Airborne Transmission of Communicable Infection — The Elusive Pathway

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What does it mean to describe an infection as having airborne transmission, and what are the clinical implications? There is a fitting symmetry between the report by Yu et al. about airborne transmission of the severe acute respiratory syndrome (SARS) in this issue of the *Journal* (pages 1731–1739) and John Snow's investigation of a cholera epidemic 150 years ago. Snow's independent investigation tested the hypothesis that cholera was waterborne. The official investigation by the General Board of Health in England, however, concluded that transmission in the epidemic was airborne, caused by nocturnal vapors emanating from the Thames River — a conclusion that was consistent with the dominant paradigm of the time. Today, the situation is reversed. Yu et al. conducted an independent investigation in which they used computational fluid-dynamics and multizone modeling to test a hypothesis that the outbreak of SARS at the Amoy Gardens apartment complex in Hong Kong was caused by airborne transmission. In the official investigation, airborne transmission was not seriously considered, because the current paradigm, as initially described by Charles Chapin in 1910, supports the belief that most communicable respiratory infections are transmitted by means of large droplets over short distances or through contact with contaminated surfaces.

What underlies the low repute of airborne transmission today? First, the two diseases whose aerosol transmission is most widely acknowledged, measles and tuberculosis, have been largely controlled through vaccination or drug therapy. As a result, the impetus to understand the aerobiology of infectious diseases has faded. Second, contamination of water, surfaces, and large-droplet sprays can be easily detected. It is difficult, however, to detect contaminated air, because infectious aerosols are usually extremely dilute, and it is hard to collect and culture fine particles. The only clear proof that any communicable disease is naturally transmitted by aerosol came from the famous experiment by William Wells, Richard Riley, and Cretyl Mills in the 1950s, which required years of continual exposure of a large colony of guinea pigs to a clinical ward filled with patients who had active tuberculosis.

The SARS epidemic provides an opportunity for the critical reevaluation of the aerosol transmission of communicable respiratory diseases (see Figure). Prevailing thought has focused on determining whether an infectious agent has "true" airborne transmission. We find it more useful to classify the aerosol transmission of diseases as obligate, preferential, or opportunistic, on the basis of the agent's capacity to be transmitted and to induce disease through fine-particle aerosols and other routes.

Tuberculosis may be the only communicable disease with obligate airborne transmission — an infection that, under natural conditions, is initiated only through aerosols deposited in the distal lung. Diseases with preferentially airborne transmission are caused by agents that can naturally initiate infection through multiple routes but are predominantly transmitted by aerosols deposited in distal airways; with these agents, infection initiated through another route usually causes modified disease. Agents that must be systemically disseminated by resident pulmonary cells in order to cause full-blown disease have either preferential or obligate airborne transmission and may include viral exanthems such as measles and smallpox. There are probably many diseases with opportunistically airborne transmission — infections that naturally cause disease through other routes (e.g., the gastrointestinal tract) but that can also initiate infection through the distal lung and may use fine-particle aerosols as an efficient means of propagating in favorable environments. For all three classes of diseases that are communicable through aerosols, the agent must be capable of initiating infection, with some reasonable probability, by means of a small dose delivered to the lung in a single airborne particle.

The current analysis of the outbreak at Amoy Gardens suggests that SARS has at least opportunistically airborne transmission. A concentrated aerosol plume is described as having originated from sewage that was contaminated by the index patient. Hydraulic aerosol experiments combined with aero-

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
22 APR 2004	**N/A**	**-**

4. TITLE AND SUBTITLE
Airborne transmission of communicable infection - the elusive pathway, New England Journal of Medicine 350:1710 - 1712

5a. CONTRACT NUMBER
5b. GRANT NUMBER
5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Roy, CJ Milton, DK

5d. PROJECT NUMBER
5e. TASK NUMBER
5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD

8. PERFORMING ORGANIZATION REPORT NUMBER
RPP-04-254

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release, distribution unlimited

13. SUPPLEMENTARY NOTES
The original document contains color images.

14. ABSTRACT
What does it mean to describe an infection as airborne and what are the clinical implacations? The concept of the air we breathe as a reservoir for disease-causing agents harkens back to the pre-Pasteur teachings of miasmic-induced disease of Sir Edwin Chadwick. Modern germ theory largely rejects the vague concepts of airborne vapors as a cause of disease, and has focused on obvious transmission patterns of infectious agents from the source to a susceptible host. Observable mechanisms of transmission such as contaminated water, direct surface contact, and large droplet sprays, can all be validated as means of disease communicability. In addition, many of the aerosol-transmitted disease agents such as smallpox and measles have been effectively eliminated or controlled through aggressive preventive and primary care of the last century. As a result, the aerobiological basis of disease transmission has faded somewhat into the more obscure theoretical milieu. Only tuberculosis frequently defied directly observable transmission by close contact. Thanks largely to the work of William Wells and Richard Riley, we now know that tuberculosis is naturally transmitted only by the airborne route. But proof of airborne transmission was an arduous task, requiring continual exposure of a guinea pig colony to active tuberculosis cases in a clinical ward. Only after satisfying Koch's postulate by demonstrating disease agent transmission from the infected patient to a naïve animal, was there recognition that tuberculosis was, in fact, an airborne-acquired disease.

15. SUBJECT TERMS
aerobiology, aerosol exposure, infectious disease, review

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
unclassified	**unclassified**	**unclassified**	**SAR**	**3**	

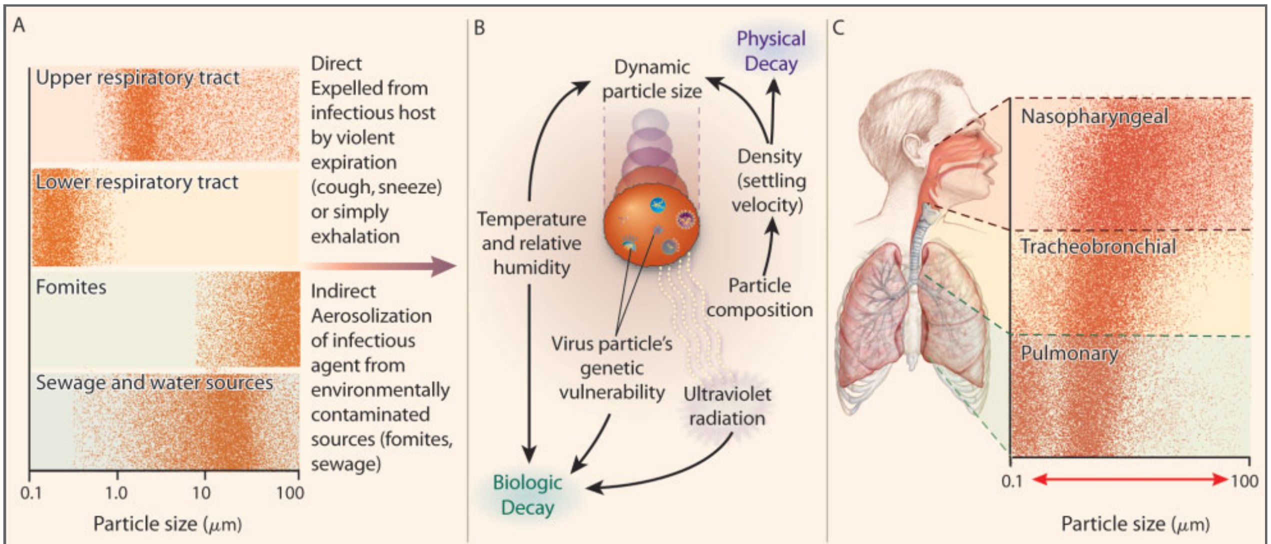

Figure. The Aerobiologic Pathway for the Transmission of Communicable Respiratory Disease.
Whether it is an infected human or a contaminated environmental matrix, each source (Panel A) generates particles with a characteristic range of sizes. The length of time a particle resides in the air (physical decay, Panel B) depends on its initial size, its composition, and environmental factors. Similarly, the length of time an airborne organism remains infectious (biologic decay) is affected by the infectious agent's initial metabolic state, genetic characteristics, and environment. The portion of the respiratory tract of a susceptible host in which inhaled particles are deposited (Panel C) is a function of the particles' aerodynamic size; in the middle of the range, particles may be deposited in both the upper and the lower airways.

sol and epidemiologic modeling clearly implicated airborne transmission within the apartment complex. The apparent novelty of the aerosol source, the novel dispersion through floor drains, and the rapid spread of the outbreak should not be considered to represent evidence that airborne infections necessarily cause explosive outbreaks or that patients with less contagious cases of SARS did not transmit infection through fine-particle aerosols. This outbreak merely reflects the fact that airborne transmission may be implicated relatively easily in cases in which there is a concentrated source of contaminated fine particles and a high probability of infection at a large distance from the source. In other cases, in which the source produces a low concentration of infectious particles, the aerosol becomes so dilute as it travels away from the source that most secondary infections occur in the immediate vicinity of the index patient. Therefore, the epidemiologic pattern associated with a dilute aerosol mimics that expected with large-droplet sprays or surface contact (i.e., face-to-face contact). Thus, as with the demonstration of the airborne transmission of tuberculosis, airborne transmission from the average case of SARS is not easily proved, but it should also not be dismissed out of hand.

The clinical implications of airborne transmission are particularly important for infection control in hospitals and in public indoor settings such as airplanes and schools. In the hospital setting, airborne precautions can be instituted once a patient is suspected of having a disease with airborne transmission. But substantial transmission from patients with unsuspected cases, especially in waiting rooms, can be expected and was observed during the SARS epidemic. The likelihood of such transmission may indicate a need for more general application of aggressive air-sanitation measures (e.g., upper-room germicidal ultraviolet irradiation) in areas where patient care is provided and in the public areas of hospitals. Airborne transmission on commercial aircraft has been implicated in a few investigations of outbreaks of tuberculosis, influenza, and SARS. Whether better air sanitation can be achieved in this highly ventilated but crowded environment remains to be determined. Schools, which are frequently poorly ventilated, are well recognized as important sites for the propagation of respiratory infections. It was fortunate that in the SARS epidemic, the disease did not develop in or disseminate among children. But the reduction of airborne transmission of influenza by means of air sanitation in schools could prove important with the emergence of the next pandemic influenzavirus.

As perplexing as it may be, the peculiarity of the transmission of the SARS coronavirus in Amoy Gardens may be a harbinger of unorthodox transmission patterns associated with emerging infectious agents in the modern built environment. It is a clear demonstration of the need for a better understanding of aerosol-acquired disease — whether airborne transmission is obligate, preferential, or opportunistic — and for improved vigilance and infection control.

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