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Deposition pattern from a nasal pump spray

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SUMMARY

The initial distribution and subsequent clearance of aerosol from a hand-operated nasal pump spray has been assessed from gamma camera scans in ten normal subjects, following labelling of placebo sprays with $^{99}Tc^{m}$ labelled Teflon particles (mean diameter 2 μm). Aerosol was concentrated chiefly in the anterior part of the nose, but the area of deposition varied between subjects. No particles reached the lungs. A mean 56% of the dose was retained at the initial site of deposition 30 minutes after administration, while the remaining 44% of the dose had cleared to the nasopharynx. The initial partitioning of nasal pump sprays between ciliated and non-ciliated zones is relevant both for effective topical therapy of the nasal cavity, and for possible systemic drug delivery by the intranasal route.

INTRODUCTION

Nasal pump sprays are used primarily to administer aqueous solutions or suspensions of drugs for a local effect in the nasal passages. These drugs include nasal decongestants (Empey and Medder, 1981) and both corticosteroids and sodium cromoglycate for the treatment and prophylaxis of allergic rhinitis (Mygind, 1985). Nasal sprays also play a role in the delivery of certain other drugs to the systemic circulation, particularly for compounds which are poorly absorbed or inactivated when given orally (Freestone and Weinberg, 1976; Parr, 1983; Chien and Chang, 1985).

The action of drugs delivered intranasally is likely to depend in part upon their initial site of deposition. In a recent study we found that aerosol administered into the nose from a pressurised metered dose inhaler is deposited entirely in the anterior one-third of the nasal cavity, with a high local concentration in this region (Newman et al., 1987). We have now extended these studies to assess the distribution and clearance of aerosol released from a nasal pump spray in a group of normal subjects.

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METHODS

A spinning disc generator was used to make insoluble Teflon particles (mean diameter 2 μm; mass median aerodynamic diameter 3.2 μm), labelled with the radionuclide $^{99}Tc^{m}$ (Newman et al., 1981). The particles simulated the suspension of budesonide crystals found in a Rhinocort® nasal spray (Astra Pharmaceuticals Ltd) and were suspended inside placebo pump sprays containing 3 ml aqueous vehicle. The nasal valves (Morén, 1985; Petri et al., 1985) released 50 μl per actuation with a spray cone angle 60° and a droplet mass median diameter 62 μm.

Ten normal subjects (5 males, 5 females, age range 22–50 years), free of upper respiratory tract infections, were studied. After firing the inhaler 10 times into a closed vessel in order to prime the valve, 2 puffs of aerosol were directed into the right nostril with the pump spray held in the sagittal plane and with the tip of the actuator inserted 1.0 cm into the nasal vestibule. Subjects held the breath while the spray was actuated, immediately inhaled rapidly through the nose, and then exhaled through the mouth via a filter (Inspiron 002290) to trap any exhaled particles.

Lateral views of the head were obtained immediately after inhalation and then 10, 20 and 30 minutes later using a General Electric Maxi Camera connected to a Nodecrest computer, where data were stored as a 64×64 matrix of cells. ^{57}Co anatomical markers were worn during the scans on the bridge of the nose, on the chin and on the nape of the neck. An anterior-posterior view of the chest was also taken immediately after inhalation.

RESULTS

The area initially covered by the spray varied in size between individuals, a mean 46 (range 27–68) cells in the gamma camera scans being contained within the 5% contour, i.e. within a line marking 5% of peak activity.

Subject 5 (Figure 1) had the largest area of deposition, consisting of two distinct zones, one in the anterior part of the nose, and the other more posteriorly. Particles deposited in the latter zone cleared subsequently into the nasopharynx, while the zone of deposition in the anterior part of the nose remained essentially unchanged.

Subject 9 (Figure 2) had the smallest area of deposition, largely confined to the anterior part of the nose. Some of the deposited particles cleared to the nasopharynx, although the main concentration of particles in the anterior part of the nose remained after 30 minutes.

The mean (range) percentage retention of particles at the initial site of deposition after 10, 20 and 30 minutes was 69(34–94)%, 61(27–82)% and 56(29–67)% respectively. Thus 44 (33–71)% of the particles had been cleared to the nasopharynx after 30 minutes.

No significant radioactivity was detected either in the lungs or on the exhaled air

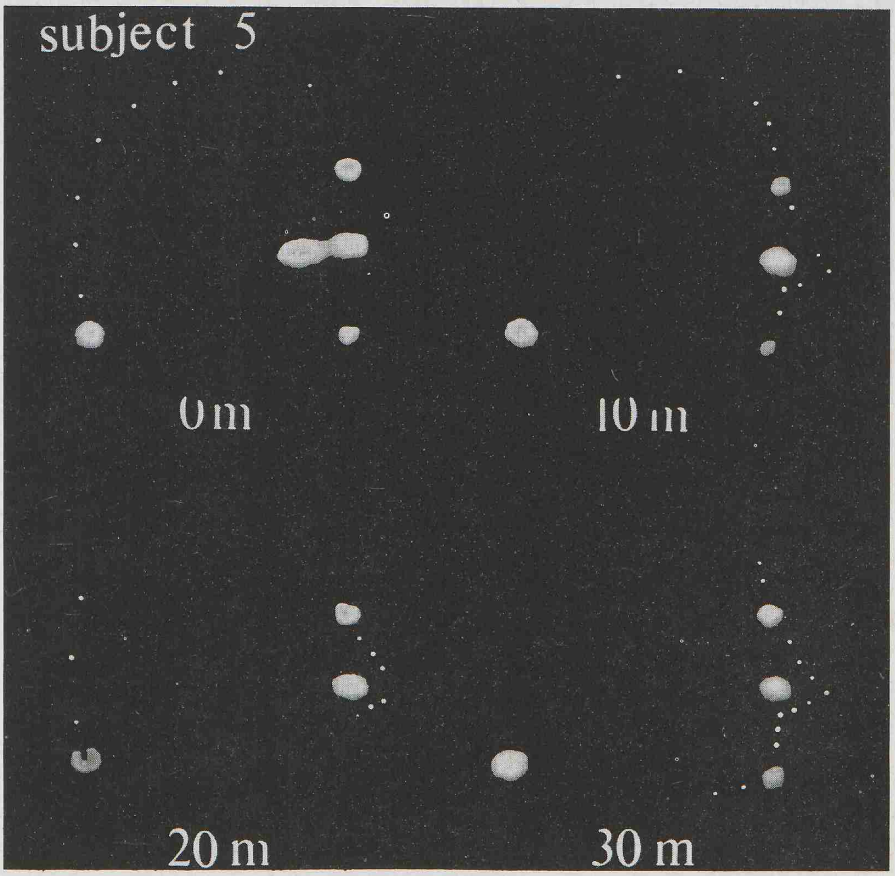

Figure 1. Particle distribution in the nose in subject 5, immediately after inhalation and then 10, 20 and 30 minutes later. ^{57}Co marker sources on bridge of nose, chin and nape of neck are marked "C".

filter in any subject, although material cleared to the nasopharynx appeared subsequently in oesophagus and stomach.

DISCUSSION

The nose acts as a very efficient filter for inhaled particles, particularly in the region of the nasal valve (Proctor 1982) where the narrow cross-section of the airway promotes a turbulent airstream and impaction of aerosol. The small radioactive Teflon particles used in the present study were enclosed within large liquid droplets (mass median diameter 62 μm), and thus it is not surprising that the spray was deposited chiefly in the anterior part of the nose with no detectable aerosol either in lungs or exhaled air. The Teflon particles were insoluble, and

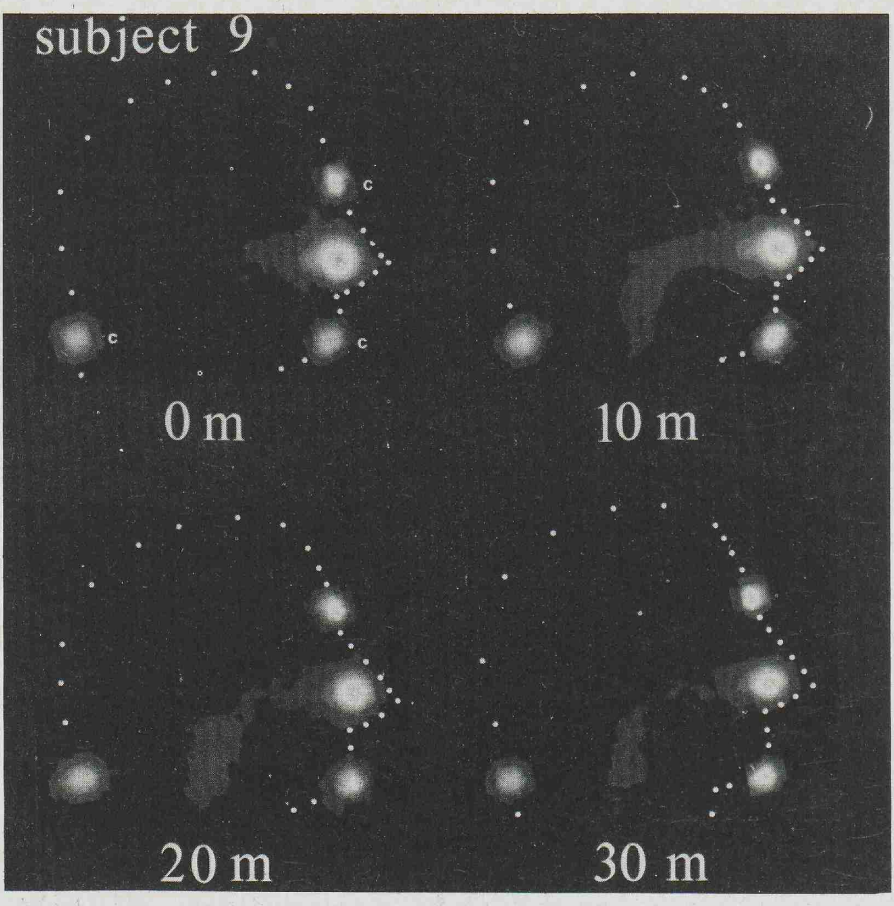

Figure 2. Particle distribution in the nose in subject 9, immediately after inhalation and then 10, 20 and 30 minutes later.

their removal to the nasopharynx presumably occurred by mucociliary action. Assuming that those particles retained in the nose after 30 minutes were deposited initially in the non-ciliated regions (i.e. in the nasal valve and on the most anterior parts of the turbinates) (Proctor, 1982), then our results suggest that on average approximately half the dose from a nasal pump spray reaches the ciliated zones in the main nasal passages where it would be required for topical therapy, and where rapid absorption of compounds into the systemic circulation might occur. The biphasic nature of deposition and clearance from nasal pump sprays has been noted in other studies (Aoki and Crawley, 1976; Bond et al., 1984; Hardy et al., 1985; McLean et al., 1985). Sprays tested *in-vitro* were deposited chiefly in the anterior zones of models of the human nose (Kim et al., 1985; Hallworth and Padfield, 1986).

Nasal drops may give a more uniform distribution pattern compared to that attained from nasal pump sprays, with solution dispersed fairly evenly throughout the length of the nasal cavity (Aoki and Crawley, 1976; Hardy et al., 1985), although complex manoeuvres are required by the patient to distribute nasal drops successfully (Mygind, 1985). By contrast, the deposition pattern from a pressurised metered-dose inhaler is more localised than that from a pump spray (Mygind and Vesterhauge, 1978), with only about 20% of the aerosol clearing to the nasopharynx, and the initial deposit covering only 20 matrix cells (Newman et al., 1986).

The present study was performed in normal subjects, and further studies are required to determine whether aerosol deposition and clearance differs in patients with abnormal nasal pathology. The presence of a blocked or runny nose, or of nasal polyps may modify aerosol penetration and clearance. The speed of inhalation, formulation of the spray and relative humidity of the environment may also influence the quantity of aerosol penetrating posteriorly into the nasal passages.

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