Experimental Corneal Infection of the Cebus Monkey with Herpesvirus hominis Type 1 and Type 2

By

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With 5 Figures

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Summary

Cebus monkeys were infected with *Herpesvirus hominis* type 1 or 2 by the corneal route in the right eye. The type 1 animals developed a keratoconjunctivitis approximately a week earlier than the type 2 animals. Although the duration of the type 1 lesions was more prolonged, there was no difference in the severity of the lesions between the two types. Lesions in the contralateral eye developed in all the animals although virus was not isolated. Virus was recovered from the lacrimal secretions of the infected eye and throat swabs. The animals exhibited a rise in serum neutralizing antibody to the homologous virus.

1. Introduction

*Herpesvirus hominis* (HVH) produces many syndromes in man, including gingivostomatitis, vulvovaginitis, dermatitis, eczema herpeticum, keratoconjunctivitis, and meningoencephalitis. In the newborn, a fatal, generalized visceral disease may be produced.

Two types of *Herpesvirus hominis* have been described which differ in their antigenic and biologic properties (1—4). HVH1 is usually isolated from non-genital lesions, whereas HVH2 is recovered from genital herpetic lesions. In addition to being the primary etiologic agent for genital herpes infection, HVH2 has also been identified as a causative agent for abortion (5) and neonatal herpes infection (6). In addition, there is evidence it is responsible for cervical neoplasia (7—10) and chronic neurological disease (1).

One of the major causes of keratoconjunctivitis and blindness in man is HVH. The typical lesions produced are unilateral conjunctivitis, superficial keratitis, and
disciform keratitis. HVH1 has been studied in the cornea of the rabbit by a number of investigators (1). Oh et al. (11) have recently compared the pathogenicity of HVH1 and 2 on the rabbit cornea.

Due to the importance of herpesviruses in keratitis and the possibility that corneal infection during parturition may result in generalized neonatal disease, we undertook a study to determine the susceptibility of the Cebus monkey to corneal infection with HVH1 and HVH2. The Cebus monkey has been shown to develop genital herpes lesions upon intravaginal inoculation (12—14).

2. Materials and Methods

2.1. Virus

The viruses utilized in this study were kindly supplied by Dr. A. J. Nahmias, Emory University Medical School (13—14). The two strains used were Shealey (type 1) and CUR (type 2). These viruses had been passaged twice in primary rabbit kidney cells followed by one or two passages in Vero cells. The titters on Vero cells were: type 1 — $10^{7.8}$ TCID$_{50}$/0.2 ml and type 2 — $10^{5.7}$ TCID$_{50}$/0.2 ml.

2.2. Animals

The Cebus monkeys (Cebus apella) were purchased from a commercial source. The animals were individually caged throughout the experiment and were shown to be free of herpesvirus by isolation attempts and by the absence of antibody to this virus upon arrival, after a four week quarantine, and at the time of inoculation. Five animals were inoculated in the right eye with HVH1 by dropping undiluted virus onto the eye and gently rubbing the eye with a moist swab. Similarly, six other animals were inoculated in the right eye with HVH2.

2.3. Virus Isolation

Routine throat and vaginal swabs were taken at regular intervals. In addition, starting on the fourth day, lacrimal secretions were collected from both eyes by touching a small disc of filter paper to the medial canthus of the eye. The discs were then placed in MEM supplemented with 10% fetal bovine serum and antibiotics (15). These samples were then inoculated onto primary baboon kidney cells (BKC) for virus isolation.

2.4. Serology

Blood samples were obtained by venipuncture prior to virus inoculation and again at regular intervals during the experiment. Antibody determinations were performed by serum neutralization (SN) test in microtiter plates with Vero cells using procedures standard for this laboratory (16). Between 20 and 50 TCID$_{50}$ virus were employed in all neutralization tests.

2.5. Clinical Observation

The eyes were examined every other day and stained with fluorescein opthalmic strips (Ayerst) to detect the presence of corneal lesions. The lesions were scored according to the method of Kaufman and Maloney (17). Briefly, the lesions were graded from 0—4 in relation to the size of the corneal lesions; 0 representing no lesion and 4 representing the involvement of the entire cornea.

3. Results

Table 1 illustrates the pattern of viral excretion from the five animals inoculated in the right eye with HVH1. Virus was recovered from the throat swabs and lacrimal secretions from the right eye in all five animals. Virus isolations started