Editorial

Three, if by Air

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One, if by land, and two, if by sea.—Henry Wadsworth Longfellow

This month's issue of *Infection Control and Hospital Epidemiology* presents studies pertaining to the transmission of two extremely important pathogens: *Aspergillus,* the scourge of the cancer ward; and *Mycobacterium tuberculosis*, the scourge of the rest of the world. With J. Craig Ventner's genome safely sequenced[1] and a cloned mule at large in the fields of Idaho,[2] it seems only fair to ask whether we know everything we would like to in 2003 about how these infections are transmitted.

Despite the high profile of *Aspergillus* on cancer and transplant floors,[3] a number of details regarding its transmission remain to be determined. For example, is the source always contaminated air, as most believe,[4-7] and could aerosolization of contaminated water play a role, as recently suggested?[8]

The two studies on *Aspergillus* in this month's issue of *Infection Control and Hospital Epidemiology*[9,10] operate on the well-accepted premise that hospital construction is a risk factor for nosocomial aspergillosis, presumably by shaking up the earth or moldy boards, thereby inundating the atmosphere with countless spores.[11,12] The study by Cooper et al. has given reassurance that infection control works at preventing such a threat.[9] They showed that during major construction, current infection control interventions designed to prevent airborne transmission prevented increases in both detectable airborne fungi and cases of aspergillosis among high-risk patients.

Such a confirmation is much appreciated, but one inconvenient fact continues to unsettle our collective attempts to answer the remaining questions about the role of the environment—air, land, or sea—in causing invasive aspergillosis. Quite a few studies have now been performed to determine the relationship between the *Aspergillus* found in the environment and the *Aspergillus* that we recover from our patients.[5,13-20] In general, these studies, employing molecular profiling techniques, have failed to establish relatedness between clinical and environmental strains, with a few notable exceptions.[5,14-16,20] Our inability to establish an environmental connection in every case in which it has been sought may relate to the heterogeneity of the hundreds or perhaps thousands of different strains of *A. fumigatus* in a single hospital, making it difficult to isolate and identify all of the environmental strains and then compare them with the patients' isolates.[5] Many patients have been shown to be infected by multiple different strains of *A. fumigatus*.[5,21-23]

Alternatively, the disjunction may derive from differences in growth characteristics of *Aspergillus* strains taken from the environment versus the patient. Perhaps whatever it takes to thrive and dominate on a potted plant or on moist particleboard has little to do with predominating in the dark shadows of the human airway. Supporting this is the always inconvenient fact that, although most studies find the air teeming with molds, *A. fumigatus*, which predominates as a human pathogen, is almost always in the distinct minority in environmental samples. Instead, other potentially pathogenic *Aspergillus* species, *Penicillium*, and other molds are what end up on the settle plates.

Tuberculosis has also withstood decades of intense scrutiny, but there are still questions to answer. In this issue of *Infection Control and Hospital Epidemiology*, Menzies, the lead sleuth on the case for the past 10 to 15 years,[24-27] adds to his ever-growing story on transmission, demonstrating that violent coughing is indeed remarkably efficient at creating infectious droplet nuclei.[28] This work, which focuses on microbes other than *Mycobacterium tuberculosis*, updates the cough-in-the-box work of Loudon,

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who showed that coughing, sneezing, or even singing produces a spike of droplet nuclei.[29] This, in turn, was an update of the admonitions of generations of mothers begging us to cover our mouths when we coughed—still an effective (and certainly the most cost-effective) way to prevent transmission of tuberculosis.

The work of Menzies is yet another reminder of how new knowledge about transmission has a funny way of presenting itself. Just when we think we understand something or believe in a certain diagnostic approach, we find new problems with that approach. His study helps to confirm that our honest attempts to diagnose individual patients may have accidentally helped create the very outbreaks that characterized much of urban North American tuberculosis a decade ago. At least one of the studies of those outbreaks showed increased spread in relation to cough-inducing therapy.[30] Thus, those of us who were vigorous enthusiasts of promoting induced sputum to diagnose one and all may inadvertently have produced a cloud of infectious droplet nuclei around each (forcibly induced) coughing patient. Oops! This humbling observation has demonstrated yet again how difficult it is to fool Mother Nature, bringing up the always unpleasant fact that too often our tricks to improve patient care end up at odds with sensible infection control.

REFERENCES

1. Anonymous. Life of Craig: he was so curious about himself, he sequenced his own DNA. *New Science* 2002;174:5.
2. Pollack A. Another milestone of cloning is reached as a mule is born in Idaho. *New York Times* May 30, 2003:22.
3. Cornet M, Fleury L, Maslo C, Bernard JF, Brucker G. Invasive Aspergillosis Surveillance Network of the Assistance Publique-Hopitaux de Paris: epidemiology of invasive aspergillosis in France. A six-year multicenter survey in the Greater Paris area. *J Hosp Infect* 2002;51:288-296.
4. Sherertz RJ, Belani A, Kramer S, et al. Impact of air filtration on nosocomial *Aspergillus* infections. *Am J Med* 1987;83:709-718.
5. Chazalet V, Debeaupuis JP, Sarfati J, et al. Molecular typing of environmental and patient isolates of *Aspergillus fumigatus* from various hospital settings. *J Clin Microbiol* 1998;36:1494-1500.
6. Fridkin SK, Jarvis WR. Epidemiology of nosocomial fungal infections. *Clin Microbiol Rev* 1996;9:499-511.
7. Patterson JE, Zidouh A, Miniter P, Andriole VT, Patterson TF. Hospital epidemiologic surveillance for invasive aspergillosis: patient demographics and the utility of antigen detection. *Infect Control Hosp Epidemiol* 1997;18:104-108.
8. Anaissie EJ, Stratton SL, Dignani MC, et al. Pathogenic *Aspergillus* species recovered from a hospital water system: a 3-year prospective study. *Clin Infect Dis* 2002;34:780-789.
9. Cooper EE, O'Reilly MA, Guest DI, Dharmage SC. Influence of building construction work on *Aspergillus* infection in a hospital setting. *Infect Control Hosp Epidemiol* 2003;24:472-476.
10. De Rosa FG, Shaz D, Campagna AC, Dellaripa PF, Khettry U, Craven DE. Invasive pulmonary aspergillosis soon after therapy with infliximab, a tumor necrosis factor-alpha–neutralizing antibody: a possible health-care-associated case? *Infect Control Hosp Epidemiol* 2003;24:477-482.
11. Arnow PM, Andersen RL, Mainous PD, Smith EJ. Pulmonary aspergillosis during hospital renovation. *Am Rev Respir Dis* 1978;118:49-53.
12. Walsh TJ, Dixon DM. Nosocomial aspergillosis: environmental microbiology, hospital epidemiology, diagnosis and treatment. *Eur J Epidemiol* 1989;5:131-142.
13. Symoens F, Burnod J, Lebeau B, et al. Hospital-acquired *Aspergillus fumigatus* infection: can molecular typing methods identify an environmental source? *J Hosp Infect* 2002;52:60-67.
14. James MJ, Lasker BA, McNeil MM, Shelton M, Warnock DW, Reiss E. Use of a repetitive DNA probe to type clinical and environmental isolates of *Aspergillus flavus* from a cluster of cutaneous infections in a neonatal intensive care unit. *J Clin Microbiol* 2000;38:3612-3618.
15. Symoens F, Bouchara JP, Heinemann S, Nolard N. Molecular typing of *Aspergillus terreus* isolates by random amplification of polymorphic DNA. *J Hosp Infect* 2000;44:273-280.
16. Thio CL, Smith D, Merz WG, et al. Refinements of environmental assessment during an outbreak investigation of invasive aspergillosis in a leukemia and bone marrow transplant unit. *Infect Control Hosp Epidemiol* 2000;21:18-23.
17. Rath PM, Ansorg R. Value of environmental sampling and molecular typing of aspergilli to assess nosocomial sources of aspergillosis. *J Hosp Infect* 1997;37:47-53.
18. Anderson MJ, Gull K, Denning DW. Molecular typing by random amplification of polymorphic DNA and M13 southern hybridization of related paired isolates of *Aspergillus fumigatus*. *J Clin Microbiol* 1996;34:87-93.
19. Birch M, Nolard N, Shankland GS, Denning DW. DNA typing of epidemiologically-related isolates of *Aspergillus fumigatus*. *Epidemiol Infect* 1995;114:161-168.
20. Buffington J, Reporter R, Lasker BA, et al. Investigation of an epidemic of invasive aspergillosis: utility of molecular typing with the use of random amplified polymorphic DNA probes. *Pediatr Infect Dis J* 1994;13:386-393.
21. Symoens F, Bertout S, Piens MA, et al. A longitudinal study of lung transplant recipients infected with *Aspergillus*: genetic polymorphism of *Aspergillus fumigatus*. *J Heart Lung Transplant* 2001;20:970-978.
22. Denning DW, Venkateswarlu K, Oakley KL, et al. Itraconazole resistance in *Aspergillus fumigatus*. *Antimicrob Agents Chemother* 1997;41:1364-1368.
23. Mondon P, Brenier MP, Symoens F, et al. Molecular typing of *Aspergillus fumigatus* strains by sequence-specific DNA primer (SSDP) analysis. *FEMS Immunol Med Microbiol* 1997;17:95-102.
24. Menzies R, Schwartzman K, Loo V, Pasztor J. Measuring ventilation of patient care areas in hospitals: description of a new protocol. *Am J Respir Crit Care Med* 1995;152:1992-1999.
25. Adhikari N, Menzies R. Community-based tuberculin screening in Montreal: a cost-outcome description. *Am J Public Health* 1995;85:786-790.
26. Fanning EA, Menzies R. Surveillance of medical students for TB urged. *CMAJ* 1995;152:327-328.
27. Menzies R, Vissandjee B, Amyot D. Factors associated with tuberculin reactivity among the foreign-born in Montreal. *Am Rev Respir Dis* 1992;146:752-756.
28. Menzies D, Adhikari N, Arietta M, Loo V. Efficacy of environmental measures in reducing potentially infectious bioaerosols during sputum induction. *Infect Control Hosp Epidemiol* 2003;24:483-489.
29. Loudon RG, Roberts RM. Droplet expulsion from the respiratory tract. *Am Rev Respir Dis* 1967;95:435-442.
30. Beck-Sague CM, Dooley SW, Hutton MD, et al. Hospital outbreak of multidrug-resistant *Mycobacterium tuberculosis* infections: factors in transmission to staff and HIV-infected patients. *JAMA* 1992;268:1280-1286.