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# A Study of Aerosol Deposition and Clearance from the Human Nasal Passage

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**A study of the deposition and clearance of inhaled particles in the human nasal passage has identified and quantified the major routes of particle transport clearance from the nose. The results of the study have been used to construct a compartment model describing extra-thoracic clearance. Experimental evidence for each of the model's clearance routes is discussed.**

*Keywords:* inhalation; nasal; clearance; human; model

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## INTRODUCTION

The Task Group of Committee 2 of the International Commission on Radiological Protection (ICRP) that developed the Human Respiratory Tract Model for Radiological Protection (HRTM) noted that data on the clearance of inhaled particles from the human nasal passage was limited and that further knowledge was desirable (ICRP, 1994). Therefore, nasal deposition and clearance by particle transport in human subjects has been studied to improve knowledge of these processes. Experiments for a range of particle sizes and work rates have measured nasal clearance over a much longer period than previous studies. The principal objective is to improve the accuracy and reliability of dose assessments of intakes by nasal inhalation.

In the HRTM the extra-thoracic compartment (ET) is divided into two sub-compartments, $ET_1$ and $ET_2$, which receive approximately equal deposits of inhaled aerosols. $ET_1$ represents the skin-lined front of the nasal passage and has lower radiosensitivity than the rest of ET ($ET_2$). The HRTM models all clearance from $ET_1$ as nose blowing. The ciliated posterior nasal passage is part of $ET_2$, from which clearance is modelled as mucociliary action to the gastrointestinal (GI) tract, except for 0.05% that is sequestrated into airway walls and slowly clears to the ET lymph nodes ($LN_{ET}$). The $ET_1$ and $ET_2$ clearance rates are 1 and 100 per day, respectively. Nasal clearance in the HRTM is deliberately simplified by not including clearance from $ET_1$ to $ET_2$, but the $ET_1$ and $ET_2$ deposition fractions have been adjusted to compensate for this simplification.

The findings of the study were used to construct the Smith–Etherington ET (S-E ET) clearance model, which aims to represent nasal clearance more realistically. This model has been used to assess doses received from ET deposition after nasal inhalation for comparison with HRTM predictions (Smith *et al.*, 2000).

## MATERIALS AND METHODS

Ethical approval was obtained from the Central Oxford Research Ethics Committee to perform the study and administer small quantities of aerosols radiolabelled with either $^{99m}$Tc or $^{111}$In to nine volunteer participants. Both spinning top and vibrating orifice aerosol generators were used to produce the insoluble, radiolabelled monodisperse polystyrene aerosols for the study (Youngman, 1997). All nine participants inhaled 3 μm aerodynamic diameter ($d_{ae}$) particles naturally through the nose while sitting at rest. Smaller groups inhaled 1.5 or 6 μm $d_{ae}$ aerosols while sitting at rest and 3 or 6 μm $d_{ae}$ aerosols while performing light exercise (80 W work rate). Breathing patterns and aerosol intakes were recorded during the inhalations. Nasal and lung retention were measured for ~50 h by γ-ray spectrometric *in vivo* measurements. Initial rapid clearance to the stomach was also measured. Participants provided nose blow samples at will. The activities of nose blow and some supplementary bioassay samples were measured by γ-ray spectrometry.

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## RESULTS

The S-E ET model (Fig. 1), like the HRTM, divides ET into $ET_1$ and $ET_2$ and also includes a sequestrated fraction. However, the S-E ET model includes additional clearance routes that were observed in the study, i.e. clearance from $ET_1$ to $ET_2$ and very rapid clearance from $ET_2$ to the GI tract. Deposition fractions and clearance rates were derived and are shown in Fig. 1 for a 5 µm $d_{ae}$ aerosol inhaled at the standard work rate (Smith *et al.*, 2000). The model's clearance routes are justified by the following experimental evidence.

### *Nose blowing*

Different participants cleared between 0.5% and 50% of initial ET deposit (IETD) by nose blowing. This inter-subject variation was typical for ET clearance fractions measured in this study. Despite this variation, nose blow activities showed a general trend with IETD and time after intake. For individual administrations this trend was best shown by the sum of nose blow activities given in each 3 h interval after intake, but the trend was most powerfully shown by the geometric means of the 3 h nose blow activities from all the administrations normalized to the IETD (Fig. 2). No relationships between nose blow clearance and particle size or exercise rate were identified.

### *Rapid transport from ET to GI tract*

Clearance of activity to the stomach in the first hour showed the expected mucociliary clearance from the posterior nasal passage ($ET_2$ in Fig. 1) with an average half-time of 16 min. Additionally, there was evidence for a very fast clearance fraction that reaches the stomach within 3 min of administration. This may be a result of swallowing particles deposited in the nasopharynx (Fig. 3).

### *Slow transport from ET to GI tract*

Nose blow activities and rapid clearance to the GI tract cannot account for a significant fraction of nasal clearance after the first hour (Fig. 4). Subtracting the measured activities from the IETD shows that there must be an additional ET clearance mechanism with a half-time of the order of 10 h, which is responsible for >50% of nasal clearance in some participants. *In vivo* measurements on the

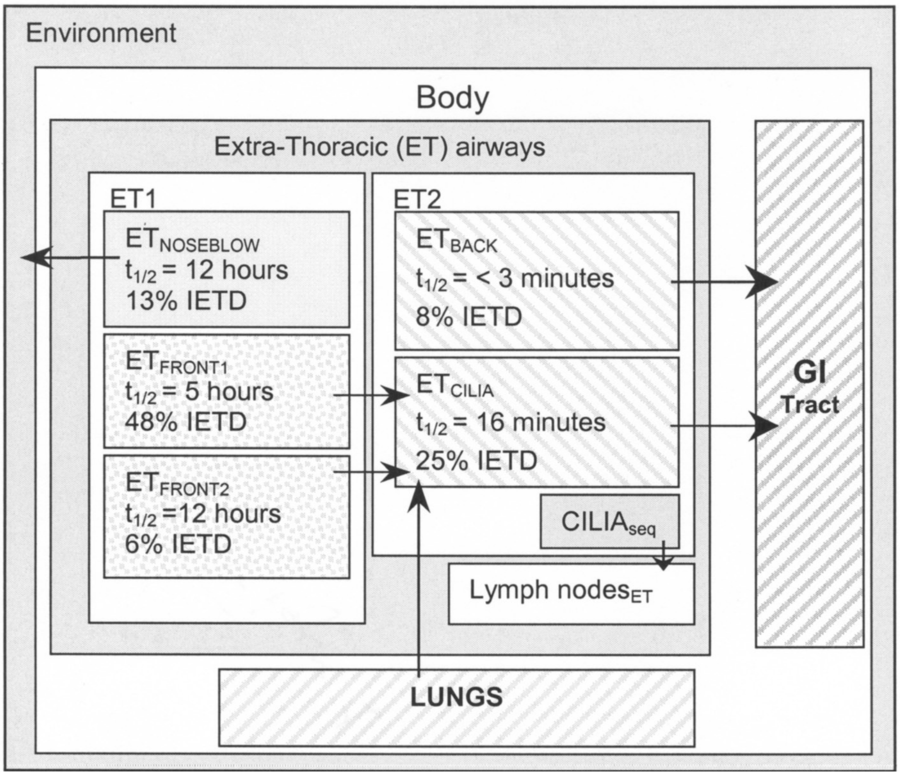

**Fig. 1.** The Smith–Etherington ET clearance model. IETD, initial ET deposit.

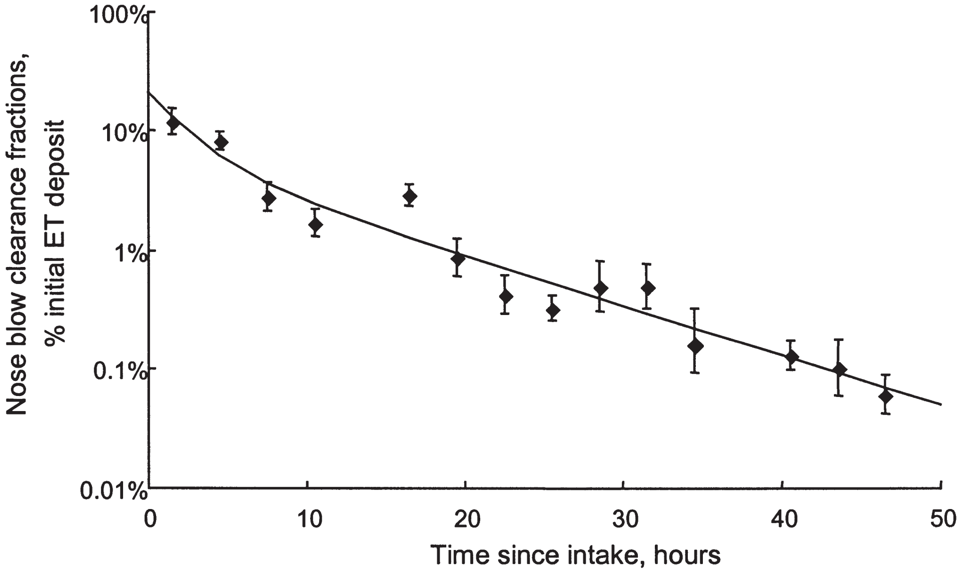

**Fig. 2.** Geometric mean and standard error of the mean of nose blow samples for all administrations in each 3 h interval.

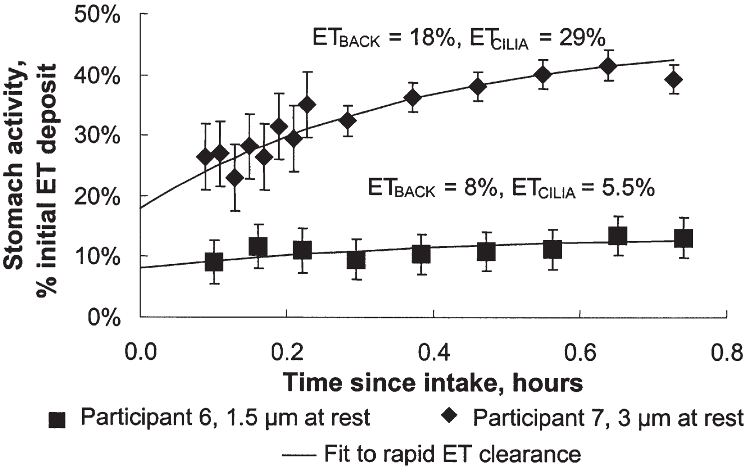

**Fig. 3.** Rapid ET clearance to the stomach for two of the participants.

head showed that after the first hour retained ET activity was predominantly at the front of the nose ($ET_1$ in Fig. 1). As this slow clearance fraction did not clear from $ET_1$ by nose blowing, it must clear through $ET_2$ to the GI tract.

The large degree of inter-subject variation means that trends in the clearance rate of the slow cleared fraction with particle size or breathing rate are best seen by comparing results for the same participant. For instance, data for participant 4 (Fig. 5), in common with data for other participants, suggests that the 50% clearance time decreases as particle size and exercise rate increase.

## CONCLUSIONS

The existence of slow clearance from the front of the nasal passage to the GI tract has been confirmed and has been shown to be responsible for the clearance of >50% of particles deposited in the nose in

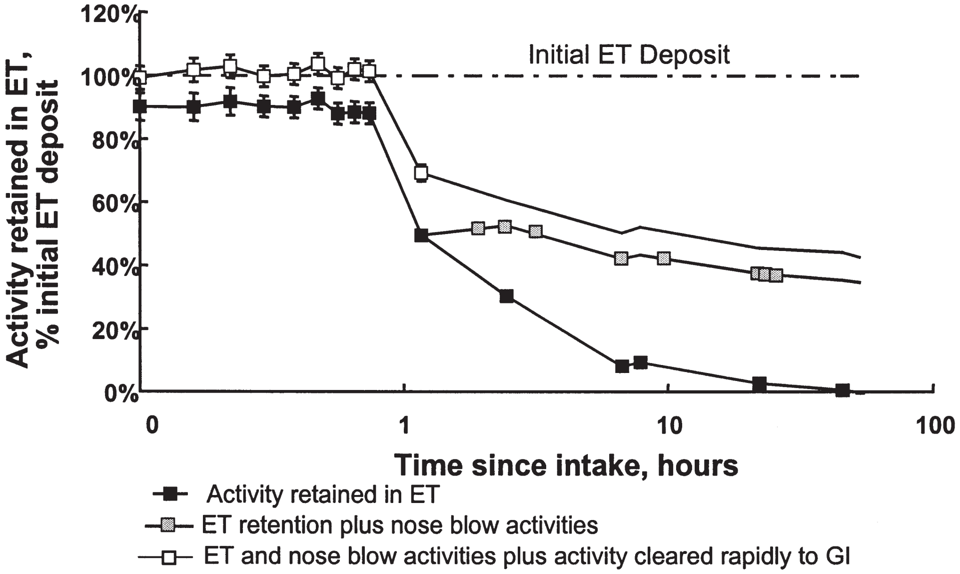

**Fig. 4.** Slow clearance route to GI tract, as shown by the activity deficit for clearance of 1.5 μm aerosol inhaled at rest by participant 6.

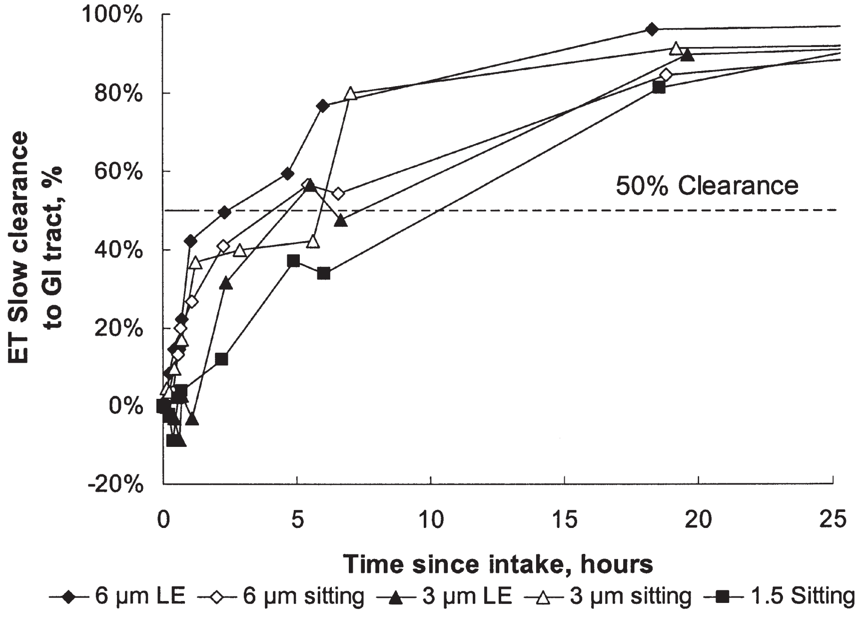

**Fig. 5.** Normalized slow ET clearance to GI tract for participant 4 showing that clearance rate increases with particle size and work rate.

some individuals. An additional rapid clearance route from $ET_2$ to the GI tract has been identified, which may be due to the swallowing of particles deposited in the naso-pharynx.

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