

A network-informed approach to investigating a tuberculosis outbreak: implications for enhancing contact investigations

P. D. McElroy,* R. B. Rothenberg,† R. Varghese,‡ R. Woodruff,§ G. O. Minns,§ S. Q. Muth,¶ L. A. Lambert,* R. Ridzon*

* Surveillance and Epidemiology Branch, Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, † Department of Family and Preventive Medicine, Emory University School of Medicine, Atlanta, ‡ Epidemic Intelligence Service, Epidemiology Program Office, Centers for Disease Control and Prevention, Atlanta, Georgia; § Department of Community Health, Wichita-Sedwick County, Wichita, Kansas; ¶ Quintus-ential Solutions, Colorado Springs, Colorado, USA

SUMMARY

BACKGROUND: To elucidate networks of *Mycobacterium tuberculosis* transmission, it may be appropriate to characterize the types of relationships among tuberculosis (TB) cases and their contacts (with and without latent TB infection) in addition to relying on traditional efforts to distinguish 'close' from 'casual' contacts.

SETTING: A TB outbreak in a US low incidence state.

OBJECTIVE: To evaluate whether social network analysis can provide insights into transmission settings that might otherwise go unrecognized by routine practices.

DESIGN: All adult outbreak-associated cases ($n = 19$) and a convenience sample of their contacts with and without latent TB infection (LTBI) ($n = 26$) were re-interviewed in 2001 using a structured questionnaire. Network analysis software was used to create diagrams illustrating important persons within the outbreak net-

work, as well as types of activities TB cases engaged in with their contacts.

RESULTS: Drug use and drug sharing were more commonly reported among cases and their infected contacts than among contacts without LTBI. TB cases central to the outbreak network used crack cocaine, uncovering the need to focus control efforts on specific sites and persons involved in illicit drug use.

CONCLUSION: Outbreaks occur even in areas with low TB incidence, frequently among groups whose drug use or other illegal activities complicate control efforts. TB programs should consider the use of network analysis as a supplement to routine contact investigations to identify unrecognized patterns of *M. tuberculosis* transmission.

KEY WORDS: tuberculosis; contact investigations; social network analysis

THE RATIONALE for tracing and investigating contacts of persons with tuberculosis (TB) is that infectious patients can transmit infection to their contacts through airborne droplet nuclei containing *Mycobacterium tuberculosis*.^{1,2} Those contacts who show evidence of latent TB infection (LTBI) can reduce by 60–70% their risk of progressing to active disease by completing a 6- to 9-month course of isoniazid.³ Aside from making decisions regarding who gets further screening for active disease or LTBI, most of the data collected as part of the contact investigation process are used by TB control programs as an indicator of program success (e.g., number of contacts identified per case, number with latent TB infection, etc.). However, the richness of contact investigation data has the potential to accomplish a great deal more when the combined, cumulative data from a community (or even a larger geographic area) are analyzed for transmission patterns.

In recent years, primarily as a result of the human immunodeficiency virus and sexually transmitted disease epidemics, disease controllers have become increasingly interested in using social network analysis to detect and understand unrecognized patterns of disease transmission.^{4–6} Network analysis permits mapping and visualization of contact investigation data, revealing connections among cases and contacts as both groups are identified over time. Instead of considering the results of each contact investigation as an independent set of information, network analysis aims to examine and describe all data accumulated from the contact investigations performed by a TB program. More advanced methods provide quantitative metrics that indicate the relative position and importance of the cases, contacts, and public sites most critical to the networks of *M. tuberculosis* transmission in a community. The recent application of network analysis in the field of TB control suggests that this

approach holds promise for improving both the understanding of transmission dynamics within a community and the effectiveness with which secondary TB cases and high-risk contacts are discovered through the contact investigation process.^{7,8}

The underlying hypothesis for using network analysis in contact investigations is that this strategy will potentially help TB controllers find additional contacts in a given social milieu. TB disease or LTBI among an infectious person's contacts may be the consequence of direct exposure either to the source patient or to another, perhaps unidentified, infectious source in the community. A network investigation may uncover persons with TB who are epidemiologically linked through a common network (e.g., social, sexual, or drug using connections) and have *M. tuberculosis* isolates with matching DNA fingerprint patterns, as well as persons who are epidemiologically linked but do not have isolates with matching DNA fingerprint patterns.

In this report, we explore the use of network analysis as an epidemiologic tool complementing routine contact tracing and DNA fingerprinting of *M. tuberculosis* isolates during the investigation of a protracted TB outbreak (1994–2001) in Wichita, Kansas, involving 19 adults and three children. The outbreak was first detected among women working as exotic dancers. Despite several years of control efforts directed at the clubs where dancers worked, transmission of the outbreak strain was not contained. Concern that the problem was escalating prompted our investigation of the role of social, sexual, and drug using network relationships in understanding ongoing *M. tuberculosis* transmission in the community.

STUDY POPULATION AND METHODS

Initial outbreak investigation

In January 2001, the US Centers for Disease Control and Prevention (CDC) assisted the Wichita-Sedgwick County Department of Health and the Kansas Department of Health and Environment in investigating a cluster of 22 TB patients diagnosed between 1994 and 2001. Patients included 10 men, nine women, and three children. Seven of the nine female patients had sputum acid-fast bacilli (AFB) smear-positive cavitary pulmonary TB at the time of diagnosis and worked as exotic dancers in the Wichita area. (Exotic dancers are usually women employed by clubs to dance nude or near-nude for the entertainment of men, although either sex can be the dancer or the observer.) All three pediatric patients had household contact with at least one exotic dancer with TB. Epidemiologic links to female patients had previously been established for the majority of male patients through routine contact investigation procedures. Concern about ongoing transmission in unrecognized sites led to the request for additional help from the CDC Division of TB Elimination. In consultation with state and local health author-

ities, all adult outbreak-associated cases and selected named and unnamed contacts were reinterviewed using a network analysis questionnaire.

Terminology

A tuberculin skin test (TST) was performed on contacts using the Mantoux method (5TU purified protein derivative [PPD] intradermally) and induration ≥ 5 mm was interpreted as a positive TST reaction. Cases are the adult outbreak-associated TB patients included in the county's routine contact investigation. Primary contacts are persons identified by TB cases and interviewed at the time of the county's original routine contact investigation, and were either TST-positive or -negative. Secondary contacts are persons named by either cases or primary contacts at the time of the network analysis interviews in 2001. As the network analysis interviews were conducted months or years after the county's routine contact investigations, the group of secondary contacts included persons previously identified at the time of the original contact investigations. Secondary contacts named by only one interviewee are referred to as terminal contacts.

Network interviews

Two categories of persons were interviewed using the network questionnaire: 1) outbreak-associated adult TB cases, and 2) a sample of primary contacts. In January 2001, the adult cases were contacted and reinterviewed using the network analysis questionnaire described below. A convenience sample from among the 90 primary contacts named at the time of the original contact investigations (128 were location-based contacts) was also interviewed. This sampling approach was necessary as a random sampling method would not have provided a sufficient number of contacts who could be located and interviewed within the allocated amount of time for data collection. In order to uncover broad differences between persons with and without evidence of latent TB infection (and their corresponding location within a transmission network), an attempt was made to interview an equal number of TST-positive and -negative contacts over a 2-week period of data collection. Interviews were conducted at the person's home or the health department, or at clubs out of business hours.

Network questionnaire

An extensive questionnaire was developed by adapting an instrument previously used in sexual network analysis.^{9,10} Data collected with the questionnaire included demographic characteristics; travel, incarceration, and employment history; drug using practices (any time in the past and the 6-month period preceding the interview); sexual activity (commercial sex work, exchanging sex for drugs or drugs for sex); and places of social aggregation with primary focus on specific exotic dance clubs, together with dates of

first and last attendance. The questionnaire asked the respondent to identify persons (secondary contacts) with whom they shared air space at home, work, leisure, or during party activities. Type of contact between the respondent and each secondary contact was elucidated by asking the respondent (in three separate questions) whether he/she had shared drugs with, or had sex with, or other very close contact with each named person within the past month. The term 'close' was not defined for the respondents. Finally, the questionnaire elicited general characteristics regarding each secondary contact named by the respondent (age, sex, race/ethnicity, relationship type, duration known, activities engaged in).

DNA fingerprinting of M. tuberculosis

IS6110 DNA fingerprint analysis of *M. tuberculosis* isolates was performed according to a standard method.¹¹ DNA fingerprint patterns were considered to match if the patterns were identical or differed by the addition or subtraction of a single band.

Data management and analysis

All network questionnaire responses were entered into a Microsoft Access[®] database. The interviewed cases and primary contacts were assigned a unique 4-digit identification number. Secondary contacts were assigned a 3-digit identification number that could be linked to each case or primary contact who named them. Secondary contacts named by more than one interviewee were considered to be the same individual if they matched on first and last names (or alias), approximate age, and ethnicity. In the absence of a last name, matches were identified using first name, approximate age, ethnicity, and street address. The data were assessed using SAS¹² for epidemiologic analysis, and Ucinet-V¹³ and PAJEK¹⁴ for network analysis and visualization.

RESULTS

General characteristics of interviewed cases and primary contacts

We interviewed all 19 adult cases and 26 primary contacts (15 TST-positive and 11 TST-negative, or 29% of the originally identified 90 contacts). Duration of interviews ranged in length from one to two hours. Demographic characteristics of the two groups are presented in Table 1. Cases and primary contacts named 198 and 273 secondary contacts, respectively. The cases were slightly older (median age, 35 years) than primary contacts (median age, 31 years) and fewer had completed high school (53% vs. 69%). Almost three fourths of both groups were white. Twelve (46%) cases were married at the time of interview compared to seven (37%) primary contacts. Five (26%) cases and four (15%) primary contacts described themselves as unemployed, while about 70% of both groups stated that a paid salary or a business was their primary source of income. Two women in each

Table 1 Demographic characteristics of cases and primary contacts interviewed with network questionnaire, Wichita, Kansas, 2001

Characteristics	Cases (n = 19) n (%)	Primary contacts (n = 26) n (%)
Median age (years)	35	31
Female	9 (47)	16 (62)
Worked as a dancer	7 (37)	9 (35)
Worked for an escort service	2 (11)	2 (8)
White	14 (74)	19 (73)
African American	4 (21)	3 (12)
High school degree or higher	10 (53)	18 (69)
Married	12 (46)	7 (37)
Ever incarcerated	12 (63)	13 (50)
Number of contacts named*	198	273

* Secondary contacts.

group stated that they had worked for escort services, and two thirds of the cases and half of the primary contacts had been previously incarcerated.

Cases and primary contacts (stratified by TST status) named secondary contacts (total n = 471) who were similar with regard to age distribution, gender, and ethnicity (Table 2). A similar proportion of cases and primary contacts lived with their secondary contacts. The types of relationships with secondary contacts and the number of months known were also similar.

Sexual and drug using activity among cases and primary contacts

Ninety per cent of those interviewed stated that they were sexually active at some time in the past, but a substantial proportion (68% of cases and 27% of primary contacts) reported having had no sex partners in the month preceding the network interview. Five (56%) of the nine women with TB reported having sex with women as well as with men. Five (26%) of the 19 cases reported sex with an injection drug user (IDU) compared to only two (8%) of 26 primary contacts. Five (11%) of 45 cases and primary contacts reported exchanging drugs or money for sex. Cases and TST-negative primary contacts showed the greatest disparity in the proportion of secondary contacts with whom they had either 'close contact' or sex (Table 2). Compared with the cases, TST-negative primary contacts reported over twice as high a proportion (26%) of 'close contact' with their identified contacts.

Drug use was more common among cases than among primary contacts (Table 3). With the exception of alcohol, drug use among cases exceeded that among primary contacts by two to four fold. Also, 19% of cases reported sharing drugs with their secondary contacts, compared to 8% of the TST-positive primary contacts and none of the TST-negative primary contacts (Table 2). Most of this predominance was attributable to female cases who, as a subgroup, had the highest proportion (as well as absolute number) of amphetamine, cocaine, crack, marijuana, and opiate use. Four

Table 2 Characteristics of secondary contacts identified by cases and primary contacts at time of social network interview, January 2001, Wichita, Kansas

	Contacts of interviewees			
	Total (n = 471) n (%)	Cases (n = 198) n (%)	TST+ primary contacts (n = 165) n (%)	TST- primary contacts (n = 108) n (%)
Median age (range)	31 (1–93)	32 (1–93)	32 (2–90)	29 (1–70)
Male	238 (51)	109 (55)	81 (49)	48 (44)
Race/ethnicity				
White	373 (79)	166 (84)	124 (75)	83 (77)
Black	70 (15)	23 (12)	32 (19)	15 (14)
Hispanic	17 (4)	4 (2)	4 (2)	9 (8)
Asian/Pacific Islander	4 (1)	0 (0)	3 (2)	1 (1)
Native American	6 (1)	4 (2)	2 (1)	0 (0)
Other	1 (<1)	1 (<1)	0 (0)	0 (0)
Interviewee lives with contact	118 (25)	51 (26)	34 (21)	33 (31)
Relationship type				
Relative	160 (34)	57 (29)	60 (36)	43 (40)
Neighbor	5 (1)	5 (3)	0 (0)	0 (0)
Co-worker	120 (25)	55 (28)	44 (27)	21 (19)
Friend	176 (37)	73 (37)	59 (36)	44 (41)
Unspecified	10 (2)	8 (4)	2 (1)	0 (0)
Months interviewee has known				
≤6	39 (8)	25 (13)	11 (7)	3 (3)
7–24	79 (17)	30 (15)	32 (19)	17 (16)
25–48	65 (13)	18 (9)	24 (15)	23 (21)
>48	263 (56)	108 (55)	92 (56)	63 (58)
Unknown	25 (5)	17 (9)	6 (4)	2 (2)
Activities during contact				
Close contact	63 (13)	23 (12)	12 (7)	28 (26)
Engages in sex	41 (9)	20 (10)	9 (5)	12 (11)
Shares drugs	51 (11)	37 (19)	14 (8)	0 (0)

TST = tuberculin skin test; + = positive; - = negative.

(44%) of the nine female cases (four of the six who used crack) reported 'shotgunning,' a drug sharing and conserving practice whereby inhaled smoke (from crack or marijuana) is exhaled or blown directly from one user's mouth into the mouth of another.¹⁵ The average number of drug partners in the past month was also highest for these same women, primarily because of one person who reported 100 drug partners.

Table 3 Frequency of drug use among persons interviewed during the investigation of a TB outbreak in Wichita, Kansas, 1994–2001

Drug	Active TB cases (n = 19) n (%)	Primary contacts	
		TST+ (n = 15) n (%)	TST- (n = 11) n (%)
Alcohol	15 (79)	7 (47)	10 (91)
Amphetamine	9 (47)	2 (13)	1 (9)
Cocaine	10 (53)	1 (7)	1 (9)
Crack	8 (42)	2 (13)	3 (27)
Marijuana	15 (79)	5 (33)	4 (36)
Opiates	7 (37)	0 (0)	1 (9)
Shotgunning	5 (26)	1 (7)	1 (9)
Mean number of drugs used	4.3	1.2	2.0

TST = tuberculin skin test; + = positive; - = negative.

Network configuration

With one exception, cases and primary contacts demonstrated considerable assortative mixing (persons with similar characteristics who connect with each other) by age and ethnicity. That is, persons aged ≥ 30 generally named others who were ≥ 30 (70% of secondary contacts named by cases; 60% of secondary contacts named by primary contacts). The secondary contacts identified by white cases and primary contacts were predominantly white (96% and 91% of secondary contacts named by cases and primary contacts, respectively). However, only 37% of the secondary contacts named by African American cases were of the same race, compared to the African American primary contacts who named predominantly other African Americans as secondary contacts (84%). Mixing by gender was, as expected, largely disassortative (with only small deviations, half the secondary contacts named by either sex were of the same sex, and half were of the opposite sex). The mixing pattern for sexual contacts mirrored that of the total group. The two sexual partners named by the four African American cases were both white, reflecting the overall disassortative mixing of this small group.

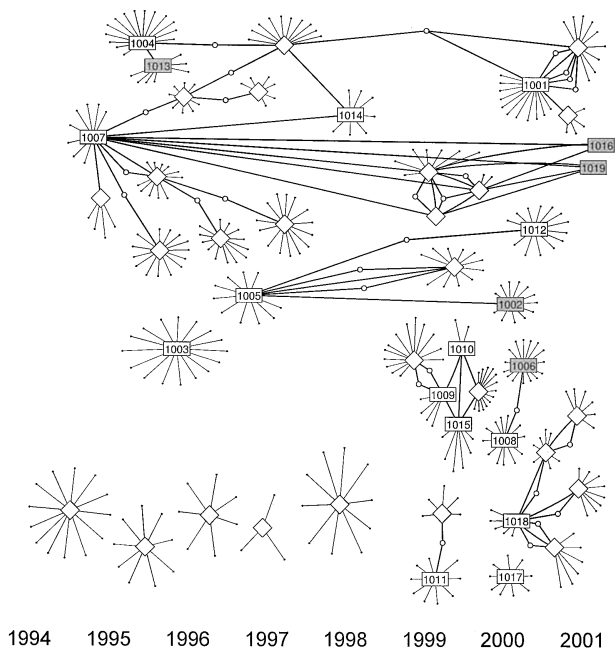
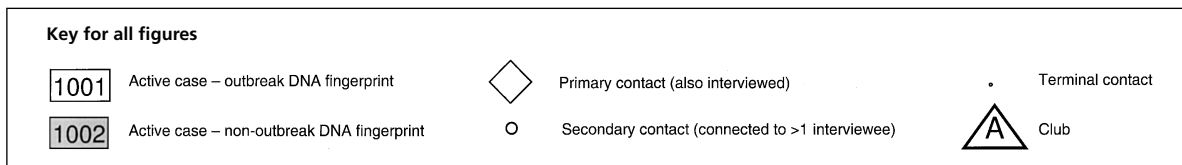


Figure 1 Diagram of all 471 identified network connections among interviewed cases and primary contacts, and their reported secondary contacts, Wichita, Kansas, 1994–2001. Dates at bottom of figure are the year each TB case was diagnosed.

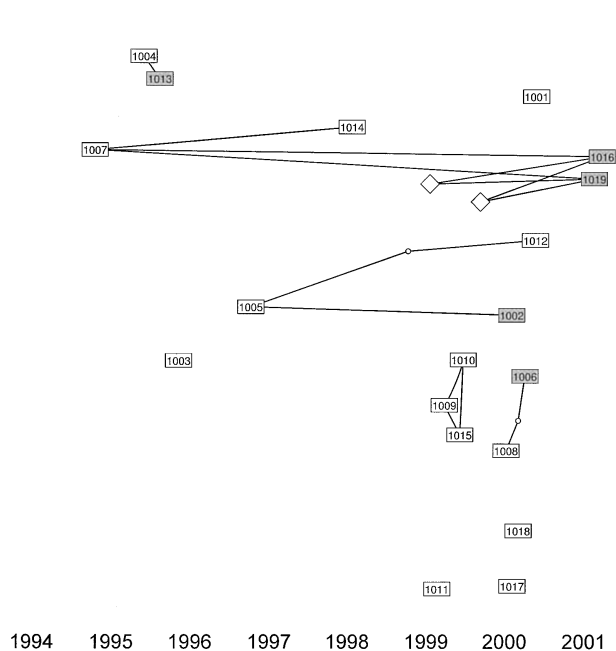


Figure 3 Diagram of interconnections among adult TB cases ($n = 19$) included in the outbreak investigation, Wichita, Kansas, 1994–2001. Dates at bottom of figure are the year each TB case was diagnosed.

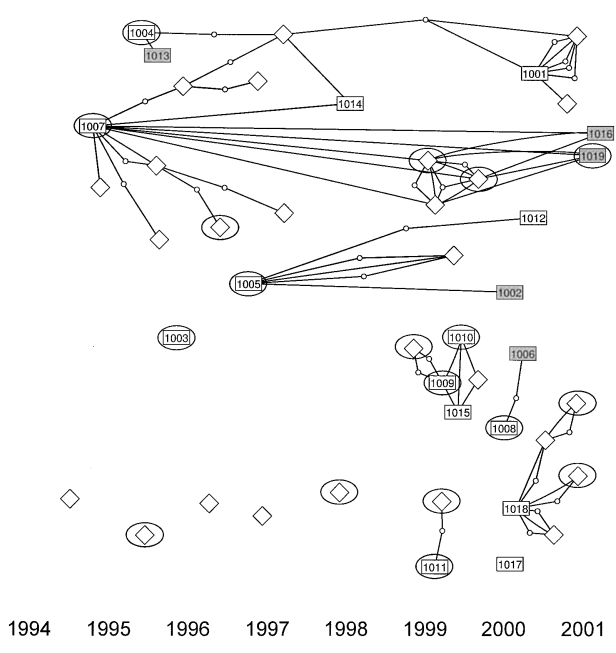


Figure 2 Diagram of interviewed cases and primary contacts and the secondary contacts connecting them ($n = 73$), Wichita, Kansas, 1994–2001. Dates at bottom of figure are the year each TB case was diagnosed.

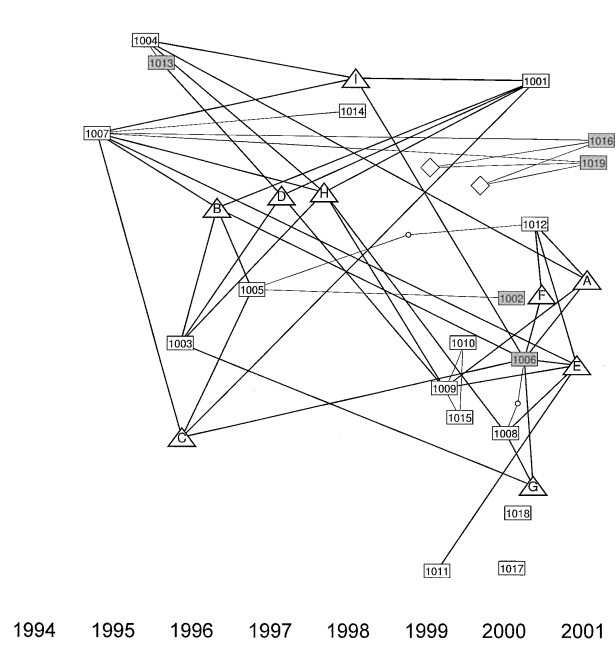


Figure 4 Diagram of interconnections among adult TB cases ($n = 19$) and places of aggregation (A-I), Wichita, Kansas, 1994–2001. Dates at bottom of figure are the year each TB case was diagnosed.

Network visualization

The complexity of the interactions among all interviewees (19 cases and 26 primary contacts) and their 471 secondary contacts is demonstrated in Figure 1, a graphic visualization of the outbreak network. Upon removal of 'terminal contacts,' the diagram is simplified to interviewees, and to all secondary contacts connected with two or more of them (Figure 2). The simplified network demonstrates the relative position of five persons (shaded) initially thought to be associated with the outbreak owing to epidemiologic links to other outbreak cases. However, subsequent DNA fingerprint analysis of isolates from all outbreak-associated cases revealed patterns among these five isolates that differed from the outbreak strain (11-band pattern) that caused disease in the remaining 14 outbreak cases. In addition, the diagram permits direct visualization of the role of crack cocaine use (circled cases and contacts) in the outbreak. In a further simplification (Figure 3) that includes only cases and the primary and secondary contacts connecting at least two cases, several small clusters are observed, but direct linkage among all cases is not demonstrated. Based on information obtained concerning attendance at exotic dance clubs (see Methods), we included the clubs as nodes in the network diagram⁸ (Figure 4). The graph establishes, with two exceptions (nodes 1017 and 1018), the potential for contact between each case and at least one other case. The isolate from case 1017 matched the outbreak strain, but investigation revealed this was likely the result of laboratory cross-contamination with a specimen obtained from case 1008, a female patient with strong epidemiologic ties to the outbreak network. Thus, with the exception of case 1018, a link to strip clubs was established as an epidemiologic connection among all cases with *M. tuberculosis* isolates having the same 11-band DNA fingerprint pattern (outbreak strain), as well as with persons infected with non-outbreak strains.

DISCUSSION

Modern TB control strategies are evolving as new approaches emerge from molecular, pharmaceutical, and diagnostic laboratories. For example, DNA fingerprinting has become a useful molecular tool for identifying persons who may be part of a common source of *M. tuberculosis* transmission.¹⁶⁻²¹ Unfortunately, epidemiologic investigation methods have not kept pace with these other advances in disease control. While current epidemiologic approaches generally identify links among outbreak-associated cases, often the majority (up to 75%) of TB cases sharing a matching DNA fingerprint pattern cannot be connected epidemiologically.²² Thus, while TB case clusters may be detected through DNA fingerprinting methods, efforts to successfully eliminate TB will be

sub-optimal if these clusters are only recognized and not investigated. Case clusters, and the infected and uninfected contacts associated with them, need to be described and understood through systematic methods, including network analysis.

Based upon our findings from the current study, we wish to highlight two main concepts regarding the use of network analysis to enhance TB contact investigations: 1) these methods may elucidate connections among cases and persons with LTBI previously unrecognized by traditional contact investigation methods; and 2) they can identify differences in behaviors in a group that help focus attention toward appropriate sub-groups despite seeming similarities among group members.

First, network-based methods may provide evidence for direct connections among cases and persons with LTBI, as well as indirect evidence, such as overlap in attendance at places of social aggregation and drug using behaviors. In combination with DNA fingerprinting, these methods can be used to verify and explain recent transmission of *M. tuberculosis*. Upon construction of the outbreak network diagram that included TB cases as well as contacts, the location of particular persons (nodes) within the network helped identify characteristics and behaviors that were likely important for maintaining *M. tuberculosis* transmission in a community. Visualization of the network members, accompanied by analysis of their characteristics, may help TB controllers find additional high-risk network members with TB or candidates for treatment of LTBI. For example, characteristics of nodes at the fringe of the network are probably less relevant for planning control strategies than are characteristics of the more centrally-located nodes in the network. In this outbreak, crack cocaine use by cases and TST-positive contacts was their single biggest difference from the TST-negative network members.

Second, network analysis can help discern behavior or relationship differences among various members of a seemingly similar group, and show the variation in behaviors that may explain transmission. As seen in Figure 2, four of the five cases with isolates having a DNA fingerprint different from the other outbreak cases in the network were persons who reported no use of crack cocaine. The fact that these cases had isolates different from the outbreak strain, and were less likely to be crack users than were the outbreak cases and their contacts, supports the finding that crack use was a characteristic of the outbreak network. These five cases with unique strains were thus retained in the network diagram to highlight the relative importance of crack use. In Figures 1 and 2, three cases with isolates that had unique DNA fingerprints (cases 1002, 1006, and 1013) did not have a single primary contact that overlapped with any other cases. The last two outbreak-associated cases in 2001 (cases 1016 and 1019) were a husband and wife in a drug sharing relationship with persons from the out-

break network. One of the couple's identified contacts was case 1007 (diagnosed in 1994). Isolates from the husband/wife pair shared a matching DNA fingerprint pattern that was different from the outbreak strain. Even prior to knowing the strain types, case 1007 was not considered the likely source of the couple's infection. Yet her close association with the husband/wife couple highlighted the interactive nature of the drug using group. This analysis permitted the construction of a network of transmission that evolved over 7 years. It identified a small, highly interactive group that transmitted *M. tuberculosis*, possibly facilitated by behaviors common to drug sharing relationships (e.g., shotgunning). Our retrospective reconstruction shows that an investigation focusing on a single epidemic DNA fingerprint pattern may ultimately identify TB cases caused by unrelated strains of *M. tuberculosis* that may be circulating in the same high-risk social environment.

The social network approach used in this report complemented the standard contact investigation. As part of the network approach, contacts of TB cases were also interviewed and asked the same questions as the cases. Comparison persons are often chosen, as was done here, from among the contacts. This group of contacts was selected to help elucidate the network relationships, rather than to serve as a 'control' group. While the use of convenience sampling may have resulted in a failure to interview contacts who were even more representative of the network, our retrospective approach and limited time for data collection precluded the selection of a sufficiently large random sample of contacts. As this is not a standard case-control study, the comparison of cases and primary contacts in this instance is purely descriptive. The calculation of odds ratios, *P* values, and confidence limits is in fact unwarranted, given the nature of the sample and lack of statistical independence among observations. The lack of such simple summary statistics may be unsatisfying from an epidemiologic perspective, but we believe this limitation is offset by insights that were gained into network structure, temporal relationships, and the ability to understand the role of particular TB cases in transmitting *M. tuberculosis* within a community.

Prior to this analysis, the Wichita TB control program had not recognized crack cocaine, and the sites where persons congregate to share it, as important factors associated with *M. tuberculosis* transmission in their jurisdiction. These findings prompted the Wichita TB control staff to ask each newly diagnosed person specific questions about drug use. Several sites (e.g., motels and private homes) were subsequently identified that previously diagnosed cases and contacts with LTBI had frequented. TB screening activities were recently conducted at these locations.

The retrospective nature of this investigation precluded an evaluation of network analysis as a tool for

interrupting, or slowing, transmission. The results suggest, however, that such an approach, undertaken in 'real time' under circumstances of heightened transmission (e.g., a network of persons in multiple sexual or drug using relationships), would be of value in finding cases of LTBI and TB disease with multiple DNA fingerprint types. Such potential remains to be determined. However, had the relevance of drug use and drug sharing behavior in this outbreak situation been detected a few years earlier, it is possible that interventions directed at such settings could have ameliorated the magnitude of transmission in this community.

In a recent report on contact investigations conducted by five TB control programs and the outcomes of these investigations, the authors concluded that improvement in the current contact investigation strategy is necessary.²³ Six approaches to improving contact investigations were proposed, with emphasis on the need to collect additional data through a prospective study. We propose a seventh approach: applying network analysis methods to data collected during contact investigations. While this strategy needs to be further refined and simplified before it can be implemented by a typical TB control program, the long-term benefits may help the United States achieve TB elimination. The current contact investigation paradigm will likely benefit from the collection of additional ethnographic data from TB patients and their contacts, but more emphasis must be placed on what is done with these data following collection by TB controllers.

Current approaches to contact investigations may leave many high-risk contacts unidentified, unscreened, and untreated. As recently noted by Mohle-Boetani and Flood, the process of prioritizing contacts for evaluation must consider not only the risk of LTBI, but also the risk that LTBI will progress to TB disease.²⁴ The elimination of TB in the US will, in part, require enhanced strategies for conducting routine contact investigations and prioritizing persons identified by infectious cases. Network analysis offers the potential to directly identify a greater number of high-risk contacts who will benefit from treatment of LTBI. In addition, the strategy may help TB controllers focus on particular locations, behaviors, or risk groups in greatest need of attention.

Acknowledgements

The authors thank the following persons for their dedication to TB control in Wichita-Sedgwick County in this investigation: Charles Magruder, Virginia Barnett, Peggy Baker, Eddie Brady, Tamika Julian, of the Wichita-Sedgwick County Department of Community Health, as well as Gianfranco Pezzino, Mindee Reece, Allison Alejos of the Kansas Department of Health and Environment. We are also thankful to Scott Jones and Zachary Taylor of the Field Services Branch, Division of Tuberculosis Elimination, CDC, for their assistance with this investigation. DNA fingerprint analysis was performed by the Arkansas Regional Laboratory of the National Tuberculosis Genotyping and Surveillance Network.

Preliminary results of this investigation were presented at the North American meeting of the International Union Against Tuberculosis and Lung Disease in Vancouver, BC, March 2002.

References

- Control and prevention of tuberculosis in the United Kingdom: code of practice 2000. Joint Tuberculosis Committee of the British Thoracic Society. *Thorax* 2000; 55: 887–901.
- Dunlop N E, Bass J, Fujiwara P, et al. American Thoracic Society: Diagnostic Standards and Classification of Tuberculosis in Adults and Children. *Am J Resp Crit Care Med* 2000; 16: 1376–1395.
- Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2002; 49(RR-6): 12–21.
- Klovdahl A S. Social networks and the spread of infectious diseases: the AIDS example. *Soc Sci Med* 1985; 21: 1203–1216.
- Morris M. Sexual networks and HIV. *AIDS* 1997; 11 (Suppl A): S209–S216.
- Rothenberg R B, Narramore J. The relevance of social network concepts to sexually transmitted disease control. *Sex Trans Dis* 1996; 23: 24–29.
- Fitzpatrick L K, Hardacker J A, Heirendt W, et al. A preventable outbreak of tuberculosis investigated through an intricate social network. *Clin Infect Dis* 2001; 33: 1801–1806.
- Klovdahl A S, Graviss E A, Yaganehdoost A, et al. Networks and tuberculosis: an undetected community outbreak involving public places. *Soc Sci Med* 2001; 52: 681–694.
- Rothenberg R B, Woodhouse D E, Potterat J J, Muth S Q, Darrow W W, Klovdahl A S. Social networks in disease transmission: The Colorado Springs Study. In: Needle R H, Coyle S L, Genser S G, Trotter R T, eds. *Social Networks, Drug Abuse, and HIV Transmission*. Rockville, MD: US Department of Health and Human Services, Public Health Service, National Institutes of Health, 1995: 3–19.
- Rothenberg R B, Long D, Sterk C, et al. The Atlanta urban networks study: a blueprint for endemic transmission. *AIDS* 2000; 14: 2191–2200.
- van Embden J D A, Cave M D, Crawford J T, et al. Strain identification of *Mycobacterium tuberculosis* by DNA fingerprinting: recommendations for a standardized methodology. *J Clin Microbiol* 1993; 31: 406–409.
- SAS Language and Procedures: usage. Version 6, 1st ed. Cary, NC: SAS Institute Inc., 1989.
- Ucinet V for Windows: Software for Social Network Analysis. Natick MA: Analytic Technologies, 1999.
- Batagelj V. PAJEK: package for large network analysis. Accessed 5/06/2002 at <http://vlado.fmf.uni-lj.si/pub/networks/pajek/default.htm>
- Perlman D C, Henman A R, Kochems L, Paopne D, Salomon N, Des Jarlais D C. Doing a shotgun: a drug use practice and its relationship to sexual behaviors and infection risk. *Soc Sci Med* 1999; 48: 1441–1448.
- Alland D, Kalkut G E, Moss A R, et al. Transmission of tuberculosis in New York City: an analysis of DNA fingerprinting and conventional epidemiologic methods. *N Engl J Med* 1994; 330: 1710–1716.
- Bauer J, Kok-Jensen A, Faurschou P, Thuesen J, Taudorf E, Andersen A B. A prospective evaluation of the clinical value of nation-wide DNA fingerprinting of tuberculosis isolates in Denmark. *Int J Tuberc Lung Dis* 2000; 4: 295–299.
- Onorato I M. Tuberculosis outbreaks in the United States. *Int J Tuberc Lung Dis* 2000; 4 (Suppl 2): S121–S126.
- Sebek M. DNA fingerprinting and contact investigation. *Int J Tuberc Lung Dis* 2000; 4 (Suppl 1): S45–S48.
- Small P M, Hopewell P, Singh S P, et al. The epidemiology of tuberculosis in San Francisco—a population-based study using conventional and molecular methods. *N Engl J Med* 1994; 330: 1703–1709.
- Van Soolingen D. Molecular epidemiology of tuberculosis and other mycobacterial infections: main methodologies and achievements. *J Intern Med* 2001; 249: 1–26.
- Bishai W R, Graham N M, Harrington S, et al. Molecular and geographic patterns of tuberculosis transmission after 15 years of directly observed therapy. *JAMA* 1998; 280: 1679–1684.
- Reichler M R, Reves R, Bur S, et al. Evaluation of investigations conducted to detect and prevent transmission of tuberculosis. *JAMA* 2002; 287: 991–995.
- Mohle-Boetani J C, Flood J. Contact investigations and the continued commitment to control tuberculosis. *JAMA* 2002; 287: 1040–1042.