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Failure of Antrycide in Treatment of Leptospirosis in Experimentally Infected Hamsters[1] (*)

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The chemotherapeutic efficacy of quinapyramine (antrycide) could not be demonstrated in hamsters experimentally infected with a virulent strain of serotype *bataviae*.

Quinapyramine (antrycide) is frequently used outside the United States for prophylaxis and treatment of trypanosomiasis and babesiasis in livestock (2, 5, 6). In many of these areas, leptospirosis is also an important disease of livestock. Therefore, reports of Roumanian workers (3, 4) that antrycide was therapeutic for leptospirosis served to emphasize its importance as a multipurpose drug. The Roumanian observations were empirical. It was deemed advisable to affirm or deny the antileptospiral activity of antrycide in experimentally infected hamsters.

The in vivo test system used to evaluate drugs was previously developed in this department to screen drugs for antileptospiral activity (A. D. Alexander, *unpublished data*).

Three- to 4-week-old weanling hamsters weighing 30 to 40 g were used. The inoculum was prepared from the liver of a moribund hamster that was infected with a virulent strain (1415) of serotype *bataviae*. The liver was triturated, suspended in 10 parts of Stuart's medium, and then centrifuged at 1,500 × g for 10 to 15 min to remove tissue particles. The concentration of organisms in the supernatant fluid was determined by microscopic counts made with a Petroff-Hausser bacteria counter. Accordingly, the supernatant fluid was diluted to provide a concentration of 26,000 leptospiras per ml. This constituted the inoculum which was given intraperitoneally in a 0.5-ml dose. The infectious inoculum dose was selected on the basis of previous virulence titrations and killed hamsters in 6 to 7 days.

The dimethosulfate salt of antrycide was diluted with distilled water to provide dilutions containing 64, 16, 4, 1, and 0.5 mg/ml. The respective dilutions were given in sufficient volume to provide drug doses of 640, 160, and 40 mg/kg which were used routinely in the drug screening test system and also to provide doses of 10 and 5 mg/kg. The two lesser doses were included because antrycide was reported to have antileptospiral activity at these levels (3, 4). Each dilution of drug was given to 10 infected hamsters by the subcutaneous route. Drug dilutions were given in a single dose 2 days after animals were infected. For comparative purposes as well as for use as a positive control, chlortetracycline was similarly administered to hamsters at dose levels of 640, 160, and 40 mg/kg. For drug toxicity controls, five uninfected hamsters were used for each dose level

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and route of administration. Twenty-five hamsters were used as infection controls.

After infection, animals were observed twice daily for signs of disease for a 16-day observation period. Dead or moribund animals in treatment and infection control groups were autopsied; blood, kidneys, and livers were obtained for microscopic and, if necessary, cultural examinations for leptospirosis (1). At least two animals in each group of surviving animals in treatment and infection control groups were similarly examined for leptospirosis.

Antrycide administered subcutaneously at dose of 640 mg/kg killed all five drug control hamsters in 1 to 4 days after inoculation. Lesser doses of antrycide were not lethal for hamsters. Chlortetracycline at various dose levels elicited no toxic effects in hamsters.

All untreated infected animals died 6 to 7 days after inoculation. Early toxic deaths occurred in the group given 640 mg of antrycide per kg. All other groups of infected hamsters treated with antrycide died of leptospirosis within the same time as that of controls. By contrast, all infected animals treated with chlortetracycline survived. No leptospiras were detected in tissues obtained 16 days after infection from two of five surviving hamsters that were treated with a 40 mg/kg dose of chlortetracycline.

The *bataviae* hamster-infectivity system which was used to determine drug activity is highly sensitive. It has served to demonstrate activity of all drugs known to have antileptospiral activity (A. D. Alexander, *unpublished data*). With this test system, antileptosiral activity of antrycide :could not be demonstrated.

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