Spread of *Mycobacterium tuberculosis* in a Community Implementing Recommended Elements of Tuberculosis Control

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During the past decade, the application of molecular epidemiology to the field of tuberculosis (TB) has advanced our understanding of the dynamics of TB transmission. Numerous descriptions of TB outbreaks have identified hospitals, prisons, congregate living settings, and homeless shelters as sites for TB transmission, to name only a few such settings.1-4 Population-based studies have identified the characteristics of cases associated with the clustering of patients with the same strain of *Mycobacterium tuberculosis*, which is believed to indicate the recent transmission of *M. tuberculosis*.5-8

Despite improved understanding of the dynamics of TB transmission and improvements in TB control, transmission of *M tuberculosis* and disease resulting from such transmission continue to occur.7 To date, a comprehensive assessment of why our current public health interventions have failed to eliminate TB from this mechanism has not been reported. Such an assessment can guide the development or implementation of interventions so that cases of TB from ongoing transmission can be reduced in our communities.

Since 1996, we have conducted a population-based molecular epidemiological study of TB in the San Francisco Bay area. As part of this study, we identified a large cluster of TB case-patients infected with a single strain of *M tuberculosis* in 1 county. Because we determined that from 1992 to 1993 a number of case-patients in this community had the same strain of *M tuberculosis*, we investigated the current cluster to identify the factors responsible for the disease development.

**Context** Despite improvements in tuberculosis (TB) control during the past decade, *Mycobacterium tuberculosis* transmission and resulting disease continue to occur in the United States.

**Objective** To determine the primary reasons for disease development from a particular strain of *M tuberculosis*.

**Design** Population-based, molecular epidemiological study.

**Setting** Urban community in the San Francisco Bay area of California with recommended elements of TB control in place.

**Patients** Seventy-three TB cases were reported in 1996-1997 that resulted from 1 strain of *M tuberculosis* as identified by TB genotyping and epidemiological linkage.

**Main Outcome Measures** Transmission patterns involving source and secondary case-patients; primary reasons for disease development.

**Results** Seventy-three (33%) of 221 TB case-patients in this community resulted from this strain of *M tuberculosis*. Thirty-nine (53%) of the 73 case-patients developed TB because they were not identified as contacts of source case-patients; 20 case-patients (27%) developed TB because of delayed diagnosis of their sources; and 13 case-patients (18%) developed TB because of problems associated with the evaluation or treatment of contacts; and 1 case-patient (1%) developed TB because of delay in being elicited as a contact. Of the 51 TB cases identified with sources, 49 (96%) were infected within the 2 years prior to diagnosis.

**Conclusions** Our results indicate that in a community that has implemented the essential elements of TB control, TB from ongoing transmission of *M tuberculosis* will continue to develop unless patients are diagnosed earlier and contacts are more completely identified.
for the propagation of this strain of *M tuberculosis*.

**METHODS**

**Study Population**

Contra Costa County, California, is located in the San Francisco Bay Area with a population of around 900,000 persons and an area of 720 square miles. The western part of the county is densely populated and there are high rates of poverty, homelessness, substance abuse, and human immunodeficiency virus (HIV) infection. The remainder of the county, which is much more sparsely populated, has suburban and rural communities.

During 1996-1997, 221 TB cases (annual rate of 12.5 cases/100,000 population) were reported in the county. 160 of these, 160 were culture-confirmed cases. *M tuberculosis* isolates were collected for *M tuberculosis*-based restriction fragment-length polymorphism analysis for 151 of the culture-confirmed cases (93.8%).

The restriction fragment-length polymorphism pattern from 72 isolates (45%) was identical to at least 1 other isolate and these were designated as clustered isolates. Sixty-five (90%) of the clustered isolates had less than 6 copies of IS6110 (5 with 1 copy, 58 with 2 copies, and 2 with 3 copies). These isolates were further analyzed with a second genotyping technique using a probe for the polymorphic guanine-cytosine rich sequence (PGRS) (previously described). All isolates with 1 copy of IS6110 had unique PGRS patterns. The 2 isolates with 3 copies of IS6110 had an identical PGRS pattern. Of the 58 isolates with 2 copies of IS6110, 56 isolates had the same PGRS pattern, and this cluster was given the designation PG004; the remaining 2 isolates had unique PGRS patterns.

We reviewed the public health record of all TB cases to identify additional cases in 1996-1997 that had epidemiological linkages to cases in the PG004 cluster. Epidemiological linkages were identified with 17 additional case-patients in whom cultures were either negative or not collected, for example, pediatric case-patients. Our final study population consisted of all 56 case-patients in the PG004 cluster and the 17 case-patients with epidemiological linkages to case-patients in the PG004 cluster.

**Data Collection**

We reviewed all available public health and medical records to collect the following data: demographic and clinical information, risk factors for TB, HIV infection, laboratory and radiographic results, date of symptom onset, date of TB diagnosis, reasons for delay in diagnosis, estimated period of communicability, treatment information, use of directly observed therapy, adherence to treatment, and information on contact investigation, including the evaluation of each contact. Additional information on acquired immunodeficiency syndrome was obtained by cross-matching these case-patients with the AIDS Registry in the California Department of Health Services.

A contact investigation was routinely performed on all case-patients with pulmonary TB and a source case-patient investigation was performed for all pediatric and extrapulmonary TB case-patients. The concentric-circle approach to contact investigation was used. Identified contacts were evaluated for TB and tuberculosis infection and then given treatment when appropriate. The routine use of directly observed therapy and contact investigation as outlined has been in place since 1985.

**Assignment of Source and Secondary Case-Patients**

For our analysis, a source case-patient was defined as a patient who was determined to have transmitted *M tuberculosis* to another person. A secondary case-patient was defined as a patient who was infected by an identifiable source. A secondary case-patient who transmitted *M tuberculosis* to other case-patients was also defined as a secondary source case. Using predetermined criteria, 3 investigators independently reviewed all available data to determine transmission linkages among patients. Results from these independent reviews were compared and differences between reviewers were resolved in a meeting. These results were presented in a cluster conference to all public health nurses and disease investigators involved with these patients. During the conference, additional information on epidemiological linkages was collected and used to form the final assignment of source and secondary case-patients.

**Determination of the Primary Reason for Disease Development**

For each case, we sought to determine the primary reason for disease development. Secondary case-patients not identified as contacts during the investigation of their sources were considered to have developed disease because they were not identified as contacts in relation to their sources. All case-patients not linked to any known source were assumed to have developed disease as a result of failure to be elicited as a contact to an unidentified source.

For those secondary case-patients who were elicited as contacts of their sources, we assumed their disease could only have been prevented if there had been sufficient time for them to be identified, evaluated, and given preventive treatment. According to established guidelines in California, contacts should have been elicited and evaluated, and receiving treatment within 2 to 4 weeks after the initial report of suspected or confirmed TB. The exact duration depends on the communicability of the index case-patient and the risk characteristics of the contact. Based on these guidelines, secondary case-patients were defined as having resulted from delayed diagnosis of their source case if they developed disease before their sources were reported to the health department or within 30 days following such reports. For each of these secondary case-patients, TB could not have been prevented unless their sources had been diagnosed and reported earlier.

For the remaining secondary case-patients, we compared their date of disease onset to the date when contact investigation was initiated for their sources,
the date when each secondary case-patient was identified as a contact, and the date when medical evaluation for each secondary case-patient was initiated and completed. This allowed us to identify those case-patients who developed disease because of delay in being elicited as contacts and delay in initiating or completing medical evaluation of these contacts.

Among those secondary case-patients who had not developed TB by the end of their medical evaluation as a contact, we assessed whether they were given appropriate treatment for tuberculous infection and whether they completed their treatment. Thus, we identified secondary case-patients resulting from failure to start or complete treatment for tuberculous infection. For those secondary case-patients who completed a course of treatment for tuberculous infection but still developed TB, we initially concluded that such treatment had failed. For case-patients with a prior history of TB, we also initially concluded that they had a relapse of TB. For these last 2 categories of case-patients, we placed them into the category of exogenous reinfection if 2 conditions were met: the case-patient had contact with another infectious TB patient after the completion of their treatment for TB infection or disease; and the M tuberculosis isolates from the case-patient and his/her putative source had the same genotype. We used the above criteria to determine why their disease was not prevented after reinfection.

Statistical software (SAS, version 6.12, SAS Institute Inc, Cary, NC; Epi Info, version 6, Centers for Disease Control and Prevention, Atlanta, Ga) was used to calculate relative risks and to generate 95% confidence intervals of point estimates, including use of exact methods when appropriate.

RESULTS

Of the 221 patients with TB reported in Contra Costa County during 1996-1997, 73 (33%) were linked by TB genotyping or an epidemiological relationship, or both, to a single strain of M tuberculosis. This strain was susceptible to all first-line anti-TB drugs. The 73 case-patients did not include 3 case-patients determined to have resulted from laboratory cross-contamination. The demographic, sociobehavioral, and disease characteristics of the 73 case-patients are reported in Table 1. Eighty-five percent of these case-patients were reported from 3 ZIP codes in the densely populated western part of the county. The involved areas had high rates of poverty, homelessness, substance abuse, and HIV infection.

Epidemiologically Linked Clusters

Initially, the 3-person review group separated the 73 case-patients into 13 epidemiologically linked clusters and was left with 20 unlinked case-patients. Based on additional information gathered at the cluster conference, the final grouping of clusters was established: 57 case-patients in 13 epidemiologically linked clusters and 16 unlinked case-patients.

Among the 57 case-patients in linked clusters, there were 6 source case-patients and 51 secondary case-patients (Figure). However, 9 of the 51 secondary case-patients also became secondary source case-patients, giving rise to other cases during 1996-1997. Ten of the 57 clustered case-patients resulted from 7 source case-patients reported prior to 1996, with 5 of 7 reported in 1995. Overall, only 2 (4%) of 51 secondary case-patients resulted from remote infection (transmission that occurred >2 years ago). When we included the case-patients reported prior to 1996 into the 13 clus-
ters, our clusters ranged in size from 2 to 19 case-patients (median, 3 case-patients).

**Primary Reason for Disease Development**

For 20 case-patients, the primary reason for disease development was delayed diagnosis of their sources (TABLE 2). These case-patients were identified and immediately evaluated during the contact investigation of their sources, but they had already developed TB. Among the cases resulting from delayed diagnosis of their sources, 12 (60%) case-patients were pediatric and 7 (35%) were not culture-confirmed. Pediatric case-patients were more likely than adult case-patients to have developed TB from delayed diagnosis of their sources (12/19 vs 8/32; relative risk [RR], 2.5; 95% confidence interval [CI], 1.2-5.0).

Problems associated with elicitation of contact resulted in discovery of 40 cases. Seventeen case-patients were not identified during the contact investigation of their sources. Therefore, the primary reason for disease development was failure to be elicited as a contact. For the 22 cases with no identifiable source (16 unlinked case-patients and 6 source case-patients reported in 1996-1997), we assumed that their primary reason for disease development was also failure to be elicited as a contact. A delay in eliciting a contact led to 1 case-patient. In this instance, the contact investigation surrounding the source case-patient occurred within 1 day of case report to the health department, but it took 72 days for the health department to elicit the contact and the patient developed TB during this period of delay.

Problems associated with evaluation of contacts resulted in 6 case-patients. Four contacts developed TB because they failed to complete their recommended evaluation—1 contact could not be located, a second contact refused any medical evaluation, and 2 other contacts were determined to have a tuberculin skin test but failed to keep multiple medical appointments. Another contact developed TB because of delay in completing his medical evaluation. At the time of initial evaluation, the patient was asymptomatic but had a positive tuberculin skin test result. However, the patient missed appointments for a chest radiograph and was found to have TB when evaluation was completed. One other contact developed TB because of improper evaluation. In this case, the health department did not repeat the tuberculin skin test in the contact who had a negative initial skin test result.

Problems associated with treatment of contacts for tuberculous infection resulted in 7 cases. Isoniazid treatment was recommended to 2 contacts, but they did not keep their medical appointments and subsequently developed TB; another contact was not offered isoniazid treatment because he had completed treatment for a prior episode of TB. One case-patient did start isoniazid treatment but discontinued her treatment and subsequently developed TB. Three contacts developed TB after completing 6 to 12 months of isoniazid treatment for tuberculous infection. Only 1 of the 3 case-patients was certain to have adhered to his treatment since he was receiving directly observed preventive therapy; the other 2 case-patients completed their self-administered preventive therapy.

Three case-patients had prior treatment for TB, but all had evidence of exogenous reinfection. They all had new exposure to an infectious case of TB after completing appropriate treatment for their prior episode of TB. One case-patient received directly observed therapy; the second case-patient did not receive directly observed therapy but had no documented treatment nonadherence. The isolates from the 2 case-patients had the same genotype as the isolates from their current putative source case-patients. Although reinfection is likely in these 2 case-patients, endogenous relapse with the original strain cannot be ruled out. One other case-patient had a history of TB but with an isoniazid-mono-resistant organism. Because the case-patient’s current isolate was pan-sensitive, we concluded that reinfection was likely. None of the 3 case-patients was immunocompromised.

Of the 51 case-patients with identifiable sources, 17 were not elicited as contacts to their sources. Out-of-household contacts were less likely than household contacts to be elicited (15/31 vs 19/20; RR, 0.51; 95% CI, 0.35-0.74). Among the out-of-household contacts, some came in contact with their sources in home settings and others occurred in nonhome settings, with illicit drug use locations being the most common sites. Out-of-household contacts in nonhome settings were less likely to be elicited than out-of-household contacts in home settings (3/13 vs 12/18; RR, 0.35; 95% CI, 0.12-0.98).

**Identified Sources:**

**Time to Diagnosis, Treatment, and Contact Investigation**

Twenty of the 23 identifiable sources were reported from 1995 to 1997. Information on their treatment and contact investigation showed that they were well managed from a public health per-

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**Table 2. Primary Reason for Disease Development**

<table>
<thead>
<tr>
<th>Reason</th>
<th>No. (%)</th>
</tr>
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<tbody>
<tr>
<td>Delay in diagnosis of the source case*</td>
<td>Pediatric cases 12 (16)</td>
</tr>
<tr>
<td>Adult cases 8 (11)</td>
<td></td>
</tr>
<tr>
<td>Problems associated with contact elicitation</td>
<td>Not elicited as a contact†</td>
</tr>
<tr>
<td>Definite 17 (23)</td>
<td></td>
</tr>
<tr>
<td>Presumed 22 (30)</td>
<td></td>
</tr>
<tr>
<td>Delay in being elicited as a contact 1 (1)</td>
<td></td>
</tr>
<tr>
<td>Problems associated with contact evaluation</td>
<td>Incomplete evaluation 4 (5)</td>
</tr>
<tr>
<td>Delay in completing evaluation 1 (1)</td>
<td></td>
</tr>
<tr>
<td>Improper evaluation 1 (1)</td>
<td></td>
</tr>
<tr>
<td>Problems associated with treatment of contact for tuberculous infection</td>
<td>Failure to start treatment 3 (4)</td>
</tr>
<tr>
<td>Failure to complete treatment 1 (1)</td>
<td></td>
</tr>
<tr>
<td>Disease following completion of treatment 3 (4)</td>
<td></td>
</tr>
</tbody>
</table>

*Delay in diagnosis of a source case that resulted in either a pediatric or adult secondary case.
†Refers to the case being elicited as a contact during the contact investigation of the source case that led to disease in the case of interest. For cases definitely not elicited as a contact, the source case is known. For cases presumably not elicited as a contact, the source case is not known.
Table 3. Twenty Identified Source Cases (1995-1997): Time to Diagnosis, Treatment, and Contact Investigation

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from symptom onset to diagnosis, d</td>
<td></td>
</tr>
<tr>
<td>≤60</td>
<td>8 (40)</td>
</tr>
<tr>
<td>&gt;60</td>
<td>12 (60)</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>Initial treatment regimen</td>
<td></td>
</tr>
<tr>
<td>Isoniazid, rifampin, pyrazinamide, and ethambutol</td>
<td>18 (90)</td>
</tr>
<tr>
<td>Isoniazid, rifampin, and pyrazinamide</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Isoniazid, rifampin, and ethambutol</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Use of directly observed therapy</td>
<td>19 (95)</td>
</tr>
<tr>
<td>Episodes of nonadherence</td>
<td>9 (45)</td>
</tr>
<tr>
<td>Treatment outcome</td>
<td></td>
</tr>
<tr>
<td>Completed treatment</td>
<td>18 (90)</td>
</tr>
<tr>
<td>Defaulted from treatment</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Died during treatment</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Moved before treatment completion</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Contact investigation*</td>
<td></td>
</tr>
<tr>
<td>Initiated contact investigation</td>
<td>19 (100)</td>
</tr>
<tr>
<td>Contact investigation initiated</td>
<td>3 (16)</td>
</tr>
<tr>
<td>&gt;7 days after case report</td>
<td></td>
</tr>
<tr>
<td>No. of contacts identified, mean [median] [range]</td>
<td>19 (16) [1-62]</td>
</tr>
<tr>
<td>No. of cases with &lt;8 contacts identified</td>
<td>3 (16)</td>
</tr>
</tbody>
</table>

*Contact investigation record not available for 1 case; 19 cases used as denominator in analysis.

In 8 of the 12 case-patients with longer than 60 days from symptom onset to diagnosis, secondary cases of TB had already developed among their contacts by the time the diagnosis was established. In contrast, only 2 of the 8 case-patients with 60 days or less from symptom onset to diagnosis had secondary cases of TB among their contacts by the time they were diagnosed (RR, 0.38; 95% CI, 0.11-1.33).

Overall, of the 10 sources with secondary cases that resulted from their delayed diagnosis, 8 took longer than 60 days from symptom onset to diagnosis. For 9 of these 10 sources, we determined that patient delay in seeking medical evaluation was the main cause of the delay in establishing the diagnosis.

**Linkage With Prior Cluster**

In 1992, a strain of M tuberculosis that had 2 copies of IS6110 was isolated from Contra Costa County. Bradford et al\(^9\) reported a cluster of 19 cases with this strain as part of a larger study. Using the pTBN12 method, one investigator (Don Cave, PhD, University of Arkansas for Medical Sciences, Little Rock) compared the current strain of M tuberculosis to the prior strain and they had the same restriction fragment-length polymorphism pattern. Case-patients in the 2 clusters resided in the same area and had similar patient demographics. We did not attempt to find direct epidemiological linkages between the 2 clusters.

**COMMENT**

In this study, we used molecular and conventional epidemiological methods, along with a detailed assessment of program data, to determine the factors responsible for the spread of a strain of M tuberculosis in a community. Over a 2-year period, this strain of M tuberculosis was responsible for one third of all cases in a community that has implemented the key elements of TB control. These cases did not result from a single source outbreak or institutional transmission but rather from multiple sources infecting others in community settings, with the vast majority of transmission occurring within the 2 years prior to disease development. A detailed examination of why this strain of M tuberculosis successfully propagated in this community revealed it was largely due to failure in contact elicitation and delay in diagnosis of infectious TB case-patients.

More than 50% of the case-patients were not elicited as contacts to their sources. This finding of TB among unidentified contacts is consistent with other studies, which showed that routine contact investigation identified epidemiological linkages in only a small percentage of case-patients with the same strain of M tuberculosis.\(^4,5,7\) Such results have led some investigators to recommend that contact investigation activities, at least in our urban communities, should be intensified.\(^5,7\) Our results lend support to this recommendation since nearly half of the missed epidemiological linkages could be established in retrospect. We believe an intensification of contact identification activities in this community can identify more infected contacts before they become TB cases.

Such intensification, at least in this community, will have to focus on out-of-household contacts because the vast majority of cases from failed contact elicitation occurred in this population. In particular, contacts in settings other than the typical household accounted for a large proportion of the TB cases from failed contact elicitation. Special effort should be targeted toward the population with a high prevalence of substance abuse and homelessness. To identify this group of contacts, investigations based on location or social network may be useful.\(^9,16,17\) Clearly, the traditional concentric-circle approach is inadequate in this community.

Although secondary cases occurred from problems in contact elicitation, it is important to point out that the county’s contact investigation program was functioning properly. The health department initiated contact investigations for all infectious TB case-patients and this was done in a timely manner for nearly all identified sources in this study. Both the mean and median number of contacts identified was high. Despite this, cases of TB due to recent infection continued to occur.

In this study, at least one quarter of the patients developed TB because of delayed diagnosis of their sources. Although delayed diagnosis of TB is believed to contribute to the transmission of M tuberculosis, the importance of this to the development of TB in a given community has not been well described. Delayed diagnosis has been identified as a major reason for community-based TB outbreaks.\(^18\) Studies on delayed diagnosis of TB have focused on determining the risk factors for delayed diagnosis, such as older age, atypical radiographic presentation, or extrapulmonary TB.\(^16,21\) Other studies have explored patients’ attitudes and beliefs to determine how they may lead to delays in diagnosis.\(^22\) To our knowledge, this is the first study to actually quantify the contribution of delayed diagnosis to the development of secondary case-patients with TB.
In this community, delayed diagnosis of TB disproportionately affected the development of TB in children. Two thirds of the pediatric case-patients with this strain of M tuberculosis developed disease because of delayed diagnosis of their sources. Pediatric case-patients were 5 times more likely than adult case-patients to have TB that resulted from delayed diagnosis of their sources.

Some studies have defined delay in diagnosis of TB by a period of at least 60 days from symptom onset to diagnosis. Our study did not focus on absolute delay but instead focused on whether any delay, regardless of duration, resulted in secondary cases. We found that even though 60% of the sources had a delay from symptom onset to diagnosis of at least 60 days, not all such delays led to secondary cases. In contrast, some secondary case-patients did develop TB even though their sources were diagnosed within 60 days from symptom onset. Although sources with delays in TB diagnoses were more likely to be linked to secondary case-patients, this association was not statistically significant. In this study, patient delay in seeking medical care was more important than physician delay as a factor for disease development. Therefore, interventions to reduce delayed diagnosis in this community will have to include efforts to get patients to seek health care earlier.

Less than 20% of the case-patients resulted from problems with the evaluation or treatment of identified contacts. Several contacts developed TB because they were nonadherent to various steps in their evaluation despite efforts by the health department. Some contacts also failed to start treatment or did not complete treatment for tuberculosis infection. A few contacts developed TB after completing a course of preventive therapy; however, the degree of adherence to such therapy is unknown. Although improvement in contact evaluation and treatment should be encouraged, it is important to point out that such improvement will only prevent a small percentage of cases in this community.

The propagation of this strain of M tuberculosis in this community is likely to have been going on for several years. The most convincing evidence of this is the identification of a cluster of case-patients with this strain of M tuberculosis dating back to 1992. Although this strain appears to be endemic in this community, most of the patients with disease from this strain were recently infected. Therefore, the presence of an endemic strain of M tuberculosis does not preclude the possibility that disease from the strain is due to recent infection.

There are limitations to this study. First, these results do not tell us how well the program actually performed in contact investigation activities, it only tells us about the cases that develop from gaps in contact investigation activities. We also cannot determine the number of cases prevented because of current activities. A control group of case-patients would be needed to determine this. Second, we could not evaluate all factors contributing to the successful propagation of this strain of M tuberculosis. The organism's virulence or the genetic susceptibility of individuals to TB may play a part in the successful propagation of the strain of M tuberculosis. Neither of these factors was assessed. Third, we cannot be certain that case-patients with epidemiological linkages to this strain of M tuberculosis, but without culture confirmation, were infected by the same strain. A recent study found that a third of the TB case-patients with epidemiological linkages were infected with a different strain of M tuberculosis. However, case-patients born in the United States (as with our study population) were more likely to have the same strain. In addition, the high number of pediatric case-patients among the culture-unconfirmed case-patients also increases the likelihood that these case-patients were infected by the same strain. Fourth, the epidemiology of TB tends to vary from location to location. Therefore our results may not be generalizable to all communities in which there is ongoing transmission of M tuberculosis. However, the methods used in this study can be used to determine why disease due to recent infection continues to occur in other communities.

Our results are consistent with molecular epidemiological studies from TB control programs in San Francisco and Baltimore, Md. These studies found that even when the treatment completion rate for TB is high and contact investigation is performed, disease due to ongoing transmission could not be eliminated and, in fact, accounted for a substantial proportion of cases. Our results extend these findings by identifying key reasons for the development of TB. Unless we can identify cases earlier and elicit a complete list of contacts, we will not be able to eliminate TB from ongoing transmission of M tuberculosis in this and likely other communities using currently available tools.

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**REFERENCES**

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The great art consists in devising decisive experiments, leaving no place to the imagination of the observer. Imagination is needed to give wings to thought at the beginning of experimental investigations on any given subject. When, however, the time has come to conclude, and to interpret the facts derived from observations, imagination must submit to the factual results of the experiments.
—Louis Pasteur (1822-1895)