LYMPHOCYTE MOBILIZATION BY DEXTRAN SULFATE IN BEAGLES

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Dogs manifesting ^{239}Pu-induced lymphopenia responded to the lymphocyte-mobilizing agent, dextran sulfate, to a degree similar to that observed in control dogs. No life-threatening increase in prothrombin times or hemorrhagic tendencies were observed.

Dogs exposed to a single inhalation of $^{239}PuO_2$ develop a dose-related and prolonged lymphopenia. It has been speculated that the lymphopenia results primarily from continuous irradiation of circulating lymphocytes via thoracic lymph nodes, but this pathogenesis has not been clearly defined. It was of interest to determine whether dogs with lymphopenia still have mobilizable pools of lymphocytes, or whether all available lyniphocytes are already in circulation.

Several polyanions have been found to induce lymphocytosis following injection in rats and primates, due mainly to mobilization of lymphocytes from lymphoid organs. Dextran sulfate (DS) was selected as a lymphocyte-mobilizing agent in this experiment because of its ready availability and lack of serious side effects.

Dogs with average initial lung burdens of ∿ 2.5 μCi $^{239}PuO_2$ 18 mo postexposure had blood lymphocyte concentrations ∿ 55% those of age-related control dogs. Dogs from both groups were given 5 mg/kg body weight sterile DS by intravenous injection, and blood samples were taken 0, 0.5, 1.0, 2.0, 3.0 and 5.0 hr later. From these samples the total leukocyte count was determined and blood smears were made for leukocyte differential counts. Since dextran interferes with clotting, plasma prothrombin times were also assayed.

The results of DS injection on blood lymphocyte, neutrophil, and monocyte concentrations, calculated as the ratio of cells at time $_x$/cells at time are shown in Figure 3.58. Although absolute lymphocyte concentrations were reduced in $^{239}PuO_2$-exposed dogs, the percent of lymphocytes mobilized after DS injection was comparable in lyniphopenic and control dogs, both as to time and degree of maximum response. Only a niodest increase in neutrophils was observed in either treatment group. Interestingly, the percent of monocytes mobilized by DS was greater in lymphopenic than in control dogs, even though the preinjection monocyte values were about equal, ($400 \pm 130/mm^3$ in the former versus $460 \pm 120/mm^3$ in the latter).

Maximal prolongation of prothrombin time occurred at the 0.5-hr sample in both groups. Mean value at that time was 1.8 times the zero-hr value, so did not represent a serious compromise of the clotting mechanism.

From the results of this study it appears that dogs manifesting prolonged ^{239}Pu-induced lymphopenia have a reserve pool of mobilizable lymphocytes. However, a major unanswered question remains: Why is a feed-back mechanism not stimulated by the prolonged lymphopenia that would return lymphocyte levels toward normal? Studies to help answer this question are being planned.

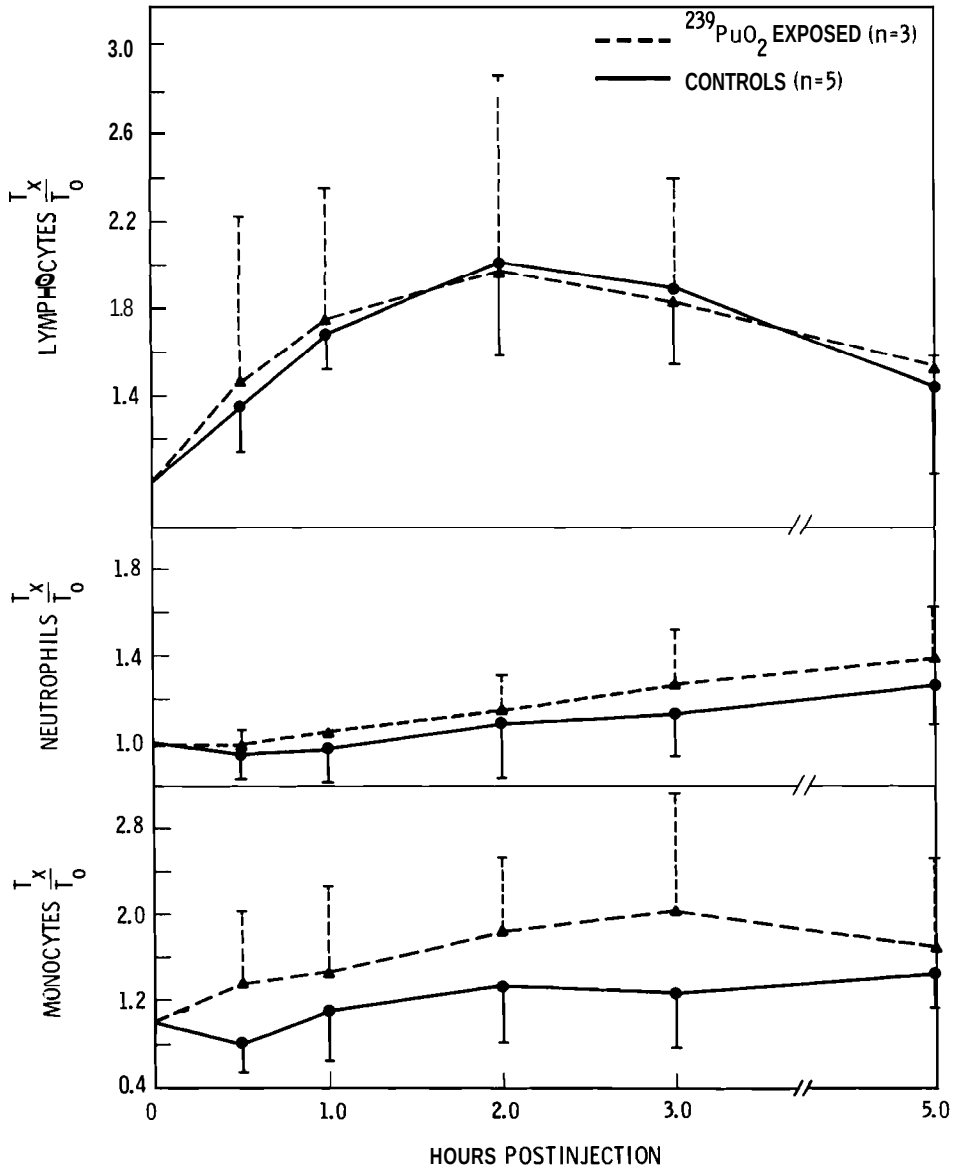

FIGURE 3.58. Leukocyte Mobilization in Dogs Following Intravenous Injection of Dextran Sulfate, Ration of cells at time x (mean ± SD)