Airborne Disease and the Upper Respiratory Tract

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**INTRODUCTION**

Studies of airborne infection have been largely directed at the identification and nature of responsible microorganisms, epidemiology, host immunological defenses, and antibacterial or antiviral drugs. A relatively small effort has involved the possible role of the respiratory mucosa and the nasal passages in the defense against airborne infection. As a result, although a highly sophisticated body of knowledge has accumulated in the former fields, we do not yet know whether the upper respiratory tract constitutes a useful defense against airborne disease, is of no use, or may possibly be a detrimental influence. G. W. Wright pointed out this fact at the first Airborne Infection Conference five years ago (85), in saying, "One might well wonder whether the nose and nasopharynx are more harmful than helpful with regard to infections of the lower air passages."

The long-term objective of the work to be reported in this paper is to discover what part the upper respiratory passages and the respiratory mucosa play in defense against airborne disease and what factors influence their function.

It is conceivable that the nasal passage in man is merely a vestigial remnant of a once highly effective olfactory organ (37, 56) (Fig. 1). Yet, anthropological studies show that evolutionary changes have resulted in nasal dimensions which vary with climate demands (18), thus suggesting that, in man's development, the nose has not entirely regressed to a useless ornament.

On the one hand, available evidence indicates that the nose is less effective in humans than in other mammals as a filter for particles in the inspired air (3, 9, 19, 58), that particles carrying infectious organisms are not only small enough to pass through the nose but also to pass through the tracheobronchial tree into the alveol (17, 28, 42, 53, 76), and that many patients survive for years while breathing through a tracheotomy (31, 61). Unfortunately, no really adequate study has been done on such patients to determine the effect of tracheotomy breathing on airborne infection.

On the other hand, it is well known that, during the first few days after tracheotomy, pulmonary infections are common and often severe; some evidence from experimental induction of respiratory infection suggests that the nose may serve to protect the lower respiratory tract (13); clinical experience suggests that a diseased nasal passage is seldom found without concomitant lower respiratory symptoms, and, in mucoviscidosis, the abnormal function of mucous membranes seems the most obvious link with the susceptibility of these patients to frequent and severe respiratory infection. At least one study has described a relationship between the effectiveness of the nasal filter and the incidence of silicosis (45).

All of this leads to the conclusion that the role of the upper respiratory tract is still in doubt and requires further investigation.

**ANATOMY OF THE UPPER RESPIRATORY TRACT**

It will be helpful if workers in this field will agree upon clear-cut definitions of terms. The upper respiratory tract is that part of the air passages which extends from the larynx to the nostrils and to the lips, including the Eustachian tubes and the paranasal sinuses (Fig. 2).

This may be divided into the nasal passage extending from the mucocutaneous junction at the nostrils to the upper border of the soft palate (including the paranasal sinuses), the nasopharynx from the posterior nasal passage downward to the lower free border of the soft palate (including the Eustachian tubes), the mouth extending from the lips backward to the soft palate,
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UPPER RESPIRATORY TRACT

Fig. 1. Upper respiratory tract of the Indian barking deer showing the relation between the epiglottis and the palate, assuring nasal air flow even when the mouth is open. This relationship exists in many mammals but not in man. From V. Negus, Comparative Anatomy and Physiology of the Nose and Paranasal Sinuses. E. & S. Livingstone, Ltd., Edinburgh, 1958, with the kind permission of the author and the publishers.

Fig. 2. Diagram of the upper respiratory tract showing the anatomical divisions suggested in the text. The mouth is included in the oropharynx. The lateral extensions of the hypopharynx downward on either side of the larynx are not shown.

The oropharynx extending downward from the free border of the soft palate to the epiglottis, the hypopharynx from the tip of the epiglottis downward into the pyriform sinuses laterally and to the aryepiglottic folds medially, and the larynx extending from the aryepiglottic folds down through the cricoid ring.

Fig. 3. Nasal airway. The cartilaginous and bony structures (horizontal hatching) fix the maximal dimensions of this portion of the airway, and the overlying vascular network and mucosa more or less narrow the passage according to their state of congestion. Communication with maxillary antra through middle meati is usually a thinner partition than shown here. Air passage is shown in solid black.

The dimensions of the nasal passage are relatively fixed by their cartilaginous and bony framework, but vary in width according to the thickness of the lining mucous membranes (Fig. 3). The nostril hairs placed at the entrance to the nose may play a part in air flow and aerosol distribution in the air stream. From the nostril to posterior nasopharynx in the adult is 8 to 11 cm and from the nasal floor to cribriform plate is 4.5 to 5 cm. The dimensions of the nasopharynx vary with the size of the adenoid mass above and with the position of the soft palate below. The mouth will vary from a broad passage when the tongue and palate are widely separated to a closed space when they are approximated. The oropharynx will be narrow or wide as the tongue is moved backward or forward and will also be affected by the size of the tonsils. The hypopharynx is relatively constant except during deglutition. The laryngeal airway is effected by both deglutition and by the motion of the true and false vocal cords.
The mucous membrane in the respiratory tract is ciliated columnar epithelium from a line just posterior to the anterior ends of the turbinates back into the nasopharynx, except for the olfactory area, but including the lining of the paranasal sinuses. In the nasopharynx there is a transition from ciliated columnar to transitional and then squamous epithelium. Over the adenoid tissue, there are alternating patches of squamous and ciliated columnar, but the crypts are entirely lined with keratinizing squamous. The common belief that adenoid tissue does not exist in the normal adult is untrue. At least small amounts of lymphoid tissue with crypts can be found in man of all ages (2). The Eustachian tubes are also lined with ciliated mucosa. The remainder of the upper respiratory epithelium with the exception of the ciliated posterior wall of the larynx is squamous.

Within the nasal passage, the vascular bed is so rich and subject to such wide changes in dilatation that it is commonly referred to as erectile tissue. There is also a particularly rich vascular supply within the tonsillar and adenoid tissue.

Goblet cells and mucosal glands supply a continuous carpet of mucus which lines the entire upper respiratory tract. This mucus is kept continually on the move by ciliary activity and swallowing from every point in the respiratory tract toward the hypopharynx and thence to the esophagus.

The ciliated mucosa of the trachea extends upward through the posterior commissure of the larynx; but motion of mucus through other portions of the larynx above the cricoid is largely determined by cough or "throat clearing" (Fig. 4).

The paranasal sinuses consist of a group of air spaces in the bones of the face communicating with the nasal air stream through small openings, and, in the case of the frontal sinuses, through long nasofrontal ducts. The direction of the mucociliary stream in all of the sinuses is toward the nasal passage.

The Eustachian tubes are normally closed channels connecting the nasopharynx with the air spaces of the middle ear. Here also ciliary activity moves mucus toward the nasopharynx. These tubes normally open during swallowing and yawning. They are essential for the maintenance of normal pressure within the middle ears and are of importance in respiratory infection as the chief passage through which pathogenic microorganisms gain access to the middle ears.

Whether or not the upper respiratory tract is an important factor in the defense against inhaled materials, it is certainly an important contributor to the adjustment of the temperature and water vapor content of inspired air and probably is important in the maintenance of normal body temperature and water (12, 15, 22, 32, 38, 51, 56-58, 72, 73).

Although it is true that these functions can be taken over by the mucosa lining the tracheobronchial tree, observation of patients with tracheotomy (even long-term) indicates that the nasal passage is best suited for this purpose. Normally, with nasal breathing, air temperature is close to body temperature, and the air is near to saturation with water vapor by the time it reaches the hypopharynx (63).

**Upper Airways, Nasal or Oropharyngeal**

Because the narrow nasal passage is the place of greatest resistance to air flow (24), when the ventilatory demand rises beyond a certain point, one resorts to mouth breathing. Under these circumstances, the tongue is depressed and the palate raised, providing a wide airway with minimal resistance to flow. What work load creates this demand and how much individual variation there is has not been determined.

In like manner, when the nasal airway is sufficiently reduced by physiological alterations in mucosal and submucosal vasculature or by pathologic processes, even quiet breathing may occur through the mouth; but in this case the oral airway consists of a narrow slit between tongue and palate. Here there is wide individual variation. Some patients will complain of nasal obstruction
FIG. 5. Pneumotachogram during nasal breathing (left), followed by talking, with brief inspiration in center. Note air flow during this inspiration is more than twice that in resting breathing. With the permission of the Editor, Inhaled Particles and Vapours II (in press), Pergamon Press, Inc., New York.

FIG. 7. Tomograms of the upper airways. To the left, lateral view, and, to the right, anterior view. Compare with Fig. 3 and 8. With the permission of the Editor, Handbook of Physiology, vol., 1 Respiration, American Physiological Society, Washington, D. C.

FIG. 6. Oropharyngeal airway during deep breathing (A) and during inspiration between conversational phrases (B). Lips may be seen to the left. Note narrow airway between tongue and palate in (B). From cine-fluorograph, with thanks to Sue McCarty and Martin Donner, Johns Hopkins Hospital. With the permission of the Editor, Inhaled Particles and Vapours II (in press), Pergamon Press, Inc., New York.

FIG. 8. (A) Obverse of cast of nasal passage taken at autopsy: (B) Model constructed from same. Nostril is to the left. With the permission of the Editor, Inhaled Particles and Vapours (in press), Pergamon Press, Inc., New York.

when their measured resistance to air flow is less than that found in others who are unaware of any difficulty in nasal breathing.

Movement of air in and out of the paranasal sinuses and middle ears occurs as a result of respiratory cycle pressure changes when these spaces are in free communication with the moving air stream, and as a result of gas absorption from these spaces when this communication is periodi-
cally interrupted. Under normal circumstances, the gas contained within the sinuses undergoes one full change every few hours (63). Under unusual circumstances, especially those associated with marked atmospheric pressure changes, ventilation of these paranasal spaces may be much greater. Rahn calculated that in the Japanese women divers (Ama) the ventilation of each middle ear approximates 1,800 ml per day (67a).

During conversation, inspiration occurs through the mouth, but here again the oral airway is narrow. During singing, when it is necessary to fill the lungs quickly for long phrases, the oral airway is wide as in high ventilatory demands (Fig. 5 and 6).

If resistance to air flow is external, as with respiratory masks, nasal breathing continues until such resistance is extremely severe.

Although it is commonly recognized that nasal congestion sufficient to cause mouth breathing may be related to a multitude of internal and external environmental factors, these relations as yet remain generally undocumented. Such influences probably include emotional stimuli, such as stress or sexual conflict, endocrine disturbances, such as hypothyroidism, and sudden changes in inspired air temperature. Especially in the case of emotional stress, changes occur in all mucous membranes but are generally more readily noticed and more pronounced in the nose (35, 49, 54, 60, 75, 84).

The function of the paranasal sinuses in man is open to question. It is clear that these air spaces provide protection for the brain against blows on the face. It seems likely that, in addition, they act as insulators and a source of mucous secretion to supplement the air-conditioning function of the nose (57, 58, 67).

CHARACTER OF UPPER RESPIRATORY AIR FLOW

The fate of inspired particulate matter depends upon the size and weight of the particle, the character of air flow, and the relationship between the moving air stream and the surfaces over which it passes. Since, within the nose the air stream is narrow (Fig. 7) and moves at a high linear velocity, and since turbulence is more likely to occur there than elsewhere in the respiratory tract, it is of importance that we understand the nature of air flow in the nasal passage and the factors which may significantly alter this flow (20, 38, 59, 66 74, 80).

Because of the difficulty in introducing measuring devices within the nose without interfering with the nasal air stream, models of the nasal cavity have been constructed from casts made at autopsy to permit measurement of simulated nasal air flow at all points (Fig. 8). These measurements
path along the middle meatus. In one model, this change occurred sharply at 16 liters per min, a flow which approximates the peak one might expect through one side of the nose in rapid nasal breathing (Fig. 11). In other models this sharp change has not been so evident, but a similar alteration in flow has been found in all (Fig. 12 and 13).

Changes in the nasal airway resulting from pathological conditions have also been studied in these models. Polyps, septal deviations, alterations at the nostril, enlarged adenoids, and generalized mucosal thickening have all been simulated. Alterations in the main nasal cavity, such as would result from polyps or septal deviations, seem to have the most effect on air flow patterns and might influence particle deposition or concentrate the air stream in small areas, thus producing an undue drying effect upon mucosa.

During expiratory flow, there is a more diffuse spread of the stream through the entire nasal passage including the olfactory area (Fig. 14 and 15). Maximal olfactory occurs just after a sniff when air may rapidly diffuse into the olfactory area.

Landahl has calculated the maximal linear velocity in the respiratory air stream to be about 2 meters per sec, and this occurs in the secondary bronchi (43). In our model studies, it is clear that peaks of at least 5 meters per sec occur briefly in the main stream of flow during quiet nasal breathing. Such velocities in a narrow curving air stream will surely influence the chances of particles contacting the surface.

If inspired particles are hygroscopic, upon entrance into the efficient humidification apparatus of the nose, they will increase in size. Theoretical considerations based on the behavior of particles in tubes or even in the experimental animal may be misleading and cannot substitute for measurements of what actually occurs in the human nose.

The relatively sharp bend of the air stream at the nasopharynx plus the fact that the main air stream at this point travels along the posterior wall increases the chance for impaction of particles on the adenoid tissue.

Studies of oropharyngeal and laryngeal air flow are needed to understand what role these portions of the respiratory tract may play in the fate of inhaled particles.

**FATE OF PARTICLES DEPOSITED ON UPPER RESPIRATORY SURFACES**

In collaboration with Henry Wagner, Jr., Betsy Bang, and James Langan, and with the advice of Anna Baetjer, three methods of following muco-
ciliary clearance of particles have been explored, one of which was combined with the use of a visible dye. For each technique, 0.02 to 0.1 ml of a saline solution containing 8 to 20 μc of radioactivity was injected with a microsyringe on the mucosal surface at the anterior nares. A head mirror and nasal speculum were used to assure placement of the material just behind the anterior end of the inferior turbinate. 131I was the isotope most frequently employed. In most studies, the isotope used labeled aggregates of human serum albumin (81), usually from 5 to 100 μ in diameter, but in one study (Fig. 17) 5 to 15 μ (64, 65). In other studies, the isotope was in the form of a solution of sodium iodide, or a solution containing fluorescein mixed with the dye Sky Blue (dimethoxydiphenyl-diazo-bis-8-amino-1-naphthol-5,7-disulfonic acid) [C9H9N4O2S4Na4]. Subjects were given Lugol's solution by mouth prior to the study to block entrance of the 131I into the thyroid gland.

For the first method, immediately after placement of the isotope, the subject lay prone on a conventional scanning table with the head turned to one side (Fig. 16). A series of scans of the nasal area were then done as quickly as possible until the radioactivity was detected in the nasopharynx (Fig. 17). In most studies, the test was completed in 10 to 30 min, but in one study scanning was continued for 70 min to demonstrate retention in the anterior unciliated area (Fig. 18).

Such relatively long scans may provide important information. Both Hilding (33) and Macklin (50) pointed out the possible importance of small areas of poor clearance in the tracheobronchial tree in the role of carcinogenesis. Whether such areas regularly occur in the upper airways or whether they result from specific environmental circumstances is not known.

One study was done on a child with mucoviscidosis (Fig. 19), but no other patients have been studied as yet.

For the second method, the subject was seated in a chair with a head rest and remained in this position throughout the test (Fig. 20). A double-channel collimated crystal scintillation detector was brought alongside the face and positioned so that the two channels pointed across the nasal passage, one just behind the point of injection, and the other 4 cm farther back. Radioactivity was then recorded at each point until the isotope had been carried backward past the second position (Fig. 21).

The third method (carried out in collaboration with Betsy Bang and James Langan) was similar to the second, except that a single detector was placed in front of the nose, pointed along the line of the nasal passage. Thus, as the isotope was carried backward, detected radioactivity fell in proportion to the square of the distance. In this series of studies, the Sky Blue was mixed with the isotope and looked for in the oropharynx about
once a minute. This dye, which is very clearly visible on mucosal surfaces, produced no unpleasant sensation in the subject, and appeared to have no unfavorable effect upon ciliary activity. In each subject, the appearance of the dye either at the edge of the soft palate or on the posterior pharynx coincided with a fall in radioactivity as detected in front of the nose. In most subjects, the visualization of the dye occurred just before the fall in detected radiation reached a plateau (Fig. 22).

The use of visible materials to study mucociliary activity has the advantage of simplicity (23, 68). Nevertheless, although the isotope technique demands complex equipment, it requires a minimum of cooperation on the part of the subject, gives a much more complete picture of the path of the mucociliary stream, allows one to de-

![Figure 12](http://example.com/fig12.png)

**Fig. 12.** Changes in linear velocity with increasing flow in another model, at points in main stream (A) and at points away from main stream (B). Points are indicated on diagram. B·5 refers to the line halfway between (B) and (C), etc.

![Figure 13](http://example.com/fig13.png)

**Fig. 13.** Changes in direction of flow with increasing flows, at points in main stream (A) and away from main stream (B) as in Fig. 12: 90° is horizontal to the floor of the nose.

![Figure 14](http://example.com/fig14.png)

**Fig. 14.** Patterns of flow in model charted in Fig. 12 and 13. (A) Expiratory flow at 11 liters per min and (B) at 44.6 liters per min. Note diffuse distribution of flow even in (B).
tect areas of retention, and permits study of portions of the respiratory tract not readily accessible to visual observation.

Thirty-six subjects have been studied in 64 tests thus far: 27 males and 9 females, ranging in age from 7 to 52 years, only one of whom had gross respiratory disease. This number is insufficient for the establishment of normal values; and studies of normal subjects in varied environmental circumstances and of patients are just beginning. There have been 23 scans, 28 studies with the double detector, and 13 with the single detector.

The mucociliary transport of surface materials in the human nose seems to occur at about the same average speed observed in previous studies of respiratory mucous membranes. It is clear, though, that this is not a uniform speed. Portions of a drop even as small as 0.02 ml may require 2 to 10 min to move 6 to 9 cm backward into the nasopharynx, whereas other portions of the same drop may require 8 to 15 min to travel the same distance; still other portions (at the anterior unci lated area) undergo no detectable motion.

There is wide individual variation, with some normal subjects showing transport times two to three times faster than others. Not enough studies have been done to discover how much variability there is in a single normal subject from time to time, or how variations may be related to environmental or other influences.

Fig. 15. Patterns of inspiratory flow in model charted in Fig. 12, 13, and 14. Hatched areas in lower part of A indicate approximate cross section of airway. Letters and numbers refer to the grid locations as shown in charts in Fig. 11, 12, and 13. In C and D, the meati were narrowed (C) and filled (D) to simulate changes in airway to be expected from swollen mucosa.

Fig. 16. Scan superimposed on skull radiogram for orientation. This scan is taken from series to left in Fig. 17 and is from same subject in Fig. 6 and 21 A. With the permission of the Editor, Arch. Environ. Health (64).

DISCUSSION

It is believed that microorganisms are airborne in droplet nuclei 2 to 3 μ in diameter (70, 82). Although there are relatively few studies of nasal particle deposition in man (and in these studies there is not complete agreement), it seems likely that many particles smaller than 5 μ will penetrate the to lower respiratory tract (29, 30, 34, 45, 53).
Three factors deserve further investigation in this connection: the possibility that droplet nuclei are hygroscopic and increase in size in the nose, the possibility that coagulation of particles may occur, and the effect of turbulence in the stream.

Since maximal exposure to airborne infection may occur in circumstances where one is indulging in animated conversation, the fate of particles in the oropharynx in these circumstances also deserves further study.

A recent report on the epidemiology of tuberculosis suggests the possibility that the nose may be an important defense. This report, and at least two other studies, indicate the likelihood that cross-infection has occurred between persons singing together, whereas infection did not occur between similar individuals sleeping in neighboring beds, sitting together in crowded classrooms or riding together on crowded buses (7, 36, 33, 78).

Two factors could combine to explain this interesting observation. The passage of air through the vibrating glottis may provide an excellent atomizer for the production of very small mucous particles. At the same time, since inspiration during singing consists of deep breaths through a wide open oropharynx and glottis, maximal opportunity for penetration of airborne particles into the depths of the lungs will result (Fig. 6).

In contrast, inspiration during conversation occurs through a narrow oral slit at relatively high linear velocity, a situation which could result in a filtration of particles similar to that normally found in the nose (Fig. 5 and 6).

If the upper respiratory tract plays a significant role in the removal of particles from the inspired air, the next question involves their fate once deposition has taken place (10, 11). Four possibilities are worthy of investigation: mucociliary clearance with dispatch through swallowing into the stomach, the passage of viable organisms through gastrointestinal mucosa, penetration through the mucous carpet into upper respiratory
mucosal cells, and deposition in the crypts of the adenoids.

Certainly, some organisms are deposited in the adenoids, but we know little about the factors which determine whether active infection ensues or whether the presence of pathogenic microorganisms in lymphoid crypts is a benign infestation leading to an opportunity for the body to thereby develop immunity to them (62).

It is evident that pathogenic bacteria may reside in the upper respiratory tract without producing signs or symptoms of disease (8, 26, 83). What enables such bacteria to institute active infection is not clear. It is conceivable that their deposition and residence, especially in the adenoid crypts, may be entirely innocuous, and that only when mucous membrane defenses are injured in some manner are such bacteria able to invade the body tissues and produce the signs and symptoms of infection.

Information is especially scarce regarding the chemical nature of respiratory-tract mucus. Mechanisms by which its water content and viscosity are varied to meet the changing demands of our everyday environment are virtually unexplored. It has been established that antibodies are found in mucus, and it is possible that such antibodies may, on occasion, be more abundant and more effective against airborne infection than those which circulate in the blood stream (4, 14, 27, 46, 65, 79).

The method by which inhaled viruses pass through the moving mucous layer and gain entrance to surface cells remains unclear (79). It does seem that such penetration will be less likely to occur when the particle carrying the virus is kept rapidly on the move in the mucociliary stream. Stasis at any point in the stream would provide the needed opportunity for contact with cells, penetration, and infection. It should be remembered that any influence which slows the stream may lead to stasis. The more slowly the mucous stream moves, the longer it is exposed to the drying effect of the moving air, and the more likely such drying and the consequent rise in viscosity are to lead to the inability of the cilia to maintain mucous motion. Any factor acting directly either to impair ciliary activity or to in-
crease viscosity of mucus may thus reduce the effectiveness of respiratory mucosa, at least as an air conditioner and perhaps as a defense organ.

Although a great many studies have been directed at mucociliary activity and particle clearance, most of this work (owing to the paucity of techniques applicable to the human subject) has been done on in vitro mucosal strips or in the experimental animal (1, 5, 6, 16, 21, 23, 25, 41, 47, 68, 71). The use of radioactive tracer materials and apparatus for their external detection permits the study of mucociliary activity in living man (1, 25, 34, 55, 64, 65).

Although it is possible that many infectious organisms travel in the inspiratory air stream directly to the alveoli, there are broad gaps in our knowledge of particulate behavior in the airways and suggestive areas of disagreement (33, 39, 40, 61).

FIG. 20. (A) Double collimated crystal scintillation detector showing slits 4 cm apart. (B) Detector in place alongside subject's face. With the permission of the Editor, Arch. Environ. Health.

FIG. 21. Redrawn record from the double detector (A) and actual record (B). (A) From same subject illustrated in Fig. 6 and 17 (left). (B) From normal 35-year-old male. With the permission of the Editor, Arch. Environ. Health and Inhaled Particles and Vapours II (in press), Pergamon Press, Inc., New York.

FIG. 22. Tracings from records obtained with single detector method: (A) 26-year-old normal male; (B) 36-year-old normal male; and (C) 32-year-old normal male. In these records, the fall of radioactivity detected at probe in front of nose results from motion of isotope backward in mucociliary stream. Plateaus in (B) and (C) probably represent material retained in anterior unciliated area. Arrows indicate time at which dye became visible in posterior pharynx.
We cannot now state with certainty whether or not the upper respiratory tract is a barrier against airborne disease. We cannot know until we first understand normal human respiratory function (air flow and mucosal function) and what influences disturb it. Only then will it be possible to search for correlations between such disturbed function and susceptibility to disease.

Many of the conclusions thus far drawn regarding the upper respiratory tract and mucous membrane function come from in vitro studies or the experimental animal. Although some of these conclusions are probably correct, it is time to check them with carefully controlled experiments on the human subject. This is especially true in regard to respiratory air flow and the fate of inhaled particles.

Clinical experience with respiratory infection has long suggested relationships between susceptibility and such factors as change of season, cold weather, allergies, exhaustion, emotional stress, etc. Studies of naturally occurring infections have not produced data leading to clear conclusions, perhaps because they have not included concomitant studies of mucosal function. Studies in the experimental induction of respiratory infection have in general failed to substantiate any of the relationships mentioned, but, instead, indicate that whether or not an individual exhibits signs and symptoms of infection is largely a matter of degree of exposure to, and immunity against, the infectious agent (10, 11, 13, 39, 60, 79).

Now and then, one does find evidence suggesting that susceptibility may vary with other factors, but the most suggestive evidence comes in children with mucoviscidosis. These children seem to have at least average capability for development of antibodies against infectious microorganisms, but, in spite of this, become infected frequently and tend to suffer from unusually severe infections. What is more significant is that their infections are almost exclusively respiratory. Here, the facts strongly indicate either that mucous membrane, when functioning normally, is a potent defense against airborne infection, or that there is some other now unknown factor involved.

To document any possible role of the upper respiratory tract or respiratory mucous membrane in general, we must be able to measure air flow and mucociliary activity in the normal human subject and in the patient before and during respiratory disease. Whether or not naturally occurring respiratory infections are most commonly transmitted through airborne droplets, droplet nuclei, or direct contact has not as yet been clearly established.

The techniques reported here represent a beginning toward the development of methods applicable to human studies aimed at the eventual answer to these questions. When applied in circumstances where environmental conditions are carefully controlled, and, especially when the isotopes are delivered in airborne suspensions comparable to naturally occurring aerosols, our knowledge should be improved. Now it should be possible to determine ranges of normal function in man of all ages, variations in normal function associated with environmental change, and association between such variations and airborne disease. It is too early to say which of the three isotope techniques thus far explored is most useful or whether some other method may prove to be more effective. At the present time, it appears that the serial scans are most helpful in picturing the path of flow and, especially, in detecting areas of poor clearance. The double collimated detector seems most useful in quantitating speed of mucociliary flow between any two points. The single detector is the simplest mechanically.

These same techniques are also applicable to the study of areas of deposition of the isotope-labeled airborne particulates, as well as the determination of the eventual fate of those deposited.

At present, more questions regarding the upper respiratory tract and mucous membranes have been raised than answered. Among these are the following.

How much of the variability already noted is really "normal," and to what degree might the extremes of these "normal" variations be related to infection if they coincide with exposure? What pathological conditions in the upper respiratory tract increase susceptibility to infection? Are significant variations attributable to alterations in ciliary activity, respiratory tract mucus, or both? How are these functions affected by variations in environmental temperature or humidity, emotional stress, endocrine activity, pharmacological agents, etc.?

When these questions are clearly answered, research in the field of airborne disease may be more logically directed toward, or away from, the upper respiratory tract or the respiratory mucosa, or both.

**Summary and Conclusions**

Certain questions regarding the role of the upper respiratory tract in airborne disease remain unanswered. Among the most urgent are the following. What airborne materials are likely to be deposited upon the respiratory mucosa? What factors influence their removal from the air stream and their point of deposition? What is the fate of materials once deposited upon mucosal surfaces?
What factors influence their clearance, not only from the respiratory tract, but from the body?

Techniques are herein reported for the study of the respiratory air stream, and, through the external detection of radioisotopes, for the study of the deposition of airborne particles and their motion in the respiratory mucociliary stream. It is hoped that pursuit of these studies may cast some light on the transmission and pathogenesis of airborne disease.

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