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Life span and spontaneous lesions in rats. The effects of ad libitum versus controlled feeding

Rats and mice are the species of choice in experiments to test the chronic toxicity and/or carcinogenicity of various compounds. Because of historic reasons and convenience these animals are fed a high quality diet ad libitum during their life span, resulting in obese animals with a high incidence of background lesions and tumours. Previous experiments, in which the effects of diet restriction on background pathology and/or tumour incidences were studied, limited the amount of diet given to the animals using a percentage of the food consumption of ad libitum fed control animals. This feeding regime has not found wide acceptance, probable because of the enormous additional labor costs involved in the daily weighing of diets.

This preliminary report covers the life span and background pathology lesions in the kidney, parathyroid, pituitary, and mammary gland in groups of 20 male and 20 female rats in which the period of food intake was restricted to 6.5 hours per day compared to a similar group with ad libitum access to food all day.

The survival rate after two years was 18/20 and 16/20 in males and females of the restricted diet group and 8/20 and 14/20 in the ad libitum group. There was a marked reduction in the incidence and severity of chronic progressive nephropathy and the associated secondary hyperplasia of the parathyroids in the diet restricted group compared to the ad libitum fed group. The incidence of renal corticomedullary mineralization, pituitary adenomas and mammary hyperplasia/tumours was also lower in female animals of the restricted diet group.

These findings are consistent with previous studies on diet restriction. A major mechanism for the increased life span and the lower incidence of background lesions is likely to be a more "normalized" hormonal status of the animals. The lower incidence of background lesions and increased life span with diet restriction may lead to a reduction of the number of animals used in chronic toxicity and carcinogenicity tests by increasing the number of "end of test" animals and reducing the "background noise" (due to a high incidence of background pathology) in the statistical analysis of the pathology data.

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