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### 3. CLINICAL SIGNS & SYMPTOMS

#### *3.1 Introduction*

When in early studies for HHV-6 prevalence 1,135 randomly chosen persons, between 18-52 years old, were tested for antibody positivity, a clinical history of all was also obtained. 295 persons tested positive for HHV-6 with following clinical symptoms (discriminative HHV-6 IgG titer was 1:40 without further tests for active or latent infection):

- HHV-6+ without any clinical symptoms 84%
- HHV-6+ with upper respiratory tract infection and mononucleosis-like symptoms 14%
- HHV-6+ with abdominal discomfort and mild diarrhea 2%
- HHV-6+ and occasional symptoms: fatigue, depression, persistent oropharyngitis, recurrent lymphadenopathy, thyroid dysfunction, non-specific abdominal complaints.

Since then (1988), clinical histories were obtained from all persons tested for HHV-6 infection at the Immunopathology Laboratory, University of Cologne, Cologne, Germany. The following list is a summary of symptoms listed in persons with evidence for active HHV-6 infection.

General

*Malaise, fatigue, chills, sweats, flu-like symptoms*

Cardiovascular

Palpitations, tachycardia, arrhythmias

Respiratory

Oropharyngitis, coryza, cough, mild bronchitis, sore throat, intermittent wheezing

Gastrointestinal

Sialoadenitis, sicca syndrome, abdominal pain, indigestion, diarrhea

Lymphatic

Tonsillar hypertrophy, peripheral blood lymphocytosis, slight splenomegaly,  
mononucleosis-like disease

Hematopoietic

Anemia, thrombocytopenia

Musculoskeletal

Weakness, arthralgia, myalgia, SLE- or fibromyalgia-like symptoms

Endocrine

Various signs of thyroid dysfunction

Skin

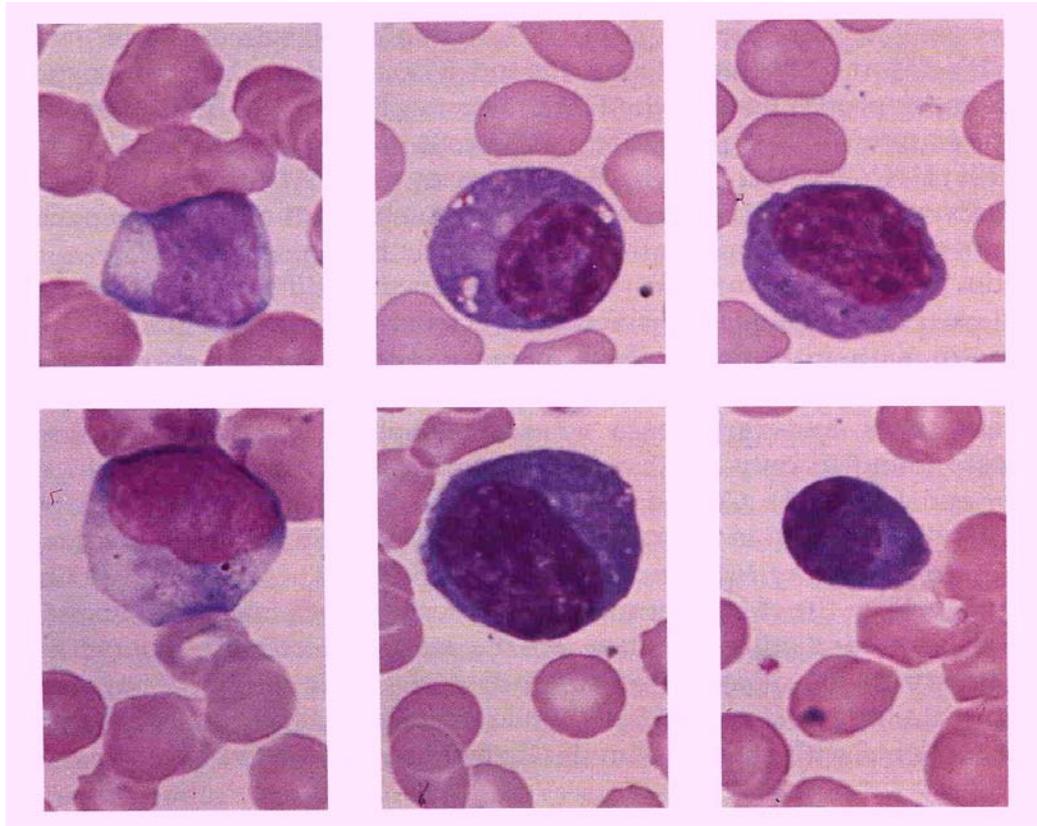
Rash, eyelid & facial edema

Central & peripheral nervous system

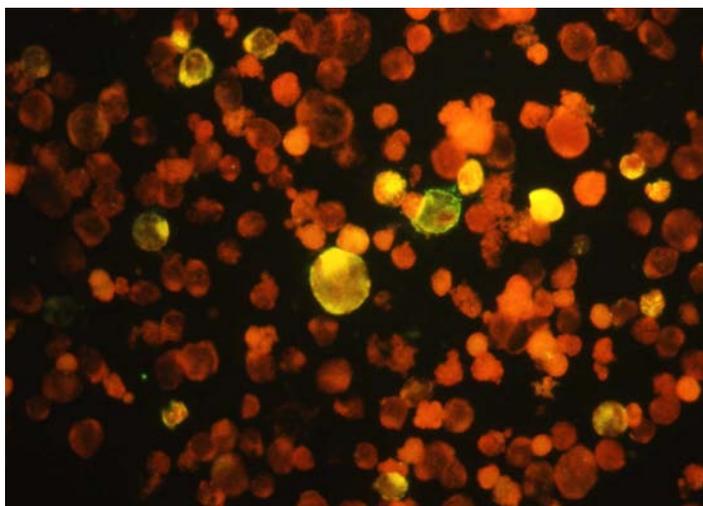
Emotional lability, irritability, lack of concentration, headache, dizziness,  
loss of memory, chronic fatigue syndrome-type symptoms, paresthesias, peripheral neuropathy

(Note: all symptoms may be helpful in the differential diagnosis, but none is specific for HHV-6 infections)

3.2 Figures



Various types of peripheral blood lymphocytes which can be seen in HHV-6 infection



HHV-6 positive (fluorescent) cells in smear from peripheral blood. Tested with known HHV-6 IgG-positive serum and IFA

Other characteristic clinical features such as rash, oropharyngitis, tonsillitis etc. are shown in the paragraphs of respective organ systems.

### 3.3 Further Reading

Krueger GRF, Koch B, Ramon A, Ablashi DV, Salahuddin SZ, Josephs SF, Streicher HZ, Gallo RC, Habermann U. Antibody prevalence to HBLV (human herpesvirus-6, HHV-6) and suggestive pathogenicity in the general population and in patients with immune

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## 4. SYSTEMIC REACTIONS

### 4.1 Introduction

Systemic reactions or better "multi organ reactions" (MOR) can be observed in both primary and non-primary HHV-6 infections. Most frequently, the infection and disease of the prime target organ (e.g. the tonsils, the CNS or a transplanted organ) is accompanied by a skin rash, and liver enzymes may be slightly elevated. There are signs of "dry" oropharyngitis, cough, malaise and fatigue, fever, iridocyclitis, arthritis and some myalgia similar to other viral infections. We have seen such MOR to accompany HHV-6 associated acute febrile illnesses in babies and small children, acute tonsillitis and mononucleosis-like diseases, and in patients with bone marrow or renal transplants. Vincent Descamps has described such MOR to occur in the context of allergies, especially drug allergies, for which he coined the *terminus* DRESS (i.e. Drug Reaction with Eosinophilia and Systemic Symptoms).

Janos Luka (personal communication) could show that EBV (Epstein-Barr virus) and HHV-6 antibody titers suggesting reactivation are more frequently observed during allergy seasons (and in allergic persons). Such reactivated lymphotropic viruses may well then further disturb the normal immune reactivity thus contributing to the illness.

In some persons preferentially with reactivated HHV-6 and persistent viral activity (replication) a clinical syndrome may occur that has been described as postinfectious chronic fatigue syndrome (CFS) or chronic fatigue immune dysfunction syndrome (CFIDS).

There are other systemic diseases such as vasculitis and collagen-vascular diseases which may be accompanied by reactivated HHV-6 infection the implication of which still needs investigation.

### 4.2 Figures

Characteristic features of systemic reactions are also shown in the paragraphs of respective organ systems (e.g. skin, oropharynx, tonsils, liver).