November 22, 1933.

Dr. A. Sabin
Bellevue Hospital
New York City

Dear Dr. Sabin:

I am enclosing a resumé of our article relative to the Brebner case which will appear shortly in The Journal of Infectious Diseases. I hope this is what you desire and I regret the delay in sending it off. I shall be interested in reading your article.

Best wishes.

Sincerely yours,

[Signature]
Margaret Holden

Encl.
MH/C
Evidence that "W.B." Virus is Closely Related to Herpes Virus.

Pathogenicity of Virus "W.B." for Rabbits.

Rabbits given intracerebral inoculations of 0.2 cc. of a 20% suspension of the original human brain, cord or rabbit passage brain die in 4 to 6 days with fever, salivation and tremors.

The brains are congested but are free from bacteria.

Sections from Ammon's horn in such an animal showed intranuclear acidophilous inclusion bodies.

Intradermal inoculations of the standard suspension of passage virus produce redness, hemorrhage and finally necrosis within 4 to 5 days. An ascending flacid paralysis beginning about the 6th or 7th day and terminating fatally on the 8th to 10th day occurs. (The lesions differ from the customary lesions produced by a known herpes virus in the relative infrequency of vesicles and the intensity of the hemorrhage and necrosis. Paralysis of this sort after dermal inoculation with certain strains of herpes virus is infrequent but has been noted by other investigators and ourselves.) It might well be a lesion caused by a herpes virus of unusual potency.

Pathogenicity of Virus "W.B." for Rhesus and Cebus Monkeys.

This virus when tested intracerebrally and intradermally in rhesus monkeys is innocuous, in this regard agreeing with observations that have been made on the virus of herpes.

Two Cebus monkeys inoculated intracerebrally with rabbit passage brains after incubation period ranging from 2 to 7 days had rise in temperature with return to subnormal temperature, tremors and lethargy until death
occurred on the 7th and 17th day respectively. Salivation and convulsive twitchings occurred just before death.

The brain of Cebus 1 which died acutely in 7 days was shown by inoculation into rabbits to contain the virus. Histologically, perivascular infiltration of mononuclear cells in meninges, cortex and white matter of the brain.

The brain of Cebus 2 which lived for 17 days contained no virus as tested intracerebrally in rabbits, thus indicating, when compared with Cebus 1 who died earlier, a process of autosterilization. Sections of the brain and cord from this monkey showed a definite meningoencephalitis.

This virus, then, shows the characteristic reaction for herpes virus when tested by comparative pathogenicity for Rhesus and Cebus monkeys.

**Immunological Tests.**

Four human and four rhesus serums that neutralize an authenticated herpes virus also neutralize W.B. virus in the rabbit.

Three human serums and four rhesus serums that fail to neutralize herpes virus also fail to affect W.B. virus with a single exception.

Antiherpes rabbit immune serum neutralizes, after proper incubation, our several strains of herpes virus as tested by intracerebral or skin inoculation. Normal rabbit serum never has this effect and is also ineffective on W.B. virus. This antiherpes serum modifies but does not completely neutralize "W.B." virus. The skin reactions produced by a mixture of "W.B." virus and rabbit antiherpes serum are negative or minimal. However, death follows although delayed beyond the period required with mixtures of W.B. and normal rabbit serum.
Monkeys whose serum fail to neutralize either virus may be successfully immunized so as to show neutralizing properties both for the virus employed and the other virus.

In addition, a rabbit recovered from dermal inoculation with the virus of Herpes simplex no longer reacts to this virus nor to the virus W.B.