BENT-TAIL
A NEW MUTATION IN THE HOUSE MOUSE, MUS MUSCULUS

Thesis for the Degree of M. S.

MICHIGAN STATE COLLEGE

Herschel L. Irons

1937

THESIS

Mice

Title

Zoology

BENT-TAIL

A NEW MUTATION IN THE HOUSE MOUSE, MUS MUSCULUS

THESIS

Submitted to the Faculty of the Michigan State College
in Partial Fulfillment of the Requirements for the Degree of
Master of Science.

by

HERSCHEL LESTER IRONS

August, 1937.

THESIS

ACKNOWLEDGMENT

The author wishes to express his gratitude and thanks to Dr. H. R. Hunt for his careful guidance and untiring effort in guiding this piece of research.

TABLE OF CONTENTS

INTRODUCTION

Distortions of the tails of animals due to the fusion of caudal vertebrae have been reported by several authors. These investigators have captioned the trait variously as, "kinky", "flexed", "wry", "screw", and fused, depending in a measure upon the amount and type of distortion.

Sometime prior to 1933 animals with bent tails were discovered in the stocks at the Michigan State College Rodent Colony. Several of these animals were mated and a bent stock maintained. This stock furnished the bent-tailed animals used to start this investigation.

The bent-tailed character is highly variable in its expression. (Fig. 1). The tails are rigid at the bends, indicating vertebral fusions. In most cases there are one or more permanent angles in the tail. The abnormality ranged from bends which were very slight, but perceptible, to spiral forms resembling cork screws. These spirals may turn clockwise or counter clockwise. It was observed that as a rule the bends were located in the distal half of the tail, though the proximal half occasionally showed fusions. The base of one of the tails formed a right angle with the bertebral column, then turned cephalad under the left leg where it again angled beneath the animal's body. The result was that the scrotum

and genital organs appeared as though framed. One animal was found which appeared straight-tailed, but palpation showed that it had definite vertebral fusions.

Such a bent-tailed condition in wild mice would extremely handicap the possessor. One of our experimental animals was caught in the wire-mesh cage top by the spiral in its tail. It was unable to extricate itself and died.

Bent tailed animals showed other abnormalities. Several male animals had double scrota. Efforts to breed these males were unsuccessful. Several females were noted in which the external genital opening and the anus were the same. One of these females was bred, and produced young without difficulty.

The bent character is very much like flexed (Hunt 1933) in its phenotypic expression, and the two traits might be regarded as the same in the absence of breeding tests. Fused (Reed 1936) is also very much like bent both in phenotypic expression, and inheritance. We will review both of these papers in some detail in order to establish the similarities and disimilarities between flexed, fused and bent.

Literature

According to Nordby (1934) the kinky tail in swine is characterized by rigid angles in the tail. The trait is distinctly evident at birth. In general the kinks are located toward the distal end of the tail.

The number of kinks per individual varies from one to three. The angles are usually lateral, but the direction of bending is variable. In exaggerated cases the tail may show a distinct hook. These hooks are formed by three rather acute angles which bend in the same direction. The vertebrae may be fused end to end. Such specimens are difficult to classify, and may be mistaken for normals unless the tails are carefully palpated. There are no bends in tails fused in this manner. Kinks are rigid and are due to the fusion of two or more caudal vertebrae.

According to Nordby (1934) the defect in cattle is due to a single recessive gene. There are certain inhibitory influences which prevent the appearance of the normal ratio.

Knapp, Emmel and Ward (1936) reported a similar condition in Red Polled Cattle. The condition is due to a fusion of one or more pairs of adjacent coccygeal vertebrae. The defect appears to be similar to the kinky tailed condition in swine. The trait is recessive.

In 1935 Atkenson and Warren reported a wry tail condition in Jersey cattle. The trait is one in which the base of the tail is set at an angle to the backbone. For a long time the defect was considered as accidental. Genetic implications were suspected when a single bull at the Idaho experiment station sired several wry-tailed calves. In all these calves the tails were set to the

left. The bull was phenotypically normal in all respects, as were the dams to which he was mated. The bull here in question had normal tailed sire and dam. This indicates that the gene for the trait is transmitted through phenotypically normal animals. The investigators showed that the character was inherited as a recessive.

The work of Chesley (1935) varifies Zavadskais's conclusion (Chesley 1935) that the short tailed condition (brachyury) in mice is due to a single dominant factor, although the manifestation of the character is highly variable. Chesley has also shown that a homozygous brachyuric animal dies, so that the gene is a recessive lethal. Thus viable short-tailed mice are always heterozygous. Differences in tail length were observed to be due to modifying factors.

Embryos homozygous for short-tailed die on the tenth or eleventh day after copulation. Both homozygotes and normal embryos appear alike up to eight and one half days after insemination, when they have from four to eight somites. The first evidence of abnormality is the appearance of small paired or unpaired blebs on either side of the mid-line. Then the neural tube becomes slightly irregular. Finally, the somites are not as clear nor as regular as those of normal mates.

Blebs are due to blistering of the dorsal epithelium. These blebs are no longer visible beyond the nine day stage (10 to 12 somites).

Ten days after insemination normal embryos have 25 to 30 somites, anterior limb-buds are present, and posterior limb-buds apparent. In the short-tailed homozygote of the same age there is no marked segmentation, and posterior limb-buds are absent. In these embryos the distance from anterior limb-buds to the posterior end is one-half that for normal embryos. In short, the posterior part of homozygous short-tailed embryos fails to develop normally, causing the mose to die in utero.

The notochord of homozygous short-tails fails to develop normally, so that on the day of the embryo's death there is no evidence whatever of this structure. The neural [illegible] very irregular at the time of closure. Some of these homozygotes show enlargement of the pericardial cavity, obliteration of the dorsal aorta, and fusion of the gut with the neural tube. The viable heterozygote shows a shortening of the embryonic tail; this shortening is first evident on the eleventh day of embryonic development.

Bean (1929) reported on limb abnormalities in mice which are also due to bleb formation. The abnormalities arose in descendants of X-rayed animals. The numerous malformations are characterized by reduction of tarsal or carpal bones due to fusions, resulting in polydactyly, brachydactyly, syndactyly, club foot, etc. Bean believes that these anomalies are due to arrests in the

circulation of blood which cause retardation in development.

Plagens also (1933) has reported on malformed limbs in mice induced by X-ray. Blebs seem to play a conspicuous part in many of the limb abnormalities reported in these papers. These blebs deserve more attention. Plagens' work reveals that blebs form, at about the thirteenth day of development, by a separation of the ectoderm from the underlying mesenchyme. The space thus created is soon filled with lymgh, forming a bleb. Later in embryological development the bleb becomes hematogenous. On the eleventh day it was noted that the marginal vein and capillaries of the limb-bud were mislocated. These blood bubbles cause abnormal development by crowding tissues which would otherwise develop normally.

Bonnevie (1934) attributed these blebs to concentrations of spinal fluid in the limbs. The fluid originates in the medullary tube, and migrates to the legs where it collects. As long as the fluid remains in motion beneath the embryonic epidermis, no ill effects are noted. In these abnormal animals there is an unusually high expulsion of cerebrospinal fluid through the foramen anterious, an opening in the roof of the mylencephalon, which exists for a short time during embryonic development. These abnormalities in the Little-Bagg animals are due to a single recessive gene which produces its effects from

the eleventh to the thirteenth day of embryonic development. The blebs also cause abnormalities in the limbs, head, kidneys, etc., of Little-Bagg's X-rayed stock ( ).

Dunn (1925 and 1936) investigated rumplessness in the domestic fowl. Rumpless birds have no prominent tail feathers, no oil glands at the base of the tail and no vertebrae in the fleshy rump. This absence of tail vertebrae is the characteristic feature of the rumpless fowl. The anterior part of the pelvis is normal. The spinal column is frequently curved. The condition is evident at the time of hatching. Dunn believes that rumplessness is due to the absence of tail vertebrae rather than to a disappearance of vertebral anlage after they have been formed.

He says that there are two types of rumplessness ----- heredity and accidental. Hereditary rumplessness is a dominant trait, and Dunn reports having found a homozygous rumpless female. About one in every thousand chicks is rumpless as a result of accident.

Hereditary duplication of parts of the mouse's body have been reported by Danforth (1930). It was thought that the anomalies were due to X-ray, but subsequent investigation showed that X-ray was not responsible. These defectives usually have four hind legs, two of which are rudimentary. Kinky tails are frequent.

There may be two rectums, two urogenital openings, two bladders, four kidneys, and four gonads. Kinky and otherwise defective tails are frequently found.

Embryological development seems to be normal until the eleventh day, when there arises a pronounced thickening of ventral tissues in the region of the cloacal pit. This pit is forced to widen, producing two cloacal membranes. Thus two rectums appear. Remnants of the caudal intestine become cystic on the sixteenth day. These cysts throw the developing caudal cartilages out of alighment, and these cartilages, fusing, form the tail kinks.

This duplication of hind parts is due to a single recessive gene.

Hunt, Mixter, and Permar (1933) studied the inheritance of a flexed tailed condition in mice. The abnormality is characterized by unions between adjacent caudal vertebrae, and usually by spiral or angular bends in the tail. The expression of the character is highly variable. Bends range from one to sometimes five in a single tail. Often the tail is markedly shortened. Occasionally an animal is found which has no visible flexure, but palpation of the tail shows that adjacent vertebrae are united.

Flexed tailed animals have two other ab-

normalities. Mixter and Hunt (1933) found that anemia during the first two weeks of life is one of these. Ventral spotting has also been reported as one of the anomalies. Flexed, anemia, and ventral spotting are thought to be alleles or to be closely linked in the same chromosome.

Data presented by these writers establishes the flexed tailed character as recessive to normal.

Kamenoff (1932) studied the embryological development of the flexed tailed mouse. The flexure is due to unilateral fusions between successive vertebrae of the tail. The abnormality begins to be noticeable on the fourteenth day of gestation. About this time fibrous tissue is formed by the mesenchyme of the invertebral anlage in normally developing mice. In kinky tailed mice this fibrous tissue is not formed on one side of the notochord. These non-fibrous anlage form cartilagenous connections between the successive vertebrae. Ossification of these connections cause unequal subepiphyseal growth, and produces bends, angles, and spirals in the tail.

The fused mutant arose in the Bussey Institute stocks prior to 1931. Until 1936 it was thought that this new mutation was, because of phenotypic similarities in expression, identical with the recessive

flexed-tail character. However, Reed (1936) has shown by his investigation that the two characters, though phenotypically alike, are genetically different. The most striking difference is the mode of inheritance. Flexed being recessive, and fused dominant, genetically.

Reed mentions the following abnormalities as frequent accompaniments of the fused character: asymmetrical vertebral fusions; absence of the tail in toto or in part; proximal fusion of ribs; tails bifurcated at the distal end, and absence of from one to three ribs. Many of the tail variations and abnormalities reported by Dr. Zavadskaia and her associates (1927-1934) are reproduced in fused animals. Dr. Reed states that fused is in the same chromosome as brachyury. Linkage studies tend to show they are allels or very closely linked. A very important fact is that genetically fused animals may be phenotypically normal; such individuals are called "normal overlaps". Reed proved that there are no modifying genes that affect the expression of the fused character.

Though fused is a simple dominant, the breeding ratios do not closely approximate those expected in monofactorial inheritance. The deviation from the expected F2 ratio is attributed to cytoplasmic or maternal inheritance. This fact is also borne out in a

study of overlap percentages. When F1 fused males are mated with unrelated normals 17.1 % of the normal progeny are overlaps; while if F1 fused females are mated with unrelated normals 57.7 % of the normals are such.

Chesley (1935) studied the embryological development of fused. He showed the notochord to be poorly aligned, and distinct curves and angles present along the neural crests.

Environmental factors, such as litter size, age of mother, or birth rank, do not affect the expression of fused.

THE BENT MUTATION

The study of the mode of inheritance of bent, which is the subject for this thesis, was begun in the summer of 1936. Some preliminary experiments were conducted in 1935. In this preliminary work one bent-tailed male from the colony stock cages was mated to several normal female mice. From the bent progeny six females and three males were saved to begin this work.

The bent trait is highly variable, ranging from bends which are very slight to spirals. Bends

are usually confined to the distal half of the tail, although the proximal half may be affected occasionally. (Fig. 1)

The mice were kept in cages which were 12 inches square, and 12 inches high. They were constructed of sheet metal, with the cage tops made of wire mesh. The mice were fed twice a week on a rolled oat diet alternated with a grain diet. Following are the ingredients of the rolled oat diet: bran, middlings, rolled oats, corn meal, alfalfa meal, powdered milk, codliver oil, and salt. The grain ration was composed of the following: sunflower seed, wheat, barley, cracked corn. This was the ration in general use throughout the laboratory, and was considered as a well balanced diet. Dog bread biscuit were kept in the cages at all times. Drinking water was always available.

Bent-tailed young could be readily classified a few hours after birth. Occasionally a slightly bent animal had to be observed again several days after birth to confirm the classification. Such doubtful cases always proved to be bent, and are recorded as such.

The three bent-tailed males were mated with nine normal females (dark eyed dilute brown), and the six bent females were mated with two normal tailed males. This was an F1 x normal backcross, since each of the bent mice used had a normal parent. These F1 bent

animals must have been heterozygous for the gene or genes responsible for the bent condition. The results are recorded in table 1 (A). Of the 313 progeny 127 (40.6%) are bent. If bent is dominant and due to a single gene we would expect 156.5 bent and the same number of straight tailed animals. We are thus deficient 29.5 bent animals. Unless there are normal overlaps, phenotypic normals which carry the bent gene, we would expect the normals to breed true. Twenty of the F1 back-cross normals were mated to unrelated normals, and of the twenty, one male and two females produced 41 progeny of which 6 (14.6%) were bent. This shows that bent can be transmitted through normal animals. On the basis of this finding one expects 3/20ths of the observed normals to be genetically bent. Hence we must deduct 27.9 from the observed normals, and reclassify them as bent. If this be done the observed and expected ratios are in close agreement. Table 3 A shows the deviation to be only 1.6 from the expected 3:1 ratio.

Such an explanation might lead one to think that bent and Reed's fused were the same. Fused is dominant, as is bent. However, Reed attributes his ratio to a cytoplasmic influence. F1 fused females mated with normal males produced 57% of normal overlaps, and F1 fused males produced only 17.1% overlaps when mated with

unrelated normal females. The evidence for bent being such a factor is not made clear in this experiment. Our data tend to show that bent males produce a slightly greater overlap percentage (table 2) than do females. When heterozygous F1 bent males and females are back-crossed to unrelated normals, the former produce 18.4% and the latter 11.2% normal overlaps. The difference between the observed and the expected normal progeny gives the number of normal overlaps; this figure divided by the number of observed normals x 100 gives the percent of normal overlaps. It would seem that the bent ratios are not due to a cytoplasmic or maternal influence.

When F1 bent females were mated to F1 bent males there were 273 bent and 208 normal progeny. Table 1, B, shows that 56.8% of the total progeny are bent, and that the observed ratio fits a two factor better than a one factor hypothesis. If nine bent to seven normal progeny are expected there would be 270.5 bent to 210.4 normals. The observed data deviate from this 9:7 ratio by 2.4 animals. The deviation from the 3:1 ratio (mono-factorial) is 87.8 animals. The evidence in the F2 leads us to believe that bent is due to two complementary factors. Reed's data also fits the 9:7 ratio more closely than it does the 3:1 interpretation. The former ratio gives a deviation of only 4.8 animals, while the latter (3:1 ratio) deviates from

Reed's observed data by 57.3 animals. The evidence favoring the expression of bent and fused being due to different genes is not conclusive. Bent-tailed animals exhibit no bifurcated tails, fused ribs, or abnormal hind legs, as do fused animals. A study of the overlap percentages also militates against their being identical. Fused females give higher percentages of overlaps than do fused males (57% and 17% respectively). This experiment does not show this to be true for bent. Bent females produce 11% normal overlaps, and bent males 18% overlaps. Although the mode of inheritance of the bent trait has not yet been demonstrated, the trait is inquestionably inherited. An increasing concentration of bent germ plasm in the parental and grand parental generations is accompanied by an increase in the percentage of bent individuals among the progeny, as the following table shows.

Type of mating	Number of bent ancestors in the parental and grand parental generations.	Percent of bent individuals in the progen-
F1 bent x normal	2	40.6%
F2 bent x normal	3	45.8%
F1 bent x F1 bent	4	56.8%

These facts prove that the trait is inherited.

If the data for bent be interpreted on the

mono-factorial basis, we expect 360.75 bent to 120.25 normals. We actually observed the F2 population: 273 bent to 208 normals. There would therefore be a deficiency of 87.75 bents and the same excess of normals. The 87.75 deviation is 42.2% of the supposed 208 normals observed. This figure (42.2%) represents the percentage of normal overlaps. If 87.75 of the F2 normals observed were genetically bent, this figure should be subtracted from the normal total and added to the bent data to give the true genetic picture. By so doing there would be 120.25 normals to 360.75 bent.

By mating F2 normals from the cross bent x bent it was observed that 13.3% of the F2 normals were overlaps. If 13.3% of the 178 supposed normals be reclassified as bent, we have a truer genetic picture of the F2 population. The corrected F2 ratio, 186.7 bent to 154.3 normal, deviates from the expected 3:1 ratio by 44 animals.

Nine bent F2 males and eight bent F2 females were mated to unrelated normals to test for homozygosity. If the monofactorial hypothesis is correct, about one-third of the F2 bents should be homozygous. None of these animals tested produced 100% of bent progeny. The range was from 14 to 71% (tables 4 & 5). A study of the table suggests that there are genetic differences between the

seventeen mice tested. We may be dealing with two types of animals, those producing a low and those a high percentage of bent. Also, there may be inhibitory factors operating against the development of the bent character when the bent gene is present.

Suppose we provisionally assume that two dominant genes are necessary for the development of the trait. When F1 bent females were mated to F1 bent males, there were 273 bent to 208 normals. Of the 481 F2 progeny, 56.8% were bent, and the observed ratio fits the two factor better than the one factor hypothesis. If nine bent to seven normal progeny are expected, there would be 270.5 to 210.4 normals among the F2 population. The observed number of bents (273) exceeds the expected (270.5) by only 2.5 animals.

Reed's data for the F2 generation, from the P1 cross fused x normal, approximates the 9:7 ratio. From the cross F1 fused male x F1 fused female 331 offspring were recorded. Of these 57.7%, or 191 were fused, and 140 were normal. If a two factor interpretation is applied, we expect 186.2 fused to 144.8 normal F2 progeny. The deviations are 4.8 from the expected result. However, Reed does not accept the two factor, but rather the monofactorial hypothesis, accompaned by a cytoplasmic influence, as the mode of inheritance for fused. Then if we expect three fused to one normal among the F2

population, the theoretical distribution would be 248.25 fused to 82.75 normal. On this hypothesis there is a deficiency of 57.25 fused animals, and a like excess of normals. According to Reed the excess of normals consists of genetically fused animals. That is, they are normal overlaps. If this is true, 40.8% of the observed F2 normals are overlaps, and should produce fused progeny when mated to normal animals. Reed has not progeny tested any of these F2 normals to determine whether some of them carry the fused gene.

The question of the mode of inheritance of the bent trait now presents itself. When F1 bent animals are mated to normals the corrected 1:1 ratio indicates that the trait is a simple dominant, with some complex of agencies which inhibits the expression of the trait, producing normal overlaps. It was noted previously that the expression of the bent trait is highly variable. Genes responsible for this variability may conceivably operate to produce the normal overlaps, and thus the ratios observed.

Several theoretical explanations may be advanved for the mode of transmission of the bent trait, a few of which follow$:

(1) It is produced by a single dominant gene, without modifiers.

(2) Sex linked dominant.

(3) Sex limited.

(4) Sex influenced; the single gene being dominant in the male or female, and recessive in the female or male.

(5) Two complementary factors, both of which are dominant, are required to produce the trait.

(6) A single dominant gene, is responsible, though its action can be suppressed by a dominant factor introduced by the normal parent.

(7) One dominant factor produces bent, but its effects can be partially or completely inhibited by several dominant suppressing factors.

(8) A single dominant gene is reponsible for the trait, and several factors showing no dominance can modify or suppress it.

(9) Diet is an inhibiting factor.

(10) A single dominant which is lethal in the homozygous condition.

(11) Bent is due to multiple factors, the degree of development of the trait depending on the number of these factors present.

These theories may now be appraised by showing whether the observed facts support or refute them.

(If bent be due to a single dominant gene without modifiers, we would expect a closer approximation to the 1:1 ratio in the F1 x normal cross than was

observed. The deviation from the expected was 29.5 animals. Also, we would expect all of the F1 normals to breed true for normality. However, we found that this was not the case, for 15% of the observed F1 backcross normals were genetically bent.

(2) The bent trait is not a sex linked dominant, for when a bent male was mated with an unrelated normal female, the mutation was found in both sons and daughters, which rules out the hypothesis of a sex linked dominant. Three bent males, when mated to unrelated normal females, produced 25 bent males, 25 bent females, 50 normal males, and 39 normal females.

(3) The character cannot be a sex limited dominant, for the trait is expressed equally in both males and females. The cross involving three bent males x unrelated normals produced 50 bent progeny, of which 50% were male, and an equal number female.

(4) If bent were dominant in the males and recessive in the females, bent females when mated to normal males would produce normal females and bent males. If B is the factor for bent; then bent males would have the constitution Bb or BB, and females the BB formula. Then bent females BB when mated to normal males bb would produce all Bb offspring. It is evident that all the females from this cross should be normal, and the males

should be bent, since bent females must have the BB formula. If bent males with the formula Bb are mated to normal females of the constitution bb, one-half of the offspring will be bent Bb, and one-half normal bb. However, we should have only bent males, and no bent females. The evidence rules out this hypothesis. When six bent females were mated to three unrelated normals 12 bent males, 18 bent females, 22 normal males, and 18 normal females. If bent is recessive in females, we expect no bent females from this cross. The three bent Bb males, when mated to unrelated normal females, produced 50 bent and 89 normal progeny. Of the bents 50% were female. The evidence rules out this hypothesis.

(5) If bent be due to two complementary factors we would expect 3 normals to 1 bent animal in the F1 x normal backcross (25% bent). The corrected F1 backcross data more nearly approximate the 1:1 ratio. The observed ratio in the F2 generation, however, approaches the 9:7 ratio very closely, the deviation being 2.5. But there is experimental evidence to show that there is some normal overlapping in the F2 generation as discussed on page 13. If the observed data be corrected for this overlapping, the 9:7 ratio does not fit so well. The corrected F2 generation deviates from the expected 3:1 ratio by 44 animals. The deviation is 38.5 from the 9:7 ratio.

Thus, the F2 ratio, as corrected, is slightly more in accord with 9:7, or two factor hypothesis than it is with the monofactorial theory.

(6) Suppose that bent is due to a dominant gene, the expression of which is suppressed by a dominant factor introduced by the normal parent. In an F1 backcross, from a P1 cross bent x normal we would expect to observe not more than one bent to three normal animals, with one-third of the normals being overlaps. No such 3:1 ratio was observed in the F1 backcross. To illustrate, if bent Bbss be mated with a normal carrying the homozygous dominant suppressor S, bbSS, the bent condition would be entirely suppressed in the progeny. If the suppressor is heterozygous, bbSs, and is mated with bent Bbss; 25% of the progeny would be bent. My cross of this type actually gave 40.6% bent progeny; which is far in excess of the maximum of 25% expected, and thus rules out this hypothesis. Occasionally, our normals should have been bbSS, and when mated with bent should have produced all normal offspring. We encountered no such normals.

(7) One dominant gene and several dominant suppressors could possibly be advanced to explain the observed data in this experiment. However, the problem then resolves itself into one of seeking the modifiers, and determining their number. If the suppressors were

recessive the number must still be determined. The possibility of several modifiers demands further study.

(8) Bent may be due to a single dominant gene which is suppressed in the overlaps by several modifying genes, which have no dominance. Again the number of modifying factors would remain to be determined. The backcross ratio, the variability observed in bent animals, and the demonstrated existence of normal overlaps support this theory.

(9) Diet might conceivably play an important part in the development of the bent trait, but if this is true the diet of the mother is the significant agency, for the mutation shows at birth. Unpublished data on the flexed tail trait tend to show that the food of the mother is a limiting factor in the development of this character. However, all the mothers in my experiment received the same food, on the whole, though lack of very careful weighing and mixing of the ingredients may have prevented all mothers from getting the same proportions of nutrient factors constantly. However, the absence of bent young in stocks of other animals in the colony when mothers were fed the same diet shows that food is not the only agent in causing bent, if it is an agent at all. There must have been genetic differentiators as well. One may entertain the hypothesis, therefore, that bent is an inherited trait whose development is helped or hindered by

dietary agents, and that the latter might occasionally produce normal phenotypes when the individual carries the bent gene.

(10) It may be argued that the bent gene is lethal in the homozygous condition, and that this accounts for the deficiency of bents in the F2 generation. Heterozygous bent animals x heterozygous bent produced 313 progeny in 47 litters, an average of 6.7 young per litter. Heterozygous bent animals x heterozygous bent produced 441 progeny in 60 litters, an average of 7.4 young per litter. If homozygotes die, we would expect one quarter of the progeny of the latter cross to be non-viable. This lethal condition would be evident in the reduction in size of the litters from two bent parents. Obviously no such reduction in F2 litters occurs, so we have no evidence of the lethality of homozygotes.

(11) If bent is due to multiple factors, the degree of development of the trait depending on the number of these factors, we would expect the trait in question to be influenced as are stature, and size. Stature and size have had a long evolutionary history. The bent trait arose suddenly and unexpectedly, and has been transmitted from generation to generation. This latter process is that of a mutation. The evolutionary

history of the bent condition refutes the argument that it is due to multiple factors.

Further experimentation is needed to establish the exact mode of inheritance of the bent trait. Linkage studies should be carried out to determine whether it is linked with brachyury, and therefore presumably the same as Reed's fused trait (Reed 1936). Efforts should be made, by a process of inbreeding and rigid selection, to establish a line of homozygous bent animals. Normal animals from the cross between two F1 bent parents should be progeny tested, to establish accurately the percentage of overlaps in the F2 generation, so that accurate corrections may be made in this generation. If normal overlaps are due to suppressing factors, they should be eliminated from the bent line by selecting only markedly bent animals, and closely inbreeding them. Finally, dietary studies should be made to determine the role of nutrition in the production of the trait.

We do not know yet whether bent and fused are genetically different traits. In some respects they differ. Bent-tailed animals exhibit no bifurcated tails, fused ribs, or abnormal hind legs, as do fused animals. A study of the overlap percentages also militates against their being identical. Fused females show a higher percentage of overlaps than do fused males in backcross

litters (57% and 17.1% respectively). Our experiment does not show this to be true for bent. In backcross litters there were 18% normal overlaps among females, and only 11% overlaps among males. To determine whether bent is the same mutation as Reed's fused, homozygous bents should be mated with homozygous fused and the progeny inbred to determine whether more normals appear than in pure bent and pure fused lines. Also, it should be determined whether bent is linked with brachyury, as fused seems to be.

SUMMARY

(1) Bent is a new mutation in the mouse. It is characterized by rigid spirals or bends in the tail. The distal half of the tail is more frequently affected than the proximal.

(2) The trait is inherited, and is dominant to normal.

(3) It is not the same as flexed, for flexed is recessive.

(4) Bent is much like fused genetically and phenotypically, and may be identical with it.

(5) Proof of the exact mode of inheritance must wait upon the crossing of homozygous bent and normal strains.

(6) Bent may be due to a single dominant gene together with inhibitory factors.

Figure 1

Phenotypic expression of the Bent tailed gene.

(8) Weakly fused .

(11) Spiral form.

(12) Angular form.

TABLE 1

Showing crosses used, total progeny from each cross, and percentages of bent progeny from each cross.

Cross	Total Progeny	Progeny Bent	Progeny Normal	% Bent
(A) F1 Bent x Normal (F1 Backcross)	313	127	186	40.6 ± 1.89
(B) ♂ F1 Bent x ♀ F1 Bent (F1 Cross)	481	273	208	56.8 ± 1.55
(C) ♂ F2 Bent x ♀ normal (F2 Backcross)	160	74	86	46.2 ± 2.63
(D) ♂ Normal x ♀ F2 Bent (F2 Backcross)	112	51	61	45.5 ± 3.17

TABLE 2

Showing the percentage overlaps in the F1 backcross generation. Reed's data show evidence of cytoplasmic or maternal inheritance, but these data fro bent show no such influence.

Cross	Progeny Bent	Progeny Normal	% Bent	% Overlaps
♂ F1 Bent x ♀ normal	75	119	38.6	18.4 ± 1.89
♂ normal x ♀ Bent	52	67	43.6	11.2 ± 1.88 7.2 ± 2.67

TABLE 3A

When F1 normals from the P1 cross Bent x normal were mated with unrelated normals, it was found that 3/20 of the observed normals produced bent progeny. Thus it became necessary that the data be corrected by re-classifying these "normal overlaps " as bent.

Cross	Bent	Normal
♂ F1 Bent xo normal (and reciprocal)	127	186
Correction	27.9	27.9
Expected ratio 1:1	156.5	156.5
Deviation	1.6	1.6

TABLE 3B

The same as for table 3A except that the F2 generation normals are the test animals.

Cross	Bent	Normal
F1 Bent x F1 Bent	263	178
Correction	23.7	23.7
Expected ratio	330.05	110.25
Deviation	44.1	44.1

TABLE 4

Results of progeny tests for homozygous F2 males. The percentage bent column shows that no homozygous males were among the nine tested. (♂ F2 Bent x ♀ unrelated normal)

Male Number	Total Progeny	Progeny Bent	Progeny Normal	% Bent
19	21	3	18	14.2
38	20	6	14	30.0
18	16	6	10	37.5
24	14	7	7	50.0
20	23	12	11	52.1
31	13	7	6	53.8
33	17	10	7	58.8
28	22	13	9	59.09
36	14	10	4	71.4

TABLE 5

The same as table 4, but F2 females are the test animals. (♀ F2 Bent x ♂ unrelated normal).

Female number	Total Progeny	Progeny Bent	Progeny Normal	% Bent
57	13	3	10	23.1
66	16	4	12	25.0
71	15	5	10	33.3
68	15	7	8	46.6
70	11	6	5	54.5
67	18	10	8	55.5
58	14	9	5	64.2
69	10	7	3	70.0

BIBLIOGRAPHY

Atkenson, T. R. Warren 1925 Inheritance of Wrytail in Jersey Cattle. The Journal of Heredity vol.26 pp. 331-334

Bagg, H. J. 1929 Hereditary Abnormalities of the Limbs, Oreign and Transmission II American Journal of Anatomy. vol. 43, pp. 167-219.

Bagg, H. J. and C. C. Little 1924 Hereditary Structural Defects in the Descendants of Mice Exposed to Roentgen ray Irradiation. American Journal of Anatomy vol. 33, pp. 119-146

Bean, A. M. 1929 A Morphological Analysis of the Foot Abnormalities occurring in the descendants of x-rayed mice. American Journal of Anatomy vol. 43, pp. 221-246

Bonnevie, K. 1934 Embryological Analysis of Gene Manifestation in Little-Bagg's Abnormal Mouse Tribe. Journal of Experimental Zoology vol. 67, pp. 443-520

Chesley, Paul 1935 Development of the Short Tailed Mutant in the House Mouse. Journal of Experimental Zoology vol. 70 pp. 429-455

Dunn, L. C. 1925 Inheritance of Rumpless in the Domestic Fowl. Journal of Heredity, vol. 16 pp. 127-134

--------- 1926 New Data on the Inheritance of Rumpless in the Domestic Fowl. Anatomical Record, vol. 34 pp. 181

Danforth, C. H. 1930 Developmental Anomalies in a Special Strain of Mice. American Journal of Anatomy vol. 45 - pp. 275-287

Hunt, H. R., Russel Mixter, Dorothy Permar, 1933 Flexed Tail in the Mouse, Mus Musculus. Genetics vol. 18 pp.335-366

Kamenoff, R. J., 1932 An Embryological Study of the Development of the Kink-tailed Mouse. Proceedings of the Sixth International Congress of Genetics vol. 2, pp. 253

Knapp, Bradford Jr., M. W. Emmel and W. F. Ward, 1936 The Inheritance of Screw-tail in Cattle. Journal of Heredity vol. 27, pp. 269-271

Landauer, W., L. C. Dunn, 1925 Two Types of Rumpless in Domestic Fowls. Journal of Heredity vol. 26 pp.153-160

Nordby, Julius E., 134 Kinky Tail in Swine. Journal of Heredity. vol. 25, pp. 171-174

Plagens, G. M., 1933 An Embryological Study of a Special Strain of Deformed x-rayed Mice. Journal of Morphology, vol. 55, pp. 151-183.

Reed, C. F. 1936 The Inheritance and Expression of Fused, a New Mutation in the House Mouse. Genetics vol. 1 pp. 1-13.