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Reply to “Missing Stowaways, Lack of Expected Concurrent Infection”

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From the Authors

We thank Drs. Sasieta and Escalante for their interest in our article (1). We certainly agree with their conclusion that we might have misclassified the apparent etiology of some of the tuberculosis (TB) recurrences in our cohort. In addition to other listed limitations that might have led to misclassification, a possibility that they correctly raise is that some of the 15% whom we classified as having novel reinfection might, in fact, have had undetected mixed infections (i.e., coinfection) during the initial TB episode.

The frequency of mixed TB infections in the United States is difficult to ascertain given that the National Tuberculosis Genotyping Service typically offers genotyping for only one isolate from every culture-positive TB case (2, 3). However, just as state public health laboratories have the option to submit multiple isolates to help investigate a possible false-positive *Mycobacterium tuberculosis* culture, they also have the option to submit multiple isolates if they suspect mixed infections (4). None of the initial or subsequent isolates in this analysis were flagged as either suspected false positives or mixed infections. The isolates from the 20 pairs of TB episodes that we classified as reinfections had substantially different

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M. tuberculosis genotype patterns (further details in Table 2 [1]), well beyond the single mycobacterial interspersed repeat units–variable number tandem repeat [MIRU–VNTR] locus or RFLP band difference occasionally seen with *in situ* clonal evolution.

Because our TB investigation experience (5) has taught us that cases along the same chain of transmission typically match by current genotyping methods (i.e., spoligotyping and 24-locus MIRU–VNTR [2,3]), we were not surprised that 85% of the recurrences that we examined had a genotype that matched that of the earlier TB episode (1), suggesting that most persons with recurrent TB in this U.S. cohort experienced reactivation of residual infection.

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