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PERSPECTIVE

F-A-S-T: a refocused, intensified, administrative tuberculosis transmission control strategy

E. Barrera,* V. Livchits,† E. Nardell‡

*Partners in Health, Boston, Massachusetts, USA; †Partners in Health, Russia; ‡Division of Global Health Equity, Brigham & Women's Hospital, Boston, Massachusetts, USA

TRANSMISSION is driving the global tuberculosis (TB) epidemic, especially where human immunodeficiency virus (HIV) co-infection is prevalent.[1,2] More than half of multidrug-resistant TB cases worldwide occur in persons who have not been treated previously, i.e., as a result of transmission.[3] Transmission occurs in the community, of course, but TB is believed to spread most efficiently in congregate settings such as hospitals, clinics, prisons and refugee camps. The well-publicized transmission of extensively drug-resistant TB (XDR-TB) in rural South Africa, and the six-fold higher risk of multidrug-resistant TB (MDR-TB) reported among hospitalized, adherent, drug-susceptible patients in Tomsk, Siberia, are two compelling examples of hospital transmission of drug-resistant TB in very different parts of the world.[4,5]

FOCUS – KNOWN OR UNSUSPECTED CASES?

Implementing comprehensive institutional interventions to control transmission, such as those promoted by the World Health Organization (WHO), has been challenging in resource-poor, high-burden settings.[6,7] Unable to implement the full range of recommendations for administrative, environmental, and respiratory protection, programs and institutions tend to focus on certain elements, such as the separation of sputum smear-positive and -negative patients, opening windows where conditions permit, and providing respirators for health care workers. In the present article, we introduce a refocused, intensified administrative approach to TB transmission control that we call *FAST*: Find cases Actively by cough surveillance and rapid molecular sputum testing, Separate safely, and Treat effectively based on rapid drug susceptibility testing (DST). This approach is based on the assumption that most transmission occurs, not from known TB patients on effective treatment, but from persons with unsuspected TB or unsuspected drug resistance. For example, active case finding of all new admissions over a 1-year period in a general medical ward in Lima, Peru, found a 16% prevalence of active TB cases, one-third of which were unsuspected, including unsuspected smear-positive MDR-TB cases.[8] More recently, in Zambia, 900 admissions were screened for TB, 70.6% HIV-infected, of whom 13.4% had unsuspected TB, including 18 MDR-TB cases, five of whom were unsuspected.[9]

Awareness and implementation of TB infection control, when present at all, is often focused on the care of known or suspected TB cases—the use of surgical masks by patients, their separation or isolation in well-ventilated airborne isolation rooms, directional airflow, and the use of respirator protection for health care workers. The irony is that such patients, once on effective treatment, are highly unlikely to be infectious at all.[10] If coughing patients with unsuspected/undiagnosed TB and/or drug resistance are quickly identified and placed on effective treatment, we contend that that intervention alone will prevent most transmission. This refocused, intensified administrative approach has only recently been made possible by the increasing availability of rapid molecular diagnostic tests, coupled with a renewed awareness of the extremely rapid impact of effective treatment on transmission—long before sputum smear or culture conversion to negative. The latter phenomenon, well-reported in the older literature, has recently been published in this *Journal*.[10,11] FAST is being implemented in hospitals and clinics around the world, including a TB hospital in the Veronesh region of Russia and a large chest hospital in Bangladesh. Preliminary results of these two pilot sites are briefly reviewed below as examples of early application.

F-A-S-T PRINCIPLES

To reiterate, the FAST approach is based on four underlying principles: 1) that TB is spread in

Correspondence to: Edward A Nardell, Division of Global Health Equity, Brigham & Women's Hospital, 641 Huntington Ave 3A03, Boston, MA 02115, USA. Tel: (+1) 617 432 2080. Fax: (+1) 617 432 6958. e-mail: enardell@gmail.com
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institutions predominantly by coughing patients with unsuspected TB or unsuspected drug resistance, 2) that most potentially infectious patients can be identified by cough surveillance, 3) that coughing TB patients most likely to be infectious can be diagnosed using rapid molecular sputum tests, including drug resistance (Xpert® MTB/RIF; Cepheid, Sunnyvale, CA, USA), and 4) that by dramatically reducing the duration of institutional exposure through effective treatment, transmission among patients and to health care workers will be reduced proportionately. While these are solid principles, like most transmission control interventions, their efficacy in preventing transmission has yet to be proven, and there are many practical barriers to implementation.

BARRIERS TO F-A-S-T IMPLEMENTATION

In many high-burden settings, health care workers are already overstretched. Who will perform cough surveillance? Who will ensure that sputum is promptly collected and delivered to laboratories, that results are obtained, and that effective treatment is started immediately? If these activities are as critical for stopping transmission as we contend, they cannot be assigned to volunteers or simply added to already full workloads. Where, then, are the sustainable funding sources for the additional human resources, Xpert machines, and laboratory supplies? If the benefits in terms of secondary cases averted were obvious, the costs of prevention through rapid diagnosis and effective treatment might be easily justified, but these are rarely clear. On the other hand, diagnosing and treating active TB is a fundamental public health and personal health imperative—it must be done sooner or later. We argue that the public health and personal health benefits of diagnosing and treating sooner through active surveillance, rapid diagnostic testing and effective treatment will far outweigh the added costs, especially for MDR-TB where the costs, both human and financial, are staggering for each additional case transmitted. We await demonstrations of both reduced transmission in clinical settings, and the formal cost-benefit analyses that are likely to follow the spread of this approach.

The goals of FAST implementation for general medical hospitals, chest hospitals, and TB-specific settings are different. In the general hospital setting, cough surveillance is aimed at diagnosing unsuspected, infectious TB and drug resistance. In the TB hospital, where all patients are TB cases or suspects, FAST entails rapid universal molecular testing for drug resistance and rapid implementation of effective MDR-TB treatment. Chest hospitals fall somewhere in-between. Respiratory symptoms may be so common as to reduce the specificity of cough surveillance, shifting the focus to sputum screening—or other potential rule-out triage diagnostic tests—to reduce the cost of molecular sputum testing. There is ample room for innovative approaches to diagnosis that might reduce the number of sputum tests required. Characteristics of optimal triage tests that might reduce Xpert testing were proposed recently.[12]

INDICATORS OF F-A-S-T SUCCESS

Unlike hand washing to prevent infection from the spread of droplets, effective FAST implementation is fundamentally not an educational campaign for employees, although understanding its rationale is important for achieving its ambitious goals. FAST implementation requires an institutional investment in resources and specific personnel to introduce new policies and procedures (and streamline old ones) to achieve the goal of reduced exposure time. Although it has proved difficult to measure the impact of any TB infection control intervention in terms of reduced transmission, the process indicators entailed (time from admission to cough detection, time from cough detection to sputum submission, Xpert turnaround time, and time from admission to effective treatment) are measurable and logically closely tied to the duration of exposure. Performance goals for these process indicators should be set, and achieving these measurable goals should be considered by institution administrators and funding agencies as primary proof of impact. Improvements and slippage in performance process indicators can be tracked over time. In the two examples that follow, pre-FAST process indicators were not available, but an impact of rapid diagnostics on exposure can be assumed and has been demonstrated elsewhere.[13]

IMPLEMENTATION OF F-A-S-T

In a TB hospital in Veronesh, Russia, 932 patients with suspected pulmonary TB were hospitalized from May 2013 to March 2014; 923 underwent Xpert testing, of whom 863 (93.5%) were tested within 2 days of admission: 407 were positive and 161 (study participants) were rifampin-resistant, of whom 159 were started on MDR-TB treatment within 3 working days of receiving the result. Under normal operating conditions before the pilot implementation of FAST, as in most Russian TB hospitals, treatment failure, often identified months after admission, was the usual criterion for DST. If DST was performed using conventional means, results were obtained after several more months.[5] Under usual practice, other patients and staff are commonly exposed for months rather than the $\leqslant 5$ days under the FAST protocol currently in effect. Although Veronesh is part of an externally funded (Lilly Foundation, Indianapolis, IN, USA) and non-governmental organization supported (Partners in Health [PIH] Russia, Tomsk, Russia) pilot project, universal rapid Xpert testing is now routine in the Vladimir Oblast TB Program in Russia under government funding (G Volchenkov, personal communication, 2014).

FAST is also being implemented as a pilot project in Bangladesh, with human and financial resources contributed through a TB Care II project (United States Agency for International Development, Washington, DC, USA) under the direction of University Research Co. Bangladesh and PIH, Boston. The site is the National Institute of Diseases of the Chest Hospital (NIDCH), a 680-bed facility in Dhaka. Because respiratory symptoms are so common among patients admitted to NIDCH, a decision for universal sputum sampling was made.

Over the first 21 weeks of implementation, a total of 1891 sputum samples from discrete patients admitted to one of the in-patient departments at NIDCH were tested using Xpert. Of these 1891 samples, approximately 11% and 1% unsuspected cases of TB and MDR-TB were identified, respectively. Of the 1453 patients admitted to the facility as non-TB patients with other respiratory diseases, about 9% actually had TB and had been misclassified upon admission. The unsuspected TB rate was more than twice as high among patients with a previous history of TB. Furthermore, of the 60 TB patients on treatment admitted to the facility, approximately 8% were identified as unsuspected, Xpert-confirmed MDR-TB cases. All 1891 samples were processed the same day of collection. Diagnoses were available for treatment initiation within 1–2 days of collection. A reporting delay of 1 day may have occurred if samples were processed at the end of the day. Treatment was initiated within 1 day of confirmed diagnosis. Implementing the FAST strategy at NIDCH has resulted in a sharp increase in the number of unsuspected TB and MDR-TB cases identified and effectively treated compared to routine practice. One limitation of the FAST strategy at NIDCH was that not all admitted patients could produce sputum, and some cases may have been missed.

We have not yet seen early results from general hospitals or clinics implementing the FAST approach, but these data will soon follow as projects are started in general hospitals in Haiti and other countries.

F-A-S-T FORWARD

In summary, we have presented FAST as a refocused TB transmission control strategy, reinforcing the priority of intensified administrative controls with an emphasis on active case finding and rapid diagnostic testing leading to prompt, effective treatment, and measurable by improved process indicators. To be clear, good building design, patient flow, separation, airborne isolation rooms, air disinfection, and respiratory protection will always play a role in managing TB patients—specifically for cases missed by active case finding, before effective treatment is started, and in managing XDR-TB, for which treatment with current regimens is unlikely to result in rapidly reduced transmission. Traditional general interventions, however, need to be replaced from the centerpiece of TB infection control to supportive roles as institutions refocus attention on a highly structured administrative approach with very clear outcome measures—specifically, reduced exposure time to previously unsuspected transmitters.

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