MTB/RIF. In epidemiological settings in which NTM diseases are more frequent than tuberculosis, the balance would be even more against replacing microscopy with Xpert MTB/RIF (2).

Moreover, although the lack of specificity of microscopy is well known (not all acid-fast bacilli are tuberculous bacilli; some are NTM), it must be underlined that Xpert MTB/RIF also lacks specificity. In the authors' study, Xpert's positive predictive value was 75%. In other words, a quarter of tuberculosis treatments started on the basis of Xpert MTB/RIF would have been done erroneously.

Overall, we believe that the Xpert MTB/RIF assay should be used as an identification test in patients who have undergone an initial screening: either positive-smear microscopy or, in case of a high clinical suspicion of tuberculosis, in case of negative-smear microscopy. ■

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Reply to Aubry and Veziris

From the Authors:

We thank Dr. Aubry and Dr. Veziris for their letter and great interest in our published study (1). They raised concerns regarding the possibility of delaying the diagnosis of nontuberculous mycobacteria (NTM) diseases when using the Xpert MTB/RIF assay alone. We consider that the clinical benefit of making an early diagnosis or excluding tuberculosis, relying solely on the Xpert MTB/RIF results, is more important than the disadvantage that could result from a delayed diagnosis of NTM disease. Moreover, this disadvantage can be minimized by considering the current diagnostic criteria for NTM lung disease (2). There are several reasons for this. First, *Mycobacterium tuberculosis* complex (MTBC) is a highly infectious and transmissible pathogen that is a global public health concern, whereas NTM are widely distributed in the environment and rarely spread via direct transmission among humans (3). Second, because most NTM lung diseases display slow progression, and the antibiotic regimen or prognosis varies depending on the causative NTM species, these diseases do not require rapid diagnosis and immediate treatment; accurate identification of the NTM species and even subspecies is more beneficial (4). Thus, at least two separate, time-consuming, positive culture results are necessary for a definitive diagnosis of NTM lung disease (2, 3). Last, even in the case of rapid progression of severe NTM lung disease (i.e., fibrocavitary disease), it can easily be suspected based on the distinct abnormalities in chest radiographs, despite negative Xpert MTB/RIF results (3).

Aubry and Veziris also expressed important concerns regarding the lack of specificity of the Xpert MTB/RIF assay, which can lead to unnecessary treatment. As summarized in Table E10 in the online supplement of our article (1), out of 66 patients with false-positive Xpert MTB/RIF results, 57 were diagnosed with clinical ($n = 45$) or subsequently culture-proven ($n = 12$) tuberculosis. In addition, 40 had been previously treated or were undergoing treatment for tuberculosis. Because the Xpert MTB/RIF assay cannot distinguish between viable, dormant, and nonviable mycobacteria, some false-positive results may be due to residual DNA from dead bacilli after treatment (5). Further advancements (e.g., the RNA-based amplification assay and the use of propidium monoazide to prevent amplification of DNA released from damaged or nonviable mycobacteria) could help to circumvent this limitation of the current Xpert MTB/RIF assay (5) and enhance the specificity of rapid molecular diagnostic methods in the near future.

Considering the delayed reporting time of smear microscopy (19.1 h) versus the Xpert MTB/RIF assay (3.1 h) in our study (1), the Xpert MTB/RIF assay should be used first. Otherwise, the conditional use of the Xpert MTB/RIF assay as an identification test after initial smear microscopy would cause delayed diagnosis and management of pulmonary tuberculosis with high infectivity. Notably, the use of smear microscopy as a complement to the Xpert MTB/RIF assay is helpful for making an early presumptive diagnosis of NTM lung disease, but it is not critical for a definitive diagnosis leading to the initiation of targeted drug therapy (4). Moreover, smear microscopy cannot differentiate MTBC from NTM, which can also mislead clinicians to initiate unnecessary treatment. We suggest that molecular methods for differentiating MTBC and NTM should be considered as alternative approaches in resource-rich areas with an increasing NTM burden, as these methods have a higher sensitivity for NTM than smear microscopy (6). Therefore, we recommend initial use of the Xpert MTB/RIF assay, followed by complementary use of the MTBC/NTM differential molecular assay. This could increase the diagnostic sensitivity for tuberculosis and reduce the use of unnecessary smear microscopy.

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Although the current technical state of the Xpert MTB/RIF assay prevents the complete retirement of smear microscopy, we hope that future technological advances in rapid molecular methods, including the Xpert MTB/RIF assay, will allow full replacement of smear microscopy for the diagnosis of mycobacterial diseases. ■

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Erratum: XBP1S Regulates MUC5B in a Promoter Variant–Dependent Pathway in Idiopathic Pulmonary Fibrosis Airway Epithelia

Because of a typesetting error, the expression "air–liquid interface" was incorrectly replaced with "acute lung injury" in the article by Chen and colleagues (1), published in the July 15, 2019, issue of the *Journal*. This error appears in the legends to Figures 1, 2, and 7. ■

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