AUTOANTIBODIES IN HUMAN CONTACTS OF SLE DOGS

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Canine systemic lupus erythematosus (SLE), consisting of hematologic, joint, and renal involvement, has recently been described (1,2). The etiology is unclear, but breeding studies have implicated the importance of environmental factors (3) and minimized the role of genetic factors (4). A filterable agent, transmissible to mice and puppies, further supports the environmental theory (3). More recently two dogs that lived in a household in which several members had SLE were discovered to have DNA antibodies in their serum associated with hypergammaglobulinemia (5). This finding argued in favor of an environmental agent transmissible from humans to dogs. Since no control families were examined in the latter study and dogs are known to have a β-globulin which nonspecifically binds DNA (6), the following study was performed to determine if markers of autoimmune disease are increased in human contacts of dogs with SLE.

The study population consisted of five families in which a lupus dog resided and seven control families who had healthy dogs at the time of the study. The family members with lupus dogs were divided into seven men with a mean age of 36 years and six women with a mean age of 41 years. Four families had a spouse pair residing with the dogs with canine SLE. Six family member controls were men with a mean age of 36 years and 11 women with a mean age of 32 years. The SLE dogs were all diagnosed at the Veterinary School of the University of Pennsylvania. All had positive antinuclear antibodies and multisystem disease. Duration of disease varied from 1 to 4 years. Only one dog was acutely ill whereas the others were in steroid-induced remission at the time of obtaining sera from the household contacts.

Lymphocytotoxic activity (LCTA) was determined as previously described (7). A positive test was one in which at least 20% of the 2,000 lymphocytes in an individual well were killed. An individual serum was considered cytotoxic if at least 20% of the tests were positive from the panel of 27 normal lymphocyte donors obtained from healthy volunteers with a broad range of HLA phenotypes.

Antibodies to double-stranded DNA and the synthetic polynucleotides poly rA and poly rA·poly rU were measured by cellulose ester filter radioimmunoassay, prefiltering the nucleotides prior to use to remove any single-stranded material which nonspecifically binds to the filter (7,8). A positive test for antibodies to polynucleotides is defined as positive if it is two standard deviations greater than the mean of controls.

Antinuclear antibodies (ANA) and rheumatoid factors (RF) were determined in the study groups by standard techniques (9,10). A positive serum had a titer of 1:20 or greater.

No difference was found between the study and control group for the incidence of LCTA, binding of polynucleotides, antinuclear antibodies or rheumatoid factor activity (Table 1). Sera from ten members of the lupus dog contacts and 13 members of the control fami-
lies killed less than 20% of the panel, whereas sera from 2 and 3 family members killed 20-39% of the panel and only one each killed 40-59%. No family member of either group displayed antibodies to two polynucleotides simultaneously.

Sera from three family members residing with lupus dogs displayed antinuclear antibodies, whereas none of 17 family member control sera showed antinuclear antibodies. The antinuclear antibodies were limited to two families in which one of the household members had antibodies to polynucleotides or lymphocytotoxic antibody. In the first family, the wife had lymphocytotoxic antibodies and antibodies to DNA, and the husband had antinuclear antibody. In the second family both husband and wife were octogenarians. The wife had antibodies to poly rA poly rU and antinuclear antibodies and the husband had only antinuclear antibodies. Rheumatoid factor was found in one control family member who had no contact with a dog with SLE.

These results show that autoantibodies are not increased in human household contacts of dogs with SLE when compared to a control group. Studies of human contacts of SLE patients have shown a varying incidence of autoantibodies in family members (7,11,12) with increased numbers of family members having LCTA when the patient is acutely ill (13). These previous data supported the hypothesis of environmental factors being important in human SLE, although studies of polynucleotides in family members stress that genetic factors are also important (7). Family members exposed to patients with active SLE tend to have increased levels of autoantibodies (13). Due to the infrequency of diagnosis of canine SLE, it was not possible to obtain sera from dogs with active untreated disease. A prospective study is now in progress to examine whether disease activity in the dog is related to autoantibody formation in the human contacts. The number of individuals in this study is admittedly small, however, these data taken together with recent findings (14) do not support the hypothesis that environmental factors are operable in transmission of autoantibody formation from dogs with canine lupus to human household contacts.

**REFERENCES**

PROPRANOLOL AND THE TREATMENT OF RHEUMATOID ARTHRITIS

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Recently we reported that propranolol can suppress rheumatoid factor release from blood lymphocytes in vitro, responsiveness to plant mitogens, and a primary antibody response in cultured mouse spleen cells (1,2). These effects were related to the membrane stabilizing, or anesthetic property of the drug, not its beta-adrenergic blocking property. Although concentrations of propranolol required for these membrane effects were higher than those which could be expected to be achieved in vivo, we decided for two reasons that a small clinical trial should be performed to determine whether propranolol could have clinical immuno-suppressive usefulness in rheumatoid arthritis: 1) Some evidence might be demonstrated of decreased lymphocyte function at lower blood concentrations of propranolol than those needed in vitro, if the drug were administered over extended periods of time. 2) We were aware of anecdotal descriptions of patients whose rheumatoid arthritis or other connective tissue disease improved coincidental to propranolol use for hypertension or angina pectoris.

We administered propranolol to 14 patients in open trial. Propranolol was given orally starting at 40 mg four times a day and increasing the dose by 1/4, or 1/2 dose increments once or twice a week (maximum doses shown in Table 1). The treatment extended over 3 to 5-month periods. In two patients, the drug was discontinued at 1 month because of rashes. One patient was dropped from the study because of unreliability in following the protocol. This report is of the remaining 11 patients.

The clinical changes in the 11 patients are indicated in Table 1. All 6 patients who initially had fewer than 40 actively affected joints, as manifested by tenderness or pain on motion, had significant reduction in the number of affected joints during propranolol therapy, but one only marginally so. Improvements in walking times and grip strength occurred in 3 patients each. Sustained changes in number of involved joints of more than 25% from baseline, walking times 10% or more, and grip strength 33% or more are considered in our clinic to represent significant change in disease activity, as judged from serial observations of patients during apparently steady disease in pretreatment control periods. All percentages considered significant are shown in Table 1.

Of the 5 patients with more than 50 actively diseased joints initially, 3 showed significant reduction in number of affected joints during propranolol therapy, but in 2 of these the reductions were minimal. Two of the 5 patients showed significant reductions in walking...