

THE GROWTH OF THE FETUS OF THE ALBINO RAT FROM THE THIRTEENTH TO THE TWENTY- SECOND DAY OF GESTATION

J. M. STOTSENBURG

The Wistar Institute of Anatomy and Biology

TWO FIGURES

For the prenatal growth in weight of the human body Jackson ('09) has presented data gathered by himself and compared these with such data as had already been published. Similarly, Lowrey ('11) has studied the prenatal growth of the pig. In both cases the authors have found it necessary to depend in part on preserved material. While preservation may not alter materially the relative weights of parts of the body, it undoubtedly does alter the total body weight and the records for that character must be interpreted, therefore, with this fact in mind.

The following study on the growth of the fetus of the albino rat forms another series of observations on the prenatal growth of the mammal and has the special virtue of being made throughout on fresh specimens.

The fetuses were all from second litters, the female having been allowed to breed once and to raise her litter under observation, so that we might be assured of her normal behavior as a breeding animal. The data have been gathered from the colony at The Wistar Institute between 1907 and 1913.

METHODS

The female was mated for the second time, under observation, and after the lapse of the desired interval, was killed with ether. The fetuses were removed, cleared of membranes, and then each placed in a previously weighed stoppered vial and the weight determined to a tenth of a milligram. The operation was al-

ways conducted within a protecting chamber to prevent the loss of moisture by evaporation. The fetus of 13 days was found to be the youngest which would stand manipulation without damage and the observations begin with that age. The litters of 38 females have been thus studied. The total number of fetuses removed was 336, giving an average of 8.8 per litter, with a range of from 3 to 16 fetuses per litter. For 330 of these the exact weights have been obtained.

The observations furnish records for the weights of the fetus from the 13th to the 22d day inclusive—the latter being about the time of birth—under usual conditions, and within these limits they give the weights of the fetus at approximately twenty-four-hour intervals. The observed weights for this series are entered in table 1.

When the data of table 1 are combined and the means taken, we obtain the mean fetal weights given in table 2. The values given in table 2 are the means of the averages for the several litters of like age. Thus the average value for each litter was given the same weight irrespective of the number of fetuses in the litter. When the data of table 2 are plotted they furnish the graph in chart 1. The form of this graph illustrates the rate of growth as given in table 2 and this agrees with the general observation that in the growing fetus the rate tends to diminish with advancing age.

It has been pointed out by Donaldson ('06) that we may assume the span of life in the albino rat to be three years—between birth and natural death—and that this span in the rat is equivalent to ninety years in man. On this assumption the rat grows thirty times as rapidly as man. If we apply this ratio to the gestation period it follows that one-thirtieth of the human gestation period is about 9 days, but the rat has a gestation period of some 22 days. The explanation of this discrepancy between the rate of prenatal and that of postnatal growth is still wanting but the recent observations of Huber ('15) on the early stages of development in the Albino show that the first phases go very slowly. Taking 22 days for the gestation period of the Albino and 271 days (Mall, in Keibel and Mall '10) for

TABLE 1

Giving the observed weights of the fetuses at different ages from the 13th to the 22d day of gestation. Where the horn of the uterus from which the fetus came and its relative position in the horn were not noted, the fetus weights are given in ascending values under the heading 'Horn and position not noted.' When these facts were noted the weights of the fetuses are given under the respective horns and in serial order, no. 1 being the fetus nearest to the ovary. In a few cases the horn was noted but the order of the fetuses not determined. All the weighings were made to the tenth of a milligram, but in the table only three digits are entered. The diet of the mother, which appears to influence the number of fetuses, is also given

SERIAL NO.	AGE OF LITTER		DIET	HORN OF UTERUS AND POSITION IN HORN		HORN AND POSITION NOT NOTED
	Days	Hours		Left	Right	
39....	13		Scrap	0.036 1 0.038 2 0.044 3	1 0.045 2 0.038 3 0.029 4 0.031 5	
21....	13	2	Bread and milk	0.— 1 0.— 2 0.041 3	0.010 1 0.055 2 0.028 3 0.068 4 0.037 5 0.042 6 0.047 7	
22....	13	2	Bread and milk	0.032 0.034 0.034 0.036 0.038 0.041 0.—	0.033 0.043 0.050	
23....	13	2	Bread and milk	0.046 1 0.046 2 0.036 3 0.049 4 0.041 5 0.046 6	0.058 1 0.049 2 0.046 3 0.038 4	

TABLE 1 (Continued)

SERIAL NO.	AGE OF LITTER		DIET	HORN OF UTERUS AND POSITION IN HORN		HORN AND POSITION NOT NOTED
	Days	Hours		Left	Right	
42....	14		Scrap	0.092 1 0.088 2 0.093 3 0.107 4 0.092 5	0.081 1 0.108 2 0.107 3 0.085 4 0.101 5 0.091 6 0.097 7 0.104 8 0.059 9	
17....	14	2	Bread and milk	0.122 1 0.145 2 0.098 3 0.127 4 0.116 5 0.136 6 0.101 7		
20....	14	2	Bread and milk	0.117 1 0. — 2 0.135 3	0.085 1 0.099 2 0.131 3	
24....	14	2	Bread and milk	0.103 1 0.144 2 0.115 3 0.120 4 0.100 5	0.108 0.101 0.091 0.096 0.102 0.104	
14....	14	2	Bread and milk			0.080 0.109 0.118 0.119 0.121 0.124 0.126
43....	15		Scrap	0.104 1 0.109 2 0.114 3 0.094 4 0.132 5 0.118 6	0.119 1 0.098 2 0.111 3 0.088 4 0.109 5 0.097 6	

TABLE 1 (Continued)

SERIAL NO.	AGE OF LITTER		DIET	HORN OF UTERUS AND POSITION IN HORN		HORN AND POSITION NOT NOTED
	Days	Hours		Left	Right	
38....	15		Scrap	0.223 1 0.202 2 0.205 3 0.217 4 0.206 5	0.228 1 0.217 2 0.244 3	
16....	15		Bread and milk	0.148 0.167 0.182 0.183 0.197 0.226	0.158 0.170 0.176 0.189 0.190	
7.....	15		Bread and milk			0.119 0.143 0.176 0.186 0.193 0.196
41....	16		Scrap	0.319 1 0.306 2 0.336 3 0.329 4 0.315 5 0.256 6	0.342 1 0.360 2 0.336 3 0.327 4 0.322 5	
15....	16		Bread and milk	0.348 1 0.310 2 0.322 3 0.347 4 0.300 5	0.258 1 0.306 2 0.306 3 0.353 4 0.288 5	
12....	16		Bread and milk			0.257 0.291 0.336
25....	16		Bread and milk			0.320 0.326 0.328 0.332 0.351 0.352 0.356 0.373 0.390

TABLE 1 (Continued)

SERIAL NO.	AGE OF LITTER		DIET	HORN OF UTERUS AND POSITION IN HORN		HORN AND POSITION NOT NOTED
	Days	Hours		Left	Right	
5.....	16		Bread and milk			0.220 0.233 0.237 0.252 0.263 0.269 0.274 0.276 0.298 0.304 0.311
18....	17		Bread and milk	0.536 1 0.474 2 0.617 3 0.543 4	0.419 1 0.529 2 0.608 3	
40....	17		Scrap			0.482 0.491 0.493 0.508 0.530 0.531 0.543 0.625
6.....	17		Bread and milk			0.518 0.536 0.580 0.595 0.649 0.650
13....	18		Bread and milk			0.898 0.934 0.955 0.101 0.105 0.105 0.106 0.108

TABLE 1 (Continued)

SERIAL NO.	AGE OF LITTER		DIET	HORN OF UTERUS AND POSITION IN HORN		HORN AND POSITION NOT NOTED
	Days	Hours		Left	Right	
30....	18		Scrap			0.825 0.938 0.941 0.944 0.958 0.961 0.962 0.973 0.978 0.980 0.983 0.986 1.000 1.010 1.020 1.090
4.....	18		Bread and milk			0.930 0.950 1.030 1.020 1.090 1.130 1.170 1.230 1.250
36....	18		Scrap			0.819 0.859 0.866 0.939 0.943 0.954 0.961 0.967 1.010 1.150
37....	19		Scrap	1.480 1 1.550 2 0.530 3 1.450 4	1.310 1 1.690 2 1.540 3 1.340 4	

TABLE 1 (Continued)

SERIAL NO.	AGE OF LITTER		DIET	HORN OF UTERUS AND POSITION IN HORN		HORN AND POSITION NOT NOTED
	Days	Hours		Left	Right	
19....	19		Bread and milk	1.930 1	1.560 1 2.020 2 1.740 3 1.910 4 1.630 5 1.860 6 1.900 7	
2.....	19		Bread and milk	1.020 1.440 1.440 1.550		
31....	19		Scrap			1.510 1.590 1.670 1.670 1.690 1.700 1.710 1.730 1.730 1.740
35....	20		Scrap	2.280 1 2.310 2 2.700 3 2.520 4 2.390 5 2.510 6	2.780 1 2.480 2 2.520 3 2.690 4	
33....	20		Scrap			2.130 2.280 2.470 2.480 2.500 2.550 2.600
26....	20		Scrap			2.770 2.830 2.870 2.900

TABLE 1 (Continued)

SERIAL NO.	AGE OF LITTER		DIET	HORN OF UTERUS AND POSITION IN HORN		HORN AND POSITION NOT NOTED
	Days	Hours		Left	Right	
26....	20		Scrap			2.940 3.000 3.060 3.200
34....	21		Scrap	3.750 3.950 4.000 4.020 4.160 4.420	3.980 4.050 4.280	
35....	21		Scrap			3.920 3.990 4.030 4.110 4.150 4.220
32....	21		Scrap			3.580 3.720 3.790 3.810 3.930 4.080 4.090 4.260 4.370
28....	21		Scrap			3.030 3.400 3.470 3.470 3.550 3.580 3.590 3.720 3.760 3.950
27....	21		Scrap			4.000

TABLE 1 (Continued)

SERIAL NO.	AGE OF LITTER		DIET	HORN OF UTERUS AND POSITION IN HORN		HORN AND POSITION NOT NOTED
	Days	Hours		Left	Right	
27.....	21		Scrap			4.020 4.120 4.150 4.220 4.330 4.380 4.460
44.....	22		Scrap	4.460 1 4.710 2	3.910 1 4.710 2 4.950 3 4.700 4 4.540 5 4.820 6 4.750 7 4.710 8	

TABLE 2

Derived from the data in table 1, and showing the mean weights of the fetuses at ten ages during gestation

AGE IN DAYS	NUMBER OF FETUSES	AVERAGE WEIGHT OF FETUS IN GRAMS	RATE OF INCREASE IN WEIGHT
			<i>per cent</i>
13.....	34	0.040	
14.....	44	0.112	179
15.....	37	0.168	50
16.....	44	0.310	83
17.....	21	0.548	77
18.....	43	1.000	83
19.....	30	1.580	58
20.....	25	2.630	65
21.....	42	3.980	51
22.....	10	4.630	16

Fetus of albino rat

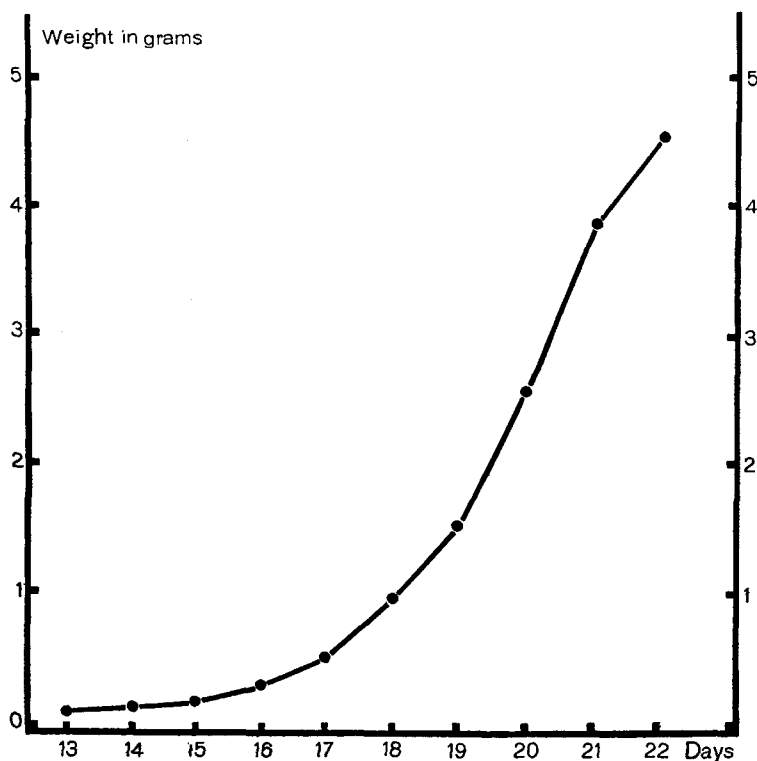


Chart 1 Showing the mean weights in grams of the fetuses of the albino rat at 24-hour intervals, from the 13th to the 22nd day of gestation, inclusive, based on the values given in table 2. The weights here given would be slightly increased if the mothers had all been fed on 'bread and milk,' and slightly diminished had the mothers all been fed on 'scrap.'

that of man we find the actual time ratio to be 1 to 13. Applying this ratio to the human records, the 13th day of gestation in the rat would correspond to the 169th day in man. If the weights in the two species—man and the rat—correspond during the gestation period, then at birth, 4.6 grams for the rat would represent 3250 grams for man. At the 13th day the rat fetus weighs 0.04 grams, so by proportion we would obtain a weight for the human fetus of 283 grams at 169 days. Speaking broadly, this seems to be too small a fetal weight for man (Jackson '09).

TABLE 3

Crown-rump length of fetus in millimeters; scrap diet only

SERIAL NO.	AGE IN DAYS	NUMBER IN LITTER	AVERAGE WEIGHT OF FETUS IN GRAMS	AVERAGE CROWN-RUMP LENGTH IN MM.	RANGE OF LENGTH IN MM.
42.....	14	8	0.093	9.5	9 -10
43.....	15	12	0.107	9.4	9 -10
38.....	15	8	0.218	12.1	12 -12.5
41.....	16	11	0.322	13.0	12.5-13
40.....	17	7	0.525	16.3	16 -17
36.....	18	9	0.947	19.1	18 -21
37.....	19	8	1.490	22.7	20.5-24
35.....	20	10	2.510	27.7	24 -32
34.....	21	9	4.070	36.7	35 -39
44.....	22	10	4.630	39.2	36 -41

It might be interpreted, however, as evidence for a still greater slowness of growth in the rat during the earlier period of gestation, but any attempt to follow the matter further must await better data on the weight of the human fetus at different ages.

The data contained in table 1 are sufficient to justify some further discussion of the characters and relations of the fetus during the period covered by the observations.

It is often desirable to have the data for fetal weight correlated with fetal length. Table 3 gives in a number of cases the crown-rump measurements of *the fresh fetus* after the membranes had been cleared away. The litters from scrap-fed mothers only have been used for this purpose.

A word of explanation touching the diets is here in place. In the course of these observations the general diet of the colony was changed. The earlier litters were from females fed on a diet in which bread and milk were the chief features—this is designated 'bread and milk,' while the later records were from females fed on a 'scrap' diet—i.e., table scraps from which materials known to be injurious to the rats had been excluded—this is designated as 'scrap.'

Two differences which are apparently related to the diet, appear, as can be seen from table 4, in which the data are arranged according to the diet of the mother.

In seven out of eight comparisons the litter number for the scrap diet is greater, while the average weight of the fetus is less for the scrap diet litters. Also in seven out of eight comparisons; the exceptional records are in parentheses. The lower average weights of the fetuses from the scrap-fed rats are about what we should expect to follow from the increase in the number in the litter (King '15) but the appearance of the larger number per litter in the scrap-fed series was an unexpected result. The distribution of the litter size (number of individuals) is a fairly symmetrical one and is shown in chart 2.

The mean value for the litter size is 8.8. Our laboratory records show a mean litter size of about 7.0 for the general

TABLE 4

Effect of diet on the number of fetuses in the litter and on the mean fetus weight

AGE, DAYS	DIET	NO. OF LITTERS	LITTER DESIGNATION	AVER- AGE NO. IN LITTER	AVER- WT. OF FETUS, GRAMS
13.....	Bread and milk Scrap	3	(21) (22) (23)	9	0.041
		1	(39)	(7)	0.037
14.....	Bread and milk Scrap	4	(20 (17) (14) (24)	8	0.117
		1	(42)	14	0.093
15.....	Bread and milk Scrap	2	(7) (16)	8.5	0.174
		2	(38) (43)	9.5	0.162
16.....	Bread and milk Scrap	4	(12) (25) (15) (5)	8	0.305
		1	(41)	11	0.322
17.....	Bread and milk Scrap	2	(6) (18)	6.5	0.560
		1	(40)	8	0.525
18.....	Bread and milk Scrap	2	(13) (4)	8.5	1.05
		2	(36) (30)	13	0.95
19.....	Bread and milk Scrap	2	(2) (19)	6	1.59
		2	(37) (31)	9	1.58
20.....	Bread and milk Scrap	1	(26)	8	2.95
		2	(33) (35)	8.5	2.47
General average: Bread and milk.....				7.8	0.848
Scrap.....				10.0	0.781

population of the colony (King and Stotsenburg '15). In the present case, however, it is to be remembered first, that we are dealing only with second litters, which tend to be large (King and Stotsenburg '15) and second, that there may be some tendency also for the fetuses to be more numerous than are the young actually born.

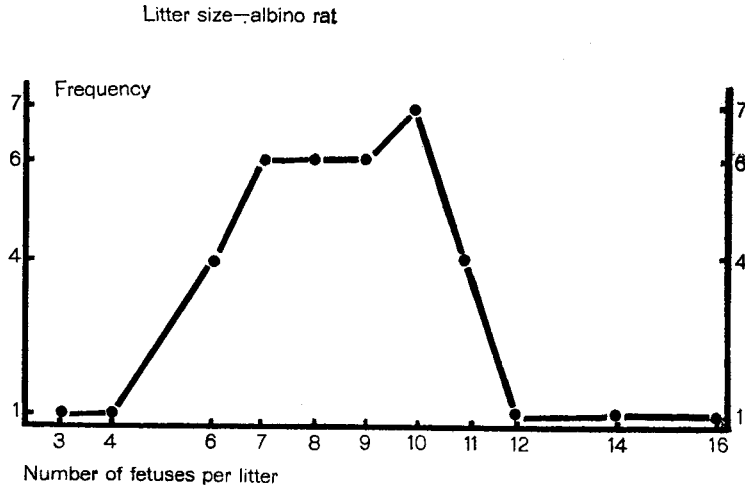


Chart 2 Showing the frequency, as indicated on the ordinate, of the litters containing from 3 to 16 fetuses, as indicated on the abscissa. The mean value is 8.8 fetuses per litter.

DISTRIBUTION OF THE FETUSES BETWEEN THE TWO HORNS OF THE UTERUS

This distribution was noted in the case of 20 litters and the details are given in table 5. *In toto* there were 90 fetuses in the right horn, 94 in the left. In two cases the right horn was sterile, and in four cases there was the same number of fetuses in each horn. If the comparison is made between the average weights of the fetuses in the two horns it is seen that in nine out of the fourteen possible comparisons the average weight of the fetus is greater in the horn containing the smaller number.

THE WEIGHT OF THE FETUS ACCORDING TO POSITION IN HORN

An examination of the fetal weights according to the position of the fetus in the horn has not revealed any correlation. At the same time, inspection of table 1 shows that marked variations in the weights of the fetuses in the same litter and even within the same horn may occur.

For the growth of the Albino from the beginning to the end of gestation, we already have the observations of Huber ('15) giving weight data for the first 3 days and 17 hours, so that there still remains to be filled the interval of about 10 days between the end of Huber's weight records, and the 13th day, which marks the beginning of the records here presented.

TABLE 5

Showing the number of fetuses in each horn of the uterus and their average weight

SERIAL NO.	AGE OF LITTER		NO. IN LITTER	LEFT HORN		RIGHT HORN	
	Days	Hours		No.	Weight	No.	Weight
21.....	13	2	10	3	0.041	7	0.041
22.....	13	2	10	7	0.043	3	0.042
23.....	13	2	10	6	0.044	4	0.048
39.....	13		8	3	0.039	5	0.036
17.....	14	2	7	7	0.121	0	
20.....	14	2	6	3	0.126	3	0.105
24.....	14	2	11	5	0.116	6	0.100
42.....	14		14	5	0.094	9	0.092
16.....	15		11	6	0.184	5	0.176
38.....	15		8	5	0.210	3	0.229
43.....	15		12	6	0.112	6	0.104
15.....	16		10	5	0.325	5	0.302
41.....	16		11	6	0.310	5	0.337
18.....	17		7	4	0.542	3	0.519
2.....	19		4	4	1.36	0	—
19.....	19		8	1	1.93	7	1.80
37.....	19		8	4	1.50	4	1.47
35.....	20		10	6	2.45	4	2.62
34.....	21		9	6	4.05	3	4.08
44.....	22		10	2	4.58	8	4.63
Total				94		90	

LITERATURE CITED

- DONALDSON, H. H. 1906 A comparison of the white rat with man in respect to the growth of the entire body. Boas Anniversary Volume, pp. 5-26. G. E. Stechert & Co., New York.
- HUBER, G. CARL 1915 The development of the albino rat (*Mus norvegicus albinus*). Part I. From the pronuclear stage to the stage of mesoderm anlage; end of the first to the end of the ninth day. Jour. Morph., vol. 26, pp. 247-358.
- JACKSON, C. M. 1909 On the prenatal growth of the human body and the relative growth of the various organs and parts. Am. Jour. Anat., vol. 9, pp. 119-161.
- KEIBEL, FRANZ, AND MALL, FRANKLIN P. 1910, 1912 Manual of human embryology. 2 vols. J. B. Lippincott Co., Philadelphia.
- KING, HELEN D. 1915 On the weight of the albino rat at birth and the factors that influence it. Anat. Rec., vol. 9, pp. 213-231.
- KING, HELEN D., AND STOTSENBURG, J. M. 1915 On the normal sex ratio and the size of the litter in the albino rat (*Mus norvegicus albinus*). Anat. Rec., vol. 9, pp. 403-420.
- LOWREY, LAWSON, G. 1911 Prenatal growth of the pig. Am. Jour. Anat., vol. 12, pp. 107-138.