

Increase in Testis Weight of Hereditary Dwarf Rats (*rdw/rdw*) with Advancing Age

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Testis weight and seminal vesicle weight (relative to total body weight) in *rdw* rats and N rats were compared with advancing age. The results obtained were as follows 1) The increase in testis weight became remarkable at 15-16 weeks of age. The weight remained constant up to 23-30 weeks of age and decreased thereafter with age. 2) Seminal vesicle weight increased rapidly in *rdw* rat at 15-16 weeks of age, reflecting elevated androgen secretion and sexual maturation. 3) From the viewpoint of histology, one of causes of the increase in testis weight may be edema. The increase in testis weight coincided with the increase in androgen secretion at 15-16 weeks of age as suggested by the relative increase in seminal vesicle weight. —KEY WORDS : aging, *rdw* rat, testis wt. increase

The *rdw* rat is a hereditary dwarf mutant [2]. The body weight of the *rdw* rat is less than half that of normal litter mates (N) at 4 to 15 weeks of age, and the mutant gene related to the expression of dwarfism is considered to be recessive on the autosomal chromosome since expression is independent of sex [2]. We have been producing these mutant rats over many generations by mating F₁ parents, and the rate of the occurrence of dwarfism has been previously reported [2].

We estimated the levels of several kinds of hormones in the blood and pituitary at 10 weeks of age or less with a radioimmunoassay technique. Findings included that *rdw* rats, as compared with normal litter mates, have remarkably lower levels of growth hormone (GH), lower levels of prolactin (PRL) in the pituitary and blood and lower blood levels of insulin like growth factor 1 (IGF-1), reflecting decreased GH synthesis and release by the pituitary [4,5]. We also observed decreased levels of blood thyroxine at 10 weeks of age [5].

At the completion of studies, when we routinely weighed gonads and accessory genital

organs at autopsy, we noticed that the increase in testis weight with advancing age was greater in *rdw* rats than in N (Fig. 1: 21 weeks of age). We subsequently examined the alteration of the testis weight and seminal vesicle weight at several ages.

F₁ parents were mated to obtain *rdw* rats, and *rdw* and N pups were fed according to similar feeding conditions as previously reported [4,5]. From 1990 to 1993, the body and organ weights (testis and seminal vesicle) of a total of 105 male rats, namely 60 dwarf and 45 N rats, at various ages were measured. Rats were sacrificed in most cases by decapitation and in some cases by bleeding from the jugular vein under ether anesthesia. The obtained data were categorized by age into eight groups as detailed in Table 1. Differences were tested for significance by Student's *t*-test to compare *rdw* rats with N rats.

Body weight : At all ages, the body weight of *rdw* rats was significantly lower (1/2 or less) than that of N rat (Table 1).

Testis weight : *rdw* rats showed a significantly lower value than N rats at 10 and 11-12 weeks of age. The difference lessened at 13-14 weeks

Table 1. Body weight and organ weight (testes and seminal vesicle) at various ages (weeks) in *rdw* and normal rats

Weeks of age	<i>rdw</i> or N (No. rats)	Body wt. (B) (g)	Testes wt. (T) (mg)	Seminal vesicle wt. (T) (mg)	T/B	S.V./B
10	<i>rdw</i> (18)	115.2***	1,691.2***	203.2***	14.4**	1.5**
		± 5.4	± 154.5	± 43.1	± 1.1	± 0.3
	N (15)	275.2	2,919.9	739.7	10.7	2.7
		± 9.9	± 63.5	± 60.1	± 0.3	± 0.2
11~12	<i>rdw</i> (8)	125.6***	1,930.0**	284.9***	15.3***	2.1
		± 11.6	± 207.8	± 70.8	± 0.7	± 0.4
	N (7)	278.3	2,977.0	753.0	11.0	2.8
		± 19.1	± 40.6	± 77.9	± 0.7	± 0.4
13~14	<i>rdw</i> (3)	147.0*	2,791.0	481.3	18.6	3.2
		± 7.8	± 743.3	± 218.5	± 4.5	± 1.4
	N (3)	321.0	3,144.0	1,082.0	10.0	3.5
		± 37.4	± 75.8	± 98.9	± 1.0	± 0.5
15~16	<i>rdw</i> (5)	160.4*	3,915.2	1,005.6	24.3***	6.2**
		± 12.2	± 387.6	± 132.6	± 1.1	± 0.5
	N (3)	321.0	3,093.7	726.3	11.5	2.5
		± 37.4	± 66.4	± 246.1	± 1.6	± 0.5
17	<i>rdw</i> (4)	189.8***	4,301.3***	1,013.3	22.8***	5.4
		± 8.0	± 71.5	± 10.5	± 1.1	± 0.3
	N (5)	376.6	3,167.2	1,190.4	8.4	3.1
		± 11.4	± 94.5	± 115.1	± 0.2	± 0.3
21~22	<i>rdw</i> (6)	165.7***	3,990.7**	924.0	24.2***	5.7*
		± 6.3	± 90.4	± 103.6	± 0.8	± 0.8
	N (4)	356.0	3,280.0	1,097.5	9.3	3.1
		± 13.2	± 110.4	± 142.9	± 0.6	± 0.3
23~30	<i>rdw</i> (4)	182.8***	4,206.5*	744.0	23.4**	4.0
		± 19.4	± 289.9	± 192.2	± 1.5	± 0.7
	N (4)	434.3	3,409.0	1,274.3	7.9	2.8
		± 31.3	± 103.8	± 241.7	± 0.3	± 0.4
31~56	<i>rdw</i> (12)	206.2**	3,656.0	493.8***	16.9***	2.4*
		± 8.6	± 267.7	± 74.5	± 1.4	± 0.4
	N (4)	491.8	3,553.3	1,706.8	7.0	3.5
		± 39.4	± 102.7	± 101.5	± 0.5	± 0.3

M±S.E. * : P<0.05 ** : P<0.01 *** : P<0.001

of age, and at 15~16 weeks of age the *rdw* rats had larger testes. The testis weight in *rdw* rats was significantly higher at 17, 21~22 and 23~30 weeks of age, but no difference between the two types of rats was seen at 31~56 weeks of age.

Testis weight relative to body weight: The value in the *rdw* rats was larger than that in the N rats at all ages examined, and there was a significant difference at all ages except at 13~14 weeks of age. Ookuma and Kawashima developed GH deficient dwarf rats and reported

that the testis weight relative to body weight in the dwarf rat is 1.8 times that in normal litter mates at 25 weeks of age [3]. The value in the *rdw* rats in the present report was about three-fold higher than that in the N rats, indicating an abnormality in the weight (Table 1).

Weight of seminal vesicles: The seminal vesicle weight in *rdw* rats was significantly lower than that in N rats at 10 and 11~12 weeks of age, and this trend was seen up to 13~14 weeks of age. Such a difference between the two groups was not seen at 15~16 to 21~22 weeks

of age. The seminal vesicle weight was decreased in *rdw* rats at 23~30 weeks of age and was remarkably lower in *rdw* rats than in N rats at 31 weeks of age (Table 1).

Seminal vesicle weight relative to body weight : The value in *rdw* rats was significantly lower than that in N rats at 10 weeks of age, and a lower value was still seen at 11~12 and 13~14 weeks of age. However, the value rapidly increased at 15~16 weeks of age. Since an increase in the value (relative to the weight of testes) reflects elevated secretion of androgen from testes, it was concluded that sexual maturation of the *rdw* rat occurs at this time. This high value was still seen at 21~23 weeks of age, but the value was significantly decreased after 31 weeks of age. The decreased weight in *rdw* rats seemed to reflect lowered secretion of androgen as it corresponded with smaller testis weight at the same age.

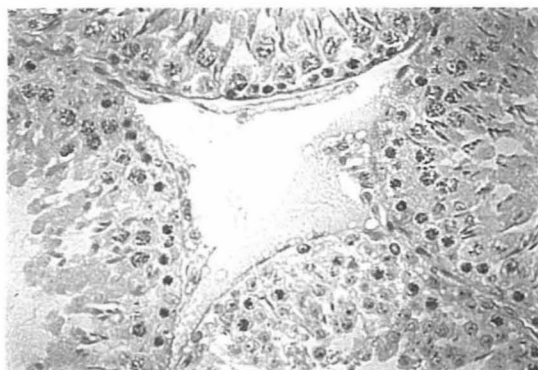
Histology of the testes : Histology of the testes was examined at 17 weeks of age, when the difference in testis weight was prominent (Fig. 2). Testes were fixed in Bouin's solution, embedded in paraffin, sectioned at 7 μ m and stained with hematoxylin-eosin. The protein component, which seemed to have originated in the blood, was lightly stained with eosin in the interstitial region between the seminiferous tubules. Since erythrocytes were not observed within the interstitial region, the staining does not seem to be due to congestion (Fig. 2(A)). On the contrary, no staining with eosin in the interstitial region between the seminiferous tubules was observed in N rats (Fig. 2(B)). From these observations, the testes of the *rdw* rats at 17 weeks of age were determined to be edema.

Up to now, this phenomenon, namely an increase in testis weight with advanced age, has not been observed in dwarf mice [6] or dwarf rats [1,3] with pituitary GH deficiency. Since the *rdw* rat is characterized by GH and PRL deficiency, it is interesting to speculate whether PRL deficiency is related to the increase in testis weight and the appearance of edema in the testis. Alternatively, some genetic defects in *rdw* rats may be directly related to this phenomenon. A further research is needed to elucidate these points.

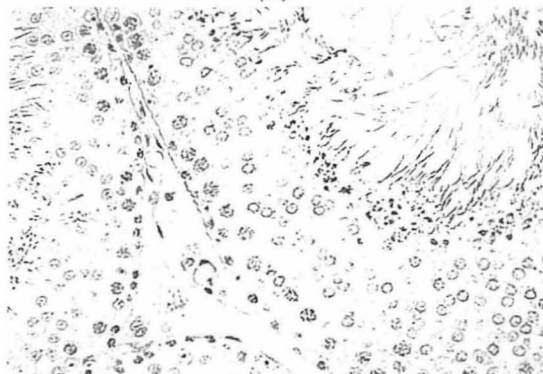
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Fig. 1. Appearance of testes in a *rdw* rat and a normal litter mate at 21 weeks of age



(A)



(B)

Fig. 2. Histology of the testis in (A) an *rdw* rat and (B) normal rat at 17 weeks of age ($\times 500$)

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遺伝的侏儒症モデルラット (*rdw/rdw*) の 加齢に伴う精巣重量の増加について

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加齢の進んだ *rdw* ラットの剖検時にその精巣重量が異常に大きいのに気付いた。従来、侏儒症マウスや下垂体 GH 単一欠乏の侏儒症ラットではこのような現象の報告は見られないので、精巣重量と精嚢腺重量の実重量と比体重重量を加齢の過程で *rdw* ラットと N ラットで比較した。結果は以下の通りであった。1) *rdw* ラットでは15~16週齢で精巣重量の増加は顕著となり、その増加は23~30週齢まで維持され、31週齢以後では

低下した。2) 精嚢腺重量は *rdw* ラットでは15~16週齢で急増し、アンドロジェンの昂進が窺われ、この時期に *rdw* ラットは成熟に達するものと考えられた。その重量は31週齢以後では低下した。3) 組織学的所見から、*rdw* ラットの精巣重量の増加の原因の一つは水腫によるものと考えられ、その出現はアンドロジェンの分泌の昂進の時期とほぼ一致した。