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Influence of Sex and Age on the Diabetic Traits in a Strain of Rats.*

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Reports by the authors[1, 2] have shown that a high percentage of the sexually mature male rats from their "Y" strain exhibit characteristics of a hyper or unbalanced secretion of the diabetogenic factors of the anterior pituitary. Thus, their fasting blood sugar is high, their glucose tolerance is low, their hyperglycemic response to epinephrine is exaggerated, and their reaction to insulin is delayed. In the earlier work females were avoided, since they offered complicating factors not found in the males, but with the diabetic characteristics of the male established, it became necessary for genetic studies to investigate the female. Also, in view of the well-recognized sex differences both in metabolism and in the incidence of spontaneously occurring diseases[3–9] an investigation of the female appeared in order. The effect of age on the glucose tolerance of females has served to introduce an extension of the data on this factor in males.

The analytical methods, general procedure and criteria were the same as those used in studies on the male, and may be summarized as follows: Glucose tolerance tests on females from the "Y" and Wistar strains, maintained on the same diet and under the same conditions for 5 to 7 generations, were made 15 to 16 hours after food had been withdrawn. The glucose was administered intraperitoneally,† 3.5 g per kg, and followed by the determination of the

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† A comparison of the results obtained by the intraperitoneal and intragastric administration of glucose was discussed in a previous paper.[1]

"true" blood sugar at appropriate intervals. The criteria for a normal curve demand that: (a) the half-hour blood sugar must be greater than the first hour value; (b) the half-hour value must be less than 300 mg %; (c) the fifth hour value must be at least 40 mg % below the half-hour or 60 mg % below if the half-hour value is over 200 mg %; (d) the fifth hour blood sugar must be below 180 mg %.

Data obtained with a large number of males from the authors' colony of the Wistar strain have failed to give a diabetic glucose tolerance in animals presenting a healthy physical appearance, and for this and other reasons[1, 2] the Wistar strain is considered normal. Tests on females of the normal strain (Table I) duplicate reasonably well those previously published on males,[1] however, the data on the females show a slightly larger probable error, and 2 of the 37 tests recorded in Table I are diabetic. Grouping the tests according to their period in the estrous cycle (Table I), both of the diabetic curves occur in diestrus, but when these tests were repeated during the same period of the cycle they were normal. The average of the tests made during diestrus is not significantly different from those in

TABLE I.

A Comparison of the Glucose Tolerance of Females from the Wistar and "Y" Strains.

Age range days	No. of rats	Fasting	Hours after glucose* ½	1	2	3	5
		"True" sugar in terms of glucose per 100 cc of blood					
		mg	mg	mg	mg	mg	mg
Wistar Strain							
114-141	18	69±1.1	172±3.0	125±3.5	110±1.5	108±2.2	105±3.8
134-148	19	72±1.1	187±3.9	119±2.8	102±1.9	101±2.0	96±2.8
Chance that deviation is due to sampling		19/100	41/100	39/100	9/100	11/100	19/100
Above tests grouped according to period in estrus cycle.							
	No. of tests						
Proestrus	9	7	70	161	120	107	103	101
Estrus and Metaestrus	14	8	68	171	120	104	103	98
Diestrus	14	8	73	186	126	107	106	102
"Y" Strain (Diabetic Curves)							
101-140		21	77	235	203	193	193	218
141-300		21	87	239	202	206	212	192
>300		12	77	216	188	211	225	250
"Y" Strain (Normal Curves)							
101-140		27	69	215	176	126	133	129
141-300		13	67	238	202	162	146	136
>300		7	79	219	192	160	150	140

* 3.5 g per kg in a 10% solution, intraperitoneally.

the other periods, nevertheless, this period was avoided in tests on the "Y" strain.

Tests on 101 females of the "Y" strain are reported in Table I, and comparisons of these data with those published on the males[1] and with those in Table III indicate no important sex differences;

TABLE II.
Statistical Significance of Age and Sex Differences in Incidence of Diabetic Curves. ("Y" Strain).

Sex	Age range	% diabetic	Compared with			Chance that deviation is due to sampling
			Sex	Age range	% diabetic	
Male	71-100	48	Male	51-70	14	.000,0007
			"	101-140	66	.02
			"	141-180	57	.27
			"	181-240	67	.018
			"	241-300	78	.0003
Male	101-140	66	"	141-180	57	.27
			"	181-240	67	.90
			"	241-300	78	.12
			Female	101-140	44	.014
			"	141-300	62	.70
			"	>300	62	.76

TABLE III.
Effect of Age on the Normal and Diabetic Glucose Tolerance Curves of Males from the "Y" Strain.

No. of rats	Age range days	Fasting	Hours after glucose* ½	1	2	3	5
		"True" sugar in terms of glucose per 100 cc of blood					
		mg	mg	mg	mg	mg	mg
		Diabetic Curves					
38	91-120	74	189	188	188	195	195
†61	121-180	78	199	204	197	201	202
43	181-240	78	188	182	177	185	186
†34	241-300	85	222	223	222	233	246
‡13	301-365	84	228	221	208	221	235
‡22	366-730	72	218	232	205	215	231
		Normal Curves					
20	91-120	76	210	195	161	146	136
40	121-180	77	210	186	155	151	133
21	181-240	83	223	205	164	159	141
10	241-300	75	217	194	157	151	135
‡3	301-365	82	212	206	166	149	155
‡2	366-730	81	220	213	179	177	115
†Chance that difference is due to sampling			9/1000	1/10	3/100	1/100	7/1000

* 3.5 g per kg in a 10% solution intraperitoneally.

‡ The ratios of diabetic to normal curves in the age groups over 300 days are grossly distorted because the normal rats have been sacrificed in other experiments.

the types of the diabetic curves are the same, the average values are of the same order, and the percentages of diabetic animals in the age groups are similar except for the group 101-140 days. Here only 44% of the females but 66% of the males are diabetic, and a statistical analysis of these data (Table II) shows that the chances are 100 to 1 that the difference is real. Thus, the females lag behind the males in the development of a low glucose tolerance and reach their maximum, 62% of diabetic curves, around 140 days of age. Attention should be called to the fact that the glucose tolerance of the males is normal to 50 days of age,[1] but thereafter the incidence of diabetic curves increases until it reaches 66% at 100 days of age with only a questionable additional increase after 240 days (Table II).

Relevant to the problem of whether or not the diabetic curves become more severe with age, Table III lists the averages for 307 tests made on males of the "Y" strain ranging in age from 90 to 730 days. The data suggest that after 240 days there is a further decrease in the glucose tolerance of the diabetic males. Normals of the "Y" strain do not show a similar change.

Summary. 1. Females of the "Y" strain exhibit a low glucose tolerance similar to that of the males. 2. The estrous cycle has no conspicuous effect on the glucose tolerance. 3. After 240 days of age, the severity of the diabetic curves in the males appears to increase.

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Androgenic Function of APL Stimulated Ovaries in Immature Rats.*

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The present authors have reported that the administration of chorionic gonadotropic hormone (APL) to very young, immature female rats causes definite growth of the clitoris.[1] This gross enlargement was associated with modifications in the male direction as

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