Cat scratch disease in Australia

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Companion animals such as cats are important for their health benefits. However, one of the risks of bringing cats into the household is cat scratch disease (CSD), with kittens or stray cats posing the highest risk. CSD is a clinical syndrome caused mainly by *Bartonella henselae* and is characterised by regional lymphadenopathy in patients with a history of close cat contact within three months of onset of symptoms. In most cases, CSD is a benign, self-limited infection, with more severe infections occurring only rarely in immunocompetent people. However, in immunocompromised patients, including those post-organ transplantation or with advanced HIV infection, the disease can be more severe and avoiding exposure needs to be considered. Improving flea control is also important, as transmission among cats occurs via the cat flea *Ctenocephalides felis*. To add to the data on *B. henselae* in Australia, I will report on some previously unpublished data on the seroprevalence and percentage of culture positives in WA domestic cats.

Bartonella henselae is considered to be the main causative agent of cat scratch disease (CSD) with previous studies showing 21 of 25 lymph nodes from suspected cased being PCR positive[1] and 88% seropositive[2]. *B. henselae* was first isolated in association with CSD in 1993[3]. We reported the first case of CSD associated with *B. henselae* in Australia in 1995[4]. The patient developed fever, lethargy and anorexia three weeks after removing fleas from his cat. This was followed by axillary lymphadenopathy (Figure 1). *B. henselae* was grown from fleas and blood from his cat and *B. hensellae* DNA was detected in a lymph node aspirate. The patient had an antibody titre to the organism of 1024. Granulomatous inflammation was found on histopathology of the lymph node with no organisms seen on staining and electron microscopy. The lymph node was culture negative. In a subsequent Queensland study which used some improved methods of culture the organism was isolated in 17 of 83 (20.5%) and detected by PCR in 104 of 297 (35.1%) of clinical specimens, most of which were from lymph nodes, but included a small number of skin biopsies[5]. The organisms from the cases in Queensland have been further characterised into genotypes with 76.1% being the Houston genotype 1 (variant Houston-1) and 23% being the Marseille genotype variant CAL-1. The diversity of strains including evidence of horizontal gene transfer among *B. henselae* strains has also been studied[6]. The multi-locus typing method has also been used to identify hyper-virulent and feline-associated clones of the organism in isolates from three continents including Australia[7].

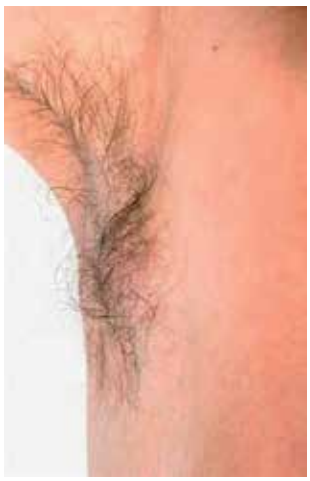

Figure 1. Patient with axillary lymphadenopathy from cat scratch disease.

The organism has also been isolated or detected in a range of other clinical presentations including bacteraemia, endocarditis, osetomyelitis, neuroretinitis, peliosis hepatitis and bacillary angiomatosis[8], although the infections associated with vascular proliferative disease occur in immunocompromised patients. Grando *et al.* have reported isolating *B.* henselae from a case of Parinaud's Ocluoglandular syndrome in Australia[9].

Members of the genus Bartonella are short, pleomorphic, gram-negative rods that are biochemically inert and both oxidase and catalase negative. On agar the colonies are small non-haemolytic, rough, dry and yellow to grey. They grow best on media with rabbit or horse blood at 37°C with 5% CO_2, but also grow in broth and tissue culture. When first isolated on solid media they tend to pit into the agar, but this changes with sub-culture. The primary culture can take two to six weeks, but laboratory adapted organisms show colonies in three to five days. The organism has been found to be inside erythrocytes and added hemin[5] can improve the isolation rates. The organism is not usually seen on

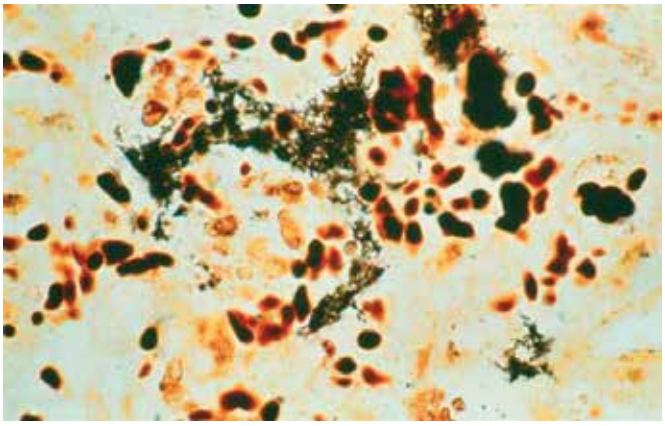

Figure 2. Warthin-Starry stain of *B. henselae* in tissue.

histopathology in lymph nodes from patients with CSD, but can be seen in tissue in some cases, although it is more commonly seen in conditions such as bacillary angiomatosis by Warthin-Starry Silver staining (Figure 2). The diagnosis of CSD can also be made by detecting DNA from the organism[1,4,5] or by serology[2,10].

A collaborative study on the seroprevalence of *B. henselae* in two Australian states was reported in 1997[10]. The survey was a retrospective study of 354 patients from WA and NSW. In that study 54% of patients with a history of cat contact and lymphadenopathy were seropositive. The percentage that were seropositive increased to 62% in those with a cat bite and increased to 90.3% if the patients had granulomatous inflammation in a lymph node with a history of cat contact and lymphadenopathy. In NSW the prevalence of antibodies to *B. henselae* in blood donors was 5%. The serology test used for the study was an indirect immunofluorescent antibody test (Figure 3). Other significant findings included data on the odds ratio of a seropositive result (titre $\geq$64) compared to the control population (titres <64) for cat contact (4.3), cat scratch or bite (4.5), lymphadenopathy (10.6), inoculation papule (5.2), systemic symptoms (2.8) and lymph node biopsy showing granulomatous inflammation (124.4) that were all statistically significant at <0.05, with the cases inclusive of the characteristic biopsy findings having a P<0.0001. Notably, only 20.5% of patients identified systemic symptoms as part of their history. However, as this was a retrospective study, some patients may not have been able to recall some specific symptoms, including fever. Serology testing can lack specificity due to cross-reaction with other organisms including *B. quintana*, *Coxiella Burnetii* and Chlamydia species. However, in the appropriate clinical setting it is still useful.

B. hensellae has been isolated previously from cats in Australia[4,5,11,12], although antibody detection to the organism has not been previously reported. In a WA study (Nora Tan and James Flexman, previously unpublished), serum was collected from 175 cats with 20 (11.4%) being seropositive positive for antibodies to *B. henselae*. Blood cultures were collected from 72 of the cats, with five being culture positive (6.9%). This is much lower than the 35% that were culture positive in a NSW study[5] and 41% in a USA study[13]. However, in the NSW study the organism was isolated more commonly from feral cats 24/59 (40%) compared to 3/18 (16%) of domestic cats. Furthermore, most of the cats were under one year, but all of the cats in the WA study were domestic and over two years of age, which may explain the relatively low percentage of culture positives. Younger cats and stray or impounded cats were also more likely to be culture-positive in the USA study[13]. The finding of 11.4% of WA cats being seropositive for *B. henselae* antibodies was similar to a study in Japan, in which 15.1% of the cats were found to be seropositive[14].

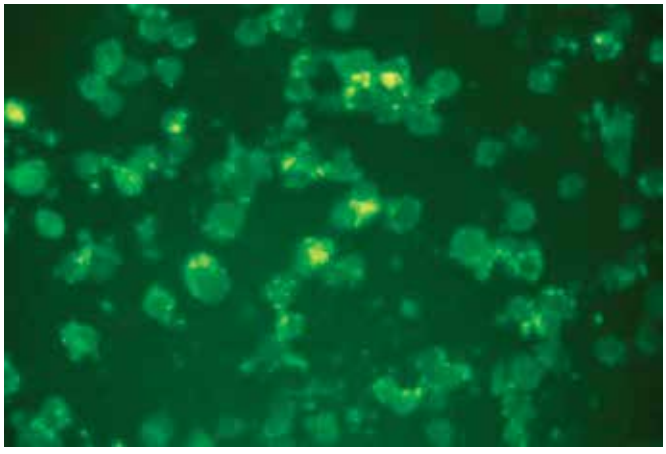

Figure 3. Indirect immunofluorescent antibody test for *B. henselae*.

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Biography

Dr James Patrick Flexman is Head of the Department of Microbiology and Infectious Diseases at Royal Perth Hospital and PathWest Laboratory Medicine WA. He is a Clinical Professor in the Department of Microbiology and Immunology, School of Pathology and Laboratory Medicine at the University of WA. He is also the PathWest Network Director of Pathology for the hospitals in the South Metropolitan Health Service in WA, which includes the new Fiona Stanley Hospital. He has a background in Science and Medicine having completed a science degree and PhD prior to studying medicine and has held two Postdoctoral Fellowships. His research and laboratory interests include hepatitis viruses, viral infections in transplant patients, serology, sexually transmitted infections and molecular microbiology.