Cat Scratch Disease (Bartonella henselae infection)

Members of the genus Bartonella have been known to infect humans for thousands of years. DNA from Bartonella quintana, the causative agent of Trench fever, has been demonstrated in a 4,000 year-old human tooth. The genus was named after a Peruvian scientist, Alberto Leonardo Barton Thompson.

The organism, Bartonella henselae, the causative agent of Cat Scratch disease (CSD) was first discovered by Henri Parinaud in 1889. This disease is also known by a number of other names such as “cat scratch fever” and “Teeny’s disease”. The organism was first found in a patient suffering from cat scratch disease and identified as such by Debre et al. in the 1950s.

The Microorganism

B. henselae, previously known as Rochalimaea henselae until it was reclassified in 1993, is an aerobic, oxidase-negative, slow-growing gram-negative rod that is slightly curved. It does not possess flagella but there is some evidence of a twitching motility. The organism is very fastidious and requires heme to grow in vitro. It is also very susceptible to pH and requires an explicit pH range (6.8 to 7.3) to grow.

Members of the species are intracellular parasites that show a preference in humans for erythrocytes and endothelial cells. It can be grown in the laboratory on blood agar or chocolate agar plates supplemented with carbon dioxide (i.e., it is microaerophilic). Since the colonies usually take up to six weeks to form, laboratory culture isn’t a procedure to be used in diagnosing the disease. This very slow growth is one of the reasons it took so long to connect the organism with the actual disease.
In addition to \textit{B. henselae}, there are a number of other species of \textit{Bartonella} that are associated with human disease. These include:

- \textit{Bartonella quintana} – the causative agent of Trench fever. This disease is transmitted by body lice and is usually associated with crowded conditions and poor personal hygiene. The disease is worldwide in distribution.

- \textit{Bartonella bacilliformis} - causative agent of Carrión’s disease (also known as Oroya fever and Verruga peruana). The disease is common in South America (especially Peru, Ecuador and Colombia) and is carried by sand flies.

Additionally, there are seven other species of \textit{Bartonella} known to be capable of causing disease in both animals and humans. Several of these are associated with disease in cats and one with dogs.

### Epidemiology and Transmission

The incubation period for the disease is usually 7 to 14 days but in some individuals, it may take as long as two months before the symptoms appear. There is no gender or age difference in transmission.

Transmission of the disease is almost always related to a cat scratch. It can, however, also be transmitted by cat bites. Even though the organism has been demonstrated in fleas, they have never been shown to be a means of transmission as is the case with other species of \textit{Bartonella}.

About 40\% of cats will carry \textit{B. henselae} at some point in their lifetime. However, infected animals show no signs of any illness. Hence, it is impossible to tell which cats are infected. Kittens are more likely to carry the organism than older cats.

### The Disease

The symptoms associated with cat scratch disease are of some help in pointing the physician in the right direction especially when a cat scratch or bite has already been involved.

The symptoms of cat scratch disease can be divided into two categories:

- Classic
- Atypical

#### Classical Disease

This form usually presents as tender and swollen regional lymph nodes one to three weeks after exposure. This is known as regional lymphadenopathy. At the site of the initial inoculation, there may be a papule or pustule.
Enlarged lymph node associated with cat scratch disease
Courtesy of The Veterinary College University of Georgia

Papule or pustules at the site of the scratch
Courtesy of CDC

Many patients will have fever, chills, headache, backache and abdominal pain. If these symptoms are going to develop, it will usually be one to two weeks after infection. However, it may take as long as two months. The swollen lymph glands may persist for several months after the other symptoms disappear.

Most cases of cat scratch disease in healthy persons are self-limited and will resolve without any antimicrobial treatment.

Atypical Disease
Atypical disease may take several different forms depending on the organ system that becomes involved.

Bacillary Angiomatosis - a vascular skin lesion that may extend to the bone or be present in other areas of the body. Usually, these patients have HIV infection or some other cause of immunosuppression.

Parinaud's Syndrome – this involves granulomatous conjunctivitis in the eye near the swollen lymph nodes. The upward gaze of the eye is paralyzed while the lower gaze is not. There are a number of other bacterial infections that can also cause this syndrome,

Bacillary Peliosis – usually involves organs in HIV-infected persons,

Acute Encephalopathy – a generalized dysfunction of the brain.

Diagnosis
There are no routine culture procedures that can be employed due to the inordinately long time it takes for this organism to grow in the laboratory.

Quest Diagnostics has two tests that are available to assist in diagnosis:

Bartonella henselae Antibodies (IgG, IgM) with Reflex to Titer
This test is performed using an immunofluorescence assay (IFA). A screen is performed and, if it is positive, a follow-up titer is then carried out.

This test has one significant limitation. There is a cross-reaction between B. henselae and B. quintana as well as members of the genus Chlamydia and Coxiella burnetii. This can lead to false-positive results.

Bartonella DNA, Qualitative Real-Time PCR
This is a highly specific and sensitive procedure for detecting the presence of Bartonella species DNA in clinical specimens. The assay cannot differentiate
between \textit{B. henselae} and \textit{B. quintana}. The diagnosis of \textit{Bartonella} infection should not rely solely on the result of a PCR assay. A negative PCR result indicates only the absence of \textit{Bartonella} species DNA in the sample tested and does not exclude the diagnosis of the disease. Patients with a positive PCR result should be evaluated with other tests to further establish the diagnosis of the disease. A positive result should be considered in conjunction with clinical presentation and additional established clinical tests.

**Treatment**

Most infections in healthy persons will resolve \textit{without} benefit of any antimicrobial treatment. In fact, treatment is \textit{not} recommended for immunocompetent persons with mild to moderate infections due to the side-effects of the antibiotics.

In the case of patients with disseminated disease or in individuals who are immunocompromised, antimicrobial therapy is usually recommended. The recommended antibiotic is azithromycin at the following concentrations:

- For adults and children >45.5 kg: 500 mg on Day One, followed by 250 mg for four days,
- For children < 45.5 kg: 10 mg per kg on Day One, followed by 5 mg per kg for four days

With infections caused by species other than \textit{B. henselae}, a number of other antibiotics have been used. In these cases, the aminoglycosides are usually the first drug of choice since they are bactericidal.

**Infection Control Practices**

The best way to prevent the transmission of this disease to humans is to follow the steps that CDC has outlined on their website:

- \textbf{Avoid} “rough play” with cats especially kittens. This includes any activities that lead to cat scratches and/or bites,
- If you do get scratched or bitten, wash the area immediately and thoroughly with soap and water,
- \textbf{Do not} allow cats to lick any open wound. Keep in mind the fact that the cat may have the organism in their saliva,
- Control fleas (even if they don’t appear to be involved),
- If you develop an infection (with pus and pronounced swelling) at the area where you were scratched or bitten by a cat or develop symptoms including fever, headache, swollen lymph nodes and/or fatigue, contact your physician immediately.

**Recommended References**

Centers for Disease Control and Prevention. 2012. \textit{Bartonella} infection. Click \textit{here} to access the entire website.

Centers for Disease Control and Prevention. 2011. Cat scratch disease (\textit{Bartonella henselae} infection). Click \textit{here} to access website.


**Free CME/CEU credits**

\textbf{FDA approvals: First cell culture influenza vaccine.} Click \textit{here} to access offering.

\textbf{New treatments, new challenges: managing side effects of treatment of chronic HCV.} Click \textit{here} to access offering.

\textbf{Determining causes of recurrent Lyme disease.} Click \textit{here} to access offering.

\textbf{HCV therapy response tied to survival.} Click \textit{here} to access offering.

**We’d Like to Hear from You**

The vast majority of feature articles that appear in our \textit{Infectious Disease Update} come about because somebody asked for them.

Often at meetings or during informal conversations, somebody will say: “Why don’t you write something about this particular subject?” Invariably, if it’s important enough for one person to be interested in it, then there’s an excellent chance that additional readers would like to hear about that subject.

Additionally, you might come across an article in a journal that you feel should be brought to the attention of other professionals. Just let us know the name of the journal, the volume, the month, and the page and we’ll try to include it in a forthcoming issue.

To contact the Editor, just click \textit{here}. 

Quest Diagnostics \textit{Infectious Disease Update} March 2013
Other Infectious Disease News

Influenza Immunizations in Connecticut Long-Term Care Facilities: 2012-2013

Every year for over a decade, the Senior Editor of Infectious Disease Update has been conducting a survey of influenza immunizations among healthcare workers in Connecticut long-term care facilities. The survey is anonymous so participants do not have to identify themselves.

This year (as of February 7, 2013), 52 facilities participated in the survey. They represented a total of 5,249 beds and 8,262 employees of which 78% were immunized.

What makes this survey different from all the previous years is that we now have a new category – those facilities that mandated the vaccine be given to all employees with the exception of those who had a bonafide medical or religious reason for not receiving it. Below is a summary of the results.

<table>
<thead>
<tr>
<th>Number of Facilities</th>
<th>Category</th>
<th>Average Immunization Rate</th>
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<tr>
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<td>2</td>
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<td>34</td>
<td>Signed declination</td>
<td>64.8</td>
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<tr>
<td></td>
<td>Required</td>
<td>Range: 38.4 – 93.1</td>
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<tr>
<td>16</td>
<td>No declination</td>
<td>44.9</td>
</tr>
<tr>
<td></td>
<td>Required</td>
<td>Range: 28.8 – 65.1</td>
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With only two facilities mandating the vaccine this year, it is not possible to make any earth-shaking comments concerning the effect of this practice but one can assume that it would have a profound effect on vaccine rates among healthcare workers. CDC and many states are working towards implementing such a mandate in the future.

The rate in those facilities where a signed declination was required averaged about 20% higher than in those facilities that did not require a signed declination. Every year, more and more facilities are requiring this practice. Hopefully, in the years to come, more healthcare facilities will be mandating the influenza vaccine as a condition of employment and/or governmental agencies will be stepping in and requiring it.

FDA Approves Recombinant Vaccine for Influenza

The U.S. Food and Drug Administration (FDA) has announced that it has approved a recombinant influenza vaccine known as FLublok® (Protein Sciences).

The preparation of this vaccine does not require eggs. In fact, it doesn’t even require the virus. The vaccine contains three recombinant HA proteins (hemagglutinins) – two for influenza A and one for Influenza B. The conventional vaccine that was used in the 2012-2013 protects against the same three HA proteins.

According to FDA, this new technology will offer the potential for faster start-up of the vaccine manufacturing process in the case of a pandemic. This is because the process is not dependent on an egg supply or on the availability of the virus itself.

The new vaccine is 44.6% effective against all circulating influenza strains – not just those that the vaccine was originally designed to cover.


New Strain of Norovirus Spreading Worldwide

A Norovirus variant, known as “Sydney 2012”, has been identified in France, New Zealand, Japan, and Australia and is rapidly becoming the predominant strain in Great Britain according to health officials there.

Fortunately, the symptoms associated with this new strain are just about the same as those associated with other strains i.e., there is no increase in virulence.

BBC News: “Why has Norovirus been so bad this winter?” January 12, 2013. Click here to go to BBC website.

Is Celiac Disease related to Infant Infections?

According to a recent study from Sweden, the answer to this question is yes. The study found that when children had repeated infectious episodes early in life (and it doesn’t make any difference what kind of infection), there was a significant increase in the risk for later celiac disease. The occurrence of at least three infections (regardless of the site) appears to be associated with increases in celiac disease later in life.

Thimerosal should stay in Vaccines
For the last 15 years, there have been numerous studies on the dangers or lack thereof of Thimerosal in vaccines. The bottom line in all these studies is that basically Thimerosal, which contains small amounts of mercury, does not represent the hazard that its cousin, methyl mercury, does. In 1999, The American Academy of Pediatrics (AAP) came out with a statement to the effect that Thimerosal should be removed from vaccines. This statement, however, was eliminated in 2002. By 2012, AAP, along with the U.S. Public Health Services, feel that its use should be continued.


More Disinfection means Less Infections
Researchers at the Veterans Administration Hospital in Cleveland, OH, conducted a study on “high touch” surfaces and the effect of frequency of disinfections on incidence of infections. They found that intensive, daily disinfection of high-touch surfaces plays an important role in the frequency of pathogens on these surfaces. Additionally, the incidence of certain pathogens decreased from 39 to 11 % for MRSA and 30 to 6.4 % for Clostridium difficile.

Kundrapu, S. et al. 2012. Daily disinfection of high-touch surfaces in isolation rooms to reduce contamination of healthcare workers’ hands. Infection Control and Hospital Epidemiology 33: 1039-1042. Click here to access abstract.

FDA approves Drug for The Treatment of Inhalational Anthrax
On 14 December 2012, The Food and Drug Administration (FDA) announced that it had approved the use of the monoclonal antibody Raxibacumab (Glaxo-SmithKline) for the treatment of inhalational or pulmonary anthrax. This disease is also known as “Cushing’s disease”. The drug has also been approved to prevent inhalational anthrax when other treatments are not available.

During the 2001 anthrax attacks that involved dissemination via the U.S. Mail, five of the 11 persons infected died despite antimicrobial therapy.

Raxibacumab is the first drug that has been approved to treat inhalational anthrax. It acts by neutralizing the toxins produced by B. anthracis. Because naturally occurring anthrax is rare and experimenting with humans would be unethical, the studies leading up to the development and release of this drug were carried out using animal models, namely rabbits.

Another advantage in the use of Raxibacumab is that it can be used to treat multidrug-resistant anthrax.

Food and Drug Administration. Press Release” FDA approves Raxibacumab to treat inhalational anthrax. 14 December 2012. Click here to access press release.

Guidelines issued on The Treatment of Prosthetic Joint Infections (PJIs)
It has long been the practice to administer routine antibiotics for persons undergoing dental procedures who have previously had joint replacements.

New guidelines from the American Academy of Orthopedic Surgeons and the American Dental Association suggest that this practice is no longer necessary. The new joint guidelines from these associations include only three recommendations:

- Practitioners should consider changing their customary practice of prescribing antibiotics prophylactically to patients undergoing dental procedures,
- There is no evidence that the use of topical antibiotics by the dentist will prevent PJIs,
- Good dental hygiene should be maintained. This in fact was the only consensus recommendation from the organizations.


Probiotics cut Clostridium difficile Infections by Two-Thirds
In a recent report published in the New England Journal of Medicine by investigators from the Hospital for Sick Children Research Institute, Toronto, Canada, it was pointed out that there may be up to a 66 % reduction in the number of cases of Clostridium difficile-associated diarrhea (CDAD) when probiotics are employed in treatment.

This report was the result of a meta-analysis of 20 trials covering 3,800 participants. Prophylaxis with probiotics appears to prevent 33 cases of CDAD per 1,000 patients. Among those patients treated with

Quest Diagnostics Infectious Disease Update March 2013
probiotics, there were 9.3% adverse events as compared to 12.6% in control patients.

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**Artificial Stool Product helps treat Clostridium difficile infections**

We don’t think that there’s any debate that *C. difficile* infections are the direct result of disruption of normal intestinal flora by a broad spectrum antibiotic.

Why not, therefore, come up with an artificial stool substitute that could be given to the patient and would in the process “restore” the normal stool flora.

Researchers at Kingston General Hospital, Queen’s University, Ontario, Canada have done just that and have come up with a synthetic stool substitute which they are calling "RePOOPulate". No kidding. This name was used right in the publication.

The investigators started with a healthy 41-year old female and isolated 33 different intestinal microorganisms in pure culture from her stool specimens. The 33 isolates that were selected represented commensal species that were (1) usually susceptible to a broad range of antibiotics and (2) were relatively easy to culture.

The mixture was given to only two patients with *C. difficile* infection but that's a start. Both were patients in their 70s and both were infected with a hypervirulent strain of *C. difficile*, ribotype O78. In addition, both of these patients had previously failed at least three courses of antimicrobial therapy.

Within two to three days, both patients treated with “RePOOPulate” had returned to normal bowel patterns and remained symptom-free for six months or more.

Petrof, E.O. et al. 2013. Stool substitute transplant therapy for the eradication of *Clostridium difficile*: “rePOOPulating” the gut. *Microbiome* (this was the inaugural issue of Microbiome, an open access journal. 1: 3 . Click [here](#) to access full article.

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**Ask The Experts**

**Ralstonia pickettii**

**Question:** We recently got a report back from the laboratory that indicated that *Ralstonia pickettii* had been isolated from a sputum specimen we submitted from a patient with very serious respiratory disease. We have never heard of this organism before.

**Answer:** First of all, *Ralstonia pickettii* has been known for many years under the guise of a number of other names. Here are some of the names that can be found in the literature over the years:

- *Pseudomonas pickettii*
- *Burkholderia pickettii*
- *Burkholderia solanacearum*
- *Alcaligenes eutrophus*

*R. pickettii* is a gram-negative long-slender rod that is capable of surviving in environments with very little nutrients. It is similar in many ways to members of the genus *Pseudomonas*. It can be found in moist environments such as the bottom of rivers and lakes and in soil. It is also found in biofilms that have formed in plastic water pipes.

No completely healthy person has ever become sick from an infection with *R. pickettii* as far as anybody knows. Serious infections apparently only occur in patients with serious health conditions. Good examples would be cystic fibrosis and Crohn’s disease.

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A good place in the woods near the Editor’s house to find *R. pickettii* growing. This is “wetlands” part of the year.
**Very mucoid colonies associated with R. pickettii**

Courtesy of Faculté de Médecine Cochin-Port-Royal, Paris, France


**Aerococcus urinae**

**Question:** Our laboratory recently reported out *Aerococcus urinae* from a urinary tract infection in an elderly male in renal failure. We have never heard of that microorganism before. Can you tell us anything more about it?

**Answer:** Members of the genus *Aerococcus* are gram-positive cocci that grow in pairs or clusters. They are also alpha-hemolytic. As a consequence, they can be easily mistaken for a *Streptococcus*, *Enterococcus* or *Staphylococcus*. This may be one of the reasons that it’s rarely identified.

Some speculate that it is far more prevalent than we think it is but many of the automated microbiological identification systems fail to identify it correctly.

Most isolates of *A. urinae* come from elderly males with predisposing conditions.


**Staphylococcus caprae**

**Question:** We recently isolated two organisms from an infected replacement joint. One of the organisms was *Stenotrophomonas maltophilia*. The other one isolated was *Staphylococcus caprae* which we had never heard of before. The species name suggests that this organism comes from goats. Can you tell us a little bit more about it?

**Answer:** First of all, Kudos to your laboratory for isolating and identifying this microorganism. It is difficult to identify correctly and the chances are that it is really more common than is suggested in the medical literature but gets misidentified. It is a coagulase-negative species of *Staphylococcus* and probably gets misidentified as *Staphylococcus epidermidis* more often than not.

It got its name originally from the fact that it was first isolated from goats. However, it can also be found on human skin as a commensal and has been isolated from the bloodstream, urinary tract and joints.


Erratum:

February 2013 issue, front page, right column

“Most viruses are inactivated by substances such as bleach, alcohol, quaternary ammonium chlorides (“quats”), due to the denaturation of the lipid envelope. In this case, there is no envelope to denature and hence this virus is not inactivated by these substances.”

Please add to the end of this statement the words: “except bleach”.

News Credits

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FROM A GUEST EDITOR'S DESK

The Great Fire of London
Stephen Mortlock, D.Sc.
Quest Diagnostics
London, England

London in the 17th Century was a thriving, growing city, with a population estimated to be about 384,000. The metropolis, was by far the country's largest and richest city, and it contained the principal royal palace, the court and parliament, and the courts of law. Its growth since the mid-sixteenth century, when its population had been roughly 120,000, had brought problems of overcrowding and shoddy housing, with buildings subdivided, gardens and yards obliterated. The only way people had to get rid of rubbish was to throw it out into the streets. This would include normal household waste as well as human waste. And mixed into this was a combination of animal dung, animal entrails from the slaughter houses and, of course, discarded beer (which not surprisingly, was safer to drink than the water!). As a result, London was filthy and a perfect breeding place for the rats carrying the plague that had been ravaging the city for almost a year.

On the night of September 2, 1666, a small fire began in the bakeshop of Thomas Farynor on Pudding Lane, baker to King Charles II. At one o'clock in the morning, a servant woke to find the house aflame, and the baker and his family escaped, but a fear-struck maid perished in the blaze. At this time, most London houses were of wood and pitch construction, dangerously flammable, and it did not take long for the fire to expand. The fire leapt to the hay and feed piles on the yard of the Star Inn at Fish Street Hill, and spread to the Inn. The strong wind that blew that night sent sparks that next ignited the Church of St. Margaret, and then spread to Thames Street, with its riverside warehouses and wharves filled with food for the flames: hemp, oil, tallow, hay, timber, coal and spirits along with other combustibles. The citizen fire-fighting brigades had little success in containing the fire with their buckets of water from the river. By eight o'clock in the morning, the fire had spread halfway across London Bridge. The only thing that stopped the fire from spreading to Southwark, on the other side of the river, was the gap that had been caused by another fire in 1633.

Lord Mayor Bludworth, worried about the cost of rebuilding, was hesitant to destroy the houses in the path of the flames, creating "fire-breaks", and by the time a Royal command was issued and conveyed by Samuel Pepys himself, the fire was too out of control to stop. The houses were demolished by gunpowder but often the rubble was too much to be cleared before the fire was at hand, and only eased the fire's way onward. The fire blazed unchecked for another three days, until it halted near Temple Church. Then, it suddenly sprang to life again, continuing towards Westminster. The Duke of York (later King James II) had the presence of mind to create a fire break, and the fire finally died down. The Great Fire of London was over.
Although the loss of life was minimal (some sources say only sixteen perished), the magnitude of the property loss was staggering. Some 430 acres, as much as 80% of the city proper was destroyed, including 13,000 houses, 89 churches, and 52 Guild Halls. Thousands of citizens found themselves homeless and financially ruined. The Great Fire, and the fire of 1676, which destroyed over 600 houses south of the river, changed the face of London forever. The one positive effect of the fire was that the plague, which had been throughout London, diminished greatly, due to the mass death of the plague-carrying rats in the blaze.

Almost immediately, allegations that the fire was begun deliberately as part of a Roman Catholic conspiracy were exploited by opponents of the court as powerful political propaganda, especially during the Popish Plot and exclusion crisis later in Charles II's reign. A sentence added to the inscription on the Monument in 1681 blaming the fire on "Popish frenzy" was not finally removed until 1831. Charles II appointed six Commissioners to redesign the city. The plan provided for wider streets and buildings of brick, rather than timber. By 1671, 9000 houses and public buildings had been completed. Sir Christopher Wren was commissioned to design and oversee the construction of nearly 50 churches, not least of them a new St. Paul's Cathedral, construction of which began in 1675. The physical consequences were more attractive, at least to the Georgians, less so to the Victorians. The streets, buildings, and distinctive skyline produced by the rebuilding were recorded by a myriad of famous artists.

Even so some of these new buildings were burnt down and twenty-seven of the churches have been demolished or were destroyed during the Second World War. But a number of the livery halls and several other post-fire buildings still remain. However, it is the surviving churches, and, most spectacularly, Wren's great cathedral, that are the striking legacy of London's great fire. The King also had Wren design a monument to the Great Fire, which still stands today at the site of the bakery which started it all, on a street now named Monument Street.