Acute ulcerative esophagitis presumed to be caused by herpes simplex virus was first described in 1943 by Pearce and Dagragn, who used cytologic techniques to make the diagnosis. Heretofore, all cases of herpetic esophagitis have been reported in severely debilitated or immunocompromised hosts and have generally lacked tissue culture support. Most often the diagnosis is made on necropsy. The following case is one of culturally and serologically proved herpes simplex virus infection occurring in an immunocompetent host and temporally associated with development of ulcerative esophagitis.

**Case Report**

The patient, a 29-year-old, previously healthy male physician, presented with severe odynophagia. Liquid antacids had given no relief, and the patient had begun to notice severe retrosternal and substernal pain, even on dry swallows. He denied nausea, vomiting, heartburn, or ingestion of very hot or corrosive substances. There was no history to suggest trauma to the esophagus such as that caused by irradiation, chemotherapy, or nasogastric intubation. He had had an upper respiratory tract infection with sore throat, fever, and myalgias of 3-days duration, beginning before the onset of odynophagia. He specifically denied ever having had "fever blisters;" however, his newlywed wife had had a recurrence of herpes labialis approximately 3 weeks before his illness.

Physical examination revealed a healthy-appearing white male whose vital signs were normal. Examination of the lips, mouth, and pharynx revealed no lesions. The neck was supple and was without adenopathy. Examination of the lungs, heart, abdomen, genitalia, and skin was normal. Stool tested negatively for occult blood.

Laboratory data included normal electrolytes, urinalysis, white blood count was 7500 with 60% polymorphonuclear leukocytes and 5% band forms. Hematocrit was 48%. Chest X-ray was unremarkable. Roentgenological examination of the upper gastrointestinal tract, including barium esophagram, was normal.

The patient underwent esophagogastroduodenoscopy on the 2nd day of his illness. Extending 20 cm from the incisors to the esophagogastric junction were diffuse, superficial esophageal ulcers, measuring from 2 mm to 1.5 cm in diameter, with coalescence of many of the ulcers distally. The area of the esophagogastric junction was diffusely hemorrhagic before advancement of the endoscope through this region. The stomach, pylorus, and duodenum were normal.

Biopsies of the margins and centers of the esophageal ulcers on subsequent histological examination revealed acute inflammatory changes. Tissue sections were negative for intranuclear inclusions and pseudopodophae. Brushings of the esophageal ulcers were submitted in trypticase soy broth for viral culture. Herpes simplex (Herpesvirus hominis), type 1 (HSV-1), was isolated on human embryonic kidney, African green monkey kidney, and baboon kidney tissue. Complement fixation titers for HSV-1 rose from 0 on the 2nd day of his illness to 1:128 on the 17th day.

The patient's immune defense status was investigated on the 5th day of his illness. Quantitation of IgG was 1203 mg per 100 ml, IgA was 250 mg per 100 ml, and IgM was 244 mg per 100 ml. T and B cell lymphocyte quantitation revealed 56% E rosettes (T lymphocytes) and 45% erythrocyte antibody-complement rosettes (B lymphocytes). Mitogen stimulation to pokeweed, phytohemagglutinin, concanavalin A, and streptokinase-streptodornase was normal.

Symptomatic treatment with antacids, viscous lidocaine, and diazepam resulted in marked resolution of odynophagia over a 3-day period. Hematocrit fell from 48% on the 1st day of illness to 34% on the 10th day without evidence of hypovolemia or hemolysis. Stools tested positively for occult blood from the 3rd to the 12th hospital days. The patient was not transfused but was given iron sulfate therapy which resulted in reticulocytosis and rise in hematocrit.

**Discussion**

Herpes simplex virus is a DNA-core virus which has been shown to be a causative agent of encephalitis, hepatitis, esophagitis, gastritis, and pneumonitis. These visceral herpetic infections have been described previously only in immunosuppressed or severely debilitated patients, frequently as a preterminal event. The patient presented here differs from previously re-
ported cases of herpetic esophagitis in that he was neither severely debilitated nor immunosuppressed. There was no evidence for antecedent injury to the esophagus. The severity of this patient's esophagitis is similar to that reported in primary herpetic infections which tend to be more severe than recrudescences or reinfections. Esophageal hemorrhage has not been described in herpetic esophagitis. In the present case, gross hemorrhage was seen in the distal 3 to 4 cm of the esophagus. Because there was no evidence of diagnostic phlebotomy or of hemolysis and because stools became positive for blood, it was assumed that this hemorrhagic lesion was responsible for a 14-point drop in the patient's hematocrit, although he remained hemodynamically stable throughout his course.

Diagnosis of visceral herpes usually rests on the cytological finding of Cowdry type A intranuclear inclusion bodies in the appropriate clinical setting. In autopsy series, the incidence of herpes as an etiology of esophageal ulceration varies from 2 to 10% if cytology is the method used for diagnosis. There are disadvantages to using cytology as the sole means of diagnosing herpetic infections. Cytology does not allow for differentiation between HSV-1 and HSV-2; furthermore, intranuclear inclusion bodies have been demonstrated in nonviral disease.

The endoscopic appearance of herpes esophagitis, as previously described, is similar to what was seen in the present case. Herpetic esophagitis begins with vesicle formation, followed by the appearance of small, punched-out, superficial ulcers covered with fibrinous exudate. These ulcers may coalesce, forming a diffuse erosive esophagitis. Biopsy of the margin of one of the ulcers may reveal evidence of herpetic involvement and should reveal pseudohyphae if Candida is the causative agent. It is known that herpetic ulcers may become overgrown with Candida; therefore, evidence of the two agents may coexist in the same tissue specimen. Tissue culture isolation of the specific herpes virus and serological confirmation of acute herpes infection by observing a 4-fold rise in complement-fixing antibody in the patient's serum to HSV-1 are extremely helpful from a diagnostic standpoint. The patient presented here had tissue culture proof of herpetic infection with no obvious lesion demonstrable except for esophagitis and had a 7-fold rise in complement-fixing antibody to HSV-1.

It is known that chronic oropharyngeal shedding of HSV-1 occurs in some asymptomatic persons. In the present case, oropharyngeal contamination was not excluded and histological confirmation of viral inclusion bodies was not established.

Treatment of herpes esophagitis is largely supportive. Important aspects of this supportive therapy are sedation and adequate analgesia. In the present case, resolution was spontaneous and occurred over a 10-day period.

The major intent and potential significance of this report is to call attention to the possibility that herpetic esophagitis may occur in immunocompetent hosts apparently without antecedent esophageal injury. The frequency with which this may occur will depend on subsequent studies done with an awareness that this disease may occur in noncompromised hosts, and utilizing methods to exclude the possibility of contamination, i.e., show the histological response characteristic of viral infection of the esophagus, or demonstrate increased quantity of virus from esophageal brushings, as opposed to throat washings.

REFERENCES