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# Use of Fungal Blood Cultures in an Academic Medical Center▽

Aaron R. Kosmin† and Thomas Fekete*

*Temple University School of Medicine, Department of Medicine, Section of Infectious Diseases, 3401 N. Broad St., Philadelphia, Pennsylvania 19140*

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**We studied the use of fungal blood cultures in our hospital. They added little compared to routine culture results, but clinicians ordered them for sicker patients, when facing diagnostic uncertainty, or after prior candidemia. We need a practical guideline for when to order fungal blood cultures.**

There are neither guidelines nor expert consensus regarding the proper use of dedicated fungal blood cultures. Although lysis centrifugation is a mature technology (2, 6), studies showing a higher yield of dedicated fungal blood culture results compared to routine blood culture results have generally been done in controlled laboratory assays (4) but not in a patient care context (5). Modern automated blood culture systems perform well for the most prevalent fungal bloodstream pathogens: *Candida* and *Cryptococcus* spp. The current gap in standard blood culture analyses is in the realm of finding molds and endemic fungi, but this need is only partially fulfilled by the use of fungal blood cultures (3).

Because we had little information about the use of fungal blood cultures in our institution, we did a pilot survey of positive fungal blood cultures. Over 8 months in 2004, 22 (6%) of 380 fungal blood cultures gave positive results, the majority representing *Candida* spp. A previously undocumented infection was found in less than one-half of the positive tests. Thus, the number of fungal blood cultures done to diagnose each fungemia was 16, and the number to find a previously undiagnosed fungemia was 34. Given this low yield, we wanted to study the characteristics of patients for whom fungal blood cultures were ordered.

The cases represented the first 100 adult patients with fungal blood cultures (obtained using an Isolator collection system [Wampole Laboratories, Cranbury, NJ]) submitted in 2005 from our urban 550-bed adult general hospital located in Philadelphia. For each patient for whom a fungal blood culture assay had been performed, a control patient was randomly selected from inpatients with routine blood culture results (determined using a VersaTREK system [TREK Diagnostic Systems, Cleveland, OH]) sent on the same date as those from the corresponding fungemia case. We performed a chart review for cases and controls to identify potential factors that could lead doctors to order fungal blood cultures, including patient demographics, comorbidities, and the use of other relevant diagnostic tests. We also conducted a subgroup analysis comparing those patients with fungal blood isolates (whether a case or a control) to those who did not have fungemia. Because of our retrospective study design, we could not collect information on the volume of blood sent for either culture system.

The mean age of cases was 51 (range, 16 to 89). Of these cases, 62% were male and 43% were in an intensive care unit (ICU). We found no gender or age differences between cases and controls. Significant ($P < 0.05$) results are shown in Table 1. The average duration of hospitalization at the time of the fungal blood culture for cases was 35 days compared to 19 for the controls. The in-hospital mortality for case patients was 24% (relative risk = 8). Of the comorbid conditions studied, only abdominal surgery and human immunodeficiency virus infection were overrepresented among cases. There was no difference in the levels of prevalence of diabetes, trauma, thoracic surgery, solid organ transplant, dialysis, cancer, or bowel disease. There was an excess among cases for several risk factors: central intravenous lines, parenteral alimentation, and prior fungal colonization. The case patients were sicker than the controls: duration of hospital stay and ICU care (especially in the surgical ICU) were greater among cases. Previously documented fungemia was also present for six cases but for no controls. Among cases, there were more total cultures, prior blood cultures, hospital days prior to index culture, acid-fast bacillus blood cultures, and tests for cytomegalovirus.

Ten cases (but no controls) had documented fungemia (7 cases of *Candida albicans* infection, 2 of *C. glabrata* infection, and 1 of *C. parapsilosis* infection). We compared them to the patients without fungemia. Of those 10 cases, only three had positive fungal blood culture results; most candidal isolates from our patients were from routine blood cultures. Having fungemia was (not surprisingly) strongly associated with parenteral nutrition and abdominal surgery ($P < 0.01$ for both). All 10 fungemic patients received appropriate antifungals. Interestingly, 50% of the other 90 cases also received antifungal treatment ($P = 0.01$).

Attempts to measure the enhanced sensitivity of dedicated fungal blood cultures over that of routine cultures may be limited by the infrequency of fungemia and the improved performance of routine blood cultures in assessing candidemia. The changing technology makes it difficult to point out a superior system for all the needs of the clinician, i.e., a system that offers rapidity of results and the spectrum of tests (bacterial, mycobacterial, and fungal) that may be needed for sick

* Corresponding author. Mailing address: Temple University School of Medicine, Department of Medicine, Section of Infectious Diseases, 3401 N. Broad St., Philadelphia, PA 19140. Phone: (215) 707-1982. Fax: (215) 707-4414. E-mail: tomfeke@temple.edu.

† Present address: Albert Einstein Medical Center, Department of Medicine, Klein Professional Building, Suite 363, 5401 N. York Rd., Philadelphia, PA 19141.

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TABLE 1. Factors that varied significantly ($P < 0.05$) between patients with dedicated fungal blood culture results (cases) and those with routine blood culture results (controls)

| Variable[a] | Value for: | | *P* value |
|---|---|---|---|
| | Positive cases ($n = 100$) | Controls ($n = 100$) | |
| Severity of illness | | | |
| Mortality (%) | 24 | 3 | <0.01 |
| Mean stay (no. of days) | 35 | 19 | <0.01 |
| ICU (%) | 43 | 26 | 0.01 |
| SICU (%) | 22 | 5 | <0.01 |
| Comorbidity | | | |
| Abdominal surgery (no. of cases) | 22 | 6 | <0.01 |
| HIV infection (no. of cases) | 35 | 5 | <0.01 |
| Fungemia risks | | | |
| Central IV line (no. of cases) | 54 | 36 | <0.01 |
| Parenteral nutrition (no. of cases) | 19 | 1 | <0.01 |
| Fungal colonization (no. of cases) | 24 | 3 | <0.01 |
| Prior fungemia (no. of cases) | 6 | 0 | 0.03 |
| Diagnostic delay | | | |
| Total no. of cultures | 7.4 | 5.1 | <0.01 |
| No. of days to collection of index BC | 13.2 | 6.6 | 0.02 |
| No. of prior BCs | 4.8 | 2.6 | <0.01 |
| Diagnostic uncertainty | | | |
| AFB BC sent (%) | 31 | 1 | <0.01 |
| CMV test sent (no. of cases) | 18 | 3 | <0.01 |

[a] Values represent the period prior to the date of collection of the index blood culture (BC) (except in cases of mortality). SICU, surgical ICU; HIV, human immunodeficiency virus; IV, intravenous; AFB, acid-fast bacillus; CMV, cytomegalovirus.

patients (7). Our clinicians tended to use these special cultures when caring for sicker patients, when facing diagnostic uncertainty, and after prior candidemia was detected with routine cultures. We did not survey our clinicians to see how familiar they were with the various kinds of blood culture technology used in our hospital, but there is no curricular training on the variations of blood cultures on offer in our clinical programs. Our study showed that even in this cohort of patients with multiple risk factors, undetected fungemia is uncommon and fungal blood cultures may not perform better than routine blood cultures.

The lack of evidence to help determine when the use of dedicated fungal blood cultures is appropriate permitted an inefficient use of this technology. We recognize the small sample size and retrospective nature of our study as limitations of our case-control study. In addition, we could not ascertain the specimen volume in our routine or dedicated fungal blood cultures. Furthermore, we may be underestimating the utility of fungal blood cultures in this geographical area because our location does not include areas of geographically defined endemicity for fungi such as *Coccidioides* spp. and is at the edge of the range for *Histoplasma* spp. (1). Even if we had a better tool for diagnosing fungemia, it might not be as useful now as it would have been in the past, since we are commonly using early, empirical treatment to manage sick patients at high risk for fungemia, as was the situation for half of our cases with negative culture results.

Several approaches could be undertaken to determine the role for fungal blood cultures. We could study whether fungal blood cultures help us in the management of known fungemia. We could try to identify specific settings in which routine blood cultures have failed to detect fungemia and see whether dedicated fungal cultures would be better. We could also ascertain whether newer tests such as PCR might be able to replace fungal blood cultures. Thus, at present and for the foreseeable future, fungal blood cultures will have limited application in most clinical settings (2, 5, 6). The manufacturers of equipment for blood cultures now have excellent "routine" media such as VersaTREK and BacT/Alert FA (bioMérieux, Durham, NC) that seem to have caught up with dedicated fungal blood cultures without sacrificing bacteremia detection. A practice guideline that could incorporate information about the specific clinical, demographic, geographic, or laboratory settings in which fungal blood cultures are warranted could enhance the clinical utility of this limited test. For example, fungal blood cultures could be discouraged for identification of *Candida* or *Aspergillus* spp. in the blood but could be encouraged when endemic mycoses are seen in the differential diagnosis. A more general problem of unvalidated tests also applies to fungal blood cultures: clinicians have come to use them with high hopes and low expectations and remember the occasional positive more than the frequent negative results. The unfettered use of low-yield diagnostic tools can give a false sense of accomplishment but is unlikely to be cost-effective or to alter subsequent diagnostic or therapeutic plans.

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## REFERENCES

1. **Bianchi, M., A. M. Robles, R. Vitale, S. Helou, A. Arechavala, and R. Negroni.** 2000. The usefulness of blood culture in diagnosing HIV-related systemic mycoses: evaluation of a manual lysis-centrifugation method. Med. Mycol. **38:**77–80.
2. **Creger, R. J., K. E. Weeman, M. R. Jacobs, A. Morrissey, P. Parker, R. Fox, and H. Lazarus.** 1998. Lack of utility of the lysis-centrifugation blood culture method for detection of fungemia in immunocompromised cancer patients. J. Clin. Microbiol. **36:**290–293.
3. **Ellepola, A. N. B., and C. J. Morrison.** 2005. Laboratory diagnosis of invasive candidiasis. J. Microbiol. **43:**65–84.
4. **Fricker-Hidalgo, H., F. Chazot, B. Lebeau, H. Pelloux, P. Ambroise-Thomas, and R. Grillot.** 1998. Use of simulated blood cultures to compare a specific fungal medium with a standard microorganism medium for yeast detection. Eur. J. Clin. Microbiol. Infect. Dis. **17:**112–116.
5. **Mess, T., and E. S. Daar.** 1997. Utility of fungal blood cultures for patients with AIDS. Clin. Infect. Dis. **25:**1350–1353.
6. **Morrell, R. M., B. L. Wasilauskas, and C. H. Steffee.** 1996. Performance of fungal blood cultures by using the Isolator collection system: is it cost-effective? J. Clin. Microbiol. 3040–3043.
7. **Vetter, E., C. Torgerson, A. Feuker, J. Hughes, S. Harmsen, C. Schleck, C. Horstmeier, G. Roberts, and F. Cockerill III.** 2001. Comparison of the BACTEC MYCO/F Lytic bottle to the isolator tube, BACTEC Plus Aerobic F/bottle, and BACTEC Anaerobic Lytic/10 bottle and comparison of the BACTEC Plus Aerobic F/bottle to the Isolator tube for recovery of bacteria, mycobacteria, and fungi from blood. J. Clin. Microbiol. **39:**4380–4386.