Short Communication

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The BACTEC MGIT™ 320 system as a laboratory tool to diagnose tuberculosis in a Brazilian hospital with a high prevalence of HIV infection

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ABSTRACT

Introduction: The World Health Organization endorses the BACTEC Mycobacterial Growth Indicator Tube (MGIT)™ system as a rapid, sensitive, and specific method to diagnostic of tuberculosis. Here, we compared the performance of this system against Ogawa-Kudoh cultures and microscopy. **Methods:** A total of 927 samples were obtained between December 2011 and December 2013 from 652 cases of suspected tuberculosis at the School Hospital of the Federal University of Rio Grande in Brazil. **Results:** The MGIT system confirmed tuberculosis in more cases in less time. **Conclusions:** The MGIT system is an effective tool for early diagnosis of tuberculosis, especially in patients with HIV/AIDS.

Keywords: Diagnosis. HIV coinfection. Tuberculosis.

A major factor driving the spread of tuberculosis is the considerable delay in diagnosis and treatment[1]. Thus, early detection is essential[2]. Tuberculosis can be diagnosed by sputum smear microscopy for acid-fast bacilli. However, this method has poor sensitivity, especially in samples with low bacterial load[3]. On the other hand, bacilli cultures are more sensitive than microscopy, are highly specific, and are thus the gold standard for detecting *Mycobacterium tuberculosis*. Moreover, isolation of the microorganism allows identification to species, determination of susceptibility to antimicrobials, and molecular studies. However, culture on solid media requires 20-40 days. In contrast, systems such as the Mycobacterial Growth Indicator Tube (MGIT), which are commercially available and are based on liquid media, require only 10-15 days[2].

Despite its advantages as high accuracy and fastness to obtain the results, the BACTEC MGIT™ 960 system is typically only used in reference laboratories with the required infrastructure. BACTEC MGIT™ 320, a more compact version more suitable for satellite laboratories, has also been released. However, any new method or approach, regardless of sophistication, commercial availability, or in-house testing and development, should be evaluated through well-designed and well-controlled clinical trials in endemic, low-resource settings, where such methods are most needed[4] [5]. One such setting is the coastal lagoon micro-region in the State of Rio Grande do Sul in Brazil, a high-priority city for tuberculosis control, with estimated population over 240,000. In 2013, the incidence of tuberculosis was 57.4/100,000 in the city[6] and 43.2/100,000 in the state, whereas the national incidence was 35.4/100,000[7]. Additionally, the incidence of patients living with HIV/AIDS was 9.1/100,000 in the state, the highest in the country[8], with 19.3% of HIV patients co-infected with *M. tuberculosis* in 2013[7].

In this study, we evaluated BACTEC MGIT™ 320 as a routine diagnostic tool for tuberculosis at the Dr. Miguel Riet Corrêa Jr. Hospital of the Federal University of Rio Grande/ Rio Grande do Sul in Brazil, a 204-bed reference hospital for the care of patients living with HIV/AIDS. Between December 2011 and December 2013, we obtained 447 pulmonary and 480 extrapulmonary samples from 652 patients with suspected tuberculosis, of whom 291 were HIV-positive. The patient population consisted of 253 females and 399 males 1-96 years. This study was grounded in ethical principles, and was approved by the Research Ethics Committee in the Area of Health of the Federal University of Rio Grande (Protocol 76/2012).

Each sample was tested by smear microscopy for acid-fast bacilli and by culture in Ogawa-Kudoh solid media and MGIT liquid media. For microscopy, smears were stained with Ziehl-Neelsen method[9]. Samples for culture were decontaminated with N-acetyl-L-cysteine and sodium hydroxide[10], centrifuged for 15 minutes at 3,000 ×*g*, and 0.1mL or 0.5mL of the pellet was inoculated into in-house Ogawa-Kudoh media[10] and commercial MGIT media. Media were supplemented with oleic acid, albumin, dextrose, catalase, polymyxin antibiotic mixture B, trimethoprim, amphotericin B, azlocillin, and nalidixic acid. Ogawa-Kudoh cultures were incubated at 37°C and checked for

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growth once per week up to eight weeks, while MGIT tubes were monitored hourly up to 42 days in the automated BACTEC MGIT™ 320 system. Growing isolates were confirmed to be *M. tuberculosis* by PCR of the IS*6110* insertion region using the primers INS-1 (5'-CGTGAGGGCATCGAGGTGGC) and INS-2 (5'-GCGTAGGCGTCGGTGACAAA)[11]. Culture methods were compared in BioEstat version 5.0 using *kappa* index and turn-around time calculated at 95% confidence interval.

Of 927 samples, 8.8% of Ogawa-Kudoh cultures were contaminated, as were 7.7% of MGIT cultures. Of 652 patients, 119 were confirmed to have tuberculosis, of whom 60 were co-infected with HIV. Microscopy was positive to presence of acid-fast bacilli in 48 (40%) confirmed cases. On the other hand, 92 (77.3%) were positive on Ogawa-Kudoh cultures, and two (1.7%) samples were contaminated. Finally, 115 (96.7%) of confirmed cases were also positive on MGIT cultures. Of the 48 samples that were positive by microscopy, 42 and 44 were confirmed by Ogawa-Kudoh and MGIT cultures, respectively. Notably, all 71 patients who were negative by microscopy were positive by MGIT culture, and 50 were also positive by Ogawa-Kudoh culture **(Table 1)**. Among patients co-infected with *M. tuberculosis* and HIV, MGIT was more sensitive (58/60) than Ogawa-Kudoh culture (45/60) and microscopy (22/60).

In general, cultures are used to increase diagnostic sensitivity or to test the sensitivity of other diagnostic techniques. Thus, cultures are expected to contribute to enhance the diagnosis of tuberculosis. Accordingly, we found that Ogawa-Kudoh and MGIT cultures accounted for 51% and 60% of positive diagnoses. respectively, as assessed by published methods[12] [13] [14]. Notably, the *kappa* index was 0.9 between Ogawa-Kudoh and MGIT cultures, indicating excellent agreement ($p < 0.0001$).

Nevertheless, the results indicate that MGIT cultures were more sensitive than Ogawa-Kudoh cultures, and detected tuberculosis in 23 more patients. This result is consistent with previous studies of MGIT 960 in Brazil and other countries[12] [13]. MGIT 320 and MGIT 960 require the same sample processing, as well as the same additional tests to confirm infection with *M. tuberculosis*. However, the MGIT 320 compact system does not require stable electricity to maintain constant temperature during incubation, and is also more suitable for laboratories with lower caseload.

An important aspect of culture methods is turn-around, which has been reported to be shorter for MGIT (10-15 days) than for solid media (20-40 days)[2]. In line with these observations, the gap between a positive test on microscopy and a confirmed diagnosis was 8.8 days for MGIT and 17.3 days for Ogawa-Kudoh cultures **(Table 2)**. Similarly, a negative result on microscopy was typically confirmed in 13.2 days by MGIT culture, and 24.1 days by Ogawa-Kudoh. These data show that the time to diagnosis by MGIT is shorter than Ogawa-Kudoh culture by an average of 10 days.

In summary, our data demonstrate that use of mycobacterial cultures as a routine diagnostic tool may significantly enhance and accelerate detection of *M. tuberculosis*, especially among patients living with HIV/AIDS. However, cost-effectiveness will have to be analyzed to fully assess the suitability of BACTEC MGIT™ systems in satellite laboratories.

TABLE 1 - Ogawa-Kudoh and Mycobacterial Growth Indicator Tube 320 cultures of 119 tuberculosis cases stratified by microscopy results.

	MGIT		OK	
	n	%	n	%
Positive microscopy				
positive culture	44	91.7	42	87.5
negative culture	4	8.3	6	12.5
total	48	100.0	48	100.0
Negative microscopy				
positive culture	71	100.0	50	70.4
negative culture	0	0.0	21	29.6
total	71	100.0	71	100.0

MGIT: Mycobacterial Growth Indicator Tube. **OK:** Ogawa-Kudoh.

TABLE 2 - Days required to confirm microscopy diagnosis by Ogawa-Kudoh and Mycobacterial Growth Indicator Tube cultures.

	MGIT	OK
Positive microscopy		
turn-around	8.8 days	17.3 days
95% confidence interval	7.9-9.3	16.7-17.5
range	3-18	7-28
Negative microscopy		
turn-around	13.2 days	24.1 days
95% confidence interval	12.4-13.8	22.5-25.3
range	2-28	14-56

MGIT: Mycobacterial Growth Indicator Tube. **OK:** Ogawa-Kudoh.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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