SIDE EFFECTS OF HYDROCORTISONE AND PREDNISOLONE ON MICE OF VARIOUS AGE GROUPS

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The action of small doses of hydrocortisone (0.25 mg) and prednisolone (0.3 mg) given for 1, 2, and 3 weeks to male and female mice, weighing from 12 to 22 g, was studied. At the end of the experiment the animals were mated with mice not receiving these substances. A marked decrease in weight was observed in the mice receiving hydrocortisone; some of the animals died; sexual maturation of the young males and females was delayed. In adult females receiving hydrocortisone and in all females receiving prednisolone, the incidence of pregnancy was five times lower than in the control. Hydrocortisone reduced the fertilizing ability in the adult males by half, while prednisolone reduced it in adult males by 33% and in young males by 80%.

Hydrocortisone and prednisolone are widely used at the present time for the clinical treatment of many diseases [1, 2]. Besides their beneficial therapeutic effect, administration of these substances also gives rise to a number of undesirable side effects [3-11]. The writers have previously shown that the prolonged administration of large doses of these substances causes a considerable mortality among sexually mature animals and reduces their fertility [6-8].

In the investigation described below the action of small doses of hydrocortisone and prednisolone was studied on albino mice of two age groups: sexually mature (20-22 g in weight) and young (12-14 g).

EXPERIMENTAL METHOD AND RESULTS

The substances were injected intramuscularly for 1, 2, and 3 weeks. The daily dose of hydrocortisone was 0.25 mg and of prednisolone 0.3 mg per animal. Control animals received no treatment. After 3 weeks the sexually mature experimental and control animals were mated for 24 h with individuals of the opposite sex which were untreated. The young mice were mated on attaining the age of 2 months (the time of onset of sexual maturity in the control animals).

Observations showed that by the end of the 2nd week of the experiment injections of hydrocortisone had a marked depressant action on the young mice (apathy, loss of appetite). By the end of the 3rd week the general condition of all the experimental animals had deteriorated, and in the group of mice receiving hydrocortisone 20% of the sexually mature males and females, 10% of the young females, and 20% of the young males had died. No mice in the control group died.

Although prednisolone did not reduce the absolute weight of the animals, the experimental mice gained less in weight (1.5 g) than the controls (1.5-2.5 g). Under the influence of hydrocortisone the adult females lost up to 2.7 g and the males up to 1.2 g in weight, while the mice of the control group gained in weight by 2.5 and 2.2 g, respectively.

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TABLE 1. Change in Reproductive Power of Females under the Influence of Hydrocortisone and Prednisolone

Nature of experiment	Age of females	Number of females		
		total	pregnant	
			abs.	%
Control	Adult	100	16	16
	Young	55	15	27.3
Hydrocortisone	Adult	60	2	3.3
	Young	30	0	0
Prednisolone	Adult	60	2	3.3
	Young	90	5	5.5

TABLE 2. Change in Fertilizing Ability of Males under the Influence of Hydrocortisone and Prednisolone

Nature of experiment	Age of females	Number of females mated		
		total	pregnant	
			abs.	%
Control	Adult	100	16	16
	Young	55	15	27.3
Hydrocortisone	Adult	114	9	7.9
	Young	90	0	0
Prednisolone	Adult	135	14	10.3
	Young	90	5	5.5

Young mice receiving hydrocortisone lost about 1 g in weight while those receiving prednisolone gained in weight (the females by up to 3 g and the males by up to 3.9 g). In the control group the weight of the females increased during this period by 4.5 g, and the weight of the males increased by 6 g.

The reproductive power of the experimental animals was lower in all cases than that of the control (Tables 1 and 2).

The results show that the sexually mature females were more sensitive to hydrocortisone than males. In the group of mice receiving the substance for 1 week, 3.3% of the animals became pregnant, compared with 16% of pregnant animals in the control group. The experimental males preserved their fertilizing ability throughout the experiment although it was lower approximately by half than that of control. The effect of hydrocortisone on the young animals was more marked. The onset of sexual maturity was delayed in both females and males, and they produced no offspring. All the mice receiving prednisolone preserved their reproductive power, but the incidence of pregnancy was much lower than in the control group.

Microscopic study of sections through the ovaries of the females receiving hydrocortisone revealed the absence of ripe follicles and corpora lutea as well as atresia of many follicles of all types. The ovaries of the females receiving prednisolone contained follicles of all types, but only solitary ripe follicles and corpora lutea were present and some follicles of all types showed atresia.

The testes of the adult males receiving both compounds differed only slightly from those of the control animals. The seminiferous tubules were filled with spermatozoa. No spermatozoa were found in the seminiferous tubules of the young males receiving hydrocortisone. The number of spermatozoa in the seminiferous tubules of males receiving prednisolone was greatly reduced compared with the control.

Young animals, before the age of sexual maturity, are thus particularly sensitive to hydrocortisone and prednisolone.

Prolonged administration of therapeutic doses of both compounds to young animals delays their sexual maturation, reduces the fertility of the females, and lowers the fertilizing ability of the males.

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