Making the most of poor diagnostics: increasing access to tuberculosis treatment through optimized smear microscopy services
Ramsay, A.R.C.

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Chapter 5

The bleach microscopy method and case detection for tuberculosis control.

A Ramsay
SB Squire
K Siddiqi
J Cunningham
MD Perkins

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The bleach microscopy method and case detection for tuberculosis control

A. Ramsay,* S. B. Squire,† K. Siddiqi,‡ J. Cunningham,* M. D. Perkins§

* UNICEF/United Nations Development Programme/World Bank/World Health Organization Special Programme on Research and Training for Tropical Diseases (TDR), Geneva, Switzerland; † EQUI-TB Knowledge Programme, Liverpool School of Tropical Medicine, Liverpool, ‡ Nuffield Centre for International Health & Development, University of Leeds, Leeds, United Kingdom; § Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland

SUMMARY

The World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Disease (The Union) recommend direct sputum smear microscopy for tuberculosis (TB) case finding in resource-poor settings. This method is associated with poor sensitivity. Digestion of sputum with bleach prior to smear preparation has been reported to increase sensitivity. Some workers, having reviewed the relevant literature, have called for the WHO and The Union to advocate for a shift to this methodology for TB case finding. This article highlights deficiencies in the scope and detail of available evidence, and cautions against the premature, and possibly counter-productive, adoption of so-called ‘bleach microscopy’. Further well-guided research is required to answer policy-relevant gaps in our knowledge about this promising technology.

KEY WORDS: bleach; hypochlorite; microscopy; tuberculosis; sputum; diagnosis

THE FACTORS determining whether research findings influence health service delivery are varied and complex. For health service providers seeking to base their services on scientific evidence, the strength of that evidence will be a major consideration. A review published in the *Journal* in 2004 concluded that there is enough evidence to promote the introduction of bleach microscopy as part of the DOTS strategy, and that relevant organisations should start to advocate a shift to this methodology.1 Although bleach microscopy is promising, we cannot agree that the disparate study results collated in this review constitute the required evidence. Despite some criticism, the review has generated a demand for the widespread adoption of bleach microscopy. We would like to caution against this. Although the review includes a caveat that country-specific evaluation should precede full-scale implementation, this glosses over important deficiencies in the existing data.

Bleach (sodium hypochlorite) was being advocated as a useful additive for sputum microscopy nearly 100 years ago2,3 and has, with a long list of other agents,4–8 been used with centrifugation or sedimentation to increase sensitivity. None have become a part of standard sputum processing, most commonly because the benefit they offered was small, or because the effect could not be replicated, especially when put into everyday use. Although the need for improved diagnostic methods for tuberculosis (TB), especially in the human immunodeficiency virus (HIV) era, is urgent, we cannot ignore the need for solid evidence prior to the introduction of new techniques.

The recommendation of the authors was based on a review of recent studies evaluating methods in which acid-fast bacilli (AFB) microscopy was performed after bleach treatment of sputum. The heterogeneous series of papers included in the review evaluated several different laboratory methodologies (e.g., various centrifugal forces or passive sedimentation periods) and study designs. Blinded and non-blinded studies were considered together. Studies in which procedures were performed on a single specimen were reviewed alongside those in which different specimens from the same patient were used for different procedures. The sensitivity benefit of bleach varied tremendously between studies, with an increase of 0% to over 100% in the number of smear-positive samples detected.

It is difficult to construct policy out of such variable results. Were we to accept the authors’ conclusions, which of the various bleach methods should be implemented? In what settings and for what patient groups would it be used? The studies included in the review do not address either of the two most impor-
tant operational questions for microscopy today. The first is whether bleach microscopy can be of benefit in peripheral clinics where the majority of patients seek care. Only three of the 19 papers included in this review were carried out in peripheral health centres, and, as the authors point out, in two of those three studies bleach showed no clinically significant sensitivity benefit over conventional microscopy. The second is whether bleach microscopy is particularly helpful in HIV co-infected individuals, where the need for improved detection of paucibacillary disease is most critical. Although some studies have been conducted in areas of high HIV seroprevalence, only a few specifically address this question.

There are many attractions to household bleach as a microscopy reagent. It is inexpensive and widely available in low-income countries, even in rural areas. However, adoption of a bleach microscopy method would not be without difficulty. As pointed out by the review, the common requirement for distilled water or for bench-top centrifuges, neither of which may be available in peripheral health centres, is a significant impediment. Other possible operational disadvantages of the bleach methods, such as the need for a timed step in microscopy preparation, the increased fragility of smear preparations, a danger of false-positives by transfer, and potentially altered storage and restaining characteristics of smears, need further study. The treatment of specimens with bleach may reduce biohazards associated with smear preparation, but more research, under operational conditions, is required. Importantly, sodium hypochlorite, the active ingredient in household bleach, degrades over time, primarily through oxidation, a process accelerated by temperature and the presence of trace impurities. At tropical temperatures (35°C), the activity of 5% unfiltered household bleach would be reduced by a half within 3 months. None of the published studies in the review described the storage history of the bleach or quartered household bleach would be reduced by a half.

The mechanism through which hypochlorite would improve sensitivity has not been investigated, aside from one careful study using radiolabelled bacille Calmette-Guérin. Whether the effect is on the buoyant density of mycobacteria, their flocculation or dispersal through digestion of sputum remains unknown.

The end result of using bleach may be to turn smears classified as ‘scanty’ into positives, an idea supported by the largest of the reviewed studies included in this review (3287 samples), which used American Thoracic Society (ATS)/Centers for Disease Control and Prevention (CDC) rather than World Health Organization (WHO)/International Union Against Tuberculosis and Lung Disease (The Union) criteria for scoring smears and found no difference between bleach-treated and direct microscopy. If this were true, simply changing reading criteria, as has been suggested, might have as much impact as changing the processing methodology. The ATS/CDC criteria for smear positivity are based on fewer AFB per 100 fields than the WHO or Union systems.

The bleach methodologies are attractive since they are likely to be appropriate in the developing country settings, where improved diagnosis of TB is desperately needed. However, given the cost and complexity of introducing a new diagnostic method, Ministries of Health, and the technical agencies that support them, will want solid data illustrating the benefit of the technology. We need more information on the relative merits of the different bleach techniques, followed by controlled multicentre clinical trials in highly structured settings to evaluate clinical sensitivity and specificity. Beyond this, operational research clarifying the feasibility, impact and cost-effectiveness of these interventions will be needed. Premature scale-up of a suboptimal technique must be avoided, as it could lead to the unwarranted discrediting of a promising technological approach. Lack of data should drive us to expand our research efforts, not to declare an early victory.

References


L’Organisation Mondiale de la Santé (OMS) et L’Union Contre la Tuberculose et le Maladies Respiratoires (L’Union) recommandent l’examen microscopique direct des frottis d’expectoration pour le dépistage des cas de tuberculose (TB) dans des contextes à faibles ressources. Cette méthode comporte une faible sensibilité. La digestion de l’expectoration avec de l’eau de Javel préalablement à la préparation du frottis a été décrite comme un moyen d’augmenter la sensibilité. Certains chercheurs ayant fait la revue de la littérature concernée ont demandé à l’OMS et à l’Union de plaider en faveur du passage à cette méthodologie pour le dépistage des cas de TB. Cet article insiste sur l’étendue et les détails des preuves disponibles et invite à la prudence à l’égard d’une adoption prématurée et peut-être contre-productive de la microscopie dite à l’eau de Javel. Des recherches ultérieures bien conduites sont nécessaires pour répondre aux carences dans nos connaissances, importantes pour la stratégie au sujet de cette technologie prometteuse.

La Organización Mundial de la Salud (OMS) y La Unión Internacional Contra la Tuberculosis y las Enfermedades Respiratorias (La Unión) recomiendan la baciloscopia directa de las muestras de esputo para la detección de los casos de tuberculosis (TB) en medios con escasos recursos. Este método presenta una baja sensibilidad. Existen informes sobre un aumento de la sensibilidad mediante digestión de la muestra de esputo con lejía (hipoclorito de sodio). Algunos autores, después de revisar la literatura pertinente, han sugerido que la OMS y la Unión preconicen un cambio hacia esta técnica para la detección de los casos de TB. En el presente artículo se resalta la insuficiencia de las pruebas existentes sobre el alcance y los detalles de este método y previene contra una adopción prematura y eventualmente contraproducente de la baciloscopia con digestión por lejía. Se precisa una investigación bien orientada para responder a las lagunas del conocimiento de los principios de esta técnica prometedora.