Particle deposition in the nose related to nasal cavity geometry*

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SUMMARY *A number of studies have been made to characterise the deposition-pattern of inhaled airborne particles in the nose. Common to all results has been considerable differences in deposition fractions between normal human subjects. It was the aim of the current study to improve our understanding of individual differences in nasal deposition of inhaled particles. Depositions were measured in ten adult normal subjects and were related to dimensional measurements by acoustic rhinometry. Five litres of a polydisperse aerosol (MMAD=0.7 μm, σ_g=1.7) were inhaled through one nostril only during 5 inspirations with flows of 10, 20, and 30 L/min with decongested mucosa. Increasing flow was found to increase the fraction deposited in the nose, while there was an inverse correlation between nasal deposition fraction and minimum cross-sectional area of the nasal cavity (Amin). Information based on acoustic rhinometry measurements significantly reduced the amount of unexplained variation between subjects in nasal deposition fraction. We conclude that an estimate of maximum linear air velocity, calculated as airflow divided by Amin, was the best single predictor of nasal deposition fraction, which was found to increase with increasing air velocity raised to a power of approximately 4/3.*

Keywords: acoustic rhinometry, nasal, particle deposition

INTRODUCTION

During the last sixty years, many experimental studies have been made to explain the deposition-pattern of inhaled airborne particles. Common to all results is a considerable difference in deposition fractions between normal human subjects. Such differences in deposition fractions may result in corresponding differences in the risk of acquiring lung diseases caused by inhaled environmental pollutants. As an example Lehmann in 1935 found that those miners who had developed silicosis were those who on the average had the lowest nasal deposition fraction. Understanding which factors determine nasal deposition may improve our ability to estimate how toxic substances are deposited upon inhalation.

When aerosols are inhaled through the nose various fractions of particles deposit along the passage. Only very few particles larger than 10 μm in diameter are able to penetrate the human nasal passage during normal inhalation, while most particles smaller than 2 μm reach the more distal airways (Heyder et al., 1986). The fraction of particles deposited in the nasal passage by impaction or inertial deposition will increase with particle size and with high velocity and changes in flow direction through the passage.

Based on cumulated experimental data from 7 studies with a total of 31 subjects, with particle sizes ranging from 0.25 to 23 μm, and flow rates from 5 to 37 L/sec Yu et al., (1981) found that the nasal inspiratory deposition efficiency could be described as a function of particle density (*r*), particle diameter (*d*), and flow (*Q*) according to the equation:

$d_{NI} = a + b\ log(\rho d^2 Q)$, where *a* and *b* are constants

Hounam et al., (1969) found, however, in a study of 3 subjects that the inter-individual variability in nasal deposition fraction was better described if deposition was plotted as a function of the pressure difference (ΔP) measured across the nasal passage during the inhalation instead of flow. ΔP would be determined by the airflow through the nose in combination with individual differences in flow resistance.

This relationship was later re-evaluated by Heyder & Rudolf (1977) in a study of 4 subjects. They also found that the results were better described by including the pressure difference in the equation instead of the airflow, but their equation included $\Delta P^{2/3}$ instead of ΔP.

However, the pressure difference across the nose is for a given flow rate determined by the geometry of the nasal passage and the minimum cross-sectional area (Amin) through the nasal passage is likely to be of special importance – not only for the flow resistance but also for localising the deposition (Itoh et al., 1985; Christensen & Swift, 1986). Kasavanathan et al., (1998) recently evaluated in a study with 40 subjects the ability of Amin in combination with other measures of nasal geometry to predict nasal deposition efficiency for a polydisperse aerosol in

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comparison with predictions based on nasal flow resistance measurements. They found that both models could predict deposition but concluded that the nasal passage geometry information was easier to obtain. However, the models they developed did not reflect a specific mechanism of deposition.

In the present study, ten healthy subjects inhaled a polydisperse aerosol through one nostril only with the other nostril closed. Flow rates through the nasal passage during inhalation were precisely recorded and dimensions of the passage were measured repeatedly by acoustic rhinometry. The purpose of the study was to describe the influence of nasal passage geometry on particle deposition in the human nose and to evaluate how such information may improve predictions of nasal particle deposition efficiency in comparison with previously published models predicting nasal deposition.

METHODS AND MATERIALS

Subjects

With approval by the local ethics committee ten healthy adult subjects (5 females, 5 males, mean age =30.1 years, range 23-51 years), all without any history of nasal problems, volunteered for the experiment. The participants had been examined by anterior rhinoscopy and had been found without abnormalities. At the first day of appearance, all subjects had their nasal mucosa decongested with ephedrine in a 0.25% solution. The side of the nose to be used in the study was selected by means of acoustic rhinometry as the side of the nasal cavity with the largest volume to ensure that it would be possible to inhale at the highest flow rates.

Scheme

Each subject was investigated in randomised order on three different days with a different flow rate on each day. Each day the nasal cavity was decongested prior to the measurements to minimise within-subject variation in nasal passage geometry between days.

Day 1:flow=10 L/min
Day 2:flow=20 L/min
Day 3:flow=30 L/min

Decongestion of Mucosa

To decongest the nasal mucosa the whole nasal cavity was washed with an isotonic NaCl solution containing 0.25% ephedrine. Measurements started after a lag-time of approximately 20 minutes.

Acoustic Rhinometry

The method has been described in details previously (Hilberg et al., 1989). We used equipment (GJ Electronics, Skanderborg, Denmark) where a sound impulse is generated by a spark. This acoustic signal was directed into the nasal cavity via a 100-cm long rigid tube with an internal diameter of 1.5 cm and a 7-cm long straight nosepiece with a short conical fit to the nostril. Sixteen cm from the upper edge of the tube a microphone measured both the incident and the reflected signals. A change in the cross-sectional area in the nasal passage changes the acoustic impedance and accordingly the pattern of the reflected signal. The incident and reflected signals, amplified and low-pass filtered at 10 kHz, were recorded by a computer at a sampling rate of 50 kHz. From these data a curve showing the cross-sectional area of the nasal passage as a function of the distance from the nostril was subsequently calculated and nasal cavity volume was calculated as the volume of the first 7 cm of the cavity. Cross-sectional areas of the nasal passage used for inhalation were measured three times immediately before and three times immediately after the inhalation and the six measurements were subsequently averaged.

Aerosol Generation

For inhalation an aqueous, polydisperse aerosol was produced from a Wright nebulizer (Raabe, 1976) using an air pressure of 1.30 bar. The nebulized solution contained isotonic NaCl and approximately 5 MBq/mL ^{99m}Technetium-diethylenetriamine-pentaacetic acid (DTPA). From the nebulizer 15 litres of aerosol was led into a plastic bag. Here the aerosol was kept for exactly 4 minutes before inhalation.

The particle size distribution of the aerosol drawn from the bag was measured with an Andersen Mk. II sampler (Andersen 2000 Inc., Atlanta, Georgia, USA) after a dwell time in the bag of 4 minutes and after a dwell time of 5 minutes and 10 seconds to evaluate how stable the aerosol was over the period of time it could take to draw the aerosol from the bag during the inhalation. After a dwell time of 4 minutes, we found a- mass median aerodynamic diameter (MMAD) of 0.67 µm with a geometric standard deviation (σ_g) of 1.72. After 5 minutes and 10 seconds MMAD was 0.70 µm and σ_g=1.63.

To evaluate to what extent the particle size distribution might change when entering the warm and humid nasal cavity we also measured the aerosol after passing it through a humidifier at 38°C., into the Andersen sampler also heated to 38°C. The aerosol changed only slightly to a MMAD of 0.81 µm and $\sigma_g = 1.72$. The particle size distributions of these aerosols are illustrated in Figure 1.

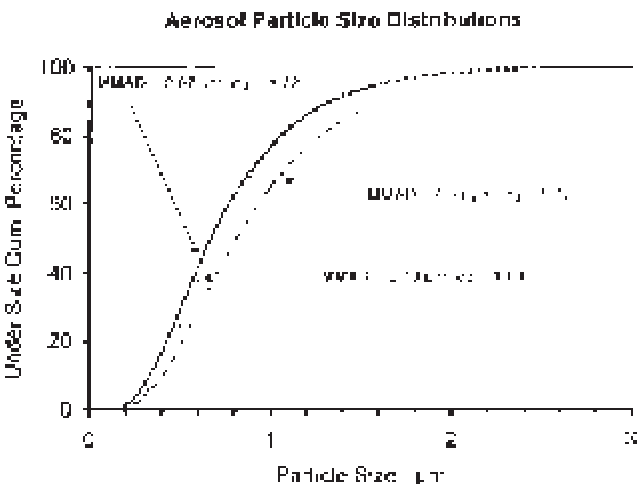

Figure 1. Particle size distributions for aerosols with MMAD and σ_g as measured in the current study.

Aerosol Inhalation

The set-up for aerosol inhalation is shown in Figure 2. The subject had one nostril sealed with tape and had a small tight fitting mask placed over mouth and nose. The subject was connected to the plastic bag and would then inhale aerosol through the one nostril followed by exhalation through the mouth. In this way aerosol deposition in the nose only took place during inhalation.

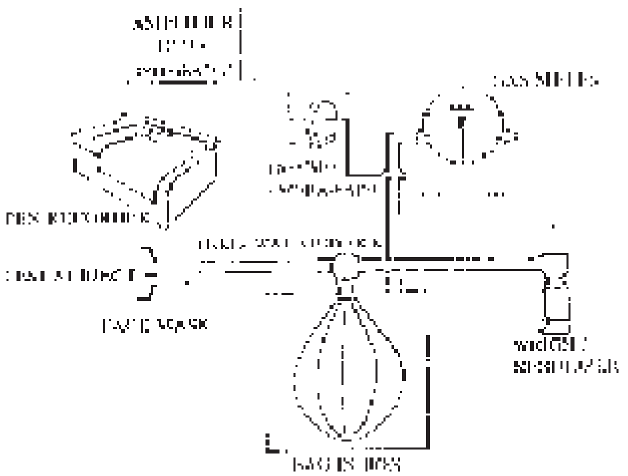

Figure 2. Set-up for Aerosol Production and Inhalation (*cf.* text).

Flow Monitoring

Air flow through the nose was measured by a pneumotachograph (Fleisch No.1) and recorded on a strip-chart recorder (Servogor 2, Goerz electro, Vienna, Austria) paper speed=10 mm/s. During inspiration the subject had the recording pen follow an already drawn pattern on the paper as shown in Figure 3. This required training beforehand. If the pattern was followed, the subject inhaled exactly one litre at each inspiration with the specified airflow (10, 20, and 30 L/min), until a total of 5 litres was inhaled.

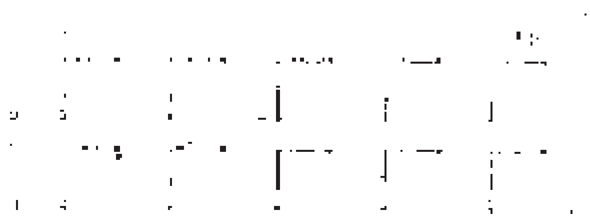

Figure 3. Inhalation Guidance. A recording of two series of inhalations, each consists of five inhalations of 1 litre each at a specified flow of 20 L/min, is shown. In each of the two series the subject attempts to follow the bold square lines corresponding to an exact flow of 20 L/min during inhalations, and with exhalations through the mouth. The thin line overlaying the bold square line is a tracing of the actual flow, while the line rising from lower left to upper right side is a tracing of the total volume inhaled with the 5 inhalations. The tracing marked '1' was obtained first and with a filter placed on the exhalation line, while the tracing marked '2' was obtained thereafter and with a filter on the inhalation line instead. During the second series the subject would adjust the duration of the last inhalation to ensure that the same total volume was inhaled in the two series.
The actual mean flow rate during the first series of inhalations was afterwards measured from the tracings. Any difference between the two series in total inhaled volume was corrected for in the subsequent calculations.

Particle Deposition Measurement

For each measurement, the subject made two inhalations, each consisting of 5 inspirations i.e. 5 litres of aerosol (Figure 3). During the first inhalation, an absolute filter was placed *on the expiration side* and immediately after inhalation two activity measurements were made in front of a scintillation detector (Harshaw-detector model 1252/3A) in identical geometric position:

1) total deposited activity in the nose and part of rhinopharynx (**A**)
2) activity of the filter in the expiratory line (**B**).

After emptying and refilling the bag with aerosol, the series of inspirations was repeated, now with an absolute filter on the inspiratory side. Inspiration was stopped, when exactly the same volume as in the first inhalation was obtained (Figure 3) after which the activity of the filter *in the inspiratory line* was measured (**C**). All measurements were corrected for background radiation and decay of ^{99m}Technetium. For measurements on filters, there was no attenuation of the radiation while radiation from particles deposited in the nose was attenuated by a factor of 0.8. After correction for radiation attenuation and for differences in the inspiratory volume between the two series of inspirations the following parameters could be expressed:

a) body deposition as % of inhaled aerosol = 100•(C-B)/C
b) nasal deposition as % of inhaled aerosol = 100•A/C

Statistics

Non-parametric tests for analyses of repeated measurements on the same group of subjects were used to test for differences between test days (Friedman's non-parametric analogy of a two-way ANOVA) (Zar, 1984). For the analysis of correlation between two variables on a single day, Spearman's non-parametric rank-based correlation analysis was used (Zar, 1984). For tests of statistical significance a p-value <0.05 has been considered significant. Conventional parametric regression analyses were used with data from several days, not as a test of statistical significance, but to provide a R^2-value as an estimate of the extent to which a straight least-square fitted line through the data could describe their distribution.

RESULTS

Nasal Dimensions

The minimum cross-sectional area (Amin) of the decongested nasal cavity varied between subjects from 0.52 to 1.00 cm^2 (average of Day 1-3). Amin did not change between days (p=0.74). The average nasal cavity volume (Day 1-3) varied between subjects from 9.5 to 15.0 mL. The average distance from the nostril to Amin (Dmin) for all ten subjects for the three days was 2.3 cm.

Particle Deposition Related to Flow and Nasal Dimensions

The overall average body deposition was 66.0% and was uninfluenced by differences in inhalation flow (p=0.74). No relation was found between nasal cavity dimensions and body deposition fraction.

The nasal deposition (as percentage of inhaled aerosol) increased with increasing inhalation flow rates from 10 L/min to 30 L/min (p=0.0007). This is shown in Figure 4, where the actual flows obtained are also shown. One subject (subject 'F') was unable to achieve the highest two flow levels.

When nasal depositions for Day 1-3 were analysed according to the equation:

$$d_{NI} = a + b \cdot \log(\rho d^2 Q)$$

with σ=1 g/cm^3 and d=0.68 µm, and the parameter $\rho d^2 Q$ ranging from an average of 78 (10 L/min) to an average of 211 g µm^2 sec^{-1} (30 L/min), then values for a and b of -0.66 (S.E.=0.21) and 0.37 (0.10), respectively, were found. R^2 for the fit between the data and the model was 0.35.

No correlation was found between Amin and nasal deposition at the lowest inspiratory flow of 10 L/min. However, as the flow was increased to 20 and 30 L/min an inverse correlation of increased nasal deposition fraction with decreasing Amin became evident (Spearman's r (r_S)=-0.71 with 30 L/min, p=0.022).

The two relationships (increasing nasal deposition with increasing flow and decreasing Amin), were then combined into a single parameter by calculating an estimate of the maximum air velocity through the nasal passage as:

$$Flow\ (m^3/sec)\ /\ Amin\ (m^2).$$

When this parameter was correlated with nasal deposition as shown in Figure 5, it was possible to reduce the amount of unexplained variation in nasal deposition fraction substantially. The best fit model had the form:

$$Nasal\ Dep.\% = 1.4 \cdot [Air\ Velocity]^{1.4}$$

with a R^2 of 0.64.

DISCUSSION

An overall observation in the present study is the variability of deposition between subjects. With a flow = 20 L/min and decongested mucosa nasal deposition varies between 3.3% and 41.6%. This finding is notable, however not unique, in comparison with earlier studies (Yu et al., 1981).

Our results are not directly comparable with those of former studies as reviewed by Yu et al., (1981). With the aerosol and flow rates used in the present study the parameter $\rho d^2 Q$ varied between average values of 78 and 211 g µm^2 sec^{-1}. However, in contrast to other studies working within the same range for $\rho d^2 Q$ the subjects of the current study inhaled the aerosol through one nostril only, while in the other studies the particles were inhaled through the nose as a whole. As a consequence, the flow per nostril has on the average been twice as high for the same value of an overall Q. So in comparison with these other studies the parameter $\rho d^2 Q$, as a predictor of deposition, may in the present study be considered to have been approximately twice the value of what is simply calculated from the air flow and would thus range between 156 and 422 g µm^2 sec^{-1}. This may explain the higher nasal deposition found in the current study for seemingly comparable values of $\rho d^2 Q$. Furthermore, it places the value range for the parameter $\rho d^2 Q$ from the current study in a transition zone between two different equations predicting nasal deposition in dependence of $\rho d^2 Q$ as calculated by Yu et al., (1981):

$$d_{NI} = -0.014 + 0.023 \cdot \log(\rho d^2 Q), \quad \text{for } \rho d^2 Q < 337 \text{ g µm}^2 \text{ sec}^{-1}$$

and

$$d_{NI} = -0.959 + 0.397 \cdot \log(\rho d^2 Q), \quad \text{for } \rho d^2 Q > 337 \text{ g µm}^2 \text{ sec}^{-1}$$

The current data was best described by the equation:

$$d_{NI} = -0.66 + 0.37 \cdot \log(\rho d^2 Q) \quad \text{with } R^2 = 0.35.$$

Another difference between the current study and most of the earlier studies is our use of a polydisperse aerosol. This seems to have been of limited importance. Heyder & Rudolf (1977) made a number of measurements on four subjects under very similar conditions for flows and inhalation pattern (flow = 7.5, 15, and 30 L/min with tidal volumes of 1 L) using monodisperse aerosols with particle diameters of 0.5 and 1.0 mm. Their results, as reported in their article, were used together with results from the current study to construct Figure 6. Here mean deposition percentages obtained in the current study at each flow level have been plotted together with mean values from Heyder & Rudolf against a common scale of log ($\rho \cdot d^2 \cdot$[Flow/Nostril]). Results from the current study are seen to be close to those from Heyder & Rudolf. For the highest flow rates, where $\rho \cdot d^2 \cdot$[Flow/Nostril] for the two studies were nearly identical, the difference between the two sets of data was not significant (p>0.40).

Between subjects the nasal deposition fraction increased with diminishing minimum cross-sectional area, which for a given flow means with increased air velocity at the narrowest site within the nasal cavity. However, with flow = 10 L/min there was hardly any variability in the nasal deposition between the subjects. Flow has probably been laminar and dimensions therefore of less importance under these circumstances. To evaluate the flow characteristics of the air as it passes through the part of the nasal passage corresponding to Amin, Reynolds number was calculated as:

$$Re = 2 \cdot \rho \cdot Q \cdot \pi^{-1} \cdot r^{-1} \cdot \eta^{-1} \text{ (Dubois, 1964)},$$

where ρ = the density of air = 1.142•10^{-3} g cm^{-3} at 34°C, Q = the airflow in cm^3•s^{-1}, r = the radius in cm [= $\sqrt{(\text{avg.Amin}/\pi)}$ = $\sqrt{(0.75\ \text{cm}^2/\pi)}$], and η = the viscosity of air in poise = 181.83•10^{-6} poise at 34°C (Miller, 1993).

Reynolds number was found to be 1327, 2655, and 3982 with the nasal dimensions measured and flows of 10, 20, and 30 L/min, respectively. As a Reynolds number of less than 2000 indicates a laminar flow through the part of the nasal passage corresponding to Amin a transition from laminar flow towards turbulent flow may be assumed to happen as the flow increased.

The fact that the nasal deposition fraction increased with increasing flow (and velocity) in all subjects emphasises the significance of the air velocity for nasal deposition. The nasal deposition percentage was found to increase proportional to the velocity raised to the power of 1.4 or approximately 4/3. With this relation, we could describe the data from the current study with considerably higher precision than with the equation relating nasal deposition efficiency to flow or $\rho d^2 Q$. Therefore, the dimensional information conveyed by the acoustic measurements of Amin of the nasal air passage may reduce the residual, unexplained variability in nasal deposition fraction compared with a model based on flow alone.

In our study, we calculated the velocity at the narrowest site in the nasal cavity as flow divided by minimum cross-sectional

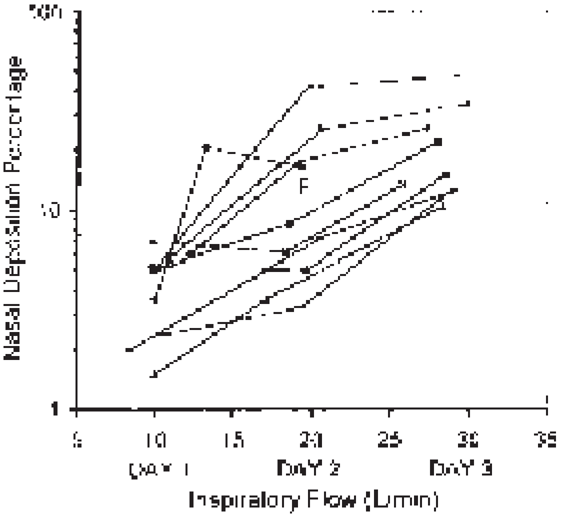

Figure 4. Effect of Inhalation Flow on Nasal Deposition Percentage. Day 1-3 corresponds to flows of 10, 20, and 30 L/min.

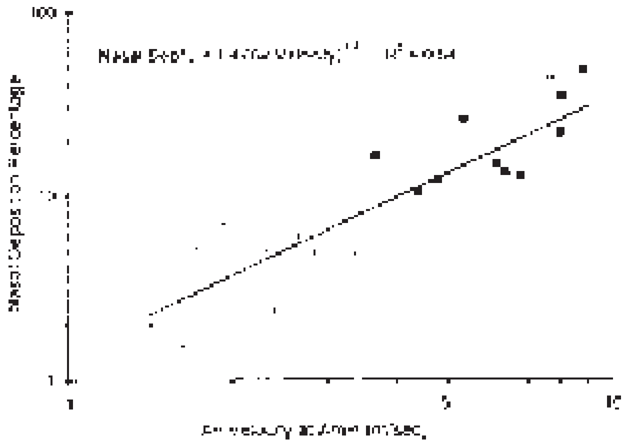

Figure 5. Nasal Deposition Percentage vs. Air Velocity through the Minimum Cross-sectional Area on all Test Days. Cross = Day 1, Open Square = Day 2, Closed Square = Day 3.
The best least square fit through the points have been drawn as well as the equation for the line.

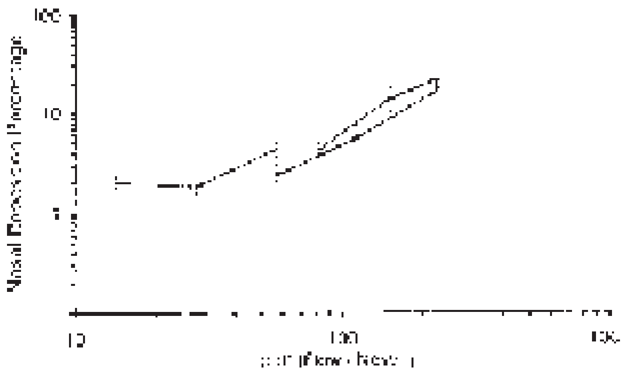

Figure 6. Mean Nasal Deposition Percentages *vs.* $\rho d^2 Q$. using data from the current study and data published by Heyder & Rudolf (1977). For comparability, the flow parameter, Q, has been calculated as *flow/nostril.* Consequently, a bi-nostril flow of 30 L/min will result in a value for Q of 15 L/min. □: H&R, d = 0.5 μm, Δ: H&R, d = 1.0 μm, +: Current study, d = 0.7 μm.
Error bars: ± S.E.M.

area. The kinetic energy of the aerosol particles is related to the pressure required to accelerate the particles at a given flow so that they can pass the narrowest cross-section of the nose. This pressure equals $1/2\rho v^2$, where ρ is density and v velocity. As the deposition by impaction is related to the kinetic energy this may explain why nasal deposition is better correlated with velocity than with flow, and is in agreement with the findings of Heyder and Rudolf (1977). Yet we found only a power of 1.4, where 2 was to be expected. However, as the pressure needed for convective acceleration accounts for only a part of the total pressure drop across the nasal cavity (Hilberg et al., 1989), and because turbulent as well as laminar flow components are included, the total pressure drop may be considered a sum of linear and quadratic flow terms, and that may explain why the exponent is smaller than two.

In comparison with the models developed in the study by Kesavanathan et al., (1998) the model derived in the current study reflects the underlying physical mechanisms of particle deposition more closely. The models developed by Kesavanathan et al. had the general format of: $d^a \cdot Amin^b \cdot E^c$ where d = particle diameter and E = the nostril length to width ratio for the model based on measurements of nasal geometry and the format: $d^a \cdot R^b$ where R = nasal passage flow resistance for the model based on nasal resistance. The coefficients would vary for different flows, but without a specific relationship to changes in flow. In the current study, the parameter of nostril length to width ratio did not add further precision to the model in predicting deposition efficiency. A possible reason could be that in contrast to the former study the participants of the current study were ethnically more homogeneous with correspondingly smaller differences in the geometry of the external nose.

The conclusion is that the nasal deposition efficiency is best described by an estimate of the maximal air velocity through the nose, calculated from the inspired flow rate and the minimum cross-sectional area measured by acoustic rhinometry. Information about Amin obtained from acoustic rhinometry reduces the residual and unexplained variability considerable compared to a model based on the flow alone.

So it appears that deposition of even rather small particles (MMAD = 0.7 μm) in the nose to a great extent is determined by the kinetic energy of the particles. As a consequence forceful inhalations through the nose would actually be the best way to avoid inhaling particles into the deeper airways by increasing the nasal deposition fraction.

In the current study we have not compared simultaneous depositions in the two sides of the nose. However, the flow rates through the two sides of the nose are likely to be different as a result of anatomical differences and the influence of the nasal cycle. The distribution of flow between the two sides will be so as to minimise the difference between the two sides in pressure drop along the nasal passages. Consequently a smaller airflow is expected through the narrowest side of the nose compared with the other side. The Bernoulli equation predicts that the air velocity at the narrowest points in the two sides will be identical. As deposition is determined by air velocity, the deposition fractions on the two sides are expected to be fairly equal, but the absolute amount of aerosol deposited in the narrower side will be smaller, because less air passes through that side.

We have not made measurements of particle deposition in diseased noses. Based on the current results, we would expect a higher deposition fraction in a partly occluded nose because the air velocity in that situation would have to be higher to maintain a certain volume of respiration per time unit provided that nose breathing is maintained.

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ANNOUNCEMENT