Failure of Adenine Arabinoside to Modify Scrapie in Mice

(Accepted 6 August 1971)

Enhanced synthesis of DNA in brains of scrapie-affected mice prompted Kimberlin & Hunter (1967) to examine the effect of inhibitors of DNA synthesis. No protection or delay was observed in mice inoculated intracerebrally, and receiving combined intracerebral-intraperitoneal treatment. The high penetrability of adenine arabinoside into the central nervous system and its relatively high activity against neurotropic DNA viral infections (Dixon et al. 1969 Schardein & Sidwell 1969; Sloan et al. 1969) inspired an examination of its possible effectiveness in scrapie.

Swiss Webster mice were inoculated intracerebrally with 0.03 ml. of 10^{-1} or 10^{-4} saline suspensions of scrapie mouse brain, using the sixth mouse passage of the Chandler strain. Beginning the day before inoculation and semi-weekly thereafter one group of mice receiving each concentration of inoculum was treated subcutaneously with adenine arabinoside (9-D-arabinofuranosyladenine), 200–300 mg./kg.; another group of mice at each concentration of inoculum received equal volumes of buffered saline solution.

Treatment had no effect and the disease was uniformly fatal in all groups. In the animals inoculated with 10^{-1} scrapie brain suspension the arithmetic mean survival times were 148 days for both treated and control groups, with 10^{-4} 182 and 178 days, for the treated and control groups respectively.

Antiviral effectiveness of adenine arabinoside was confirmed by demonstrating its activity against vaccinial pneumonia in mice. Three groups of mice were inoculated intranasally with the Western Reserve strain of vaccine virus (0.05 ml. of 10^{-1.5} infected mouse lung suspension). Groups were treated subcutaneously with adenine arabinoside, 100 or 200 mg./ml./day for 6 days starting the day before virus. Fifth-day lung lesion scores, scoring '1' for each 25% of consolidation, averaged 1.4 for the group receiving the saline placebo. The score for each treated group was essentially zero, with only one mouse in each ten exhibiting a visible patch of consolidation too small to score as '1'.

In the present study, treatment with an antiviral compound active against certain viral encephalitides failed to alter scrapie in mice. These results are similar to those of Kimberlin & Hunter (1967), who found that combined central and peripheral treatment with hydroxyurea of 5-iodo-2'-deoxyuridine failed to alter scrapie. The results support the conclusions (Adams, 1970; Adams, Caspary & Field, 1969; Kimberlin, 1969; Kimberlin & Hunter, 1967; Kimberlin & Anger, 1969) that altered DNA synthesis is not a primary feature of the pathogenesis of scrapie in the central nervous system.

Department of Epidemiology and Virus Laboratory
School of Public Health, University of Michigan
Ann Arbor, Michigan 48104

REFERENCES

Short Communications


(Received 6 July 1971)