

Bartonella quintana

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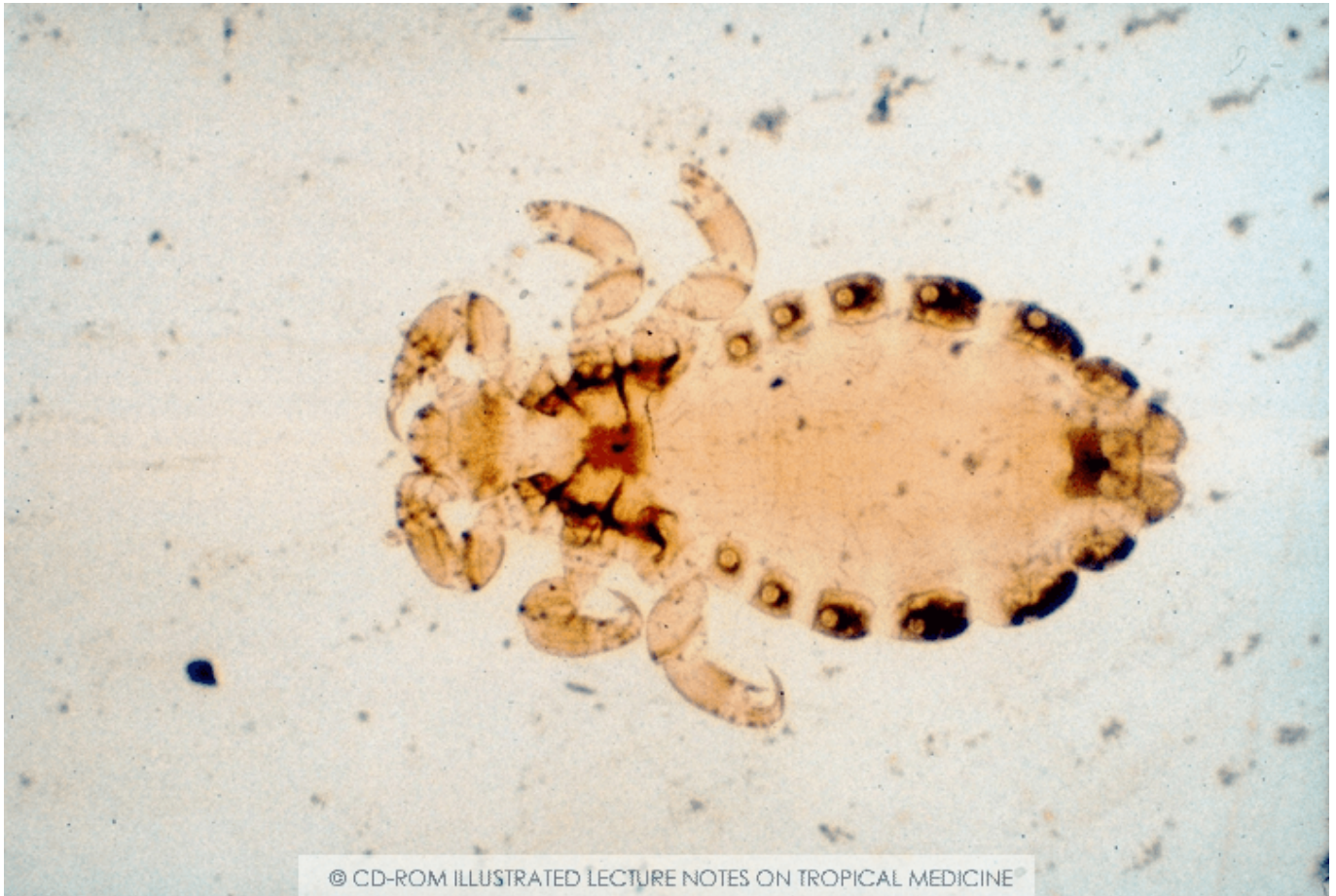
General

Bartonella quintana is a very small Gram-negative rod-shaped bacterium, responsible for a whole range of infections. Infections with this bacterium occur where **people are living in wretched circumstances and are infested with lice**. **Trench fever** was the first clinical manifestation of infection with *Bartonella quintana* to be recognised. 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 at the time of 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) of *B. henselae*, which itself 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 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 faeces. **Wounds caused by scratching** facilitates the entry of the **bacteria contained 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. More study of possible reservoir hosts is clearly needed. It is possible that an important animal reservoir might be identified.



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 was 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**. They may be subfebrile and may have symptoms of pharyngitis. People can be asymptomatic carriers and act as a reservoir. In 1995 *B. quintana* was found in 14% of the homeless in Marseilles, who presented without symptoms or with general vague aspecific symptoms.

Chronic endocarditis can occur. The main characteristics are fever, haematuria, 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, anaemia 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 haemorrhages under the nails, Osler's nodules (painful lesions on the fingers), Roth's spots on the retina.

Classical trench fever. The patient develops 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, enlargement of the spleen 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.

Continuous fever can develop for several weeks (typhoidal form), accompanied by splenomegaly and a fleeting rash (roseola).

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 either by the pathogen itself or by the host's response to infection. This leads to proliferation of endothelial cells, with typical neovascularisation. **Bacillary angiomatosis** is characterised by the emergence of a few to hundreds of skin lesions, from a few mm to several cm in diameter. They are reddish purple may be ulcerated and then resemble 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. **Peliosis hepatitis** is a condition in which numerous, blood-filled cystic spaces appear in the liver.

Diagnosis

The pathogen can be cultured axenically (in absence of all other bacterial contamination) but this takes a long time (up to 45 days). It is best to use a combination of cultures on solid medium, liquid medium and cell cultures. Since *Bartonella* is a facultative intracellular bacterium, the lysis-centrifugation system (Isolator) is recommended for the cultivation of *Bartonella* sp. from blood. Inoculation of material from the Isolator tube and from tissue onto freshly made chocolate agar plates

facilitates growth of the organism. Incubation in a humid atmosphere with 5% to 10% CO₂ for several weeks is required for isolation. Serologically, antibodies display a great deal of cross-reactivity. Cross-absorption is indicated before performing any serological tests. Indirect immunofluorescence is the reference method. IgG of > 1/50 indicates *Bartonella* infection. Endocarditis patients usually have titres 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 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.

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