Diagnosis of tuberculosis in developing countries in the era of high HIV transmission; alternative approaches
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Chapter 7

Comparison of scanty AFB semars against culture in an area with high HIV prevalence

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Comparison of scanty AFB smears against culture in an area with high HIV prevalence

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To verify among tuberculosis (TB) suspects attending hospitals in Abuja, Nigeria, if sputum smears graded as scanty are false-positive, sputum smears from 1068 patients were graded with the International Union Against Tuberculosis and Lung Disease classification. One specimen was cultured. Eight hundred and twenty-four (26%) smears were positive, 137 (4%) scanty and 2243 negative. Of 1068 cultures, 680 (64%) were positive.

**SUMMARY**

One hundred and thirty (95%) scanty and 809 (98%) positive smears were culture-positive. Twelve of 18 patients with a single scanty smear and 51 of 52 with ≥2 scanty smears were culture-positive. Fewer than <5% scanty results, <1% of the patients treated for TB, are false-positive.

**KEY WORDS:** tuberculosis; diagnosis; Nigeria; scanty bacilli; smears

PATIENTS WITH SYMPTOMS suggestive of pulmonary tuberculosis (PTB) often have direct sputum smears graded as 'scanty' (<10 acid-fast bacilli [AFB] per 100 high power fields [HPF]). The World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Diseases (IUATLD) international recommendations indicate that a single smear with scanty AFB should not be accepted as diagnostic unless confirmed by further smears.1 This is, however, not uncommon: Van Deun et al. reported that sputum smears classified as 'scanty' were observed in about 10% of their Bangladeshi patients.2 Although Van Deun et al. documented that only 1.5% of these smears were false-positive, few recent studies have validated scanty smear results against culture, which is considered the gold standard. In sub-Saharan Africa, the number of patients presenting with scanty bacilli has increased due to the high incidence of human immunodeficiency virus (HIV) in the region.3,4 Studies that compare the value of a single smear with scanty AFB against culture in areas of high HIV prevalence are critical for the proper management of patients.

**STUDY POPULATION AND METHODS**

We investigated all consecutive patients with symptoms suggestive of PTB attending eight hospitals in Abuja, Nigeria, from September 2003 to September 2004. Patients presenting with a history of cough for more than 3 weeks were requested to submit three sputum samples over 2 consecutive days for direct smear microscopy. One smear was prepared from each sputum sample and stained using the hot Ziehl-Neelsen (ZN) method.1 All smears were then read independently by two laboratory technicians. A third technician recorded the results from the two readings and reconciled discrepant smear results to reach a consensus. Smears were graded using the IUATLD classification,1 and the number of bacilli observed per 100 HPF was counted for smears graded as scanty. One of the three sputum specimens was randomly selected and cultured using the BACTEC 960 system (Becton Dickinson, Erembodegem, Belgium). Sputum specimens were digested/decontaminated with Petroff's method, using 4% sodium hydroxide and centrifugation at a relative centrifugal force of 3000 g prior to inoculation of the BACTEC bottles.

Material was removed from BACTEC bottles showing growth and used to prepare ZN smears. BACTEC bottles growing AFB were considered positive. The laboratory in Abuja was unable at that time to confirm AFB isolates as Mycobacterium tuberculosis. A positive result was therefore interpreted as growth of AFB, which is likely to be M. tuberculosis. Previous work by our group has shown that 31% of the patients in our setting are considered 'definite' sputum smear-positive cases on the basis of two or more positive direct smears and a further 29% are smear-negative, culture positive.5 Smear results were tabulated according to the number of AFB seen in the scanty bacilli.
### Table  Smear results of patients with scanty AFB grades by culture

<table>
<thead>
<tr>
<th>Culture</th>
<th>Scanty Negative n (%)</th>
<th>Scanty Negative n (%)</th>
<th>Scanty Negative n (%)</th>
<th>Scanty Positive Negative n (%)</th>
<th>Scanty Positive n (%)</th>
<th>Scanty Positive n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 AFB in all scanty smears</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>15 (79)</td>
<td>6 (60)</td>
<td>5 (100)</td>
<td>3 (100)</td>
<td>1 (100)</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>4 (21)</td>
<td>4 (40)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>One or more scanty smears with &gt;3 AFB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>48 (94)</td>
<td>6 (75)</td>
<td>8 (89)</td>
<td>3 (100)</td>
<td>22 (100)</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>3 (6)</td>
<td>2 (25)</td>
<td>1 (11)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

AFB = acid-fast bacilli.

smears (< or ≥3 AFB/HPF) and whether they had single scanty smears or one scanty smear with further scanty, positive or negative smear permutations. These permutations are presented in the same order for all smears, independently of the timing of the sputum sample that was graded as scanty (spot or early morning specimens) to facilitate its interpretation.

### RESULTS

A total of 1068 consecutive patients were screened during the study period and a total of 3204 direct smear results were available. Of these, 824 (25.7%) were graded as positive (+, ++ or +++), 137 (4.3%) as scanty and 2243 (70%) as negative. Forty-eight (1.5%) first on-the-spot, 38 (1.2%) morning and 51 (1.6%) second on-the-spot specimens were graded as scanty. Six hundred and eighty (64%) of the 1068 BACTEC cultures were positive.

One hundred and thirty (95%) of the 137 scanty and 809 (98%) of the 824 positive smears belonged to patients with positive cultures. Eighteen patients had only one scanty smear plus two negative smears (Table). Of these, 10 had <3 and 8 ≥3 AFB counts per 100 HPF. Six of the 10 smears with <3 AFB were culture-positive, compared to 6 of the 8 with ≥3 AFB per 100 HPF (P > 0.1). Fourteen patients had two scanty plus one negative smear and only one of them had negative culture. A further 38 patients had three scanty or one scanty plus other positive smears. All of these patients were confirmed by culture.

### INTERPRETATION

Our findings confirm that in TB control programmes with adequate quality control, smears reported as 'scanty' are more likely to be true than false-positives. Our results are in agreement with previous studies that have demonstrated that the majority of scanty smears belong to patients with active PTB. Although about 50% of our patients with PTB are co-infected with HIV (unpublished data), accepting scanty smears as positive would result in less than 1% of the patients being wrongly classified as having PTB (7/1068), and a further 34 patients could have been identified for treatment. This would be particularly useful in African countries with high TB prevalence (where the test would have a high positive predictive value), whose populations often have low access to services and overburdened diagnostic facilities.

### References


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Pour vérifier chez des suspects de tuberculose (TB) se rendant dans des hôpitaux d'Abuja, Nigéria, dans quelle mesure les frottis d'expectoration classés comme avec de rares bacillus sont des faux positifs, des frottis d'expectoration provenant de 1.068 patients ont été codifiés secondo la classification de l'Union internationale contre la tuberculose et les maladies respiratoires. Un des échantillons est mis en culture. Il y a eu 824 frottis positifs (26%), 137 avec de rares bacillus (4%) et 2.243 négatifs. Sur 1.068 cultures, 680 cultures ont été positives (64%).
Les cultures ont été positives chez 130 frottis de rares bacillus (95%) et chez 809 frottis positifs (98%). Douze des 18 patients dont un seul frottis avait de rares bacillus et 51 des 52 patients dont deux frottis ou davantage avaient très peu positifs ont eu une culture positive. Moins de 5% des résultats avec de rares bacillus sont des faux positifs, ce qui représente moins de 1% des patients traités pour TB.

Para verificar en pacientes con sospecha de tuberculosis en Abuja, Nigeria, si frotes de esputo con escasos bacilos son falso-positivos, 1068 frotes fueron clasificados (escala Unión Internacional Contra la Tuberculosis y Enfermedades Respiratorias). Un especimen fue cultivado. Ocho ciento veinte y cuatro (26%) frotes fueron positivos, 2243 negativos y 137 (4%) tenían escasos bacilos. De 1068 (64%) cultivos, 680 fueron positivos; 809 (98%) frotes positivos y 130 (95%) con escasos bacilos tenían cultivos positivos. Doce de 18 pacientes con un frote y 51/52 pacientes con ≥2 frotes con escasos bacilos tenían cultivos positivos. Menos de 5% de los frotes con escasos bacilos es falso-positivo, lo que corresponde a <1% de los pacientes tratados.