JOURNAL OF CLINICAL MICROBIOLOGY, Feb. 1997, p. 364–368 Vol. 35, No. 2
0095-1137/97/$04.00+0

Comparison of the Mycobacteria Growth Indicator Tube (MGIT) with Radiometric and Solid Culture for Recovery of Acid-Fast Bacilli

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Received 7 June 1996/Returned for modification 13 August 1996/Accepted 31 October 1996

In a multicenter study involving three reference centers for mycobacteria, the rate of recovery of acid-fast bacilli (AFB) and the mean time to their detection from clinical specimens was determined by using the Mycobacteria Growth Indicator Tube (MGIT). These parameters were compared to those assessed by the radiometric BACTEC 460 TB system and by cultivation on solid media. Clinical specimens (n = 1,500) were pretreated with *N*-acetyl-L-cysteine (NALC)-NaOH. The contamination rates for MGITs were 2.0% (center 1), 13.8% (center 2), and 6.1% (center 3). A total of 180 mycobacterial isolates were detected (*M. tuberculosis* complex, n = 113; nontuberculous mycobacteria [NTM], n = 67). When using a combination of liquid and solid media (the current "gold standard" for culture), MGIT plus solid media detected 156 (86.7%) of the isolates, whereas BACTEC plus solid media recovered 168 (93.3%) of all AFB. Between these two gold standards there was no statistically significant difference ($P > 0.05$). The combination of MGIT plus BACTEC detected 171 (95.0%) of all isolates (compared with MGIT plus solid media, $P < 0.01$; compared with BACTEC plus solid media, $P > 0.05$). Considering the efficacies of the different media separately, MGIT was superior to solid media (although not significantly; $P > 0.05$) in detecting AFB but was inferior to the BACTEC system ($P < 0.01$). The mean time to the detection of *M. tuberculosis* complex was 9.9 days with MGIT, 9.7 days with BACTEC, and 20.2 days with solid media. NTM needed, on average, 11.9, 13.0, and 22.2 days to appear by the three methods, respectively. In conclusion, MGIT proved to be a valuable alternative to the radiometric cultivation system.

Despite promising progress in the direct detection of tuberculosis by molecular biological methods, e.g., PCR or transcription-mediated amplification (11), cultures still remain indispensable in the clinical mycobacteriology laboratory. The reasons for this are manifold: (i) the commercial kits presently available detect *Mycobacterium tuberculosis* complex only and do not yet offer a *Mycobacterium* genus screen; (ii) a simple differentiation within the *M. tuberculosis* complex, i.e., *M. tuberculosis* versus *Mycobacterium bovis*, can only be achieved by biochemical methods, which are dependent on the availability of cultures; and (iii) susceptibility testing, when done routinely, again requires ample biomass. Although cultivation is straightforward on solid medium such as Löwenstein-Jensen (LJ) or Middlebrook agar, it is insensitive and may take several weeks. Newer techniques that use liquid medium such as the SeptiChek AFB biphasic system (Becton Dickinson Microbiology Systems, Cockeysville, Md.) or the BACTEC 460 TB radiometric system (Becton Dickinson Diagnostic Instrument Systems, Sparks, Md.) are able to detect mycobacteria within considerably less time (1, 13), but as a whole, they are labor-intensive or have other limitations. This holds true in particular for the BACTEC system, for which the high costs of acquisition, the accumulation of radioactive waste, and the potential danger of needle punctures among laboratory technicians are the most serious drawbacks.

The Mycobacteria Growth Indicator Tube (MGIT; Becton Dickinson Microbiology Systems) has been developed to circumvent some of the limitations described above. MGIT contains a modified Middlebrook 7H9 broth in conjunction with a fluorescence quenching-based oxygen sensor (silicon rubber impregnated with a ruthenium pentahydrate) and can be used for the rapid detection of acid-fast bacilli (AFB) as well as for susceptibility testing (6, 10). MGIT allows for the good growth of most mycobacterial species (16). Preliminary studies report that MGIT detects AFB from clinical specimens with a high degree accuracy and does so rapidly (4, 6, 8, 10, 16). However, those studies were carried out with a limited number of samples (85 sputum specimens [10] up to 500 sputum specimens [8]). Also, MGIT was compared with only a single medium, either with the radiometric BACTEC system medium (6) or with LJ agar (10, 16). In addition, the ratio of smear-positive to smear-negative specimens sometimes remained unknown (8). This parameter is of crucial importance since both recovery and the time to detection of AFB are considerably influenced by the number of organisms present in a clinical specimen.

Our report summarizes the results of a European multicenter study which compared the MGIT technology with the radiometric cultivation system and with the use of solid medium (the current "gold standard" for culture [5, 9]) for both recovery rates and the mean time required to detect mycobacteria from 1,500 clinical specimens.

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MATERIALS AND METHODS

Specimens. A total of 1,500 clinical specimens were consecutively received for culture by the three reference centers for mycobacteria participating in the study (center 1, Zurich, Switzerland; center 2, Borstel, Germany; center 3, Cordoba,

TABLE 1. Rates of recovery of mycobacteria from clinical specimens using liquid and solid culture media

Isolates (no. of isolates)	No. (%) of isolates detected by:					
	MGIT plus solid media (combination A)	BACTEC plus solid media (combination B)	MGIT plus BACTEC (combination C)	MGIT	BACTEC 460 system	Solid media[a,b]
Total (180)	156 (86.7)	168 (93.3)	171 (95.0)	137 (76.1)	158 (87.8)	125 (69.4)
M. tuberculosis complex (113)	104 (92.0)	107 (94.7)	108 (95.6)	92 (81.4)	101 (89.4)	85 (75.2)
All NTM (67)	52 (77.6)	61 (91.0)	63 (94.0)	45 (67.2)	57 (85.1)	40 (59.7)
MAC only (40)	33 (82.5)	39 (97.5)	40 (100)	31 (77.5)	35 (87.5)	30 (75.0)

[a] The values given are means.
[b] Center 1 used LJ medium and Middlebrook 7H10/sel7H11 (biplate), center 2 used LJ medium (with PACT) and Stonebrink, and center 3 used LJ medium only.

Spain). Samples originated from patients admitted to hospitals or consulting private physicians. The bulk of the specimens were from the respiratory tract (sputum samples, bronchial and tracheal aspirates, and bronchoalveolar lavage specimens; 1,062 specimens); urine (177 specimens), pleural fluid (82 specimens), gastric fluid (41 specimens), and miscellaneous samples such as cerebrospinal fluid, lymph node, and biopsy specimens (138 specimens) were also included. Upon receipt, the specimens were kept at 4°C prior to processing with *N*-acetyl-L-cysteine (NALC)-NaOH (see below).

Specimen processing. In all three centers, respiratory, urine, and gastric fluid specimens were liquefied and decontaminated with NALC-NaOH, as recommended by the manufacturer. Lymph nodes and tissue specimens were homogenized in a Ten Broeck mortar. In centers 1 and 3, 100 μl of these homogenates as well as 100 μl of other, normally sterile body fluids (cerebrospinal fluid samples, biopsy samples, pleural aspirates, etc.) were applied to Chocolate II agar (Becton Dickinson Microbiology Systems), and the agar plates were incubated for 48 h at 36 ± 1°C. If the chocolate medium grew contaminants (bacteria or fungi), lymph nodes, tissue specimens, and body fluids were treated with NALC-NaOH; otherwise, these types of specimens were directly inoculated onto mycobacterial growth medium (i.e., without NALC-NaOH pretreatment). Center 2, however, did not use Chocolate II agar since all clinical specimens were pretreated with NALC-NaOH. As described earlier (12), an equal volume of the material used to digest the specimens (3% NaOH, 1.45% sodium citrate, 0.5% NALC [Sigma Chemical Company, St. Louis, Mo.]) was added to 10 ml of a specimen (adjusted to 10 ml with sterile distilled water) and processed as described by Kent and Kubica (5).

Use of MGIT. (i) Quality control. Reference strains (*M. tuberculosis* ATCC 27294, *Mycobacterium kansasii* ATCC 12478, *Mycobacterium fortuitum* ATCC 6841, *Pseudomonas aeruginosa* ATCC 27853, and *Staphylococcus epidermidis* ATCC 12228) were tested initially in each new lot of MGITs. According to the study protocol, mycobacterial suspensions (in sterile saline) were prepared from LJ subculture slants (up to 14 days old) and bacterial suspensions from Columbia agar with 5% sheep blood (24 to 48 h old). Multiple serial dilutions (derived from a 0.5 McFarland nephelometer standard) were made and were finally inoculated into the MGITs.

(ii) Reproducibility. Prior to testing mycobacterial isolates from clinical specimens, reproducibility testing was performed. On 5 consecutive days, a suspension of *M. tuberculosis* ATCC 27294 was prepared to a turbidity equal to that of a 0.5 McFarland nephelometer standard and diluted in sterile saline to 1:5 and 1:500, and each dilution was inoculated into a set of five MGITs. Each set of MGITs was read by two independent observers in absolute darkness. The MGIT was compared to the chemical positive control (0.4% sodium sulfite solution in an uninoculated MGIT from which the broth had been emptied) and the negative control (uninoculated MGIT tube). Tubes were initially read at day 2 and then daily until they were positive. The fluorescence of positive tubes was manifested by a bright orange color on the bottom of the tube and at the meniscus when the tubes were screened with a 365-nm UV lamp. When fluorescence resembled most closely that of the sodium sulfite positive control, the tubes were considered positive.

Cultivation of clinical specimens. Cultivation of mycobacteria was done in liquid medium and on solid media. These included the MGIT and the radiometric BACTEC medium (centers 1 to 3) and an LJ slant without antibiotics (centers 1 and 3) and LJ with polymyxin B, amphotericin B, carbenicillin, and trimethoprim (PACT; Becton Dickinson) (center 2), Stonebrink (center 2), and Middlebrook 7H10/sel7H11 (biplate; Becton Dickinson) (center 1). All media were incubated at 36 ± 1°C. Specimens taken from superficial wounds were inoculated to an additional set of media (MGIT, BACTEC, and solid media) and were incubated at 30°C in order to recover mycobacteria at a lower optimum temperature (e.g., *Mycobacterium marinum*).

A total of 0.5 ml of a specimen of the processed sediments was added to each MGIT (BBL catalog no. 4345111) after 0.5 ml of MGIT oleic acid-albumin-dextrose-citrate (OADC) enrichment and 100 μl of MGIT medium containing polymyxin B, amphotericin B, nalidixic acid, trimethoprim, and azlocillin (PANTA; Becton Dickinson) were added. The tubes were incubated at 36 ± 1°C (with 6% CO_2). For 30 days the tubes were examined daily for fluorescence and thereafter they were examined twice weekly for the last 4 weeks of the study. The time to detection in the MGIT was considered the interval between specimen inoculation and tube fluorescence. The acid fastness of the microorganisms was confirmed by Ziehl-Neelsen staining. Half a milliliter of sediment was cultivated in BACTEC medium (7). Each BACTEC Middlebrook 7H12 medium vial (Becton Dickinson Diagnostic Instrument Systems) was supplemented with 0.1 ml of an antimicrobial mixture (PANTA). The vials were incubated at 36 ± 1°C for 8 weeks. The growth index was read twice per week for the first 2 weeks and weekly thereafter for an additional 6 weeks. The time to detection in the BACTEC system was the interval between specimen inoculation and a vial growth index of >50. Finally, 0.25 ml of the sediments was inoculated onto the solid media, incubated at 36 ± 1°C in 6% CO_2, and inspected weekly for 8 weeks. The acid fastness of the cells was always verified by Ziehl-Neelsen staining.

Microscopy. Smears were stained with auramine-rhodamine fluorochrome. Positive slides were confirmed by Ziehl-Neelsen staining (5).

Identification of mycobacteria. Routine biochemical methods (5, 9) and the Accuprobe culture confirmation kits (Gen-Probe, San Diego, Calif.) were used to identify the isolates. Some of the isolates were identified by their cellular fatty acid patterns (14).

Statistical analysis. χ^2 values were calculated by using Epi Info (version 6.03; Centers for Disease Control and Prevention, Atlanta, Ga.).

RESULTS

In our multicenter study, a total of 1,500 clinical specimens including 70.9% respiratory and 29.1% nonrespiratory specimens were cultivated in liquid (MGIT and BACTEC 460) and on solid (egg- and agar-based) media. Each laboratory processed 500 specimens. Reading of the MGITs with a 365-nm UV lamp was very rapid and was easiest in complete darkness. Only in rare instances were the readings ambiguous. In these cases the tubes were incubated for another 24 h and were read the next day. Contamination rates for MGIT, BACTEC, and solid media were 2.0, 2.4, and 8%, respectively, for center 1; 13.8, 12.4, and 6%, respectively, for center 2; and 6.1, 8.5, and 9.2%, respectively, for center 3.

Cultures positive for AFB were obtained for 180 specimens, of which 70 (38.9%) were smear positive and 110 (61.1%) were smear negative. The mycobacterial isolates included *M. tuberculosis* ($n = 110$), *M. bovis* BCG ($n = 3$), *M. avium* complex (MAC; $n = 40$), *M. fortuitum* ($n = 7$), *M. xenopi* ($n = 6$), *M. gordonae* ($n = 5$), *M. chelonae* ($n = 3$), *M. kansasii* ($n = 3$), *M. gastri* ($n = 1$), *M. celatum* ($n = 1$), and *M. marinum* ($n = 1$).

When comparing the recovery rates on liquid and solid media in combination (gold standard), MGIT plus solid medium (combination A) recovered 156 (86.7%) of all mycobacterial species, while BACTEC plus solid media (combination B) yielded 168 isolates (93.3%; Table 1). Combination A detected 104 of 113 *M. tuberculosis* complex isolates (92.0%) and 52 of 67 isolates of nontuberculous mycobacteria (NTM) (77.6%), whereas combination B detected 107 of 113 *M. tuberculosis* complex isolates (94.7%) and 61 of 67 isolates of NTM (91.0%; Table 1). There was no statistically significant difference between the two gold standards either for the recovery of *M. tuberculosis* complex ($P > 0.05$) or for that of NTM ($P > 0.05$). The two mycobacterial broths (MGIT plus BACTEC; combination C) yielded 108 of 113 (95.6%) isolates of the *M. tuberculosis* complex and 63 of 67 (94.0%) isolates of NTM; i.e., 171 of 180 (95.0%) of all isolates were recovered (Table 1). A

TABLE 2. Detection of mycobacteria from clinical specimens according to initial smear[a]

Isolates (no. of isolates)	No. (%) of isolates detected by:		
	MGIT	BACTEC 460	Solid media[b]
Total of smear-positive specimens (70)	62 (88.6)	67 (95.7)	60 (85.7)
Total of smear-negative specimens (110)	75 (68.2)	91 (82.7)	65 (59.1)
Smear-positive *M. tuberculosis* (54)	47 (87.0)	52 (96.3)	45 (83.3)
Smear-negative *M. tuberculosis* complex (59)	45 (76.3)	49 (83.1)	40 (67.8)
Smear-positive NTM (16)	15 (93.8)	15 (93.8)	15 (93.8)
Smear-negative NTM (51)	30 (58.8)	42 (82.4)	25 (49.0)

[a] A total of 1,500 clinical specimens were tested. Pretreatment with NALC-NaOH was used.
[b] See footnotes *a* and *b* of Table 1.

statistically significant difference was found between combination A and C for the recovery of all mycobacteria ($P < 0.01$) and for NTM ($P < 0.05$), but not for the *M. tuberculosis* complex ($P > 0.05$). Conversely, when combination B was compared with combination C, no statistically significant differences could be found, whether it was for all isolates, *M. tuberculosis* complex only, or NTM only.

Focusing on each type of cultivation system separately, mycobacteria mostly grew in or on more than one type of medium. Recovery rates for mycobacteria in each culture system (MGIT, BACTEC, and solid media) are also summarized in Table 1. MGIT and the BACTEC system detected 76.1 and 87.8% of all isolates, respectively, whereas the solid media used in this study detected 69.4% of all isolates (MGIT versus solid media, $P > 0.05$; MGIT versus BACTEC, $P < 0.01$; BACTEC versus solid media, $P < 0.01$). Similar values were obtained for the isolation of *M. tuberculosis* complex, demonstrating again that MGIT and BACTEC were more sensitive than conventional solid media (81.4 and 89.4% for MGIT and BACTEC, respectively, versus 75.2% for solid media; MGIT versus solid media, $P > 0.05$; MGIT versus BACTEC, $P > 0.05$; BACTEC versus solid media, $P < 0.01$). For NTM, recovery by MGIT was also higher than that on solid media (67.2 versus 59.7%, respectively; $P > 0.05$) but inferior to recovery by BACTEC (85.1%; MGIT versus BACTEC, $P < 0.05$; BACTEC versus solid media, $P < 0.01$).

The rates of recovery for mycobacteria from smear-positive and smear-negative specimens are presented in Table 2. Overall, MGIT and BACTEC detected 88.6 and 95.7% of the smear-positive specimens, respectively, whereas solid media detected 85.7% of the smear-positive specimens (no statistical difference for *P* values). In smear-negative specimens the rates of recovery of mycobacteria were 68.2 and 82.7% with MGIT and BACTEC, respectively, compared to 59.1% with solid media (MGIT versus solid media, $P > 0.05$; MGIT versus BACTEC, $P < 0.05$; BACTEC versus solid media, $P < 0.01$). For *M. tuberculosis* complex, whether the strains were isolated from smear-positive or smear-negative specimens, there was no statistically significant difference between the performance of the media. Except for smear-positive specimens which grew NTM, the sensitivity of MGIT for NTM was significantly lower than that of BACTEC ($P < 0.05$) but higher (although not significantly; $P > 0.05$) than that of solid media.

Many isolates grew only on a single medium, while they did not grow on any of the other ones. MGIT alone detected six additional isolates of *M. tuberculosis* (which were missed by BACTEC and solid media), while BACTEC detected seven additional isolates of the *M. tuberculosis* complex (*M. tuberculosis*, $n = 4$; *M. bovis* BCG, $n = 3$) as well as 13 isolates of NTM (MAC, $n = 4$; *M. fortuitum*, $n = 6$; *M. marinum*, $n = 1$; and *M. xenopi*, $n = 2$). Solid media, finally, detected eight isolates (five *M. tuberculosis* isolates on LJ medium and three isolates of NTM [*M. kansasii*, *M. fortuitum*, and *M. gordonae*] on Middlebrook agar) which could not be recovered by either liquid medium.

Overall, the mean times to detection for all mycobacterial isolates were 14, 13.5, and 23.1 days in MGIT, in BACTEC, and on solid media, respectively (Table 3). *M. tuberculosis* complex was detected from smear-positive specimens after 9.9 days, on average, when using MGIT, 9.7 days when using BACTEC, and 20.2 days when using solid media. For smear-negative specimens, the values were 20.3, 18.0, and 27.2 days, respectively. Growth of *M. tuberculosis* complex in smear-positive and smear-negative specimens occurred in the MGIT after a few days (4 and 5 days, respectively), similar to what has been observed for the BACTEC system (2 and 4 days, respectively). In contrast, the earliest growth of *M. tuberculosis* on solid media was not observed before 9 days (smear-positive specimens) and 17 days (smear-negative specimens). MGIT detected NTM ($n = 67$) in a mean time of 11.9 days, BACTEC detected NTM in a mean time of 13.0 days, and solid media detected NTM in a mean time of 22.2 days. Of all NTM, MAC exhibited the shortest mean time to detection: 7.2 days in MGIT, followed by 8.9 days in BACTEC and 22.9 days on solid media. For all other NTM species (*M. fortuitum*, *M. xenopi*, *M. gordonae*, *M. chelonae*, *M. kansasii*, *M. gastri*, *M. celatum*, and *M. marinum*; $n = 27$), the average time to detection in liquid media exceeded that observed on solid media (36.1 days for MGIT, 30.4 days for BACTEC, and 26.2 days for solid media).

DISCUSSION

The worldwide increase in the incidence of tuberculosis (15) and the growing number of mycobacterioses in immunocom-

TABLE 3. Mean time to detection of mycobacteria in clinical specimens[a]

Culture method	Average no. of days (range) to detection of:				
	All isolates ($n = 180$)	*M. tuberculosis* complex ($n = 113$)		All NTM ($n = 67$)[b]	MAC ($n = 40$)[c]
		Smear-positive specimens ($n = 54$)	Smear-negative specimens ($n = 59$)		
MGIT	14.0 (2–53)	9.9 (4–20)	20.3 (5–46)	11.9 (2–53)	7.2 (2–17)
BACTEC 460 system	13.5 (2–51)	9.7 (2–23)	18.0 (4–38)	13.0 (2–51)	8.9 (2–34)
Solid media[d]	23.1 (8–54)	20.2 (9–49)	27.2 (17–47)	22.2 (8–54)	22.9 (8–54)

[a] Pretreatment with NALC-NaOH was used.
[b] Smear-positive specimens contained 16 isolates (14 MAC, 1 *M. kansasii*, and 1 *M. celatum*); smear-negative specimens contained 51 isolates.
[c] Smear-positive specimens contained 14 isolates; smear-negative specimens contained 26 isolates.
[d] See footnotes *a* and *b* of Table 1.

promised patients (3) require fast and efficient cultivation strategies that can easily be applied in a clinical mycobacteriology laboratory. One of the most recent developments, MGIT, points in this direction: it is easy to handle, is nonradiometric, and at present does not need costly instrumentation. Our multicenter study compared MGIT with established cultivation techniques for AFB and defined two of the most important parameters of a medium, the rate of recovery and mean time to detection, i.e., sensitivity and speed. We are well aware that comparative studies of this type bear two major biases which cannot, however, be eliminated in a routine clinical laboratory, where standardized protocols for cultures must be strictly followed. First, the inoculum size was not equal for each of the different media (0.5 ml of the sediment for MGIT and BACTEC and ≤0.25 ml for solid media), and second, the reading frequency was not the same for all media (for MGIT reading was daily for the first 4 weeks and twice weekly thereafter; for BACTEC reading was initially three times per week for the first 2 weeks and once weekly thereafter; for solid media reading was once weekly).

Contamination was not a serious problem, at least as far as centers 1 and 3 were concerned (2 and 6.1%, respectively, for MGIT; 2.4 and 8.5%, respectively, for BACTEC; and 8 and 9.2%, respectively, for solid media). These values compare well with those reported by Palaci et al. (10) (7.8% for MGIT and 4.5% for LJ medium) and Sewell et al. (13) (5.5% for BACTEC and 7.0% for LJ medium). In contrast, the contamination rate seen at center 2 for both liquid media was unusually high (13.8% for MGIT and 12.4% for BACTEC) and parallels the findings of Cornfield et al. (2). In our case, it is most likely explained by the commonly encountered delays in sample processing due to the late arrival of the specimens at that particular center (2 to 5 days after specimen collection).

It is generally accepted that the use of a combination of liquid plus solid media (gold standard) is essential in good laboratory practice for the isolation of mycobacteria. Our study design complied well in this respect. The use of solid media differed, however, among the study centers (center 1 used LJ plus agar-based medium, center 2 used two egg-based media, and center 3 used LJ medium only). Nevertheless, recovery rates were about equal on all solid media, and the same held for the mean time to detection. Our results demonstrated that there was no statistically significant difference between a gold standard consisting of MGIT plus solid media (combination A) or BACTEC plus solid media (combination B) for the recovery of *M. tuberculosis* isolates (92 versus 94.7%, respectively; $P > 0.05$). The same held for NTM, in which 77.6 and 91.0% of the isolates could be detected by combinations A and B, respectively ($P > 0.05$). The combination of the two liquid media (MGIT plus BACTEC, combination C) was, however, even more efficient in isolating mycobacteria than the use of the gold standards described above (combination A, 86.7%; combination B, 93.9%; and combination C, 95.0%). Statistically significant differences between combinations C and A were found for the total number of mycobacterial isolates ($P < 0.01$) and NTM ($P < 0.05$), but not for the *M. tuberculosis* complex, while no significant difference was found between combinations C and B. These data suggest that a combination of two liquid media may be more attractive than the use of a liquid plus a solid medium (the traditional gold standard). However, in light of the drawbacks of radiometric growth technology, future studies should primarily aim at defining the efficacy of combined liquid media which do not contain radioisotopes.

Considering each cultivation method separately, both liquid media were superior to the conventional solid media, a result which had previously been shown for BACTEC and a biphasic system (SeptiChek) (1, 13). For the isolation of *M. tuberculosis* by using MGIT, the difference in our study was statistically not significant when compared with that for solid media ($P > 0.05$), in contrast to the results for BACTEC versus solid media ($P < 0.01$). Similar findings were reported by others (6, 16). In a comparison of the two liquid media with each other, there was, again, no significant difference ($P > 0.05$); MGIT detected 87.0% of the smear-positive *M. tuberculosis* complex isolates, while BACTEC recovered 96.3% of the smear-positive isolates; of the smear-negative specimens that grew *M. tuberculosis* complex, MGIT detected 76.3% and BACTEC detected 83.1%. Except for the 16 smear-positive specimens which have grown MAC (recovery rate, 93.8% on all media), detection of NTM from smear-negative specimens by MGIT was unsatisfactory. MGIT detected 58.8%, BACTEC detected 82.4%, and solid media detected 49.0% (MGIT versus solid media, $P > 0.05$; MGIT versus BACTEC, $P < 0.05$; BACTEC versus solid media, $P < 0.01$). These data emphasize that BACTEC may be better for recovering NTM from smear-negative specimens.

Our study demonstrates, furthermore, that the isolation rate conceivably increased with the number of media used: six more isolates of *M. tuberculosis* could be found when MGIT was added to the gold standard consisting of BACTEC plus solid media (combination B). Conversely, BACTEC detected 4 more *M. tuberculosis* isolates, 3 more *M. bovis* BCG isolates and 13 more NTM isolates, respectively, which had been missed by MGIT plus solid media (combination A). Workload, financial resources, and in particular, the restricted amount of sediment of a clinical specimen are, however, the limiting factors in working with too many different types of media in a laboratory. Thus, cultivation of mycobacteria always remains a compromise.

The mean time to detection of *M. tuberculosis* complex from smear-positive specimens by MGIT was equal to that of the BACTEC (9.9 versus 9.7 days, respectively) and was half of that observed for solid media. The average time of 9.5 days for the detection of *M. tuberculosis* given by Kodsi et al. (6) is thus confirmed by our much larger study. Also, for smear-negative specimens there was an insignificant difference in the mean time to detection between MGIT and BACTEC (20.3 versus 18.0 days, respectively), and the mean time to detection in MGIT was again much faster than that on solid media. Excellent values were also obtained for NTM (11.9 days in MGIT 13.0 days in BACTEC) as well as for all mycobacterial isolates (14.0 versus 13.5 days, respectively). Most remarkably, MGIT provided for the very early detection (as little as 2 days) of MAC (7.2 days versus 8.9 days for BACTEC).

From our data, three major conclusions can be drawn. (i) Although a combination of two liquid media (MGIT plus BACTEC) yielded a higher rate of recovery of mycobacteria than a combination of liquid with solid media, such an approach is limited by the cost and logistical disadvantages of handling and disposing of radioactive materials within the BACTEC technology. (ii) As long as a combination of liquid and solid media is maintained, MGIT can be considered a replacement for the radiometric component in the current cultural gold standard, since no statistically significant difference between combinations A and B (MGIT plus solid media versus BACTEC 460 plus solid media, respectively) was found. (iii) The rapidity by which mycobacteria are detected is the most obvious advantage of MGIT, allowing for the detection of mycobacteria within the same amount of time as BACTEC. These facts, together with the simplicity and flexibility of the system, make MGIT a suitable nonradiometric alternative to other mycobacterial liquid media. Should an automated system incorporating MGIT technology be made available, the elim-

ination of current sources of errors, such as the visual reading of fluorescence, may further enhance performance.

ACKNOWLEDGMENTS

We thank Alexander von Graevenitz for helpful suggestions. Becton Dickinson provided us with the MGIT medium.

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