Reviewer's report

Title: Bacteriophage-based tests for the detection of Mycobacterium tuberculosis in clinical specimens: a systematic review and meta-analysis

Version: 1 Date: 15 May 2005

Reviewer: John Bernardo

Reviewer's report:

General
This paper examines results of published studies in the English language literature that evaluate the performance of commercially-available and proprietary (in-house) bacteriophage-based tests for M. tuberculosis in clinical samples. Studies chosen for review were identified through electronic database searches as well as by referrals from experts and by manufacturers of bacteriophage tests. Thirteen studies met eligibility criteria and were analyzed in detail, assessing the overall potential utility of these tests versus microscopy. Data analyzed included those from head-to-head comparisons between sputum smears and phage-based tests, and subgroup analyses of smear-positive and negative sputum. The authors report that despite having generally high specificity, these tests display variable, and, in some cases, very low sensitivity; overall, their performance is similar to that of microscopy. Given the high costs of these tests (including materials, facilities, and expertise) and their lack of significantly better performance, the authors conclude that bacteriophage-based tests for TB cannot replace conventional microscopy in these clinical settings.

This is an important study, since there is great need to identify a rapid, inexpensive test that will establish a diagnosis of TB with a higher degree of precision than currently is available and rule out the disease where it is not present. Clinically-based studies should help define such a test and the conditions under which its performance is optimized. However, as a review and analysis of others work, it suffers from the variable nature and small size of its study population. Relatively few published studies have examined the performance of phage-based tests against microscopy, using culture-confirmation (or NAA) as reference standard in clinical settings. The methods used in different studies vary, and the quality of the work performed is not standardized. Yet, in their analysis of the 13 studies that met their entry criteria, the authors found that reported performance of these tests does not justify their use in place of smear-microscopy. This calls for additional studies, as pointed out by the authors, preferably standardized, to define the optimal ways to make use of these tests.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

None

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Abstract; para 1. The sputum smear may be highly specific, but only in appropriate populations. This should be clarified in the text.
2. Abstract; para 2. The authors presumably performed a review of the published literature for this study. The sentence should be completed.
3. p. 5, para 2: Figure 1 only depicts only the principles of the plaque assay methodology. The
designation of Figure 1, in line 1, should be moved to reflect this (perhaps to line 3).
4. p. 5, para 2: Define PhaB.
5. p. 6, para 1: Some studies analyzed were referred (or sponsored/performed) by test manufacturers. If results can be analyzed separately, was test performance in these studies different from others?
6. p. 10, para 2, ff. Some studies (3) analyzed sputum specimens other than sputum. In these studies, can data from these samples be separated from sputum data and analyzed separately?
7. Discussion: In these studies, TB disease was defined by growth in culture; clinical diagnoses are not accepted. Inclusion of clinical diagnoses may affect both sensitivity and specificity analyses, and should be mentioned in the discussion.
8. SP is identified in several places in the manuscript as a reviewer (p. 6, para 2 and 3) and as an author (p. 18, para 2). I assume the correct initials are SK, referring to the first author.

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions
Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No
Declaration of competing interests:
I declare that I have no competing interests