Criteria for Identification of Cross-Contamination of Cultures of *Mycobacterium tuberculosis* in Routine Microbiology Laboratories

Recent years have seen a dramatic rise in the number of cases of tuberculosis worldwide, and as a result, there has been an upsurge in the demand for the isolation and characterization of *Mycobacterium tuberculosis* isolates. In their recent articles, Ruddy et al. (4) and de Boer et al. (2) described the incidence of false-positive cultures of *M. tuberculosis* in routine microbiology laboratories in London and the Netherlands, respectively. While we agree with their findings in principle, we feel that their experience does not translate well to the situation that prevails in laboratories serving areas with a high incidence of tuberculosis. While their rates of cross-contamination were low (0.54 and 2.4%), so was the average number of positive isolates handled by each laboratory per week, which in itself limits the potential for cross-contamination. We particularly feel that one of their criteria for the definition of a cross-contamination event, i.e., an isolate with a fingerprint that is identical to that of another isolate processed within 7 days, is unrealistic. In a recent paper (1), we reported on the implementation of a set of measures that resulted in the reduction of the cross-contamination rate for the processing of sputum cultures, from 7.3 to 2.1%. In contrast to the situation in London and The Netherlands, our laboratory has a culture positivity rate of 55%, which translates into approximately 24 positive cultures per week. In addition, the incidence of tuberculosis in the area is very high (3), with a high degree of molecular clustering. In such a scenario, the exclusion, as a cross-contamination event, of isolates with identical DNA fingerprints that were cultured within 7 days of each other cannot always be correct. We found that the majority of cross-contamination events were associated with processing of culture-negative specimens in the same batch as smear-positive samples obtained within the first 3 days of treatment. The modifications we made to laboratory procedures were designed to limit the opportunity for the transfer of bacilli from positive to negative samples without increasing the workload. As we could not limit the number of smear-positive samples processed per day, we ensured that the order of sputum processing went from negative to positive specimens. We also designated a specific safety cabinet for dealing exclusively with sputum samples, and all positive cultures, whether in liquid or on solid media, were dealt with in another cabinet.

It is necessary to point out that these options are accessible to all laboratories, regardless of their level of expertise and financial support. The procedural modifications we implemented were effective at reducing the rate of cross-contamination but did not have an impact on our output, and they can be effectively applied by any laboratory, whether in a routine or clinical-trial situation, without extensive economic outlay.

REFERENCES


Authors’ Reply (reference 2)

With interest we took notice of the letter to the editor of our colleagues N. M. Carroll et al. dealing with the definition of and the measures against laboratory cross-contaminations of Mycobacterium tuberculosis. Although we appreciate the point that the detection of false-positive M. tuberculosis isolates is more difficult when the background prevalence of tuberculosis is high and/or the variety of strains circulating in the community is low, we do not agree with the main criticism of Carroll et al. of our definition of cross-contamination because this comment does not justify the criteria we used to register an M. tuberculosis isolate as false positive. We do not simply register an isolate as false positive if the fingerprint is identical to that of another isolate processed within 7 days, but rather, we only suspect the isolate to be false positive if the fingerprint is identical to that of another isolate processed within 7 days in the same laboratory. An isolate is only officially registered as false positive if the respective fingerprint is identical to that of another isolate from the same laboratory processed within 7 days, if the patient had no clear tuberculosis symptoms, and if the peripheral laboratory confirms the false-positive laboratory diagnosis after verification with the clinician involved (1).

Finally, we applaud the idea of reserving one safety cabinet for primary cultures from clinical specimens and another for dealing with positive cultures. Laboratories throughout the world can add this measure to the excellent list of procedures to minimize the occurrence of false-positive cultures described by Small et al. (2).

REFERENCES


Annette S. de Boer*  
Center for Infectious Diseases Epidemiology

Dick van Soolingen  
Diagnostic Laboratory for Infectious Diseases and Perinatal Screening  
National Institute of Public Health and the Environment  
Antonie van Leeuwenhoeklaan 9  
3721 MA Bilthoven, The Netherlands

*Phone: 31 30 274 3691  
Fax: 31 30 274 4409  
E-mail: Annette.de.Boer@rivm.nl