"PIGTAIL," A HEREDITARY TAIL ABNORMALITY IN THE HOUSE MOUSE, *MUS MUSCULUS*

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(With Plates 7 and 8 and Two Text-figures)

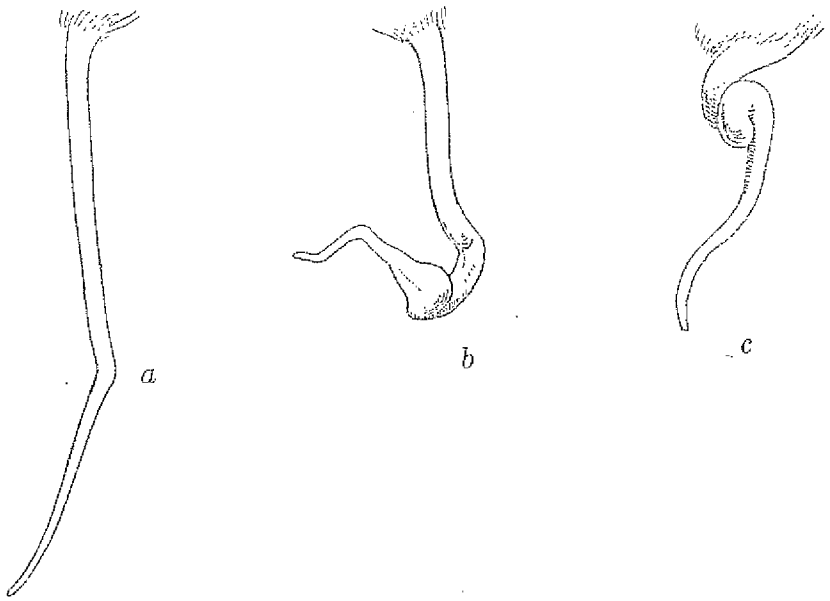
Among the mice supplied by a commercial breeding farm, there occurs occasionally a tail abnormality which, as it appeared to be of a hereditary nature, was subjected to genetical studies. It was intended to supplement these by histological and embryological investigations and to clear up doubtful genetical points by further breeding tests. Since, however, present conditions do not allow of further research, the data gained so far will be presented below without much attempt at interpretation, which, at the present stage of the investigation, must needs be very hypothetical.

Description

The abnormality in question has been called "pigtail", for in its more pronounced degrees of manifestation, the tail forms a complete curl similar in appearance to the curled tail of a pig. The pigtail condition as observed by external inspection, without the aid of X-rays or sections, varies from a slightly perceptible thickening at some point in the tail to complete single or even double curls (Text-fig. 1). Intermediate stages are single or multiple kinks varying from obtuse to right angles, with more or less pronounced bony thickenings at the bending points. The direction of the curls may be right-handed or left-handed. In the case of multiple kinks the direction may remain the same from one kink to the next, or it may change and thus produce a zigzag pattern. When a strong kink or curl occurs at the root of the tail the position of the sacrum and the pelvis bones may be affected so as to become markedly asymmetrical when seen from above. The lowest grade of pigtail may become manifest only some weeks after birth. Thus the various degrees of expressivity of pigtail arrange themselves into a series, the lowest member of which is just recognizable on inspection of the live animal and remains unidentified should the animal die in infancy. A continuation below this level would lead to a condition which is no longer manifest to the unaided observer, though indications of it might be discovered by

special techniques, such as histological preparations. In other words, variable expressivity will be combined with incomplete penetration (Timoféeff-Ressovsky, 1934). As will be seen below, the actual breeding results allow of a reasonable interpretation only when it is postulated that a considerable proportion of genetically pigtail animals overlap normal.

It was thought possible that X-ray photographs might reveal bone abnormalities in all or most of these overlaps. A great number of radiograms gave not the least support to this assumption. Whereas the



Text-fig. 1. Various degrees of expression.

manifest pigtail condition exhibits more or less marked abnormalities of the shape of the tail vertebrae (Pl. 7, fig. 1), combined with ankylosis and fusion of vertebrae, the skeleton of the overlaps (Pl. 8, fig. 3) resembles that of the controls (Pl. 8, fig. 4) in every detail. It should be pointed out, however, that the inspection of the X-ray photographs was a purely qualitative one, no measurements of vertebrae being taken, since there was not much reason to suppose that a quantitative study would reveal differences between controls and phenotypically normal, genotypically pigtail individuals.

Tail skeletons freed from the adhering tissues corroborated the evidence from X-ray photographs: the overlaps were indistinguishable

from the controls, while the manifest pigtails exhibited abnormally shaped and fused vertebrae.

Bone abnormalities in parts of the skeleton, other than the tail, were not observed; but in later generations a number of young were born with a spina bifida aperta (Pl. 7, fig. 2).

Genetical results

Table 1 summarizes the results gained by breeding from the various types within the stock and by outcrossing and backcrossing to pigtail. Classification for abnormality was done on the basis of naked eye

Table 1. *Results of experimental matings*

	Crosses within pigtail stock					Outcrosses				
	I (*a*) Both parents manifest pigtails	II (*b*) Only father manifest pigtail	III (*c*) Only mother manifest pigtail	IV (*b*) and (*c*) combined	V Both parents phenotypically normal	I F_1, father from pigtail stock	II F_1, mother from pigtail stock	III F_1, combined	IV F_2	V Backcross F_1 to pigtail stock
No. of litters	36	10	9	19	21	20	9	29	—	—
No. of young	219	66	51	117	143	173	61	234	311	142
Litter-size	6·1	6·6	5·7	6·2	6·8	8·7	6·8	—	—	—
No. of abnormal young	52	14	10	24	24	0	0	0	5	6
Proportion of manifest pigtails, 1 in	4·2	4·7	5·1	4·9	6	—	—	—	62·2	23·7
No. of litters with spina bifida	4	3	1	4	2	0	0	0	0	0
No. of young with spina bifida	4	6	1	7	2	0	0	0	0	0

inspection and palpation of the tail, counting as abnormal each individual which revealed even a slight abnormality to these methods. As mentioned above, the lowest degree of pigtail may become manifest only at several weeks of age. The inaccuracy introduced by this practice is considerable: in a series of litters which were carefully observed from birth to weaning, eight cases of delayed manifestation occurred among 56 young which at birth were classified as normal and survived the weaning age of 21 days. Therefore, all litters for computation of segregation ratios were kept for 21 days and classified twice, once immediately after birth, a second time at 21 days of age. Even this precaution is, of course, not sufficient to avoid completely the inaccuracy due to delayed manifestation. Deaths at birth or during the suckling period may remove infant mice which were on the way to manifesting a low grade of pigtail. However, as

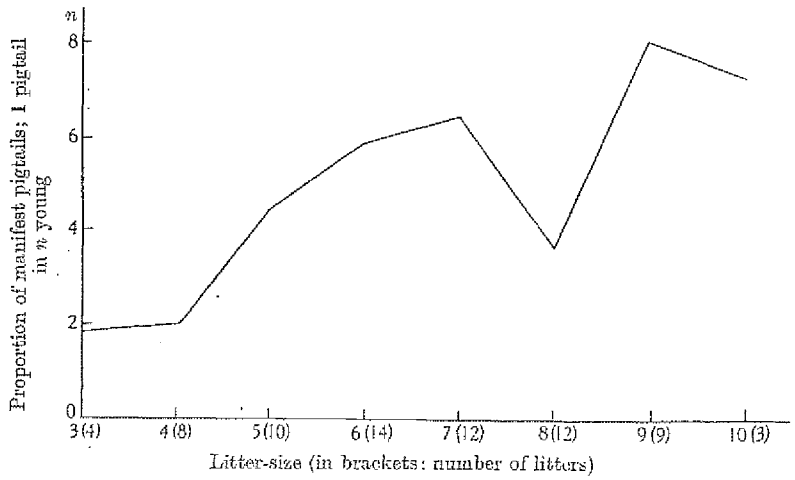
there is no indication of a selective pre-natal or post-natal mortality of the pigtail young—apart from the spinae bifidae, none of which survived weaning age—it may be assumed that losses due to these causes are evenly distributed among normal and abnormal young.

Outcrosses. Twenty litters by manifest pigtails mated to unrelated inbred agouti, albino, or lemon (**bbppc^{ch} c^{ch}**) mice contained 173 young without a single pigtail. Since at this stage of the experiment, litters were often discarded before weaning, a second series of outcrosses was made, in which the young were kept for 21 days. No pigtail was found among sixty-one young from nine litters. It therefore seems safe to conclude that the genetical basis of pigtail is either a recessive gene or a combination of genes, one at least of which is recessive. In Table 1, the data for the outcross F_1 are grouped according to which parent was pigtail. It will be seen that the pigtail ♀♀ in this series were definitely less fertile than the not-pigtailed ones. The difference in litter size is 1·9 +0·84 which is 2·3 times its standard error.

Inbreeding. Manifest pigtails, when mated together, produce pigtails as well as normals. The proportion of pigtail young in litters from such matings is a little less than 25%. The normal young from these litters when tested adequately, always produced pigtails in a somewhat lower, but not significantly different percentage (columns II–V in Table 1). This fact suggests that the manifest pigtails are not genetically different from the normal litter-mates. From Table 1, it would appear as though the fertility of the manifest pigtail ♀♀ was lower than that of the phenotypically normal ♀♀ (compare columns II and V with I and III), but this difference is not significant on these data. The breeding results do not point to the action of genetic modifiers as responsible for the different degrees of expressivity and penetration, for good pigtails were obtained from normal parents and vice versa. Moreover, selection for high penetration was not successful, but as the highest number of generations in any selected line is only four, this negative evidence is only of slight value. If the degree of penetration depended on the cumulative action of several recessive modifiers for which the strain would become more homozygous through inbreeding, it would be expected that inbreeding *per se* would tend to alter the percentage of manifestation. The coefficient of inbreeding (computed after Wright 1922) without selection varied from 0 to 0·5. Within this range no significant correlation between penetration and degree of inbreeding could be established. The coefficient of correlation, though positive, namely, +0·191, is not significant for 74 degrees of freedom.

Among extraneous conditions, the position of the foetus *in utero*, the size of the litter and the physiological state of the mother might be of importance for the development of the abnormality. Dissections of six pregnant manifest pigtail females mated to similar ♂♂ gave no indication of a relationship between visible abnormality and position in the uterus at a stage when the abnormality is already visible in the foetus (16th to 17th day). The age of the mother varied between 2 and 8 months, and within these rather narrow limits no correlation between age of mother and penetration could be established.

As seen from Text-fig. 2, there was a tendency for penetration to decrease with the size of the litter. This observation was borne out by



Text-fig. 2. Relation between litter-size and manifestation in genetically pigtail litters.

computation of the coefficient of correlation between litter-size and penetration in litters from two pigtail parents. The coefficient, though small, is significantly negative, namely, 0·23 for 76 degrees of freedom, with the 5% point at 0·217 and the 1% point at 0·283. This fact seems to suggest an influence of uterine conditions on the development of the abnormality.

The last two rows of Table 1 show that young with a spina bifida aperta occurred in litters from all types of mating within the pigtail stock. There appears to be a relationship between the degree of inbreeding and the occurrence of spina bifida aperta, for the average inbreeding coefficient (as calculated from the last four generations) for the ten litters with spina bifida was 0·31 as compared with the average for all matings within the stock of 0·20. The difference is $0·11 \pm 0·019$. Pene-

tration in litters with one or more young with spina bifida was unusually high. This cannot be due to differences in litter size, for the average litter-size in the ten litters containing spinae bifidae was 6·1 as compared with the grand average of 6·3. The percentage of manifestation in spina bifida litters was 56·6, whereas it was only 22·3 in all genetically pigtail litters. When the actual spina bifida young were left out of the calculation, the penetration in the litters from which they came, was still as high as 31·2%. This indicates a connexion between spina bifida and the skeletal abnormalities by which pigtail is characterized. It might be thought that the spina bifida was the original disturbance, the bone abnormalities having arisen secondarily through lack of properly developed nerve supply as suggested for skeletal abnormalities in man (e.g. Beck, 1922). The fact that out of 12 spinae bifidae only one was not pigtail as well, would seem to support this idea. The data, however, are too small to allow of any definite conclusion. Moreover, no evidence of a spina bifida occulta was found in X-ray photographs of manifest pigtail individuals or phenotypically normal, genotypically pigtail individuals.

Later generations from outcrosses

The data on the outcross F_2 and the backcross progeny from outcross F_1 individuals mated to pigtails are presented in the last two columns of Table 1. Obviously, they cannot be interpreted on the basis of a simple Mendelian recessive. A comparison with Table 2 shows that the

Table 2. *Expected ratios with different genetical assumptions*

(*a*) Backcross of F_1 outcross to manifest pigtail
Observed: 6 in 142. S.E. = 2·4

No. of recessive factors	No. of pigtails expected: With complete manifestation	With manifestation 1 in 5	In a total of 142	D./S.E.
1	1 in 2	1 in 10	14	Approx. 3
2	1 in 4	1 in 20	7	,, 0·5
3	1 in 8	1 in 40	3·4	,, 1
4	1 in 16	1 in 80	1–2	,, 2

(*b*) Outcross F_2
Observed: 5 in 311. S.E. = 2·2

No. of recessive factors	No. of pigtails expected: With complete manifestation	With manifest 1 in 5	In a total of 311	D./S.E.
1	1 in 4	1 in 20	16	Approx. 5
2	1 in 16	1 in 80	4	,, 0·5
3	1 in 64	1 in 320	1	,, 2
4	1 in 256	1 in 1280	0	,, 2

assumption of two recessive complementary factors gives a good fit, if it is assumed that for certain non-genetical reasons in all crosses only roughly one out of five genotypically pigtail individuals will be phenotypically abnormal. However, the assumption of complementary factors where there is no means of separating them genetically or physiologically, is not a very satisfactory hypothesis. Moreover, the assumption that the degree of penetration remains unchanged by outcrossing is almost certainly inaccurate, although it has to be considered that little or no inbreeding had been carried out before outcrossing, and that the outcrosses were made to various unrelated stocks, so that the variability of genotypical background in all crosses taken together should be large enough to warrant a chance distribution of the variations in penetration due to differences in genotypical milieu, and thus to smoothe out inaccuracies arising from this source. No evidence of an influence of the kind of stock used for outcrosses on manifestation was observed although the data are not large enough to allow of a statistical comparison. On the whole, the assumption of one main recessive gene and a number of modifiers, each with only a slight effect on penetration, seems less open to criticism.

Phenotypically, pigtail bears a striking resemblance with the flexed tail described by Hunt *et al.* (1933). Flexed tail, too, is a recessive, which, however, seems to be much more independent of the genotypical environment. Moreover, flexed tail young are usually anaemic at birth (Mixter & Hunt, 1933), whereas pigtail young are born with a normal skin colour. However, Mixter & Hunt suggest that the anaemia may be due to a different recessive gene linked with the one causing flexed tail. Thus, the differences between flexed tail and pigtail do not seem to exclude identity, or at least allelomorphism, of the underlying genes and might be due only to differences in the associated genotypical background. Prof. L. C. Dunn has kindly undertaken to test pigtails against flexed tails for allelomorphism.

The occurrence of spina bifida aperta in pigtail litters offers particular interest in view of the fact that in man spina bifida appears to have a genetical basis and to cause or at least to be connected with a number of skeletal abnormalities. An embryological study of pigtail promises to throw some light on these much-debated questions.

SUMMARY

A skeletal abnormality, termed pigtail, in the house mouse is described which phenotypically resembles flexed tail. In a certain small proportion of litters, one or more young with spina bifida aperta occurred, especially in the more highly inbred litters. Genetically, pigtail is a recessive character, caused either by two complementary factors, or—more probably—by one main gene interacting with a number of modifiers which affect the penetration. Penetration is never 100%. In genetically pigtail litters, it varies round about 20%. It is not noticeably dependent on age of mother, degree of expression in the parents, degree of inbreeding or selection; but there exists a significant, though slight, negative correlation between litter-size and percentage of manifestation in homozygous litters, suggesting some intra-uterine, non-genetical influence on the development of the abnormality.

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EXPLANATION OF PLATES 7 AND 8

PLATE 7

Fig. 1. X-ray photograph of the tail of an adult manifest pigtail.

Fig. 2. Spina bifida aperta in new-born young.

PLATE 8

Fig. 3. Skeleton of normal control ♀.

Fig. 4. Skeleton of phenotypically normal, genetically pigtail ♀.

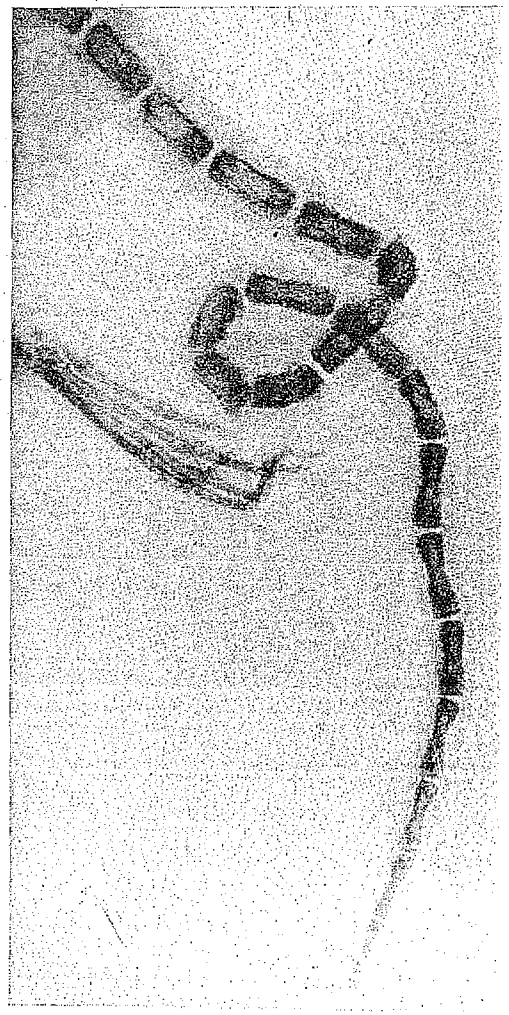

Fig. 1.

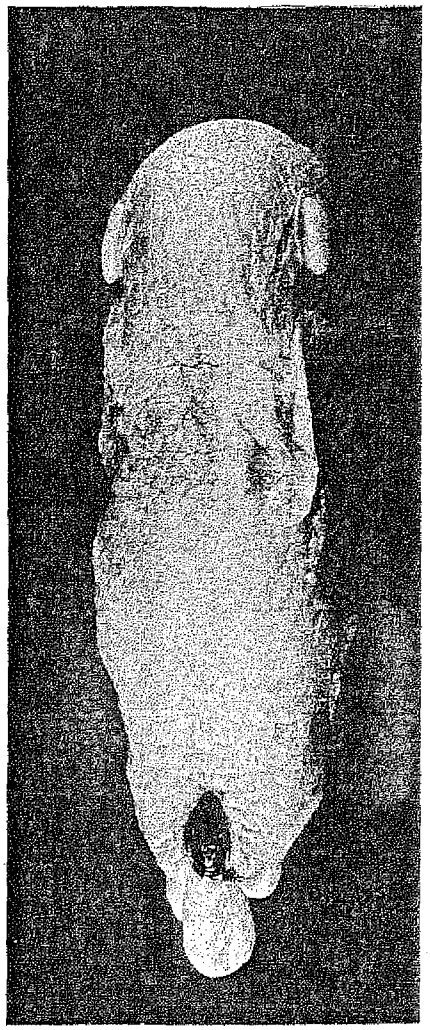

Fig. 2.