INHERITANCE OF BENT-NOSE IN THE RAT (RATTUS NORVEGICUS) WITH OBSERVATIONS ON THE EFFECT OF NUTRITION

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Walter E. Heston

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INHERITANCE OF BENT-NOSE IN THE RAT (RATTUS NORVEGICUS) WITH OBSERVATIONS ON THE EFFECT OF NUTRITION

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by

Walter E. Heston

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INTRODUCTION

Our most important problems often are encountered during the study of anomalies which at first appear quite simple. We can never predict with accuracy the nature of these problems nor the field in which they will occur. The bent-nose condition of the rat was first attacked as a simple Mendelian trait, but it has since appeared to involve more complicated genetics as well as factors which are not of a genetic nature.

The name "bent-nose" was chosen because it describes the actual condition encountered in the rat. As the name implies, the nose is bent to one side. This bending may be to the right or left and to a varying degree. No other abnormalities occur. Plate I shows an adult bent-nosed animal, while Plate II presents skulls of such individuals.

It is interesting to note that the character does not appear at birth. Throughout the experiment, the youngest animal to show the character was thirty-four days old. Others have not manifested it until they were 120 days old,and still others were not found to be bent until their skulls were examined after they were full grown and etherized.

The author has found no other case of this character, nor any similar character, described in the literature. Other skull abnormalities such as hydrocephalus and "high-brow" of the rat have been studied, but none are comparable to the bent-nose condition. However, a few cases of a similar character have been observed by Dr. H. W. Feldman and Mr. Alan L. Mitchell of the University of Michigan among their mice which have an ear abnormality. These observations have not been published

HISTORY OF THE BENT-NOSED RAT

The "bent-nose" character of the rat was first discovered in the elementary Zoology laboratory here at Michigan State College in 1930. Rats from the rodent colony here are used for study of the mammalian skeleton. During the spring of 1930 several of the skulls which were being studied were found to be bent, the bend being so evident that it could not escape notice.

Immediately an investigation was begun by Dr. H. R. Hunt to see whether the condition could be found in any other animals of the colony. In a red-eyed-yellow strain derived from Dr. W. E. Castle's stock, the abnormality was quite prevalent, but it did not occur in any of the other stocks of the colony. The author since found it occurring in a meager strain of black-hooded agouties which were believed to be related to the red-eyed-yellows. However, it was never found in the other colony strains: the black-hoodeds and the pink-eyed-yellows derived from Dr. W. E. Castle's stock, nor the blacks descended from Dr. C. A. Hoppert's animals. These three strains were not known to have been related to the red-eyed-yellows.

During 1931 and 1932 Mr. L. W. Wiren attempted to determine whether or not the character was inherited. He made nine P_1 matings of bent x normal animals from the bent stock and two matings of bent x bent. The data of Mr. Wiren's work are given in Table I.

Table I

SUMMARY OF MR. L. W. WIREN'S BREEDING EXPERIMENTS

Type of Mating	No. of matings	Total progeny	Normal progeny	Bent progeny
P_1 Mating Bent x Normal from bent stock	9	63	54	9
Bent x Bent	2	7	7	0

As can be seen in the table, nine bent-nosed animals in a total of 63 appeared in the F_1 generation. This would tend to indicate that the character was inherited, possibly as the result of interaction of several genes. Note that the seven progeny from the bent x bent matings were all normal.

This concluded Mr. Wiren's work. At this point the author first attacked the problem.

GENERAL SURVEY OF THE STUDY OF THE BENT-NOSED RAT

The fact that the character was so prevalent in one strain but occurred in none of the other strains of the colony indicated that bent-nose was inherited. The author initiated an experiment to determine definitely whether the character was or was not inherited, and to study its mode of inheritance.

During the fall of 1932 P_1 matings and matings of Wiren's animals were made. Backcross and F_1 matings were planned to follow according to the conventional method of analyzing a genetic character. However, the train of progress has since been derailed so often that no definite plan could be consistently followed during the analysis of the problem.

The first complication encountered was the result of a change in food on January 1, 1933. Before that time the animals had been fed on a varied diet, getting cooked corn meal one day, possibly cooked wheat the next, and perhaps rice pudding the third, depending on what the man who prepared the food decided to give them. On January 1, 1933, fox-chow was introduced as a food. This is a well balanced diet manufactured in a pellet form which can be very conveniently fed, convenience in feeding having been the primary reason for adopting it.

The new diet brought about a very important change in the frequency of bent-nose. Until January 1, 1933, five animals out of a total of 112 from the various matings were bent. No animals reared on fox-chow developed the bent-nose, though in all, 191 animals were reared with this food.

Fox-chow was continued until May 5, 1933. At this time, the author returned the breeding stock to the old ration fed previous to the fox-chow. Other matings favorable for producing the character were also made. The results of the change back to the old diet were amazing. Bent-nose animals began to appear in comparative large numbers. In the 27 progeny of four inbred crosses between normal animals from bent-nose x bent-nose matings, 67% were bent-nosed.

However, these results among animals fed on this uncontrolled diet could not be used as definite proof that the character was hereditary in nature. The food was so coarse and so incompletely mixed that there was a chance for individuals to eat only certain constituents. It was possible that those rats which were developing bent-nose were selecting a deficient diet.

To eliminate this possibility a controlled diet was made by finely grinding and thoroughly mixing all the different ingredients that had been fed during the period in which the character appeared. The stock was transferred to this controlled diet on November 18, 1933, and there it has remained until the present time (May, 1934).

Three phases have appeared in this problem. Nutrition appears to be quite as important a factor as heredity. The third phase of the investigation is the anatomy of the anomaly. The body of this thesis will deal with each of these phases separately. First, the anatomy of the bent-nosed rat will be taken up. Second, nutrition in relation to bent-nose will be discussed; and third, the author will deal with the inheritance of the trait.

PART I

ANATOMICAL STUDY OF THE BENT-NOSED RAT

External observations of "bent-nosed" animals showed that they were very much like their normal sibs except that their noses appeared bent to the right or left. The body in general appeared quite normally healthy, the only exception being that the animals often were a little underweight. This could be attributed to their slight handicap in eating. The lower jaw was normal, and, since the nose was diverted, the incisor teeth did not articulate as they would normally.

The point at which the nose bent appeared rather definite externally, being a little anterior to the eyes, but the degree of bend was quite variable. In some animals one had difficulty in detecting any bend while others showed a very noticeable deflection.

In general, the heads of the bent animals appeared shorter. An extremely afflicted animal gave the impression of being very "pug-nosed". Such a condition of short-headedness has been found in a few of the normal animals. A more thorough analysis of this condition will be discussed later.

Purpose of the Anatomical Study

It was evident that external observations told us little about the osseous anatomy of the "bent-nosed" rat; so a thorough study of the skeleton was made.

Often one bone abnormality is accompanied by others. It is quite reasonable to suspect that any set of factors causing one bone anomaly would cause others in different parts of the body. Rickets may make a child bow-legged, and this be accompanied by a curved spine or sternum. Abnormal vertebrae in the lumbar region have been found in flexed-tailed mice. Thus it was important to determine whether or not other bone abnormalities accompanied the bent-nose condition in the rat.

A careful study was made to determine just which bones of the skull were bent. Was it the nasal bones or the frontals that were deflected? Did this affect the maxillaries or the pre-maxillaries, and were there any bones posterior to these which were included in the bending?

As before mentioned, the bent-nosed animals' heads appeared unusually short. It was desirable to make a more careful study to determine if the skull was abnormal in respects other than having a bent-nose. Was the skull relatively short, wide, and deep? Did the bending of the rostrum deform other bones? In other words, in how many respects did the skulls from the bent-nosed animals differ from normals?

It was observed that the skulls were bent either to the left or the right. A study was made to determine the frequency with which they were turned to the right. Related to direction of bend was angle of bend. What were the range and mean degree of flexure? Also, were those which were deflected to the right bent to a greater degree than skulls bent to the left?

These were the questions whose answers were sought in the following anatomical study.

Study of the Skeleton Other Than the Skull.

This study of the skeleton as a whole was made by two different methods: (1) by X-ray pictures, and (2) by cleaned whole skeletons. The structure of bones can be studied quite well in a good X-ray picture. However, it is desirable to supplement this with a study of the actual skeleton.

The X-ray study.

X-ray photographs were made of eight bent animals and, for comparison, of two normals. These photographs are included in plates V to XIII inclusive, with the exception of one of the normal animals.

The technique in taking the X-ray pictures was as follows: First the animal was anesthetized with ether. Care was taken not to give enough to cause death. The rat was then tied to a board, back down, with the four legs stretched out as shown in the pictures. A cloth muzzle suspended on two wire loops was placed over the nose to hold the head down in place. The film was slid in between the animal and board and both were placed under the X-ray tube at a distance of 30 inches. For four and one-half seconds the rat was subjected to the rays of the machine which was set at 4.6 If (filament current), 20 M.A. (milliamperes, and 58 K.V. (kilo-volts). The films were then taken to the dark room where they were opened and immersed in the developing fluid for five minutes and then in the fixing fluid for five minutes or longer.

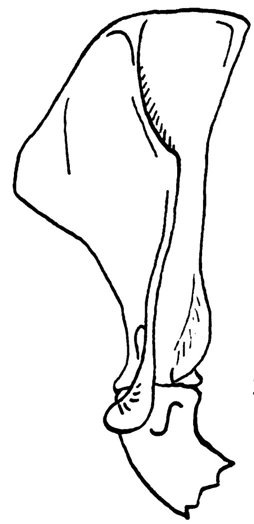
A careful detail study was made of these photographs, comparing the bent-nosed with the normal animals. F_2 ♂ 375,

F_2 ♂ 369, ♂ 1B, ♂ 19B, and ♀ 10B appeared to have curved spines, the condition being most pronounced in ♀ 10B. F_2 ♂ 375, F_2 ♂ 369, and ♂ 1B, which are still in the breeding cages, have been examined, and by palpating their spines one can detect no curvature. ♀ 10B and ♂ 19B were etherized and on the examination of their spines no abnormality was found. The appearance of curved spines may be explained as follows. When the animals were tied back down to the board their muscles had a tendency to contract. As the four legs were stretched out tight the spine was pulled out of shape. The fact that the head of ♀ 10B is thrust caudad against her body tends to verify this reasoning. All the other bones of the bent animals appear to be normal with the exception of the rostrum, the deflection of which can be easily detected.

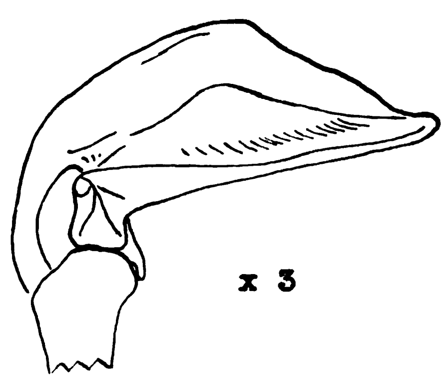
Study of whole skeleton.

The skeletons of eight bent-nosed rats were cleaned and thoroughly studied. The animals were boiled for about 20 minutes in a soap solution which loosened the flesh, making the cleaning of the bones quite easy.

With one exception, no bone abnormalities aside from the bent skull were found in these animals. An abnormal scapula was observed in one case. The scapular blade was bent medially causing the acromion process to be elongated. The scapular spine was much more prominent than normal. The opposing scapula was normal. Figure 1 shows an anterior and a lateral view of this abnormal bone. Since only one anomalous scapula was found in the 16 bent-nosed animals examined as whole skeletons and by X-ray photographs, one could not conclude that this peculiarity was related to the bent-nose character. One might find one such aberrent bone in an equal number of normal animals.



Lateral view



Posterior view

Fig. 1 Malformed scapula of bent-nose F_2 ♂ 444.

From these two studies one must conclude that the factors causing the bent-nose condition are not general, but quite specific in their expression. They cause the anterior bones of the skull to become bent, but do not alter other bones in the body. This would indicate that the character was influenced by heredity as one would expect the anomaly to be accompanied by several other defects were it caused by a dietary insufficiency acting alone. This point will be discussed further in Part III which deals with heredity.

Study of the Skull

Sixty-six thoroughly cleaned bent-nosed skulls and 78 normal ones from the experiment were the subjects of anatomical study. These were selected at random from P_1, F_1, and F_2 animals, and the progeny of backcrosses.

First the bent skulls were studied to determine which bones were affected. It was found that the angle of bend was quite definite, occurring at or just in front of the suture between the nasal and frontal bones. The bones affected on the dorsal side were the nasal, premaxillaries and maxillaries. The zygomatic arches appeared normal. (See plate II.) On the ventral side of the skull the bend seemed more uniformly distributed from the basisphenoid bone to the incisors. The bones in the posterior region, the occipitals, parietals, inter-parietals, squamosals, the tympanic bullae and the petrosal bones all appeared normal.

The anatomical study included also definite measurements on all 66 bent-nosed skulls and 78 normal ones. The measurements of the two types of skulls were compared. (Tables II and III.) Five major precautions were taken for accuracy:

(1) All skulls were thoroughly cleaned of flesh in order that the points for measurements would be well defined.

(2) All skulls were complete.

(3) The skulls of no animals less than 100 days of age were used.

(4) The skulls were dried for at least two weeks in a mean temperature of approximately 130° F.

(5) Points for measurement were selected where the bone was relatively thick.

The following measurements were made. (Fig. 2.) The length AB was defined as the distance from the dorsal border of the foramen magnum to the most anterior point of the upper incisors. The width CD was taken from a point on the squamosal bone just dorsal to the zygomatic process of the squamosal and directly ventral to the descending portion of the suture between the squamosal and parietal bones, to the same point on the opposite side of the cranium. A posterior thickness EF was taken as the distance from the point E at which the sutures separating the two parietal bones and the interparietal bone unite to a point F midway between the two tympanic bullae on the suture between the basioccipital and the basisphenoid bones. An anterior thickness GH was measured. This measurement was defined as the distance from the point G at the union of the sutures between the frontal and nasal bones to the point H which is even with the anterior border of the first molars on the suture between the maxillaries. The fifth measurement was the width outside the

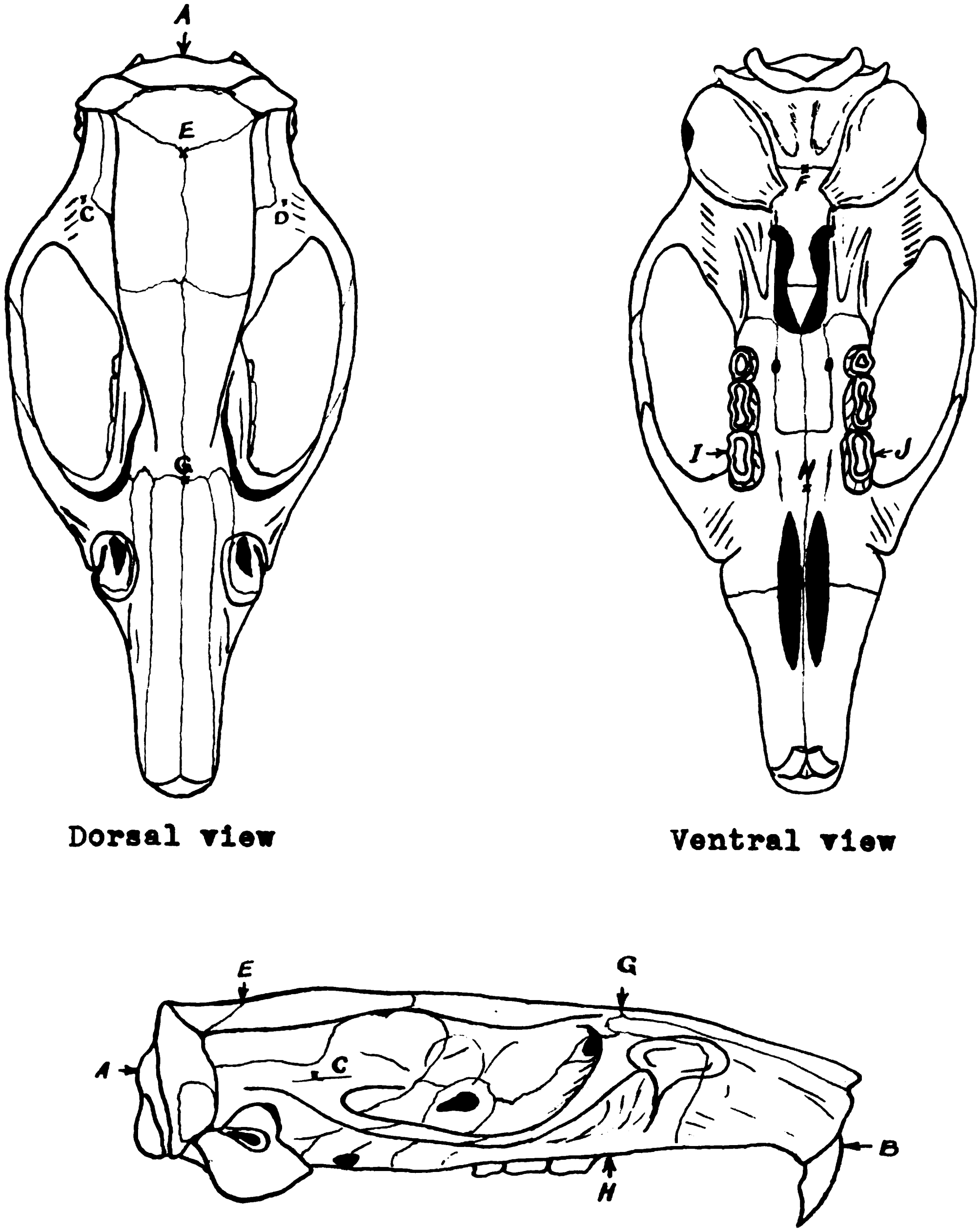


Fig. 2 Points A, B, C, D, E, F, G, H, I, and J on which measurements were made.

Length AB

Posterior thickness EF

Width CD

Anterior thickness GH

Width outside 1st molars IJ

first molars, or IJ. I and J were the most distant opposing points on the lateral borders of the first molars.

These distances were accurately measured to .01 inch. The apex of the angle of bend was first marked with the fine line of a 5H lead pencil across the internasal suture. The skull was then placed on a surface plate between two steel blocks with square faces, making sure that points A and B articulated squarely with the faces of the steel blocks. One block was only slightly thicker than the skulls. This minimised the error of parallax. The length was calculated as the sum of the distances from the faces of the steel blocks to the apex of the angle. A magnifying glass was used to make this reading accurate. The other measurements were made with a strain gage so set up that the skull could be placed between two steel points, the dimension being measurable to .001 inch. This apparatus is shown in plate III.

The date thus gathered were attacked with the idea of determining differences and likenesses between the normal and the bent-nosed skulls.

It is interesting to compare the means of these five measurements. (Table IV.) The mean lengths differ by .064 inch, the normal skulls being longer, while all other measurements are much the same, differing by .008 inch and less. This would tend to indicate that the bent-nosed skulls are the shorter.

Table II

SKULL MEASUREMENTS AND INDICES OF BENT-NOSED ANIMALS

Skull Number	Age in Days	Angle & direction of bend	Length AB in inches	Width CD in inches	Posterior thickness EF in inches	Anterior thickness GH in inches	Width outside 1st molars IJ in inches	Width-Length Index $\frac{CD\times100}{AB}$	Posterior Thickness-Width Index $\frac{EF\times100}{CD}$	Anterior Thickness-Width Index $\frac{GH\times100}{CD}$
P_1 ♀ 69	568*	Right 17°	1.53	.60	.42	.42	.38	39.2	70.0	70.0
P_1 ♀ 81	245*	Right 20°	1.55	.58	.42	.42	.34	37.4	72.4	72.4
P_1 ♂ 42	493*	Right 28°	1.53	.59	.42	.39	.35	38.6	71.2	66.1
P_1 ♀ 68	493*	Right 29°	1.51	.58	.44	.45	.36	38.4	75.9	77.6
P_1 ♀ 504	200*	Left 17°	1.47	.58	.41	.40	.35	39.5	70.7	69.0
P_1 ♀ 70	568*	Right 22°	1.51	.59	.41	.42	.37	39.1	71.2	71.2
P_1 ♂ 52	365*	Right 19°	1.45	.57	.42	.40	.33	39.3	73.7	70.2
P_1 ♀ 63	422*	Right 13°	1.55	.59	.43	.42	.35	38.1	72.9	71.2
P_1 ♀ 16	602*	Right 21°	1.46	.56	.41	.41	.36	38.4	73.2	73.2
P_1 ♂ 48	204*	Left 23°	1.52	.57	.40	.41	.37	37.5	70.2	71.9
P_1 ♂ 41	480*	Right 31°	1.48	.61	.41	.42	.36	41.2	67.2	68.9
P_1 ♀ 74	388*	Right 13°	1.44	.58	.40	.41	.36	40.3	68.9	70.7
P_1 ♀ 7	216*	Right 19°	1.41	.46	.39	.38	.34	32.6	84.8	82.6
P_1 ♀ 9	147*	Right 18°	1.60	.61	.42	.43	.36	38.1	68.9	70.5

* These animals were at least as old as tabulated.

Table II Continued

Skull Number	Age in Days	Angle & direction of bend	Length AB in inches	Width CD in inches	Posterior thickness EF in inches	Anterior thickness GH in inches	Width outside 1st molars IJ in inches	Width-Length Index $\frac{CD \times 100}{AB}$	Posterior Thickness-Width Index $\frac{EF \times 100}{CD}$	Anterior Thickness-Width Index $\frac{GH \times 100}{CD}$
F_1 ♂ 14	551	Right 25°	1.49	.58	.41	.42	.33	38.9	70.7	72.4
F_1 ♂ 602	266	Left 20°	1.50	.58	.41	.38	.34	38.7	70.7	65.5
F_1 ♂ 255	234	Left 8°	1.56	.58	.41	.38	.32	37.2	70.7	65.5
F_1 ♀ 22	546	Left 18°	1.56	.59	.39	.42	.36	37.8	66.1	71.2
F_1 ♂ 652	163	Right 15°	1.41	.54	.39	.35	.31	38.3	72.2	64.8
F_1 ♂ 18	508	Left 35°	1.43	.57	.40	.38	.34	39.9	70.2	66.7
F_1 ♀ 17	447	Left 16°	1.46	.56	.42	.41	.34	38.4	75.0	73.2
F_1 ♀ 243	325	Left 7°	1.55	.56	.40	.39	.34	36.1	71.4	69.6
F_1 ♂ 7	552	Left 25°	1.55	.61	.44	.44	.38	39.4	72.1	72.1
F_1 ♀ 613	262	Right 4°	1.40	.56	.40	.32	.31	40.0	71.4	57.1
F_1 ♂ 250	248	Left 20°	1.53	.58	.42	.41	.34	37.9	72.4	70.7
F_1 ♀ 254	234	Right 21°	1.49	.57	.42	.40	.33	38.3	73.7	70.2
F_1 ♂ 252	234	Left 14°	1.52	.58	.42	.37	.34	38.2	72.4	63.8
F_1 ♂ 28	450	Left 7°	1.60	.58	.42	.43	.34	36.3	72.4	74.1

Table II Continued

Skull Number	Age in Days	Angle & direction of bend	Length AB in inches	Width CD in inches	Posterior thickness EF in inches	Anterior thickness GH in inches	Width outside 1st molars IJ in inches	Width-Length Index $\frac{CD \times 100}{AB}$	Posterior Thickness-Width Index $\frac{EF \times 100}{CD}$	Anterior Thickness-Width Index $\frac{GH \times 100}{CD}$
F_1 ♀ 23	421	Right 18°	1.56	.58	.41	.42	.36	37.2	70.7	72.4
F_1 ♂ 605	261	Left 17°	1.51	.58	.42	.39	.33	38.4	72.4	67.2
F_1 ♂ 610	262	Left 23°	1.37	.54	.40	.35	.31	39.4	74.1	64.8
F_1 ♀ 604	261	Right 5°	1.55	.59	.43	.40	.34	38.1	72.9	67.8
F_1 ♂ 609	262	Right 18°	1.40	.55	.41	.35	.32	39.3	74.5	63.6
F_2 ♂ 438	315	Left 15°	1.45	.59	.47	.41	.36	40.7	79.7	69.5
F_2 ♂ 140	327	Left 11°	1.47	.57	.41	.39	.34	38.8	71.9	68.4
F_2 ♀ 364	167	Left 15°	1.41	.55	.39	.36	.31	39.0	70.9	65.5
F_2 ♀ 456	194	Left 12°	1.50	.60	.45	.39	.35	40.0	75.0	65.0
F_2 ♀ 367	167	Right 15°	1.41	.55	.38	.37	.31	39.0	69.1	67.3
F_2 ♀ 488	273	Left 17°	1.49	.57	.40	.40	.36	38.3	70.2	70.2
F_2 ♂ 320	305	Left 17°	1.50	.57	.41	.38	.35	38.0	71.9	66.7
F_2 ♂ 458	315	Left 27°	1.50	.57	.44	.41	.34	38.0	77.2	71.9
F_2 ♀ 323	183	Right 14°	1.48	.54	.38	.36	.31	36.5	70.4	66.7

Table II Continued

Skull Number	Age in Days	Angle & direction of bend	Length AB in inches	Width CD in inches	Posterior thickness EF in inches	Anterior thickness GH in inches	Width outside 1st molars IJ in inches	Width-Length Index $\frac{CDx100}{AB}$	Posterior Thickness-Width Index $\frac{EFx100}{CD}$	Anterior Thickness-Width Index $\frac{GHx100}{CD}$
F_2 ♂ 339	222	Left 23°	1.53	.59	.41	.43	.35	38.6	69.5	72.9
F_2 ♂ 136	327	Left 27°	1.58	.57	.42	.45	.35	36.1	73.7	78.9
F_2 ♀ 487	273	Right 19°	1.50	.58	.41	.38	.35	38.7	70.7	65.5
F_2 ♀ 322	291	Left 20°	1.46	.58	.41	.36	.34	39.7	70.7	62.1
F_2 ♂ 450	194	Right 13°	1.49	.58	.43	.38	.34	38.9	74.1	65.5
F_2 ♂ 317	310	Right 18°	1.47	.57	.41	.39	.34	38.8	71.9	64.8
F_2 ♂ 338	252	Left 20°	1.57	.57	.41	.40	.34	36.3	71.9	70.2
F_2 ♂ 444	319	Right 17°	1.57	.62	.45	.43	.37	39.5	72.6	69.4
F_2 ♂ 446	319	Right 20°	1.60	.60	.45	.41	.36	37.5	75.0	68.3
F_2 ♂ 463	315	Left 16°	1.47	.59	.44	.38	.35	40.1	74.6	64.4
♀ 13	314	Left 14°	1.54	.59	.42	.39	.35	38.3	71.2	66.1
♀ 14	310	Left 10°	1.51	.58	.43	.42	.36	38.4	74.1	72.4
♂ 479	289	Right 16°	1.52	.60	.44	.41	.35	39.5	73.3	68.3
♀ 17	310	Left 22°	1.53	.59	.43	.39	.35	38.6	72.9	66.1

Table II Continued

Skull Number	Age in Days	Angle & direction of bend	Length AB in inches	Width CD in inches	Posterior thickness EF in inches	Anterior thickness GH in inches	Width outside 1st molars IJ in inches	Width-Length Index $\frac{CD \times 100}{AB}$	Posterior Thickness-Width Index $\frac{EF \times 100}{CD}$	Anterior Thickness-Width Index $\frac{GH \times 100}{CD}$
♀ 7B	244	Right 9°	1.43	.57	.40	.37	.32	39.9	70.2	64.9
♂ 11	312	Left 17°	1.53	.60	.44	.41	.36	39.2	73.3	68.3
♂ 481	180	Right 10°	1.60	.61	.42	.39	.35	38.1	68.9	63.9
♀ 10	231	Right 6°	1.51	.57	.43	.38	.33	37.7	75.4	66.7
♀ 477	298	Right 20°	1.47	.57	.39	.38	.35	38.8	68.4	66.7
♀ 473	299	Left 19°	1.50	.58	.41	.39	.35	38.7	70.7	67.2
♀ 20	213	Right 12°	1.49	.58	.41	.39	.33	38.9	70.7	67.2
♀ 18	273	Right 15°	1.42	.55	.39	.36	.32	38.7	70.9	65.5
♂ 14	273	Right 24°	1.42	.55	.38	.37	.33	38.7	69.1	67.3
♀ 83	232	Right 20°	1.45	.57	.40	.40	.35	39.3	70.2	70.2

Table III

SKULL MEASUREMENTS AND INDICES OF NORMAL ANIMALS

Skull Number	Age in Days	Length AB in inches	Width CD in inches	Posterior thickness EF in inches	Anterior thickness GH in inches	Width outside 1st molars IJ in inches	Width-Length Index $\frac{CD \times 100}{AB}$	Posterior Thickness-Width Index $\frac{EF \times 100}{CD}$	Anterior Thickness-Width Index $\frac{GH \times 100}{CD}$
P_1 ♀ 52	149*	1.53	.57	.43	.42	.36	37.3	75.4	73.7
P_1 ♀ 705	207*	1.65	.59	.42	.41	.35	35.8	71.2	69.5
P_1 ♀ 50	375*	1.51	.57	.43	.39	.33	37.7	75.4	68.4
P_1 ♀ 54	483*	1.50	.57	.43	.38	.35	38.0	75.4	66.7
P_1 ♀ 4	426*	1.51	.59	.43	.40	.34	39.1	72.9	67.8
P_1 ♀ 706	200*	1.60	.56	.42	.41	.33	35.0	75.0	73.2
P_1 ♀ 6	468*	1.53	.58	.40	.40	.33	37.9	69.0	69.0
P_1 ♂ 51	337*	1.61	.58	.44	.43	.34	36.0	75.9	74.1
P_1 ♀ 703	200*	1.62	.56	.44	.41	.35	34.6	78.6	73.2
P_1 ♀ 707	200*	1.65	.58	.45	.42	.35	35.2	77.6	72.4
P_1 ♀ 702	200*	1.60	.60	.42	.42	.35	37.5	70.0	70.0
P_1 ♀ 704	200*	1.66	.61	.44	.41	.36	36.7	72.1	67.2
P_1 ♀ 701	200*	1.69	.70	.44	.41	.36	41.4	62.9	58.6

* These animals were at least as old as tabulated.

Table III Continued

Skull Number	Age in Days	Length AB in inches	Width CD in inches	Posterior thickness EF in inches	Anterior thickness GH in inches	Width outside 1st molars IJ in inches	Width-Length Index $\frac{CD \times 100}{AB}$	Posterior Thickness-Width Index $\frac{EF \times 100}{CD}$	Anterior Thickness-Width Index $\frac{GH \times 100}{CD}$
♀ 480	180	1.54	.58	.42	.39	.33	37.7	72.4	67.2
F_1 ♂ 24	413	1.65	.59	.42	.44	.35	35.8	71.2	74.6
F_1 ♂ 241	243	1.59	.60	.46	.42	.36	37.7	76.7	70.0
F_1 ♂ 650	163	1.40	.54	.39	.36	.32	38.6	72.2	66.7
F_1 ♀ 227	362	1.65	.60	.43	.40	.35	36.4	71.7	71.7
F_1 ♀ 226	362	1.64	.59	.43	.41	.36	36.0	72.9	72.9
F_1 ♀ 651	163	1.37	.56	.39	.34	.32	40.9	69.6	60.7
F_1 ♀ 229	362	1.64	.60	.43	.42	.36	36.6	71.7	70.0
F_1 ♀ 232	355	1.64	.61	.43	.43	.36	37.2	70.5	70.5
F_1 ♂ 11	393	1.61	.60	.43	.42	.36	37.3	71.7	70.0
F_1 ♂ 606	261	1.56	.58	.43	.40	.34	37.2	74.1	69.0
F_1 ♂ 244	243	1.59	.60	.43	.40	.34	37.7	71.7	71.7
F_1 ♀ 649	163	1.38	.54	.38	.34	.30	39.1	70.4	63.0
F_1 ♀ 233	344	1.58	.59	.41	.41	.35	37.3	69.5	69.5

Table III Continued

Skull Number	Age in Days	Length AB in inches	Width CD in inches	Posterior thickness EF in inches	Anterior thickness GH in inches	Width outside 1st molars IJ in inches	Width-Length Index $\frac{CD \times 100}{AB}$	Posterior Thickness-Width Index $\frac{EF \times 100}{CD}$	Anterior Thickness-Width Index $\frac{GH \times 100}{CD}$
F_1 ♀ 236	121	1.65	.59	.42	.41	.36	35.8	71.2	69.5
F_1 ♀ 242	336	1.54	.57	.41	.39	.34	37.0	71.9	68.4
F_1 ♀ 241	336	1.57	.58	.42	.40	.34	36.9	72.4	69.0
F_1 ♂ 242	243	1.62	.61	.43	.40	.36	37.7	70.5	65.6
F_1 ♂ 229	346	1.73	.61	.43	.46	.37	35.3	70.5	75.4
F_1 ♀ 234	344	1.59	.59	.41	.39	.35	37.1	69.5	66.1
F_1 ♂ 607	262	1.38	.56	.40	.36	.32	40.6	71.4	64.3
F_1 ♂ 239	345	1.58	.60	.42	.41	.35	38.0	70.0	68.3
F_1 ♂ 240	345	1.59	.59	.42	.41	.35	37.1	71.2	69.5
F_1 ♀ 16	325	1.58	.60	.41	.42	.36	38.0	68.3	70.0
F_1 ♀ 231	355	1.65	.59	.42	.43	.37	35.8	71.2	72.9
F_1 ♂ 603	266	1.53	.58	.42	.38	.34	37.9	72.4	65.5
F_1 ♂ 243	243	1.66	.61	.45	.42	.35	36.7	73.8	68.9
F_1 ♂ 245	343	1.63	.61	.44	.41	.35	37.4	72.1	67.2

Table III Continued

Skull Number	Age in Days	Length AB in inches	Width CD in inches	Posterior thickness EF in inches	Anterior thickness GH in inches	Width outside 1st molars IJ in inches	Width-Length Index $\frac{CDx100}{AB}$	Posterior Thickness-Width Index $\frac{EFx100}{CD}$	Anterior Thickness-Width Index $\frac{GHx100}{CD}$
F_1 ♀ 240	336	1.55	.57	.41	.38	.34	36.8	71.9	66.7
F_1 ♀ 228	260	1.65	.59	.42	.41	.37	35.8	71.2	69.5
F_1 ♀ 244	336	1.56	.58	.43	.39	.35	37.2	74.1	67.2
F_1 ♀ 245	345	1.57	.59	.41	.40	.34	37.6	69.5	67.8
F_1 ♀ 239	340	1.63	.59	.43	.43	.35	36.2	72.9	72.9
F_1 ♀ 235	344	1.58	.60	.40	.40	.34	38.0	66.7	66.7
F_1 ♀ 611	262	1.41	.56	.40	.36	.31	39.7	71.4	64.3
F_2 ♂ 183	144	1.53	.58	.42	.38	.32	37.9	72.4	65.5
F_2 ♀ 165	147	1.52	.57	.41	.39	.32	37.5	71.9	68.4
F_2 ♀ 133	167	1.60	.60	.44	.42	.34	37.5	73.3	70.0
F_2 ♂ 175	144	1.48	.57	.41	.38	.32	38.5	71.9	66.7
F_2 ♀ 167	147	1.54	.58	.43	.39	.33	37.7	74.1	67.2
F_2 ♂ 166	147	1.59	.58	.40	.40	.33	36.5	69.0	69.0
F_2 ♀ 182	144	1.43	.55	.40	.36	.31	38.5	72.7	65.5

Table III Continued

Skull Number	Age in Days	Length AB in inches	Width CD in inches	Posterior thickness EF in inches	Anterior thickness GH in inches	Width outside 1st molars IJ in inches	Width-Length Index CDx100/AB	Posterior Thickness-Width Index EFx100/CD	Anterior Thickness-Width Index GHx100/CD
F_2 ♀ 163	147	1.54	.58	.41	.38	.33	37.7	70.7	65.5
F_2 ♂ 160	146	1.58	.60	.43	.40	.34	38.0	71.7	66.7
F_2 ♀ 135	165	1.54	.60	.41	.40	.33	39.0	68.3	66.7
F_2 ♂ 178	144	1.53	.58	.43	.39	.32	37.9	74.1	67.2
F_2 ♂ 180	144	1.56	.57	.44	.40	.34	36.5	77.2	70.2
F_2 ♀ 159	127	1.46	.57	.40	.36	.31	39.0	70.2	63.2
F_2 ♂ 157	127	1.53	.59	.41	.37	.33	38.6	69.5	62.7
F_2 ♂ 156	127	1.53	.59	.41	.37	.33	38.6	69.5	62.7
F_2 ♂ 134	165	1.63	.60	.43	.42	.34	36.8	71.7	70.0
F_2 ♂ 162	147	1.62	.60	.42	.42	.33	37.0	70.0	70.0
F_2 ♂ 176	144	1.54	.56	.41	.40	.33	36.4	73.2	73.2
F_2 ♀ 179	144	1.45	.55	.40	.37	.31	37.9	72.7	67.2
F_2 ♂ 161	147	1.55	.58	.41	.40	.33	37.4	70.7	70.7
F_2 ♀ 445	203	1.51	.58	.44	.37	.33	38.4	75.9	63.8

Table III Continued

Skull Number	Age in Days	Length AB in inches	Width CD in inches	Posterior thickness EF in inches	Anterior thickness GH in inches	Width outside 1st molars IJ in inches	Width-Length Index $\frac{CD \times 100}{AB}$	Posterior Thickness-Width Index $\frac{EF \times 100}{CD}$	Anterior Thickness-Width Index $\frac{GH \times 100}{CD}$
F_2 ♀ 164	147	1.49	.57	.40	.38	.33	38.3	70.2	64.9
F_2 ♀ 142	111	1.46	.57	.40	.37	.33	39.0	70.2	64.9
F_2 ♀ 141	117	1.47	.56	.41	.38	.32	38.1	73.2	67.9
F_2 ♀ 120	118	1.49	.56	.41	.38	.33	37.6	73.2	67.9
F_2 ♂ 177	144	1.52	.57	.42	.40	.32	37.5	73.7	70.2
F_2 ♂ 181	144	1.47	.56	.40	.38	.32	38.1	71.4	67.9
F_2 ♀ 132	165	1.55	.60	.42	.39	.34	38.7	70.0	65.0
F_2 ♂ 131	165	1.66	.61	.44	.43	.35	36.7	72.1	70.5
F_2 ♀ 237	121	1.65	.60	.42	.41	.36	36.4	70.0	68.3

Table IV

COMPARISONS OF THE MEANS OF THE FIVE MEASUREMENTS MADE OF THE 66 BENT-NOSED ANIMALS AND THE 78 NORMAL ANIMALS

Measurement	Bent-nosed animals	Normal animals	Difference
Length AB	1.497 in.	1.561 in.	.064 in.
Width CD	.576 in.	.584 in.	.008 in.
Posterior thickness EF	.415 in.	.420 in.	.005 in.
Anterior thickness GH	.396 in.	.398 in.	.002 in.
Width outside 1st molars IJ	.344 in.	.339 in.	.005 in.

Table V

COMPARISON OF INDICES OF BENT-NOSED AND NORMAL SKULLS

Index	Bent-nosed skulls total 66				Normal skulls total 78				Difference between means	Ratio $\frac{Dif.}{P.E.}$
	Mean	Mean Deviation	σ	P.E. of the Distribution	Mean	Mean Deviation	σ	P.E. of the Distribution		
Width-Length Index $\frac{CD \times 100}{AB}$	38.5 ± 0.105	0.9	1.27	0.86	37.5 ± 0.095	0.9	1.25	0.84	1.0 ± 0.14	7.14
Anterior Thickness-Width Index $\frac{GH \times 100}{CD}$	68.7 ± 0.33	3.1	3.97	2.68	68.3 ± 2.44	2.5	3.2	2.16	0.4 ± 0.41	0.98
Posterior Thickness-Width Index $\frac{EF \times 100}{CD}$	72.1 ± 0.23	1.98	2.79	1.88	71.9 ± 0.19	1.8	2.46	1.66	0.2 ± 0.296	0.676

A more reliable comparison is by means of indices, which are the ratio of one measurement to another. This is the method used in the study of Anthropometry. Aleš Hrdlička, in his work on Anthropometry (1920), defines several different indices of the head and skull. The cephalic index is $\frac{\text{Breadth} \times 100}{\text{Length}}$. By this index humans are classified; one having a cephalic index up to 74.9 is classed as dolichocephalic; 75.0 to 79.9, mesocephalic, and 80.0 and above, brachycephalic. Other indices for the skull are: Mean Height Index - $\frac{\text{Height} \times 100}{\text{Mean of Length \& Breadth}}$; Height-Length Index - $\frac{\text{Height} \times 100}{\text{Length}}$. Not only in the study of skulls are indices used but also for other bones of the body, as the femur, the scapula, or the sternum.

Three indices were calculated for comparing bent-nosed skulls with normals, namely:

(1) Width-Length Index $\frac{CD \times 100}{AB}$

(2) Posterior Thickness-Width Index $\frac{EF \times 100}{CD}$

(3) Anterior Thickness-Width Index $\frac{GH \times 100}{CD}$

These different indices are tabulated in tables II and III, while the results of the comparative study are given in table V. Note that the one index only, the Width-Length index, shows a statistically significant difference between the bent-nosed and normal skulls. The results prove that the bent-nosed skulls are shorter in relation to the width than are the normal skulls. This is not due to the variation in the width measurement, since the means of the other two indices do not show a statistically significant variation.

Since the method used in measuring the bent-nosed skulls was not the same as for the normals, one questions whether or not this variation in length was due to faulty measuring of the bent-nosed skulls. It is hardly probable that this is the case. The mean Width-Length Index for the normal skulls was 37.5. The mean width of the bent-nosed skulls was .576 inch. Therefore, a mean length of 1.536 would be necessary for the bent-nosed skulls to give a Width-Length Index identical to that of the normal skulls. This would be .039 inch greater than the actual mean length. It is highly improbable that an average error of .039 inch was made in measuring the bent-nosed skulls. With successive measurements of the same skull the error never exceeded .01 inch.

The next phase of this skull study was centered on the bend of the skull, the direction, degree and variation of the deflection. Table VI gives the data for this study.

A method was devised for measuring the angle of bend by means of a glass straightedge and a protractor. (See plate IV.) The skull was placed on a mass of plastic clay and pressed down so that the clay held it firmly. The sagittal and frontal sutures were then placed in line with a glass straightedge which was held firmly by a clamp on a ring stand. With the apex of the angle taken at the suture between the nasal and frontal bones, the protractor was brought in line with the distal end of the internasal suture. The angle of deflection was read to the nearest degree at the point where the protractor crossed the straightedge.

Analysis of these data reveals the following points.

(1) The degree of flexure ranges from as low as 4° to 35°. It is interesting to note that these two extremes were F_1 animals.

(2) The mean degree of flexure was 17.5°.

(3) The frequency of the left bends was not significantly different from the right. Of the 66 animals, 31 bent to the left, and 35 to the right.

(4) No statistically significant difference occurs between the mean angles to the left and right. This comparison is given in table VI.

TABLE VI

COMPARISON OF SKULLS BENT TO THE LEFT AND SKULLS BENT TO THE RIGHT

	Mean angle of bend	Mean Deviation	σ	P. E. of the Distribution	Dif. of Means	Ratio $\frac{Dif.}{P.E.}$
Skulls bent to left Total 31	17.8° ± 4.13°	4.71°	6.13°	4.13°		
					0.5° ± 1.016	0.49
Skulls bent to right Total 35	17.3° ± 4.12°	4.56°	6.11°	4.12°		

Conclusions on Anatomical Study.

(1) The expression of the factors causing bent-nose in the rat is centered on the bones of the anterior region of the skull. No other bone abnormalities have been found normally accompanying this bent-nosed condition.

(2) The mean Width-Length Index is significantly greater for the bent-nosed than for the normal skulls. That is, the length is less in comparison to the width in the bent-nosed than in the normals.

(3) No significant difference occurs between the mean Posterior thickness-Width Indices, and the same is true of the mean Anterior thickness-Width Indices.

(4) The range of the degree of flexure is from 4° to 35° with a mean of 17.5°.

(5) No significant difference is found between the number, or mean angle of those animals bent to the right and those bent to the left.

PART II

OBSERVATIONS ON EFFECTS OF NUTRITION

The boundaries of the science of Genetics will never be truly defined, any more nearly than will the boundaries of Nutrition, Physiology, Chemistry or any other science. Genes cause the expression of characters only with the cooperation of all necessary physiological and environmental factors. Thus, we have the different sciences overlapping. When one attempts a genetic problem he is likely to find himself automatically carried into the adjoining territory of any of the other fields, and just where one crosses the boundary cannot be determined.

When the author began the study of the bent-nosed rat, he had no intentions of making a nutritional study, but he had not progressed far until some marked effects of the change of diet became evident. On fox-chow no bent-nosed animals appeared, while on a mixed diet a certain percentage of animals appeared bent, this percentage varying somewhat with the type of matings of which they were progeny.

The author regrets that a thorough analysis of the effects of nutrition on the bent-nose character has not been made. Such an analysis will be necessary before all the genetics of the problem can be understood. However, some of the observations on the effects of different foods merit further discussion; also some tests for the determination of rickets will be discussed.

The experiment could be divided into four different periods according to diet:

(1) From the beginning of the work in September, 1932 to January 1, 1933, during which time the animals were fed on a varied diet.

(2) The period from January 1, 1933, to May 5, 1933, when fox-chow only was fed.

(3) On May 5, 1933, the animals were returned to the imperfectly mixed varied diet again. This period ran to November 18, 1933.

(4) From November 18, 1933, to the date of writing (May, 1934) the animals were fed on a controlled diet.

Each period will be discussed separately, dealing with the types of food and the results of feeding each type.

First Period - Results of the Varied Diet.

When the experiment was begun the animals were kept on the cooked diet that they had been fed for the past several years. This diet consisted of a great variety of grains including corn, oats, wheat, barley, and rice, all these in their many different preparations. It also included some vegetables such as potatoes and carrots with lettuce and cabbage occasionally. Raisins were added for fruit, and now and then cocoanut was mixed in. Some meats were fed, this usually being salmon, though occasionally meat scraps were added. Cod-liver oil was furnished about once a week, about a half cupful being poured into the 8 or 10 pounds of feed for one day. The animals could detect this, and the feed with cod-liver oil in it was seldom eaten as well as that without. With all these different foods, the rats could have had a good diet had not they have been fed cooked corn or cooked wheat too often due to the ease with which they could be prepared.

During this period 112 animals were born, five or 4.5% of which developed bent-nose. (Table IX) These 112 were from various types matings such as F_1 (progeny of bent x normal mated inter se), backcross (F_1 x bent), and P_1 (bent x normal), all of which will be discussed later. More rats might have developed the bent-nose condition had not they have been put on the fox-chow feed while still quite young. As the reader will recall, the bent-nose character does not develop until the animal is about 32 days old or older.

Second Period - Results of Fox-chow Diet.

As previously mentioned, the stock of the colony was put on the fox-chow diet for convenience. Small wire mesh containers were made which would hold a week's supply of food, thus eliminating the daily chore of feeding. All experimental animals were put on this diet January 1, 1933.

Fox-chow is a quite well balanced diet in pellet form manufactured by the Purina Company in St. Louis, Missouri. It was evidently primarily intended for a fox food, hense the name fox-chow. However it is relished by most rodents as well. The rats ate it readily. They grew and bred well on it.

According to the manufacturers, fox-chow is composed of the following materials: meat (beef), wheat germ meal, dried skim milk, cod-liver oil, barley malt, blackstrap molasses, oat cereal, corn, wheat bran, and iodized salt. These materials were mixed in proportions which gave the following percentages:

protein	20% *
fat	3%
fiber	6%
nitrogen-free extract	50%
carbohydrates	56%
Ash	6%

The caloric value was calculated as 1500 calories per pound; the nutritive ratio was 1 to 3, and the calcium phosphorus ratio, 1.4 to 1. This would indicate a slight excess of phosphorus in relation to the amount of calcium. The ratio of calcium to phosphorus in the body is usually considered to be about 2 to 1, and, therefore, the ratio of calcium to phosphorus in a food should be about the same.

A total of 191 F_1 (progeny of bent x normal) and backcross (F_1 x bent) animals were reared to maturity (at least 120 days) on fox-chow. None of these animals developed the bent-nosed character, as their skulls were all normal when they were etherized at 120 days of age or older. Eighty-nine F_1 animals and 32 progeny of bent x bent or a total of 121 were reared on fox-chow to partial maturity ranging from 8 to 103 days of age. None of these animals appeared bent while on the fox-chow ration. They were later put back on the varied diet, and some of the younger animals afterwards developed the bent-nosed character. This point will be discussed more fully in the next section.

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* Some fallacy occurs in these percentages as they total 141%.

Third Period - Results of Return to the Varied Diet.

On or about May 5, 1933, all breeding animals, F_1 animals and progeny of bent x bent, were returned to the varied diet fed previous to the introduction of fox-chow. This was done in an attempt to regain bent-nose. In addition to the crosses already started, four inbred matings were made with progeny of bent x bent matings which had been reared on fox-chow and were normal, and 12 F_1 matings were made of bent-nose x normal animals from the bent-nose stock.

Of the 89 F_1 animals which were returned to the varied diet before reaching maturity, four developed the bent-nose, while of the 32 progeny of bent x bent which were treated in a like manner, six later became bent-nose. Table VII lists these litters with the age at which they were returned to the varied diet. Note that no animal which had been fed on fox-chow for more than 32 days after birth developed a bent-nose. One animal in a litter of seven developed a bent-nose after having been fed fox-chow until it was 32 days old; two animals out of a litter of six developed bent-nose after being returned to the varied diet at the age of 15 days; two bent-nosed animals appeared in a litter of five after being returned to the varied diet at the age of eleven days; one animal in a litter of two developed a bent-nose after being returned to the varied diet at ten days of age; and four out of a litter of five developed bent-nose after being returned to the varied diet at 8 days of age. This means that animals which were transferred to the varied diet while still nursing

Table VII

INDICATING AGE AT WHICH ANIMALS COULD BE TRANSFERRED FROM FOX-CHOW TO VARIED DIET AND DEVELOP BENT-NOSE

Type of mating	Normal offspring		Bent-nosed offspring		Age in days at which offspring were transferred from fox-chow to varied diet.
	♂	♀	♂	♀	
P_1 mating *	2				103
P_1 mating	3	1			95
Bent-nose x bent-nose	2	1			93
P_1 mating		5			91
P_1 mating	2	2			89
P_1 mating	4	2			82
P_1 mating	1	3			79
P_1 mating	1	2			79
P_1 mating	1	4			60
Bent-nose x bent-nose	3				55
P_1 mating	4	4			49
P_1 mating	4	3			42
Bent-nose x bent-nose	2	4			40
Bent-nose x bent-nose		4			40

Table VII Continued

Type of mating	Normal offspring ♂	Normal offspring ♀	Bent-nosed offspring ♂	Bent-nosed offspring ♀	Age in days at which offspring were transferred from fox-chow to varied diet.
P_1 mating	5	3			40
P_1 mating	4	4			36
P_1 mating	2	4		1	32
Bent-nose x bent-nose	1	4			31
P_1 mating	5	2			30
P_1 mating		2			17
Bent-nose x bent-nose	2	2		2	15
P_1 mating	1	2	1	1	11
P_1 mating	1			1	10
P_1 mating	1	1			10
Bent-nose x bent-nose		1	1	3	8
Total	111		10		

* P_1 matings were bent-nose x normals unrelated to the bent stock.

No animals appeared bent-nose while being fed fox-chow.

were for the most part the only ones developing bent-nose. Forty-five percent of the animals transferred before 17 days of age developed bent-nose.

A total of 204 animals were born after May 5, 1933, and fed on the varied diet. One hundred twelve of these animals were normal and 93, or 45%, developed bent-nose. One hundred seventeen animals, of which 52, or 44%, developed bent-nose, were reared from the matings which produced 191 animals, all normal, while on the fox-chow diet. Since all other environmental factors were identical, this proves that diet is a factor in determining whether or not animals will be bent-nosed.

Fourth Period - Results of Controlled Diet.

On November 18, 1933, a controlled diet was introduced to enable the author to investigate further the inheritance of the character. (See part III.) Though the results of this diet were not so striking as of the other two diets they should be discussed.

This controlled diet was formulated with two views in mind: (1) it was to contain the same materials as the varied diet of the third period but to be of known proportions; (2) the controlled diet was to be so finely ground and thoroughly mixed that there would be no chance for selection of food by the individual rat.

The following materials constituted this diet in the proportions indicated:

Material	Proportion by weight
Rolled oats	10 parts
Whole wheat	10 parts
Bran	10 parts
Middlings	10 parts
Corn meal	10 parts
Barley	10 parts
Rice	10 parts
Macaroni	10 parts
Navy beans	5 parts
Lima beans	5 parts
Cocoanut (shredded)	5 parts
Raisins	5 parts
Potatoes (pared)	10 parts
Carrots (pared)	10 parts
Salmon	10 parts
Whole milk	10 parts
NaCl	0.5 parts
Cod-liver oil	1 tablespoonful for each 14 pounds of food.

The grains, macaroni, beans, cocoanut and raisins were thoroughly mixed and finely ground together. Each day ten pounds of this mixture was cooked into a mush with tap water and later the proper proportions of milk, potatoes, carrots, salmon and cod-liver oil were added. The cooked potatoes and carrots were run through a fruit press as was the salmon to make it possible to mix them thoroughly.

This diet contained all the materials fed in the varied diet of the third period. However, the proportions were not the same since those of the varied diet were not known. The amount of wheat and corn was probably greater in the varied diet than in this one.

It is evident that this diet, though intended to be deficient, was too well balanced to produce many bent-nosed animals. By January 27, 1934, no bent-noses had appeared in 143 animals. At this time milk and cod-liver oil were eliminated from the diet. On February 9, 1934, one backcross animal was found to be bent-nosed, and February 17, 1934, one progeny of bent-nose x bent-nose was observed to be bent. Also, another such progeny was found to be bent February 19, 1934. These three animals, 2.1%, from a total of 143 were all that developed the bent-nose while the controlled diet was fed. The 143 animals included only those which had been reared to maturity (120 days of age), etherized, and had their skulls examined.

During this fourth period four control matings of normal rats imported from the Wistar Institute produced 64 animals all of which appeared normal externally. However, only 19 of these animals were over 120 days of age though all were 63 days old or older when the final observation was made (May 12, 1934).

Tests for Rickets in the Bent-nosed Stock.

Sherman defines rickets as a condition in which the mineral metabolism is disturbed in such a way that calcification of the bones does not take place normally. Three types of rickets may occur: (1) Low-phosphorus rickets - when there is an excess of calcium in proportion to the amount of phosphorus; (2) Low-calcium rickets - an excess of phosphorus in proportion to the amount of calcium; and (3) Low-calcium low-phosphorus rickets - when both are reduced.

Rickets is usually accompanied by one or more of several bone abnormalities, as crooked sternum (pigeon breast), knobs forming on the ribs at their union with the costal cartilage which produces the rachitic rosary, curvatures of the spine, and bending of the longer bones causing bowed-legs or knock-knees in children. Thus, when one finds a bone abnormality influenced by food, he immediately suspects rickets; as did the author when he discovered that the appearance of bent-nose was influenced by diet.

The next logical step was to make some tests to determine whether these bent-nosed animals were rachitic. Quoting Sure (1933): "At least four methods are used for detection of rickets experimentally: (1) X-rays; (2) total mineral and calcium content of the bones; (3) phosphorus content of blood; (4) line test." Brief tests were made by three of these methods, each of which will be taken up. There was no determination for phosphorus content of the blood.

The X-ray test.

Eight animals were subjected to the X-ray test, the X-ray photographs of which are given in plates VI to XIII inclusive. Plate V gives the photograph of a normal animal for comparison. These are the X-ray photographs which were used for the anatomical study, and the technique for taking them was given during the discussion of that phase of the problem.

In examining X-ray photographs for signs of rickets there are several points for which one should look. The skeleton of a rachitic rat in general looks "scrubby"; the "pigeon breast" character appears in the sternum; the ribs show the typical "rachitic rosary"; the spine is apt to be curved; and the long bones may be poorly formed with enlarged ends. From the plates one observes that none of these characteristics appeared in these pictures, with two possible exceptions. Three of the skeletons appear to have curved spines, but, as the author explained in Part I, he believes this was due to muscle contraction under anaesthesia rather than abnormalities in the vertebrae. The skeletons of the bent-nosed animals are not as large as the normal skeleton, but this difference is not great enough to justify one's concluding that they were rachitic.

Thus, the X-ray test indicates that at the time the X-ray pictures were taken the animals were not rachitic.

The bone ash percentage determination.

Determination of ash percentage compared to percentage of organic matter has been used extensively as a test for rickets. It has been found that after fat has been extracted and the bones dried, normal bones will range from an extreme low of about 45% ash to 60% or above, varying with food, age and sex. Proper proportions of calcium and phosphorus in the food with ample vitamin D tend to increase the ash percentage. Also the ash percentage increases with age, and females tend to have a higher percentage of ash than do males. The ash percentage of rachitic animals is exceedingly low, often being below 30%.

To make this test, a normal and his bent-nosed sib 91 days of age, two normals and their three bent-nosed sibs 163 days of age, and one lactating bent-nosed ♀ 299 days of age were used. In accordance with the usual custom only the femurs were tested. The animals were etherized and their femurs removed. After all the flesh had been rubbed and scraped from the bones the fat was extracted with alcohol for 50 hours, that being more than ample time. They were then dried and weighed. For three hours they were burned in a combustion furnace after which they were weighed again. From the weights before and after igniting the ash percentage is calculated. The results of these procedures and calculations are given in Table VIII. Precautions for accuracy, as handling crucibles with tongs rather than fingers, using crucibles at constant weight, etc., were observed throughout the analysis.

Bent ♂ 1501 and normal ♂ 1506 had been fed throughout on the controlled diet. Male 1501 had appeared bent February 17, 1934, and 24 days later was used for the ash percentage test. No significant difference appears between the ash

Table VIII

RESULTS OF BONE ASH PERCENTAGE DETERMINATION

Animal	Age in days	Femur	Weight of bone* before igniting in gms.	Weight of ash after igniting in gms.	% Ash
Normal ♂ 1506	91	Right	0.1206	0.0559	46.35
		Left	0.1219	0.0577	47.33
Bent ♂ 1501	91	Right	0.1503	0.0704	46.84
		Left	0.1403	0.0674	48.04
Normal F_1 ♀ 651	163	Right	0.1275	0.0699	54.82
		Left	0.1267	0.0710	56.04
Normal F_1 ♂ 650	163	Right	0.1419	0.0764	53.84
		Left	0.1510	0.0805	53.31
Bent F_1 ♂ 652	163	Right	0.1591	0.0877	55.12
		Left	0.1568	0.0861	54.91
Bent F_1 ♂ 648	163	Right	0.1510	0.0795	52.65
		Left	0.1540	0.0813	52.79
Bent F_1 ♂ 655	163	Right	0.1394	0.0756	54.23
		Left	0.1481	0.0814	54.96
**Bent ♀ 473	299	Right	0.1751	0.0875	49.97
		Left	0.1659	0.0822	49.55

* Weight after extraction of fat and drying.

** ♀ 473 had been lactating for 28 days.

percentages of the femurs of these two animals nor is either below what would be expected for normal rats of that age. The animals which were 163 days old had been fed on the varied diet for a short time during their early life but from the age of 48 days had been placed on the control diet after which time bent-nose in the three animals became apparent. Note that no significant difference occurs between the bent and normal sibs nor is the ash percentage for any of the five lower than normal expectancy. Female 473 had no animal with which to be compared. The ash percentage for ♀ 473 is a little low for an animal of that age, but this is due to her having been lactating for 28 days.

In summary, these results indicate that these bent-nosed animals were not rachitic. It is certain they were not rachitic at the time the test was made. *

The line test.

Four bent-nosed and two normal animals from the experiment were subjected to the line test in an attempt to discover whether the bent-nosed animals tended to be rachitic or not.

The primary purpose of the line test, formulated by Steenbock and others, was not a means by which rickets could be detected in animals, but to aid in determining the vitamin content in a food, — usually milk. However it is convenient for giving an indication of rickets in animals.

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* These conclusions were drawn after consultation with Dr. C. A. Hoppert of the Chemistry Department, Michigan State College.

The method of using this test is as follows: The animals are etherized and the radius and ulna removed. Any long bone would suffice, but the radius and ulna, being most convenient, are nearly always used. Care must be taken in removing these bones not to break off the epiphysis. The distal 1/3 to 1/2 of these bones is cut from the rest of the bone and longitudinally split, then submerged in a solution of silver nitrate. The silver nitrate reacts with the calcium phosphate forming silver phosphate. In the presence of light, silver phosphate is reduced, setting free the silver. This enables one to distinguish between calcified areas and cartilaginous areas as the former appear dark.

A rachitic bone can be detected by the appearance of the metaphysis and the size of the end of the bone. A normal bone has a very narrow cartilaginous metaphysis while that of a rachitic bone is quite broad due to the decalcification of the adjoining portions of the diaphysis and epiphysis. This normal metaphysis plus the decalcified areas on both sides is often referred to as a rachitic metaphysis. The end of a rachitic bone becomes much larger than normal as if to compensate for the strength lost by decalcification. This enlargement can usually be detected by palpation.

Five of the animals, 3 bent and 2 normal, subjected to the test ranged from 91 to 105 days of age. A fourth bent animal was 183 days old. Had the animals ever been rachitic it should have shown up in the animals from 91 to 105 days of age. The animal 183 days of age was old enough that it could have recovered from the condition.

When the readings on these bones were made, it was discovered that all animals with but one exception showed no increase in width of the metaphysis. This exception was bent ♀ 491 (Figure 3) and the metaphysis was not sufficiently wide to be classed as rachitic. Most of the animals showed a very slight bulging of the end of the diaphysis but this was not comparable to that of a rachitic animal. All readings were verified by Dr. C. A. Hoppert of the Chemistry Department. There was no difference between the appearance of the bones from the bent animals and those from the normals.

Figure 3 gives sketches of the bones of these rats and that of a standard rachitic animal, i.e., one fed on the Steenbock rachitic ration for 31 days.

Conclusions Drawn From Observations on the Effects of Nutrition.

(1) Diet is a factor influencing the expression of the character bent-nose of the rat (Rattus norvegicus).

*(2) X-ray photographs indicated that the bent-nosed animals were not rachitic at the time the photographs were taken.

*(3) Of the animals subjected to the bone ash determination of the femurs, no significant difference appeared between bent-nosed animals and their normal sibs, nor were any of the animals abnormally low in percentage of ash.

*(4) None of the animals subjected to the line test showed rachitic metaphyses, and no significant difference was detectable between bent-nosed and normal animals.

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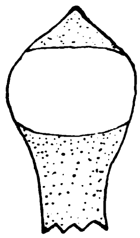
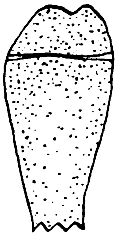
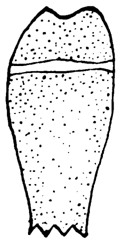
* These three statements are indications rather than conclusions due to the paucity of animals subjected to each test.



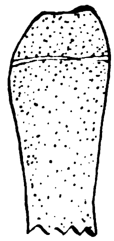
Negative of a standard rachitic rat, i.e., one fed on Steenbock rachitic ration for 31 days.



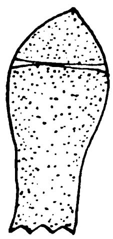
Normal ♀ 490



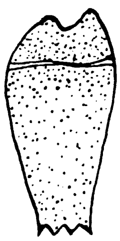
Bent ♀ 491



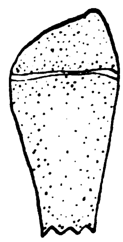
Bent ♂ 492



Bent F_1 ♀ 617



Normal F_1 ♀ 629



Bent F_2 ♀ 323

Fig. 3 Negatives of the line test with one standard rachitic negative for comparison.

Note that these negatives show normal metaphyses with one exception which is only slightly wider than normal; also, all negatives show little or no bulging.

PART III

HEREDITY OF THE BENT-NOSED RAT

When one attempts to review genetic literature, he is struck by the paucity of bone abnormalities which are definitely explained on an hereditary basis. More malformations of the bone are attributed to nutrition factors than to those of heredity. It is quite probable that in many cases both types of factors are working together to bring about the expression of the character.

The work done on the flexed tail mouse by Hunt, Mixter and Permar is one of the most thorough genetic analyses ever made of a bone abnormality. This is an anomaly in which the caudal vertebrae are malformed and fused, causing the tail to appear flexed in varying degrees. The condition has been found to be inherited as a recessive with modifying factors.

Brown and Green (1932) made a study of hereditary variations in the skull of the rabbit. Quoting from their paper which appeared in Science, "Genetically, the importance of the observations recorded lies in the fact that a profound variation in the form of the skull can be transmitted, unaltered, from parent to offspring; by crossing an animal possessing a skull of this type with a normal, the original variation can be resolved into a group of component parts which bear little or no resemblance to the original condition, but these are inherited as distinct entities; they are differentiated into right and left sided characters and can be recombined to form the parental type as well as new types which are capable of further transmission."

A genetic craniometric study of two species of mice, by Green (1932), has shown that the size of the skull tends to be inherited. However Green states that a thoroughly satisfactory genetic explanation appears impossible with the data he has gathered.

Another study more closely related to the bent-nose study was that reported by H. S. Colton on the "high-brow" rat (1929). This was a brief study and it failed to demonstrate whether the character was or was not inherited.

As the reader has observed, with one exception these investigators have found no definite genetic explanation for the bone anomaly with which they were working. The author regrets that he too has found no genetic solution for his respective problem.

However, an attempt was made to determine the inheritance. The primary purpose of the experiment was to determine whether bent nose is inherited, and if so, how. Other phases of the situation were unexpectedly encountered. Had not the analysis been divided into so many periods, thus distributing the data into four categories, more definite discoveries concerning the genetics of the character might have been made. Nevertheless, the data gathered do throw some light on the solution and are well worth presenting.

Technique Used in Conducting Breeding Experiments.

In order to prosecute an experiment with sufficient accuracy, several precautions must be adhered to. The subsequent rules were followed throughout the experiment.

(1) No animal entered the experiment without receiving a number which was marked in its ear.

(2) No females were mated which had not previously been isolated for at least twenty-one days.

(3) Females were usually isolated before parturition. In a few cases they were allowed to remain with the male, but these were instances in which no other female was in the breeding cage.

(4) Young were weaned and marked at the age of 28 days or less in all cases when the mother was remated before 21 days after weaning her progeny.

(5) Though the date at which an animal appeared bent-nosed was always recorded, no animals were definitely pronounced bent-nosed or straight until after they were mature, at least 120 days old, and their skulls had been removed and examined with a straightedge. A few exceptions to this statement are animals now running in the experiment, but which are definitely bent-nosed.

(6) With the exception of food, which has been discussed previously, all environmental factors were controlled.

Presentation and Discussion of Data.

Due to the changes made in food and the radical results of these changes, it is necessary to divide these data into the four periods used in the study of nutritional effects.

<u>Data obtained during first period.</u>

As the reader will recall, the author began the experiment with a number of Mr. Wiren's animals. These could be classed in the following categories: (1) F_1 animals with no bent-nosed sibs, (2) F_1 animals with bent-nosed sibs, (3) bent-nosed rats, and (4) normal progeny of bent x bent. By F_1's is meant progeny of bent x normal. The results of the matings of these animals are given in table IX. Progeny of other P_1 matings are included. These P_1 matings were not of rats from Mr. Wiren's stock but were of bent-nosed animals from the red-eyed-yellow stock x normal animals from stock unrelated to the red-eyed-yellows.

The results of the matings were not very striking in this period. Only five bent-nosed animals, compared to 107 normal, were reared. The paucity of the number of bent-nosed animals is evidently due partly to the animals having been put on the fox-chow ration before reaching maturity. The ages of these rats when put on fox-chow ranged from 7 to 63 days. Two of the bent-nosed animals appeared in the progeny from the mating, F_1 (with bent sibs) x F_1 (with bent sibs). One appeared in a backcross mating of F_1 ♂ (with no bent sibs) x bent ♀, and the other two appeared in the backcross mating of F_1♀ (with bent sibs) x bent ♂. Of the six F_1 animals reared, all were normal.

These data indicate that if the character were inherited, it followed no simple Mendelian scheme, and since no F_1 animals were bent-nosed one would suspect that the character was recessive.

Table IX

ANIMALS BORN BEFORE JANUARY 1 , 1933

Type of mating	Total offspring		Normal offspring		Bent-nosed offspring	
	♂	♀	♂	♀	♂	♀
F_1 (with no bent sibs) x F_1 (with no bent sibs)	3	6	3	6		
F_1 ♂ (with bent sibs) x F_1 ♀ (with no bent sibs)	25	17	25	17		
F_1 ♂ (with no bent sibs) x F_1 ♀ (with bent sibs)		2		2		
F_1 (with bent sibs) x F_1 (with bent sibs)	5	6	3	6	2	
F_1 ♂ (with no bent sibs) x Bent ♀	4		3		1	
F_1 ♂ (with bent sibs) x Bent ♀	7	3	7	3		
Bent ♂ x F_1 ♀ (with bent sibs)	11	8	10	7	1	1
F_1 ♂ (with bent sibs) x Normal ♀ (progeny of bent x bent)	6	3	6	3		
P_1 Matings (Bent ♂ x Normal ♀ unrelated to bent stock)	2	4	2	4		
Total	112		107		5	

Data obtained during second period.

The matings made during the first period were kept breeding during the second period. A total of 191 animals were reared during this period, but since the fox-chow suppressed the character these data are of no value in studying the inheritance of bent-nose. Results of this period are given in table X.

Data obtained during third period.

The most valuable data for the inheritance study were gathered during this period. These data are tabulated in table XI.

Matings of the previous periods were continued and in addition were made five more F_1 matings, four brother-sister matings of normal progeny from bent x bent matings, and 12 P_1 matings of bent x normal animals from the bent-nose stock. The latter is not a true P_1 mating as these normals might carry some of the factors for the expression of bent-nose, but not show the character as they lacked the complete necessary set-up. As the reader will recall, the author was sorely in need of bent-nosed animals, this being his reason for setting up these matings which were quite likely to produce such animals.

On analyzing these data one finds several points which indicate that the character is influenced by heredity. In table XI one will observe that inbreeding tends to produce more bent-nosed animals. In the 27 progeny of brother-sister matings of the normal animals from the bent x bent matings,

Table X

ANIMALS REARED ON FOX-CHOW

Type of matings	Progeny ♂	Progeny ♀
F_1 (with no bent sibs) x F_1 (with no bent sibs)	41	35
F_1 ♂ (with no bent sibs) x F_1 ♀ (with bent sibs)	10	18
F_1 ♂ (with bent sibs) x F_1 ♀ (with no bent sibs)	13	12
F_1 (with bent sibs) x F_1 (with bent sibs)	7	4
F_1 ♂ (with no bent sibs) x bent ♀	15	10
Bent ♂ x F_1 ♀ (with no bent sibs)	2	5
Bent ♂ x F_1 ♀ (with bent sibs)	1	3
F_1 ♂ (with no bent sibs) x normal ♀ (progeny of bent x bent mating)	6	9
Total	191	

All animals were normal.

Table XI

ANIMALS BORN AFTER MAY 5, 1933,
AND FED ON VARIED DIET.

Type of mating	Total offspring		Normal offspring		Bent-nose offspring		% Bent
	♂	♀	♂	♀	♂	♀	
F_1 (with no bent sibs) x F_1 (with no bent sibs)	55	40	34	22	21	18	41 %
Backcross F_1 ♀ (with bent sibs) x Bent ♂	3	2	1	2	2		40 %
Backcross F_1 ♂ (with no bent sibs) x Bent ♀	6	6	3	2	3	4	58 %
Bent-nose x Bent-nose	2	2			2	2	100 %
P_1 mating (Bent ♂ x normal ♀ unrelated to bent-nose stock)	6	3	4	2	2	1	33 %
Normal progeny of bent-nose x bent-nose, mated inter se	16	11	4	5	12	6	67 %
P_1 mating (Bent-nose ♂ x normal ♀ from bent-nose stock)	30	22	20	12	10	10	38.5%
Total	204		111		93		45.6%

67% were bent. The four progeny of the bent x bent mating were all bent-nosed. Of the 12 progeny of the backcross F_1 ♂ (with no bent sibs) x bent ♀, 58% were bent-nosed, 41% of the 95 F_2 animals were bent-nosed, and of the 52 F_1 animals from the P_1 mating (bent x normals from the bent stock) 38.5% were bent-nosed, while of the nine F_1 animals from the P_1 mating (bent x normals from unrelated stock) 33% were bent-nosed. In only three classes are the numbers of individuals great enough to give frequency percentages of statistical value. These were: (1) progeny whose parents were normals from bent x bent, mated inter se, (2) progeny of bent ♂♂ x normal ♀♀ from the bent stock, and (3) F_2's from F_1's (with no bent sibs) x F_1's (with no bent sibs). Between the first and second class, a frequency of bent percentage difference of 28.5 ± 7.61 exists, while between the first and third class there is a difference in frequency of bent percentages of 26 ± 6.99. These are both significant, but the difference between classes two and three is 2.5 ± 5.68 which is not statistically significant. (Table XII.) The first two differences would indicate that there is an apparent decrease in the percentage of bent-nosed animals as the concentration of bent-nose declines.

It is true that the animals were not fed on a controlled diet, which might account for one animal developing bent-nose when his sib was normal, since there was a chance for some rats to select certain ingredients and to reject others in the imperfectly mixed ration; but it is hardly probable, considering the group as a whole, that one would

Table XII

PERCENTAGE OF BENT-NOSED PROGENY WITH DECREASING PROPORTION OF BENT ANCESTRY

Parent	Number of progeny	% bent among progeny
Bent x bent	4	100
Normals from bent x bent, inter se	27	67 ± 6.10
F_1 ♀ (with bent sibs) x bent ♂	5	40
F_1 ♂ (with no bent sibs) x bent ♀	12	58
Bent ♂ x normal ♀ from bent stock	52	38.5 ± 4.55
F_1 (with no bent sibs) x F_1 (with no bent sibs)	95	41 ± 3.41
Bent ♂ x normal ♀ from non-bent stock	9	33

find such marked differences in the percentage of bent-nosed animals in the different classes were due wholly to selection of food. It would be possible for animals to inherit certain tastes which the inbreeding brought out, but still the character would be indirectly influenced by heredity. In short, if the bent-nosed condition is due wholly to dietary influences, why do not all the types of matings produce substantially the same percentage of bent animals irrespective of ancestry?

If the character is hereditary, it must be influenced by dominant factors as bent-nose F_1 animals appear. One could not conclude that it was or was not sex-linked since, due to the shifting from one period to another, data on reciprocal crosses were not obtained.

In all, only 204 animals were reared in this period; and since these were divided into so many different categories, the numbers from any one type of mating are not great enough to justify one's drawing definite conclusions. The percentage differences may have been due exclusively to non-genetic causes operating within small numbers.

Data obtained during fourth period.

The data of the fourth period were obtained under a condition in which every factor was controlled with the exception of heredity. Any variation in the frequency of bent-nose in these animals could not be attributed to food. If heredity were not a factor in the production of the bent-nosed character, one would expect all animals to be either bent-nosed if the food was sufficiently deficient to cause the character, or normal if the food was of such a constitution to prevent the development of the anomaly. Three animals from a total of 143 developed bent-nose during this period. (See table XIII for data.) Two of the bent-nosed animals were derived from bent-nose x bent-nose crosses, while the third was from a backcross. None of the F_1 or F_2 animals developed the character. It would have been necessary to have had more bent-nosed animals appear to prove that the character was influenced by heredity. However, only on the assumption that hereditary influences exist can the appearance of the three bent-nosed animals be explained.

It is quite possible that this controlled diet was much more nearly balanced than the combination fed during the third period. Though this contained the same ingredients of the varied diet, the proportions were not the same since those of the latter were not known. Probably a higher frequency of bent-nosed animals would have appeared during this fourth period had the diet constituents been in the same proportions as those in the preceding period.

Four females and two males were imported from the Wistar Institute October 13, 1933, and were mated to secure some control animals. From these control matings 64 animals were reared, all of which were fed on the controlled diet. None of these animals has shown the bent-nosed character. However, as previously cited, only 13 are older than 120 days, though the remainder are over 63 days of age. Since none of these animals has been etherized, only a superficial examination has been made.

Table XIII

ANIMALS BORN AFTER NOVEMBER 18, 1933,
FED ON CONTROLLED DIET.

Type of mating	Total offspring ♂	Total offspring ♀	Normal offspring ♂	Normal offspring ♀	Bent-nosed offspring ♂	Bent-nosed offspring ♀
F_1 (with no bent sibs) x F_1 (with no bent sibs)	21	29	21	29		
Backcross F_1 x Bent	24	33	24	32		1
Bent-nose x Bent-nose	11	8	9	8	2	
P_1 mating (bent ♂ x normal ♀ unrelated to bent-nose stock)	11	6	11	6		
Total	143		140		3	
Control matings (normal x normal Wistar animals)	37	27	37	27		
	64		64			

Another aspect of the problem which was presented during the anatomical study, but which gives evidence of heredity, was the specifity with which the factors causing bent-nose manifested themselves. As the reader will recall, the condition is normally accompanied by no other bone abnormality. Though this does not prove that bent-nose is inherited it is more characteristic of the action of hereditary factors while nutritional deficiencies alone usually have a more generalized effect.

Summary of Heredity Study.

Until more complete data have been obtained, definite conclusions will not be drawn as to whether the bent-nosed character is inherited or not. The following facts are evidence that bent-nose is inherited.

(1) The character appeared in the red-eyed-yellow stock and not in the three stocks of the colony that were unrelated to the red-eyed-yellows, though all were subjected to similar environment.

(2) It appears to be possible to breed for high frequency of occurrence of the bent-nosed character.

(3) Three animals developed bent-nose in a total of 143 animals when all factors but heredity were controlled.

(4) The factors causing bent-nose are specific in their manifestation. Normally no other structural anomaly accompanies the bent-nosed character.

GENERAL DISCUSSION

Though the data are not conclusive, it appears that bent-nose is the resultant of the interaction of several causative agents including both environmental and heredity factors. It seems that a definite genetic constitution is necessary for the appearance of the anomaly, but this can be manifested only when the diet is deficient.

It has been definitely proved that food is a factor. From matings which produced 191 animals, all normal, on fox-chow, breeding with a varied diet yielded 117 of which 52, or 44%, developed bent-nose. Many facts indicate that the character is genetic. The causative factors are specific in their manifestation; inbreeding tends to increase the frequency of bent-nosed animals; the condition was prevalent in only one strain of the colony; and when all environmental factors are controlled three animals developed the anomaly. All of these tend to prove that the character is inherited, and when a thorough analysis has been completed, heredity may be found to be quite as important as diet.

The most nearly conclusive evidence of bent-nose being hereditary is the apparent increase in the percentage of bent-nosed progeny with increasing proportion of bent ancestry. (Table XII.) If the character were genetic, one would expect a higher frequency of bents among the progeny of normals from bent x bent, mated inter se, than among the F_2's from F_1's with no bent sibs x F_1's with no bent sibs. Of the first class 67%

were bent, while only 41% of the F_2's were. This is a statistically significant difference. The frequency of bent-nose among the progeny of bent ♂♂ x normal ♀♀ from the bent stock was 38.5% which is also significantly less than that of the progeny of normals from bent x bent, mated inter se. This difference is of less value than the former, due to the possible variability in the genotypes of the normal females from the bent stock.

One would expect the character to be rachitic in nature. However, the tests have indicated that the animals are not rachitic. Those examined did not show a rachitic metaphysis, an abnormally low percentage of bone ash content, nor other structural anomalies usually present in rachitic animals. However, as yet these tests are not conclusive.

The problem is not solved; only some of its phases have been revealed. Before the genetics can be analyzed, a controlled diet which will give a high frequency of bent-nosed animals must be formulated. A homozygous bent-nosed strain that could be crossed with normals should be developed by inbreeding. Then with a controlled and deficient diet and a homozygous strain it should be possible to discover many facts on the inheritance of the character.

Though it has been proved that food is a factor, its causative elements are unknown. These should be determined. The study of rickets should be continued more extensively to determine whether there is some bone deficiency just at the time bent-nose is developing.

GENERAL CONCLUSIONS

(1) Bent-nose, a character of the rat, has its expression centered on the rostrum of the skull.

(2) Diet is a factor in determining whether or not animals will be bent-nosed.

(3) Though the data are inadequate to prove definitely that bent-nose is inherited, many facts strongly indicate the presence of genetic factors.

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EXPLANATION OF PLATES

Plates I and II are photographs of the bent-nosed character. Plate I is an external view while II is a dorsal view of cleaned bent skulls.

Plates III and IV demonstrate apparatus and technique used in measuring skulls.

The remainder of the plates are X-ray photographs, the first (plate V) being a normal animal while the remaining eight are bent-nosed animals. These photographs had two purposes, namely: (1) anatomical study, (2) rachitic test.

Plate I

External appearance of a bent-nosed animal. Adult animal with nose bent to the right.

Plate II

Skulls showing the bent-nosed condition. Female 6 normal. Female 7, Female 9 and Female 11 bent.

The absence of the zygomatic bone is not an anomaly as in each case it was lost while the skull was being cleaned.

Plate III

Strain gage mounted with points for making all skull measurements except the length. Micrometer to the right used for measuring the length of the normal skulls.

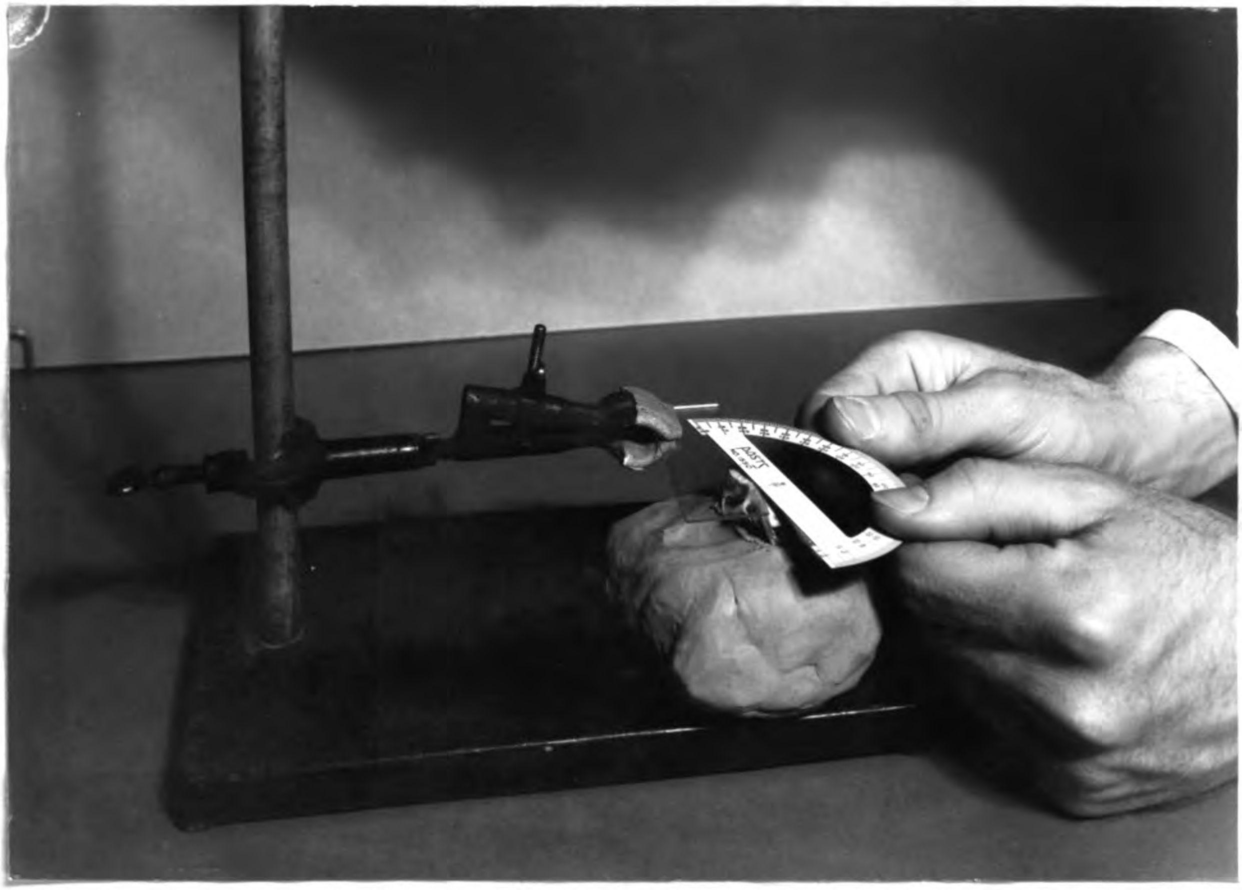

Plate IV

Demonstrating method used for measuring the angle of bend in the skulls.

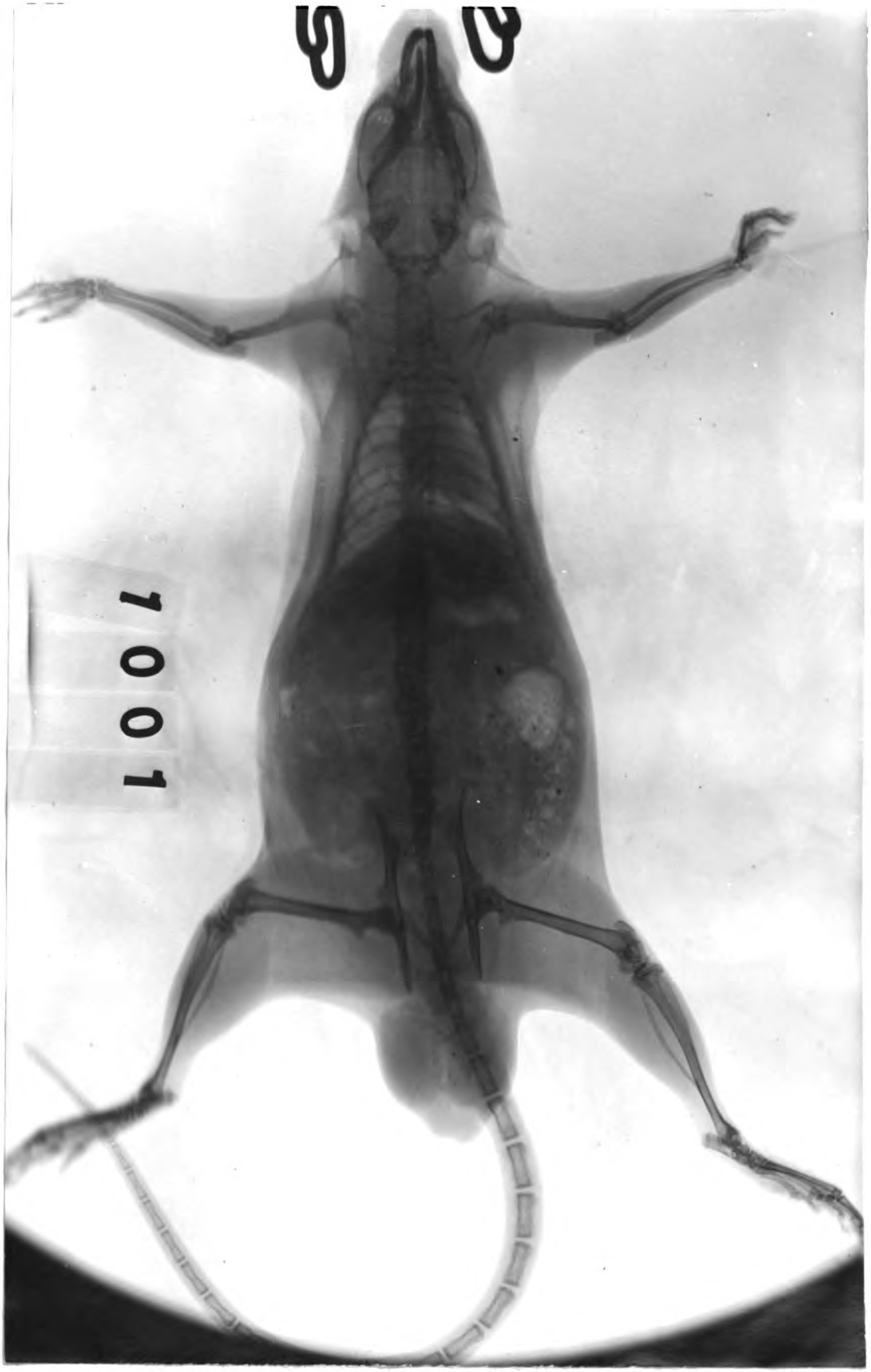

Plate V

An X-ray photograph of normal Male 1001
from the control stock.
Age 108 days.

Plate VI

An X-ray photograph of bent Male 1B, a progeny of a brother-sister mating of normal animals derived from a bent x bent mating.
Age 217 days.

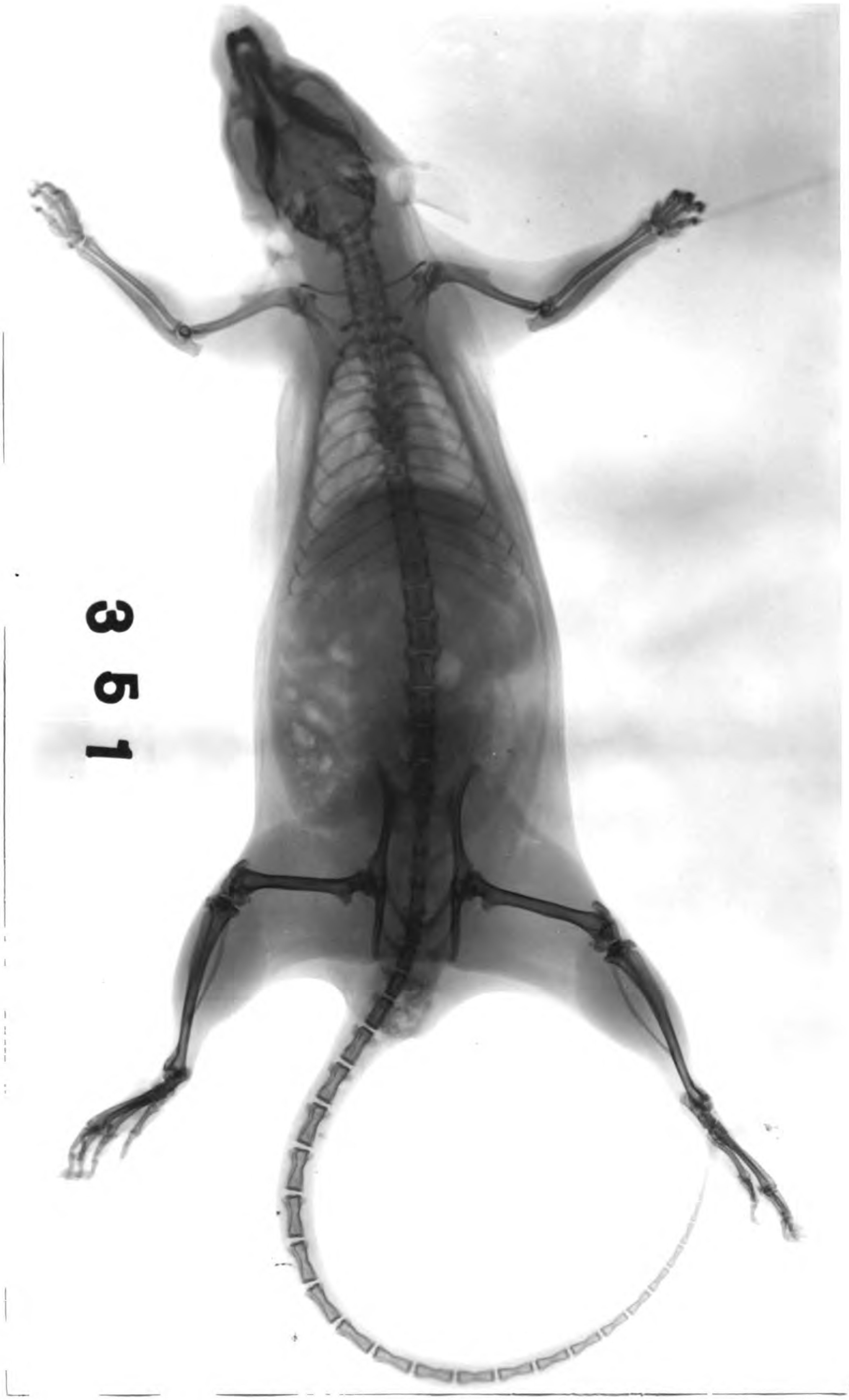

Plate VII

An X-ray photograph of bent F_2 Female 351,
Age 167 days.

Plate VIII

An X-ray photograph of Bent F_2 Male 375
Age 167 days.

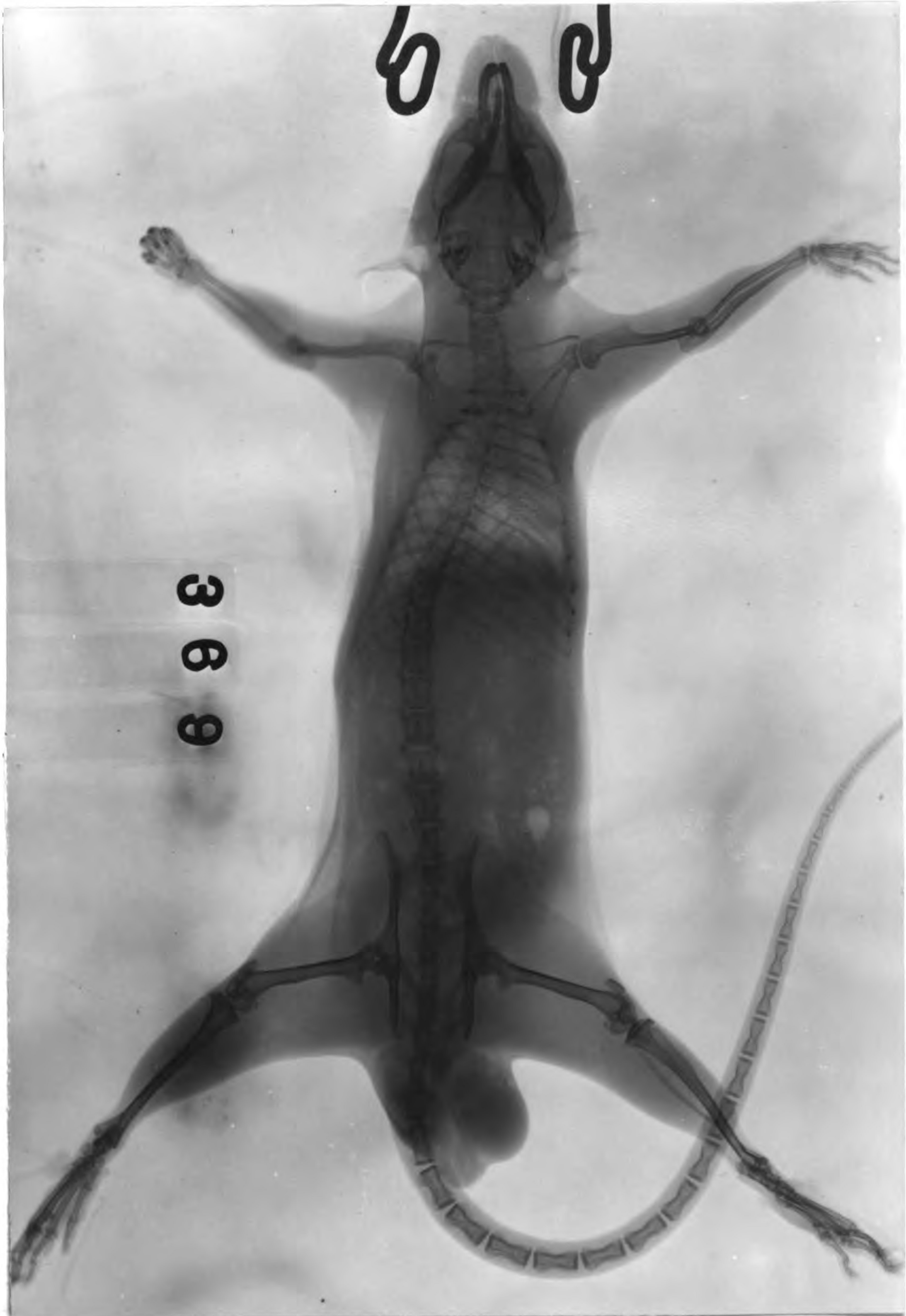

Plate IX

An X-ray photograph of bent F_2 Male 369,
Age 167 days.

Plate X

An X-ray photograph of bent Male 5B, a progeny of a brother-sister mating of normal animals derived from a bent x bent mating.
Age 217 days.

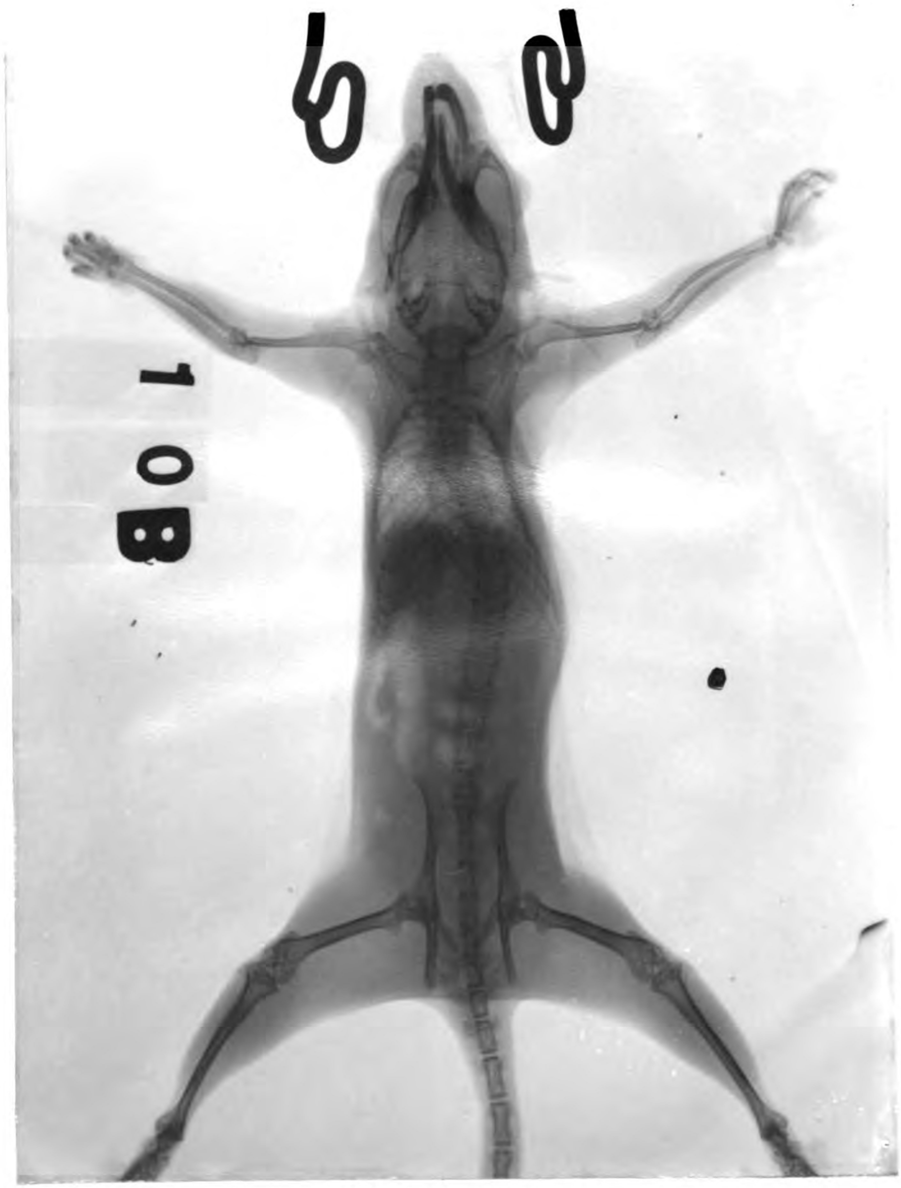

Plate XI

An X-ray photograph of bent Female 10B, a progeny of a brother-sister mating of normal animals derived from a bent x bent mating.

Age 164 days.

Plate XII

An X-ray photograph of bent Male 6B, a progeny of a brother-sister mating of normal animals derived from a bent x bent mating.

Age 204 days.

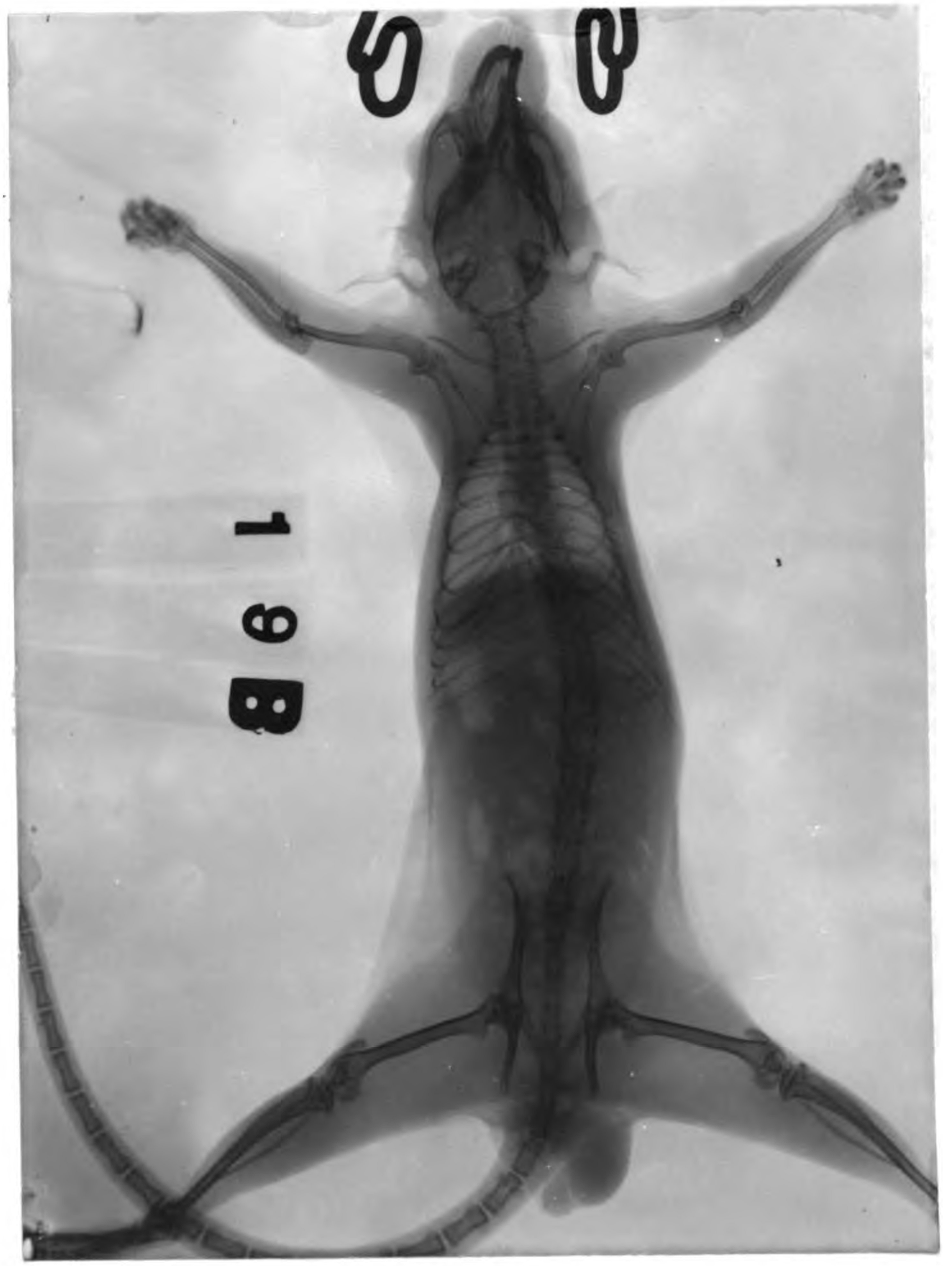

Plate XIII

An X-ray photograph of bent Male 19B, a progeny of a brother-sister mating of normal animals derived from a bent x bent mating.

Age 193 days.

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