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correlations between IFN- $\alpha$  and the other parameters showed that IFN- $\alpha$  levels correlated positively with high levels of triglycerides ( $P = .004$ ) and with the wasting syndrome ( $P = 0.002$ ), and correlated negatively with an elevated hematocrit ( $P = .04$ ). Moreover, 6 (75%) of the 8 patients with wasting but only 18 (25%) of the 71 patients without wasting had detectable levels of IFN- $\alpha$  ( $P = 0.01$ ). The mean ( $\pm$ SD) levels of IFN- $\alpha$  were  $3.6 \pm 6.8$  pg/mL and  $1.6 \pm 6.4$  pg/mL, respectively, in patients with and without active opportunistic infections at the time of sampling ( $P = \text{NS}$ ).

Grunfeld and colleagues [3] also found high levels of IFN- $\alpha$  in HIV-infected patients and a strong correlation between IFN- $\alpha$  and hypertriglyceridemia in these patients. This is the first report, to our knowledge, of a correlation between IFN- $\alpha$  and the wasting syndrome. Interferon has been shown to induce anorexia [4], and it might play an important role in the wasting syndrome of HIV-infected patients. In our study TNF- $\alpha$  does not appear to be strongly implicated in AIDS-related wasting. Moreover, repeated administration of TNF- $\alpha$  in animals does not induce cachexia [5]. It is interesting that only eight of our patients had a wasting syndrome. Studies of the role of cytokines in the wasting syndrome should be conducted in greater numbers of HIV-infected patients. Patients should be matched to controls according to other factors such as opportunistic infections or CD4 lymphocyte count, and levels of both TNF- $\alpha$  and IFN- $\alpha$  should be measured.

### Active Human Herpesvirus 6 Infection in an Adolescent Male

**SIR**—Active infection with human herpes virus 6 (HHV-6) in immunocompetent adolescents and adults may be more common than is generally believed [1]. We describe a case of active HHV-6 infection in a healthy adolescent.

A 17-year-old male was admitted to Saint Jozef Hospital (Kerkrade, the Netherlands) for a high recurrent fever (spikes to  $39.5^{\circ}\text{C}$ ) and a generalized erythematous skin rash. Physical examination revealed bilateral conjunctivitis, tonsillar pharyngitis, and cervical lymphadenitis. Jaundice and mild hepatomegaly were also noted. The hemoglobin level was 14.1 g/dL. The following hematologic alterations that were associated with toxicity and that were consistent with the presence of an infectious disease were noted. The erythrocyte sedimentation rate was elevated (38 mm/h). The WBC count was  $15,600/\text{mm}^3$  (8% band forms; 76% neutrophils, with Döhle's bodies and toxic granulation [both found in  $\sim 30\%$  of neutrophils]; and 3% lymphocytes). The platelet count was  $130,000/\text{mm}^3$ . Hepatic dysfunction was evidenced by the significant increase in the levels of bilirubin and liver enzymes. Other clinical findings were nor-

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### References

1. Landman D, Sarai A, Sathe SS. Use of pentoxifylline therapy for patients with AIDS-related wasting: pilot study. *Clin Infect Dis* 1994;18:97-9.
2. Lebon P, Daffos F, Checoury A, Grangeot-Keros L, Forestier F, Toublanc JE. Presence of an acid-labile alpha-interferon in sera from fetuses and children with congenital rubella. *J Clin Microbiol* 1985;21:775-8.
3. Grunfeld C, Kotler DP, Shigenaga JK, et al. Circulating interferon- $\alpha$  levels and hypertriglyceridemia in the acquired immunodeficiency syndrome. *Am J Med* 1991;90:154-62.
4. Dixon RM, Borden EC, Keim NL, et al. Decreases in serum high-density-lipoprotein cholesterol and total cholesterol resulting from naturally produced and recombinant DNA-derived leukocyte interferons. *Metabolism* 1984;33:400-4.
5. Patton JS, Peters PM, McCabe J, et al. Development of partial tolerance to the gastrointestinal effects of high doses of recombinant tumor necrosis factor-alpha in rodents. *J Clin Invest* 1987;80:1587-96.

mal, and the results of hematologic and biochemical tests were within normal range.

The patient's rash subsided during the week after admission, but with gradual desquamation, especially on the palms of his hands and the bottoms of his feet. The patient recovered uneventfully. Because of the patient's symptoms, the differential diagnosis included a variety of infectious diseases. The patient did not have a history of travel outside of his hometown and the surrounding regions. Histologic examination of a biopsy specimen of a cervical gland revealed a nonspecific inflammatory process. Histochemical staining of the biopsy specimen was not performed. Appropriate microbiological cultures and paired serological tests were performed for detection of the following agents or diseases: *Streptococcus pyogenes*; Q fever; *Brucella* species; *Leptospira* species; *Mycoplasma pneumoniae*; *Chlamydia* species; *Toxoplasma gondii*; adenovirus; measles virus; parainfluenzae virus; parvovirus B19; rubella virus; hepatitis A, B, or C virus; and HIV. The results of these cultures and serological tests were uninformative or negative. ELISAs for cytomegalovirus (CMV) and Epstein-Barr virus were negative for IgM, but CMV IgA was detected on day 58 of hospitalization. Serum specimens were tested by indirect immunofluorescence [1], which showed a significant rise in the titer of HHV-6 IgG (the titer was 1:20 on day 9 of hospitalization and 1:640 on day 18). HHV-6 IgM was detected on day 18 of hospitalization (titer, 1:160) and day 58 (titer, 1:10), but it was not detected at a later date (table 1). Six months after the patient initially presented, an ELISA for detection of HIV antibodies was negative.

Despite the absence of lymphocytosis, our patient's clinical picture resembled a recently published description of an acute

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**Table 1.** Antibody titers for an immunocompetent adolescent with active HHV-6 infection.

Viral antibody	Titer of antibody by day of illness				
	9	18	58	150	170
HHV-6 IgG	1:20	1:640	1:1,280	1:1,280	1:640
HHV-6 IgM	<1:10	1:160	10	<1:10	<1:10
CMV IgG (AU)	>43	>70	>1,500	>1,500	>1,500
CMV IgM	...	...	...	...	...
CMV IgA	...	...	+	...	...
EBV-VCA IgG/IgM	<1:8	<1:8	<1:8	<1:8	<1:8

NOTE. AU = arbitrary laboratory units; EBV-VCA = Epstein-Barr virus viral capsid antigen; ... = negative.

HHV-6 infection [2]. Simultaneous rises in the titer of antibody to HHV-6 and CMV have been attributed to cross-reactivity [3]. The delay in the rise of the titer of CMV antibody (compared with the rise in the titer of HHV-6 antibody) suggests a concomitant reactivation of CMV. The absence of IgM and the presence of IgA are also consistent with reactivation of CMV [4].

Niederman et al. [1] described a mild spectrum of symptoms caused by HHV-6 infection in three adults who did not have fever but who had an HHV-6 IgM response, as was the case for our patient. However, it may be difficult to differentiate between a primary HHV-6 infection and a reactivation of HHV-6 infection [5]. Almost 100% of individuals are seropositive for HHV-6 by the time they are 4 years old [2]. The percentage of individuals who are seropositive for HHV-6 declines with age, presumably due to a loss of antibody that results in a level of antibody that cannot be detected.

Our patient's illness may have been caused by a primary HHV-6 infection, by an exogenous reinfection by another variant of HHV-6, or by endogenous reactivation (we were not able to determine the cause of our patient's illness after examining these three possibilities) [5]. The likelihood of HHV-6 infection must be considered when searching for the origin of an acute exanthemous febrile disease in adolescents.

### Teicoplanin Selects for *Staphylococcus aureus* That Is Resistant to Vancomycin

SIR—We are currently experiencing an ongoing epidemic of infection with multiply-resistant, methicillin-resistant strains of staphylococci in the United States and other countries [1–4]. The cyclic glycopeptides, including vancomycin and teicoplanin, are thought to be the preferred therapeutic agents for serious infections caused by methicillin-resistant strains [5] or

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### References

1. Niederman JC, Liu CR, Kaplan MH, Brown NA. Clinical and serological features of human herpesvirus-6 infection in three adults. *Lancet* 1988;2:817–9.
2. Akashi K, Eizuru Y, Sumiyoshi Y, et al. Brief report: severe infectious mononucleosis-like syndrome and primary human herpesvirus 6 infection in an adult. *N Engl J Med* 1993;329:168–71.
3. Adler SP, McVoy M, Chou S, Hempfling S, Yamanishi K, Britt W. Antibodies induced by a primary cytomegalovirus infection react with human herpesvirus 6 proteins. *J Infect Dis* 1993;168:1119–26.
4. Van Loon AM, Van der Logt JTM, Heesen FWA, Van der Veen J. Quantitation of immunoglobulin E antibody to cytomegalovirus by antibody capture enzyme-linked immunosorbent assay. *J Clin Microbiol* 1985;21:558–61.
5. Morris DJ. Primary human herpesvirus 6 infection in an adult [letter]. *N Engl J Med* 1993;329:1817–8.

for serious staphylococcal infections occurring in patients allergic to  $\beta$ -lactam antibiotics. Teicoplanin, which is currently undergoing clinical trials, is a member of the cyclic glycopeptide class and has already been marketed in Europe and may be marketed in the United States. Resistance to teicoplanin and vancomycin has already been reported for clinical isolates of coagulase-negative species of staphylococci such as *Staphylococcus hemolyticus* [6].

It is also known that teicoplanin therapy for serious infection caused by *Staphylococcus aureus* can result in emergence of strains resistant to teicoplanin; however, these strains remain susceptible to vancomycin [7]. We have carried out a preliminary characterization of a susceptible strain of *S. aureus* and the teicoplanin-resistant derivative that emerged during teicoplanin therapy for endocarditis [8]. We showed that the resistant strain expresses a new membrane protein of ~35 kD in molecular weight, that it shows increased expression of the two polypeptides of penicillin-binding protein (PBP2), and that it is more susceptible to lysis by lysostaphin, an endopeptidase that

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