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# Aspects of B Virus Infection in Laboratory Monkeys

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B virus infection of monkeys appears to be analogous to herpes simplex infection of man. The virus causes vesicular lesions of the lips, tongue, and buccal mucosa following periods of stress. Encephalitis in monkeys due to B virus, as with herpes simplex in man, occurs but is rare. The disease appears most commonly in epizootic proportions in recently imported monkeys.<sup>5</sup> Like other vesicular diseases of the oral cavity, it causes loss of condition as a result of the monkeys failing to eat. There are two profound reasons why veterinarians involved with laboratory animal care must be concerned with B virus infection. First, when transmitted to man, the disease, with few exceptions,<sup>1</sup> produces a fatal ascending myelitis and encephalitis.<sup>6,8,10</sup> Second, in experiments utilizing monkeys, B virus encephalitis may give confusing results. The latter was especially true during investigations of poliomyelitis virus infection in monkeys.<sup>3</sup> Monkeys inoculated with human brain material suspected of containing poliomyelitis virus succumbed with B virus encephalomyelitis.<sup>7</sup>

In 1932, a physician (patient B) working with poliomyelitis in rhesus monkeys, was bitten by an apparently normal monkey. Within three days, vesiculopustular lesions were present at the site of the wound and regional lymphangitis and

adenitis had developed. A week later, an acute ascending myelitis was manifested by motor and sensory disturbances in the lower extremities and bladder. Death occurred 17 days after onset of the first symptoms. When brain material from the autopsy was injected into rabbits, a similarly fatal encephalomyelitis was produced.<sup>14</sup> Subsequent investigations revealed the filterable agent to be a herpes virus closely related to herpes simplex and pseudorabies.<sup>12,13</sup>

Since 1932, B virus transmitted by monkey contact has caused over 25 deaths in veterinarians, physicians, and animal managers. The clinicopathologic appearance has been similar to the original case description. Infection has occurred from monkey bites, contamination of hand wounds by monkey saliva, cuts from broken culture bottles containing B virus, and cleaning monkey bones in preparation of a skeleton. In addition, many cases have not been traced to the source or time of infection.

## VIRUS ISOLATION

Infected tissue, serum, or vesicle fluid can be inoculated into several systems for viral isolation. Subcutaneous injection of suspected materials into young adult rabbits appears to be the most accessible and reliable method.<sup>11,13</sup> This results in encephalomyelitis with death occurring in 7-10 days. Intracerebral inoculation

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causes death in 5–8 days. Intradermal challenge results in local vesicular lesions in 3–5 days, but rabbits so treated have been reported to survive.

Inoculation of B virus onto the chorio-allantoic membrane of the 11-day-old embryonating hen's egg produces small, white pocks in 7–9 days.<sup>2</sup> The pocks are, as a rule, slightly smaller and less prone to give secondary foci than are pocks produced by the virus of herpes simplex and pseudorabies. B virus produces generalized infection with death of the embryo when the virus is passed in eggs. After 30

quantity of the virus is present in the inoculation material.

Many other laboratory animals are susceptible to infection with B virus but are not as sensitive. Suckling guinea pigs, rats, mice, and hamsters succumb after receiving intracerebral inoculations but do not develop clinical signs when inoculated by other routes.

Rhesus monkeys develop local lesions when given intradermal injections with viral suspensions, but only rarely develop encephalitis. Intracerebral inoculation of monkeys is invariably fatal.

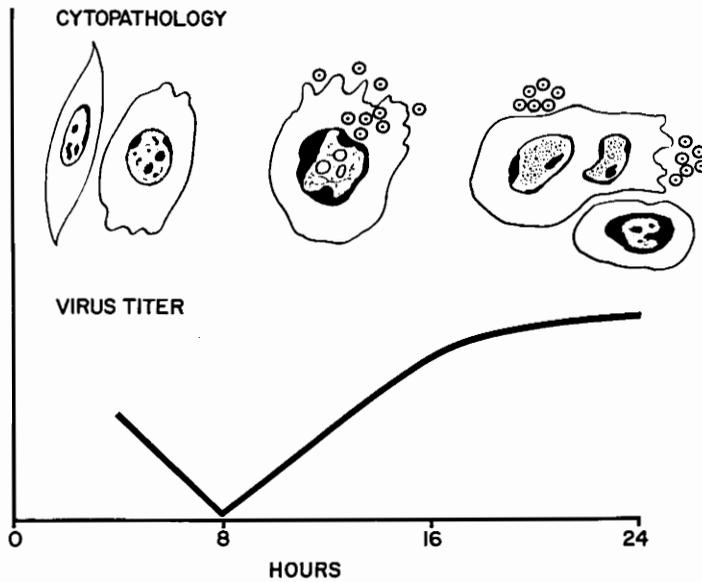


Figure 1. A diagram of the cellular changes and virus titer of cell cultures with Herpes B virus (modified from Reissig and Melnick, 1955).

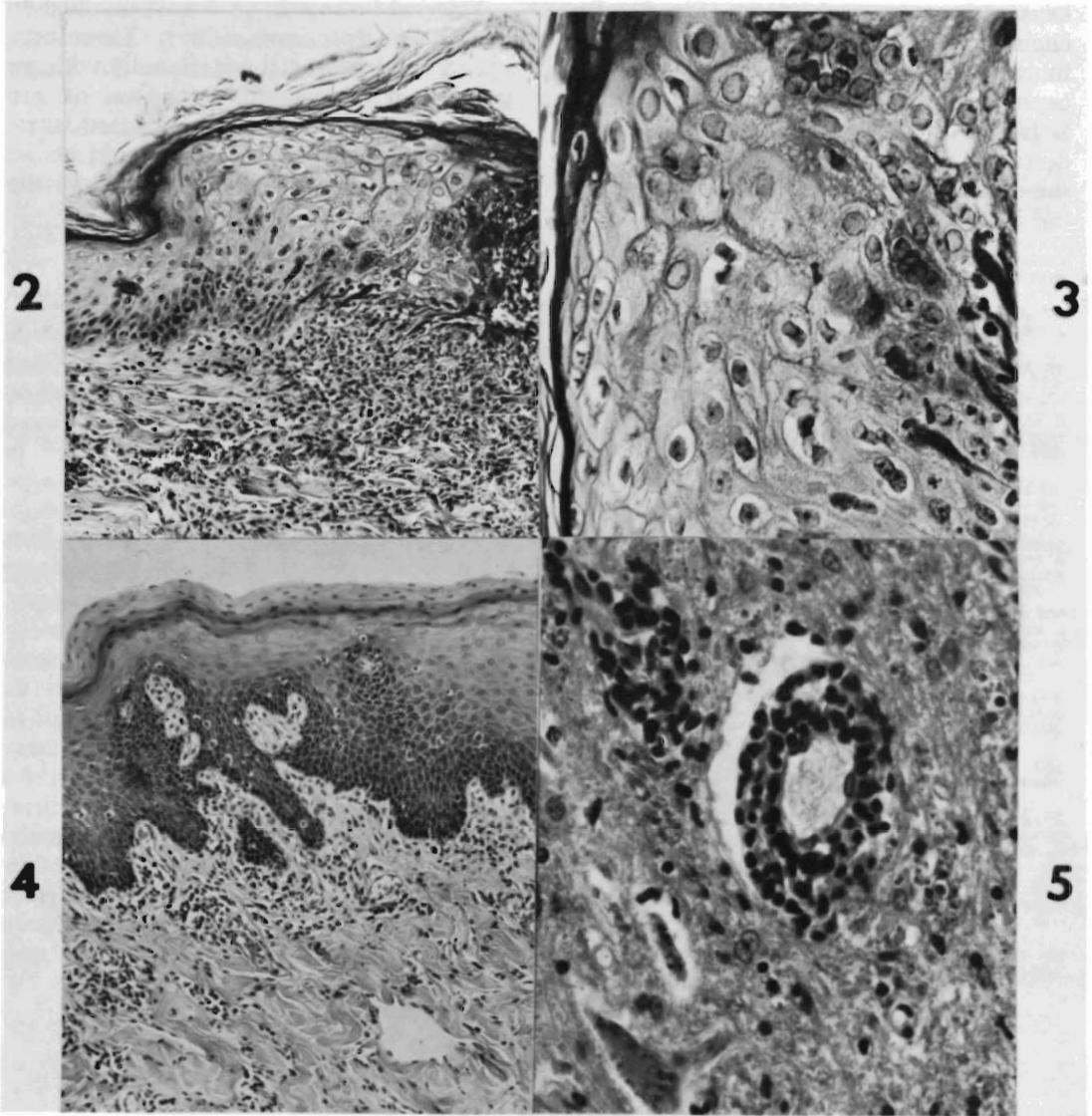
passages on the chorioallantoic membrane, the embryo is killed in 3–5 days.

Cell cultures are as sensitive to B virus infection as rabbits. Primary rabbit kidney cells, primary monkey kidney cells, and HeLa cells have been used for virus isolation (Fig. 1). Three days postinoculation, focal areas of cell necrosis develop.<sup>9</sup> Formation of giant cells and intranuclear inclusions occurs. The cells shrink, become round and granular, and detach from the glass. The cell sheet is usually destroyed in 5–6 days providing sufficient

#### ***PATHOLOGY OF B VIRUS IN MONKEYS***

Macroscopic lesions in monkeys are usually confined to the lips, tongue, and buccal mucosa. As with other viral vesicular diseases, the lesions develop through successive stages of erythema, vesiculation, pustule formation, and ulceration.<sup>12</sup>

Affected epithelial cells swell and develop intranuclear eosinophilic inclusion bodies (Fig. 2). Well-defined inclusion bodies are not common. The usual appear-



**Figure 2.** The margin of a herpes B virus lesion from the lip of a rhesus monkey. Epithelial cells are swollen and a severe mononuclear infiltrate is present in the dermis.  
**Figure 4.** A healing lesion of herpes B virus infection from the oral cavity of a rhesus monkey.

**Figure 3.** High power of Figure 2. The nucleus is filled with pale, homogeneous material and the chromatin is located at the nuclear membrane.  
**Figure 5.** Perivascular lymphocyte cuffing located near the nucleus of the trigeminal nerve (cranial nerve V) in a monkey with severe lesions of herpes B virus.

ance is a very pale, finely granular area occupying the majority of the nucleus. Vesiculation results from the coalescence of swollen epithelial cells. Ulceration with secondary bacterial infection occurs in vesicular areas (Fig. 3). Healed lesions

contain thickened epithelial layers with subepithelial infiltration of lymphocytes (Fig. 4).

Perivascular cuffing and glial nodules can often be seen near the nucleus of the trigeminal nerve (cranial nerve V) in mon-

keys with severe oral lesions (Fig. 5). Encephalomyelitis is rare except in monkeys inoculated intracerebrally. B virus encephalomyelitis is usually fatal in monkeys and is characterized by widespread destruction of nervous tissue, especially in the spinal cord and medulla oblongata.

Visceral lesions have been described in the spleen, liver, and kidney. These consist of focal necrosis, occasionally with intranuclear inclusions. Such lesions are characteristic of animals inoculated intraperitoneally with B virus but should not be confused with the necrotic lesions in the

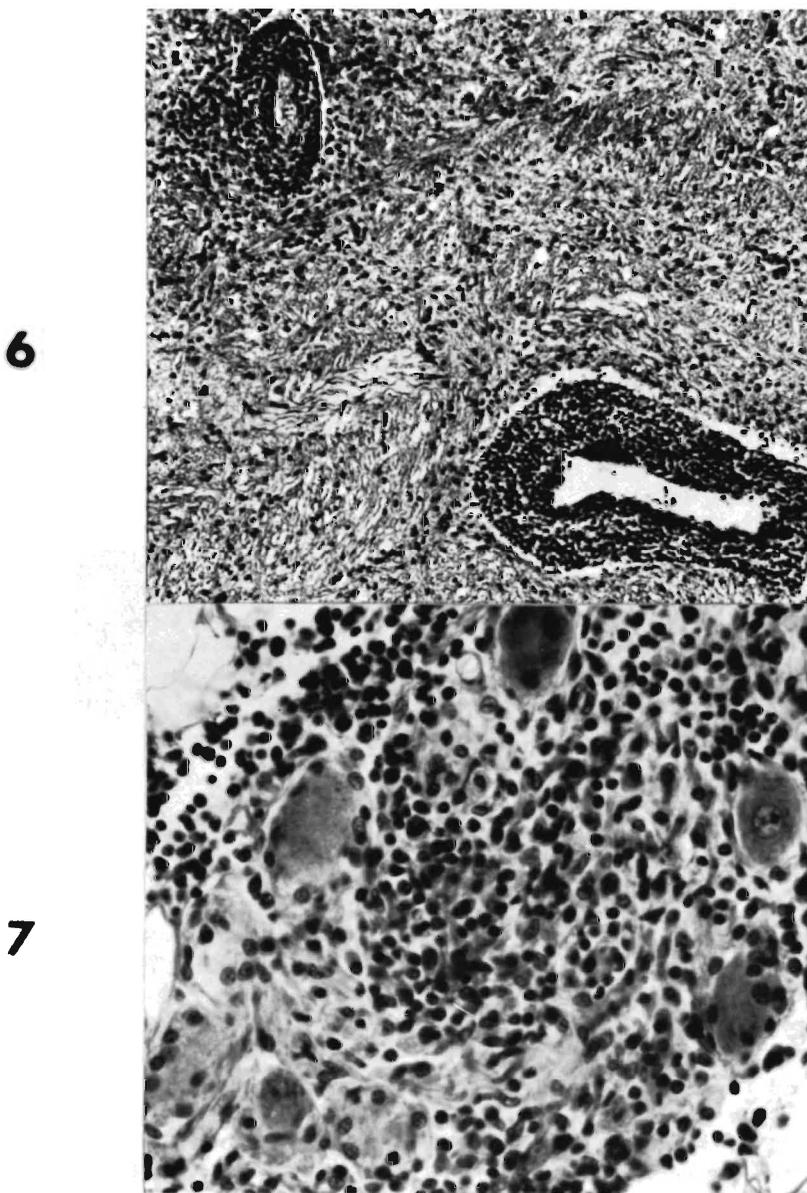


Figure 6. Necrosis and Severe perivascular lymphocyte cuffing in the medulla of a human patient who died of herpes B virus infection.

Figure 7. Lymphocytic ganglionitis and radiculitis near the base of the heart. Same patient as Figure 6.

viscera produced by Herpes M virus in marmosets.<sup>4</sup> Bronchopneumonia commonly accompanies B virus infection in rhesus monkeys. Measles virus produces an interstitial pneumonia characterized by the formation of giant cells and intranuclear inclusion bodies.<sup>15</sup>

**THE PATHOLOGY OF B VIRUS INFECTION IN MAN**

The clinical course of B virus infection in man is quite variable. This is due, in part, to the ability of the virus to remain latent in the infected host. Many cases have not been traced to the source or time of infection. Motor and sensory disturbances appear first in the lower limbs and bladder and are accompanied by fever, chills, and headache. Paralysis then progresses to the upper limbs, throat, and respiratory centers.

Destruction of nervous tissue is usually most severe in the spinal cord and medulla although lesions are common in the cerebellum and cerebral cortex. Necrosis, perivascular cuffing, and increased glial cell formation are prominent throughout the central nervous system (Fig. 6). Severe edema and secondary demyelination are widespread. Lymphocytic radiculitis and ganglionitis (Fig. 7) may be responsible for many of the symptoms of B virus infection.

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