

Research

Serologic testing for *Bartonella* in Manitoba, Canada, 2010–2020: a retrospective case series

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Abstract

Background: Bartonella are gram-negative bacilli not identified by routine bacterial culture. The objectives of this study were to review the results of all serologic testing for Bartonella ordered in Manitoba, Canada, and to review cases with positive test results among adults to assess species identification, risk factors, clinical manifestations and outcomes.

Methods: This retrospective study included all *Bartonella* serologic tests ordered in Manitoba and performed at the National Microbiology Laboratory, Winnipeg, from Jan. 1, 2010, until Dec. 31, 2020. We analyzed the aggregate data for all serologic tests for *Bartonella* for patients of all ages. We reviewed the charts of adult (age ≥ 18 yr) patients with serologic positivity for *Bartonella* who had a medical chart at 1 of Winnipeg's 2 largest hospitals (Health Sciences Centre and St. Boniface Hospital) to extract clinical and demographic data and create a case series. Descriptive statistics were performed.

Results: During the study period, 1014 *Bartonella* serologic tests were ordered in adult and pediatric patients, of which 24 (2.4%) gave a positive result. Sixteen adults (12 men and 4 women; mean age 48 yr) seen at a participating hospital had a positive result. Molecular species-level identification occurred on explanted cardiac valves in 5 (31%) of the 16 cases; *B. quintana* was identified in all 5. Six patients (38%) were diagnosed with probable *B. quintana* infection, for a total of 11 *B. quintana* cases (69%); 8 (73%) of the 11 had endocarditis. Four cases of *B. quintana* infection (36%) were associated with rural residence. Four cases (25%) of probable *B. henselae* were identified; 2 patients had fever and lymphadenopathy, and 2 had endocarditis. The remaining patient was deemed to have a false-positive result as his *B. henselae* titre was at the threshold for positivity, his *B. quintana* serologic test gave a negative result, and his clinical syndrome was not suggestive of *Bartonella* infection. Two patients died; both had multivalvular *B. quintana* endocarditis with ruptured intracranial mycotic aneurysms.

Interpretation: Bartonella quintana was a common cause of Bartonella serologic positivity among adults in Manitoba in 2010–2020 and was associated with endocarditis and systemic embolization. As *B. quintana* is transmitted by body lice, active case finding for people who lack suitable housing, both in urban and rural settings, should prioritize those with elevated Bartonella titres to receive echocardiography and detect endocarditis before systemic embolization occurs.

This genus of bacteria evades identification by routine culture owing to its slow replication time and niche within erythrocytes.^{3,4} Although more than 45 *Bartonella* species and subspecies infect various mammals, human disease due to *Bartonella* in North America is caused primarily by 2 species: *B. henselae* (cat scratch disease) and *B. quintana* (trench fever).^{2,5} Cat scratch disease usually occurs after a feline scratch or bite.^{6,7} Its most common clinical manifestation is regional lymphadenopathy.⁷ *Bartonella quintana* is transmitted in the feces of body lice, entering the systemic circulation via abrasions in the skin.^{8–10} Body lice live on clothing and bedding (Figure 1, Figure 2) and feed intermittently on the human host.^{8,10,11}

Clinical disease due to *B. quintana* was first described in 1915 among World War I soldiers and was thus coined "trench fever." Although *B. quintana* was historically associated with a relapsing febrile illness, chronic bacteremia with

B. quintana may be associated with few to no symptoms. ^{12,13} Infection with *B. quintana* has since emerged among urban populations experiencing houselessness owing to infestations with body lice. ^{8,9,14–17} Both *B. benselae* and *B. quintana* may cause endovascular infections such as infective endocarditis and mycotic aneurysms. ^{18,19} Although patients with uncontrolled HIV infection may develop other manifestations of bartonellosis, such as bacillary angiomatosis and peliosis hepatis, most cases of *Bartonella* infection are not associated with HIV. ²⁰

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Figure 1: Long underwear stained with human blood due to body lice ectoparasitosis acquired in Winnipeg, Canada.



Figure 2: Body lice, *Pediculus humanus humanus*, seen on clothing acquired from a patient experiencing houselessness in Winnipeg.

Given the difficulties in identifying *Bartonella* with culture-based methods, serologic testing is often used to diagnose bartonellosis.^{2,3} A large diversity of clinical syndromes, including lymphadenopathy after a cat scratch, vegetations seen on echocardiography, visual loss due to possible infectious causes and febrile illness with negative culture results, prompt ordering of *Bartonella* serologic testing. Clear documentation of what prompted ordering testing is sometimes lacking.

In Canada, serologic evidence of exposure to *B. henselae* is common, reflecting local endemicity.²¹ Although Canadian data regarding other zoonotic *Bartonella* species are scant, serologic positivity for *B. tribocorum*, a species associated with rats,²² was described among people who inject drugs in Vancouver's Downtown Eastside.²³ Human infection with *B. tribocorum* is very rare;²⁴ to our knowledge, no Canadian cases of clinical disease have been reported. The first Canadian case of *B. quintana* infection was described in 1996.²⁵ Twenty years elapsed before a subsequent case was identified, in 2016.²⁶ Since 2018, 6 cases of *B. quintana* infection have been described in Canada, from both inner-city and rural areas of Alberta and Manitoba.^{27–29} All cases were associated with endocarditis, a rare and severe manifestation of *B. quintana* infection, which suggests an undescribed burden of community transmission.³⁰

As bartonellosis is not a reportable disease, little is known about *Bartonella* infection in Canada.³¹ The objectives of this study were to review the results of all serologic testing for *Bartonella* ordered in Manitoba from 2010 to 2020, and to review cases with positive test results to assess speciation, risk factors, clinical manifestations and outcomes.

Methods

Study design and setting

This study was a case series of adults with serologic positivity for *Bartonella* in Manitoba. Aggregate data included all serologic tests for *Bartonella* ordered from 2010 to 2020 for patients of all ages. We reviewed the charts of adult patients with positive test results to extract clinical and demographic data and to create a case series. We reported this study using the Preferred Reporting of Case Series in Surgery (PROCESS) guidelines.³²

Participants

Inclusion criteria for chart review were age 18 years or more at the time of testing, serologic positivity for *Bartonella* and having a medical chart at 1 of Winnipeg's 2 largest hospitals (Health Sciences Centre and St. Boniface Hospital). Pediatric cases were not included in the chart review owing to ethics approval considerations.

Data sources

We obtained the results of all serologic tests for *Bartonella* ordered in Manitoba from Jan. 1, 2010, until Dec. 31, 2020, from the database of Cadham Provincial Laboratory, Manitoba's provincial public health laboratory, in Winnipeg. *Bartonella* serologic testing was performed at the National Microbiology Laboratory, Winnipeg. An indirect immunofluorescent antibody assay was used to test for immunoglobulin G



antibodies to *B. henselae* and *B. quintana* antigen.³³ A positive test result was defined as a titre of 1:256 or greater.³³ Titres of 1:64 and 1:128 were considered equivocal, and titres less than 1:64 were considered negative.³³ Before 2017, the National Microbiology Laboratory reported results of *Bartonella* serologic testing exclusively for *B. henselae*. There is known serologic cross-reactivity between *B. henselae* and *B. quintana*.^{2,34}

C.B. and Y.K. retrospectively reviewed the electronic medical records and paper charts of adults who had positive results of *Bartonella* serologic testing, and extracted clinical, laboratory and demographic data from emergency department visits and hospital admissions to the Health Sciences Centre and St. Boniface Hospital (Appendix 1, available at www.cmajopen.ca/content/10/2/E476/suppl/DC1). Records were reviewed for the period 2 years before and 1 year after the serologic testing result. Clinical data included comorbidities, housing status, animal exposures, clinical syndrome, treatment and outcome. Laboratory data included *B. quintana* and *B. henselae* serologic titres and molecular speciation, if applicable. Demographic data included age, gender and geographic area based on home postal code.

Case definitions

We classified cases as confirmed or probable B. quintana or B. henselae infection by extrapolating from definitions of infections under public health surveillance.³⁵ Confirmed cases had molecular confirmation to species level by means of 16S rRNA sequencing, species-specific polymerase chain reaction or gene sequencing. Patients with probable infection showed Bartonella positivity on serologic testing, compatible clinical syndrome and risk factors consistent with B. henselae or B. quintana acquisition, without molecular confirmation. Epidemiologic risk factors differ between B. benselae and B. quintana infection:16,36 B. henselae infection is associated with cat exposure, whereas B. quintana infection is associated with houselessness and body lice ectoparasitosis.³⁶ Cases with lowgrade serologic positivity but failure to fulfill the criteria for compatible clinical syndrome and epidemiologic risk factor were considered to have a false-positive result. Given the lack of suitable housing in many communities in northern Manitoba, we considered residence in a remote area known to have inadequate housing without a description of feline exposure a risk factor for B. quintana infection. 26-28,37

Statistical analysis

We classified the aggregate data, which included data for both pediatric and adult patients, according to positive, equivocal or negative result of serologic testing for *Bartonella*. We performed descriptive statistics using R Statistical Software, version 3.5.3 (R Foundation for Statistical Computing).

Ethics approval

The study was approved by the University of Manitoba Bannatyne Campus Health Research Ethics Board (H2020:374), the Health Sciences Centre Research Ethics Board (RI2020:147), St. Boniface Hospital's Research Review Committee (RRC/2020/1978), Shared Health and Winnipeg Regional Health Authority's Research Access and

Approval Committee (2020-059) and the Manitoba Health Information Privacy Committee (2020/2021-79).

Results

During the study period, 1014 *Bartonella* serologic tests were ordered for adult and pediatric patients, of which 896 (88.4%) gave a negative result, 94 (9.3%) gave an equivocal result, and 24 (2.4%) gave a positive result (Table 1).

There were 16 adults (12 men and 4 women; mean age 48 yr) who had positive test results and received care at a participating hospital (Table 2). Twelve of the 16 patients lived in Winnipeg, and 4 cases of infection (all with *B. quintana*) were associated with rural geography: 3 patients resided in northern Manitoba, and 1 lived in Nunavut. One case of *B. quintana* infection was acquired in Eritrea before immigration. Two cases of *B. henselae* were acquired in Winnipeg, and 2 cases were acquired internationally. Of the 7 patients who acquired *B. quintana* infection in Winnipeg, 6 experienced a lack of suitable housing. Overall, 3 people were experiencing houselessness at the time of *Bartonella* testing, 4 lived in single rooms, and 2 depended on shelters for food and clothing. Although 3 of the 4 patients from northern communities were housed, 2 did not have running water, which indicated a lack of suitable housing.³⁸

Causative pathogen and clinical manifestations

Molecular species-level identification occurred on explanted cardiac valves in 5 cases (31%); the pathogen was *B. quintana* in all 5 (Table 3). Six patients (38%) were diagnosed with probable *B. quintana* infection, for a total of 11 *B. quintana* cases (69%). People infected with *B. quintana* described infestation with "bedbugs" and "itchy bugs" but not body lice per se. Of the 11 cases, 8 (73%) were associated with endocarditis. Seven (88%) of the 8 patients had evidence of embolization: 4 showed

Table 1: Results of *Bartonella* serologic tests ordered in Manitoba, 2010–2020*

	Result; no. (%) of tests							
Year	Negative	Equivocal	Positive	Total				
2010	46 (90.2)	5 (9.8)	0 (0.0)	51				
2011	56 (83.6)	9 (13.4)	2 (3.0)	67				
2012	57 (86.4)	9 (13.6)	0 (0.0)	66				
2013	46 (97.9)	0 (0.0)	1 (2.1)	47				
2014	72 (93.5)	4 (5.2)	1 (1.3)	77				
2015	80 (82.5)	15 (15.5)	2 (2.1)	97				
2016	70 (80.5)	15 (17.2)	2 (2.3)	87				
2017	101 (91.8)	6 (5.4)	3 (2.7)	110				
2018	125 (89.3)	13 (9.3)	2 (1.4)	140				
2019	105 (91.3)	8 (7.0)	2 (1.7)	115				
2020	138 (87.9)	10 (6.4)	9 (5.7)	157				
Total	896 (88.4)	94 (9.3)	24 (2.4)	1014				
*For both adult and pediatric nationts								

For both adult and pediatric patients



Patient no.	Age, yr	Gender*	Home area†	Year	Comorbidities	Substance use	Housing	Animal exposure
1	48	Male	Winnipeg	2020	HIV infection, ectoparasitosis	Alcohol, intravenous crystal methamphetamine use	Single room, previously houseless	None
2	35	Male	NE-MB1	2020	Rheumatic heart disease, schizophrenia, ectoparasitosis	Alcohol, cannabis	Housed	None
3	33	Male	NE-MB1	2020	Anxiety, depression	Intravenous crystal methamphetamine use, alcohol	Houseless	None
4	53	Male	Winnipeg	2020	None	Alcohol, baclofen	Single room, meals at shelter	None
5	62	Male	Winnipeg	2020	Depression, ectoparasitosis	Alcohol	Single room (clothes, food at shelter)	None
6	57	Male	Winnipeg	2020	HIV infection, HCV infection	Alcohol, intravenous crystal methamphetamine use	Houseless	None
7	63	Male	Winnipeg	2020	Anxiety	Unknown	Single room, previously houseless	None
8	65	Male	Winnipeg	2020	Syphilis, HCV infection	Unknown	Housed	None
9	63	Male	Winnipeg	2020	Unknown	Unknown	Houseless (shelter)	None
10	38	Female	Winnipeg	2019	HIV infection, HCV infection, tuberculosis	Intravenous crystal methamphetamine use, alcohol	Housed	Cat
11	31	Female	Winnipeg	2018	Congenital patent ductus arteriosus	None	Housed	None
12	39	Male	Winnipeg	2017	Nephrolithiasis	Alcohol	Housed	Cat
13	20	Female	Winnipeg	2017	None	None	Housed	Cat
14	53	Male	Winnipeg	2017	Neuroendocrine tumour, pulmonary embolism	None	Housed	Cat
15	47	Male	Nunavut	2015	None	Alcohol	Housed	None
16	62	Female	NW-MB2	2014	Type 2 diabetes	Alcohol	Housed	Hunting

intracranial complications with embolization or ruptured mycotic aneurysms or both, and 3 had evidence of splenic infarcts. Mitral and aortic valve involvement was most common. Among cases of endocarditis with documented vegetation size, the average size was 17 mm × 7 mm. All cases of *B. quintana* endocarditis were associated with elevated *Bartonella* titres (> 1:1024). Two patients with *B. quintana* endocar-

†As determined by the postal code in the medical chart.

Four cases (25%) of probable *B. henselae* infection were identified. All 4 patients had a history of a cat scratch, 2 had fever and lymphadenopathy, and 2 had endocarditis. Patient 8

ditis had concomitant Streptococcus pneumoniae bacteremia.

was deemed to have a false-positive result as his *B. henselae* titre was at the threshold for positivity, his *B. quintana* serologic test gave a negative result, and his clinical syndrome was not suggestive of *Bartonella* infection.

Comorbidities

Three patients (19%) were living with HIV infection, and 3 were coinfected with hepatitis C virus (Table 2). Two patients had previous valvular disease, rheumatic heart disease in 1 and a patent ductus arteriosus in the other. Three (27%) of the 11 patients infected with *B. quintana* had a description of



Patient	Clinical presentation/		B. henselae	B. quintana	Species	Antimicrobial (duration of	Surgical	Outcome (length of
no.	test indication	Interpretation	titre	titre	identified*	treatment, d)	treatment	follow-up, mo)
1	AV/MV endocarditis (14 mm × 6 mm†), aortic root abscess, pulmonary and splenic emboli, arterial aneurysms	Confirmed B. quintana	8192	8192	B. quintana (16S AV)	Gentamicin (4), ceftriaxone (42), doxycycline (42)	AV/MV replacement	Survived (12)
2	MV endocarditis (18 mm × 7 mm†), intracranial aneurysm	Probable B. quintana	8192	8192	No	Ceftriaxone (43), vancomycin (21), daptomycin (22)	Endovascular coiling (MCA aneurysm)	Survived (6)
3	MV endocarditis (16 mm × 9 mm†), ruptured intracranial mycotic aneurysm	Probable B. quintana	8192	8192	No	Ceftriaxone (56), vancomycin (56), doxycycline (56), gentamicin (14)	Endovascular coiling (MCA aneurysm)	Survived (6)
4	AV/MV endocarditis (14 mm × 6 mm†), intracranial emboli	Probable B. quintana	8192	8192	No	Ceftriaxone (15), vancomycin (15)	None (declined)	Died
5	MV endocarditis (21 mm × 6 mm†), splenic emboli	Confirmed <i>B. quintana</i>	8192	8192	B. quintana (16S AV)	Gentamicin (14), doxycycline (42)	MV replacement	Survived (3)
6	Ectoparasitosis, cellulitis	Probable B. quintana	512	256	No	Doxycycline (7)	None	Survived (0)
7	Fever, rash, ectoparasitosis	Probable B. quintana	64	256	No	None	None	Survived (0)
8	Gastroduodenal artery hemorrhage	False-positive	256	Negative	_	None	Arterial embolization	Survived (0)
9	Ectoparasitosis, shin pain	Probable B. quintana	64	256	No	None	None	Survived (0)
10	PV endocarditis‡	Probable B. henselae	256	Negative	No	None	None	Survived (0)
11	AV/PV endocarditis,‡ splenic infarcts	Confirmed B. quintana	8192	8192	B. quintana (16S AV)	Gentamicin (14), doxycycline (42)	AV replacement, PDA closure	Survived (12)
12	Axillary lymphadenopathy, fever	Probable B. henselae	1024	512	No	Azithromycin (5)	None	Survived (0)
13	Axillary lymphadenopathy, fever	Probable B. henselae	512	NA	No	Azithromycin (5)	None	Survived (0)
14	AV endocarditis‡	Probable B. henselae	4096	2048	No	Doxycycline (42), rifampin (14)	AV replacement	Survived (6)
15	AV/MV/PV endocarditis,‡ ruptured intracranial aneurysm	Confirmed B. quintana	4096	NA	B. quintana (rpoB gene sequencing)	Ceftriaxone (42), doxycycline (42), gentamicin (14)	AV/MV replacement, PV repair, craniotomy, aneurysm clip	Died
16	AV/MV endocarditis,‡ aortic dissection	Confirmed B. quintana	1024	NA	B. quintana (16S AV)	Ceftriaxone (42), doxycycline (42)	AV/MV replacement	Survived (6)

Note: 16S = 16S rRNA sequencing, AV = aortic valve, MCA = middle cerebral artery, MV = mitral valve, NA = not applicable, PDA = patent ductus arteriosus, PV = pulmonary

ectoparasitosis in their medical chart. Ten patients (62%) had alcohol listed in their substance use history, and 6 (38%) had previous emergency department visits for withdrawal or intoxication. Four patients (25%) had a history of intravenous injection of crystal methamphetamine.

Treatment and outcome

Six patients (38%) underwent valve replacement surgery, and 2 patients (12%) underwent intravascular coiling of a middle cerebral artery aneurysm (Table 3). All patients with endocarditis were prescribed antimicrobial therapy; doxycycline + gentamicin,

or ceftriaxone, or both, were the most common regimens. One patient was prescribed doxycycline and rifampin. Patients diagnosed with cat scratch disease were treated with azithromycin.

Fourteen patients (88%) survived. The 2 patients who died had multivalvular B. quintana endocarditis with ruptured intracranial mycotic aneurysms.

Interpretation

Bartonella quintana was a common cause of Bartonella serologic positivity among adults in Manitoba from 2010 to 2020. As

^{*}On explanted cardiac valves.

[†]Largest vegetation documented

[‡]Vegetation size was not documented in the available medical chart.



B. quintana infection is transmitted by body lice, it is inherently tied to access to suitable housing and running water. The presence of *B. quintana* infection in urban and rural Manitoba indicates extreme conditions of privation, mimicking the trenches of World War I.³⁹

It is unknown how many people with *Bartonella* serologic positivity will develop endocarditis. Data from an outbreak of *B. quintana* infection among people experiencing houselessness in Seattle suggest that endocarditis will develop in 20% of people with bacteremia due to *B. quintana*.³⁰ Considering that only a minority of people with *Bartonella* serologic positivity are bacteremic, the elevated frequency of endocarditis in our study, 62%, suggests a substantial burden of undiagnosed trench fever in Manitoba.¹⁵

Endocarditis was present in 10 of our 16 patients. Of the 10 cases, 8 were due to *B. quintana* and 2 to *B. henselae*. Endocarditis due to *B. quintana* predominantly involved the mitral and aortic valves, as described previously. ^{40,41} Embolization, including intracranial complications, was present in 7 of the 8 cases of *B. quintana* endocarditis. As embolization is not a salient feature of other reports, our cases may reflect a prolonged time to diagnosis and thus a greater burden of disease with higher propensity to embolize. ^{18,40}

Two cases of *B. quintana* endocarditis were associated with concomitant *S. pneumoniae* bacteremia. To our knowledge, only 1 other case of polymicrobial *B. quintana* endocarditis has been described, with *Staphylococus aureus*.⁴² The presence of gram-positive cocci on the gram stain of patient 16's explanted valve suggests acute on subacute endocarditis: subacute *B. quintana* infection creates valvular damage and large vegetations, which provide a substrate for seeding when acute bacteremia occurs with a different pathogen.

Bartonella serologic positivity was identified predominantly in men in our study, a finding described elsewhere. 14,16 This may reflect the disproportional number of cases due to B. quintana and the known preponderance of men within the population experiencing houselessness in Canada. 43 Although the association of B. quintana with alcohol use is well established, the association with intravenous crystal methamphetamine use has rarely been described.¹⁴ A Baltimore-based study showed that 37.5% of people who used intravenous drugs had serologic positivity for Bartonella. 14 As the subacute bacteremia due to B. quintana may last many months, it is possible that B. quintana may be transmitted by shared syringes in addition to body lice ectoparasitosis. 15 Although ectoparasitosis was described in the medical charts of 3 patients infected with B. quintana in our study, body lice were not mentioned explicitly in the charts. People 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 people who are underhoused.

Of the 4 patients who had a history of injecting crystal methamphetamine, 3 were living with HIV infection, and 2 were coinfected with hepatitis C virus. The association of *Bartonella* infection with HIV infection, hepatitis C and intravenous stimulant use exemplifies a convergence

of houselessness, substance use and infection described by the syndemic theory of disease.⁴⁴

In this study, 3 cases of *Bartonella* infection were likely acquired in rural Manitoba and 1 in Nunavut. The association of *B. quintana* with urban houselessness is wellestablished, leading to the designation of "urban trench fever." However, rural transmission of *B. quintana* is largely underrecognized. A recent case from northern Alberta suggests a hidden endemicity of *B. quintana* and body lice ectoparasitosis in remote communities in Canada. ²⁷ 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. ³⁷

To understand the full burden of B. quintana in Manitoba, seroprevalence and ectoparasite surveillance studies are necessary. Patients with elevated Bartonella titres should then undergo echocardiography to identify endocarditis before valvular damage or mycotic aneurysms develop. To prevent additional cases of B. quintana, a program sponsored by government and directed by the Indigenous community is needed to provide suitable housing and washing facilities in both inner-city Winnipeg and 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.⁴⁵ The establishment of accessible washing and laundry facilities is a necessary measure that can be implemented immediately to interrupt B. quintana transmission.39 Finally, 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.31

Limitations

This study is limited by the known serologic cross-reactivity between different *Bartonella* species and other infectious pathogens, albeit at lower titres. ⁴⁶ Occasional cases of *Bartonella* bacteremia and endocarditis have been associated with negative results of serologic testing for *Bartonella* despite molecular confirmation of *Bartonella*. ¹⁵ Although all 16 adults with serologic positivity for *Bartonella* in our study had medical records at Manitoba's 2 largest hospitals, limiting our chart review to these 2 facilities may have limited information regarding milder clinical manifestations.

Conclusion

Bartonella quintana was a common cause of Bartonella serologic positivity among adults in Manitoba in 2010–2020 and was associated with endocarditis and systemic embolization. The presence of B. quintana infection in urban and rural Manitoba indicates the need for improved access to suitable housing and running water, both in inner-city Winnipeg and in remote Manitoba communities. Improved case finding through sero-prevalence studies and subsequent echocardiographic surveillance for people with elevated Bartonella titres are needed to prevent endovascular complications such as endocarditis and mycotic aneurysm rupture.



Research

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