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A clonal outbreak of tuberculosis in a homeless population in the interior of British Columbia, Canada, 2008–2015

J. M. CHENG[1]*, L. HISCOE[2], S. L. POLLOCK[2,3], P. HASSELBACK[4], J. L. GARDY[3,5] AND R. PARKER[2]

[1] *Public Health Agency of Canada, Guelph, ON, Canada*
[2] *Interior Health Authority, Kelowna, BC, Canada*
[3] *School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada*
[4] *Vancouver Island Health Authority, Nanaimo, BC, Canada*
[5] *British Columbia Centre for Disease Control, Vancouver, BC, Canada*

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SUMMARY

A tuberculosis (TB) case was reported May 2008 in Kelowna, British Columbia, leading to a multi-year outbreak in homeless persons. The epidemiological characteristics and social networks of cases are described. Outbreak-related cases were identified from epidemiological information in medical records and from genotyping of TB isolates. Social network information from case interviews were used to identify potential locations of TB transmission, where symptom screening and tuberculin skin testing was conducted. Fifty-two cases that were predominantly male (47/52), Canadian-born (44/50), and were homeless or associated with homeless individuals (42/52) were reported from May 2008 to May 2014. Many isolates (40/49) had partial resistance to isoniazid. Transmission primarily occurred at two homeless shelters, with potential further transmission at sites visited by the general population. TB outbreaks in homeless populations can occur in small, low-incidence cities. Social network information helped prioritize sites for TB screening, thereby improving detection of persons with TB disease or latent infection for treatment.

Key words: Infectious disease epidemiology, investigation, outbreaks, resistance to drugs, tuberculosis (TB).

INTRODUCTION

Tuberculosis (TB) outbreaks often occur in homeless populations [1–3]. These individuals are more likely to live in crowded conditions, have compromised immune function, and have poor access to healthcare – all conditions that facilitate TB infection and transmission. TB in the homeless has been reported in major urban centres in Canada [4–6], presenting an ongoing public health challenge for TB outbreak control and containment.

The city of Kelowna is a rapidly developing small urban centre located in the Okanagan Valley in British Columbia (BC), Canada with a population of ~120 000. The region's mild climate, recreation opportunities, and popularity with retirees attract both tourists and migrants from BC and the neighbouring province of Alberta. Agricultural activities also attract seasonal farm workers to the area during harvesting season. With Kelowna's rapid growth, homelessness is a growing issue. A 'point-in-time' count of the homeless population conducted over a

* Address for correspondence: Ms. J. M. Cheng, 255 Woodlawn Road West, Unit 120, Guelph, Ontario, N1H 8J1, Canada. (Email: joyce.cheng@phac-aspc.gc.ca)

24-h period in April 2007 found 279 homeless people in the Kelowna area and estimated that 1489 individuals had been 'hidden homeless' at some point in the past year [7]. The incidence of TB in Kelowna's homeless population is not available; however, the Okanagan health service delivery area, which includes Kelowna, had rates of active TB between 0 and 1·8/100 000 population in the 3 years prior to the outbreak we describe here [8].

From 2008 to 2015, a large outbreak of TB occurred in Kelowna's homeless population, with spread to the general population and the surrounding Okanagan Valley. The index case was first reported to public health authorities in May 2008 and an outbreak was declared at the end of 2008 following the detection of six epidemiologically linked cases. In the ensuing years, efforts were made to control and contain the TB outbreak in this small, low-incidence setting through case management and the introduction of multiple case-finding strategies. By 2015, the outbreak had grown to include 52 cases; here, we describe their epidemiology and the outbreak investigation.

METHODS

This epidemiological investigation was done as part of a public health outbreak control response as a legislated responsibility of the local Medical Health Officer under the provincial Public Health Act of BC. TB cases were investigated and managed according to the Canadian Tuberculosis Standards [9].

Laboratory analysis

Sputum or other samples from suspected TB cases in BC are sent to the BC Public Health Microbiology and Reference Laboratory (Vancouver, BC, Canada) for diagnosis and phenotyping. Laboratory-confirmed cases of active TB are defined as those with *Mycobacterium tuberculosis* (MTB) complex present on culture; all 52 suspect cases referred to the laboratory by the outbreak investigation team were culture-positive. Bacillary loads are quantified using acid-fast bacilli (AFB) smear testing; results are reported using the semi-quantitative grading system [9], in which 4+ is the highest grade. Drug susceptibility testing is performed for all first-line antibiotics using line probe assays (Hain Lifescience, Germany).

Genotyping of isolates is performed only upon request of a physician, typically to confirm suspected community transmission. All suspected outbreak cases were referred for genotyping, which was performed at the Public Health Agency of Canada's National Microbiology Laboratory (Winnipeg, Manitoba, Canada) using the mycobacterial interspersed repetitive unit-variable number of tandem repeats (MIRU-VNTR) typing scheme. Isolates typed prior to 2009 were interrogated at 12 loci; subsequent isolates were analysed using 24-loci MIRU-VNTR. A case was considered as belonging to the outbreak if it had a MIRU-VNTR pattern equal to or within a single repeat's difference of 224325153323 444234423373, using the locus ordering scheme MIRU02/04/10/16/20/23/24/26/27/31/39/40, 424/577/1955/2163/2165/2347/2401/2461/3171/3690/4052/4156.

Case data

A clustered TB case was defined as a TB case linked to the outbreak through: (1) having an epidemiological connection to another case or an outbreak location; and, (2) having the characteristic MIRU-VNTR genotype. Case data were collected by public health nurses using a standardized case interview form and routine public health nursing assessments. Information was collected on: demographics, employment, incarceration history, medical history, TB symptoms and onset, contacts with TB symptoms or active TB, daily routine, places of social aggregation, social networks, places of residence/sleeping locations, and recent travel. Information on bacillus Calmette-Guérin (BCG) vaccination was not collected because BCG vaccine is only given in selected Aboriginal communities with high TB incidence in Canada; the cases in this outbreak were mostly Canadian-born, non-Aboriginal individuals. Data on age, sex, diagnosis date, sputum smear status, culture results, chest X-ray findings, disease site, and outcome were also collected.

Contact tracing

A concentric circle approach to contact investigation was used to identify individual named contacts. Screening began with close contacts, defined as individuals sharing the same air space with a case for >4 h per week. For cases staying in homeless shelters, close contacts were those who stayed in the beds immediately surrounding the case's bed for $\geqslant 5$ nights. If there was evidence of transmission between close contacts, the circle of contact tracing was widened to include casual contacts or those who stayed in more distant shelter beds until there was no evidence of further transmission. To assist with locating individuals for

contact tracing, lists of contact names were provided to local police, homeless shelters, a community drop-in centre, and street outreach nurses.

In addition to contact tracing around individual cases, location-based mass TB screening events were also conducted regularly at homeless shelters, soup kitchens, addiction recovery homes, and urban health clinics in Kelowna and the surrounding area. In April 2011, based on the recommendations of an expert review panel, quarterly sputum sweep screening of all residents in the two affected homeless shelters in Kelowna was added.

Screening and surveillance

Initial screening of individual contacts and at mass screening events involved a symptom review and a tuberculin skin test (TST). Clients with a positive TST, defined as an induration of $\geqslant 5$ mm at 48–72 h, were followed up with a chest X-ray. Clients experiencing cough or other TB symptoms were referred for chest X-ray and sputum collection. Clients found to have latent TB infection (LTBI) upon screening were offered 4 months of rifampin as preventative therapy; those who opted not to receive preventative therapy were placed on surveillance, consisting of monthly symptom reviews and bi-annual chest X-ray and sputum sampling, for 2 years. In 2013, the surveillance period was extended to 3 years.

Medical, public health, and laboratory records were reviewed retrospectively. Homeless shelter records were accessed to prioritize contacts for follow-up.

RESULTS

Index case

We traced the outbreak to a single highly infectious index case. In May 2008, a 20-year-old male culture-positive for MTB with AFB smear results of 4+ and low-level isoniazid resistance was reported to public health. Chest radiographs revealed a cavitary lesion and the case reported a history of cough beginning October 2007. He had recently moved to Kelowna from Vancouver's Downtown Eastside, an impoverished urban neighbourhood with a high incidence of TB and other communicable disease, addiction and mental health issues, and high crime rates [8]. The case became well-known within Kelowna's homeless community, sleeping in camps and parks in the city and sporadically residing at Kelowna's sole permanent, year-round men's homeless shelter ('shelter A').

Nine of the index case's close contacts developed active TB genotypically identical to the index case's isolate. Interviews with these individuals revealed common links to shelter A, triggering enhanced screening and case-finding around the shelter and its clients.

Outbreak epidemiology

Ultimately case-finding and screening yielded a total of 52 clustered TB cases, including the index case. Patients' characteristics are detailed in Table 1. The majority of cases were adult males (90%, $n = 47$), many (81%, $n = 42$) with a history of homelessness or contact with homeless individuals through social circles, volunteering, or working at a shelter or other location frequented by outbreak cases. HIV status was recorded for 37 cases; of these, two were HIV-positive. Country of birth was recorded for 50 cases, 88% ($n = 44$) were Canadian-born. Case report dates ranged from May 2008 to May 2014 (Fig. 1).

Most cases (94%, $n = 49$) were diagnosed solely with respiratory TB. One case had concurrent respiratory and non-respiratory TB, and two cases were infected with non-respiratory TB only, including TB in fluid taken from the shoulder and a case of TB meningitis. Of the 50 respiratory TB cases, 54% ($n = 27$) were smear-positive. Thirteen of the smear-positive respiratory cases were recorded as AFB 4+.

Drug susceptibility testing results were available for 49 of the 52 cases. Of these, 40 (82%) isolates demonstrated resistance to low concentrations of isoniazid (0·1 μg/ml) but not high concentrations (0·4 μg/ml), while nine isolates were sensitive to all first-line drugs. Resistant and susceptible isolates had identical MIRU-VNTR genotypes, with many of the susceptible isolates occurring in the earliest outbreak cases.

Forty-four cases required hospitalization. When the outbreak was declared over in January 2015, 44 cases had completed treatment and one was receiving treatment. One case completed 7 months of treatment and had his health status monitored for an additional 3 years due to HIV co-infection. Three cases died before treatment could be completed and two cases moved out of the province and their treatment completion results are unavailable. One case was treated in 2009 and reactivated in 2012. Both his isolates had the outbreak strain MIRU-VNTR genotype; however, his first isolate was isoniazid resistant while the isolate from the second episode was fully sensitive to all front-line drugs.

Table 1. *Socio-demographic and clinical characteristics of cases in an outbreak in the BC interior, 2008–2015*

Case characteristic	All cases ($N = 52$)	Homeless cases only ($N = 42$)
Sex		
Male	47/52 (90%)	40/42 (95%)
Age		
Median	50 years	51 years
Range	20–82 years	20–71 years
<40 years	11/52 (21%)	6/42 (14%)
40–59 years	30/52 (58%)	27/42 (64%)
⩾60 years	11/52 (21%)	9/42 (21%)
Site of infection		
Respiratory	49/52 (94%)	39/42 (93%)
Non-respiratory	2/52 (4%)	2/42 (5%)
Respiratory and non-respiratory	1/52 (2%)	1/42 (2%)
Clinical findings for respiratory TB cases		
Sputum smear acid-fast bacilli positive	27/50 (54%)	22/40 (55%)
Abnormal chest X-ray	46/50 (92%)	36/40 (90%)
Clinical outcome		
Hospitalization	44/51 (86%)	36/41 (88%)
Death	3/52 (6%)	2/42 (5%)
Treatment outcome		
Completed treatment or monitoring	46/50 (92%)	37/40 (93%)
Treatment ongoing	1/50 (2%)	1/40 (3%)
Case deceased	3/50 (6%)	2/40 (5%)

Social networks of the cases

Using data from the case interviews, we observed substantial clustering of cases within social settings, social networks, and geospatially. Forty-two (81%) cases occurred in homeless individuals. Shelter A in Kelowna emerged as a primary site of disease transmission, with 31 of the 42 homeless cases reporting a history of accessing shelter A's services or staying overnight. Three additional homeless cases did not report using shelter A but are named contacts of cases that did stay there. Nine of the 31 homeless shelter A cases also reported staying at a second homeless shelter in Kelowna ('shelter B'). One additional case reported only staying at shelter B, but not at shelter A. Other common places of social aggregation in the downtown Kelowna area were also mentioned by cases, including: a drop-in centre ($n = 10$), an Aboriginal services centre ($n = 6$), an outdoor park ($n = 7$), the library ($n = 6$), and a neighbourhood pub ($n = 3$). Given these overlapping locations, transmission at other community sites in addition to shelter A and shelter B may have occurred.

Six homeless cases lived in Penticton, a smaller city 63 km south of Kelowna in the Okanagan Valley. These cases had contact with one shelter A-associated case who frequently travelled throughout the Okanagan Valley, often using a soup kitchen in Penticton. In addition, a seventh Penticton case had a history of homelessness but no confirmed epidemiological links to any other cases or sites of social aggregation.

Ten cases occurred in individuals who were not homeless themselves, but were potentially in contact with homeless individuals and shelter clients. Four of these cases were staff or volunteers at shelter A ($n = 2$), shelter B ($n = 1$), and the Aboriginal services centre ($n = 1$). Three cases visited or were named contacts of cases who sought daily work assignments from temporary labour agencies often accessed by homeless individuals, including five shelter A cases. One case was a regular patron at a neighbourhood pub frequented by three shelter A cases. One case was diagnosed in another city, having recently arrived from Kelowna, and another case regularly used public transportation and frequented the recreation centre, two activities also common in some homeless individuals in Kelowna.

Contact investigation

The results of contact tracing and screening efforts, which includes both named contact follow-up and mass screening, are summarized in Figure 2. Between June 2008 and March 2015, the local health authority completed TB screening on 2007 (83%) clients out of 2419 individuals identified as potentially exposed. In addition to the 52 active TB cases genotypically linked to this outbreak, 374 individuals with LTBI or previous active TB disease were identified. Preventative therapy – 4 months of rifampin, in light of the isoniazid resistance observed in the majority of cases – was recommended for 272 individuals, of which 119 have completed or are undergoing treatment and 54 have been placed on surveillance to monitor changes in health status.

DISCUSSION

Our epidemiological and laboratory investigation revealed a clonal outbreak of TB in BC's Okanagan Valley. Stemming from a single highly infectious index case who was symptomatic for at least 7 months

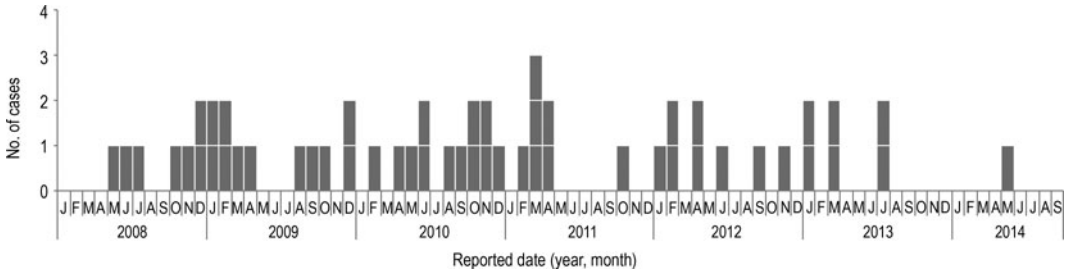

Fig. 1. Tuberculosis cases by reported date, Okanagan Valley, 2008–2014 ($n = 52$).

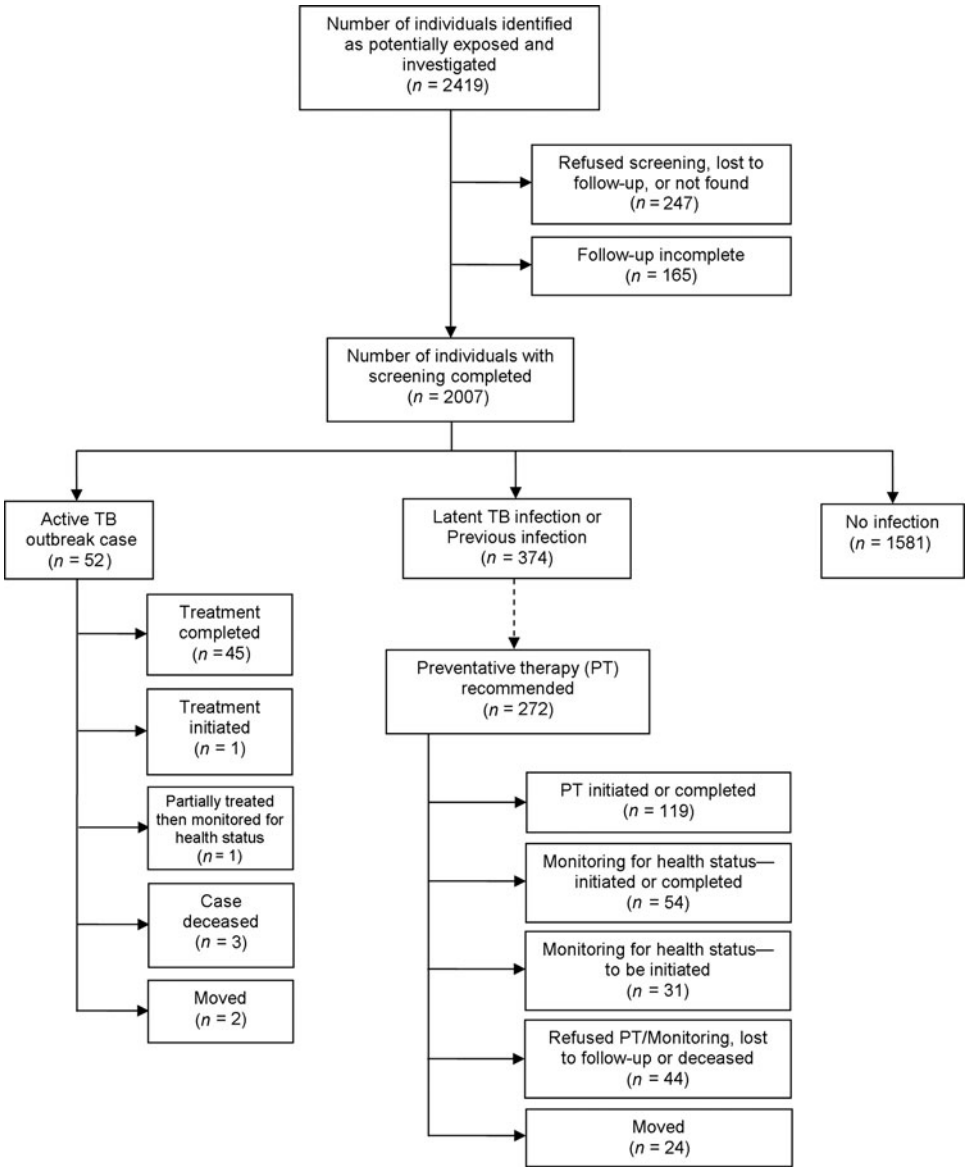

Fig. 2. Outbreak-associated contact screening outcomes in a tuberculosis outbreak in the British Columbia interior, 2008–2015.

before diagnosis, the outbreak primarily affected middle-aged males with a history of homelessness. Social network data suggested that transmission of the outbreak strain occurred largely through homeless shelters, with limited onward transmission to members of the general population. Outside of the shelter setting, transmission occurred through social service agencies and sites visited by both the homeless and general populations. Recent North American TB outbreaks occurring in homeless populations have demonstrated similar epidemiological characteristics and homeless shelters have been identified as primary sites for transmission [2, 10–14]. Transmission of TB in other settings, such as transportation hubs, bars, and temporary labour agencies, has also been previously described in the literature [1, 2, 11, 12]. Although Kelowna's population is small relative to urban centres such as New York City [3] and Toronto [4], where large TB outbreaks have occurred, this outbreak highlights the growing issue of homelessness in small cities in Canada and with it the risk of TB outbreaks. The index case, who moved from a large urban centre to Kelowna, and the sub-cluster of cases in Penticton demonstrate how even in smaller centres, highly transient individuals can spread TB to other cities, presenting new challenges for infection control and outbreak containment.

Given the concentration of transmission in the highly mobile homeless population, targeted mass screening at key sites was used for case-finding in addition to the standard contact tracing protocol. Location-based mass screening has been previously employed in outbreaks [1–3, 12, 13] and was successfully used here to identify additional cases of active TB and LTBI and target individuals for preventative therapy. A study of homeless males in Vancouver and Kelowna found that the services most frequently used by those interviewed were shelter/housing services, meals, social services/disability, and the health clinic [15], therefore our screening focused on these locations. We were able to fully assess the majority of individuals identified as potentially exposed, indicating that location-based screening is an important tool in shelter-associated outbreaks, particularly in the small city setting.

Laboratory data revealed a clonal outbreak, with all organisms having an identical or near-identical genotype; only a single isolate was mismatched at one MIRU-VNTR locus, which may be due to the gain of a repeat element at this site or misinterpretation of the VNTR length at the laboratory. In BC, isolates are genotyped when community transmission is suspected – cases occurring in Canadian-born individuals are generally referred for testing, while those in foreign-born individuals are not. Although all Kelowna-area cases were genotyped to rule them in or out of the outbreak investigation, it is possible that some cases were missed because they had moved out of the Kelowna area and their history did not suggest an epidemiological link to the region. Two of the 52 outbreak cases were diagnosed in other health authorities but were epi-linked to Kelowna.

The MIRU-VNTR genotype we observed in this outbreak was not unique to Kelowna. A review of provincial genotyping records indicates the strain has been circulating in the Vancouver area since at least 1997, and it may also be present in other areas of BC in isolates that have not been genotyped. A retrospective genotyping project currently underway at the BC Public Health Microbiology and Reference Laboratory will capture any of these overlooked cases. Furthermore, an investigation of the outbreak strain at the whole-genome level is presently underway; we anticipate this analysis, which also includes 33 genomes from the Kelowna outbreak, will reveal differences between the Vancouver and Kelowna isolates supporting a single introduction into Kelowna. The genomic data will also be used to identify potential transmission events within the Kelowna outbreak, using a model we have previously established [16].

Interestingly, the low-level isoniazid resistance phenotype we observed was not present in all cases. Although many of the earliest cases displayed isoniazid sensitivity, the origin of this phenotype could not be traced to the index case, whose isolate displayed the partial resistance phenotype. We believe the most likely explanation for this observation is that over the several months that the index case was symptomatic, a portion of his MTB bacilli – perhaps resident in a single lesion – evolved the resistance phenotype. During his infectious period, he may have been expelling sensitive bacilli at some points and resistant bacilli at others, depending on which lesions were active at a given point in time.

Our outbreak investigation has two notable limitations. First, the database used to track screened individuals evolved during the course of the outbreak and the case questionnaire was not always administered, thus data were not always captured completely or consistently. When a case questionnaire could not be administered, efforts were made to collect as much information as possible through public health nursing

assessments according to usual practice. In future outbreak investigations, including an interview as part of the clinical standard of care may facilitate a more complete epidemiological dataset, while the use of a standardized ontology would ensure that information is being captured in a consistent fashion, such as using an agreed-upon format for recording dates and observations. Second, epidemiological information was largely gleaned from interviews with cases that were not always able to provide reliable or detailed information. As a result, there could be unrecognized links between cases. Where possible, case histories were validated with supplementary information such as shelter records and attempts were made to gather more information about outbreak cases reported in other jurisdictions.

Although the incidence of TB is declining in Canada [9], this outbreak demonstrated that TB outbreaks in vulnerable populations still occur, even in small cities. We anticipate that due to reactivation after long periods of latency, we will continue to detect further active TB cases with the outbreak genotype. Furthermore, both the arrival of new homeless individuals to the Okanagan Valley, who may import TB from larger urban centres, and a higher index of suspicion of TB in healthcare providers will also likely result in more diagnoses of active TB in the region. Staff and clients of homeless shelters and other social service agencies should be informed of TB signs and symptoms so that those who are potentially ill can undergo clinical evaluation without delay, and prevent a situation such as the one here – in which a patient symptomatic for several months was residing in a crowded shelter environment – from turning into a large outbreak.

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DECLARATION OF INTEREST

None.

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