THE INHERITANCE AND EXPRESSION OF FUSED, A NEW MUTATION IN THE HOUSE MOUSE

SHELDON C. REED
Bussey Institution, Harvard University, Boston, Massachusetts

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INTRODUCTION

THIS mutation of the house mouse arose in the stocks at the Bussey Institution previous to 1931. Because of its phenotypic similarities the character had been confused with the recessive flexed-tail (HUNT 1933) and its independence of flexed was not realized until these experiments were made. Fused is in the same chromosome as Brachyury, as will be shown in this paper, while flexed is not in this chromosome (CLARK 1934). It follows that recessive flexed and dominant Fused are entirely distinct, genetically.

DESCRIPTION OF FUSED

Some of the most frequent expressions of Fused consist of various types of asymmetrical fusions of vertebrae, of lack of the whole tail or part of it, and of ribs fused at their proximal ends but separating into the component ribs at any place along their length. Sometimes the embryonic manifestations of the character cause bifurcation of the tail distally with growth proceeding from each part of the divided growth center.

It is proposed that the name "Fused" be used for all expressions of the character, and that its symbol be "T^f" indicating its probable allelism with Brachyury (T).

Many of the variations of Fused have been studied in whole specimens cleared in potassium hydroxide and glycerine. Nitric acid macerations which leave the nervous system intact have also been employed.

Practically all the variations of brachyury figured in the papers of ZAVADSKAIA and associates (1927–1934) have counterparts in Fused variants. All types and degrees of tail abnormalities are noted with both characters. Of the variants peculiar to Fused, the bifurcated tails, fused ribs, and an occasional rudimentary hind leg lacking the metatarsals and other bones, are most noticeable. The vertebrae of the Fused animals are often fused in the thoracic and lumbar regions with resultant angles in the vertebral column.

The bifurcation of the tail may prove to be a problem of general interest. The normally unilateral blood vessels and vertebrae become double posteriorly allowing functional vertebrae in each half of the bifurcation. Nitric acid macerations seem to show that in the normal animals the main nerves innervating the tail come from the sacral region and grow into the tail—a bilateral system. In the bifurcated part of the tail, each half of this bilateral system went into a part of the bifurcation. Thus the normal part of the tail is bilaterally innervated while the bifurcations are each unilaterally innervated.

Extensive rib abnormalities are often present. One animal shows on the left side alone, the fourth rib incompletely ossified for the middle third of its length. The seventh and eighth ribs leave their respective vertebrae separately but fuse immediately and continue joined for about a centimeter before separating again. The thirteenth rib comes off at the same place as the twelfth but separates from it almost immediately.

Another animal showed the most extreme lack of ribs noted; she was also tailless. On the right side only 9 of the usual 13 ribs were present. One of the 9 was of double thickness out to the end where the components separated. Counting the fused rib as two ribs, there are still three entirely absent.

An embryological study of Fused showed the first observable abnormalities to be poor alignment of the notochord and distinct curves and angles of the neural crests. CHESLEY (1935) found that it was the notochord which first became abnormal in homozygous brachyuric mice. Indeed, the embryological pictures of fused and brachyury are quite similar.

In the search for effects of environmental factors it was found that there is no correlation ($r=0.05\pm0.10$) between the size of the litter in which an animal was born and the degree of expression of Fused. Neither was there an apparent effect of the age of the mother upon the degree of expression of Fused in the offspring. Birth rank is also a factor of negligible importance in determining the variability of the character.

GENETIC BASIS OF FUSED

Fused is a dominant character but animals which are genetically fused often appear entirely normal. Proof that such phenotypically normal animals may be genetically Fused comes from crosses of them with inbred strains known to be genetically normal. As an example, a male (T^f16) gave 25 fused and 2 phenotypically normal young, when crossed with normal females. Both phenotypically normal young produced fused young when mated with the normal Strong albino strain and therefore both were "normal overlaps." This case was selected because it proves this male to be homozygous for T^f, as all 27 F_1 young were fused. Several other animals were proved to be homozygous for T^f as a result of testing their phenotypically normal progeny, though the test was usually not complete because of the death of one or more of the normals of a sibship before testing. Another male gave 28 young, all Fused, when crossed with normal females.

Animals tested and proved to be homozygous for Fused were all extreme grades of expression but an occasional heterozygous animal has been found to exhibit as marked abnormalities, so that progeny tests are necessary to prove whether an animal is homozygous for T^f.

Many fused animals have been crossed with animals from various inbred normal strains. The Fused animals used here exhibited strong expression of the character and the evidence shows that they were homozygous for the gene. The F_1 derived from these crosses consisted of 253 Fused and 83 animals with phenotypically normal tails. Table 2 includes these 336 animals as well as others.

TABLE 1

The increase in Fused expression (dominance) when selected strongly Fused animals of successive generations are backcrossed to a normal strain (Pincus).

PARENTS OF THE GENERATION	GENERATION	FUSED	NORMAL	% FUSED
Homozygous Fused ♂ T^f16×Pincus ♀♀	G_1 (or F_1)			
Strongly Fused G_1 ♀♀×Pincus ♂	G_2	22	73	23.2
Strongly Fused G_2 ♀♀×Pincus ♂	G_3	32	87	26.9
Strongly Fused G_3♂×Pincus ♀♀	G_4	24	30	44.5

The increase in Fused expression is of the same (or greater) order when selected weakly Fused animals of successive generations are backcrossed to the normal strain.

PARENTS OF THE GENERATION	GENERATION	FUSED	NORMAL	% FUSED
Homozygous Fused ♂ T^f16×Pincus ♀♀ (same as above)	G_1 (or F_1)			
Weakly Fused G_1 ♀♀×Pincus ♂	G_2	49	133	27.1
Weakly Fused G_2 ♀♀×Pincus ♂	G_3	26	70	27.1
Weakly Fused G_3♂×Pincus ♀♀	G_4	10	10	50.0

The F_2 derived from matings of some of these F_1 Fused animals was composed of 191 Fused and 140 straight-tailed. With complete dominance we would expect 248.25 Fused and 82.75 normal. Some of the F_1 animals were backcrossed to the normal parent races and a progeny of 2057 animals recorded. This backcross generation consisted of 786 Fused and 1271 straight-tailed.

Should there be modifiers in the various normal strains affecting the dominance of fused directly it should be easy to increase the percentage of Fused with successive backcrosses if only those Fused animals were used in backcrossing which exhibited the most extreme expression of the gene. The genes for extreme expression in the original Fused strain would be saved and added to those derived from the normal strain. If the opposite practice of selecting for weak expression is followed, the percentage of Fused should fall with each generation.

Table 1 shows that selection for modifiers controlling the degree of Fused expression (strong or weak) was entirely ineffective. Actually the strain selected for slight expression gave a higher percentage of Fused at the end of the experiment than did the strain in which there was selection for extreme Fused. It is clear, from the table, that the percentage of Fused increases in both cases whether selection was for weak or strong Fused. It is suggested that modifiers of the normal (Pincus) strain allowed more frequent expression of Fused but did not determine the degree of expression.

Continuous outcrossing of this sort is a method for determining whether there is only one important gene which causes the Fused effect when present in the heterozygous or homozygous state. We would not expect clear 1 : 1 ratios of Fused to normal in the *later* generations of the outcrossing if there were several genes, each of which, independently, brought about the

TABLE 2

The difference in overlapping of Fused in reciprocal crosses.

CROSS	FUSED	NORMAL	PERCENT OVERLAPS
♀ Fused × ♂ normal produced an F_1 of	123	127	50.8
♀ Normal × ♂ Fused produced an F_1 of	199	52	20.8
n = 501 $\chi^2 = 4.8$ P = between .05 and .02			

Fused condition. Nor would we obtain such a ratio if their action were cumulative. Table 1 shows that with repeated outcrossing the approximation to a 1 : 1 ratio becomes better, whereas on a multiple factor hypothesis the percentage of Fused would decrease with continued outcrossing and the approximation to a 1 : 1 ratio become worse.

As a test, a strongly Fused male of the first outcross generation (G_1) was backcrossed to normal females, with the resulting production of 45 Fused and 42 non-Fused animals. There was practically no overlapping with the normal if we assume a single dominant; but if the father was heterozygous for two factors which could cause Fused independently, then about half of the 42 non-Fused animals were normal overlaps. The first 24 of these 42 normal were reserved at birth for testing to ascertain whether they were genetically fused.

It will be shown that non-Fused animals which *are* overlaps usually produce good percentages of Fused when crossed with normal strains Therefore it should be easy to distinguish which of these 24 phenotypically normal animals were overlaps if each is crossed with the normal and sufficient progeny raised. One genetically Fused animal was found among the 17 which survived till tested. It produced 38 non-Fused and 36 Fused, a fine approximation to a 1 : 1 ratio. The 16 sibs of this male produced only normal young; they were not overlaps. These 16 produced between 25 and 278 normal young each.

Conclusive evidence that there is a single dominant gene, Fused, would follow from a proof of linkage between this dominant and some one of the other characters of the mouse with known linkage relations. Such evidence will be presented in a later section of this paper.

POSSIBLE INTERACTION BETWEEN A MODIFIER (OR MODIFIERS) AND THE FUSED GENE BEFORE FERTILIZATION OF THE EGG

A favorite method of attack upon the problem of maternal inheritance consists of reciprocal crosses between animals exhibiting the character in question and normal animals. Should the F_1 from the cross of normal

TABLE 3

The difference in overlapping of Fused in reciprocal crosses (F_1 fused × normal).

CROSS		FUSED	NORMAL	PERCENT OVERLAPS
♀ F_1 Fused × ♂ normal	produced	33	120	57.0
♀ normal × ♂ F_1 Fused	produced	68	96	17.1
	n = 317 $\chi^2 = 15.6$	P = <.01		

mothers with Fused fathers differ significantly in percentage of overlaps from the F_1 of the reciprocal cross, it might be concluded that the mother had a non-chromosomal effect upon Fused expression. The reciprocal crosses yielded strong evidence that there is some kind of "maternal influence" concerned with the overlapping of Fused. The significant difference in the F_1 from the reciprocal crosses is shown in table 2. This amount of overlapping may be compared with that in the offspring of known homozygotes; known homozygotes mated together produced 175 Fused and 88 phenotypically normal which is equivalent to 33.5 percent overlapping.

Chromosomally the two classes of F_1 should be identical (as Fused is not sex-linked). There must be some other factor affecting the expression of fused because of the extremely small probability that such a large difference between the reciprocal crosses is due to chance alone.

Both male and female F_1 Fused were backcrossed to normal strains of various derivations to ascertain whether the possible "maternal effect" is inherited. It appears to be a regular feature. Table 3 shows the reciprocal crosses of the F_1 Fused animals backcrossed to the normal. Again the normal mothers produced fewer overlaps.

Such a pronounced "maternal effect" merits further investigation. The experiment was repeated and extended with confirmatory results. The following data are not related to those just presented except that the same gene is under scrutiny. The normal animals were especially procured for the new study and had not been used in the previous one.

Fused males and females were crossed with a strain of normal albino mice obtained from Dr. Pincus. These mice had been inbred, brother with sister, for many generations and were probably genetically homozygous. Fused females (F_1 or G_1) from the cross of Pincus normal females by Fused males were backcrossed to the Pincus strain and produced the second generation (G_2). No G_2 was produced from Fused males by normal females. Fused males and females of the G_2 generation were again backcrossed with the Pincus strain and a third generation produced (G_3). Fused animals of both sexes of the G_3 generation were once more backcrossed with

TABLE 4

Inheritance of the significant difference in Fused expression in reciprocal crosses.

CROSS		FUSED	NORMAL	PERCENT OVERLAPS	GENERATION
♀ Fused (parental) × ♂ normal (Pincus)	produced	13	13	50.0	G_1
* ♀ Fused (G_1) × ♂ normal (Pincus)	produced	72	230	52.3	G_2
♀ Fused (G_2) × ♂ normal (Pincus)	produced	57	156	46.5	G_3
♀ Fused (G_3) × ♂ normal (Pincus)	produced	48	88	29.4	G_4
♀ Fused (G_4) × ♂ normal (Pincus)	produced	1	7		G_5
♀ Fused (G_1–G_4) × ♂ normal (Pincus)	produced	178	481	46.0	G_2–G_5
♀ normal (Pincus) × ♂ Fused (parental)	produced	25	2	7.7	G_1
♀ normal (Pincus) × ♂ Fused (G_1)	produced		None		G_2
♀ normal (Pincus) × ♂ Fused (G_2)	produced	52	48	0.0	G_3
♀ normal (Pincus) × ♂ Fused (G_3)	produced	34	40	8.1	G_4
♀ normal (Pincus) × ♂ Fused (G_4)	produced	53	67	11.7	G_5
♀ Normal (Pincus) × ♂ Fused (G_2–G_4)	produced	139	155	5.4	G_3–G_5

* From normal ♀ × Fused ♂

the Pincus strain and the resulting (G_4) Fused males and females were again backcrossed to the Pincus normal strain for a fifth (G_5) generation. One may see in table 4 that the reciprocal effect persists through all these generations. The difference between the 46 percent overlapping when the mothers of the various generations were Fused and the 5 percent overlapping when the fathers were Fused is highly significant ($\chi^2 = 40$, $n = 1$).

The criticism could be raised that the fathers were of a higher, more extreme grade of fused than the mothers due to chance selection. The criticism is not valid if we judge the grade of Fused from its phenotypic expression. Careful tracings were made of the tails of each of the Fused parents just after death of the animal. A comparison of the tracings and the breeding records shows that the most extreme Fused female (D327,

G_3) produced 10 fused and 28 normal offspring, with 47 percent overlapping, whereas a male (D194, G_3) with but a slight manifestation of Fused at the tip of the tail, produced 52 Fused and 48 normal, with no overlapping.

If some property of the Y chromosome accounts for the small amount of overlapping among the progeny of Fused males, then the daughters of Fused males should be straight-tailed more frequently than the sons, which possess the Y chromosome. However, table 5 shows that there are no more straight-tailed females than males in undepleted litters. Therefore, the expression of Fused is not dependent upon some special property of the Y chromosome.

TABLE 5

Sex of Fused animals in undepleted litters from various Fused crosses (Fused×Fused and Fused×normal).

	GOOD FUSED	FAIR FUSED	NON-FUSED
Males	80	29	56
Females	81	34	55

Maternal inheritance in plants and animals has been well established. Plastid inheritance and male sterility in plants are among the generally recognized features. In animals the situation has been less thoroughly developed, but there are a few cases where extra-chromosomal influence has been clearly demonstrated (PLOUGH and IVES, 1935).

Fused might be regarded as a case in which cytoplasmic inheritance could be inferred from the data in tables 2, 3, and 4. It might be assumed that the Fused gene happened to mutate in a race of which the cytoplasm is inhibitory toward Fused expression, thus yielding the large percentage of overlapping in the inbred Fused strains and in any other crosses in which the cytoplasm of the zygote is supplied by the Fused race. The cytoplasm of most normal races would be less inhibitory toward the Fused gene, so fewer overlaps would result if the male supplies the Fused gene and the normal female supplies the cytoplasm not inhibitory to expression of the Fused gene.

But this explanation is invalid. In table 4 the cytoplasm of all the various *backcross* generations came directly from the normal Pincus strain. Thus the cytoplasm of all the animals of table 4 is from the normal rather than from the Fused strain, in the backcross generations. It will be recalled that *all* G_2 animals were offspring of G_1 Fused females and Pincus normal males (top half table 4). There was no reciprocal G_2 from normal females and G_1 Fused males, such a cross having been intentionally omitted. But all the G_1 Fused females (used to produce the G_2) were daughters of normal females by Fused males (G_1 of bottom half of table 4). Thus *all* the G_2 animals developed from eggs with Pincus cytoplasm and as all G_3, G_4 and G_5 animals in both halves of table 4 descended from G_2 (with normal cytoplasm) they all had cytoplasm inherited only from the Pincus normal strain. As the cytoplasm of the eggs came from the Pincus strain and not from the Fused strain it would have been impossible to have any inhibitory effect of Fused cytoplasm because none is present. Though we can no longer consider continuous inheritance of what looks like a maternal effect, through an unbroken line of cytoplasm, still we must admit the existence of a very definite effect of some sort.

Two remaining possibilities will be considered. Both assume the action of genetic modifiers inhibiting the expression of Fused. Both explanations fit the facts well but neither can be proved to be the correct one at present. The different results of the reciprocal crosses might be due to an effect of modifiers of the genotype of the mother working through the uterus to inhibit Fused expression. One might question the probability of genetic agencies taking effect on the young through the uterus of the mother. Further, it might be expected that such uterine influences would increase rather than decrease the percentage of abnormal young.

The second possibility is that there are genetic modifiers which *interact* with the Fused gene to weaken or inhibit its expression. Such interaction must take place, if at all, *before* fertilization of the egg. It may be assumed that the modifiers are present to a greater or lesser degree in all strains of mice and that if the Fused gene is also present in the unfertilized egg the inhibitory reaction prevents the embryo from expression of Fused in many cases, and thus the number of overlaps increases. If the Fused gene is not present in the unfertilized egg the modifiers cannot interact with it so that at the proper time (after fertilization) the Fused gene introduced by the sperm will cause its effect, uninhibited, and there will be little, if any, overlapping.

It should be understood that the interaction between the Fused gene and inhibitory modifiers is assumed to take place very early in development and to "condition" the cytoplasm before entrance of the sperm and fertilization. After this interaction has occurred and the cytoplasm is conditioned, entrance of the sperm probably has less effect on the expression of Fused. Whether or not a second Fused gene is introduced (at fertilization) seems to make some difference (12.5 percent) in the expression of fused, for there were 46 percent overlaps if no Fused gene entered at fertilization (table 3) and 33.5 percent overlaps if a Fused gene did enter (progeny from homozygous parents).

If the conditioning of the cytoplasm *did not* take place before fertilization (in normal females no fused gene was present to interact with the modifiers) the Fused gene, brought into the normal egg by the sperm, was allowed nearly complete expression and fewer (5.4 percent) overlaps resulted.

Fused behaved in an interesting way in a species cross between the house mouse, *Mus musculus*, and the Asiatic mouse, *Mus bactrianus*. The inhibitory effect was greater to the extent that Fused lost its dominance completely. All 20 young from the cross of 2 homozygous Fused *musculus* females by normal *bactrianus* males were straight-tailed (normal). When two of the F_1 males, which were straight-tailed but must have carried the Fused gene, were crossed to normal *musculus* females 48 backcross young resulted. All were straight-tailed. Apparently so many inhibitory modifiers have accumulated in *bactrianus* that the Fused gene cannot express itself at all in this species; the modifiers in *bactrianus* probably take effect after fertilization.

GREEN'S (1935) observations on crosses of brachyuric *Mus musculus* with normal *Mus bactrianus* were that the dominance of Brachyury, which is usually observed in pure *musculus* crosses was lost when one of the parents was *bactrianus*. Because Brachyury is similar to Fused and probably allelic to it one might speculate that the same *bactrianus* inhibiting modifiers affect both mutants.

A modifier interaction with the Fused gene as accounting for most of the overlapping of animals carrying Fused genes is tentatively indicated as the factor predominantly responsible for the incompleteness of dominance of the character. If such is the case this interaction produces an effect simulating maternal or cytoplasmic inheritance.

BIFURCATION OF THE TAIL

Early in the Fused investigations an animal exhibiting a bifurcation of the tail appeared. The tail was like that of other Fused animals except that at the distal end it divided into two approximately equal parts. Other bifurcated animals appeared from time to time in the Fused stock; usually the bifurcation resulted in unequal parts, the smaller part never exceeding 3 centimeters in length.

We observed 125 Fused animals showing this bifurcation of the end of the tail. Never were there any animals with bifurcations which did not also exhibit vertebral fusions and displacements typical of Fused. It is possible that there is a particular modifier of Fused which causes the bifurcation and an attempt was made to test this. Animals with bifurcated tails crossed together produced 20 bifurcated and 181 Fused but not bifurcated (10.0 percent of the young were bifurcated). Bifurcated crossed with Fused, but non-bifurcated, gave 18 bifurcated and 143 non-bifurcated (but Fused) offspring or 11.2 percent bifurcated. Bifurcated animals crossed with normal non-Fused strains produced 7 bifurcated and 46 Fused, non-bifurcated, young (13.2 percent bifurcated).

It may be, then, that the bifurcated condition is not determined by specific modifiers because no more bifurcated young are produced when both parents were bifurcated than when only one was affected. Probably bifurcations result from a particular type of mechanical variation of the Fused gene expression during embryonic development.

TABLE 6

Tests for linkage of Fused.
The expectation of equal frequencies of parental and crossover gametes is realized with these characters.

LINKAGE GROUP	GENE	PARENTAL COMBINATIONS	RECOMBINATIONS
1.	Albinism	91	87
	Pink-eye p_1	37	31
2.	Non-agouti	85	72
	Pink-eye p_2 (Robert's)	12	14
3.	Brown	51	59
4.	?{ Dilution	84	82
5.	Wavy (Crew)	43	41
6.	Piebald	68	69
7.	Dominant spotting	85	89
8.	Waltzing	17	17
9.	Rodless retina	21	25
10.	Naked	116	111
11.	Leaden	61	60
12.	Shaker sh_2	32	32
13.	Harelip	5	2

LINKAGE OF FUSED

The tendency of Fused to overlap could complicate a linkage study but fortunately such complications were removed automatically by the nature of the crosses which caused the overlaps to fall into a parental and a crossover class in equal proportions. Tests showing that there is no association between Fused and certain of the other independent characters are summarized in table 6. In this table no deviation, when divided by the probable error, was greater than 1.4; therefore none was significant.

The characters dwarf and hydrocephalus (CLARK) require different treatment because breeding experiments with them are made with heterozygous dwarf and hydrocephalus and not with homozygotes which are usually infertile or of low vitality. F_1 animals heterozygous for both Fused and dwarf, when mated, produced an F_2 of which one fourth of the dwarfs would be expected to be non-Fused. Owing to particularly great overlapping of Fused in the dwarf cross there is not a very good agreement between observed and expected, but if correction is made for the overlapping, the agreement is satisfactory (see table 7).

On account of phenotypic similarities between Fused and the character flexed-tail (which is closely linked with anaemia) it was necessary to test for linkage between anaemia and Fused in this manner. Fused animals were crossed with homozygous anaemics. Fused F_1 (but not anaemic) animals were crossed *inter se*. Three fourths of the F_2 anaemics from this cross should be Fused if there is no linkage, while with complete linkage none of them should be Fused. Seventeen of these anaemics were raised and crossed with normal strains unrelated either to the Fused or anaemic

TABLE 7

Absence of linkage between Fused and the two independent characters dwarf and hydrocephalus (CLARK'S).

LINKAGE GROUP	GENE	PARENTAL	RECOMBINATION
		(BOTH CLASSES CORRECTED FOR OVERLAPPING)	
14.	Dwarf		
Observed		3	10
Expected		3.25	9.75
15.	Hydrocephalus		
Observed		8	19
Expected		6.75	20.25

strains, to test for the presence of Fused and to distinguish it from the recessive flexed-tail. Ten of the 17 were found to be Fused and probably more were Fused but not detected. It is safe to conclude that there is no close linkage between Fused and anaemia.

One character remains which will be tested extensively. CLARK (1934) found Brachyury to be independent of the characters which we have tested against Fused. Assuming that the independence of these characters is real and not due to failure to detect loose linkages, we can state that Fused and Brachyury are both independent of perhaps 15 of the 20 chromosome pairs of the mouse. Therefore there is 1 chance in 5 that they are linked with each other. The evidence indicates a close linkage, with the possibility that the two genes are alleles.

As a test, F_1 animals heterozygous for both Brachyury and Fused were outcrossed to normal unrelated stocks. If the two genes are in different chromosomes one fourth of the offspring would lack both and would be completely normal.

The progeny observed at birth when F_1 (heterozygous for both Brachyury and Fused) were crossed with normal animals, consisted of 205 Brachyuric or Fused and 40 normal. It is quite probable that some, if not all, of these 40 are normals. If all of them are overlaps, the proof is excellent that Brachyury and Fused are either alleles or very closely linked.

Of the 40 phenotypically normal 17 survived until tested for Fused. Twelve proved to be genetically Fused; the other five were females and did not produce any Fused young when mated with normal, though only one of them produced as many as 26 normal young. It is noteworthy that *all* the straight-tailed normal males were found to be genetically Fused and that the five animals not proved to be Fused were all females. Probably they are Fused also, but owing to the tendency of females to give more normals in any type of cross than do males, the tests were probably not extensive enough.

If the overlaps that were discovered are added to the visible Fused (and subtracted from the straight-tailed class) the total is now 217 Fused or Brachy and 28 straight. Of the 28 remaining straight-tailed 23 died before a test could be completed. Considering all these to be actually straight (which is highly improbable) we know that were Brachyury and Fused independent, we should expect 61 straight and 184 Fused or Brachy. The deviation from this expectancy is very large, and, divided by the probable error, is equal to 7.2. The odds against such a large deviation being due to chance alone are greater than 500,000 to 1.

On an assumption of linkage, there is less than 10 percent crossing-over between Fused and Brachy. It is impossible to tell at present whether it is much less than 10 percent, or even whether Fused and Brachy are alleles. The proof that they are in the same chromosome seems quite satisfactory.

An F_2 from the F_1 animals heterozygous for both Fused and Brachyury consisted of 58 abnormal and 1 phenotypically straight. This experiment corroborates the previous ones, for if Fused and Brachyury were not borne in the same chromosome, at least one-twelfth of the F_2 animals should have been normal.

As Brachyury and Fused are near together in the same chromosome they may be alleles. Both are dominant genes with phenotypic effects which have a similar embryology. The variations produced by one of the characters are paralleled by those of the other. Fused behaves as would a less severe allele of Brachyury. Fused and Brachyury behaved the same in the species cross with *Mus bactrianus;* both lost dominance. The evidence that Fused and Brachyury are not identical is chiefly this. Fused differs from Brachyury in overlapping with the normal and in that Fused homozygotes are viable; homozygous Brachyuric animals die during the eleventh day of embryonic life.

SUMMARY

Fused is a dominant mutation in mice causing various types of asymmetrical fusions of the vertebrae, lack of the whole tail or part of it, absence

of from one to three ribs on each side of some animals and occasional fusions of ribs. Embryologically the gene seems to affect the neural crests and notochord. The factor predominantly responsible for the incompleteness of dominance of Fused seems to be an interaction of genetic modifiers with the Fused gene which takes place before fertilization of the egg. The observed results could be due also to maternal genetic modifiers working on the young through the uterus of the mother. This interaction produces an effect simulating maternal or cytoplasmic inheritance.

When the Fused gene is introduced into another species of mice, *Mus bactrianus*, the dominance observed in the house mouse (*Mus musculus*) is lost completely.

Fused is in the same chromosome as Brachyury and probably the two characters are alleles.

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