

Evaluation of BACTEC MYCO/F Lytic Medium for Recovery of Mycobacteria, Fungi, and Bacteria from Blood

DeANNA D. FULLER,^{1*} THOMAS E. DAVIS, JR.,¹ GERALD A. DENYS,² AND MARY K. YORK³

Wishard Health Services, Indiana University School of Medicine,¹ and Methodist Hospital,² Indianapolis, Indiana, and University of California, San Francisco, California³

Received 15 February 2001/Returned for modification 21 March 2001/Accepted 3 June 2001

MYCO/F Lytic medium (MFL), a liquid medium developed for use with the BACTEC 9240 blood culture system, was compared to the Isolator system (IS) for the recovery of fungi and to the BACTEC 13A medium for the recovery of mycobacteria. Recovery of bacteria was compared to routine BACTEC Plus Aerobic/F (AF) blood cultures. Microbial growth was detected in 203 (17%) of 1,166 blood cultures. Fifty-seven specimens were positive for fungi: 35 were positive with both IS and MFL; six were positive with IS only (three *Candida albicans*, one *Histoplasma capsulatum*, one *Candida glabrata*, and one *Fusarium* species isolate); three were positive with AF only (two *C. albicans* and one *Candida parapsilosis* isolate); and 13 were positive with MFL only (five *C. glabrata*, three *C. albicans*, two *Candida krusei*, two *Candida tropicalis*, and one *C. parapsilosis* isolate; $P > 0.05$ versus IS). Eighteen of 19 blood cultures positive for *H. capsulatum* grew in both IS and MFL, although the time to detection for MFL was greater. The mean time to detection for all fungi was 8.15 days for IS and 12.07 days for MFL. Seven hundred forty specimens were also cultured for mycobacteria with MFL and 13A. Forty-four grew mycobacteria; 38 were positive with both 13A and MFL; and 16 were positive with MFL only. *Mycobacterium avium* was recovered from 41 specimens; 36 were positive for both systems and 5 were positive for MFL alone. MFL was also compared to the AF bottle for the same 740 specimens. MFL and AF both detected 34 of the 40 clinically significant bacteria, while IS detected only 15 of 40. In summary, MFL is an excellent medium for the recovery of fungi, mycobacteria, and bacteria; however, the time to detection of *H. capsulatum* is increased.

Blood cultures have become one of the most critically important and frequently performed tests in the clinical microbiology laboratory (1, 5, 9). Various culture systems may be used to recover microorganisms from these specimens, but for optimal recovery, a fully automated system and media that are directly inoculated with the specimens are most desirable (1, 11). Several systems are available for the detection of fungemia, which perform relatively well for the recovery of yeasts (3, 7–9, 12, 15). The Isolator system (IS) (Wampole Laboratories, Cranbury, N.J.) has been the method of choice for the recovery of *Histoplasma capsulatum*, although other systems do show promise (11; D. Fuller, J. Daily, T. Davis, G. Denys, C. Hazelrigg, and M. York, Abstr. 97th Gen. Meet. Am. Soc. Microbiol., abstr. C-231, p. 160, 1997). Several automated systems reliably detect mycobacteria from blood, but often specimens must first be processed by lysis-centrifugation, as with the IS, and the pellet must be inoculated into the medium. Many automated systems exist for the detection of bacteria in blood, and some have well-documented recovery from sterile body fluids as well (1, 9). Often patients with a higher probability for fungemia will also be at risk for mycobacteremia. Therefore, a fully automated blood culture system with a medium that can be directly inoculated with blood and that can recover fungi, mycobacteria, and bacteria would enhance effectiveness in the microbiology laboratory. If that same medium could also recover bacteria with the same efficiency as complementary aerobic culture systems, then the amount of sample needed from

the patient would potentially be decreased without compromising recovery of microorganisms.

Becton Dickinson (Sparks, Md.) has developed such a medium, MYCO/F Lytic medium (MFL). This medium was developed for use on the BACTEC 9000 series of instruments specifically for the recovery of fungi and mycobacteria; however, the growth of bacteria is also detected. Whole blood (3 to 5 ml) is directly inoculated into the MFL bottle, which is placed in the BACTEC 9000 blood culture system instrument (6).

The purpose of this study was to evaluate the BACTEC 9240 instrument and MFL for the recovery and time to detection of fungi and mycobacteria from patients at high risk. We were particularly interested in the growth and detection of *H. capsulatum*, since previous studies indicated that broth culture systems were not optimal (15). We were also interested in the system's capability for recovering both yeast and/or dimorphic fungi and mycobacteria from the same specimen in the same medium. Additionally, we were interested in the recovery of bacteria and how it compared to routine aerobic bacterial cultures, as well as seeing if bacterial detection interfered with the growth and detection of fungi or mycobacteria.

MATERIALS AND METHODS

This study was performed at Wishard Memorial Hospital, Methodist Hospital, and Richard L. Roudebush Veterans Administration (VA) Hospital in Indianapolis, Indiana, and at the University of California at San Francisco (UCSF) from May 1996 to May 1997. Methodist Hospital, VA, and UCSF compared BACTEC MFL to Wampole's IS for the recovery of fungi in blood. Wishard Hospital evaluated BACTEC MFL and its ability to recover fungi compared to that of the IS, as well as the recovery of mycobacteria compared to that of the BACTEC 460TB system using 13A medium. Additionally, at Wishard, a BACTEC Plus Aerobic/F (AF) blood culture bottle was collected and bacterial and/or yeast growth was noted.

An adjunct evaluation was performed at Wishard Hospital, which evaluated

* Corresponding author. Mailing address: Wishard Health Services, Dept. of Pathology, 1001 W. 10th St., Indianapolis, IN 46202. Phone: (317) 630-8060. Fax: (317) 630-6202. E-mail: dfuller@iupui.edu.

the feasibility of a manual reading of the fluorescence of the MFL bottles at and shortly following instrument positivity and at the end of the protocol (42 days) for instrument-negative bottles. The ability to determine visual positivity with a UV light source such as a Wood's lamp or Transilluminator might be helpful if a BACTEC instrument was at full bottle capacity or if the instrument was not available. This manual reading would allow the site to select a shorter BACTEC instrument protocol length (i.e., 14 to 21 days instead of the normal 42-day protocol) and would increase the bottle throughput on the BACTEC instrument. The remaining 21- to 28-day incubation could occur in a 35°C incubator with a periodic visual inspection using the Wood's lamp or Transilluminator. Each MFL bottle was visually inspected (on the same day as instrument positivity or at the end of the 42-day protocol) and was compared to a negative bottle (uninoculated control) by holding the bottles directly on the Transilluminator (365-nm-wavelength UV light) to check the fluorescent sensor on the bottom of the MFL bottle. A negative bottle showed no fluorescence, similar to the negative control, while a positive bottle showed the sensor's bright orange glow on the bottom. If a reading was negative (no fluorescence) or indeterminate (i.e., a very low level of fluorescence), the bottles were placed in an offline incubator and held at 35 to 37°C for 3 days following removal from the BACTEC 9000 instrument. Each bottle was then tested for three consecutive days or until visually positive for fluorescence. If a bottle remained fluorescence negative at the end of 72 h, the contents of the bottle were incubated and read weekly until the end of the 42-day protocol. The manually read fluorescence was compared to that of the BACTEC 9000 system for positivity rate and time to positivity. It was also evaluated for false positivity and false negativity rates compared to smear and subculture results.

Patient selection. At each site, BACTEC MFL bottles were made available to wards and/or clinics caring for patients with a higher probability of fungemia and/or mycobacteremia than would be expected in a general population.

Blood culture collection. Skin was disinfected by a standard technique (8). Following venipuncture, 19 to 30 ml of blood was withdrawn into a sterile syringe and was randomly and aseptically transferred to the following study bottles: 3 to 5 ml in the MFL bottle; 8 to 10 ml in the IS tube; 8 to 10 ml in the AF bottle. At Wishard, an additional 3 to 5 ml of blood was also placed in a BACTEC 13A bottle. All bottles and tubes were gently rocked back and forth to mix the contents of each with the inoculated blood and were transported to the microbiology laboratory. The bottles and tubes were compared against standards filled with known volumes, and those bottles with an inoculum of less than 3 ml for MFL were excluded from the study.

Blood culture processing. All blood culture sets were processed for purposes of patient care, but only complete culture sets with adequate volumes that were received within 16 h of collection were included in the study. The BACTEC MFL and AF bottles were placed in the BACTEC 9240 blood culture instrument as soon as possible after receipt in the laboratory. The BACTEC MFL and AF bottle contents were incubated at 35°C and were continuously monitored by the instrument for microbial growth until indicated as instrument positive or until the end of the incubation period (42 days for MFL and 5 days for AF). The BACTEC 13A bottle contents were incubated in a 37°C incubator for 42 days and were read on the BACTEC 460TB instrument daily for the first 5 days and three times weekly for the remaining 5 weeks. Any BACTEC MFL, AF, or 13A bottle which gave a positive signal by the BACTEC 9240 instrument or the BACTEC 460TB instrument was smeared and stained with acridine orange and Gram's stain for MFL and AF and with auramine-rhodamine for 13A. Regardless of smear results, all positive bottle contents were also subcultured to appropriate media as follows: BACTEC AF to a blood agar plate (BAP) and chocolate agar plate; BACTEC MFL to BAP, a brain heart infusion (BHI) agar plate (with 10% sheep blood, gentamicin, and chloramphenicol), a Middlebrook 7H11 (MB) agar plate, and a Lowenstein Jensen (LJ) agar slant; and BACTEC 13A to BAP, MB, and LJ. The contents of the BAPs were incubated at 35°C in an atmosphere of 5 to 10% CO₂, while the BHI was incubated at 30°C in non-CO₂ and the MB and LJ were incubated at 37°C in 5 to 10% CO₂. All plates were examined daily for the first week. All plates, except the BAPs and chocolate agar plates, which were discarded after 1 week, were examined twice weekly thereafter for a maximum of 42 days.

At the same time that the BACTEC bottles were entered into the 9240 system, the IS tubes were processed according to the manufacturer's recommendations. The centrifuged pellet was inoculated directly to one plate of chocolate agar incubated at 35°C in 5 to 10% CO₂, one plate of Sabouraud dextrose agar incubated at room temperature (non-CO₂), and two plates of BHI with blood (and gentamicin and chloramphenicol) agar (contents of one were incubated at 30°C, while the other's contents were incubated at room temperature [both non-CO₂]). Some sites (Wishard and Methodist) included an additional MB plate (from the IS inoculum), the contents of which were incubated at 37°C in 5

to 10% CO₂. All IS plates were examined daily for the 1st week. The remaining fungal and mycobacterial plates (Sabouraud dextrose agar, BHI, and MB) were examined twice weekly thereafter for the remainder of the 42-day protocol.

All plates and bottles were treated independently. When any bottle or plate grew a microorganism, the other bottles or plates from that set continued to be processed for the remainder of the protocol. Subculturing or staining was not performed on the other bottle and/or the IS tube plates unless evidence of growth was present. At the end of the 42-day testing protocol, terminal subculturing was performed on all negative BACTEC bottles (MFL and 13A). The negative MFL was subcultured to BAP, BHI, and MB, while the 13A was subcultured to MB. The subculture plate contents were incubated as previously described. For each positive culture, the following were recorded: time to positivity, identity of any microorganisms recovered and from which bottle or plate they were recovered, and the clinical significance of each microorganism. One site (Wishard) also recorded the presence of antimicrobial therapy at the time that the blood culture was collected. Additionally, the Transilluminator protocol (manual fluorescence reading) was performed on all MFL bottles as described above.

Clinical assessment. Patients with positive blood cultures were evaluated by a pathologist, an infectious-disease consultant, or an attending clinician to determine whether microorganisms isolated from the blood culture were clinically significant. This assessment was made in accordance with published criteria (12).

Data analysis. The data were collated and analyzed initially for three separate comparisons: MFL versus IS, MFL versus BACTEC 13A, and MFL versus BACTEC AF. The three BACTEC bottles and the IS tube were compared for ability to recover microorganisms (yield) and for the time required to detect microbial growth. Additionally, the Transilluminator and BACTEC 9000 system positivity rates were compared. All comparisons were analyzed statistically with McNemar's chi-square test with Yates correction for small numbers when necessary (4) and with the Student *t* test (2) for time to detection. Differences in yield or time to detection were considered statistically significant if the chi-square value was ≥ 3.84 (i.e., if $P < 0.05$).

RESULTS

A total of 1,166 blood cultures were included in this study. Seven hundred forty were collected from Wishard, 371 from Methodist, 36 from UCSF, and 19 from VA. Clinically significant microbial growth, including the growth of fungi, mycobacteria, and bacteria, was detected in 162 (14%) cultures; a fungus and/or mycobacterium was recovered from 122 (10%) cultures.

Fifty-seven specimens from 19 patients were positive for fungi; of these, 35 specimens were positive with both the MFL system and IS. Six specimens were positive with IS only, three specimens were positive with AF only, and 13 specimens were positive with MFL only (for IS versus MFL, $P < 0.05$; for AF versus MFL, $P < 0.25$). Nineteen blood culture samples from eight patients were positive for *H. capsulatum*; 15 cultures (from six patients) grew *Candida glabrata*; 13 cultures (from seven patients) grew *Candida albicans*; 3 cultures (from two patients) grew *Candida parapsilosis*; 2 cultures (from two patients) grew *Candida krusei*; 2 cultures (from two patients) grew *Candida tropicalis*; and *Cryptococcus neoformans*, *Cryptococcus albidus*, and a *Fusarium* species were each recovered from one blood sample (Table 1).

Of the 1,166 specimens cultured for fungi in this study, a corresponding culture for mycobacteria was done for 740 samples using MFL and 13A. Sixty-eight of these (from 30 patients) grew mycobacteria; 54 were positive with both MFL and 13A, while 14 were positive with MFL only ($P < 0.001$). Sixty-five samples (from 27 patients) grew *Mycobacterium avium* complex on culture; 54 *M. avium* complex samples were positive from both systems, while 14 were positive with MFL only. One sample was positive for *Mycobacterium tuberculosis* in both systems, one sample was positive for *Mycobacterium ce-*

TABLE 1. Comparison of recovered microorganisms from IS and BACTEC 13A and AF systems with those from MFL^a

Fungal isolate(s)	No. of isolates detected from:			
	IS only	AF only	MFL only	Both MFL system and IS
All (n = 57)	6	3	13	35
<i>H. capsulatum</i>	1	0	0	18
<i>C. albicans</i>	3	2	3	5
<i>C. glabrata</i>	1	0	5	9
<i>C. neoformans</i>	0	0	0	1
<i>C. parapsilosis</i>	0	1	1	1
<i>C. krusei</i>	0	0	2	0
<i>C. tropicalis</i>	0	0	2	0
<i>C. albidus</i>	0	0	0	1
<i>Fusarium</i> species	1	0	0	0

^a P for MFL versus AF is 0.25; P for MFL versus IS is <0.05.

latum in both systems, and one sample was positive for *Mycobacterium kansasii* in MFL only. Additionally, 30 *M. avium* isolates (from 15 patients) were recovered from MB and LJ media inoculated from IS.

Although the remaining 426 specimens were not cultured in 13A, it should be noted that 16 *M. avium* isolates (from six patients) were recovered from both the MFL bottle and the IS MB plates and 8 (from four patients) were recovered from MFL alone. For the 740 blood culture specimens that were cultured for both fungi and mycobacteria, an AF culture bottle was also collected which yielded 16 fungal organisms, 3 of which were recovered from the AF bottle alone.

Because MFL can also recover bacteria, we compared it to AF and IS for recovery of bacteria from the same 740 specimens. MFL and AF both detected 34 isolates (from 26 patients) out of 40 clinically significant bacterial isolates, while the IS detected only 17 (from 16 patients) out of 40 ($P < 0.005$). Isolates included eight *Staphylococcus aureus* specimens; five coagulase-negative staphylococci; eight *Enterococcus* species; nine *Enterobacteriaceae* isolates; seven nonfermenters; and three *Streptococcus pneumoniae* isolates (Table 2).

Multiple clinically significant organisms were detected in five patients. One specimen recovered *C. albicans* and *Enterobacter cloacae* both from MFL, *E. cloacae* only from AF, and *C. albicans* only from IS; one specimen recovered *M. avium* and *H. capsulatum* from MFL, while *H. capsulatum* only was re-

TABLE 2. Comparison of recovered clinically significant bacteria from IS, AF media, and MFL^{a,b}

Bacterial isolate(s)	No. of isolates detected from:		
	IS	AF	MFL
All (n = 40)	17	34	34
<i>S. aureus</i> (n = 8)	3	6	6
CNS ^c (n = 5)	3	5	4
<i>Enterococcus</i> spp. (n = 8)	2	6	8
<i>S. pneumoniae</i> (n = 3)	1	3	2
<i>Enterobacteriaceae</i> (n = 9)	3	8	8
Nonfermenters (n = 7)	5	6	6

^a Wishard Memorial Hospital only.

^b P for IS versus MFL is <0.005.

^c CNS, coagulase-negative staphylococci.

covered from both IS and AF; one specimen recovered *Escherichia coli* and *H. capsulatum* from both MFL and IS and *E. coli* only from AF; one specimen grew *H. capsulatum* and *M. avium* from MFL, whereas IS grew only *H. capsulatum* and 13A grew only *M. avium*; and lastly, one specimen grew *C. glabrata* and *Enterococcus* species from MFL and *Enterococcus* only in both IS and AF.

The time to detection was evaluated for the recovery of both fungi and mycobacteria. Thirty-five fungal isolates were recovered from both IS and the BACTEC MFL. Of those 35, 15 grew faster in IS, while 10 grew faster in MFL. It should be noted that 14 of the 15 isolates that grew faster in IS were *H. capsulatum* ($P < 0.01$). The mean time to detection for this organism was 9.67 days (range, 4 to 23 days) for IS versus 18.4 days (range, 6 to 26 days) for MFL. The eight *Candida* species recovered faster in MFL and had a mean detection time of 5.5 days (range, 2 to 9 days) for IS versus 0.98 days (range, 0.68 to 2.48 days) for MFL.

For the mycobacteria, 38 isolates were recovered from both the BACTEC 13A and BACTEC MFL. Fourteen *M. avium* isolates grew faster in 13A, while 17 grew faster in MFL, with a mean detection time of 13.29 (range, 4 to 36 days) versus 13.16 (range, 6 to 33 days), respectively ($P > 0.05$, not statistically significant). The remaining mycobacterial isolates that grew faster in MFL were *M. tuberculosis* (23 versus 37 days) and *M. celatum* (16 versus 19 days).

Fifty-eight percent of positive blood cultures yielding clinically significant isolates were collected from patients receiving antimicrobial therapy. MFL detected 89% of these isolates, while IS recovered 59%, AF recovered 39%, and 13A recovered 37%; however, this information was documented for only 740 of the 1,166 cultures collected.

Sixty-five specimens (6%) were positive for contaminant organisms, including coagulase-negative staphylococci, *Streptococcus viridans*, *Bacillus* species, *Micrococcus* species, *Corynebacterium* species, and *Penicillium* species. Forty-three (4%) MFL cultures were positive with contaminating organisms, while IS had 17 (1.5%) and AF had 41 (4%).

The adjunct evaluation of the feasibility of a manual reading of the fluorescence of MFL using a Wood's lamp or Transilluminator was performed on 625 blood culture specimens. Of these, 91 MFL bottles were detected as positive by the BACTEC 9240 system and subsequently grew microorganisms. The Transilluminator exhibited fluorescence for 90 out of 91 samples (99% sensitivity and 100% specificity), most within 24 h of instrument positivity.

The BACTEC MFL had 22 (2%) false-positive signals. No organisms were recovered from the terminal subcultures of negative MFL bottles.

DISCUSSION

Although MFL was optimized for the recovery of fungi and mycobacteria in blood, the recovery of bacteria was also evaluated. Furthermore, as previously stated, we were particularly interested in the detection and recovery of *H. capsulatum*, since its recovery seems to be problematic for automated blood culture instruments (15). Despite dissimilar data from studies comparable to ours (11), we found that the recovery of *H.*

capsulatum from MFL was almost equivalent to that from IS; however, the time to detection is much slower in MFL for this organism.

We have also evaluated MFL for the recovery of *H. capsulatum* only in a Mycoses Study Group study (L. J. Wheat et al., submitted for publication). In that study, *H. capsulatum* was recovered from 70 positive cultures. IS recovered 70 out of 70, while MFL recovered 63 of 70. The time to detection was again longer for MFL than for IS, which seemed to correlate inversely with the number of CFU recovered from the IS. That is, the fewer CFU recovered from IS, the greater the time to detection and the likelier that MFL would be falsely negative. We observed the same correlation in this study as well. The one culture that recovered *H. capsulatum* in IS alone grew only 2 CFU. Likewise, the time to detection was greater for MFL from those specimens that had fewer than 5 CFU recovered from the IS.

MFL recovered more *Candida* species, although the difference was not statistically significant. The time to detection for *Candida* was faster in MFL than in IS. Significantly more mycobacteria were recovered from MFL than from the MB plates inoculated with the IS sediment or the 13A blood culture medium. This could be explained by the fact that a smaller volume of IS sediment was inoculated to the 13A medium and to the MB plate (per the study protocol) than the volume of blood that was inoculated into MFL. MFL demonstrated shorter times than did 13A or IS for detection of all mycobacteria recovered.

Although BACTEC MFL has not been marketed for recovery of bacteria in blood cultures, we were very interested in the utility of this product as an "all-purpose" medium for the recovery of clinically significant fungi, mycobacteria, and bacteria from blood. MFL performed better than BACTEC AF and IS for the recovery of bacteria from blood. Additionally, we recovered multiple organisms from the same sample for two specimens. Specifically, from one patient's specimen, we recovered both *H. capsulatum* and *M. avium*; from another, we recovered *H. capsulatum* and an enteric, gram-negative bacillus. From this, one might deduce that optimal recovery of mixed cultures requires a battery of selective and enrichment media that are incubated at a suitable temperature for an appropriate period (4 weeks for fungi and 6 weeks for mycobacteria); however, this warrants further investigation since the numbers are so small.

The adjunct evaluation of using the Wood's lamp or Transilluminator for manual reading of fluorescence did prove reliable but was time consuming. We feel, however, that it would be a good backup should the number of blood culture specimens unexpectedly exceed the instrument capacity. In that situation, the older MFL bottles could be manually removed from the instrument and read by this method for the remainder of the testing protocol.

We believe that MFL and the BACTEC 9240 instrument are an excellent alternative to IS even for the recovery of *H. capsulatum*. It should not, however, be used exclusively for diagnosis of disseminated histoplasmosis due to the delayed time to detection. Other serum- and urine-based tests are available that offer a more rapid turnaround time (14). Another advantage of this medium is direct inoculation of blood into the blood culture bottle. In summary, the 9240 system is nonradiometric and fully automated and continuously monitors growth of fungi, mycobacteria, and bacteria.

ACKNOWLEDGMENT

MFL for this study was provided by Becton Dickinson.

REFERENCES

- Fuller, D. D., and T. E. Davis. 1997. Comparison of BACTEC plus Aerobic/F, Anaerobic/F, Peds Plus/F, and Lytic/F media with and without fastidious organism supplement to conventional methods for culture of sterile body fluids. *Diagn. Microbiol. Infect. Dis.* **29**:219–225.
- Istrup, D. M. 1990. Statistical methods in microbiology. *Clin. Microbiol. Rev.* **3**:219–226.
- Jorgensen, J. H., S. Mirrett, L. C. McDonald, P. R. Murray, M. P. Weinstein, J. Fune, C. W. Trippy, M. Masterson, and L. B. Reller. 1997. Controlled clinical laboratory comparison of BACTEC Plus aerobic/F resin medium with BacT/Alert aerobic FAN medium for detection of bacteremia and fungemia. *J. Clin. Microbiol.* **35**:53–58.
- McNemar, Q. 1962. Psychological statistics, 3rd ed., p. 209–239. John Wiley & Sons, Inc., New York, N.Y.
- Morris, A. J., S. J. Wilson, C. E. Marx, M. L. Wilson, S. Mirrett, and L. B. Reller. 1995. Clinical impact of bacteria and fungi recovered from broth cultures only. *J. Clin. Microbiol.* **33**:161–165.
- Nolte, F. S., J. M. Williams, R. C. Jerris, J. A. Morello, C. D. Leitch, S. Matushek, L. D. Schwabe, F. Dorigan, and F. E. Kocka. 1993. Multicenter clinical evaluation of a continuous monitoring blood culture system using fluorescent-sensor technology. *J. Clin. Microbiol.* **31**:552–557.
- Petti, C. A., A. K. M. Zaidi, S. Mirrett, and L. B. Reller. 1996. Comparison of Isolator 1.5 and BACTEC NR660 aerobic 6A blood culture systems for detection of fungemia in children. *J. Clin. Microbiol.* **34**:1877–1879.
- Pohlman, J. K., B. A. Kirkley, K. A. Easley, B. A. Basille, and J. A. Washington. 1995. Controlled clinical evaluation of BACTEC Plus Aerobic/F and BacT/Alert aerobic FAN bottles for detection of bloodstream infections. *J. Clin. Microbiol.* **33**:2856–2858.
- Reimer, L. G., M. L. Wilson, and M. P. Weinstein. 1997. Update on detection bacteremia and fungemia. *Clin. Microbiol. Rev.* **10**:444–465.
- Reller, L. B., P. R. Murray, and J. D. MacLowry. 1982. Cumitech 1A, Blood cultures II. Coordinating ed., J. A. Washington II. American Society for Microbiology, Washington, D. C.
- Waite, R. T., and G. L. Woods. 1998. Evaluation of BACTEC Myco/F Lytic medium for recovery of mycobacteria and fungi from blood. *J. Clin. Microbiol.* **36**:1176–1179.
- Weinstein, M. P., L. B. Reller, J. R. Murphy, and K. A. Lichtenstein. 1983. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. I. Laboratory and epidemiologic observations. *Rev. Infect. Dis.* **5**:35–53.
- Weinstein, M. P. 1996. Current blood culture methods and systems: clinical concepts, technology, and interpretation of results. *Clin. Infect. Dis.* **23**:40–46.
- Wheat, L. J., P. Connolly-Stringfield, R. Blair, K. Connolly, T. Garringer, and B. P. Katz. 1991. Histoplasmosis relapse in patients with AIDS: detection using *Histoplasma capsulatum* variety *capsulatum* antigen levels. *Ann. Intern. Med.* **115**:936–941.
- Wilson, M. L., T. E. Davis, S. Mirrett, J. Reynolds, D. Fuller, S. D. Allen, K. K. Flint, F. Koontz, and L. B. Reller. 1993. Controlled comparison of the BACTEC high-blood-volume fungal medium, BACTEC Plus 26 aerobic blood culture bottle, and 10-milliliter Isolator blood culture system for detection of fungemia and bacteremia. *J. Clin. Microbiol.* **31**:865–871.