Editorial

Candida Species: Emerging Hospital Bloodstream Pathogens

Richard P. Wenzel, MD, MSc; Michael A. Pfaller, MD

For years, the conventional wisdom was that ***Candida*** infections occurred rarely among hospitalized patients, that when they occurred, they represented a terminal event in a patient dying primarily of his or her underlying disease, and that the infecting organism was always unique to the dying patient. Recent studies suggest that these assumptions were not valid.

To begin with, it is obvious that ***Candida*** bloodstream infections are not rare. Data from the Centers for Disease Control and a Statewide Surveillance Program showed a dramatic increase in rates from 1980 to 1990,[1,2] and currently, 10% of all nosocomial bloodstream infections are caused by ***Candida*** species. High-risk patients include those with leukemia, solid tumors and leukopenia, bone marrow transplant recipients, those with gastrointestinal diseases, burn patients, and premature infants.[3-7] Whereas the overall rate of candidemia is 5 to 10 per 10,000 patients admitted, it is considerably greater for these high-risk patients.

Risk factors for infection have now been examined in controlled studies using multivariate analyses to correct for confounding variables. What emerges is that the important independent predictors include the number of antibiotics used prior to infection, the presence of a central venous or tunneled vascular catheter, the isolation of ***Candida*** at another anatomic site, and prior hemodialysis.[5,6,8,9] The odds ratios will vary among the different studies depending on whether the controls are matched for the underlying diseases.

Once infected, the crude (overall) mortality of ***Candida*** bloodstream infection for most series is over 50%. In an earlier study of nosocomial bloodstream infections, it was shown that infection with ***Candida*** independently predicted mortality apart from the underlying disease.[10] This was surprising because of the prevailing notion of a nonvirulent pathogen that caused infection only in association with moribund patients. In fact, some authors used the term "benign candidemia" to highlight the perceived lack of need for extended antifungal therapy for vascular catheter-associated ***Candida*** bloodstream infection. An historical control study by Wey et al[8] confirmed the malignant nature of ***Candida*** bloodstream infections: 57% of cases died and 19% of diagnosis-matched controls died, leaving a 38% attributable (direct) mortality. The latter figure refers to the mortality of the infection above and beyond that expected from the underlying diseases alone.

Recently, it has been shown that bone marrow transplant patients and patients with leukemia tend to acquire a bloodstream infection with a unique *Candida* strain after a mean of eight days of colonization with the same strain.[11] It is likely that these patients are usually in a private room with assiduous infection control practices observed by healthcare workers. The epidemiology of ***Candida*** bloodstream infections for patients in busy critical care units, however, may be different. With currently available typing systems, it is now possible to show that small epidemics of cross-infection with a single ***Candida*** species probably have occurred.[12,13] The inferences are derived by recognizing infections caused by the same strain clustered in time and space and different from control strains at the same institutions. Moreover, serious postoperative wound infections have been recognized to be caused by a single strain of ***Candida*** *tropicalis* and traced to a circulating operating room nurse.[14] Because ***Candida*** species have been found to stick to

From the Division of General Medicine, Clinical Epidemiology, and Health Services I&search, Department of Internal Medicine, The University of Iowa Hospitals and Clinics, Iowa City, Iowa *(Dr. Wenzel), and the Clinical Laboratory, Department of Pathology, Oregon Health Science University, Portland, Oregon (Dr. Pfaller).*

Address reprint requests to Richard I? Wenzel, MD, MSc, Division of General Medicine, Clinical Epidemiology, and Health Services Research, C41 GH, The University of Iowa Hospitals and Clinics, Iowa City, IA 52242.

Wenzel RP, Pfaller MA. Candida ***species: emerging hospital bloodstream pathogens.*** Infect Control Hosp Epidemiol. *1991;12:523-*524.

https://doi.org/10.1086/646403 Published online by Cambridge University Press

latex gloves in experimental situations even after disinfecting the gloves,[15] and because 5% of healthcare workers' hands in critical care units at The University of Iowa have been found to harbor ***Candida*** species, the hypothesis of cross infection is strengthened. Prospective studies may confirm this idea.

In rough figures, one might view the outcome of ***Candida*** bloodstream infection as follows: 35% will survive hospitalization; 30% will die of their underlying disease; and 35% will die as a direct consequence of the infection (attributable mortality). To improve the outcome, we need better drugs to treat the underlying disease and better antifungal agents to improve the attributable mortality. Better still, if we could prevent colonization or interrupt it should it occur, we would greatly reduce the morbidity, mortality, and economic burden incurred by infection in high-risk patients. Future studies might include controlled clinical trials of prophylactic agents to prevent colonization of empiric agents for early treatment of suspected infections and of therapeutic agents to treat recognized ***Candida*** bloodstream infections. Additionally, epidemiological studies of the effectiveness of various components of infection control, antibacterial drug use, and optimal vascular catheter guidelines for insertion and management are urgently needed.

As we approach the year 2000, there is a great opportunity for young investigators to tackle an increasingly important problem in hospitals. The prevention and control of life-threatening ***Candida*** infections will require a pioneering spirit, energy, tenacity, and above all, an open mind that questions the conventional wisdom of the day.

REFERENCES

1. Horan T, Culver D, Jarvis W, et al. Pathogens causing nosocomial infections: preliminary data from the national nosocomial infectious surveillance system. *Antimicrob Newsletter* 1988;5:65-67.
2. Morrison AJ Jr, Freer CV, Searcy MA, Landry SM, Wenzel RI? Nosocomial bloodstream infections: secular trends in a statewide surveillance program in Virginia. *Infect Control.* 1986;7:550-553.
3. Harvey RL, Myers JP. Nosocomial fungemia in a large community teaching hospital. *Arch Intern Med.* 1987;147:2117-2120.
4. Prasad JR, Feller I, Thompson PD. A ten-year review of *Candida* sepsis and mortality in bum patients. Surgery. 1987;101:213-216.
5. Weese-Mayer DE, Fondriest DW, Brouillette RT, Shulmas ST Risk factors associated with candidemia in the neonatal intensive care unit: a case-control study. *Pediatr Znfect DN J.* 1987;6:190-196.
6. Karabinis A, Hill C, Leclercq B, Tancrede C, Baume D, Andremont A. Risk factors for candidemia in cancer patients: a case control study. *J Clin Microbiol.* 1988;26:429-432.
7. Wey SB, Mori M, Pfaller MA, Woolson RF, Wenzel RF! Hospital acquired candidemia: the attributable mortality and excess length of stay. *Arch Intern Med.* 1988;148:2642-2645.
8. Wey SB, Mori M, Pfaller MA, Woolson RF, Wenzel RP. Risk factors for hospital acquired candidemia: a matched case-control study. *Arch Intern Med.* 1989;149:2349-2353
9. Bross J, Talbot GH, Maislin G, Hurwitz S. Risk factors for nosocomial candidemia: a case-control study in adults without leukemia. *Am J Med.* 1989;87:614-619.
10. Miller PJ, Wenzel RI? Etiologic organisms as independent predictors of death and morbidity associated with bloodstream infections. */Infect Dis.* 1987;156:471-477.
11. Reagan DR, Pfaller MA, Hollis RJ, Wenzel RI? Characterization of the sequence of colonization and nosocomial candidemia using DNA fingerprinting and a DNA probe. *J Clin Microbiol.* 1990;28:2733-2738.
12. Burnie JP, Odds FC, Lee W, Williams JD. Outbreak of systemic candida albicans in intensive care unit caused by cross infection. *Br Med J.* 1985;290:746-748.
13. Phelps M, Ayliie GAJ, Babb JR. An outbreak of candidiasis in a special care baby unit: the use of resistogram typing method. *J Hosp Infect.* 1986;7:13-20.
14. Doebbeling BN, Pfaller MA, Houston AK, Wenzel RP. Removal of nosocomial pathogens from the contaminated glove: implications for glove reuse and handwashing. *Ann Intern Med.* 1988;109:394-398.
15. Doebbeling BN, Hollis RJ, Isenberg HD, Wenzel RP, Pfaller MA. Restriction fragment analysis of a Candida *tropicalis* outbreak of sternal wound infections. *J Clin Microbiol.* 1991;29:1268-1270.

https://doi.org/10.1086/646403 Published online by Cambridge University Press