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THE EFFECT OF PREDNISOLONE PHOSPHATE ON THE LIFE-SPAN OF DBA/2J MICE

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Abstract—Ninety-eight female DBA/2J mice were separated into two groups, and to one group prednisolone sodium phosphate was administered orally via the drinking water at a concentration between 3·0 and 3·2 μg/ml. The treatment was started when the animals were 232-days-old. No significant differences could be observed in the mortality curves for the control and experimental animals. The mean life-span of the mice was about 785 days, somewhat greater than the previously reported life-span for DBA/2J mice of 714 days.

INTRODUCTION

PREVIOUS work (Bellamy, 1968) suggested that prednisolone phosphate may have a marked influence on the life-span of short-lived mice. The earlier experiment was carried out on young mice (males and females—an inbred colony at the University of Sheffield) and commenced shortly after weaning to coincide with the period of rapid growth and the development of the lymphoid system (Bellamy, 1971). In the present experiment, a long-lived species was used and the administration of prednisolone was initiated after the plateau of the growth curve was reached.

MATERIALS AND METHODS

Ninety-eight female DBA/2J mice (Jackson Laboratories, Bar Harbor, Maine) were separated by random-number tables into two groups. One of the groups was treated as a control group and to the other group, prednisolone sodium phosphate (samples were kindly provided by Merck, Sharp and Dohme and by Schering) was administered orally via drinking (tap) water.

The concentration of prednisolone in the drinking water was between 3·0 and 3·2 μg/ml, and the average volume of water consumed was about 5·0 ml per day, representing the sole source of drinking water, so that an average dose of 15–16 μg/day was given to the experimental animals. Fresh water or prednisolone solutions were provided twice per week. The water containing prednisolone for the experimental animals was prepared by dilution of a stock solution (0·6 mg/ml) of prednisolone phosphate. The stock solution was prepared as necessary, about every 4–6 weeks, during the experiment and was stored in the refrigerator. A stock solution was tested after storage at the end of the experiment for prednisolone by two methods (U.S. Pharmacopeia, 1970) and no significant change could be detected in the prednisolone concentration of the stock solution.

The mice were housed two animals per cage in plastic cages; food (laboratory chow) and water were provided *ad lib.* The animals were weighed monthly. Throughout the study, the colony was maintained in a room separate from any other animals. Normally, only 2 persons were allowed to enter the room; the animal caretaker who had no contact with other rodents and who wore a clean uniform and disposable boots and a technician who had no contact with other laboratory animals. Cages and water bottles were kept separate from those used for other animals. The animal room was checked twice daily and any dead

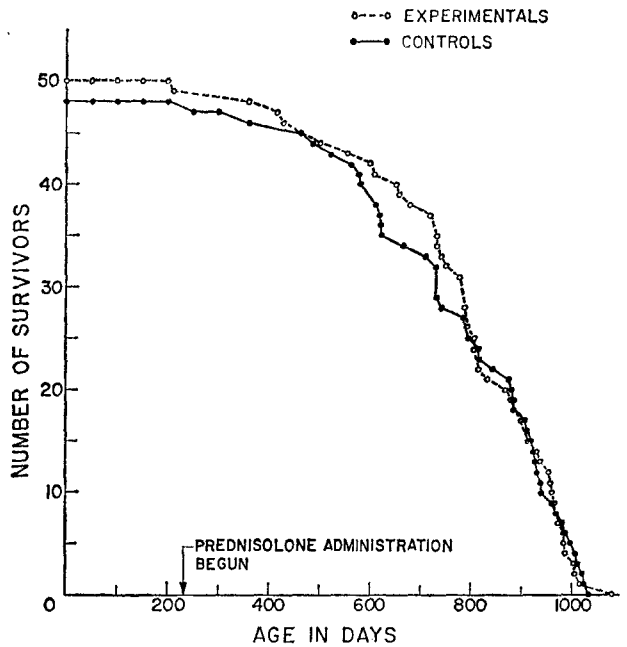

FIG. 1. Survival curves for mice receiving 3·0–3·2 μg/ml prednisolone phosphate in their drinking water (– – –) and for control animals (——).

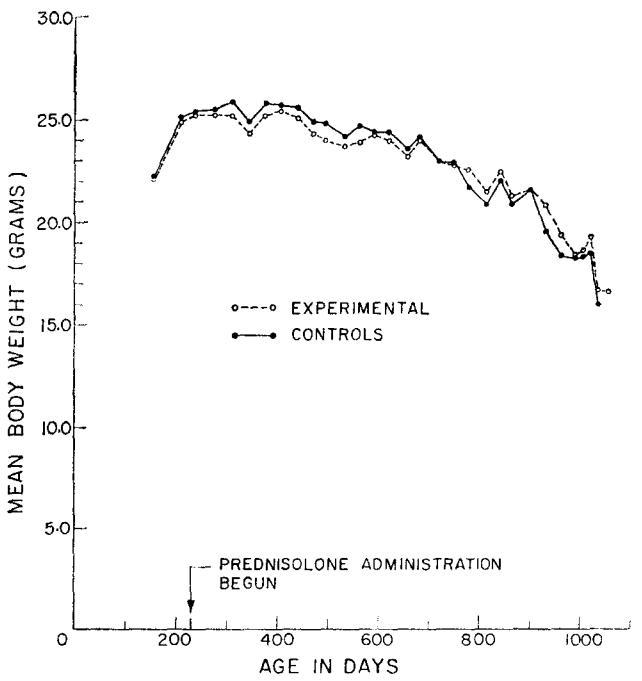

FIG. 2. Mean body weights plotted versus age for mice receiving 3·0–3·2 μg/ml prednisolone sodium phosphate in their drinking water (– – –) and for control animals (——).

animals were removed and retained for postmortem examination if autolysis had not set in. Occasionally animals whose death appeared imminent were killed.

The treatment was started when the animals were 232-days-old.

RESULTS

The mortality curves for the two groups of animals are shown in Fig. 1. The mean life-span of the controls was 784 days (maximum 1035 days) and that of the treated animals 787 days (maximum 1080 days). These life spans and the shape of the mortality curves suggest that the mice died from normal causes. Storer (Storer, 1966) reports the mean life span of 714 days for virgin female mice DBA/2J strain. No significant differences could be observed in the mortality curves for the control and experimental animals, nor for body weight (see Fig. 2) or the average water consumption. Post-mortem histopathological examinations (Dr. E. H. Fowler and Dr. R. Garman) also did not indicate any substantial differences. The pathologists were not aware whether animals were experimental or control. The lesions observed were mainly those incidental to old age.

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