EFFECTS OF CNS DEPRESSANT DRUGS ON MOUSE ENCEPHALOMYELITIS VIRUS

HAROLD E. PEARSON AND DOROTHY L. LAGERBORG
Los Angeles County General Hospital, Los Angeles, California

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Previous work (Pearson, 1950; Pearson et al., 1952; and Visser et al., 1952) showed that various compounds may inhibit Théiler's GDVII strain of mouse encephalomyelitis virus in vitro; none tested so far was effective in vivo. It was of interest to determine if compounds capable of depressing central nervous system activity would also repress viral activity. The present report gives the results of trials with various agents tested, mostly in vitro.

MATERIALS AND METHODS

Théiler's GDVII strain of mouse encephalomyelitis virus which had been passed 50–60 times in tissue culture of one day mouse brain was used (Pearson, 1950). Virus was added to tissue cultures in a final concentration of 10⁻⁴, which is approximately 100 intracerebral LD₅₀'s for mice. Viral content of tissue cultures was tested by hemagglutination using 0.25 per cent human RBC and serial, twofold dilutions of virus. By this technique the hemagglutination titer usually observed was 1,280–2,560.

Tissue cultures of minced brain tissue aseptically removed from mice one day of age were prepared in 50 ml Erlenmeyer flasks containing 3 ml of Simms' solution with virus and the drug to be tested. The stoppered flasks were incubated at 35 °C for 48 hours. After incubation, the contents of the flasks were transferred to test tubes, and the tissue was sedimented by centrifugation. Supernatant fluids from three tubes were pooled and tested for viral content. Control flasks without drugs always were included in the test.

RESULTS

The results of the tests are shown in table 1. It is seen that all drugs except luminal, para-
tains 20 per cent propylene glycol and 10 per cent ethyl alcohol. Neither of the last two compounds is inhibitory in the amount used.

Apressoline was tried in infected mice. A single intraperitoneal dose of 2 mg was lethal for mice in one day, but other mice tolerated 1 mg daily for 3 days and survived for at least 18 days. Twenty mice (10–12.5 g) were injected intracerebrally, each with 0.03 ml of 10^-4 tissue culture virus (approx 1 MLD). Beginning the second day after infection 10 mice received aresoline intraperitoneally, 1 mg in 0.5 ml saline daily for 3 successive days; 10 control mice were given only saline. Deaths occurred from 4 to 17 days after virus inoculation as follows: test mice: 4,5,6,7,7,10,17,2 survivors; controls: 5,6,7,7,8, 4 survivors. It is seen that aresoline at nearly the maximal tolerated dosage failed to protect mice from infection with a small amount of virus.

**DISCUSSION**

The various sedatives and hypnotics tested presumably act in various ways. If they affect cell permeability or interfere with enzyme systems of nervous tissues, they might also be expected to have some effect on a virus which was dependent on such systems for propagation. In a closed tissue culture of the type used in this study, continuous inhibition of virus could occur in contrast to the failure to affect the course of viral infection in vivo. In the latter instance evidently the drugs have only transient effects or perhaps do not affect at all reactions which are sensitive to the drug in vitro. Schaeffer et al. (1949) reported that treatment with drugs similar to those used in the present study failed to protect mice from infection with equine encephalitis, poliomyelitis, or influenza. Cutting et al. (1947) found that urethan, among other drugs tested, did not alter vaccinia infection in embryonated eggs.

**SUMMARY**

Various hypnotics and sedatives inhibited propagation of Theiler's GDVII strain of mouse encephalomyelitis virus in tissue cultures of mouse brain. 1-Hydrazinophthalazine (aressoline), the most effective agent in vitro, failed to alter the course of infection in mice.

**REFERENCES**


