Hemoprotezoan Infections of Domestic Animals

Trypanosomiasis, Babesiosis, Theileriosis, and Anaplasmosis

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1. INTRODUCTION

Arthropod-transmitted hemoparasitic diseases, caused by Trypanosoma, Babesia, Theileria, and Anaplasma, occur throughout the world but are frequently of greatest importance in the tropics and subtropics, where conditions are favorable to the maintenance of vector populations. Vector control and chemotherapy are the primary defenses against these disease agents. Vaccines that prevent these infections have yet to be developed. The attenuated or live vaccines described for anaplasmosis, babesiosis, and theileriosis often depend on specific therapy to reduce the severity of infection while allowing the development of a preemunizing immunity (Kuttler, 1979; Todorovic, 1974; Radley, 1981). Chemotherapy, chemoimmunization, and chemoprophylaxis thus continue to play an important role in hemoparasitic disease management and prevention. Even so, chemotherapy is not without problems; drug-resistant microorganisms arise, drug residues in tissues of food animals may be detected and prompt removal of the drug from its approved status, and the cost of drugs may be too high for use by poor farmers. The expense and difficulty in developing new replacement compounds for those no longer used for one reason or another are also a serious problem in the world today.

2. EXPERIMENTAL METHODS

Experimental rodent models are available for most of the pathogenic trypanosomes that lend themselves to drug-screening trials. Although useful, the need persists for

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trials with the primary host because of such factors as host tolerance, tissue residues, and differences in drug susceptibility among the many pathogenic trypanosomes.

Until the development of methods for the *in vitro* growth of *Theileria*, treatment trials were limited to inducing infection followed by treatment of the infected animals at various time intervals. The expense and time required for such trials severely limited the number of compounds that could be tested. The *in vitro* cultivation of *T. parva* macroschizonts in lymphoblasts (Malmquist *et al.*, 1970) contributed to the development of screening techniques that led to the discovery of the more effective quinone compounds (McHardy *et al.*, 1976). These techniques continue to provide the method of choice for screening potentially new compounds.

The absence of suitable *in vitro* methods of growth for *Anaplasma* and the *Babesias* (except for *B. bovis* and *B. divergens*) has created problems in mass screening of compounds for therapeutic efficacy. Most preliminary experimental drug trials designed to evaluate drug efficacy for anaplasmosis are conducted using splenectomized calves. In these cases, infection is induced and treatment given at the onset of parasitemia and the course of infection among the treated and nontreated (or placebo group) calves compared. Drug efficacy is usually determined using parameters such as packed cell volume (PCV), percentage drop in PCV, parasitemia, rate of recovery, and survivability.

A unique treatment consideration for anaplasmosis is the need in some circumstances to remove clinically nonapparent carrier infections. These trials are expensive and time consuming, requiring lengthy observation following treatment. To ensure that the infection has been entirely eliminated, subinoculation of blood from the treated cow to a susceptible splenectomized calf is usually required. The disappearance of a serological response, as measured by complement fixation, is presumptive evidence of a successful treatment program but cannot be relied on.

The same basic methods are used to evaluate drugs with potential babesiacidal activity. In addition to these methods, some rodent and tissue-culture models can be used. *Babesia rodhaini* infections in mice have been used to screen potential babesiacidal compounds (Beveridge, 1953; Lucas, 1960). Caution is recommended in such trials, since results can be misleading. An example is that diminazene, while highly effective against *B. bigemina* and *B. bovis*, is not equally as effective against *B. rodhaini* (Kuttler, 1981). The recent development of tissue-culture techniques for the *in vitro* propagation of *B. bovis* (Erp *et al.*, 1978; Levy and Ristic, 1980), the adaptation of *B. divergens* to the Mongolian gerbil (Lewis and Williams, 1979), and its growth on tissue cultures (Vayrynen and Tuomi, 1982) provide additional models for evaluating drug efficacy. It has been found that babesiacidal drugs will inhibit the uptake of tritiated purines such as hypoxanthine (Irvin and Young, 1977, 1979). This *in vitro* technique should prove a valuable asset in future drug-screening programs.

3. TRYPANOSOMIASIS

3.1. Clinical Importance of Chemotherapy and Chemoprophylaxis

In the absence of effective vaccines, and because of the limitations of vector control, chemotherapy and chemoprophylaxis (Table I) remain the major defenses against trypanosomiasis of livestock.