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ON THE GROWTH OF THE ALBINO RAT (MUS NORVEGICUS VAR. ALBUS) AFTER CASTRATION. By J. M. Stotsenburg, M.D., *Curator and Junior Associate in Anatomy at The Wistar Institute.*

No systematic study of the growth of any mammal after castration has yet been reported. The existing literature on castration deals mainly with its application to domestic animals for economic purposes. There are, however, some general descriptions and measurements made during life on human castrates; Matignon ('96), Pelikan ('76) and Jameson ('77), also several reports of dissections of eunuchs; Ecker ('64-'65), Gruber ('47), Lortet ('96), Becker ('99), Tandler and Grosz ('09), together with a considerable number of investigations on animals showing the dependence of the secondary sexual characters on the integrity of the testes; Ribbert ('98), Rörig ('99, '99A, '01), Sellheim ('98) and Foges ('02).

Further we have some literature, based on animal experiments, touching the interdependence of the hypophysis and of the thyroid gland on the testes: Fichera ('05, '05A), Richon and Jeandelize ('05, '05A).

In chickens, rabbits and dogs studies have been made on the growth of parts of the skeleton, especially the growth of the limb bones which become longer than normal: Poucet ('78), Richon and Jeandelize ('05B, '05C), Sellheim ('99).

Finally, McCrudden ('08) has studied the metabolism of castrated dogs, using the excretion of salts as an index. These experiments show the operation to be without any marked influence on metabolism in this animal.

The chief result of the experimental work is, therefore, to show that many secondary characters in mammals and birds are modified in their development by injury or removal of the testes, and that the latter probably produce their effect through some form of internal secretion, as shown by the observations of Walker ('08). The growth of parts of the skeleton and some of the ductless glands are also in a measure and in some animals affected by castration.

In the present communication, however, we shall consider the influence of castration only in relation to the increase in body

weight with age, making incidentally one application of the results to the phenomenon of prepubertal growth in man.

The observations to be presented were made on the albino rat (mus norvegicus var. albus) and are arranged in three series; one made for Dr. Donaldson in the Neurological Laboratory of the University of Chicago by Dr. S. W. Ranson in 1905-6, and the others by myself at The Wistar Institute in 1907 and 1908.

The comparison in growth was made always between members of the same litter, some of which were castrated, while the others were left intact to serve as controls. All the members of one litter were reared together in the same cage and fed similarly. The diet was ample and varied and included milk, except in series two.

The operation proved to be simple, and was performed on the fourteenth or fifteenth day after birth, at which time the sexes can be easily distinguished.

The males of the litter were removed from the nest and weighed to determine whether they were of normal weight. Each one was then marked upon the pinna of one or both ears. Those selected for controls were returned to the nest, while those assigned for operation were placed in warm cotton. For operation the animal was anæsthetized and the operation conducted under antiseptic precautions:—

The incision was made in the mid-line of the perineum and each testis drawn forward and its connections severed. The wound was washed with bichloride and dressed without stitches with thin celloidin. No case of infection of the wound occurred, and all the operations were successful.

All traces of blood or its odor must be removed before the rat is returned to the nest, otherwise the mother is apt to kill it.

In returning the operated rats to the nest, the mother was first removed and kept away until the operated animals had become satisfied to remain with the balance of the litter and had acquired the odor and warmth of the nest.

The mother was then allowed to enter and was not disturbed for twenty-four hours, after which time it was found there was not much danger that the young would be destroyed by her.

The weight record was taken at regular intervals, increasing

from daily records to those taken once a week. The rats were disturbed as little as possible in the process, the cage always being taken to the balance table, the rat gently placed in a perforated tin box (balanced by a counterweight) and weighed as quickly as possible, and the record set down opposite the record of the distinguishing ear-mark.

It was found best not to attempt to weigh the rats immediately after any unusual excitement in the colony-room, as under such conditions they show a temporary loss of weight; even the presence of strangers may cause them to become unusually restless and easily frightened.

The weighing was continued as long as the animals remained in a healthy condition, and the weights of a litter maintained a comparative uniformity.

During the period between 150 and 200 days, the albino rat is subject to numerous affections which disturb its growth, so it was found impracticable to follow more than a few litters beyond 200 days.

The data for these records are based on 99 animals, of which 52 were castrated and 47 were controls. These fall into three series.

While the observation of no one series was continued during an entire year, the combined records include the 12 months, so that any pronounced seasonal influence, if present, could be noted. No indication of such influence has thus far been observed.

In series No. 1, the records for which were made by Dr. S. W. Ranson at the University of Chicago during the summer and fall of 1905, continuing into the spring of 1906, there were ten litters numbering 40 animals, of which 21 were castrated and 19 were controls. The constitution of the series was the following:

Litter	Number of castrated.	Number of controls.
1	3	3
2	2	2
3	3	3
4	1	1
5	2	2
6	2	1
7	4	4
8	2	1
9	1	1
10	1	1

In series No. 2, the records for which were made at The Wistar Institute, Philadelphia, during the summer and fall of 1907, there were 8 litters numbering 27 animals, of which 14 were castrated and 13 were controls. The constitution of the series was the following:

Litter	Number of castrated.	Number of controls.
1	1	1
2	2	2
3	1	1
4	2	1
5	3	3
6	1	1
7	1	1
8	3	3

In series No. 3, the records for which were made at The Wistar Institute during the winter, spring and summer of 1908, there were 9 litters numbering 32 animals, of which 17 were castrated and 15 were controls. The constitution of the series was as follows:

Litter	Number of castrated.	Number of controls.
9	3	2
10	2	2
11	1	1
12	1	1
13	2	2
14	2	2
15	3	2
16	1	1
17	2	1

It will be impracticable to give the records for all the litters in each series, but to show how the two groups in each litter change during growth, three examples will be given as represented by litters 2, 4 and 5 of Series 2. The tabulated results are not given, but the curves based on them are shown in Figure 1.

These three records serve to illustrate what took place in all the series, *i. e.*, in some litters the castrated grew faster, in some the con-

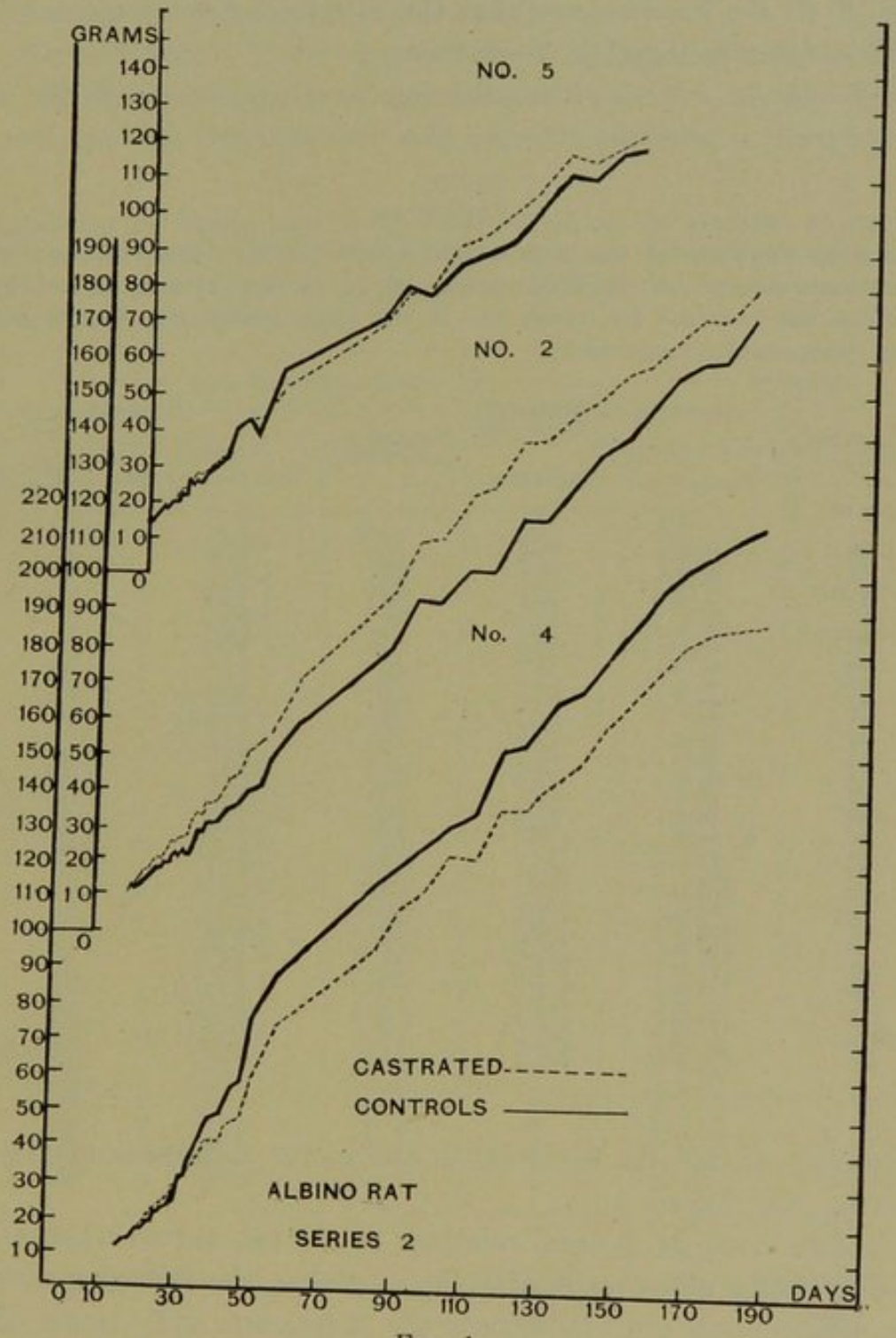
GRAMS
NO. 5
NO. 2
No. 4
CASTRATED
CONTROLS
ALBINO RAT
SERIES 2
DAYS

Fig. 1

trols, and in others the two curves were nearly identical. The immediate effect of the operation on growth was not detectable. A review of all the litters shows that the castrated surpass the controls about as often as they fall below them.

Moreover in a given litter the incidental variations in the two groups tend to coincide, showing that the castrated rats are just as

TABLE 1.

Showing for Series 1 the body weight based on the average of the litters at different stages. In the fifth column are given the numbers of the litters on which the averages are based, and in the sixth column the number of the litters permanently removed.

Average Age. Days.	Body Weight in Gms.		Number of Individuals.	Litters.	
	Castrates.	Controls.		Used for Averages.	Permanently Removed.
16	17.6	17.8	15	1–10.	
20	21.4	22.0	20	1–10.	
27	27.2	27.9	20	1–10.	
27	32.5	32.7	20	1–10.	
31	42.0	37.4	10	1–10.	
33	40.6	40.7	10	1–10.	
36	43.5	43.9	10	1–10.	
39	46.8	47.2	10	1–10	
42	48.2	51.7	9	1–3, 5–10	
45	52.5	56.7	9	1–3, 5–10	
48	58.2	60.9	9	1–3, 5–10	
51	63.0	67.1	8	1–4, 6–8, 10	
54	68.8	70.5	10	1–10.	
57	78.9	77.7	8	1–7, 9, 10.	
60	78.0	79.5	10	1–10.	
63	84.8	79.9	8	1–7, 9.	
66	95.2	93.8	8	1–8.	
74	102.8	101.8	12	1–9.	
78	108.0	103.7	9	1–7, 10	
83	116.3	116.9	12	1–9.	
87	122.4	123.1	10	1–8, 10	
93	130.6	130.0	9	2–7, 9.	
99	137.9	141.2	11	1–10.	
106	148.8	144.7	10	1–7.	
116	151.7	147.8	4	1, 4, 5, 10.	
125	157.0	165.3	9	1, 4, 6–8.	
134	165.8	174.6	7	1, 2, 4, 7, 10.	
143	179.9	191.4	5	1, 4, 8.	5, 7, 10.

susceptible as are the controls, to the minor influences modifying growth. See Figure 1.

To determine the general relations of the two curves when all of the litters of a given series are taken together, the following method was used:

The average weights of the individuals in each group of each litter was determined at the time of each weighing.

These averages were tabulated according to age in days.

The results were then averaged for all of the litters in the series and again tabulated according to age in days.

Since different litters vary widely in their growth, it seemed best in the final, averages just mentioned to take the average for each

TABLE 2.

Showing for Series 2 the body weight based on the averages of the litters. at different ages. In the fifth column are given the numbers of the litters on which the averages are based, and in the sixth column the number of the litters permanently removed.

Average Age. Days.	Body Weight in Gms.		Number of Individuals.	Litters.	
	Castrates.	Controls.		Used for Averages.	Permanently Removed.
16	15.5	15.2	12	1–8.	
18	16.7	16.6	16	1–8.	
20	18.4	18.3	16	1–8.	
22	20.6	20.3	16	1–8.	
24	22.9	22.4	16	1–8.	
26	25.0	24.6	16	1–8.	
28	26.6	26.5	16	1–8.	
30	28.8	28.5	14	1–8.	
32	30.6	31.2	14	1–8.	
34	31.4	32.7	12	1–6.	
36	35.1	36.5	11	1–5, 7, 8.	
38	42.9	43.6	8	1, 2, 5–8.	
40	43.2	44.9	7	1–4, 6.	
42	45.3	48.3	6	1, 3–5, 7, 8.	
44	54.2	56.4	5	1, 2, 5–7.	
46	44.9	45.0	4	2–4, 6.	
48	48.6	52.9	5	1, 3–5, 8.	
50	60.6	62.0	4	1, 2, 5, 6.	
52	60.7	63.5	4	2, 3, 4, 7.	
55	69.4	77.8	5	1, 2, 5, 6.	
66	76.3	78.5	5	1–4, 8.	
80	94.6	92.6	4	5–8.	
87	99.9	102.0	8	2, 3, 5–8.	
94	106.7	107.5	8	2–8.	
101	110.8	112.0	8	1–8.	
108	119.0	118.0	8	1–8.	
115	122.4	121.8	8	1–8.	
122	129.0	126.0	7	2–8.	1.
130	131.9	133.3	10	2–8.	
137	140.4	140.6	5	2, 4–7.	
144	143.5	144.6	5	2, 4–7.	3, 8.
151	149.1	149.4	5	2, 4–7.	
159	156.6	160.3	6	2, 4–7.	
166	166.8	166.7	4	2, 4, 6, 7.	
174	175.3	170.5	4	2, 4, 6.	7.
185	182.6	190.7	4	2, 4.	6.

litter as a unit, and not to weight it by the number of individuals in the litter. The averages of the observations are made at short intervals for the first fifty or sixty days, and then at longer intervals to the end of the series.

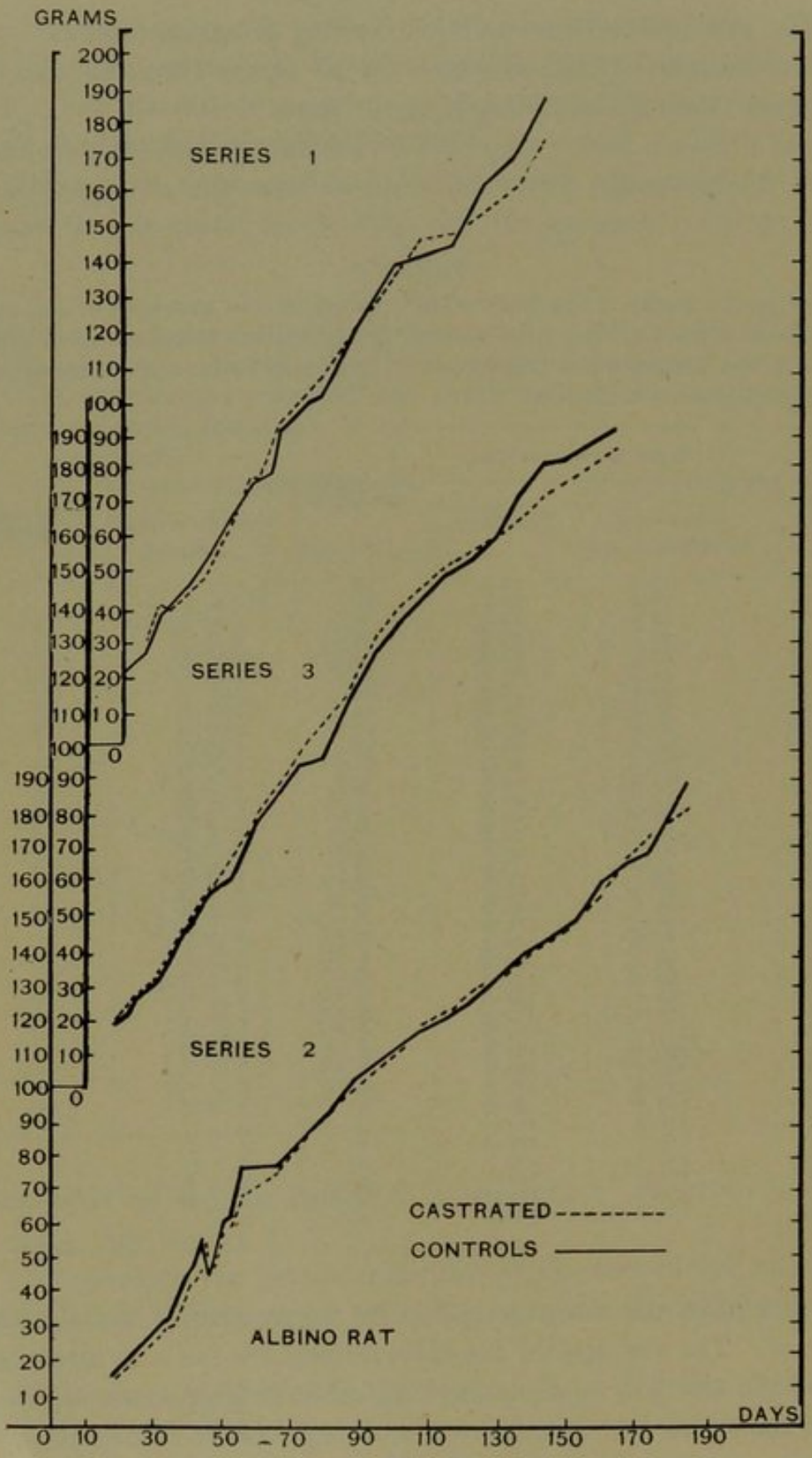
GRAMS
SERIES 1
SERIES 3
SERIES 2
CASTRATED
CONTROLS
ALBINO RAT
DAYS

Fig. 2.

The results thus obtained are given in tables 1, 2 and 3 and in Figure 2. In explanation of tables 1, 2 and 3, the following comments are in place.

In the age groupings used, not all the litters are represented every time. This of course tends to alter the direction of the curves, but does not modify the value of the comparison between the castrates

TABLE 3.

Showing for Series 3 the body weight based on the averages of the litters at different ages. In the fifth column are given the numbers of the litters on which the averages are based, and in the sixth column the numbers of the litters permanently removed.

Average Age. Days.	Body Weight in Gms.		Number of Individuals.	Litters.	
	Castrates.	Controls.		Used for Averages.	Permanently Removed.
18	18.9	18.9	8	9–16.	
21	22.0	21.4	8	9–14, 16, 17.	
23					
25	25.9	26.1	8	9–15, 17.	
28	29.2	28.5	8	9–14, 16, 17.	
30					
32	33.5	32.3	7	9–14, 17.	
35	41.3	38.9	8	9–14, 16, 17.	
38	45.4	44.7	7	9–14, 16, 17.	
42	50.4	49.8	9	9–17.	
45	56.0	56.4	9	9–17.	
49	60.3	59.4	9	9–17.	
52	67.2	65.5	9	9–17.	
56	72.4	71.0	9	9–17.	
60	78.3	76.5	9	9–17.	
63	82.4	80.9	9	9–17.	
67	88.3	86.3	9	9–17.	
72	97.2	94.0	16	9–17.	
79	107.0	102.5	11	9–17.	
86	114.8	113.4	10	9–17.	
93	129.0	125.3	9	9–17.	
100	140.0	135.3	9	9–17.	
107	146.4	143.4	9	9–17.	
114	153.2	150.1	9	9–17.	
121	157.2	155.0	8	9–17.	
128	161.3	159.2	9	9–17.	
135	168.5	174.3	8	9–11, 13–17.	12.
142	177.0	182.7	7	9–11, 14–17.	13.
149	181.5	183.5	7	9–11, 14–17.	
156	184.1	187.6	7	9–11, 14–17.	17.
164	189.6	190.3	9	9–11, 14–16.	
172	188.7	198.3	6	9–11, 15, 16.	
181	195.2	202.4	6	9–11, 14–16.	

and controls. A notable instance of this occurs at 46 days in Series 2. See Table 2 and Figure 2. In column 5 of the tables, the litters involved in each average are indicated by their numbers.

Moreover, towards the end of the series, observations on some litters ceased earlier than on others, and the effect on the curve is simi-

lar to that described above, with the additional effect of permanently reducing the number of cases and hence the general significance of the averages.

Observation in the case of any litter was usually brought to a close by some illness which interfered with the normal growth of one or more of the animals.

In such a case, observations on that litter were discontinued. When this occurred, the fact is noted in the last column of each table.

Conclusions.

1. In the case of albino rats, the growth curve for the castrates is similar to that for the normals.

2. Castrates are as susceptible as normals to the incidental influences modifying growth.

3. Castrates are as susceptible as normals to the forms of disease and digestive disturbances which hinder normal growth.

Although these observations show that in the albino rat the normal growth curve is not modified by castration, yet it is not uncommonly assumed that in man prepubertal growth is casually related to the maturing of the reproductive system at puberty.

Against this assumption, in addition to the direct evidence furnished by the foregoing observations, the following facts may be adduced:

In man castration is not usually practised before the ninth year (Möbius, '96). Castrates are never described as dwarfed, and are often stated to be heavier (*i. e.*, fatter) or to have longer limb bones than normal (Ecker, '64, '65), (Lortet, '96), (Tandler and Grosz, '98).

The amount of growth is then certainly not diminished, and it seems probable therefore that prepubertal growth it not retarded by castration. Indeed there are positive statements in the literature to the effect that it is increased.

Further in support of the idea that the relation between puberty and prepubertal growth in man is merely incidental, we have the fact that in the rat the corresponding point in the growth curve,

where the females are heavier than the males, comes to end at 50 days, while puberty does not occur until about 70 days (Donaldson, '06) and in the guinea-pig the corresponding period comes to an end at 19 to 31 days and puberty is not attained until 150 days (Minot, '91).

It seems highly probable therefore that puberty in man is not a factor in stimulating prepubertal growth.

It is desirable to emphasize in closing that these conclusions are not to be interpreted as invalidating the view, which rests on good experimental evidence, that the full development of secondary sexual characters in some birds and mammals at least, is dependent on the integrity of the testes which act directly or indirectly through some form of internal secretion.

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