Experimental Cardiac Necrosis in the Japanese Quail (*Cotournix cotournix*)[1] (36356)

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The induction of experimental myocardial infarct-like necrosis by isoproterenol has been studied in several mammalian forms. The severity of the lesion induced by this drug has been shown to be influenced by numerous factors including temperature (1), altitude acclimation (2), muscular exercise (3), pretreatment with isoproterenol (4–6), nutritional status (7), body composition (8) and species, strain and age of the animals (9, 10). It has also been shown in rats that the male is more sensitive to necrotizing doses of this agent than the female (10, 12, 14) this difference having been attributed to the greater rate of body weight gain of the male (10, 12).

This study was undertaken to determine the effect of isoproterenol on the heart of the Japanese Quail (*Cotournix cotournix*), an avian species in which the body weight gain of the female is greater than that of the male.

Methods. Sexually mature male and female Japanese Quail, hatched and raised in our facilities, were used in these experiments. Isoproterenol in doses of 80, 60, or 40 mg/kg of body weight was injected sc on two consecutive days at 24-hr intervals. On the third day the animals were sacrificed, the hearts removed under ether anesthesia and the degree of damage evaluated macroscopically. The extent of the lesions were graded using a scheme similar to that devised by Rona *et al.* (11) and used by us previously (7). (0, no necrosis; 1, diffuse paling of the tip; 2, limited necrosis of the tip; 3, necrosis involving one-third of the left ventricle; 4, more than one-half of the left ventricle effected by necrosis).

Results. The body weights of the three groups of birds are shown in Table I. At the beginning of the experiment the mean body weights of the females were approximately 25 g more than the males in each group even though all birds were of the same age.

Both males and females lost body weight in response to the first and second doses of isoproterenol (Table I). However, while body weight losses generally increased with increasing doses of isoproterenol in both sexes, they were considerably greater for the female at each dose level.

The loss of body weight was due in part to a reduction in food intake and in part to a severe diuresis induced by the drug. The diuresis observed in these experiments was particularly notable because it began within minutes of injection and frequently before the bird could be returned to its cage.

The myocardium of the quail suffered necrosis similar in appearance to that seen earlier in rats using comparable techniques and doses of isoproterenol (7). However, a clear sex difference was noted in the greater resistance of the female Japanese Quail to this type of cardiac necrosis. (Fig. 1). Hearts from male birds suffered more extensive damage compared to those from females at the same dose levels. Thus, male birds injected with 40 mg/kg body wt sustained infarcts which had a mean necrotic rating of 1.5 compared to 0.3 for the female birds. The extent of the lesion increased to 2.3 and 1.3, respectively, for the males and females when 60 mg/kg of isoproterenol was injected. Myocardial damage increased still further to 3.4 in the male birds injected with 80

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TABLE I. Mean Body Weights and Percent Body Weight Loss ± SEM in Male (m) and Female (f) Japanese Quail 24 hr After Administration of the First (I) and Second (II) Doses of 40 (A), 60 (B), and 80 (C) mg of Isoproterenol per kg of Body Weight.

Group			Body weight	I	II
A	m	(6)	97.3 ± 2.6	4.84 ± .88	7.48 ± 1.30
	f	(6)	129.2 ± 1.1	9.80 ± .77	12.94 ± 1.63
B	m	(6)	101.7 ± 1.7	7.13 ± 1.45	9.75 ± .79
	f	(6)	128.4 ± 0.8	9.26 ± 1.40	17.77 ± 2.65
C	m	(10)	107.0 ± 2.3	11.81 ± 1.04	14.99 ± 2.02
	f	(9)	125.6 ± 2.7	12.96 ± 2.17	18.41 ± 2.35

mg/kg, but remained at approximately the same level in the female birds as when they were treated with 60 mg/kg.

The distribution of the necrotic ratings for both sexes at each dose level are detailed in Table II.

At the lowest dose level (40 mg/kg) more than 50% of the male hearts received a score of 2 while none of the female hearts were damaged to this degree. At the median dose level (60 mg/kg) better than 80% of the male hearts were scored 2 or more while less than 35% of the female hearts were so damaged. At the highest dose level (80 mg/kg) 90% of the male hearts sustained cardiac damage which was scored as 3 or more while less than 25% of the female hearts were damaged this extensively. One female died after the first injection of 80 mg/kg isoproterenol.

Discussion. The results obtained in these experiments indicate that the response of at least one member of the class Aves (*C. cotournix*) to necrotizing doses of isoproterenol is similar to that reported for rats (1, 5, 7, 10, 13). As previously mentioned, Rona *et al.* (10) demonstrated that male rats were more sensitive to isoproterenol necrosis if compared with females on the basis of age but that the difference in sensitivity disappeared if the comparison was made on the basis of weight. These authors concluded that the greater sensitivity of male rats to cardiac necrosis was due to their greater rate of body growth. This explanation cannot be applied to the present studies because the female birds which weighed more than males of the same age were also more resistant to the necrotizing effects of the drug at three different dose levels. In addition, the damage to the hearts of the males increased in severity as drug dosage was increased while the damage to the female hearts did not continue to increase but rather reached a plateau at the second highest dosage.

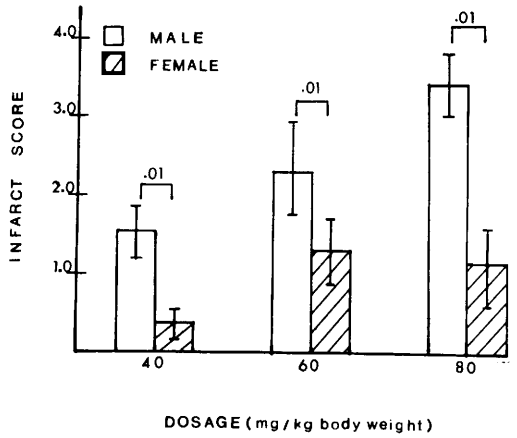

FIG. 1. Severity of myocardial infarcts of male and female Japanese Quail treated with various doses of isoproterenol.

TABLE II. Distribution of Necrotic Ratings and Mortality Among Male (m) and Female (f) Japanese Quail Administered 40 (A), 60 (B), and 80 (C) mg of Isoproterenol per kg of Body Weight.

Group	No. of birds	Ratings 0	1	2	3	4	No. birds died
A	6 m	1	1	4	0	0	0
	6 f	4	2	0	0	0	0
B	6 m	1	0	2	2	1	0
	6 f	1	3	1	1	0	0
C	10 m	1	0	0	2	7	0
	10 f	4	3	0	1	1	1

Both male and female quail lost weight in response to isoproterenol administration and weight loss increased with increasing doses of the drug. However, body weight loss was considerably greater than that reported by us earlier for rats at comparable dose levels (7) and was greater at each dose level for the female. Isoproterenol injection was accompanied in both groups by a severe diuresis and hyperventilation within minutes of injection. Since no attempt was made to quantitate the respiratory response or urine loss, it is unknown whether the greater loss of body weight in the female can be explained on the basis of water loss.

Summary. Japanese Quail (*C. cotournix*) treated with isoproterenol at three different dose levels showed cardiac necrosis similar to that seen in rats. The extent of the lesion and the amount of body weight lost after isoproterenol administration increased with increasing doses of the drug. Female quail suffered less extensive cardiac lesions but lost more body weight at each dose level. Since the male of this species weighs less than the female, the increased susceptibility of the male to the necrotizing effects of this drug cannot be explained on the basis of body weight.

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