Letter to the Editor

To the Editor—In the 15 August 2010 issue of Clinical Infectious Diseases, Fitzwater et al report on serial acid fast bacilli smear and culture conversion rates over 26 weeks in a cohort of 93 sputum culture–positive tuberculosis (TB) patients started on standardized first-line treatment in a Lima, Peru, directly observed therapy short-course (DOTS) program [1]. The authors note that median conversion times for smears and cultures, respectively, were 17.5 days and 38.5 days, and that at 60 days (a time point at which treatment failure is commonly suspected in individuals remaining smear or culture positive),
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complete treatment [2]. Moreover,

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Epidemiologic studies have confirmed

the disassociation between smear and culture positivity and infectiousness in

effectively treated patients. In Madras,

risk of infection or disease among household contacts of TB pa-
tients was no different between contacts of patients treated in the hospital and

contacts of those returning home to complete treatment [2]. Moreover,

Gunnels and colleagues demonstrated no difference in conversion rates among

household contacts of effectively treated patients regardless of sputum-smear status [3]. However, the most direct evidence of the impact of treatment on reducing patient infectiousness comes from several experiments wherein large numbers of guinea pigs (an animal model well established to quantify TB trans-

mission) breathed the air exhausted from experimental TB wards. In Riley’s study

60 years ago, all transmission to guinea pigs was interrupted when sputum

smear–positive patients were admitted to the ward on the same day they started
effective therapy for drug-susceptible TB, and resumed when drug-resistant pa-
tients on ineffectiva
treatment were ad-

[4]. In a second, similar study, Riley and colleagues directly compared the infectiousness of treated and un-
treated patients and demonstrated the extremely rapid effect of treatment on reducing transmission. Compared with untreated sputum smear–positive pa-
tients with drug susceptible TB, those started on treatment the same day as admission were only 2% as infectious

[5]. Recently, Escombe et al found similar results by exposing guinea pigs to air from an experimental ward of TB/HIV co-infected patients in Lima, Peru. They found 97% of guinea pig infections were attributable to just 8 unsuspected or inadequately treated MDR-TB patients [6]. Transmission of TB to 3 guinea pigs occurred from just 3 patients with drug-susceptible TB who experienced delays in starting ef-
tective treatment or who were off therapy because of side effects [6].

Unfortunately, the study by Fitzwater et al does not assess infectiousness per se. Smear or culture positivity does not necessarily equate with prolonged in-
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ness. To demonstrate prolonged infectiousness, one would need to exam-

ine transmission from these patients. One could evaluate household contact con-

version or disease rates after initiation of source-case treatment, for example. Alternatively, in the context of a well-

functioning DOTS program like the one described in the paper, one could com-

pare TB-skin test conversion or disease rates among household contacts strat-

tified by effective versus ineffective (eg, receiving a first-line regimen for MDR-

TB) treatment for the source case’s TB.

As we point out, critically relevant to any discussion on infectiousness is whether patients receive effective ther-

apy for TB. In Fitzwater et al’s study, the authors note that only 4 of 9 MDR-TB patients received tailored regimens based on in vitro drug-susceptibility testing results, and that only 2 of these 4 re-

ceived such regimens more than 2 weeks before study completion. If any of the patients in this study were likely to have been infectious for a prolonged time, it would be the 7 MDR-TB patients who did not receive timely tailored therapy but instead received a first-line regimen of rifampicin, isoniazid, ethambutol, and pyrazinamide.

Whereas the use of 2-month time points of smear and culture conversion may be appropriate for gauging an individual patient’s response to or the failure of a given treatment regimen, it may not be appropriate for assuming an individual’s ongoing infectiousness. In-
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ness is related not just to the presence of viable Mycobacterium
tuberculosis on sputum smear or in cul-
ture but also to the ability of patients to generate transmissible aerosols of M. tuberculosis and the ability of trans-
mit
ted organisms to cause disease. Each of these factors may be significantly mitigated when one considers the com-
plex, yet poorly defined, interactions between microbe, host, and drugs that are bound to occur within the lungs and airways of TB patients and within microscopical droplets after aerosolization.

Although we contend that the evidence from Fitzwater et al’s study is insufficient to conclude prolonged in-
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to
ness of patients, we applaud the emphasis the authors place on the need to expand rapid culture methods, im-
plement timely DST, and start early MDR-specific treatment regimens in patients needing them. Scaling up these processes is critical to getting TB pa-
tients on effective drug regimens with their demonstrable rapid and profound effect on infectiousness.

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