Nasal mucociliary function in normal man

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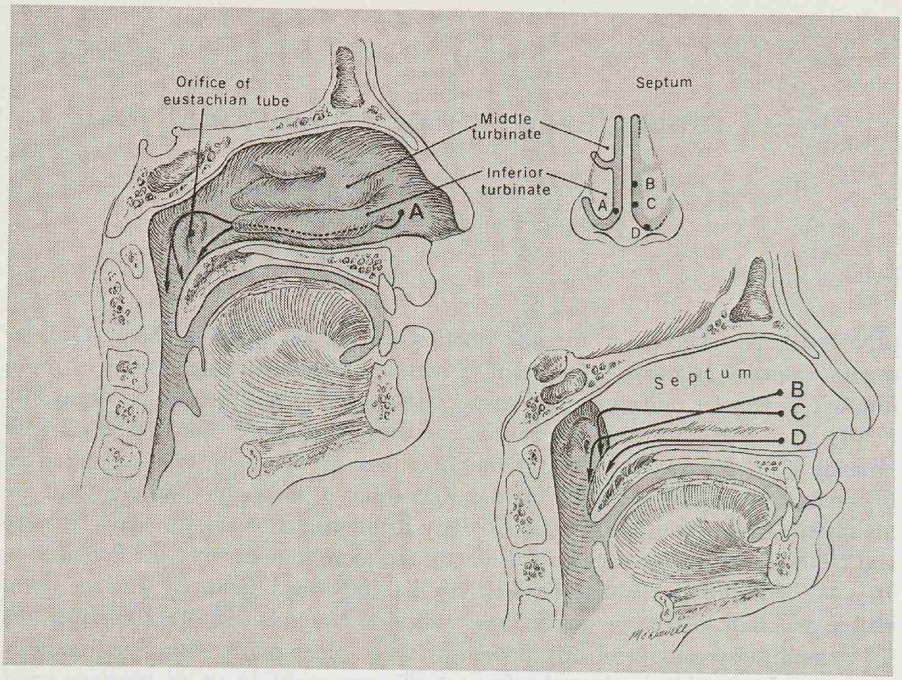
SINCE Sharpey detected a "peculiar motion excited in fluids by the surfaces of certain animals" nearly a century and a half ago, many investigations have been directed at a better understanding of mucociliary transport mechanisms. Especially in the past fifty years attempts have been made to measure this function in the nose of man. Because the nose is the first part of the body to be exposed to inspired ambient air, defenses on nasal mucosal surfaces are important to the maintenance of human health. Mucocciliary maintenance of a warm moist surface and clearance of foreign materials is among the more important of the defenses.

In 1931 Hilding published the first of his important series of studies using visible materials to observe mucociliary transport. A number of other investigators have employed variations of this method of study. Since much of the nasal passage is not readily visible, we sought for a technique enabling us to measure nasal mucociliary transport throughout the nasal passage and in 1965 reported the external detection of a radioactive tracer (Proctor and Wagner, 1965). This first technique proved difficult to quantify and in 1969 Quinlan reported a method developed in our laboratory assuring exact measurement of transport rate throughout the nasal cavity. This paper summarizes some of the methods we have used and the results we have obtained since 1969.

METHODS

Quinlan's techniqupe involved the placement of a radioactive particle (diam 0.5 mm) on the anterior nasal mucosa and tracking its subsequent motion on the oscilloscope of a gamma camera (Figure 1). Many of our studies since then have been conducted in a climate control chamber in Aarhus, Denmark. In these we have employed a particle labeled with Technicum (TC 99 m) 3 to 6 microcuries, and detected its motion by means of collimated detectors. The collimation enables us to detect the position of the particle at 5 to 6 points through the nasal passage, thus yielding 4 to 5 measures of transport speed (Andersen et al., 1971, 1972 and 1974).

Two collimated detectors face across the nasal passage. A third uncollimated detector is placed in front of the nose. Through it we obtain a continuous record of motion of the particle in the anterior-posterior direction, seen as declining radioactivity with backward motion, steady activity if no anterior-posterior motion is occuring, and increasing activity wth anterior motion. Steady activity may



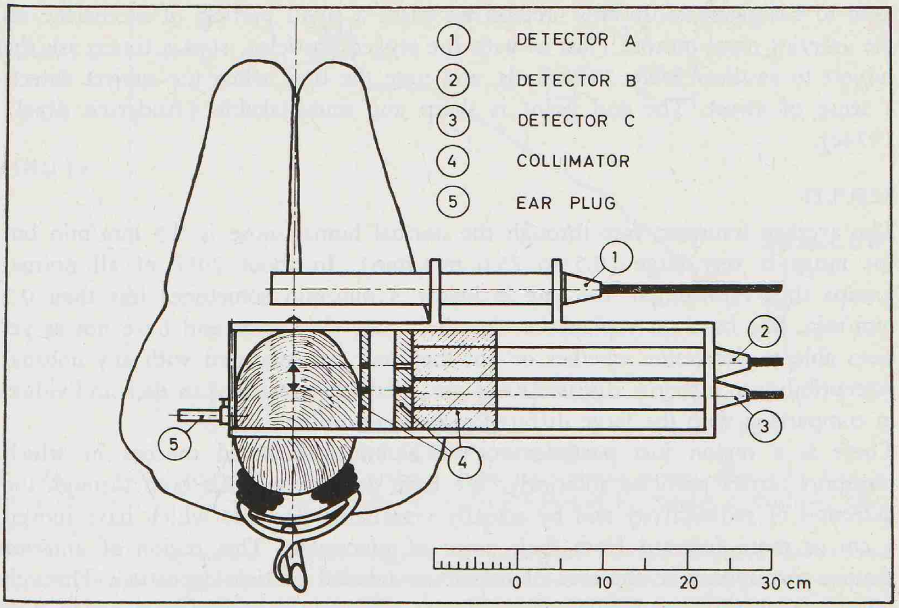
1. Paths of mucociliary clearance as detected in Quinlan's study (1969). (With the permission of the Editor, American Review of Respiratory Disease).

reflect stasis or may be associated with motion of the particle upward or downward as when curling around a turbinate (Figure 2).

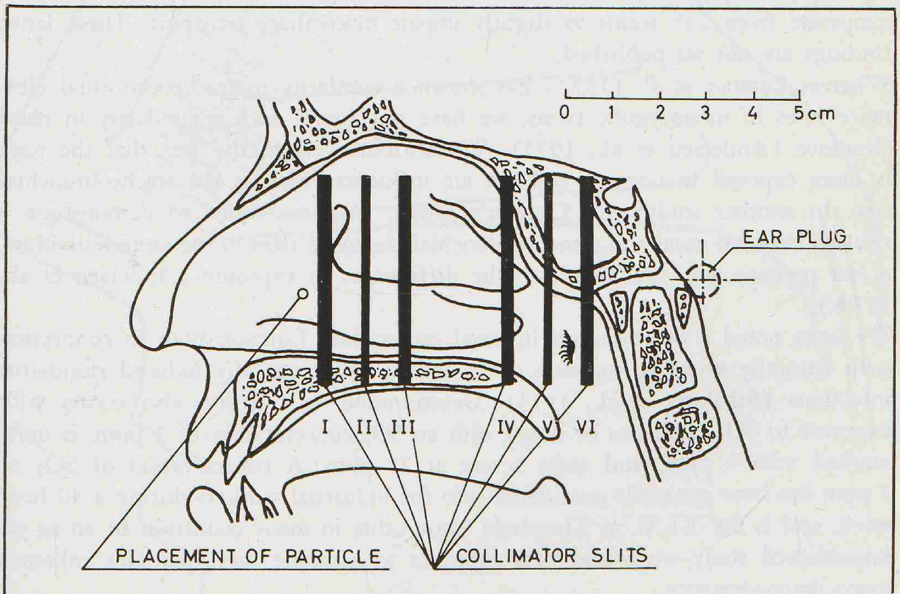
We have chosen to place the particle on the superior surface of the anterior end of the inferior turbinate since that area is in the main path of the inspiratory air stream. It is placed under direct vision with a metal applicator. Care must be taken that the point of placement is far enough back to be in the posterior moving current, about 4 cm from the nasal tip. Immediately after placement of the particle, the subject is seated in a chair with a head rest and the detection equipment attached to the head by solid plugs in the external auditory canals (Figure 2).

To date we have studied 197 normal subjects, 32 females and 165 males, average age of 24 years (range 18 - 46). Many of the studies have been done in the Aarhus climate chamber where all environmental parameters except one under study can be kept contant. (Andersen et al., 1971, 1972; Proctor et al., 1973, 1974; Andersen et al., 1974b).

Because we felt the need of an alternative technique applicable to field studies and studies in children, two years ago we developed a method for such problems. Although it does not yield the same detailed information, it does correlate well with the radioactive method and gives an overall transport rate from anterior



2. Diagram showing the subject in the chair and (above) the regions viewed by the collimated detectors (below). (With the permission of the Editors, American Review of Respiratory Disease and Archives of Environmental Health; Andersen et al 1972, 1974).



nose to nasopharynx. In this method we place a small particle of saccharine on the anterior nasal mucosa (just as with the tagged particle), start a timer, ask the subject to swallow every 30 seconds, and note the time when the subject detects a sense of sweet. The end point is sharp and unmistakable (Andersen et al., 1974c).

RESULTS

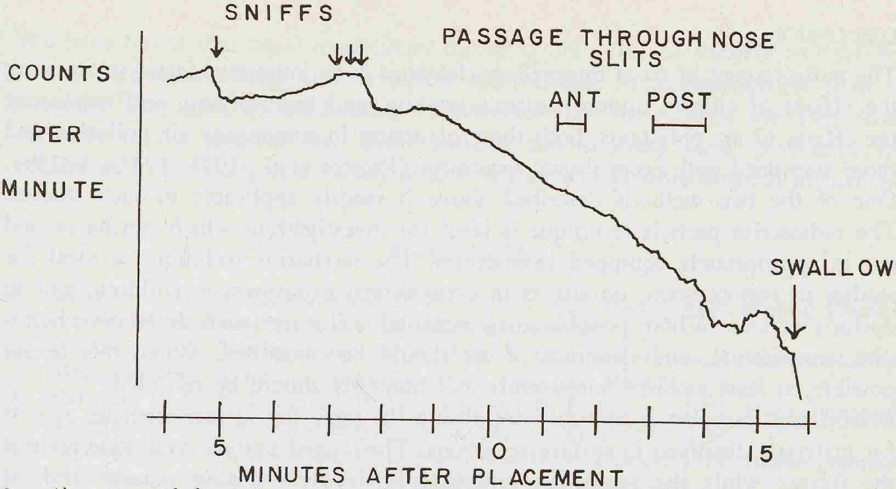
The average transport rate through the normal human nose is 5.3 mm/min but the range is very large (0.5 to 23.6 mm/min). In about 20% of all normal groups thus far studied, the rate is below 3 mm/min sometimes less than 0.5 mm/min. We have no explanation for these very slow rates and have not as yet been able to determine whether or not they may be associated with any unusual susceptibility to airborne disease. Rates are relatively consistent in each individual in comparison with the large differences between individuals.

There is a region just posterior to the anterior unciliated mucosa in which transport carries particles anteriorly. We have determinted this both through the detection of radioactivity and by actually visualizing particles which have moved 1 cm or more forward from their point of placement. This region of anterior motion corresponds to the area of maximum inhaled particle depostion. Through this mechanism, many inhaled materials are moved to a region from which they may be removed from the body by nose blowing and cleaning, thus preventing any further access to the body (Figure 3).

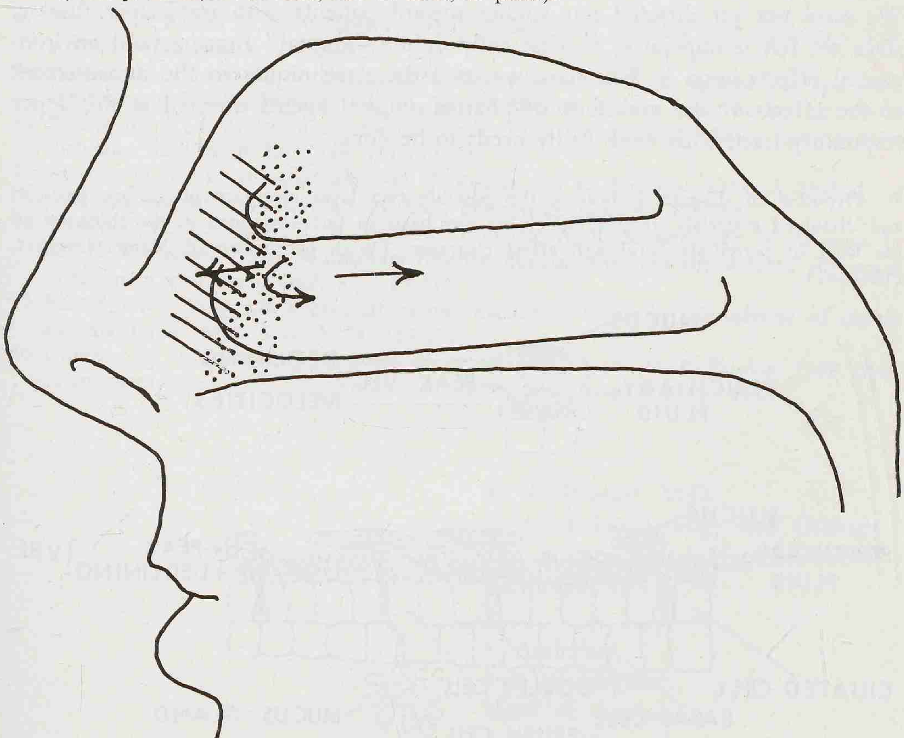
When ambient temperature is held at 23° relative humidity (R.H.) has no effect on transport rate. A relative humidity of 70% for 8 hours fails to improve mucociliary transport and even 9% R.H. for 78 hours fails to impair it (Andersen et al., 1971, 1972, 1974b). When R.H. is held constant at 50%, lowering or raising temperate from 23° seems to slightly impair mucociliary transport. These latter findings are not yet published.

Whereas Camner et al. (1972) has shown a similarity in tracheobronchial clearance rates in monozygotic twins, we have not found such a similarity in nasal clearance (Andersen et al., 1975). We attribute this to the fact that the nose is more exposed to noxious ambient air influences than is the tracheobronchial tree. In another study with Camner's group, we have failed to demonstrate a relation between nasal and trancheobronchial clearance rates in the same individual, a fact perhaps also attributable to the differences in exposure (Andersen et al., 1974c).

We have noted a deterioration in nasal mucociliary function both in connection with naturally occuring common colds and in experimentally induced rhinovirus infections (Sakakura et al., 1973). Deterioration in function also occurs with exposure to SO_2. This can be noted with an SO_2 concentration of 1 ppm, is quite marked with 5 ppm, and quite severe at 25 ppm. A concentration of SO_2 of 5 ppm has been generally considered safe for industrial workers during a 40 hour week, and is the T.L.V. or Threshold limit value in many countries. In an as yet unpublished study we found that exposure to airborne inert particles enhances mucociliary clearance.



3. *Above:* record from the anterior detector. Note the anterior motion shown by line of rising radioactivity and posterior motion on sniffing followed by regular mucociliary clearance (minutes 9 - 15).
Below: a chart indicating probable regions of unciliated mucosa (hatched lines) and anterior motion (stippled) area. There seems to be a narrow region from which anterior and downward motion begins and then posterior motion follows. (With permission of Marcel Deckker, Publisher. Will be published in a monograph, Respiratory Defnese Mechanisms, Ed. J. Brain, D. Proctor, and L. Reid, in press).



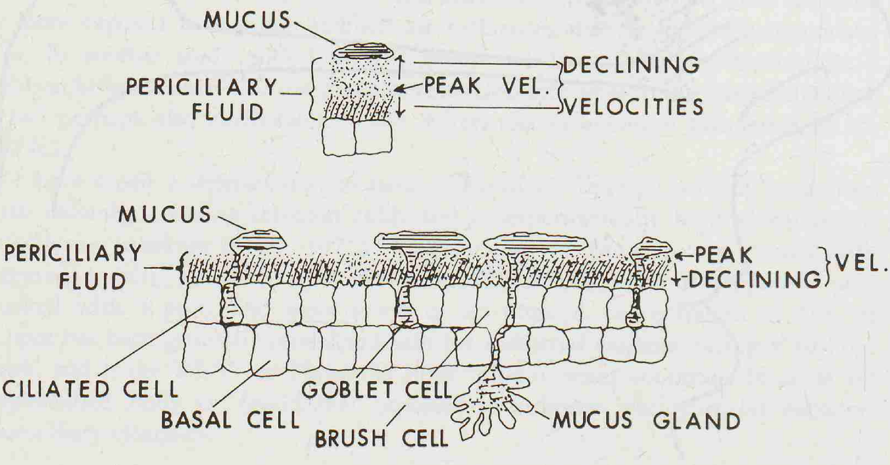
DISCUSSION

The measurement of nasal mucociliary clearance is an important factor in studying the effects of climate, indoor heating, cooling, and humidifying, and measuring the effects of air pollutants, both those occurring in community air pollution and those associated with occupational exposures (Proctor et al., 1971, 1973a, 1973b). One of the two methods described above is readily applicable to such studies. The radioactive particle technique is ideal for investigations which can be carried out in appropriately equipped laboratories. The saccharine technique is ideal for studies in remote areas, on site as in occupational exposures, in children, and in doctor's offices. Where possible environmental influences such as relative humidity, temperature, and cleanness of air should be controlled. When this is not possible, at least ambient temperature and humidity should be recorded.

Mucociliary transport is probably not always the same for surface particles as it is for materials dissolved in surface secretions. The tagged particle technique reflects the former while the saccharine undoubtedly dissolves during passage and, at least in part, reflects the latter. The glycoproteins in surface mucus are probably of importance to the former (surface particles) while some soluble materials are undoubtedly cleared in the underlying periciliary fluid (Proctor et al., 1973e). Our knowledge of the exact nature of mucociliary clearance is still imperfect, but it seems increasingly likely that cilia beat in a serous fluid and propel some of it along with the overlying mucus and surface materials (Figure 4).

We have not yet directed our studies toward patients with respiratory disease, since we felt it imperative to first fully define "normal" function and environmental effects upon it. Nor have we used these techniques in the measurement of the effects of the multitude of pharmacological agents directed at the upper respiratory tract. This work badly needs to be done.

4. Hypothetical diagram indicating the possible two layer clearance of surface particles and dissolved materials. If this model has any basis in fact variations in the thickness of the layer of periciliary fluid will affect clearance. (With permission of Marcel Deckker, Publisher).



We have found that nasal mucociliary transport both for the particle and saccharine is somewhate faster and definitely less variable in laryngectomees than in normals. This may be attributable to the fact that their noses are free from exposure to the ambient air. These patients should make ideal candidates for volunteers in the study of a variety of ambient air and pharmacological influences.

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