

Outbreak of tuberculosis in a homeless population involving multiple sites of transmission

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SUMMARY

SETTING: During 2002–2003, a large outbreak of tuberculosis (TB) occurred among persons using multiple homeless facilities in King County, Washington.

OBJECTIVE: To control the transmission of TB in multiple settings.

DESIGN: In 2002, contacts exposed to patients in homeless facilities were screened using tuberculin skin tests (TSTs) and symptom review. Based on these screening results, sites of transmission were identified and prioritised, and exposed cohorts at these sites were offered intensive screening tests in 2003 (e.g., symptom review, TST, chest radiograph [CXR], sputum examination and culture). *Mycobacterium tuberculosis* isolates from patients were genotyped using PCR-based methods to identify outbreak-associated patients quickly.

RESULTS: During 2002–2003, 48 (15%) of 313 patients

diagnosed in King County were outbreak-associated; 47 culture-positive patients had isolates that matched the outbreak strain by genotyping. Three facilities visited by >12 patients in 2002 had a higher prevalence of TST positive results (approximately 30%) among clients compared with the background rate (7%) in the homeless community. Screening contacts with one sputum culture was as sensitive as CXR in detecting TB disease (77% vs. 62%, respectively).

CONCLUSIONS: A comprehensive, resource-intensive approach likely helped to control transmission. This outbreak highlights the vulnerability of homeless populations and the need to maintain robust TB programs in urban settings.

KEY WORDS: *Mycobacterium tuberculosis*; tuberculosis; homeless persons; disease outbreak

ALTHOUGH THE INCIDENCE of tuberculosis (TB) is declining in many industrialized countries, TB outbreaks among homeless populations continue to challenge TB programs.^{1–4} Obstacles to controlling transmission among homeless persons include identifying, locating, and screening contacts and treating those diagnosed with TB disease and latent TB infection (LTBI). Improved strategies are needed to respond to sudden increases in TB among marginalized populations.

The incidence of TB in King County (population 1.7 million, including approximately 8000 homeless persons), Washington, was 7.9 cases per 100 000 in 2001. During May–October 2002, the Public Health–Seattle and King County (PH-SKC) TB Control Program reported 22 homeless TB patients, almost twice the average annual number of 13 homeless patients during 1999–2001. An outbreak was suspected in July and confirmed in October 2002 when IS6110-based restriction fragment length polymorphism (RFLP)

analysis of four patients' isolates revealed a matching DNA fingerprint pattern.⁵ This TB outbreak differed from others previously described because it was substantially larger and transmission occurred simultaneously, over a short duration, in multiple settings, rather than in a single homeless facility.^{6,7} This report describes the epidemiology of the outbreak and the approach used to control it.

STUDY POPULATION AND METHODS

Case definition

Outbreak-associated patients presented with TB or were diagnosed through screening in King County during January 2001–December 2003, and had isolates with identical spacer oligotype (spoligotype) and mycobacterial interspersed repetitive unit (MIRU) patterns and a highly conserved RFLP pattern.⁵ Culture-negative TB patients were outbreak-associated if they

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Article submitted 23 August 2005. Final version accepted 24 January 2006.

had close contact with an infectious patient whose isolate matched the outbreak genotype.

Ethical review at the Centers for Disease Control and Prevention (CDC) determined that this urgent public health response and intervention was not human subjects research. Oral informed consent was obtained from participants at the time of the field work.

Contact investigations

Identification of contacts and prioritization of sites of transmission

We used a standardized questionnaire to elicit names of contacts and places where patients slept, worked, travelled, sought health care, ate, used drugs, and spent time during their infectious period. Intake logs from facilities frequented by infectious patients were reviewed to quantify the time they spent in each facility while infectious. We assumed transmission occurred in facilities visited by infectious patients when the rate of tuberculin skin test (TST) positive clients significantly exceeded the baseline for the homeless in King County determined by routine screening (approximately 7% in 2002, PH-SKC, unpublished). Facilities visited by infectious patients were prioritised for TB screening based on the number of infectious patients who visited the facilities and the prevalence of positive TST results compared with other homeless sites.

Identification of exposed cohorts

We reviewed registries at suspected sites of transmission to identify exposed cohorts. If attendance records were available, we determined when infectious patients were in the facility, then identified clients who visited the facility during this period. Contacts were prioritized for screening based on their cumulative number of exposed visits. If attendance records were not available, we asked staff to name persons present at least once a week. These persons were prioritized for screening.

Screening of named contacts and exposed cohorts

In 2002, contacts were screened using symptom review and TST. Health department staff performed on-site screenings for exposed cohorts at each facility. In 2003, contacts exposed to outbreak-associated patients were offered a chest radiograph (CXR), one sputum smear and culture, and voluntary human immunodeficiency virus (HIV) counselling, testing and referral in addition to symptom review and TST. Results from on-site screenings performed in 2002 assisted in identifying sites of transmission of the outbreak strain. Treatment was offered to contacts with LTBI.

Case-case and case-place epidemiologic linkages

Diagrams were constructed to illustrate case-case and case-place epidemiologic links.⁸ Patients were plotted based on the estimated onset of their infectious period to determine patterns of transmission throughout the outbreak. Lines were drawn to connect patients who

named another patient as a contact, and to link patients to places they reported visiting at least weekly while infectious.

Genotyping of isolates

We genotyped *Mycobacterium tuberculosis* isolates from 64 of 65 homeless TB patients diagnosed in King County in 2002 and 2003. Isolates from homeless TB patients diagnosed in 2002 were genotyped at the University of Arkansas for Medical Sciences using the standardized method for IS6110-based RFLP analysis⁹ and at the Seattle Biomedical Research Institute using spoligotyping¹⁰ and the standardized method for IS6110-based RFLP analysis.⁹ Isolates from homeless TB patients diagnosed in 2003 were genotyped at the Centers for Disease Control and Prevention (CDC), where spoligotyping and MIRU analysis were first performed. Isolates with the spoligotype and MIRU pattern of the outbreak strain were then genotyped using IS6110-based RFLP. Spoligotyping¹¹ was performed using the modifications of Cowan et al.¹² MIRU analysis was performed using the methods of Supply et al.,¹³ with modifications designed to facilitate analysis on a CEQ8000 capillary electrophoresis instrument.¹⁴ To determine the extent of the outbreak, we also genotyped *M. tuberculosis* isolates from non-homeless patients diagnosed in King County during 2002–2003 ($n = 44$), prioritizing US-born patients and foreign-born HIV co-infected patients. Isolates from 18 (51%) of 35 US-born and 26 (12%) of 213 foreign-born non-homeless patients were genotyped.

Case finding outside King County

TB controllers in Washington and surrounding states were interviewed for strain type details of other recently identified clusters. The 15-band outbreak RFLP pattern was compared with patterns in a CDC database containing RFLP patterns of isolates from patients diagnosed during 2000–2003 in six states with low TB incidence.

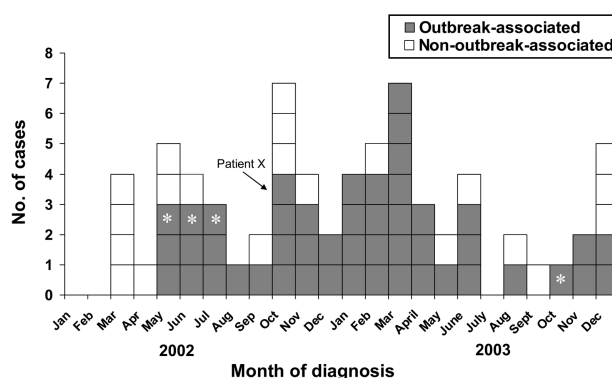


Figure 1 King County outbreak-associated TB patients ($n = 48$) and non-outbreak-associated homeless TB patients ($n = 21$) by month of diagnosis, 2002–2003. * Four outbreak-associated patients were not homeless at the time of diagnosis.

Table 1 Characteristics of outbreak and non-outbreak-associated homeless TB patients diagnosed in King County, January 2002–December 2003 ($n = 65$)

Characteristics	Outbreak patients ($n = 44$) n (%)	Non-outbreak patients ($n = 21$) n (%)	P value*
Demographic			
Male	36 (82)	18 (86)	0.695
US-born	42 (95)	15 (71)	0.006
Age (years)			
Range	22–71	27–78	N/A
Median	44	48	N/A
Race			
White	7 (16)	10 (48)	0.007
Black	14 (32)	7 (33)	0.903
American Indian/Alaska Native	23 (52)	3 (14)	0.003
Asian/Pacific Islander	0 (0)	1 (5)	—
Clinical			
Pulmonary TB (including extra-pulmonary involvement)	40 (91)	17 (81)	0.253
Sputum smear positive	24 (60)	9 (53)	0.621
Cavitary disease	7 (18)	4 (24)	0.598
HIV-infected	7/44 (16)	4/18 (22)	0.555
Habits			
Excessive alcohol use in past year	31/40 (78)	10/20 (50)	0.031
Intravenous drug use	4/37 (11)	2/20 (10)	0.924
Non-intravenous drug use	10/35 (29)	3/19 (16)	0.294

* P values are based on χ^2 statistic.

TB = tuberculosis; N/A = non-applicable; HIV = human immunodeficiency virus.

RESULTS

Characteristics of outbreak-associated patients

During January 2002–December 2003, 48 (15%) of 313 patients with TB diagnosed in King County were outbreak-associated (Figure 1). Of the isolates genotyped ($n = 108$), 58 (54%) had the spoligotyping pattern of the outbreak strain, and 47 (81%) of these had the MIRU pattern of the outbreak strain. Of the 47 isolates with the outbreak spoligotype and MIRU pattern, 42 had an identical 15-band RFLP pattern and four had highly conserved 15- or 16-band RFLP patterns (RFLP analysis was not performed on one isolate). One clinically diagnosed case was a close contact of a patient with the outbreak strain. Table 1 compares demographic, clinical, and behavioural characteristics of homeless outbreak vs. homeless non-outbreak patients. Four (8%) outbreak-associated patients identified strictly by genotyping were not homeless at the time of diagnosis. All HIV-infected patients were diagnosed with TB within 9 months of the first outbreak-associated patient in May 2002.

Forty-two (88%) of 48 outbreak-associated patients were diagnosed with pulmonary TB. Of these, 13 (81%) of the 16 diagnosed in 2002 were sputum smear-positive compared to 13 (50%) of 26 diagnosed in 2003 ($\chi^2 = 4.10$, $P = 0.043$).

Screening of contacts

In 2002–2003, the median number of named contacts per infectious outbreak-associated patient was 3.5 (mean 4.8). Six (14%) infectious outbreak-associated

patients named no contacts. In 2002, approximately 1000 contacts were evaluated at 10 homeless facilities visited by infectious outbreak patients. Of 895 TSTs placed, 654 (73%) were read and 98 (15%) were positive. Of those with a positive TST, 49 (50%) underwent CXR and 34 (69%) initiated treatment for LTBI.

TST-positive rates among clients at Facilities A–D correlated with the number of infectious outbreak patients who visited the facility (Table 2). Facility A temporarily housed chronic inebriants, and clients rarely returned to have TSTs read. Facilities B and C were daytime facilities with high clientele turn-over. Exposed cohorts from facilities A, B and C were prioritized for intensive re-screening in early 2003.

In 2003, review of facility data yielded 569 contacts at high risk for TB infection who warranted intensive screening (Table 3). During January–September

Table 2 Facility associations for infectious homeless outbreak and non-outbreak patients diagnosed in 2002

Facility	Pulmonary outbreak patients ($n = 15$) n	Pulmonary non-outbreak patients ($n = 9$) n	Positive TST among clients/patient/TSTs read n/N (%)
A	4	0	5/17 (29)
B	8	0	36/104 (35)
C	4	1	8/26 (31)
D	2	0	10/59 (17)
G	2	0	15/98 (15)
X	0	0	5/73 (7)*

* Background rate in the community (PH-SKC, unpublished data). TST = tuberculin skin test.

Table 3 Contacts identified for intensive TB screening, January–September 2003

	n (%)
Contacts identified for 5-part screening	569
Contacts evaluated	425 (75)
Contacts diagnosed with TB	13 (3)
Contacts with prior positive TST	79 (19)
Contacts with ≥ 1 TST read	286 (67)
Positive TST	99 (35)
Active TB ruled out	80 (81)
LTBI candidates	77
Initiated therapy	46 (60)

TB = tuberculosis; TST = tuberculin skin test; LTBI = latent tuberculosis infection.

2003, PH-SKC staff performed 385 CXRs, 400 sputum cultures and 342 HIV tests. Of 13 (3%) contacts diagnosed with TB disease through this screening process, 10 (77%) grew *M. tuberculosis* from their first sputum culture and eight (62%) had CXRs consistent with TB. Five HIV-negative patients had normal CXRs and sputum cultures positive for *M. tuberculosis*. Four of these five patients had ≥ 2 positive cultures processed several weeks apart.

Case-case and case-place epidemiologic linkages

Figure 2 demonstrates case-case epidemiologic links and Figure 3 demonstrates case-place epidemiologic links. We were unable to detect epidemiologic links to other patients or sites of transmission for six patients, including the four non-homeless patients.

Patient X was diagnosed in October 2002 with sputum smear-positive cavitary pulmonary TB and

clinically diagnosed laryngeal TB. This patient's likely infectious period began at least 6 months before diagnosis, one of the earliest in the outbreak.

Genotyping of isolates

The CDC provided spoligotyping and MIRU analysis results 3 weeks earlier than the RFLP results. The median number of days from receiving an isolate to reporting a spoligotyping and MIRU analysis result was 4 days (range 1–54) and 6 days (range 2–54), respectively. In contrast, the median number of days to reporting RFLP results was 26 days (range 20–96).

The pan-sensitive outbreak strain is part of the N subfamily of the W-Beijing family of *M. tuberculosis*.⁵ From January 1995 to April 2002, isolates from 62 (52%) King County homeless patients were genotyped. None matched this outbreak strain.¹⁵

Case finding outside King County

The CDC database containing RFLP patterns from low-incidence states included three patients with isolates that matched the outbreak strain. All three patients were diagnosed in a rural area of Montana during October 2000–March 2001. None were homeless when diagnosed. Patient X lived in the same area of Montana until the mid-1990s, and likely visited the area in 2000.

We also found an individual diagnosed with the Seattle outbreak strain in the same area of Montana in 1998. This patient previously lived in Minneapolis and frequented the bar that was the focus of an out-

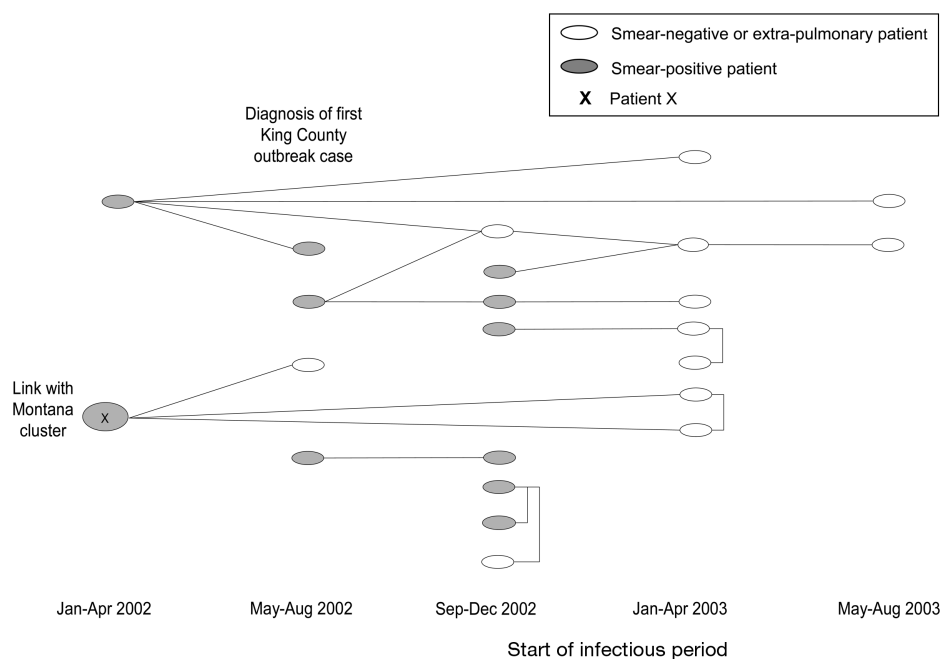


Figure 2 Timeline showing outbreak TB patients and case-case epidemiologic links, 2002–2003. Ovals represent individual patients on the timeline indicating the start of the patient's estimated infectious period. Lines connect patients determined to be named contacts. Patients without epidemiologic linkages to other patients ($n = 25$) are not shown.

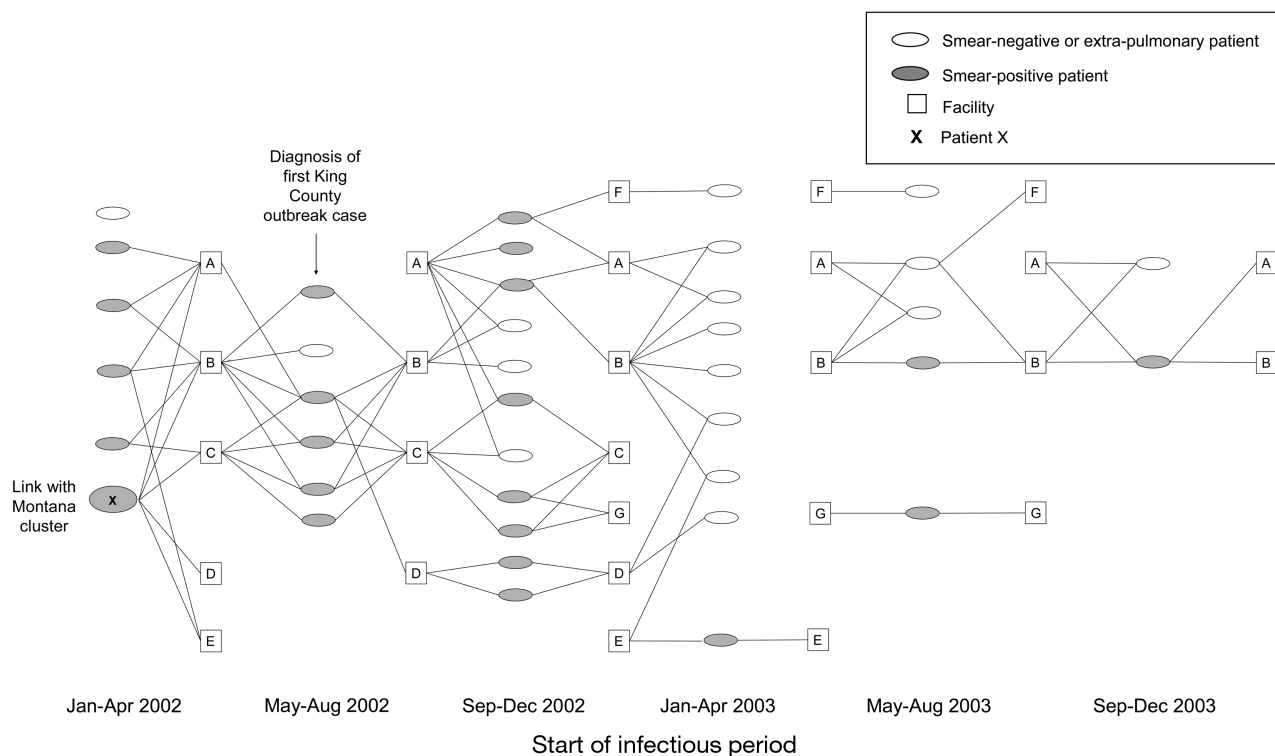


Figure 3 Timeline showing outbreak TB patients and case-place epidemiologic links, 2002–2003. Ovals represent individual patients on the timeline indicating the start of the patient's estimated infectious period. Squares represent place; each place is indicated by a letter (A–G). Lines to the left of patients represent places where persons might have been exposed to and infected with *M. tuberculosis*. Lines to the right of patients represent places where patients reported spending time at least once a week during their infectious period. To simplify the diagram, lines to the right of patients represent only patients with smear-positive sputum results, i.e., those considered more infectious. Patients without epidemiologic linkages to sites of transmission ($n = 9$) are not shown.

break in 1992 described by Kline et al.¹⁶ The genotype of the Minneapolis outbreak strain matches the Seattle outbreak strain.

DISCUSSION

During 2002–2003, King County experienced one of the largest TB outbreaks recently described in the United States. Transmission of the outbreak strain occurred in multiple homeless facilities, complicating contact investigations and increasing the resources required to slow transmission. We hypothesize that this outbreak originated from one person who, after being infected in Montana, developed active disease in King County and frequented several homeless facilities while infectious. Although this strain only caused TB disease among a few non-homeless persons in rural Montana, it caused TB disease in >40 homeless persons sharing multiple shelters in King County.

In addition to homelessness and crowded living conditions, we speculate that the outbreak was partly driven by its initial size and the fact that transmission was not confined to one homeless facility with stable residents. When the first outbreak-associated patient was diagnosed in May 2002, there were likely seven additional undiagnosed outbreak patients with spu-

tum smear-positive TB in the community (Figure 3). These initial patients frequented at least five different facilities. Of these facilities, only one housed a consistent group of residents every night. It is not known whether mycobacterial virulence factors drove transmission, as virulence studies were not performed due to lack of funding.

Several control strategies were used during the outbreak. As investigators struggled to elicit the names of contacts from outbreak-associated patients, site-based contact investigations became critical. If the PH-SKC TB Control Program had not focused on sites of transmission, they would have evaluated only a minimal number of named contacts and would not have explained transmission in approximately half of the outbreak-associated patients (Figures 2 and 3). Previous reports have described the difficulty of identifying contacts of homeless persons¹⁷ and the importance of site-based contact investigations.¹⁶ As TB patients who name no contacts are more likely to generate a secondary case of TB,¹⁸ TB programs need to pursue alternative strategies for patients who fail to report contacts.

Another strategy used in the investigation was intensive screening of contacts. Interestingly, 5 of 13 patients detected through screening had a negative CXR

and a positive sputum culture. As all five patients were treated for TB, we will never know how their illness would have naturally progressed. However, we suspect these patients either shed bacteria transiently during spontaneous resolution of primary pulmonary TB or had clinical TB in the absence of radiographic findings possibly due to malnutrition or alcohol abuse suppressing the immune response. Hardy and Schmidek similarly detected CXR-negative, sputum culture-positive patients while intensively screening contacts during an outbreak. Of 25 persons diagnosed with TB, nine had negative CXRs and positive sputum cultures.¹⁹ Similar to Kimerling et al.,²⁰ we found sputum screening to be simple and effective in detecting patients with TB in homeless shelters. Given the sensitivity and ease of collecting sputum samples compared to CXRs in the field, TB control programs investigating large outbreaks should consider using sputum examination and culture to screen contacts.

We used two polymerase chain reaction (PCR) based tests, spoligotyping and MIRU analysis, recently developed and validated for genotyping *M. tuberculosis* isolates.^{10,21} Compared to RFLP analysis, these methods are faster and less costly. During our investigation, results from spoligotyping and MIRU analysis were available on average 3 weeks before the RFLP results. Rapid genotyping of *M. tuberculosis* isolates helped to distinguish quickly between outbreak-associated and non-outbreak-associated patients (Figure 1). The immediate genotyping feedback helped motivate investigators to continue their intensified efforts and improved cooperation at affected homeless facilities by quickly verifying the outbreak strain among their clients.

We believe the strategies described above helped control transmission of the outbreak strain. However, proving that these strategies accelerated control of transmission is difficult because no control group was available. The success of our approach was supported by the fact that patients diagnosed with pulmonary TB in 2003 were significantly less likely to be sputum smear-positive at diagnosis than patients diagnosed with pulmonary TB in 2002 (82% vs. 50%). This suggests that outbreak-associated patients diagnosed in 2003 were detected earlier in the course of the illness. Furthermore, isolates from 21 of 23 homeless TB patients diagnosed in 2004 were genotyped and 11 were the outbreak strain, a 59% decrease from homeless outbreak cases in 2003.²² PH-SKC continues to monitor the extent of this outbreak strain and assess the contributions of LTBI treatment among contacts.

CONCLUSIONS

This TB outbreak highlights the vulnerability of homeless populations and shows that a comprehensive, resource-intensive approach is needed to control transmission of large TB outbreaks.

Acknowledgements

We acknowledge staff who participated in this investigation: M Elcock, M Dunbar, N Mills, J Pang, L Haba, H Wollaston, E Oren from Public Health-Seattle & King County TB Control Program; Heather Barr from Healthcare for the Homeless; K Field, T Kuss, and A Exarchos from the Washington State Department of Health; D Ingman from the Montana Department of Public Health and Human Services and M McConnell, R Groves, J Kuharik, T Cropper, and T Albrecht from the Centers for Disease Control and Prevention (CDC). J Milan and K Hauge at the Seattle Biomedical Research Institute (SBRI), J Aharchi at the Washington State Department of Health and B Metchock at the CDC assisted in genotyping isolates. Strain typing at SBRI was supported by SBRI Trustees and grants from the Puget Sound Partners for Global Health, Firland Foundation, Seattle Foundation, and the M J Murdock Charitable Trust. We thank K Ijaz, J Blair and J Hofmann for assistance during manuscript preparation.

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R É S U M É

CONTEXTE : Au cours des années 2002–2003, dans le King County, Washington, une importante mini-épidémie de tuberculose (TB) est survenue chez des personnes recourant à de multiples services pour sans-abri.

OBJECTIF : Contrôler la transmission de la TB dans des sites multiples.

SCHEMA : En 2002, les contacts exposés à des patients dans des services pour sans-abri ont été dépistés grâce aux tests cutanés tuberculiniques (TST) et à une révision des symptômes. Sur la base des résultats du dépistage, on a pu identifier les sites de transmission et leur donner la priorité. On a offert aux cohortes exposées dans ces sites des tests intensifs de dépistage en 2003 (par ex., révision des symptômes, TST, cliché thoracique, bacilloscopie et culture des expectorations). Les isolats de *Mycobacterium tuberculosis* provenant des patients ont fait l'objet d'un génotypage par des méthodes basées sur la PCR afin d'identifier rapidement les patients appartenant à la mini-épidémie.

RÉSULTATS : Au cours des années 2002–2003, 48 (15%) des 313 patients diagnostiqués dans le King County appartenaient à la mini-épidémie ; lors du génotypage, chez 47 patients dont la culture des isolats était positive, les germes correspondaient à la souche de la mini-épidémie. Dans trois services fréquentés par plus de douze patients en 2002, la prévalence de résultats positifs du TST (environ 30%) s'est avérée plus élevée parmi les clients par comparaison au taux de base de la collectivité sans-abri (7%). Pour la détection de la maladie tuberculeuse, le dépistage des contacts par une culture d'expectoration s'est avéré aussi sensible que le cliché thoracique (respectivement 77% et 62%).

CONCLUSIONS : Une approche complète et bénéficiant de ressources importantes a probablement contribué au contrôle de la transmission de la TB. Cette mini-épidémie éclaire la vulnérabilité des populations sans-abri et la nécessité de maintenir de solides programmes antituberculeux dans les contextes urbains.

R E S U M E N

MARCO DE REFERENCIA : Entre 2002 y 2003 se detectó un extenso brote epidémico de tuberculosis (TB) entre las personas que acudían a los múltiples establecimientos para personas sin domicilio en King County, Washington.

OBJETIVO : Controlar la transmisión de la TB en múltiples entornos.

MÉTODOS : En 2002, se practicó la detección sistemática de la TB entre contactos expuestos a pacientes en los establecimientos de albergue mediante la prueba cutánea de la tuberculina (TST) y una evaluación de los síntomas. Con base en los resultados de esta campaña se reconocieron y clasificaron por orden de prioridad los focos de transmisión y se ofrecieron exámenes de detección complementarios (como revisión de los síntomas, TST, radiografía de tórax, baciloscopia y cultivo del esputo) a las cohortes expuestas en estos centros, en 2003. Se realizó el genotipado de los aislados clínicos de *Mycobacterium tuberculosis* de los pacientes, mediante métodos basados en la PCR, con el objeto de reconocer rápidamente los pacientes vinculados con el brote epidémico.

RESULTADOS : De los 313 pacientes diagnosticados con TB en King County entre 2002 y 2003, 48 (15%) formaron parte del brote epidémico; 47 pacientes con cultivos positivos presentaron aislados clínicos cuyo genotipado coincidió con la cepa del brote. La prevalencia de resultado positivo a la TST en los usuarios de tres centros de albergue frecuentados por >12 pacientes en 2002 fue superior a la prevalencia en la población de referencia (7%) constituida por la comunidad sin domicilio fijo. La detección en los contactos mediante cultivo de una muestra de esputo tuvo una sensibilidad equivalente a la sensibilidad de la radiografía de tórax para el diagnóstico de TB (77% y 62%, respectivamente).

CONCLUSIONES : La estrategia exhaustiva con múltiples recursos contribuyó muy probablemente a interrumpir la transmisión de la TB. Este brote epidémico pone de manifiesto la vulnerabilidad de las poblaciones sin domicilio y la necesidad de mantener programas de TB intensos en los medios urbanos.