PART IV. BACTERIAL DISEASES

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AIRBORNE PULMONARY TUBERCULOSIS[1]

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The mechanism of transmission of epidemic respiratory infection can be studied from many points of view, one of which is represented by our work on airborne pulmonary tuberculosis. We shall discuss this work and also two studies which approach the problem from entirely different directions, after some introductory remarks on the use of the word contagion.

Contagion means contact, and the use of the word contagion can be limited to infections transmitted by direct contact. However, by common consent the closeness required for contact has been extended to include the distance of 2 or 3 ft through which relatively coarse respiratory droplets travel before falling to the floor or impinging on another person. In accord with Wells (7), I shall extend the concept of contact still further to include the invisible exchange of droplet nuclei which occurs between people occupying the same room at the same time. This extension involves only a few feet since it is ordinarily limited by the distance between the walls of a room. It is justified by the epidemiologically significant fact that droplet nuclei disperse rapidly throughout enclosed atmospheres. Furthermore, since droplet nuclei are removed from enclosed atmospheres by ventilation, the concentration of infectious droplet nuclei, and hence the chance of this type of infection, is inversely related to ventilation. For purposes of this presentation, epidemic respiratory contagion will be defined as that form of epidemic respiratory infection in which the chance of infection is inversely related to the ventilation of the room. This is equivalent to saying that we shall deal with those forms of epidemic respiratory infection which we believe to be transmitted by droplet nuclei.

If our definition of contagion seems arbitrary and rather far from the strict meaning of the word contact, it would be justified if most of the forms of epidemic respiratory infection which are commonly considered to be contagious were in fact transmitted by droplet nuclei rather than by direct contact. The likelihood that this may be so is implicit in what is to follow. We shall illustrate the interdependence of infection and ventilation, first by our work on the infectivity of the air of a tuberculosis ward, then by the epidemiological demonstration of Wells, Wells, and Wilder (5) of the relationship between sanitary ventilation and the chance of catching measles, and finally by a gigantic experiment of nature, analyzed by Wells (6), in which seasonal patterns of infection are related to indoor ventilation.

Infectivity of Air of a Tuberculosis Ward

The original purpose of this experiment was to demonstrate the presence of droplet nuclei containing tubercle bacilli in the air of a tuberculosis ward. A ward containing six single rooms was chosen and its ventilation was carefully controlled. Patients with far-advanced disease and large numbers of tubercle bacilli in the sputum occupied the ward. They were given the usual instructions regarding hygiene, including advice to cover their mouths when they coughed. Air from the ventilating system of the ward was discharged through a large guinea pig exposure chamber on its way to the outdoors. This chamber was located in a penthouse above the ward. Preliminary experiments demonstrated that the air in the exposure chamber was as infectious as that in the patients' rooms (3). An average of 156 guinea pigs occupied the exposure chamber, with replacements as necessary to maintain an approximately constant census. Each month all the guinea pigs were tuberculin-tested and positive reactors were removed. During the first 2 years of the experiment 71 guinea pigs were infected by breathing the air vented from the tuberculosis ward (4). The monthly infection

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rate varied from 0 to 10, with an average of approximately 3. The average time required to infect a guinea pig was 10 days. One guinea pig breathes about ⅓ ft^3 an hour, or 8 ft^3 per day. One hundred fifty-six guinea pigs breathe approximately 1,248 ft^3 a day, or 12,480 ft^3 in 10 days. The air of the tuberculosis ward thus contained, on an average, one quantum of tuberculosis infection in about 12,000 ft^3 of air. Infections appeared at random among the animals distributed throughout the chamber, and the characteristic *single* tubercle which each animal developed was found randomly distributed in the lungs. The only infectious particle capable of traversing the extensive ductwork between the patient and the animal chamber and being distributed randomly with the air is a particle having the aerodynamic characteristics of the droplet nucleus.

This experiment clearly indicated that droplet nuclei containing tubercle bacilli capable of infecting guinea pigs were present in the air of a tuberculosis ward. However, because of the implications with respect to control, the experiment was expanded and repeated, following the suggestions of members of the Committee on Veterans Medical Problems of the National Research Council. A second animal exposure chamber was constructed and filled with an equal number of guinea pigs. Air from the ward was divided so that approximately 100 ft^3 per minute passed through each chamber. On the way to one chamber, the air was intensely irradiated with ultraviolet light to kill all airborne organisms. Air going to the other chamber was not irradiated and hence was representative of ward air. During the 20 months of operation to date, none of the animals receiving irradiated air has developed tuberculosis, whereas the animals receiving unirradiated air have continued to acquire tuberculosis at a rate approximately the same as that during the first 2 years of the experiment. The two-chamber experiment has demonstrated beyond question that the guinea pigs were infected by organisms in the air they breathed and not by any other mechanism of transmission.

The quantitative importance of infectious droplet nuclei in the air of the tuberculosis ward can be assessed in an approximate way. In the days before the present chemotherapy of tuberculosis many careful studies were made of the rate of conversion of the tuberculin test in nurses working on tuberculosis wards. In general, the tuberculin test converted to positive in from 6 to 18 months. We shall take 1 year as a rough average. The fact of conversion indicates that the nurse developed a tubercle somewhere in her body. We shall assume that conversion of the tuberculin test signaled the presence of a pulmonary tubercle in the vast majority of cases and that this resulted from the inhalation of a "TB quantum" (infectious dose) of airborne tubercle bacilli. We can now estimate the volume of ward air containing a TB quantum by estimating the amount of ward air breathed by a nurse in 1 year. If a nurse breathes ward air for 6 hr a day, 5 days a week, and 40 weeks per year, this would amount to 1,200 hr a year, which, at the rate of 20 ft^3 per hour (9 liters per minute), would total 24,000 ft^3 in a year. Since 1 year is the average time required to inhale a TB quantum, something of the order of 24,000 ft^3 must be the average volume of ward air containing one TB quantum for a nurse. It will be recalled that it was concluded from the guinea pig exposure studies that the air of the test ward contained, on an average, one TB quantum for a guinea pig in 12,000 ft^3. In view of the fact that the data on tuberculin conversion rates for nurses were obtained before the era of chemotherapy, without knowledge of ward ventilation, and with patients suffering from different amounts of disease, we consider that one TB quantum in 24,000 ft^3 for a human being is an excellent check with one TB quantum in 12,000 ft^3 for a guinea pig. The conclusion from this line of reasoning is that the amount of airborne tubercle bacilli demonstrated in the air of the test ward is sufficient to account for the spread of tuberculosis in nurses. It is reasonable to infer that tuberculosis is spread in the community by the mechanism which operates in hospitals. The evidence therefore points toward droplet nuclei as the predominant mechanism. Under the controlled conditions of this experiment, it is clear that the concentration of airborne droplet nuclei was inversely related to the amount of dilution by ventilation.

Sanitary Ventilation and Measles

In seeking to decide whether this mechanism is applicable to other forms of respiratory infection, we have re-analyzed epidemiological data from three major studies of measles in school children. In each study, ultraviolet irradiation was used as a means of eliminating infectious droplet nuclei without affecting other forms of infectious contact. We shall use the term sanitary ventilation in referring to the elimination of airborne organisms either by ventilation or by irradiation since irradiation is the sanitary equivalent of ventilation. The studies carried out in Swarthmore and Germantown during the epidemic of 1941 and during the succeeding 5 years show that the spread of measles in classrooms can be controlled by reducing the concentration of infectious droplet nuclei (5, 7). Comparable results were not obtained in the Cato-Meridian School (2) or in the Southall Schools (1), possibly because transmission outside of the classrooms was more important.

We have tested the detailed data from Swarthmore and Germantown by recalculating the effective contact rates for each generation in each classroom and by examining the rates of nonproductive exposure and the threshold densities of susceptibles over the entire 5-year period. The data show that an impressive degree of control was consistently achieved in the irradiated classes. Since children breathe classroom air only about 20% of the time (5 out of 24 hr and 5 out of 7 days each week), it is remarkable that disinfection of classroom air alone produced an appreciable degree of control in any of these tests. Clearly the activities of the children when not in school were of the utmost importance. Only when the chance of catching measles out of school was relatively slight was the importance of the classroom so overwhelming that disinfection of classroom air alone could reduce the incidence of measles. The social structure in the Quaker communities of Swarthmore and Germantown was consistent with the inference that in these towns the chance of catching measles out of school was much less than in the Cato-Meridian or Southall districts. However, the important scientific fact is not that some tests failed but that one succeeded.

Since ultraviolet irradiation of the upper air does not affect mechanisms of transmission other than droplet nuclei, we conclude that measles in school children is predominantly borne by droplet nuclei and that the chance of catching measles in a given enclosed atmosphere, such as a classroom, is inversely related to the sanitary ventilation per susceptible occupant.

Seasonal Patterns of Measles and Chickenpox in Relation to Climate

Nature performs a gigantic experiment based on the simple fact that when the weather gets cold, people try to keep warm. They close the windows and stay indoors. Thus more susceptible people crowd into less well-ventilated atmospheres, sanitary ventilation per susceptible person is reduced, and according to the droplet nucleus hypothesis, the chance of airborne infection should be increased. Wells (6) made an extensive study of the seasonal incidence of measles and chickenpox based on state health reports. She took monthly records of various states along the eastern seaboard and superimposed data for corresponding months in a given state for 20 consecutive years. Characteristic seasonal patterns were found which changed in a systematic way as one proceeded from north to south. These findings are summarized in Fig. 1, where average curves for measles are shown for Maine, Virginia, and Florida. In Maine, measles starts earlier in the fall and continues later in the spring, whereas in Florida, measles starts later and ends sooner but reaches a higher peak. In Virginia, an intermediate situation exists. The length of the measles season thus bears a direct relation to the length of the cold season.

The same relationship was found to be true in the case of chickenpox, as shown in Fig. 2. The seasonal patterns in measles and chickenpox are by no means identical, but the same trends are seen from north to south, and these trends are consistent with the belief that ventilation is of predominant importance. This thesis gains further support from the relative lack of seasonal variation in regions where the temperature is almost constant throughout the year. This effect was noted with respect to measles in Puerto Rico and Panama.

The seasonal pattern of scarlet fever, on the other hand, showed no significant difference in northern relative to southern states, suggesting that ventilation per susceptible was not of predominant importance in the spread of this disease. Dr. Wells' paper demonstrates that ventilation per susceptible can be used as a powerful tool to investigate the mechanism of transmission of epidemic respiratory infection under natural circumstances.

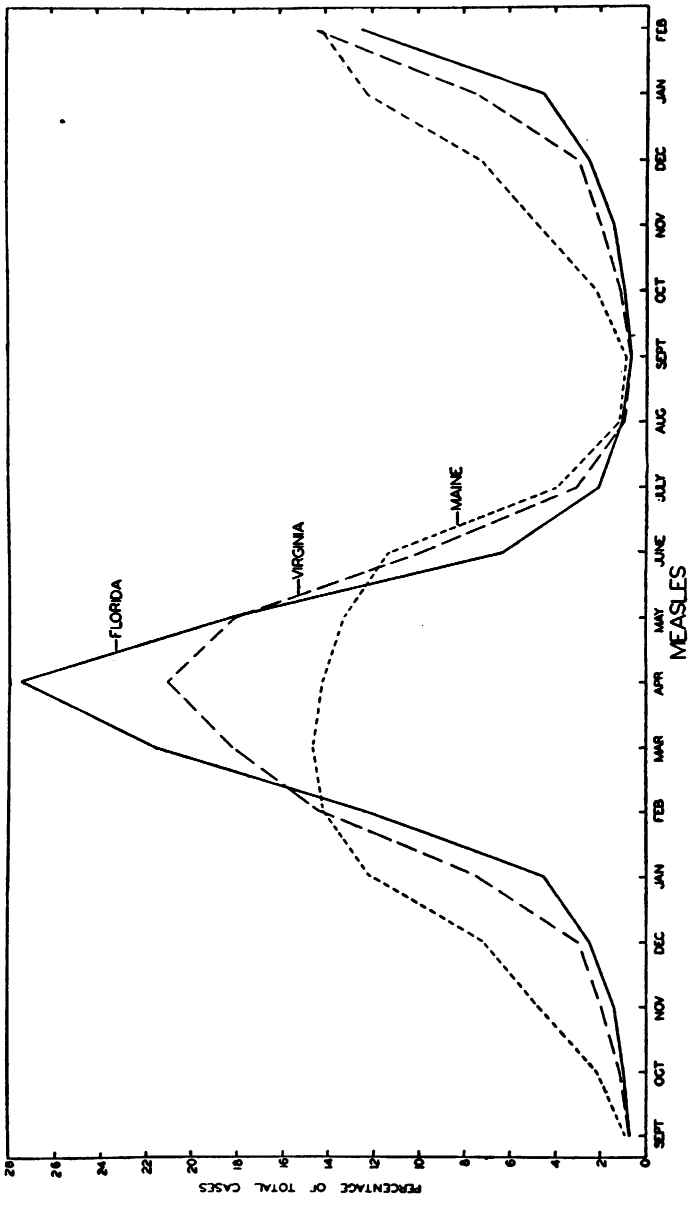

FIG. 1. *Effect of latitude on seasonal dispersion of cases of measles*

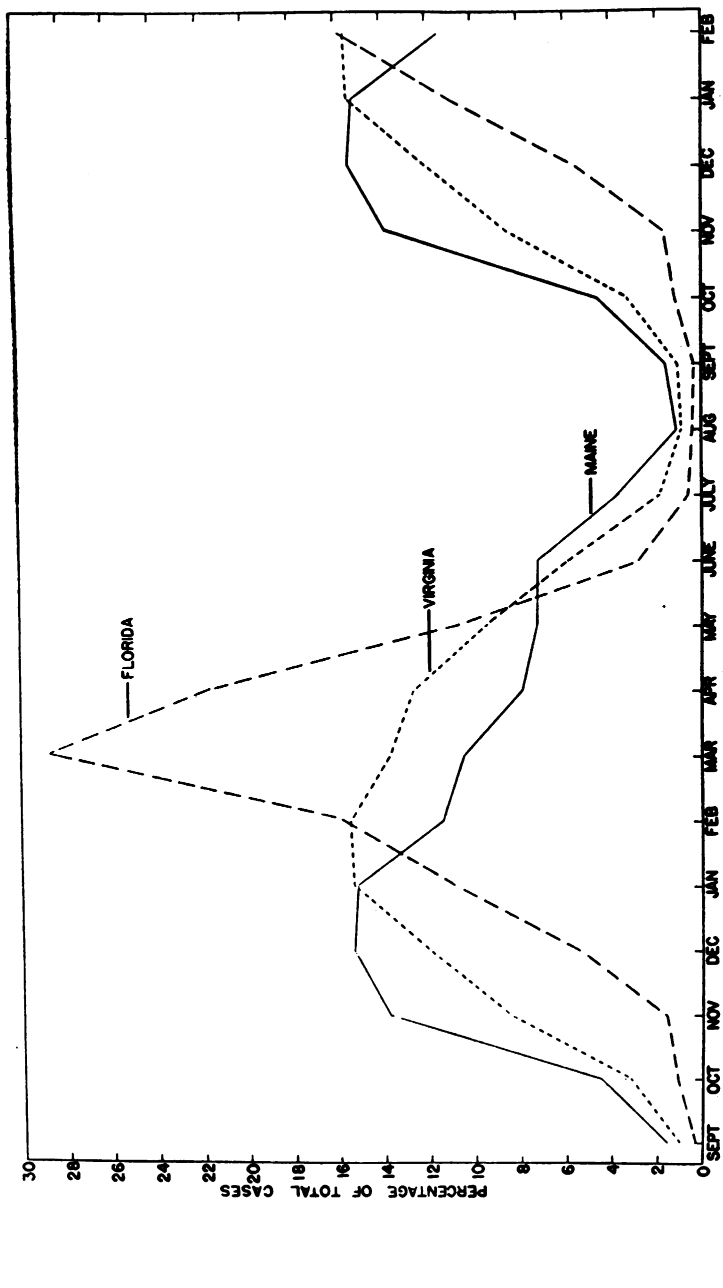

FIG. 2. *Effect of latitude on seasonal dispersion of cases of chickenpox*

It has been stated that the mechanisms of transmission of the various forms of epidemic respiratory infection must be demonstrated one by one and that no generalization is permissible. I take exception to this statement on both practical and theoretical grounds. From the practical point of view it is hardly feasible to take the acute virus diseases one by one, because in many instances neither the virus nor the disease can be identified readily. From the theoretical point of view, I see no objection to categorizing a group of diseases on the basis of mechanism of transmission. There are only four mechanisms of transmission of respiratory disease which have to be seriously considered: direct contact, dust, respiratory droplets, and droplet nuclei, and only the latter involves the inverse relationship between sanitary ventilation per susceptible and chance of infection. Therefore, we have a means of identifying a group of infections which is transmitted by droplet nuclei, based on its susceptibility to a specific type of environmental control.

The predominant importance of sanitary ventilation per susceptible in the spread of contagion is the common thread that runs through the otherwise diverse studies which have been discussed. I close with the suggestion that other forms of acute epidemic respiratory infection may be contagious, in the sense in which we use the word, and that sanitary ventilation is a powerful tool with which to test this hypothesis.

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