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*TECHNICAL NOTE*

# Oropharyngeal deposition of 3.5 μm particles inhaled through an elongated mouthpiece

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*Oropharyngeal deposition of 3.5 μm particles inhaled through an elongated mouthpiece. K. Svartengren, M. Anderson, M. Svartengren, K. Philipson, P. Camner. © ERS Journals Ltd 1996.*

**ABSTRACT: We previously studied the deposition of inhaled particles in the oropharynx of asthmatic patients, and found that a pharyngeal narrowing during inhalation seems to be one reason for high oropharyngeal deposition. In the present study, we investigated whether by-passing a larger part of the oral cavity by using an elongated mouthpiece would reduce deposition in the oropharynx, and increase deposition in the lungs.**

**Deposition in the oropharynx and in the lungs was estimated in nine patients with obstructive airway diseases. In earlier investigations, three of these patients had repeatedly shown extremely high oropharyngeal deposition (>70%). In the present study, the patients inhaled 3.5 μm (aerodynamic diameter) radiolabelled Teflon particles at 0.5 $L \cdot s^{-1}$, with and without an individually adapted elongated mouthpiece. Radioactivity was measured using a profile scanner.**

**On average, oropharyngeal deposition was 27% (range 12–45%) and 30% (range 11–77%) of the total amount of particles deposited in the body, with and without elongated mouthpiece, respectively. There was no significant difference between these values ($p>0.05$), nor between the values of lung deposition. However, oropharyngeal deposition was markedly reduced, with a corresponding increase in lung deposition, by the elongated mouthpiece in the one and only patient who still showed extremely high oropharyngeal deposition (>70%).**

**Our study shows that lengthening of the mouthpiece is not sufficient to reduce average deposition of aerosol particles in the oropharynx in patients with comparatively normal deposition values. This result, however, does not exclude a beneficial effect in patients with extremely high oropharyngeal deposition.**

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Aerosols are extensively used for administration of drugs. The therapeutic effect of the inhaled aerosols depends, among other things, on where they are deposited. A certain fraction of the aerosol will always be deposited in the oropharynx, and this fraction may be extremely large in about 25% of asthmatics [1, 2]. Consequently, the therapeutic effect of the aerosol in the lungs is difficult to predict and is sometimes suboptimal. Furthermore, adverse effects may arise locally, such as oral candidiasis and dysphonia of inhaled corticosteroids [3, 4]. It is, apparently, highly desirable to reduce a high oropharyngeal deposition. In recent studies of patients with asthma, pharyngeal narrowing during inhalation seemed to be one important factor for high oropharyngeal deposition [2, 5]. Deposition in the oropharynx can be reduced by adding a spacer to a metered-dose inhaler [6], or by adding an external resistance during inhalation [5], and possibly also by changing the design of the mouthpiece used.

The aim of the present study was to investigate the effect of lengthening of the mouthpiece on deposition in the oropharynx and in the lungs. Our hypothesis was that an elongated mouthpiece would reduce deposition in the oropharynx and increase deposition in the lungs, by having the aerosol by-pass a larger part of the oral cavity and tongue.

## Methods

### *Design*

Nine patients with obstructive airway diseases inhaled monodisperse Teflon particles (3.5 μm aerodynamic diameter), labelled with $^{111}In$. Inhalation was performed on two occasions, with a 7 day interval between the two exposures. At one exposure, the inhalation was performed through a standard mouthpiece, and at the other an elongated mouthpiece was used. The two different mouthpieces are illustrated in figure 1. The inhalations were performed in a randomized fashion. Regional deposition was estimated by adjusting the gamma counts recorded in the measurements of head and neck, lungs and stomach to absolute values, using factors for self-absorption obtained from measurements in a phantom. The total inhaled activity was obtained by adding the activities

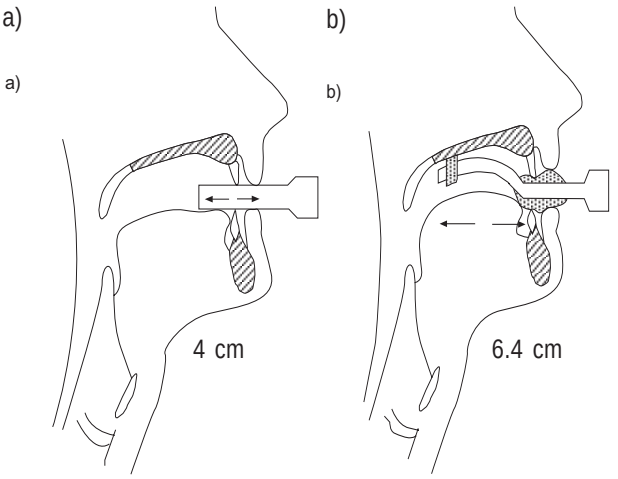


Fig. 1. – Illustration of the two mouthpieces: a) standard mouthpiece; and b) elongated mouthpiece.

from an exhalation filter. Immediately before profile scanning, all subjects drank some water to clear particles from the oropharynx and oesophagus. The total amount of particles deposited in the oropharynx was estimated from the measured activities in head and neck, and stomach, immediately after the inhalation of the test particles. The particle size used in the present study is within the range of most therapeutic aerosols.

The elongated mouthpieces were made out of ordinary upper airway tubes (Universal Airway®, Guedel type, No. 4; London, UK). For each patient, these were cut off at the level of the edge of the hard palate to obtain comfortable and relaxed inhalations. A further lengthening was not feasible without inconvenience for the patients. To obtain a standardized position of the mouthpiece in the oral cavity, dental paste was used (Coltène President®; Coltène AG, Switzerland). This was applied to the anterior and posterior parts of the mouthpiece, and was conveniently fitted to the anterior row of teeth and the hard palate (fig. 1). The average length of the mouthpieces, measured between the anterior row of teeth and the edge of the hard palate, was 6.4 cm (table 1). For the standard mouthpiece, the distance between the anterior part of the lips and the posterior part of the mouthpiece was about 4 cm (fig. 1). Inhalation of cool air through the different mouthpieces was tested before exposure to the test particles, giving different sensations. There was a sensation of airflow directed towards the tongue with the standard mouthpiece, and towards the larynx with the elongated mouthpiece.

### *Subjects*

Seven patients with asthma and two with chronic bronchitis volunteered for the study, which was approved by the Ethics Committee on Human Research of the Karolinska Institute. Personal and lung function data, duration of airway diseases, and length of the mouthpieces are given in table 1. The patients had a history of airway disease for, on average, 21 yrs. Six had a history of allergy. All used beta$_2$-agonists (inhaled and/or oral), six inhaled steroids daily, two used oral steroids, and one oral theophylline. Seven patients had participated in earlier studies, and three of them (Nos. 3, 5 and 8) were known, from two earlier investigations, to have extremely high oropharyngeal deposition (>70%).

### *Lung function tests*

Forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) were measured in a standing position using a Vitalograph spirometer (Vitalograph-Compact Ltd; Buckingham, UK). The lung function parameters were determined according to the criteria proposed by QUANJER [7].

### *Deposition measurements*

*Production and inhalation of the test particles*. The Teflon (Teflon 120; Du Pont Instruments, Newtown, CT, USA) particles were produced and labelled with $^{111}$In (half-life 68 h) by a spinning disc technique [8, 9]. The mean geometric diameter was 2.4 μm for both exposures, estimated by measurements in a light microscope (Visopan projection microscope; Reichert, Austria). The coefficient of variation was 7%. From the density of the Teflon

Table 1. – Personal and lung function data, and length of mouthpieces

| Subj. No. | Sex | Age yrs | Height cm | Weight kg | Length of mouthpiece* cm | Duration of airway disease yrs | FEV1 L | FEV1 % pred | FVC L | FVC % pred# |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F | 28 | 172 | 64 | 7.7 | 24 | 3.21 | 92 | 4.28 | 108 |
| 2 | F | 43 | 167 | 58 | 6.8 | 15 | 2.95 | 100 | 4.32 | 128 |
| 3 | F | 51 | 150 | 55 | 5.4 | 9 | 1.55 | 76 | 2.54 | 105 |
| 4 | M | 72 | 170 | 70 | 7.0 | 8 | 1.88 | 67 | 2.74 | 75 |
| 5 | F | 41 | 160 | 59 | 5.8 | 21 | 3.06 | 114 | 4.30 | 138 |
| 6 | F | 49 | 164 | 65 | 5.7 | 49 | 1.38 | 54 | 2.43 | 80 |
| 7 | F | 67 | 160 | 55 | 6.8 | 15 | 0.91 | 44 | 2.40 | 97 |
| 8 | M | 41 | 173 | 79 | 6.1 | 40 | 3.04 | 80 | 4.37 | 97 |
| 9 | F | 24 | 158 | 58 | 6.5 | 6 | 2.70 | 89 | 3.40 | 98 |
| Mean | | 46 | 164 | 62 | 6.4 | 21 | 2.30 | 80 | 3.42 | 103 |
| SD | | 16 | 7 | 8 | 0.7 | 15 | 0.87 | 22 | 0.90 | 20 |

*: Distance between the anterior row of teeth and the edge of the hard palate; #: predicted values according to QUANJER [7]. Subj.: subject; F: female; M: male; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; % pred: percentage of predicted.

particles, 2.13 g·cm$^{-3}$ [9], the mean aerodynamic diameter was calculated to be 3.5 μm. Before the particles were aerosolized into a glass bulb, they were washed in water at 37°C. The leakage of $^{111}$In in water of the washed particles was <1% per day. The Teflon particles were suspended in water (0.7 mg particles·mL$^{-1}$) and 0.2–0.3 mL of the suspension was sprayed once into a 25 L glass bulb with a Beckman Atomizer [8]. Before inhalation started, we ascertained that there was no visible mist and, if necessary, dry air was let into the bulb. The subjects inhaled the particles with 8–10 deep inhalations at a flow of 0.5 L·s$^{-1}$ during 2 min, with a pause of 1–2 s between inhalation and exhalation in order to allow all particles to deposit. The subjects were in a sitting position and wore a noseclip. The flow was measured with a pneumotachograph positioned between the bulb and the mouthpiece and was recorded graphically. By looking at the recorder needle, the subjects could inhale at a fairly constant rate throughout the inspiration. All subjects were trained to inhale in a relaxed manner before they inhaled the test particles. During exposure the exhalations were performed through a low-resistance filter in order to collect exhaled particles. The total amount exhaled was at the most 2% of the inhaled radioactivity. The radioactivity deposited in the lungs was about 0.1 MBq at each exposure.

*Measurements of radioactivity*. Radioactivity was measured using two 13×5 cm NaI crystals fitted with collimators. Profile scanning over head and neck, lungs and stomach of the supine subjects was performed twice immediately after inhalation. The counts from the two detectors were measured and recorded separately to permit discrimination between the activities in the lungs and stomach. Radioactivity in exhalation filters was also measured using the profile scanner. Factors used for calculation of self-absorption of radioactivity in head and throat, lungs and stomach were 2, 2.5, and 4, respectively. These factors were obtained from measurements using an Alderson Rando Phantom [10]. Calculations using rather large changes in the interrelationship between these self-absorption factors affected the calculated deposition in the oropharynx to only a minor extent [1].

## Results

Oropharyngeal deposition of particles inhaled through the standard mouthpiece ranged 11–77% (mean±SD 30±21%), and through the elongated mouthpiece from 12–45% (mean±SD 27±11%) (table 2). We found no significant difference between these values ($p>0.05$, Wilcoxon matched-pairs signed-ranks test). In this small study group, only one patient (No. 5) had extremely high oropharyngeal deposition, and this patient was the only one who showed a marked change in body particle deposition with an elongated mouthpiece (table 2). Deposition in the lungs, in percentage of the total amount of particles deposited in the body, was changed correspondingly to the changes in oropharyngeal deposition (table 2).

Table 2. – Deposition in the oropharynx, and in the lungs of 3.5 μm particles inhaled through two different mouthpieces

| Subj. No. | Oropharyngeal deposition* | | Lung deposition* | |
|---|---|---|---|---|
| | - | + | - | + |
| 1 | 17 | 21 | 83 | 79 |
| 2 | 14 | 26 | 86 | 74 |
| 3 | 39 | 45 | 61 | 55 |
| 4 | 38 | 37 | 62 | 63 |
| 5 | 77 | 28 | 23 | 72 |
| 6 | 20 | 21 | 80 | 79 |
| 7 | 42 | 36 | 58 | 64 |
| 8 | 16 | 12 | 84 | 88 |
| 9 | 11 | 15 | 89 | 85 |
| Mean | 30 | 27 | 70 | 73 |
| SD | 21 | 11 | 21 | 11 |

*: deposition in percentage of the total amount particles deposited in the body; -: with standard mouthpiece; +: with elongated mouthpiece. Subj: subject.

## Discussion

Studies of oropharyngeal deposition in healthy subjects [11–13] and patients with asthma [1, 2] have shown great interindividual variations, even during well-standardized inhalation procedures. Furthermore, deposition patterns are highly reproducible [1, 5], strongly indicating individual factors. As estimated from two inhalations in 20 asthmatics, the coefficients of correlation and of variation are 0.84 and 27%, respectively, with the present method of investigating aerosol deposition in the oropharynx [1]. For patients receiving lifelong medication with therapeutic aerosols, it is of importance whether 10 or 70% deposit in the oropharynx.

A pharyngeal narrowing during inhalation seems to be one reason for high oropharyngeal deposition in asthmatics [2, 5]. This finding, assessed by use of a fibreoptic laryngoscope, agreed well with the findings on radioactivity profiles, where the maximum activity was anatomically located over the oropharynx and not over the larynx. A high deposition in the oropharynx can be influenced by the use of a spacer [6], or by adding an external resistance during inhalation [5]. The spacer, among other effects, traps larger high-velocity particles from a metered-dose inhaler, thereby reducing oropharyngeal deposition. However, the decrease in the size of the particles reduces deposition not only in the oropharynx but also in the tracheobronchial region. An added external resistance, on the other hand, not only reduces a high oropharyngeal deposition but also correspondingly increases deposition and retention of aerosol particles in the lungs, possibly due to improved aerodynamic conditions.

In spite of a thorough fibreoptic examination of the pharynx and larynx, we were unable to provide simple criteria for the identification of patients with high oropharyngeal deposition. There are obviously other factors besides the shape of pharynx and larynx that are also important in determining this pattern of deposition. The fibreoptic examination included the pharynx and the larynx, but the anterior oral cavity and the behaviour of the tongue cannot be assessed by the instrument. Deposition might occur in these regions as well. The middle part of the tongue was a part we were unable to control. The anterior part of the oral cavity, about 4 cm, was covered by the standard mouthpiece. The posterior region is where oral air flow bends downward and deposition by impaction should be significant. This part was easily examined by

the laryngoscope and we did not detect any abnormal movements of the tongue at this level.

The aim of the present study was to investigate the effect of lengthening of the mouthpiece on deposition in the oropharynx, as well as in the lungs. Our hypothesis was that an elongated mouthpiece would by-pass a large part of the oral cavity and tongue such that deposition by impaction would be significantly reduced in this region, especially in patients with extremely high oropharyngeal deposition. This was the case in one patient, but not in the group as a whole. In the present study, only one patient (No. 5) still showed an extremely high oropharyngeal deposition (>70%), which could be reduced by about 50% units, with a corresponding increase in lung deposition, by use of an elongated mouthpiece. The other two patients (Nos. 3 and 8), who in two earlier investigations showed extremely high oropharyngeal deposition (>70%), were at the time of this investigation unusually well-controlled in their airway disease. They were well aware of their high oropharyngeal deposition, and also, from fibreoptic examinations, of the narrowing of their pharynx during inhalation, and had probably improved their inhalation technique. Obviously, an extremely high deposition in the oropharynx is not necessarily permanent over time in patients becoming aware of their situation.

The mean values of oropharyngeal deposition in the present study, about 30%, agree well with our previous findings in asthmatics [2, 5] and healthy subjects [14] at similar inspiratory flow and particle size. Our results, thus, show that lengthening of the mouthpiece generally does not offer an advantage over shorter devices in patients with comparatively normal deposition in the oropharynx. Comparing these results with those obtained previously with an added external resistance [5], even a moderate increase (>30%) in oropharyngeal deposition could be reduced with the increased resistance, but not with the elongated mouthpiece.

Turbulent flow is known to influence particle deposition in the oropharynx, as estimated for particles inhaled in air or helium-oxygen mixture [13, 14]. In the present study, the use of an elongated mouthpiece did not have much influence on the aerodynamic conditions in the patients, with the probable exception of patient No. 5.

In conclusion, this study shows that an elongated mouthpiece does not reduce deposition of aerosol particles in the oropharynx in most patients with relatively normal deposition values. However, the results are compatible with the hypothesis that patients with an extremely high oropharyngeal deposition may benefit from lengthening of the mouthpiece. Further clinical and experimental studies of larger populations are obviously needed to allow an appropriate identification of patients with difficulties in inhaling their medication, as well as to develop and evaluate different technical facilities for them. The results further show that an extremely high oropharyngeal deposition in some asthmatics may not be permanently high and can fall, probably due to a learning effect, indicating that inhalation training programmes may be valuable.

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