Urban and rural trench fever in Manitoba- associated with culture negative endocarditis and systemic embolization: a retrospective chart review study of *Bartonella* serologies from 2010-2020

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Keywords: *Bartonella*, serology, endocarditis, Canada

Running title: *Bartonella* serologies Manitoba, Canada

Word count: 2513

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40-word Summary:

This retrospective study includes all *Bartonella* serologies ordered in Manitoba, Canada from 2010 until 2020. We reviewed the charts of adult patients with positive *Bartonella* serologies to extract clinical and demographic data.

Funding statement: This work is supported by the Hector Ma University of Manitoba Internal Medicine Resident Research Award.

Competing interests: No competing interests.

Abstract:

Background:

Bartonella are Gram-negative bacilli not identified by routine bacterial culture. Human disease in North America is predominantly caused by *B. henselae* (cat scratch disease), and *B. quintana* (trench fever). *B. quintana* is transmitted by body lice and has emerged among populations experiencing homelessness. It is a leading cause of culture-negative infective endocarditis.

Methods:

This retrospective study includes all *Bartonella* serologies ordered in Manitoba from January 1st 2010 until December 31st, 2020. We reviewed the charts of adult patients with positive *Bartonella* serologies to extract clinical and demographic data. Descriptive statistics and Mann Kendall trend test were performed using R Statistical Software (https://www.r-project.org/).

Results:

16 adults with positive *Bartonella* serologies were identified. Molecular species-level identification occurred on explanted cardiac valves in 5 cases (31.3%): *B. quintana* was identified in all 5 cases. Six (37.5%) individuals were diagnosed with probable *B. quintana* infection, leading to a total of 11 *B. quintana* cases (68.8%). Of these, 8 (72.7%) were associated with endocarditis. Four cases of *B. quintana* (36.4%) were likely associated with rural acquisition. Four (25.0%) cases of probable *B. henselae* were identified. Of these, 2 (50%) had fever and lymphadenopathy and 2 had endocarditis (50%).

Interpretation:

B. quintana is the leading cause of clinical disease among adults with positive *Bartonella* serologies in Manitoba and is associated with severe endovascular infection. Transmission of *B.*

quintana in urban and rural settings reflects a lack of suitable housing both in inner-city Winnipeg as well as in remote communities.

Introduction:

Bartonella are Gram-negative intra-erythrocytic bacilli.(1,2) This genus of bacteria evades identification by routine culture due to its slow replication time and niche within red blood cells.(3,4) While over 45 different *Bartonella* species and subspecies infect different mammals, human disease due to *Bartonella* in North America is primarily caused by two species: *B. henselae* (cat scratch disease), and *B. quintana* (trench fever).(2,5) True to its name, cat scratch disease usually occurs after a feline scratch or bite.(6,7) Its most common clinical manifestation is regional lymphadenopathy.(7) *B. quintana* is transmitted in the feces of body lice, entering the systemic circulation via abrasions in the skin (see figures 1 and 2).(8–10) Clinical disease due to *B. quintana* was first described in 1915 in association with a relapsing febrile illness afflicting World War I soldiers, thus coined "trench fever".(11) *B. quintana* has since emerged among urban populations experiencing homelessness.(8,9,12–15) Both *B. henselae* and *B. quintana* may cause endovascular infections such as infective endocarditis and mycotic aneurysms.(16,17) Serology is often used to diagnose *Bartonella* infections due to the difficulties in identifying *Bartonella* with routine culture-based methods.(2,3) While patients with uncontrolled HIV may develop other manifestations of *Bartonella* such as bacillary angiomatosis and peliosis, most cases of *Bartonella* are not associated with HIV.(18)

In Canada, serologic evidence of exposure to *B. henselae* is common, reflecting local endemicity.(19) However, few cases of *B. quintana* have been documented in Canada.(20–24) While the first Canadian case of *B. quintana* was described in 1996, 20 years elapsed before a subsequent case was identified in 2016.(23,24) Since 2018, 6 cases of *B. quintana* have been described among people experiencing under-housing from both inner-city and rural areas of

Alberta and Manitoba.(20–22) All of these cases were associated with endocarditis, a rare and severe manifestation of *B. quintana,* suggesting an undescribed burden of community transmission.(25) No systematic description of human body lice has occurred in Canada.

Canadian data on *Bartonella* infection is based on low-quality evidence: only a handful of case reports and case series exist.(20–22,24) As bartonellosis is not a reportable disease in Canada, *Bartonella* disease prevalence is unknown.(26) No Canadian studies have attempted to describe *Bartonella* infection at a provincial level. The objective of this study is to retrospectively review cases with positive *Bartonella* serologies ordered in Manitoba from 2010 to 2020 to assess species type, demographic risk factors, clinical manifestations and treatment outcomes.

Methods:

Ethics approval:

The study protocol was approved by the Research Ethics Board of the University of Manitoba's Bannatyne Campus (H2020:374), Winnipeg's Health Sciences Centre (*RI*2020:147), St. Boniface Hospital's Research Review Committee (RRC/2020/1978) and approved by the Shared Health and Winnipeg Regional Health Authority's Research Access and Approval Committee (2020-059). Approval from Manitoba's Health Information Privacy Committee (No. 2020/2021-79) was obtained to enable access to provincial serology results.

Setting, patients and data acquisition:

We obtained the results of all *Bartonella* serologies ordered in the province of Manitoba from January 1st 2010 until December 31st, 2020. Serological information was acquired from Cadham Provincial Laboratory, Manitoba's provincial public health laboratory. *Bartonella* serology was performed at Canada's National Microbiology Laboratory in Winnipeg, Manitoba using an indirect immunofluorescent antibody assay (IFA) to test for immunoglobulin G (IgG) antibodies to *B. henselae* and *B. quintana* antigen.(27) A positive test was defined as a titer greater or equal to 1:256. Maximum calculatable titer was 1:8192. Titers of 1:64 and 1:128 were considered equivocal and titers below 1:64 were considered negative. Prior to 2017, Cadham Provincial Laboratory reported *Bartonella* serology results exclusively for *B. henselae* antigen. In 2017, reporting included IgG response to both *B. henselae* and *B. quintana* antigens. There is known serologic cross-reactivity between *B. henselae* and *B. quintana*.(2,28)

Aggregate data was divided and analyzed according to positive, equivocal and negative result. While aggregate data included both pediatric and adult patients, all tests from individuals under

18 years of age at the time of serology request were discarded prior to chart review. We retrospectively reviewed the charts of patients, 18 years and older at the time of *Bartonella* serology request, who had positive *Bartonella* serologies. We extracted clinical, laboratory and demographic data from emergency room visits and hospital admissions to Winnipeg's two largest hospitals, the Health Sciences Centre and St. Boniface Hospital.

Case definitions:

Cases were classified as confirmed or probable *B.quintana* or *B. henselae* infection according to case definitions for infectious conditions under public health surveillance.(29) Confirmed cases had molecular confirmation of pathogen to species-level using either 16S rRNA sequencing, species-specific polymerase chain reaction (PCR) or gene sequencing of *rpoB* gene. Probable cases demonstrated *Bartonella* serologic positivity, compatible clinical syndrome and risk factors consistent with either *B. henselae* or *B. quintana* acquisition, without species-level molecular confirmation. Epidemiologic risk factors differ between *B. henselae* and *B. quintana*.(14,30) *B. henselae* is associated with a history of a cat scratch or bite, whereas *B. quintana* is associated with inadequate access to suitable housing and body lice ectoparasitosis.(30) Cases with low-grade serologic positivity but failure to fulfill the criteria for compatible clinical syndrome and epidemiologic risk factor were considered not to be a case of *Bartonella*, thus a false positive. Considering the lack of suitable housing in many Northern communities in Manitoba, residence in a remote area known to have inadequate housing without a description of feline exposure was considered a risk factor for *B. quintana.*(20,22,24,31)

Statistical analysis:

Descriptive statistics and Mann Kendall trend test were performed using R Statistical Software (version 3.5.3, 2019-03-11) with the Mann Kendal statistical package.(32)

Results:

Aggregate data:

During the study period, a total of 1014 *Bartonella* serologies were ordered, of which 24 were positive (2.4%), 94 (9.3%) were equivocal and 896 (88.4%) were negative (see table 1). Testing volume increased during the study period from 51 in 2010 to 157 in 2020. An abrupt increase in positive cases occurred in 2020 with 5.7% positivity (9 cases), compared to the average positivity of 2.4% during the entire study period. The Mann Kendall trend test did not show a statistically significant difference in percent test positivity over time (P= 0.15858; Kendall's tau statistic= 0.3522).

Causative pathogen and clinical manifestations:

16 adults with positive *Bartonella* serologies were identified (see table 2). Molecular species-level identification occurred on explanted cardiac valves in five cases (31.3%): *B. quintana* was identified in all five cases. Six (37.5%) individuals were diagnosed with probable *B. quintana* infection, leading to a total of 11 *B. quintana* cases (68.8%). Of these, eight (72.7%) were associated with endocarditis. Seven of the eight patients with endocarditis had evidence of peripheral embolization (87.5%): four demonstrated intracranial complications with either embolization and/or ruptured mycotic aneurysms and three had evidence of splenic infarcts. Mitral and aortic valve involvement was most common. Among cases of endocarditis with documented vegetation size, average vegetation size was 17 mm x 7 mm. Of the positive cases associated with endocarditis, all but two were associated with elevated initial *Bartonella* titers of 8192 or 4096. Two individuals with *B. quintana* endocarditis had concomitant *Streptococcus pneumoniae* bacteremia. Four (25.0%) cases of probable *B. henselae* were identified. Of these,

all had history of cat scratch, 2 (50%) had fever and lymphadenopathy and 2 had endocarditis (50%).

Treatment and outcome:

Six patients underwent valve replacement surgery and two patients underwent intravascular coiling of a middle cerebral artery aneurysm. All patients with endocarditis were prescribed antimicrobial therapy, with doxycycline and gentamicin and/or ceftriaxone, as the most common regimens. One patient was prescribed doxycycline and rifampin. Individuals diagnosed with cat scratch disease were treated with azithromycin. 14 of the 16 individuals with positive *Bartonella* serologies survived (87.5%). The two individuals who died had multi-valvular *B. quintana* endocarditis with ruptured intracranial mycotic aneurysms.

Epidemiology:

The average age among individuals with positive *Bartonella* serologies was 48 years. Of the 16 individuals with positive *Bartonella* serologies, 12 were men and 4 were women, with gender described as per hospital chart documentation. 12 individuals acquired their infection in Winnipeg. Four cases of *B. quintana* (36.4%) were associated with likely rural acquisition according to postal code. Three individuals resided in Northern Manitoba and one individual lived in Nunavut. Of the four individuals with rural postal codes, only one individual lived in an urban center (Winnipeg) for a prolonged period, according to hospital records. One case of *B. quintana* was acquired in Eritrea prior to immigration. Two cases of *B. henselae* were acquired in Winnipeg and 2 cases were acquired internationally. Of the cases of *B. quintana* acquired in Winnipeg, 7 individuals experienced a lack of suitable housing. While 3 individuals were

homeless at the time of *Bartonella* testing, 4 individuals lived in supportive housing or in single room occupancy but depended on shelters for food and clothing. While the four individuals from Northern communities were housed, 2 individuals from remote communities articulated a lack of running water at home and the presence of more than two people per bedroom, indicating a lack of suitable housing.(33)

Comorbidities:

Three of the 16 individuals (18.8%) with positive *Bartonella* serologies were living with HIV and three were co-infected with Hepatitis C. Two individuals had previous valvular disease, one with rheumatic heart disease and one with a patent ductus arteriosus. Three of the eleven individuals (27.3%) infected with *B. quintana* had a description of ectoparasitosis in their medical chart. Nine individuals (56.3%) had alcohol listed in their substance use history and six individuals (37.5%) had descriptions consistent with alcohol use disorder in the medical chart (emergency room visits for withdrawal or intoxication). Four individuals (25.0%) had a history of injecting intravenous crystal methamphetamine.

A table describing cases with equivocal *Bartonella* results is available in the appendix.

Interpretation:

B. quintana is the most common cause of *Bartonella* serologic positivity among adults in the province of Manitoba. This differs from other high-income jurisdictions where cat scratch disease caused by *B. henselae* is the predominant form of *Bartonella* infection.(17) Endocarditis was present in the majority of our cases (62.5%). Of the 10 cases of endocarditis, 8 cases were due to *B.quintana* and 2 were due to *B. henselae*. Unlike *B.henselae,* transmission of *B.quintana* occurs via body lice ectoparasitosis and is thus inherently tied to public health concerns such as access to suitable housing and running water. An exact quantification of *B. quintana* endocarditis among those with positive *Bartonella* serologies is unknown. However, data from an outbreak of *B. quintana* among homeless individuals in Seattle suggests that 20% of individuals who are bacteremic with *B. quintana* will develop endocarditis.(25) Considering that only a minority of individuals with positive *Bartonella* serology are bacteremic, the elevated proportion of endocarditis in our study suggests a significant burden of undiagnosed trench fever and *B.quintana* bacteremia in Manitoba.(13)

In the cases described here, endocarditis due to *B. quintana* predominantly involved the mitral and aortic valves. This valvular predilection corroborates descriptions of *B. quintana* found elsewhere.(34,35) Seven of the eight cases of *B. quintana* endocarditis (87.5%) demonstrated embolization, including intracranial complications. This degree of embolization exceeds descriptions from other studies where embolization is not often a salient feature.(16,34) This may reflect a prolonged time to diagnosis and thus a greater burden of disease with higher propensity to embolize and cause mycotic aneurysms.

Two cases of *B. quintana* endocarditis were associated with concomitant *Streptococcus pneumoniae* bacteremia. To our knowledge, only one other case of polymicrobial endocarditis has been described with *B. quintana* and *Staphylococcus aureus*.(36) The presence of gram-positive cocci on the gram stain of patient 16's explanted valve suggests the possibility of acute on subacute endocarditis: subacute *B. quintana* creating valvular damage and large vegetations that provide a substrate for seeding when subsequent acute bacteremia occurs with a different pathogen.

Bartonella serologic positivity was predominantly identified in men in our study, a finding that has been described elsewhere.(12,14) This may reflect the disproportional number of cases due to *B. quintana* and the known preponderance of men within the homeless population in Canada.(37) While *B. quintana*'s association with alcohol use is well-established, the association with intravenous crystal methamphetamine use in our study has rarely been described.(12) One Baltimore-based study demonstrated that over 37% of people who use intravenous drugs have positive *Bartonella* serologies.(12) As *B. quintana's* subacute bacteremia may last many months, it is possible that *B. quintana* may be transmitted by shared syringes in addition to body lice ectoparasitosis.(13) While ectoparasitosis was described in 3 individuals infected with *B.quintana*, body lice were never explicitly mentioned in the medical chart. Individuals infected with *B. quintana* described infestation with "bedbugs" and "itchy bugs" but not body lice per se. This may reflect a lack of familiarity with body lice ectoparasitosis among health care providers as well as individuals who are under-housed.

Among the four individuals who had a history of injecting crystal methamphetamine, three were living with HIV and two were co-infected with hepatitis C. The association of *Bartonella* infection with HIV, hepatitis C and intravenous stimulant use exemplifies a convergence of homelessness, substance use and infection described by the syndemic theory of disease.(38)

In this study, three cases were acquired in rural Manitoba and one in Nunavut. *B. quintana's* association with urban homelessness is well-established, leading to the designation of "urban trench fever".(15) However, rural transmission of *B. quintana* is largely under-recognized. A recent case from Northern Alberta suggests a hidden endemicity of *B. quintana* and body lice ectoparasitosis in remote communities in Canada.(20) Local transmission of *B. quintana* in Northern Manitoba, Northern Alberta and Nunavut reflects the ongoing lack of suitable housing and running water within many indigenous communities throughout Canada.(31)

To understand the full burden of *B. quintana* in Manitoba, seroprevalence and ectoparasite surveillance studies both in urban and rural areas are necessary. Cases with elevated *Bartonella* titers should then undergo echocardiography to identify endocarditis prior to the development of valvular damage or mycotic aneurysms. To prevent additional cases of *B. quintana* in both urban and rural Manitoba, a government-sponsored and Indigenous-community directed program is necessary to provide suitable housing and running water to both inner-city Winnipeg as well as many remote communities. A similar Indigenous-rights approach has been proposed to curb rheumatic heart disease among Indigenous people in Canada, Australia and New Zealand.(39) Lastly, including *B.quintana* among the list of nationally and provincially notifiable diseases could serve as a flagship diagnosis to reflect the state of housing accessibility in Canada.(26)

Our study is limited by its retrospective nature and the limitations of serology. All cases described here were a consequence of a provider ordering testing for an under-recognized disease. As most healthcare providers rarely if ever think about *Bartonella,* this study does not describe the true burden of *Bartonella* infection in Manitoba. The study is further limited by the known cross-reactivity of *Bartonella* serology between different *Bartonella* species and other infectious pathogens, albeit at lower titers.(40) Furthermore, occasional cases of *Bartonella* bacteremia and endocarditis have been associated with negative *Bartonella* serology despite molecular confirmation of *Bartonella*.(13)

Conclusion:

The emergence of *B. quintana* in urban and rural Manitoba indicates the need for improved access to suitable housing and running water, both within inner-city Winnipeg as well as in rural Manitoban communities. Improved case finding with seroprevalence studies and subsequent echocardiographic surveillance for individuals with elevated titers is needed to prevent endovascular complications as endocarditis and mycotic aneurysm rupture.

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Tables 1 and 2.

Please see tables attached separately.

Caption Table 2.

AV: aortic valve, MV: mitral valve, PV: pulmonary valve, AKI: acute kidney injury, CRRT: continuous renal replacement therapy, HIV: Human Immunodeficiency Virus, IV: intravenous, CM: crystal methamphetamine, MCA: middle cerebral artery, MB: Manitoba, AMA: against medical advice, GERD: gastro-esophageal reflux disease, SRO: single room occupancy, MRSA: methicillin-susceptible staphylococcus aureus, BHA: bilateral hip arthroplasty, VL: viral load, HCV: hepatitis C virus, AVR: aortic valve replacement, NU: Nunavut, T2DM: type 2 diabetes mellitus

Figure 1. Legend

Long underwear stained with human blood due to body lice ectoparasitosis acquired in Winnipeg Canada. Photo courtesy: Dr. Robbin Lindsay.

Figure 2. Legend

Body lice, *Pediculus humanus humanus*, seen on clothing acquired from a patient experiencing homelessness in Winnipeg, Canada. Photo courtesy: Dr. Robbin Lindsay.

Figure 1.

Figure 2.

Please see file attached separately.

Table 1. *Bartonella* serologic testing numbers and percentages in Manitoba from 2010 to 2020

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	total study period
negative	46 (90.2%)	56 (83.6%)	57 (86.4%)	46 (97.9%)	72 (93.5%)	80 (82.5%)	70 (80.5%)	101 (91.8%)	125 (89.3%)	105 (91.3%)	138 (87.9%)	896 (88.4%)
equivocal	5 (9.8%)	9 (13.4%)	9 (13.6%)	0 (0.0%)	4 (5.1%)	15 (15.5%)	15 (17.2%)	6 (5.5%)	13 (9.3%)	8 (7.0%)	10 (6.4%)	94 (9.3%)
positive	0 (0.0%)	2 (3.0%)	0 (0.0%)	1 (2.1%)	1 (1.3%)	2 (2.1%)	2 (2.3%)	3 (2.7%)	2 (1.4%)	2 (1.7%)	9 (5.7%)	24 (2.4%)
total	51	67	66	47	77	97	87	110	140	115	157	1014

Number	Age	Gender	area	year	*B. henselae* titer	*B. quintana* titer
1	48	M	Winnipeg	2020	8192	8192
2	35	M	Island lake	2020	8192	8192
3	33	M	Island lake	2020	8192	8192
4	53	M	Winnipeg	2020	8192	8192
5	62	M	Winnipeg	2020	8192	8192
6	57	M	Winnipeg	2020	512	256
7	63	M	Winnipeg	2020	64	256
8	65	M	Winnipeg	2020	256	negative
9	63	M	Winnipeg	2020	64	256
10	38	F	Winnipeg	2019	256	negative
11	31	F	Winnipeg	2018	8192	8192
12	39	M	Winnipeg	2017	1024	512
13	20	F	Winnipeg	2017	512	n/a
14	53	M	Winnipeg	2017	4096	2048
15	47	M	Baker Lake	2015	4096	n/a
16	62	F	Pukatawagan	2014	1024	n/a

molecular speciation	clinical presentation	Embolic complications	documented endovascular infection
16S rRNA aortic valve: *B. quintana*	culture-negative AV and MV endocarditis, aortic root abscess, AKI (CRRT), pulmonary embolization, splenic infarcts, aneurysms of abdominal aortic branches.	Yes	Yes (largest vegetation: 14 x 6 mm)
No	culture negative MV endocarditis, ruptured intracranial mycotic aneurysm (hemorrhage)	Yes	Yes (largest vegetation MV: 18x7 mm)
No	culture negative MV endocarditis and ruptured intracranial mycotic aneurysm	Yes	Yes (largest vegetation: 16x9mm)
No	culture-negative AV and MV endocarditis, AKI (CRRT), intracranial emboli, concomitant *Streptococcus pneumoniae* bacteremia	Yes	Yes (largest vegetation: 14x6mm)
16S rRNA aortic valve: *B.quintana*	culture-negative MV endocarditis, splenic infarct	Yes	Yes (largest vegetation: 21x6mm)
No	ectoparasitosis, cellulitis	No	No. No echocardiography performed.
No	malaise, rash, ectoparasitosis	No	No. No echocardiography performed.
No	gastroduodenal artery mycotic aneurysm rupture (hemorrhagic shock)	No	Yes (gastroduodenal artery aneurysm: unclear etiology)
No	rash evidence of body lice (treated with permethrin), presentation to emergency room with shin pain (no	No	No. No echocardiography performed.
No	pulmonary valve endocarditis	No	Yes. (vegetation size not retrievable).
16S rRNA aortic valve: *B.quintana*	AV and PV endocarditis, splenic infarcts, anemia	Yes	Yes. (vegetation size not retrievable).
No	axillary lymphadenopathy and fever	No	No.
No	axillary lymphadenopathy and fever	No	No.
No	culture-negative encarditis (unclear valve by available documentation)	No	Yes. (vegetation size not retrievable).
rpoB gene sequencing: *B. quintana*	endocarditis (AV, MV, PV), intracranial aneurysm ruptured, intracranial hemorrhage, anemia	Yes	Yes. (vegetation size not retrievable).
16S rRNA: *B. quintana*	endocarditis AV and MV, type A aortic dissection, concomitant *Streptococcus pneumoniae* bacteremia and endocarditis: gram positive cocci on explanted valve	No	Yes. (vegetation size not retrievable).

antimicrobial therapy	surgical treatment	comorbidities	Pre-existing valvular disease	substance use	housing
gentamicin (4d), ceftriaxone (42d), doxycyline (42d)	AV and MV valve replacement	HIV (CD4=94, VL= <20), solitary kidney, ectoparasitosis	No	alcohol (binge, active), IV CM (remission)	supportive housing, previous homelessness
ceftriaxone (43d), vancomycin (21d), daptomycin (22d)	endovascular coiling of MCA aneurysm	rheumatic heart disease, schizophrenia, previous ectoparasitosis	Yes	occasional alcohol, smoked cannabis	housed with family in remote community, limited running
ceftriaxone(56d), vancomycin (56d), doxycycline(56d), gentamicin (14d)	endovascular coiling of MCA aneurysm	anxiety, depression	No	IV CM (daily, active), alcohol	homeless, recent incarceration, previous housing in
ceftriaxone (15d), vancomycin (15d)	No (declined, AMA).	GERD	No	daily alcohol, baclofen	underhoused (SRO), meals and clothing at shelter
gentamicin (14d), doxycycline (42d)	MV replacement	hypertension, dyslipidemia, depression, previous ectoparasitosis	No	alcohol	supportive housing (clothes, food at shelter)
Doxycycline (7d: MRSA cellulitis)	None.	HIV (CD4=322, VL<20 copies/mL), HCV (untreated), BHA, orthopedic fractures	No	alcohol (active), IV CM (remission)	homeless
None.	None.	Anxiety	No	unknown	underhoused (current SRO, previously homeless)
Pen G and ceftriaxone (total 14d, neurosyphilis)	embolization gastroduodenal artery	neurosyphilis, Hep C	No	unknown	Housed.
None.	None.	Unknown.	No	Unknown.	homeless (shelter)
No dedicated *Bartonella* treatment (left AMA).	None	HIV (CD4=300, Vl<20), Hep C, TB	No	polysubstance use with IV CM (admissions with meth induced psychosis), intermittent alcohol	housed
gentamicin 14 days and doxycycline 6 weeks post-AVR	bioprosthetic AVR and PDA closure	congenital patent ductus arteriosus	Yes	none	housed
azithromycin (5d)	none	nephrolithiasis	No	alcohol	housed
azithromycin (5d)	none	none.	No	none.	housed
doxycycline (42d) and rifampin(14d)	bioprosthetic AV replacement	neuroendrocrine tumor,PE, CAD, HTN	No	none	housed
ceftriaxone (42d), doxycyline (42d), gentamicin (initial 14d)	bioprosthetic AVR, MVR, PV repair, craniotomy, intracranial hematoma evacuation, aneurysm	not documented	No	alcohol	housed (remote community)
ceftriaxone (42d post-AVR/MVR), doxycycline (42d post AVR/MVR)	bioprosthetic AVR, MVR	HTN, T2DM, DLP	No	Alcohol	housed (remote, no running water)

animal exposure	outcome	geographic acquisition	interpretation
none	survived (1 year follow-up)	local urban	confirmed *B. quintana*
none	survived (6 month follow-up)	rural MB	probable *B. quintana*
none	survived (6 month follow-up)	rural MB	probable *B. quintana*
none	deceased	local urban	probable *B. quintana*
none	survived (3 month follow-up)	local urban	confirmed *B. quintana*
none	survived (no follow-up)	local urban	problable *B. quintana*
none	survived (no follow-up)	local urban	probable *B. quintana*
None.	survived (no follow-up)	local urban	not a case (suspected false positive).
None.	survived (no follow-up)	local urban	probable *B. quintana*
cat (recent scratch)	survived (no follow-up)	local urban	probable *B. henselae*
none	survived (1 year follow-up)	Eritrea (via Ukraine)	confirmed *B. quintana*
cat (recent scratch)	survived (no follow-up)	Bosnia	probable *B. henselae*
cat (recent scratch)	survived (no follow-up)	Thailand	probable *B. henselae*
cats (previous scratch)	survived (6 month follow-up)	local urban	probable *B. henselae*
none.	deceased	rural NU	confirmed *B. quintana*
subsistence hunting.	survived (6 month follow-up)	Rural MB	confirmed *B. quintana*

Long underwear stained with human blood due to body lice ectoparasitosis acquired in Winnipeg Canada. Photo courtesy: Dr. Robbin Lindsay.

Body lice, Pediculus humanus humanus, seen on clothing acquired from a patient experiencing homelessness in Winnipeg, Canada. Photo courtesy: Dr. Robbin Lindsay.

Number	Age	Gender	area	year	*B. henselae* titer	*B. quintana* titer	clinical presentation
1	25	F	Winnipeg	2020	64	64	Culture-negative AV endocarditis AV, anemia
2	52	F	Island Lake	2020	64	64	rash
3	71	M	Winnipeg	2020	64	64	CN IE AV, bioprosthetic AVR/hemiarch replacement
4	43	F	Winnipeg	2020	128	0	visual changes
5	58	M	Swan River	2019	64	64	visual changes
6	50	F	Oxford House	2019	64	64	visual changes
7	45	M	Norway House	2019	64	64	visual changes
8	67	M	Lynn Lake	2019	128	64	CN MV IE, hemorrhagic stroke, splenic infarct, R colic branch artery aneurysm
9	45	F	St. Andrews	2018	64	64	no data
10	71	M	Dauphin	2018	64	64	no data
11	39	M	Winnipeg	2018	64	128	axillary lymphadenopathy
12	21	M	Winkler	2018	64	n/a	no data
13	32	M	Hudson	2018	64	n/a	lymphadenopathy (positive pathology stain for *Bartonella*)
14	82	F	Winnipeg	2018	128	n/a	no data
15	83	M	Winnipeg	2016	64	n/a	fever NYD
16	55	F	The Pas	2016	64	n/a	no data
17	54	M	Winnipeg	2016	128	n/a	visual changes
18	31	F	Winnipeg	2016	128	n/a	visual changes
19	30	M	Winnipeg	2016	128	n/a	visual changes
20	26	F	Steinbach	2016	64	n/a	visual changes
21	29	F	Winnipeg	2016	64	n/a	visual changes
22	69	M	Winnipeg	2016	128	n/a	Q fever aortic valve endocarditis, ruptured infected aortic aneurysm (abdominal aorta repair)
23	46	M	Arviat	2016	125	n/a	visual changes
24	54	M	Selkirk	2015	64	n/a	lymphadenopathy (cervical)
25	46	M	Winnipeg	2015	64	n/a	visual changes
26	28	M	Winnipeg	2015	64	n/a	visual changes
27	18	M	East St. Paul	2015	64	n/a	visual changes

28	45	F	Winnipeg	2015	64	n/a	no data
29	53	F	Winnipeg	2015	64	n/a	no data
30	55	F	Winnipeg	2015	64	n/a	hematochezia
31	34	F	Winnipeg	2014	64	n/a	rash
32	18	F	Winnipeg	2012	64	n/a	no data
33	68	M	Warren	2012	64	n/a	visual changes
34	49	M	Island Lake	2012	128	n/a	no data
35	57	F	Gilbert Plains	2011	64	n/a	no data
36	64	F	Winnipeg	2011	64	n/a	no data
37	27	F	Winnipeg	2011	64	n/a	rash and fever (diagnosed with Lyme disease)
38	56	M	Winnipeg	2010	64	n/a	cervical lymphadenopathy

documented endovascular infection	antimicrobial therapy	comorbidities/ co-infection	substance use	housing	animal exposure
Yes. (AV 2 x 9 mm)	ceftriaxone (21d), vancomycin (21d), doxycycline (21d), then AMA	unknown	IV opiate use disorder	homeless	none
no	none	IgA nephropathy, ESRD on HD	none	housed remote community	none
Yes (AV IE and abscess)	ceftriaxone (42d)	DLH, HTN, GIB, hypothyroidism	alcohol	housed	dog
no	ceftriaxone (14d)	neurosyphilis, PTSD, depression	polysubstance use disorder with	institutionally housed	none
no	none	no data	alcohol	housed	unknown
no	none	T2DM, DLP, *H. pylori* ab IgG positive, syphilis negative.	none	housed	none
AV fistula embolization in R carotid	none	T2DM, DLP, HTN, CAD, NASH cirrhosis	none	housed	unknown
Yes (MV IE, intracranial and splenic emboli)	ceftriaxone (3d: premature antimicrobial cessation as MRP team equated "culture negative" with "non-infectious")	HTN, GERD	alcohol	housed	unknown
no data	no data	no data	no data	no data	no data
no data	no data	no data	no data	no data	no data
no	TMP-SMX (7d)	unknown	alcohol, IV	homeless	unknown
no data	no data	no data	no data	no data	no data
none.	azithromycin (5d)	ITP and is status post-splenectomy	none	housed	hunter, skins his own animals, domestic cats and dogs
no data	no data	no data	no data	no data	no data
no data	no data	CAD, MI, bipolar d/o	no data	housed	no data
no data	no data	no data	no data	no data	no data
none.	ceftriaxone (14d)	ocular syphilis (1:16 VDRL), coronary artery	no data	no data	no data
no data	no data	no data	no data	no data	no data
no data	no data	no data	no data	no data	no data
no data	no data	no data	no data	no data	no data
no data	no data	no data	no data	no data	no data
Yes.	hydroxychloroquine (18m) and doxycycline (18m)	none	none	housed	none documented
none.	syphilis	unknown	no data	housed	unknown
no	no data	no data	no data	no data	no data
none.	ceftriaxone (14d)	HIV (CD4=540, VL undetectable), neurosyphilis.	no data	housed	no data
none.	none	UC, colorectal CA (paraneoplastic syndrome)	none	housed	none
none.	none	no infectious diagnosis.	no data	housed	none

no data	no data	no data	no data	housed	no data
no data	no data	no data	no data	housed	no data
none.	none.	colorectal CA, IgA nephropathy, hypothyroid, celiac disease	no data	housed	no data
none.	none	HIV (CD4 = 70, 24%); VL= undetectable, HCV cirrhosis, portal HTN, varices	no data	previous homelessness	no data
no data	no data	no data	no data	housed	no data
no data	no data	trauma	no data	housed	no data
no data	no data	ESRD (HD), T2DM, DLP	no data	housed remote community	no data
no data	no data	CAD	no data	housed	no data
no data	no data	ESRD (HD)	no data	housed	no data
none.	doxycycline (14d)	none	no data	housed	no data
none.	none	no data	no data	housed	no data

interpretation
possible *B. quintana*
possible cross reaction:
possible *Bartonella* spp.
possible cross-reaction: syphilis
false positive
possible cross-reaction: H. pylori
false positive
possible *Bartonella* spp.
no data
no data
possible *B. quintana*
unclear
probable *B. henselae*
unclear
unclear
no data
possible cross-reaction: syphilis
unclear
unclear
unclear
unclear
possible cross-reaction: *Coxiella burnetii*
possible cross-reaction: syphilis
unclear
possible cross-reaction: syphilis
possible cross-reaction: auto-immunity
unclear

unclear
unclear
possible cross-reaction: auto-immunity
possible *B. quintana*
no data
no data
possible remote *B. quintana* exposure
unclear
unclear
possible cross-reaction with *Borrelia*
unclear

Data Collection/Capture Sheet

(To be used with Master List)

Protocol Title: "Bartonella quintana, "trench fever", in Manitoba: epidemiology, risk factors, clinical manifestations and vector surveillance"

Principal Investigator: Dr. Carl Boodman, Room 543 - 745 Bannatyne Avenue, University of Manitoba, Winnipeg, Manitoba R3E 0J9, Canada, 431-374-4187

Co-Investigator: Dr. Yoav Keynan, Room 543 - 745 Bannatyne Avenue, University of Manitoba, Winnipeg, Manitoba R3E 0J9, Canada, 204 977-5609

Data to be collected on paper: No

Data to be entered directly into computer spread sheet Yes

Data Elements to be collected:

Demographic data and identifiers

Age: _____

Gender: _____

First three digits of postal code (if applicable): _____

Admission date (if applicable): _____

Discharge date (if applicable): _____

Data elements from chart or database:

Comorbidities:

Bartonella serology titer: IgG/IGM

16 s Bartonella speciation (if available):

Antimicrobial therapy and duration:

Significant laboratory abnormalities:

Significant abnormalities on imaging (? Vegetations, mycotic aneurysms):

Description of housing history (eg: shelters, "tent encampments"):

Immunosuppression (eg: steroids):

Substance use disorder (specifically, alcohol):

Clinical manifestations, specifically:

- Endocarditis
- abdominal pain (splenomegaly?)
- Rash or evidence of ectoparasitosis and location:
- Mycotic aneurysms
- neurologic symptoms
- Fever
- Arthralgia (specifically shin or leg pain?)
- Embolization events

Clinical outcome?:

Data collected by (printed name and signature): _____

Date Data collected: _____