PART III. RESPIRATORY SYSTEM AND AIRBORNE INFECTION

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STRUCTURE AND FUNCTION OF RESPIRATORY TRACT IN RELATION TO INFECTION

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I would like to confine my remarks to a discussion of some of the mechanisms whereby the respiratory system attempts to prevent or limit infestation by living agents transmitted through an air medium. The mechanisms whereby infection or disease ensues following such infestation will be considered only to the extent that a breakdown of the defense mechanisms may permit an accumulation of living agents within the boundaries of the respiratory tract. The mechanisms of phagocytosis will be discussed only briefly and those of immunity will be only mentioned. This course has been elected not because I fail to realize the importance of phagocytosis and immunity but because my background and training in no way permits me to review these subjects in other than a most superficial manner.

It is conveneient to divide our considerations into those events that transpire in the supralaryngeal area as differentiated from those occurring below the larynx in the bronchial and alveolus-bearing portions of the lung. That events in these two anatomical areas are interrelated is obvious.

Most of our knowledge concerning the dynamics that govern the entrance of particulate material into the respiratory apparatus and its ultimate fate in the body stems from study of inanimate material. The indestructibility of these materials, the ease of their identification, and the facility with which they may be handled experimentally have favored their use in such studies rather than the more difficult to handle living materials. By comparison, relatively little is known concerning the pulmonary penetration and ultimate fate of living agents capable of producing respiratory disease. Nevertheless, some important and useful information in this regard is available. Because of the large body of information currently extant concerning inanimate particulates, one is tempted to extrapolate this information to similarly sized particulates of living agents. Although this is undoubtedly useful as a first approximation, one must exercise caution. The factors governing entrance and lodgment within the respiratory system would of necessity be similar but surely one cannot assume that the ultimate disposition of living agents would be the same as that of the inanimate particulates.

The effect of inanimate particulates upon the host is a function of amount and location of deposition, amount and location of retained particulates, length of their residence in contact with tissues, and the nature of the material, specifically its chemical and physical states and its ability to excite cellular reaction. These factors are strongly interrelated in that any one facet may influence the other. When one considers living particulates, all of the factors just mentioned must be considered plus the ability of the living agent to survive, multiply, and elaborate products that may influence the host.

Air passing into the nose enters a chamber having a large surface by virtue of the turbinates and septum. The shape of the passage is such as to cause the air stream to assume rather narrow dimensions so that all particulate matter is forced to pass in rather close proximity to the walls of the turbinates and septum. Air flow within the nose is a mixture of laminar and turbulent and eddy flow, the latter occurring about the turbinates. In the posterior portion of the nose, the air is somewhat decelerated but again

becomes accelerated as it passes through the constriction between the soft palate and the posterior pharyngeal wall. This narrowing again causes turbulence and eddying. The air stream proceeds down into the oral pharynx where it then enters the larynx. About the epiglottis there is a considerable curling and eddying of the streams of air flow. Proetz (12) has made an extensive study of these air currents and of the points where particulate materials tend to accumulate on the walls of the nose and pharynx.

The nose acts as an air filter in several ways. The rather narrow openings into the nose and the hair at the inlet filter out only very gross particles such as leaves and insects. Smaller airborne particles are removed by direct impingement against the mucosa and also to some unknown degree by electrostatic precipitation. For large particles, above 10 μ in diameter (the importance of density and shape in determining settling velocity is recognized but the convention of diameter alone will be used in this discussion), there may be some effect of gravity tending to permit settling out of particles in the less rapidly moving air streams or in the areas where eddy currents are set up. The degree to which some precipitation of particulates occurs on the basis of thermal gradients is speculative.

Studies using various techniques for measuring nasal filtration in normal individuals (4, 17) indicate that the removal of particulates larger than 10 μ in diameter is virtually complete, but smaller particles tend to pass through without deposition. Ordinary house and street dusts are of a size large enough to be almost completely removed from the air as it passes through the nose; hence, living particulates attached to such dust for the most part will be filtered from the air before entering the larynx. Droplet nuclei, however, comprise a most important state of airborne infectious material, and the nose with the nasal pharynx is a poor filtering mechanism for nuclei because they tend to be smaller than 2 μ in diameter. It is important to realize that although the majority of the particles less than 10 μ in diameter tend to pass through the nose and into the larynx, trachea, and bronchi, not all of the smaller particles escape deposition on the way through the nose. Pattle has shown that 10 to 20% of particles even as small as 0.4 μ in diameter may be trapped on the mucosa of the supralaryngeal passages. As will be commented upon later, it is of interest that some gases, for example, sulfur dioxide, ammonia, and iodine vapor, are virtually completely retained during one passage through the nose and nasopharynx. It is apparent that most of the dustborne living particulates and an appreciable fraction of the droplet nuclei are deposited in the nose and nasopharynx, whereas the majority of the droplet nuclei pass into the sublaryngeal regions.

Once deposition of particulate material occurs in the nose and nasopharynx, what is its fate? The mucosa lining these passages, with the exception of the immediate entrance to the nose, is made up largely of ciliated epithelium with numerous mucus-secreting cells interspersed. Normally, a thin blanket of mucus covers this membrane and the particulate materials deposited thereon are carried by ciliary action toward the posterior nasopharynx, where the mucus accumulates. Swallowing then occurs and the soft palate wipes the mucus down into the oral pharynx, where, as further accumulation occurs, it is either expectorated or swallowed. In addition to the mucus secreted by the lining of the nose and nasopharynx, there is a discharge of similar material from the accessory nasal sinuses and also a flooding of the area with secretions of the lachrymal glands discharged into the nose by way of the lachrymal duct. These materials, aided by the effects of gravity and ciliary motion, constantly wash the surface of the supralaryngeal mucous membranes. Few quantitative data exist concerning the actual fate of particulates deposited in the nose and pharynx. It is assumed that the majority of the particulate matter is slowly moved posteriorly and into the oral pharynx where it is either expectorated or swallowed. The transit time of particulates beginning at the most remote point from the oral pharynx is estimated to be approximately 10 to 20 min. As pointed out by Proetz (12), it is of interest that the areas of maximal accumulation of particulates coincide with the areas of major lymphoid tissue formation in the pharynx. The role of the pharyngeal, faucial, and lingual tonsils in the ultimate disposition of particulates has not been examined in a quantitative fashion and but little in a qualitative fashion. The placement of this mass of lymphoid tissue at the point of greatest deposition of particulates may be meaningful or may be simply fortuitous. The nasal secretions plus those of the

lachrymal glands deposited in the nose may have an additional role to that of acting as a carrier for particulates. A number of investigators attribute bacteriostatic activities to these secretions. The merits of these allegations will not be discussed here.

I have been unable to find any information concerning the quantitative aspects of the deposition of material introduced via air currents through the mouth. One would assume, on the basis of anatomical structure, that some deposition by impingement and perhaps even by electrostatic precipitation might occur.

Before proceeding to an examination of the deposition and fate of particulate material in the sublaryngeal areas, we must consider a sometimes little thought of feature. In a meeting devoted to airborne infection, one is apt to concentrate upon airborne particulates as related to infestation not only of the upper respiratory tract but also of the lower respiratory tract. To do so would be to fail to give due importance to the fact that once infestation of the upper region has occurred, the lower or sublaryngeal tract is now in jeopardy, not only from the airborne materials that enter through the larynx but also from liquid materials formed in the supralaryngeal portion of the respiratory tract. Such secretions may and do contain living particulate agents deposited and growing therein. Do these particulate agents contained in a liquid medium ever enter the sublaryngeal regions? The answer is most certainly in the affirmative. It has been repeatedly demonstrated that materials suspended in a liquid phase dropped into the nares of experimental animals will find their way quite rapidly in a matter of minutes into the deepest portions of the lung. That this also occurs in man is attested to by the fact that lipoid pneumonia occurs as a complication of oily materials dropped into the nose. A direct demonstration of this fact has been made in man by the simple process of dripping a small amount of radiopaque material into the pharynx of sleeping individuals (1). A roentgenogram of the chest made several hours later demonstrates the contrast media dispersed in a patchy fashion throughout both lungs. The deeper the sleep, as during moderate degrees of narcosis or fatigue, the more readily this occurs. Much of the material will also be found in the gastrointestinal tract, demonstrating that some is swallowed and some is aspirated. However, when this experiment is carried out in normal small children and babies, one finds little or no evidence of aspiration of secretions during sleep. It appears that the adult either produces much more in the way of nocturnal secretions or has lost effectiveness of the swallowing reflex. With this information, one would predict that in the presence of a clinically significant infection involving the oral pharynx, especially if attended by pain on swallowing, the tendency to accumulate secretions heavily laden with living organisms in the presence of reduced effectiveness of swallowing reflex would lead to an even greater than usual opportunity for these secretions to be aspirated into the lower portions of the lung. These simple observations have many clinical implications with regard to sublaryngeal pulmonary infections.

That airborne inanimate particulates can pass through the larynx and be distributed distally has been demonstrated repeatedly and will be discussed subsequently in some detail by Professor Hatch. Particles of all sizes may escape entrapment above the larynx and find their way into the trachea and distal compartments. The majority of the particles entering through the larynx will be smaller than 10 μ in diameter. The bulk of those measuring more than 2 μ in diameter will be deposited in the divisions of the bronchial system down to and including the terminal bronchioles. Most of the particles found to be deposited within the alveolus-bearing structures of the respiratory system will be smaller than 2 μ. It should be re-emphasized, however, that many of these smaller particles will be found deposited throughout the respiratory system although the fraction of those introduced that are thus retained in other areas is rather small.

The introduction of particulate materials suspended in a liquid medium has not been subjected to quantitative study but its qualitative aspects are known and as might be expected are somewhat different from airborne particulate distribution. First of all, the quantity of particulates that can be introduced in a liquid medium per unit time far exceeds that which can be introduced in an airborne fashion. This has been repeatedly demonstrated to those of you who are familiar with bronchoradiography. Instillation of radiopaque material in a watery or even a more viscid solution is promptly followed by its dispersal throughout all of the macroscopic divisions

of the bronchial tree with intense radiopaqueness. Some of the materials ultimately enter into the alveolus-bearing portions of the lung as well. Attempts to outline the bronchial passages by the inhalation of radiopaque material suspended in air fail to deliver and deposit enough particles to cast a visible shadow. Particulates introduced via liquid media are also apt to be distributed in a somewhat more patchy manner than those introduced via the airborne route. Regardless of whether the introduction is via the air or a liquid there is a tendency to a patchy nature of the distribution, some areas receiving more of a deposit than others. Perhaps the most important difference between these two methods of penetrating the lung is that with liquid penetration the normal defenses are usually overwhelmed by the large concentrated dosage of particulates, and the time course of subsequent events is quite different.

Materials deposited upon the walls of the tracheobronchial tree from the terminal bronchioles up to the larynx fall upon a blanket of mucus, which under the influence of ciliary action is constantly moving from the deeper parts of the lung toward the larynx. In this way, the deposited materials are removed by the mucus escalator either directly or assisted by the mechanism of cough. For the most part, particulates lodging anywhere in the respiratory tract above the respiratory bronchioles tend not to be carried through the membranes and into the fixed tissue cells and interstices of the body. Mostly, they remain on the surface entrapped within the secretions and are removed rather rapidly by mechanical means. On the basis of reasonably good measurements, it has been estimated that particulates deposited anywhere on the mucociliary apparatus will be carried to an area where they will be expectorated or swallowed within a matter of minutes, provided this escalator system is operating normally. The behavior of air-suspended particulates and movement of air within the lung play a role in determining the area where particles will be initially deposited. Particles larger than 0.5 μ in diameter do not move by active diffusion but are transported only by actual air movement. For this reason, such particles can be brought into immediate surface contact only with those parts of the lung across which actual air movement occurs. It is known that a major part of the change in lung volume attending each breath occurs in the trachea and more distal bronchial tubes. Recent evidence raises a question as to whether or not alveoli per se participate at all in actual mass movement of air. For these reasons, particles larger than 0.5 μ tend predominantly to fall upon the mucociliary mechanism directly, whereas those that are smaller in diameter may move by diffusion into the most distal air-containing structures.

Particulates that lodge in the more distal, nonciliated portions of the lung may follow several pathways. Some may pass through the surface membranes into the interstitial substance of the lung either as naked particles or entrapped within mobile macrophages. Other particles may remain on the surface of the deep respiratory passages either as naked particles or entrapped within macrophages. The majority of the particles, however, are rather rapidly taken up by the macrophages and carried out onto the mucociliary apparatus to be disposed of in the same manner as if they had originally been deposited thereupon. The rapidity and effectiveness of this latter process is rather astonishing. LaBelle and Brieger (11) appear to have demonstrated that under circumstances of moderately intense deposition of particulates within the deep portions of the lung, the vast majority of these particulates are engulfed by mobile macrophages carried to the mucociliary escalator and discharged up the trachea. To some degree, the effectiveness of removal is related to the quantity introduced. Particulates moving either directly or inclosed within macrophages through the alveolar membranes into the interstitial tissues may remain locally or pass to regional lymphoid collections, and also into the blood stream or into quite remote lymph nodes via the lymphatics. Many factors influence the macrophage response, the migration of the particles, and their ultimate fate.

That the region immediately distal to the mucociliary apparatus may possess special attributes for defense against injury has recently been demonstrated by Jerome Kleinerman. He has shown that within a matter of 2 hr after exposure to sublethal intensities of nitrogen dioxide, small animals begin to show evidence of repair of the alveolar epithelium and the epithelium lining alveolus-bearing ducts. It is striking that the most active manifestations of macrophage activity and reduplication of cells lining

the surface of ducts occur in the region of the respiratory bronchiole. Moreover, this is the area where the reaction persists the longest. It is as though this particular area situated just beyond the ciliary-mucus mechanism is especially prepared to take part in the defense and repair mechanisms. Within a matter of some 8 to 12 days following the sublethal exposures to nitrogen dioxide, the lung has an essentially normal appearance. Kleinerman has shown that animals are able to go through this train of events repeatedly at intervals of 1 month or even shorter with no apparent interference with the reactions of repair and with no permanent residual abnormalities.

The degree to which this sort of information can be extrapolated to the behavior and fate of living particulates is not known. That living agents attached to inanimate particulates, enclosed within minute droplets, or occurring as droplet nuclei can penetrate rapidly into the deepest portions of the lung and even into the pleural space has been amply demonstrated. Stillman and Branch (15) were able to isolate microorganisms from the periphery of animal lungs within 1 hr after exposure of the animals to the inhalation of air-dispersed pneumococci. Robertson (13), without giving the details of the experiments, speaks of spraying cultures of pneumococci into the lungs of dogs and recovering the organisms from snips of tissue taken from the surface of the lung 5 min after completing the spraying procedure. The relative roles of liquid versus aerosol transmission in this experiment cannot be judged. Wells (18), in an elegant experiment, demonstrated that droplet nuclei of less than 3 μ diameter and containing tubercle bacilli readily infected the lungs of rabbits, whereas airborne particulates of 10 to 12 μ in diameter containing many more organisms caused far fewer lesions because the particles were trapped on the mucociliary blanket and promptly removed from the lungs. That dust may play a role as a transmitter of organisms is evidenced by the work of Jones (10), who found that organisms could be isolated from the periphery of the lungs of animals whose diet consisted of hay and oats in the dusty state. If these same animals were fed on wet feed and kept away from the dusty materials, their lungs were sterile or yielded fewer colonies.

One must consider not only the implantation of organisms but also their survival. Cannon and Walsh (5) and Stillman and Branch (15) have shown that although viable organisms reach the deep parts of the lungs, they tend not to survive. In some instances, the organisms seem unable to propagate. In others, a moderate activity of macrophages appears to overwhelm the organisms. In still other instances, for example, the reaction to inhaled tubercle bacilli, there is little macrophage activity. The organisms apparently are engulfed but not killed. Ultimately, they grow and cause disease. It appears certain that, in humans, living particulate material must be distributed throughout the respiratory tract on occasions. Nevertheless, attempts to grow living agents from the deeper structure of the lung either by culture of actual tissue or of washings obtained via bronchoscopy have demonstrated that for the most part the lung distal to the major bronchi in healthy individuals appears to be sterile. It seems that the great speed with which organisms deposited on the mucociliary blanket are removed and disposed of by swallowing or expectoration is effective in preventing the establishment of a bacterial flora in the sublaryngeal airways in healthy persons. Viable organisms reaching the deeper parts of the lung distal to the ciliary mechanisms persist there for some period of time but die or are destroyed before growth can be established. The degree to which the macrophage system participates in the day-to-day defenses of the respiratory system against the usual onslaughts of living particulates is relatively little explored, in part because of the great difficulty in doing so. The anatomical arrangements suggest that, in the cilia-bearing portions under normal circumstances, macrophages play a relatively minor role. In the distal parts beyond the ciliary mechanism, the macrophages probably play the major role. To some extent, they act as carriers to bring the particulates up onto the mucociliary blanket for further removal. Evidence exists that the regional lymph nodes of the lung become infested with viable organisms within a matter of several hours or perhaps sooner after they have been introduced into the deeper parts of the lung. Perhaps some of these organisms move to the lymphoid tissue collection without prior macrophage engulfment. On the other hand, it seems more logical that most of them are transported contained in macrophages. The manner in which the macrophages

contain and overwhelm the infestation by living particulates will not be discussed here. Suffice it to say that, under some circumstances, the mechanism is not completely successful.

We can summarize the defenses of the *normal* respiratory apparatus against airborne living particulates with regard to simple physical infestation in the following manner: Little is known about the number of, or degree to which, living particulates penetrate the human respiratory apparatus. Such information as is available has to do with the *survival* of organisms and their ability to grow when appropriate smears or washings are cultured. It appears that the nose does act as a filter for the purpose of entrapping living particulates, especially those that are dustborne. So little is known concerning the numbers and types of organisms thrust upon the nasal filter that we are unable to assess the effectiveness of this apparatus completely. It appears that speed of mechanical cleansing and possibly some inhibition of growth of organisms play the major role in preventing the development of infection. The extent to which fixed or mobile cells take part in this control of infestation under normal circumstances is not fully known. It seems that relatively few organisms are introduced below the larynx. The deeper parts of the lungs are sterile and relatively few organisms grow in the secretions obtained from the deeper portions of the tracheobronchial tree itself. Even the mucus discharged directly from the trachea without contamination from oral contents contains few culturable organisms. The degree to which rapid removal by the various mechanisms described plays a role in preventing infection and the degree to which fixed or mobile phagocytes prevent the development of infection are unknown, but both must be assumed to play some role.

That clinical infection by the propagation and rapid multiplication of the living particulates on the surface or within the tissue cells of the respiratory apparatus does occur is undeniable. A number of factors can be thought of which might account for the development of infection. Among these would be the accumulation of unusually large numbers of living particulates as a result of impaired ability to remove the organisms or because the amounts introduced exceed the ability of the removing apparatus to keep pace. Such a circumstance would lead to the prolongation of residence of the organisms with an opportunity for multiplication and invasion. The accumulation of secretions in the supralaryngeal area with multiplication of organisms therein might lead to an unusual mode of inoculation of the sublaryngeal areas by liquid-phase rather than by airborne distribution. This circumstance might lead to the overwhelming of those protective and cleansing mechanisms existing below the larynx. It is apparent that these circumstances might develop should the normal cleansing and protective mechanisms break down.

It is reasonable to assume that there must be a limit to the ability of these various defense mechanisms to hold the size of the "dose" or intensity of the invasion to subinfectious levels. There is undoubtedly a temporal factor in that it probably requires time for full development of those forces preventing infection. Most of the mechanical equipment for the removal of organisms appears to be available at full strength at virtually a moment's notice. This feature is probably one of the strongest advantages possessed by the respiratory apparatus as a deterrent to the establishment of infection. Mobilization of the macrophage system probably takes an appreciable period of time and it is perhaps fortunate that the heaviest onslaught of organisms appears to occur in the upper respiratory portions as contrasted to the alveolus-bearing parts of the lung.

The defense mechanisms can, however, be influenced in such a manner as to make them less effective. Direct observations have demonstrated that drying markedly impairs the mobility and effectiveness of ciliary action. Moreover, the secretions forming the blanket tend to become inspissated and are more difficult to move. Localized drying is not infrequent in the nose and nasopharynx with the result that cleansing is impaired and organisms may have an unusual opportunity to accumulate in sufficient numbers and to remain long enough to begin to multiply and establish an infection. Proetz believes that the increased incidence of the common cold coincident with the beginning of heat in homes in the early winter is a manifestation of this phenomenon. Chilling of the body as a whole or even localized chilling may change the state of congestion of the highly vascularized tissues of the nose in a manner to direct most of the air flow through one relatively small channel with consequent drying of the mucosa locally. Hilding

(8), Dalham (6), and more recently Ballenger (3) have demonstrated that cigarette smoke contains materials that seriously interfere with ciliary beating. Other gases such as ammonia and sulfur dioxide have this same effect. These and other forms of injury may act as the initial impairment of normal nasal pharyngeal cleansing that leads to the establishment of infection.

Once infection has been established, the tissues react with a profuse production of mucus, sometimes of a very thick nature and sometimes of a thin watery type. Too little is known about the production of mucus both as to the quantity and character to warrant a discussion of this feature. It seems reasonable to assume, however, that under some circumstances alterations of mucus production or character may lead to impairment of the defense mechanism and the establishment of infection. Insofar as a primary causal factor is concerned, the profuse production of mucus in chronic sinusitis and in chronic bronchitis apparently bears little relationship to bacterial infection. Clinical experience suggests that though these diseases are of a primary mucous gland nature, they do become complicated at times by infection. Evidence is beginning to gather that cigarette smoking over a long period of time will promote, at least in some individuals, an unusually profuse discharge of mucus and hypertrophy of the mucus-producing glands. The inability of the body to handle the mucus properly may lead to stasis and prolongation of this material within the respiratory apparatus, giving time for infection to develop. What has been said with regard to mucus and ciliary action in the supralaryngeal areas applies equally to sublaryngeal portions of the respiratory tract.

The accumulation of bacteria-laden liquid in the supralaryngeal portion may by aspiration overwhelm the mucociliary mechanisms of the sublaryngeal portion of the tract and lead to the development of infection. The development of sublaryngeal infection consequent to an acute coryza is a common clinical experience. In a well-controlled study during World War II (9), it was shown that the incidence of pneumococcal pneumonia was to some degree related to the incidence of acute respiratory disease. It seems possible that the volume of the nasal pharyngeal secretions which characterized acute respiratory disease would favor an increase in the dosage of living organisms introduced into the sublaryngeal areas by aspiration, especially during sleep. In addition, other products favorable to the development of infection may exist in these secretions. Thus, the defenses of the sublaryngeal passages may simply be overcome by secretions from above. Less obvious factors may be operating also. These may have to do with cellular and immune reactions. In the study just referred to, "influenza" appears to have increased the incidence of pneumococcal pneumonia. Influenza is not particularly characterized by copious nasal and pharyngeal secretions, but it may be that it depresses the cellular response and thus permits the development of pneumococcal pneumonia. In addition, the virus is known to injure the cells of the mucociliary mechanism, thus interfering with adequate lung cleansing and possibly also permitting direct infection of the ciliated cell areas. Flooding of the alveoli with serum occurs during influenza and may, as shown experimentally by Harford and Hara (7), favor the development of pneumococcal pneumonia by protecting the pneumococci and nourishing their propagation once they reach the alveoli.

The extent to which the supralaryngeal mechanisms might influence those below the larynx both favorably and unfavorably could be tested by studying the experience with regard to disease of the lower respiratory tract in those persons who have undergone exteriorization of the trachea following laryngectomy. I am unable to find any systematic study of such a group. Thomson (16) refers to his clinical observation that tracheotomized humans and horses do not seem to suffer from any unusal incidence of pulmonary or bronchial infections. Personal inquiries made during the past few weeks concerning the experience of my confreres who have large numbers of such persons under observation appear to confirm Thomson's statement. One might well wonder whether the nose and nasopharynx are more harmful than helpful with regard to infections of the lower air passages.

Thus far nothing has been said with regard to cough. Cough is the natural mechanism whereby material accumulating in the major bronchi and trachea is forcibly ejected into the pharynx where it is swallowed or expectorated. The mechanism of this maneuver has been the subject of study using cineradiographic techniques at 30 frames per second with simultaneous recording of intrathoracic pressure and oral air flow. Ross, Gra-

miak, and Rahn (14) have shown that the train of events in a cough is essentially as follows:

> Following inspiration, expiration is initiated against a closed glottis with an elevation of intrapleural pressure to 100 or more mm of mercury. When the glottis is suddenly opened, the pressure falls within the trachea and major bronchi to a much lower figure. A high transmural pressure is set up across the bronchial wall, and an immediate reduction in the caliber of the bronchus ensues. At the same time, the rate of flow from the lung through the bronchi and trachea is greatly augmented. The bronchus and trachea can be narrowed to as little as one-fifth their previous diameter. Two helpful features develop as a result of this. First of all, the linear acceleration of air flow is enormously augmented through the narrowed airway so that velocities approaching 85% of the speed of sound are reached. Secondly, any secretions that have accumulated on the walls of the bronchus will occupy a larger portion of the area of the lumen and may in fact completely occlude it momentarily. As a result, the high velocity of air flow moves the slug of mucus along in the airway in a manner analogous to a pea-shooter.

It appears from these studies that the narrowing of the tracheobronchial tree is of equal or perhaps even greater importance than the increase in rate of air flow that characterizes cough.

Ross and his associates are inclined to believe that their studies fail to demonstrate a peristaltic mechanism acting in a manner that milks the airways in the direction of the larynx. In our laboratory, we have made a few preliminary observations of cough using this same technique. The patients studied had bronchiectasis. Examination of sequential frames indicates that there is virtual closure of the second and third order bronchi and abolition of the lumen of the trachea for a fraction of a second during the act of cough. In one explosive cough, there may be two or even three openings and closings of these lumens. One can see the radiopaque material spurt forward in the small bronchi. In normal, healthy persons, cough is apparently a very effective mechanism for removing secretions. In some diseases, notoriously in diffuse obstructive emphysema, cough is not effective. In part this is due to the increased tenacity and viscosity of the secretions and in part also to a change in the compliance of the tracheobronchial tree. The actual mechanics underlying the impaired cough remain to be worked out. Although no study of the mechanics of cough has been made in laryngectomized individuals with an exteriorized trachea, it is of great interest that such persons are able to cough quite effectively and can project thin mucus several feet from the ostium in the neck. As to whether or not this form of cough is as effective as when a glottis is present, I do not know, but it is obvious that a glottis is not necessary to develop an effective cough mechanism.

Some evidence exists concerning the influence of loading the macrophage and mucociliary system with inanimate particulates and the possible influence this might have on defense against infection. Laboratory animals exposed for various prolonged intervals of time to inhalation of particulate materials appear to show neither greater nor lesser susceptibility to those intercurrent infections that from time to time ravage colonies of laboratory animals. Baetjer (2) found no unusual incidence of pneumococcal pneumonia among controls infected with pneumococci suspended in mucin and similarly inoculated animals which had been previously exposed to the inhalation of Portland cement dust for periods of 1 to 30 weeks. Kleinerman and I, in a preliminary series of experiments, have studied the effect of chemical pneumonia produced by the inhalation of sublethal concentrations of nitrogen dioxide in small animals upon the incidence and extent and recovery from bronchopneumonia induced by the intratracheal spraying of influenza bacilli. We have been unable to demonstrate any difference in the reaction between controls and those animals previously exposed to nitrogen dioxide and having chemical pneumonia at the time of the subsequent bacterial instillation. In contrast to this is the clinical experience that those persons, who have been sufficiently exposed to certain irritant fumes to develop subsequently a chemical pneumonitis, seem particularly prone also to develop bronchopneumonia on a bacterial basis. It appears from this that in humans, at least, the defenses to infection can be impaired by exposure to certain of the irritant gases. It could well be that more viable and virulent organisms contaminate the lower respiratory tract in humans.

It is difficult to assess fully the effectiveness with which the respiratory apparatus defends itself against invasion and infection by living

particulates. There is a scarcity of data concerning the quantity, state of dispersal, and viability of airborne pathogenic organisms met with in various environments. Lacking such data, one can only speculate regarding many of the interesting facets of this problem.

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