**CHAPTER 16**

**Cat Scratch Disease**

**RICHARD C. TILTON**

**Disease:** Cat scratch disease (cat scratch fever).

**Etiologic Agents:** Bacterial (genus/species unidentified).

**Source:** Presumably cats, dogs, and other animals implicated.

**Clinical Manifestations:** Regional lymphadenitis, encephalitis, and Parinaud's syndrome (oculoglandular syndrome).

**Pathology:** Lymphocytic infiltrate with epithelioid granuloma formation; necrosis of the granuloma.

**Laboratory Diagnosis:** Warthin-Starry silver stain of the lymph node to reveal characteristic microorganisms.

**Epidemiology:** Cat scratch disease is seasonal, most cases occurring during the summer; not easily acquired and no person-to-person transmission has been shown.

**Treatment:** None (at present); surgery is not recommended.

**Prevention and Control:** Avoid cats.

---

**Description of Disease**

Cat scratch disease (CSD) was first recognized at the University of Paris by Debre and co-workers (1950). They described CSD in a 10-year-old boy who had many scratches on his arm as well as regional lymphadenitis. These investigators did not isolate the organism or speculate on its etiology. Cat scratch disease is now recognized as a subacute regional lymphadenitis that occurs after inoculation of organisms through the skin. Although complications of CSD have been reported, it usually resolves in 2 to 3 months without treatment.

Several case reports as well as clinical reviews have appeared in the literature over the past half-century (Carithers, 1985; Spaulding and Hennessy, 1960; Warwick, 1967). These reports have established CSD as a distinct clinical syndrome. However, the exact identification of the etiologic agent, now thought to be a bacterium, is elusive.

---

**Etiologic Agent**

Numerous efforts have been made to isolate bacteria, viruses, mycoplasma, chlamydia, and fungi from excised lymph nodes, drainage, and the eyes of patients with Parinaud syndrome (a form of CSD). With the exception of one recent study (Gerber et al., 1985), there has been little success in defining an etiologic agent even when multiple artificial and cell culture systems have been employed. Cultural and microscopic studies have implicated chlamydia, viruses, and acid-fast bacilli in CSD, but none has withstood scrutiny (Hadfield et al., 1985b).

In the past, *Chlamydia* was the leading candidate for the etiology of CSD due to some early descriptions of inclusion bodies in lymph node materials (Boyer and Cherry, 1981) and the similarity of CSD to lymphogranuloma venereum. Some serologic studies have also shown an increase in specific antibodies to certain chlamydial antigens in patients with...
CSD (Spaulding and Hennessy, 1960). However, several lines of investigation have shown that *Chlamydia* is probably not the etiologic agent. Present techniques of chlamydial isolation permit most chlamydiae to be readily cultured in cell lines or visualized with fluorescent antibodies, but they cannot be isolated from suspect specimens. In addition, patients with CSD do not respond to skin testing for lymphogranuloma venereum. Antibiotics used to treat chlamydial infection, such as tetracycline and erythromycin, seem to have no activity against CSD.

Atypical mycobacteria were cultured from the lymph nodes of eight patients who presumably had CSD (Boyd and Craig, 1961). However, other investigations using atypical mycobacterial skin tests showed no difference in skin test reactivity between children with or devoid of a history of CSD.

Because no bacterial agents had been isolated, many early investigators thought that a viral etiology was possible. Turner et al. (1960) isolated a herpeslike organism from chick embryos that were inoculated with pus from lymph nodes of patients with CSD, and Kalter et al. (1969) saw herpeslike particles by electron microscopy from such patients. None of these findings, however, has been confirmed immunologically.

Although some of the newer techniques for viral diagnosis have not been applied to patients with CSD, there seems to be little evidence that viruses are involved. Recently, Wear et al. (1983) described the presence of pleomorphic bacilli in lymph node sections from 29 of 34 patients with CSD. The organisms were within capillary walls in areas of follicular hyperplasia and within microabscesses. At present, the best way to visualize these organisms in lymph nodes is by using the Warthin–Starry silver impregnation stain. These pleomorphic bacteria have been described not only from lymph nodes, but also from primary skin lesions of patients with CSD and conjunctival biopsy specimens of patients with Parinaud oculoglandular syndrome.

Hadfield et al. (1985a) indicated that the causative agent is a small, pleomorphic, gram-negative rod, which can be seen clearly in lymph nodes that have not yet become suppurative. In such specimens, the alleged bacteria are much more difficult to observe. These bacteria are not acid fast and are gram negative when stained with the Brown–Hopp tissue Gram stain. They are approximately 0.2 μm in diameter and 0.5 to 1 μm in length, but appear larger when stained with a silver impregnation stain. Warthin–Starry stained sections of lymph node showing the bacteria can be seen in Fig. 1.

Microscopic details have been confirmed by many laboratories, including our own. Hadfield et al. (1985a) again reported the presence of bacilli in lymph nodes of patients with CSD and showed electron micrographs of the etiologic agent. These lymph nodes showed focal necrosis. The silver-stained slide revealed numerous bacteria, and the tissue Gram stain suggested that the bacteria were small, pleomorphic, and gram negative. The electron micrographs were of poor quality, and the ultrastructure of the host cells and the microorganisms were very difficult to see. According to the authors, the ultrastructure of the cell wall consisted of an outer glycocalyx and a thin peptidoglycanlike layer surrounding the protoplasm.

Margileth et al. (1984) and Hadfield et al. (1985a) have attempted to grow the organism, with little success to date. They have inoculated many artificial media incubated under a wide variety of environmental conditions. Animal inclusions and experiments have also been unsuccessful. These investigators reported injecting mice, guinea pigs, monkeys, and the embryos of chickens, quails, and duck. Various organisms, including rickettsiae and legionellae, have been eliminated by failure to demonstrate serologic reactivity in the host.

Gerber et al. (1985) reported on the isolation of a suspected etiologic agent of CSD. They indicated that a highly pleomorphic gram-positive bacterium was cultured from an excised lymph node of a patient with CSD. The organism was morphologically identical to bacteria observed in Warthin–Starry stains of lymph node sections from many patients with CSD. Extensive biochemical and physiologic analysis of this isolate suggested that it was a member of the genus *Rothia*. This organism resembles a bacterium that was identified as the etiologic agent of Parinaud oculoglandular syndrome more than 70 years ago. In 1913, Verhoeff observed microorganisms in conjunctival scrapings from patients with Parinaud syn-