, diameter 500 mm, General Electric) in the anterior position. Sixty-four images of a 64 x 64 matrix were recorded with an exposure of 30 s per image. The cinematographic technique was used for qualitative
data evaluation and orientation; the quantitative evaluation was
done with the condensed image.  For this purpose, a region of
interest of the cinematographically visualized area of transport of
the radioactive deposit was defined. For each row, the maximum
count per matrix element was determined on the first image and
entered into the first column of a new matrix. This procedure was
repeated for all 64 images. One column in the condensed image
was assigned to each image. This path-time diagram served as a
basis for further image processing; transport processes now appear
as nonhorizontal radioactivity streaks. Tangents to these streaks
were drawn interactively under visual control. From the slope of
these straight lines, the known length of the picture elements (6.2
mm) and the exposure time per image (30 s), the transport velocity
of the radioactive deposit in millimeters per minute can be
calculated. Our method was described in detail previously.

Patients Studied

The study was approved by the Ethics Committee of the
University of Ulm. The significance and the purpose of this study
were explained to the patients preoperatively. All patients had
given their written consent to participate in the study. For patients
who were admitted to the ICU in an emergency (eg, multiple
trauma) and who were unconscious, written consent was obtained
from their relatives.

A total of 32 orally intubated patients at the Ulm University
Medical Center with an expected period of mechanical ventilation
of at least 4 days were studied in a convenience sample trial.
Patients for whom this period was unexpectedly shorter (two
patients) were not included in the evaluation. Patients receiving
catecholamines (dopamine/dobutamine > 3 μg/kg min or any therapy
with epinephrine or norepinephrine), β-blockers, theophylline,
cortisone, or atropine were excluded from the study, since these
drugs can influence mucociliary clearance. Excluded also were
patients undergoing heart surgery, patients younger than 18 years,
and patients with retention of secretion or pneumonia at the time
of admission.

In all 32 patients, BTV was determined within the first 3 days
following the beginning of mechanical ventilation. Mechanical
ventilation was volume controlled (Siemens Servo 300), and the FIO2,
positive end-expiratory pressure (PEEP), and the inspiratory-
expiratory ratio were adjusted depending on the extent of respira-
tory failure. A cascade nebulizer (Bennett) was used for humidifi-
cation. The temperature of the inspiratory gases, measured
between the tube and the ventilation hoses, was between 34° and
35°C. All patients received 2 μg/kg min of dopamine, their
cardiovascular system was stable, and their hourly urine excretion
was between 1 and 2 ml/kg/h. Stress ulcer prophylaxis was per-
formed with 2 × 10 mg of pirenzepine per day. Midazolam and
fentanyl were used for analgesic sedation. For the measurement of
bronchial transport velocity, pancuronium was used as muscle
relaxant.

Pulmonary Complications and BTV

To record all retentions of secretion with the need of bronchoscopic
suctioning and the development of pulmonary infection (both were
defined as pulmonary complications), all patients were examined
on each of the 4 days following the BTV determination. The
examination was performed by an experienced intensivist who did
not know the BTV values. The indication for bronchoscopic
suctioning was based on clinically and/or radiologically diagnosed
atelectasis presumably caused by retention of secretions. The
bronchoscopies were counted as complications only in patients
with more than two segmental ostia obstructed by secretions. Less
secretion was regarded as clinically not relevant. This occurred in
two patients.

The following criteria of pneumonia were used: new infiltration
on the radiograph, purulent tracheal secretion, temperature above
38.5°C, leukocyte count over 12,000/mm3, and deterioration in gas
exchange. For diagnosis of pneumonia, at least three of these
criteria had to be met. Furthermore, a plausible organism had to be
isolated in the bronchoalveolar lavage (BAL) in a concentration
> 106 colony-forming units (CFU)/ml BAL fluid or the "bacterial
index" of Johanson et al had to be 5 or more, respectively.

Statistics

The statistical analysis is based on Wilcoxon’s test for unpaired
samples and the χ2 test, with the significance level set at p < 0.05.
For descriptive statistics, we calculated the median with range.

RESULTS

Bronchial Transport Velocities

Table 1 provides information about diagnoses or operations, respectively. Demographic data, medication, duration of mechanical ventilation (MV) up to the time of measurement, APACHE II score,17 and BTV are listed in Table 2. The median BTV in the right primary bronchus was 0.8 mm/min and in the left it was 1.4 mm/min. In 9 of 32 patients studied, both radioactive drops remained at the application site. In these patients, a further measurement was performed 1 h later. Once again, no transport was observed.

Pulmonary Complications and BTV

In 14 patients, a total of 19 pulmonary complications were observed. The development of postoperative pulmonary complications was associated with impaired BTV. Patients with pulmonary complications had statistically significant lower BTV compared with patients without pulmonary complications; in the left bronchus 0 (0 to 6.5) mm/min (median with range) vs 3.5 (0 to 10.5) mm/min (p < 0.01) and in the right bronchus 0 (0 to 3.0) mm/min vs 4.7 (0 to 11.7 mm/
min (p < 0.01). Eight of nine patients without measurable mucus transport had one or more pulmonary complications. Six of the remaining 23 patients had one pulmonary complication (p < 0.01; χ2-test).

Nine patients suffered from pneumonia. The isolated microorganisms are listed in Table 3. In seven of these patients, no transport velocity was measureable in either of the two primary bronchi. Because of secretion retention, five patients with pneumonia were also subjected to bronchoscopy.

A total of ten bronchoscopic bronchial suctionings

<table>
<thead>
<tr>
<th>Diagnosis or Operation</th>
<th>No.</th>
</tr>
</thead>
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<td>Polytrauma</td>
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<tr>
<td>Peritonitis</td>
<td>8</td>
</tr>
<tr>
<td>Major aseptic abdominal and/or thoracic operations</td>
<td>10</td>
</tr>
<tr>
<td>Status after cardiopulmonary resuscitation</td>
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</tr>
<tr>
<td>Acute respiratory failure</td>
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</table>

Table 1—Diagnosis or Operations of the Investigated Patients
were carried out, with two patients receiving two bronchoscopies. In six of these patients, BTV was 0 in both primary bronchi, and in the other three patients it was below 5 mm/min.

**Discussion**

In man, the average tracheal transport velocity using bronchofiberscopic methods is reported to be about 10 mm/min.\(^6\) We determined the transport velocity in both primary bronchi, not in the trachea, in order to avoid methodical errors, specifically related to intubated patients. Depending on the anatomic conditions, the distance from the distal end of the trachea to the tip of the tube, and thus the measuring distance, can be very short.\(^9\) In addition, mucus transport presumably ends at the blocked tube cuff leading to an accumulation of secretions in the trachea that usually must be sucked out by regular tracheobronchial toilet, particularly during long-term mechanical ventilation. Since suction-induced microlesions and secretion spots in the trachea must be expected under these conditions,\(^9,10\) reduced tracheal transport velocity does not allow conclusions to be drawn from the remaining bronchial system.

Under general anesthesia with midazolam, fentanyl, and pancuronium, intubated patients who had healthy lungs and normal results of lung function tests preoperatively and did not smoke showed a median BTV of about 9 mm/min.\(^10\) These values are in agreement with data obtained from animals.\(^21,22\) However, the values for mucociliary transport rates using bronchofiberscopic methods are usually higher than those using the radioaerosol techniques. With a special noninvasive radioaerosol technique, Foster et al\(^23\) determined mucus velocity in the main bronchi in man. Bronchial velocities were found to average only 2.4 mm/min. A similar difference occurs between tracheal rates using different methodologies.\(^24\) This

*\(^1\)S = smoker; NS = nonsmoker; a = antibiotics; b = H₂-blockers; c = metoclopramide; d = antihypertensive drugs (eg, nitrates, Ca-antagonists, clonidine); e = diuretics; MV = mechanical ventilation; BTV = bronchial transport velocity.

---

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age, yr/ Sex</th>
<th>APACHE</th>
<th>Fio₂</th>
<th>PaO₂, mm Hg</th>
<th>PEEP, cm H₂O</th>
<th>Duration of MV, h</th>
<th>BTV, mm/min</th>
<th>Pulmonary Complications (P = Pneumonia; S = Retention of Secretion)</th>
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</thead>
<tbody>
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<td>25</td>
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<td>0</td>
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<td>26</td>
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<td>-</td>
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<td>-</td>
</tr>
</tbody>
</table>

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*Table 2—Demographic Data, Medication, APACHE-II Score, Fio₂, PaO₂, PEEP, Duration of MV up to the Time of Measurement, BTV, and Pulmonary Complications of Each Individual Patient*
could be caused by the variable degree of trauma caused by the bronchoscope that may locally stimulate the mucosa.25

Patients in the ICU with expected long-term mechanical ventilation had a median BTV of about 1 mm/min with a considerable intersubject range. At the moment, we can only speculate about the reasons underlying the slow BTV. Our patients constituted a heterogeneous caseload from a general surgical ICU. The number of smokers was 50 percent; although in some studies mucociliary function was not different between smokers and nonsmokers.26,27 Most authors found a slower clearance in smokers.26-30

Numerous drugs have been shown to influence mucus transport and could have been operative in our patients. Patients receiving drugs that showed an effect on mucociliary clearance in animal or human studies were excluded. To our knowledge, whether mucus transport is influenced by other medication, eg, H2-blockers, antibiotics or long-term administration of midazolam and fentanyl, has not been studied. However, other factors may have played an even greater role. Ventilation with high oxygen concentrations,31 activation of inflammatory mediator systems,32-35 colonisation by bacteria,36-38 suction-induced lesions of the mucus membrane,39 and infection with respiratory viruses39,40 combine to form a formidable potential insult to the mucociliary clearance mechanism. No attempt could be made in our study to elucidate the part played by these and other factors.

Gamsu et al41 reported on a possible correlation between impaired mucus transport and the postoperative development of atelectasis. At the end of the operation, those investigators insufflated a radiopaque powder into the tracheobronchial system and followed its disappearance radiographically. In 7 patients who underwent orthopedic surgery, there was complete clearance of tantalum within 48 h, whereas in 14 of 18 patients after abdominal surgery, the tantalum was retained for up to 6 days. Impairment of mucociliary clearance was significantly associated with the development of postoperative lobar and segmental atelectasis. In our study, impaired BTV was associated with the development of secretion retention or nosocomial pneumonia. More recent studies have shown that the mucus is important for microbial persistence and for the multiplication of potentially pathogenic microorganisms in the tracheobronchial tree, with the retained secretion serving as a reservoir.42-44 For many microorganisms, adherence to and colonization of an intact respiratory epithelium are hardly possible. They do occur in the presence of mucus and/or damaged epithelial cells, however. Our findings, of course, require further confirmation, since the causes for retention of secretion and the high pneumonia rates observed in patients in the ICU are multiple. Additional risk factors or variables must be taken into account as, for example, the extent to which tussive clearance is restricted or the adequacy of the host's systemic defenses.

In summary, our study demonstrated that patients in the ICU frequently have an impaired mucus transport that is associated with the development of retention of secretion and pneumonia. Therefore, mucociliary clearance seems to be an important nonspecific defense mechanism of the lung in intubated patients.

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### Table 3—Isolated Microorganisms in the BAL Fluid of Patients With Pneumonia*

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Microorganisms</th>
<th>CFU/ml</th>
</tr>
</thead>
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<td>4</td>
<td>Staphylococcus aureus</td>
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</tr>
<tr>
<td>5</td>
<td>Streptococcus viridans</td>
<td>2 x 10^5</td>
</tr>
<tr>
<td>6</td>
<td>Haemophilus parainfluenzae</td>
<td>5 x 10^5</td>
</tr>
<tr>
<td>7</td>
<td>Streptococcus pneumoniae</td>
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</tr>
<tr>
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<td>Candida species</td>
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<tr>
<td>11</td>
<td>Pseudomonas aeruginosa</td>
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</tr>
<tr>
<td>12</td>
<td>Escherichia coli</td>
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<td>Candida species</td>
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*BAL = bronchoalveolar lavage; CFU = colony-forming units.


18 Wanner A. Alteration of tracheal mucociliary transport in airway disease. Chest 1980; 80:867-58


20 Todd DA, John E, Osborn RA. Tracheal damage following conventional and high-frequency ventilation at low humidity. Grit Care Med 1991; 19:1310-16


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