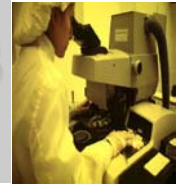


# Center for Diagnostic Sciences BULLETIN



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Issue #2

This bulletin focuses on Cytomegalovirus and its association with periodontal disease. We thank Dr. Hessam Nowzari for his contribution to this issue. As always, we invite your comments, questions, and suggested topics for future bulletins. Please forward your comments to Ms. Latresa Lawson at [llawson@usc.edu](mailto:llawson@usc.edu) or (213) 821-2336.

## **DIAGNOSIS: CYTOMEGALOVIRUS-ASSOCIATED PERIODONTITIS (Gum Disease)**

### **What is Human Cytomegalovirus (HCMV)?**

HCMV is a member of a group of DNA viruses widespread in the general population and characterized by persistent latent infections. HCMV can replicate only in humans or cells of human origin.

This virus encodes a large number of proteins that modulate cellular functions and we are still far from understanding all aspects of this intricate interplay between HCMV and the infected host cell. Infected cells may become enlarged (cytomegalia), showing intra-nuclear inclusions, and co-survival of cell and virus is often established. During acute infection, HCMV, present in most body fluids, infects circulating leukocytes and eventually persists latently in those cells. In addition, latent infection has been demonstrated in the endothelial cells lining the walls of blood vessels. Viral nucleic acid integrates into the host cell's DNA and replicates with the host cell. At any stage the integrated virus can become active, resulting in an acute episode.

### **How is the virus passed around?**

In utero transmission affects up to 2.5% of all live births. HCMV is the most common congenital viral infection in humans. Globally, 50% to 100% of adults are infected by HCMV. The prevalence increases with age from late

childhood onwards; in endemic areas the prevalence can reach 100% in young adults. For more than 25 years, HCMV has been recognized as a potentially serious complication of blood transfusion, but only in certain patient groups. Infection in healthy immuno-competent individuals is usually asymptomatic or resembles a mild glandular fever-like illness that is clinically insignificant unless occurring during pregnancy.

Transmission can occur via oro-pharyngeal secretions (saliva), urine, cervical and vaginal secretions, semen, breast milk (most common mode world wide), tears, blood transfusion, or solid organ transplantation.

Generally, transmission is either community acquired or hospital acquired. Increased risk for community acquisition includes frequent contact with young children (e.g. exposure to children in daycare) and sexual transmission (engaging in intercourse at a young age, many sexual partners, homosexuality, history of other STD's).

### **Is there a therapy?**

At present, therapeutic antiviral compounds against HCMV are limited. Acyclovir, commonly used to treat other herpesviruses, is generally ineffective for HCMV. Gancyclovir, cidofovir and foscarnet inhibit HCMV genome replication, either directly or indirectly, but these drugs may induce the formation of resistant viruses, have low oral bioavailability, and show dose-dependent toxicity. Side effects include leukopenia, thrombocytopenia, rash, CNS abnormalities, GI symptoms, abnormal spermatogenesis, and teratogenesis. Gancyclovir may predispose patients to bacterial and fungal infections. Foscarnet inhibits HCMV DNA polymerase directly. Side effects include renal toxicity.

The course of therapy is usually 14-21 days. Resistance to both agents is becoming increasingly common.

### **How about prophylaxis and vaccine?**

Given the serious clinical complications caused by HCMV in populations at risk, prophylaxis is a major goal. Unfortunately, no vaccine for HCMV is currently available.

### **Is the periodontium a source of HCMV infection?**

Recent analyses of subgingival organisms at the USC Advanced Periodontics clinic implicated HCMV in the pathogenesis of human periodontal disease. HCMV seems to infect mainly periodontal monocytes, macrophages and, less frequently, T lymphocytes. Herpesviruses are found to be more prevalent in HIV seropositive periodontitis patients than in HIV seronegative periodontitis patients. Our more recent studies have also identified HCMV in the pathogenesis of periodontal disease in immuno-compromized individuals affected by Trisomy 21, Fanconi anemia, and kidney-transplanted patients. Viral infection may reduce the periodontal defense and promote growth of putative periodontopathic bacteria such as *Bacteroides forsythus*, *Prevotella intermedia* and *Capnocytophaga* species.

Periodontitis may be an indicator of viral activity, and the periodontium may serve as a reservoir for the virus even when the virus is not detected in serum. In view of the impact of HCMV disease, great resources are dedicated to evaluate different strategies for the management of HCMV infection. Elimination of HCMV-associated periodontitis reduces the risk of HCMV infection. Analysis of HCMV mRNA in saliva and gingival crevicular fluid can be conducted at the USC Advanced Periodontics clinic.

### **How can virus-associated gum disease be treated?**

Patients with a diagnosis of "Cytomegalovirus-Associated Periodontitis" are instructed in oral hygiene. Subgingival debridement is done with ultrasonic scalers and hand instruments under local anesthesia.

Analysis of sub-gingival periodontal pathogens and local or systemic antimicrobial therapy will enhance treatment outcomes. Patients may receive periodontal surgery to eliminate periodontal defects by soft tissue plasty, osteoplasty-ostectomy and tissue adaptation.

Post-treatment periodontal probing depths of less than 4 mm provide access to diseased radicular surfaces for oral hygiene by patients and by the therapist. Weekly post-surgical recall for 4 to 6 weeks, and monthly thereafter, insure optimal conditions for periodontal wound healing. Patients are recalled monthly to optimize plaque control, promote stability of the periodontium, and further analyze HCMV mRNA activity in saliva and gingival crevicular fluid.

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### **Did you know?**

- Axium was implemented in the Center for Diagnostic Sciences (CDS) on 9/29/03.
- 798 screenings were done in CDS between 9/29/03 and 12/12/03.
- 635 new patients were accepted for treatment in Group Practices during that period.
- 116 patients were referred to other programs at USCSD during that period.