

General

Bartonella quintana is a very small Gram-negative intracellular rod-shaped bacterium responsible for a range of clinical presentations. Infections with this bacterium are **linked to louse infestation** and occur where **people lack access to adequate water to maintain personal hygiene, such as homeless encampments in high-income countries and refugee camps and remote rural areas in low-income-countries**. The bacterium is **not recognized by routine bacterial culture**. **Trench fever** was the first clinical manifestation of infection with *Bartonella quintana* to be recognized. The name refers to its association with the German and Allied troops in the First World War. It is estimated that more than one million people were infected during the war. British troops took the disease to Mesopotamia during Lawrence of Arabia. After the war, the incidence fell very sharply. The disease broke out again during the Second World War with large-scale epidemics. As the taxonomic understanding improved over the years, the pathogen underwent several name changes: *Rickettsia quintana*, *Rickettsia weigli*, *Rochalimaea quintana* and finally, *Bartonella quintana*.

The 1.6 Mb genome of *Bartonella quintana* has been sequenced. It is closely related (maybe a degenerative form) to *B. henselae*, which can be considered a shortened version of the *Brucella melitensis* genome.

Transmission

The natural reservoir is still uncertain. The **body louse** *Pediculus humanus corporis* is the **predominant vector**. These insects bite an average of 5 times per day. The bacteria multiply in the lice. *Bartonella quintana* survives up to a year in louse faeces. Since *B. quintana* propagates in the intestinal lumen of the body louse, not in the intestinal epithelial cells, infection probably results from contact with contaminated louse feces. **Wounds caused by scratching** facilitates the entry of the **bacteria in louse faeces**. *Bartonella quintana* has also been detected in *Pulex irritans* fleas, cat fleas, cat dental pulp, monkey fleas, and has been isolated from *Pediculus humanis capitis*, the human head louse. The significance of this latter finding is still unclear, but recent genomic studies link head lice infestation to *B. quintana* bacteremia in low-resource settings (e.g.; rural Senegal). Recent studies identify *B. quintana* in various macaque species, but more studies of possible

reservoir hosts are needed.



Pediculus humanus, human louse. Copyright ITM

Clinical aspects

The clinical spectrum of trench fever was described in 1919 via experimental infections in volunteer soldiers. In 1949, an accidental epidemic among 104 laboratory workers resulted in 90 symptomatic cases, which were described in detail. The incubation period varies from **15 to 25 days** (sometimes extremes of 3-38 days are mentioned). Infection can lead to several distinct clinical forms:

The patient **may have no or very few symptoms while having *B. quintana* bacteremia (bloodstream infection)**. They may be afebrile. People can be asymptomatic carriers and act as a reservoir. *B. quintana* bacteremia is chronic may last many months or years (the

most extended duration recorded is 8 years, though more recent studies describe a period of up to one year). In 1995 *B. quintana* was found in the blood in 14% of people without homes in Marseilles, who presented without symptoms or with general, vague unspecific symptoms.

Chronic endocarditis can occur. The main characteristics are fever, splenomegaly and heart murmurs. The symptoms can be divided into (a) symptoms of infection such as fever, weight loss, malaise, nocturnal sweating, clubbing, enlargement of the spleen, anemia and mycotic aneurysms, (b) heart murmurs and heart failure, (c) embolic phenomena such as CVA or a peripheral arterial embolism, (d) vasculitis such as microscopic haematuria with or without renal failure, splinter hemorrhages under the nails, Osler's nodules (painful lesions on the fingers), Roth's spots on the retina. As the bacterium is not identified by routine 5-day bacterial culture, *B. quintana* endocarditis is referred to as a common type of **culture-negative infective endocarditis**.

Classical trench fever. The patient develops a fever which persists for 5 days. This is accompanied by severe headache and muscle pain, particularly in the legs ("shin pain"). Retro-ocular pain, red conjunctivae, spleen enlargement, and leukocytosis can occur. After a fever-free interval, the fever can return. These cycles can recur 3-5, even up to 8 times. The term "quintan fever" derives from the recurring five-day attacks. Mortality is very low. The pathogen may be present in the human body long after the symptoms have disappeared. Classical trench fever is rarely described in contemporary times.

Continuous fever can develop for several weeks (typhoidal form), accompanied by splenomegaly.

The pathogen can be isolated from cutaneous angioproliferative skin lesions in patients with bacillary angiomatosis (*Bartonella henselae* can also be cultured from similar lesions). Many of these patients are immune-deficient (HIV). The pathogen is phagocytosed by endothelial cells and survives in a vacuole. Angiogenic factors are secreted by the pathogen or the host's response to infection, leading to the proliferation of endothelial cells, with typical neovascularisation. **Bacillary angiomatosis** is characterized by the emergence of a few to hundreds of skin lesions, from a few mm to several cm in diameter. They are reddish-purple and may be ulcerated, resembling a pyogenic granuloma or Kaposi's sarcoma. The lesions bleed heavily when injured. They can also affect the lymph nodes, bone, bone marrow, liver

and spleen. The growth of new blood vessel cells resembles the late stages of the skin lesions of verruga peruviana triggered by *Bartonella bacilliformis*. The pathogen can be detected by Warthin-Starry staining.

Diagnosis

The pathogen is not identified by routine bacterial culture (5-day incubation), but can be cultured axenically which takes a long time (up to 45 days) and requires special techniques. It is best to use a combination of cultures on solid medium, liquid medium and cell cultures. Since *Bartonella* is a facultative intracellular bacterium, to release the bacterium from the erythrocyte, lysis techniques such as “freeze-thaw” or the lysis-centrifugation system (Isolator) are recommended for the cultivation of *Bartonella* sp. from blood. Inoculation of material from the Isolator tube and tissue onto freshly made chocolate agar plates facilitates the growth of the organism. For isolation, incubation in a humid atmosphere with 5% to 10% CO₂ for several weeks is required. Serologically, antibodies display a great deal of cross-reactivity. Indirect immunofluorescent antibody (IFA) testing is the reference serologic method. IgG of > 1/50 indicates *Bartonella* infection. Endocarditis patients usually have titers of > 1/800. It is sometimes possible to reveal the bacteria in biopsy material using a Warthin-Starry stain (a complex silver stain) or immunohistochemistry. At present, PCR has a central role.

Treatment

Not much is known about the treatment of this pathogen. To treat classical trench fever and bacillary angiomatosis, administration of doxycycline or azithromycin is recommended. In treating endocarditis and chronic bacteremia, it is preferable to use doxycycline with either gentamicin or rifampicin, as well as considering surgery in cases of endocarditis. Bacillary angiomatosis takes 4-12 weeks to treat.

Not much is known about this pathogen. In vitro it is susceptible to beta-lactam antibiotics and it can also be killed in vitro by gentamicin, doxycycline, rifampicin, erythromycin and the new macrolides. To treat classical trench fever, once-daily administration of azithromycin or doxycycline is recommended.

In treating endocarditis, it is preferable to use doxycycline with gentamicin or rifampicin as well as considering surgery. Bacillary angiomatosis takes 4-12 weeks to treat.