日本実験用マウスの尾曲りに関する遺伝学的研究

誌名	The Japanese journal of genetics
ISSN	0021504X
著者	野沢, 謙 近藤, 恭司
巻/号	46巻2号
掲載ページ	p. 109-123
発行年月	1971年5月

JAPAN. J. GENETICS Vol. 46, No. 2: 109-123 (1971)

GENETICAL STUDY ON THE JAPANESE CROOKED-TAIL IN THE MOUSE

KEN NOZAWA* AND KYOJI KONDO

Department of Animal Genetics, Faculty of Agriculture,
Nagoya University, Nagoya, 464

Received October 26, 1970

INTRODUCTION

The authors (1956) have reported the results of morphological and genetical studies on the crooked-tail character appeared in the Japanese laboratory mice. The occurrence of this abnormality depends on the existence of a rudimentary coccygeal vertebra showing a triangular or echelonar form, and the differentiation of the abnormal vertebra has been considered to originate in the dorsal displacement of the calcification center. The variants, regardless of the sex, have no other abnormal structure than that and show no deficiency in viability and fertility; therefore, the strain has easily been kept in the Department of Animal Genetics, Nagoya University.

The results of mating tests to make clear the mode of inheritance of the character have been reported preliminarily in the paper mentioned above: the authors have considered that the character be controlled by multiple factors. Since then mating experiments have been continued and the confirmation has been given for the multi-factoriality of the Japanese crooked-tail. The results will be reported in the present article.

MATERIALS AND METHODS

The crooked-tail character could be identified after the seven days of age. At the first step of investigation the mice of several inbred strains which were kept in the Department of Animal Genetics, Nagoya University were examined and the frequencies of sporadic occurrence of the abnormality were calculated. These strains were classified into five groups as shown in Table 1: Japanese Kasukabe group, Japanese fancy mouse group, German mouse group, the group of strains originated from crossbred between above three, and the imported strain group of European and American origins. For detailed description of the strains belonging the first four groups refer to KONDO, HIMENO, IKOMA and KATSURAGI (1953) and KONDO, NOZAWA, TOMITA and ESAKI (1957).

The frequency of sporadic appearance of the crooked-tail was comparatively high in some strains of Kasukabe group. Therefore the selection experiment was carried out in order to establish a strain of the Japanese crooked-tail. For making clear the mode

* Present address: Primate Research Institute, Kyoto University, Inuyama, Aichi-ken, 484.

of inheritance, the mating experiments were performed within the Kasukabe group, and by using the crooked strain on the one hand and the KK, NSc, DDK and CF♯1 strains on the other, the latters being considered as representatives of the Kasukabe, fancy mouse, German and imported groups, respectively.

All mating experiments were made in wooden cage 20×30×15 cm in size with wire netting on the upper surface. Mice were given daily with corn-wheat-fishmeal mixture and allowed to drink water ad lib. Cages were put in a room which was warmed only in winter season; then room temperature fluctuated between about 10°C in winter and about 30°C in summer. Such a system of rearing mice has been good enough for ordinary mouse experiments in the authors' laboratory.

EXPERIMENTAL RESULTS

Sporadic crooked-tail

The frequencies of sporadic occurrence of crooked-tail in several mouse strains are shown in Table 1. As any sexual difference is not observed, the frequencies of the both sexes are pooled in this data. It may be considered that the tail-crooking is not always the expression of Japanese crooked-tail genotype in the imported strain group, because many kinds of tail abnormalities have been discovered and analyzed genetically in various strains of European and American origins. But it has been recognized that at least in the strains of Japanese origin the tail-crooking is of the same anatomy described in the introduction of the present paper. From this table it can be considered that the frequency of sporadic occurrence of the crooked-tail is remarkably high in some strains of Kasukabe group and in three strains of crossbred origin which have genetic relationship with Kasukabe group.

Regular mating experiments

The mice with crooked-tail appearing sporadically in the Kasukabe group were mated to those of German DDK strain which had been completely isolated from those of Kasukabe group and almost free from the crooked abnormality. F_1, F_2 and backcross populations were counted. The results shown in Table 2 indicate that the frequencies of occurrence of crooked-tail are much lower than those expected from simple Mendelian recessiveness. But it is not doubtful that the abnormality is hereditary, since a remarkably high rate of appearance was obtained from the backcrosses.

Moreover, the crooked mice which were extracted from the 28th generation of the high selection line described below were mated to the mice of KK, KSc, DDK and CF♯1, and F_1 and F_2 populations were counted. The results shown in Table 3 indicate that the frequency of the crooked-tail progeny is remarkably high from the cross between the crooked stock and KK strain which has been reared from Japanese Kasukabe group. Then, it can be considered that Kasukabe group of mice has such a gene constitution that the crooked-tail character be appreared with a high probability. Furthermore, it is of some interest that in the progeny of the cross between the crooked strain and the imported CF♯1 strain the incidence of crooked-tail is comparatively high, because the latter strain can not be regarded to have any genetic relationship with Japanese Kasukabe group.

Table 1. Frequencies of occurrence of sporadic crooked-tail in various strains of mice kept in the Department of Animal Genetics, Nagoya University

Group	Strain	Frequency of sporadic crooked-tail		
		Number of mice counted	Number of crooked-tail mice	Percentage with its standard error
Kasukabe	Original Kasukabe	297	26	8.7±1.6
	KK	483	13	2.6±0.7
	KSB	104	11	10.5±2.9
	KR	106	0	0.0
	AIII	148	3	2.0±1.1
	Kpa	132	6	4.5±1.8
	vl	143	3	2.0±1.1
Japanese fancy	NBC	354	8	2.2±0.7
	NC	375	5	1.3±0.6
	NCc	167	0	0.0
	NSc	210	2	0.9±0.6
German	DDK	770	1	0.1±0.1
Crossbred origin	AI	158	0	0.0
	SII	146	14	9.5±2.4
	SIII	239	0	0.0
	SIV	181	0	0.0
	SV	124	14	11.2±2.8
	CS	488	57	11.6±1.4
	DCR	64	0	0.0
	DCS	165	0	0.0
	BHC	108	0	0.0
Imported	DBA/2	235	0	0.0
	C57BL/6J	132	0	0.0
	C57L/HeMs	148	0	0.0
	CBA/Ms	107	0	0.0
	A/HeMs	65	0	0.0
	C3H	61	0	0.0
	Yellow lethal (A^y)	348	1	0.2±0.2
	CF♯1	44	1	2.2±2.2

Table 2. Results of crosses between the sporadic crooked individuals and German DDK strain

Original cross	Generation	Progeny		
		Number of mice counted	Number of crooked-tail mice	Percentage with its standard error
DDK×crooked	F_1	182	3	1.6±0.9
	F_2	529	19	3.6±0.7
	F_1 to crooked	256	45	17.5±2.3
Crooked×DDK	F_1	8	0	0.0
	F_2	71	3	4.2±2.3

Table 3. Results of crosses between crooked individuals extracted from the 28th generation of the high selection line on the one hand and KK, KSc, DDK and CF♯1 strains on the other

Original cross	Generation	Progeny		
		Number of mice counted	Number of crooked-tail mice	Percentage with its standard error
Crooked×KK	F_1	52	6	11.5±4.4
	F_2	1189	358	30.1±1.3
Crooked×KSc	F_1	32	0	0.0
	F_2	661	42	6.3±0.9
Crooked×DDK	F_1	18	0	0.0
	F_2	270	14	5.1±1.3
Crooked×CF♯1	F_1	81	1	1.2±1.2
	F_2	1758	184	10.4±0.7

Table 4. Results of selective matings among crooked-tail mice P: Frequency in the Kasukabe group, Sh 1–Sh 42: Generations of high selection

Generation	Progeny			Generation	Progeny		
	Number of mice counted	Number of crooked mice	Percentage with its standard error		Number of mice counted	Number of crooked mice	Percentage with its standard error
P	297	26	8.7±1.6	Sh 22	62	53	85.4±4.4
Sh 1	105	14	13.3±3.3	Sh 23	80	78	97.5±1.4
Sh 2	132	30	22.7±3.6	Sh 24	79	75	94.9±2.4
Sh 3	86	30	34.8±5.1	Sh 25	51	47	92.1±3.7
Sh 4	42	27	64.2±7.3	Sh 26	61	58	95.0±2.7
Sh 5	70	54	77.1±5.0	Sh 27	65	58	89.2±3.8
Sh 6	102	80	78.4±4.0	Sh 28	44	39	88.6±4.7
Sh 7	40	34	85.0±5.6	Sh 29	94	92	97.8±1.5
Sh 8	18	15	83.3±8.7	Sh 30	112	108	96.4±1.7
Sh 9	8	6	75.0±15.3	Sh 31	98	96	97.9±1.4
Sh 10	17	15	88.2±7.8	Sh 32	77	74	96.1±2.2
Sh 11	55	49	89.0±4.2	Sh 33	78	73	93.5±2.7
Sh 12	95	79	83.1±3.8	Sh 34	93	91	97.8±1.5
Sh 13	35	33	94.2±3.9	Sh 35	76	72	94.7±2.5
Sh 14	26	26	100.0	Sh 36	127	120	94.4±2.0
Sh 15	76	76	100.0	Sh 37	88	86	97.7±1.5
Sh 16	64	61	95.3±2.6	Sh 38	127	125	98.4±1.1
Sh 17	26	26	100.0	Sh 39	78	74	94.8±2.5
Sh 18	56	56	100.0	Sh 40	65	62	95.3±2.6
Sh 19	77	75	97.4±1.8	Sh 41	51	48	94.1±3.3
Sh 20	33	31	93.9±4.1	Sh 42	93	90	96.7±1.8
Sh 21	55	53	96.3±2.5				

High and low selection experiments

The preceding experiments suggested strongly that Japanese crooked-tail might be controlled by some hereditary factors. So selection experiment was started from the mating among sporadic crooked individuals in the Kasukabe group, and crooked in-

dividuals were mated selectively generation after generation (high selection line). Rates of appearance of crooked offspring in each generation are presented in Table 4 and Fig. 1. From the results it can be seen that the selection was effective and that one line of the crooked-tail was established after the 13th generation.

From a pair of normal-tailed mice in the offspring of 10th generation of the high selection line, a low selection line was started. In this line normal-tailed mice were mated selectively generation after generation. Frequencies of occurrence of crooked offspring in each generation are shown in Table 5 and Fig. 1. The results indicate that a remarkable selection response was obtained at the starting point of the low selection line and thereafter the responses were rather slight and the frequencies of appearance of crooked offspring were on about 35% level up to the 31st generation when the low selection line was terminated.

The low selection line was started from mating between one male and one female normal-tailed individuals which appeared in the progeny population of 10th generation of the high selection line. A slight selection responses after the 2nd generation of low selection may be ascribed to exhaustion of genetic variation after passage of a bottle neck of population size. In order to examine this possibility a comparison was made between the frequencies of occurrence of crooked individuals in the progeny of normal selective mating and of crooked selective mating at the 18th-19th generations of low selection line. The result is shown in Table 6. Between the two kinds of selective mating a significant difference ($P<0.01$) was observed, therefore some genetic variations were still considered to exist at that stage of low selection.

Table 5. Results of selective matings among normal-tailed mice
Sh 10: 10th generation of high selection, Sl 1–Sl 31: generations of low selection

Generation	Progeny			Generation	Progeny		
	Number of mice counted	Number of crooked mice	Percentage with its standard error		Number of mice counted	Number of crooked mice	Percentage with its standard error
Sh 10	17	15	88.2±7.8	Sl 16	47	21	44.6±7.2
Sl 1	14	6	42.8±13.2	Sl 17	72	26	36.1±5.6
Sl 2	114	59	51.7±4.6	Sl 18	71	15	21.1±4.8
Sl 3	29	15	51.7±9.2	Sl 19	187	46	24.5±3.1
Sl 4	122	65	53.2±4.5	Sl 20	83	18	21.6±4.5
Sl 5	80	50	62.5±5.4	Sl 21	79	15	18.9±4.4
Sl 6	15	4	26.6±11.4	Sl 22	143	39	27.2±3.7
Sl 7	44	17	38.6±7.3	Sl 23	92	31	33.6±4.9
Sl 8	159	78	49.0±3.9	Sl 24	124	37	29.8±4.1
Sl 9	96	49	51.0±5.1	Sl 25	162	54	33.3±3.7
Sl 10	143	63	44.0±4.1	Sl 26	129	48	37.2±4.2
Sl 11	133	53	39.8±4.2	Sl 27	136	43	31.6±3.9
Sl 12	102	48	47.0±4.9	Sl 28	110	43	39.0±4.6
Sl 13	51	12	23.5±5.9	Sl 29	153	56	36.6±3.8
Sl 14	117	40	34.1±4.3	Sl 30	57	22	38.5±6.4
Sl 15	51	21	41.1±6.8	Sl 31	115	41	35.6±4.4

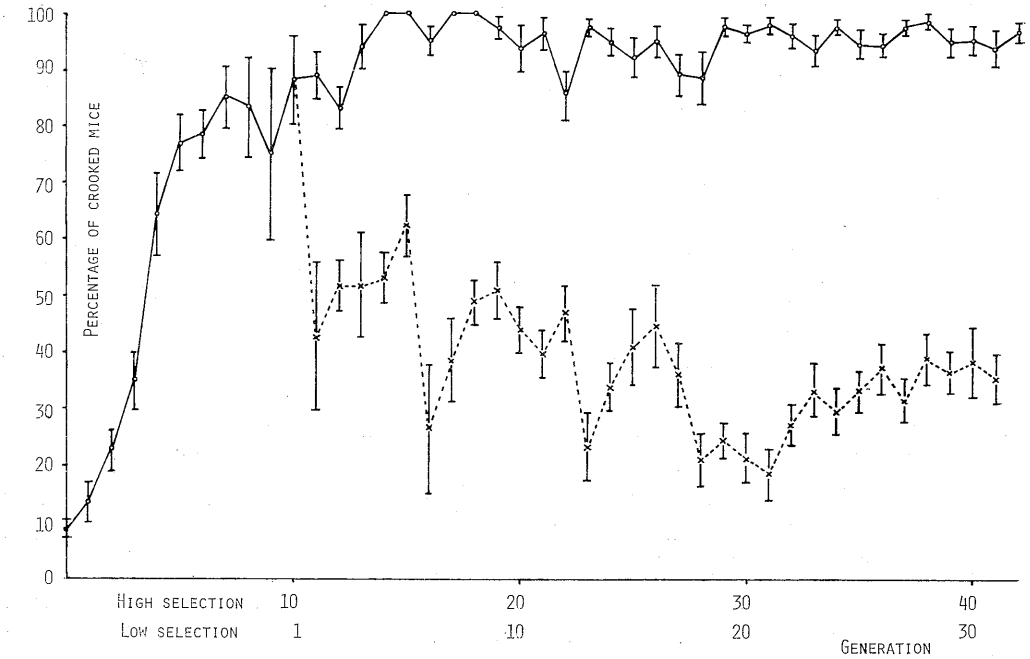

Fig. 1. Results of high and low selections

Table 6. Comparison between the frequencies of occurrence of crooked progeny from normal selective mating and from crooked selective mating at the stage of 18th-19th generations of low selection

Kind of selective mating	Progeny			
	Number of mice counted	Number of mice crooked	Percentage with its standard error	Significance of difference
Normal×normal	258	61	23.6±2.6	$P<0.01$
Crooked×crooked	231	81	35.0±3.1	

Successive backcrosses

The results of preceding mating experiments suggested the possible multifactoriality of Japanese crooked-tail. Then the following experiments were carried out to confirm it. Members of the crooked strain were crossed to random individuals of KK, NSc, DDK or CF ♯1 strain. F_1 mice with normal tail were backcrossed to the crooked strain, and normal progeny were backcrossed again to the crooked strain. Such backcrosses were continued generation after generation. If this character was controlled by a single gene difference, dominant or recessive, it would be expected that the percentages of the crooked offspring in each backcross generation might be at a certain definite level. So these experiments can be considered as a discriminative test between single-factor inheritance and multifactoriality of the crooked abnormality. The original crooked individuals were derived from members of the high selection line already

Table 7. Results of successive backcrosses between normal segregants to the crooked

Generation	Progeny			Generation	Progeny		
	Number of mice counted	Number of crooked mice	Percentage with its standard error		Number of mice counted	Number of crooked mice	Percentage with its standard error
Original cross: Crooked (offspring of 19th generation of high line)×KK							
F_1	29	4	13.7±6.3	B_5	191	156	81.6±2.8
B_1	171	74	43.2±3.7	B_6	84	79	94.0±2.5
B_2	86	51	59.3±5.2	B_7	45	40	88.8±4.7
B_3	72	56	77.7±4.9	B_8	57	55	96.4±2.4
B_4	96	75	78.1±4.2				
Original cross: Crooked (offspring of 19th generation of line)×NSc							
F_1	23	0	0.0	B_5	159	139	87.4±2.6
B_1	163	64	39.2±3.8	B_6	90	81	90.0±3.1
B_2	174	105	60.3±3.7	B_7	49	46	93.8±3.4
B_3	180	147	81.6±2.8	B_8	28	25	89.2±5.8
B_4	97	74	76.2±4.3	B_9	6	6	100.0
Original cross: DDK×crooked (offspring of 11th generation of high line)							
F_1	18	0	0.0	B_7	66	56	84.8±4.4
B_1	94	28	29.7±4.7	B_8	62	58	93.5±3.1
B_2	168	114	67.8±3.6	B_9	37	30	81.0±6.4
B_3	154	127	82.4±3.0	B_{10}	87	80	91.9±2.9
B_4	168	151	89.8±2.3	B_{11}	51	48	94.1±3.2
B_5	107	96	89.7±2.9	B_{12}	34	27	79.4±6.9
B_6	69	66	95.6±2.4	B_{13}	46	46	100.0
Original cross: CF♯1×crooked (offspring of 25th generation of high line)							
F_1	22	0	0.0	B_7	207	202	97.5±1.0
B_1	80	34	42.5±5.5	B_8	41	38	92.6±4.0
B_2	134	99	73.8±3.7	B_9	91	85	93.4±2.6
B_3	161	127	78.8±3.2	B_{10}	139	134	96.4±1.5
B_4	224	185	82.5±2.5	B_{11}	163	160	98.1±1.0
B_5	168	140	83.3±2.8	B_{12}	153	149	97.3±1.3
B_6	132	118	89.3±2.6				

described; the offspring of the 11th generation were crossed with DDK, those of the 19th generation with KK and with NSc, and those of 25th generation with CF ♯1. The results of the successive backcrosses were given in Table 7. This table shows a pronounced increase in percentage of the crooked abnormality with generations in every series of successive backcross experiments. It can be considered that the multifactoriality of the Japanese crooked-tail is strongly confirmed by these mating experiments.

In addition, it is interesting to note that the frequency of crooked individuals is much higher in the offspring of the first backcross generation (B_1) of the successive backcross experiments using DDK strain (29.7%) than in those of the backcross in the regular mating experiments (17.5%, Table 2). Since these two crosses were carried out in the same manner, the difference ($0.01<P<0.02$) may be ascribed to a possible accumulation of the crooked factors in the course of selective matings of more than ten

generations.

"Outcross, high selection and between-line cross" experiment

If the determinants of the Japanese crooked-tail phenotype are of multifactorial or polygenic nature, it would possibly be considered that the crooked character can be brought to expression by only a partial accumulation of such polygenes. And it would also be interesting to get insight into dominance or recessivity of the crooked polygenes. The following experiments were carried out on the basis of such a consideration. From the fully established crooked strain six females were sampled and they were divided into three groups. Each group of two crooked females was crossed to a male from DDK strain and three lines (I, II and III) were started. In each line the individuals with crooked-tail were selected as parents of next generation except in early generations when crooked individuals could not always be obtained because of low frequencies of that phenotype. The selection was successful in increasing crooked frequency in every lines as shown in Table 8. However, unfortunately, the selection line I was terminated

Table 8. Results of selections of crooked-tail from F_1 population of DDK×crooked and frequencies of crooked phenotypes in crossbred populations between two selection lines

Generation	Progeny		
	Number of mice counted	Number of crooked mice	Percentage with its standard error
Selection line I			
F_1 from DDK × crooked	29	3	10.3±5.6
SI_1	210	9	4.2±1.3
SI_2	91	16	17.5±3.9
SI_3	63	23	36.5±6.0
Selection line II			
F_1 from DDK × crooked	26	1	3.8±3.7
SII_1	245	10	4.0±1.2
SII_2	162	3	1.8±1.0
SII_3	254	38	14.9±2.2
SII_4	196	83	42.9±3.5
SII_5	51	37	72.5±6.2
SII_6	30	25	83.3±6.8
Selection line III			
F_1 from DDK × crooked	38	5	13.1±5.4
$SIII_1$	250	27	10.8±1.9
$SIII_2$	197	56	28.4±3.2
$SIII_3$	114	48	42.1±4.6
$SIII_4$	133	69	51.8±4.3
$SIII_5$	98	73	74.4±4.4
$SIII_6$	102	81	79.4±4.0
Crossbred (CB) between selection lines			
CB from $SII_3 \times SIII_3$	67	18	26.8±5.4
CB from $SII_4 \times SIII_4$	121	53	43.8±4.5
CB from $SII_5 \times SIII_5$	4	?	75.0±21.6

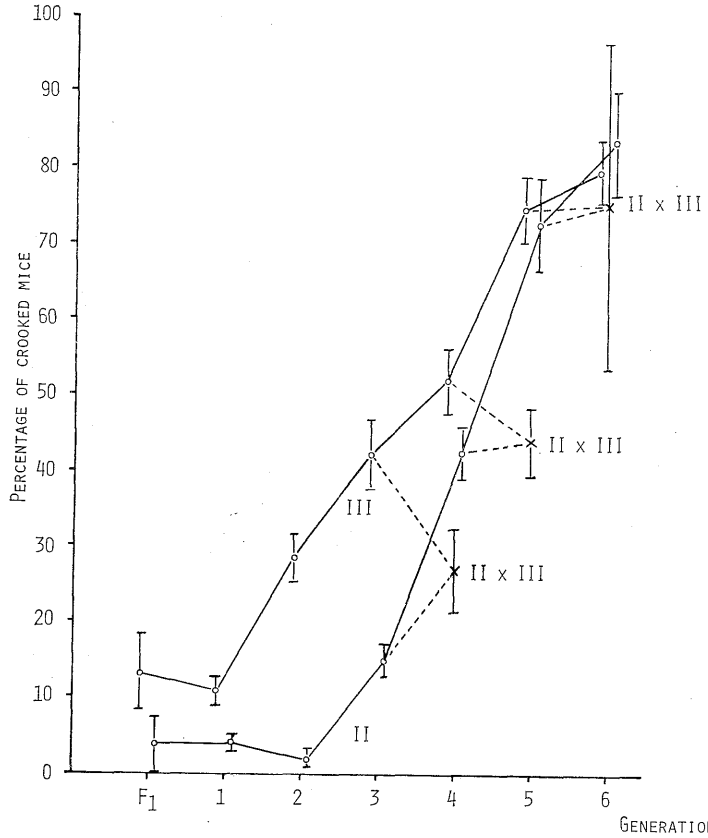

Fig. 2. Crooked frequencies in the selection lines II and III, and in crossbred populations of "Outcross, selection and cross" experiment.

in the 3rd selective generation on account of low fecundity; that was considered as a probable effect of inbreeding depression.

Now, in the 3rd, 4th and 5th selective generations the crooked individuals were sampled randomly from both selection lines II and III and crosses were made between lines. Then the frequencies of occurrence of crooked abnormality in the crossbred populations were compared with those in the next generations of the selection lines. The results are presented in Table 8 and Fig. 2. The crooked frequencies in the three crossbred populations were lower than those in the corresponding generations of both selection lines, two cases of them showing statistical significance. From such experimental results it can be considered that the expression of crooked character does not necessitate a complete accumulation of the crooked polygenes and that the polygenes are in general of recessive nature.

Pleiotropism and environmental influences

The crooked genes have such a peculiarity that they do not express pleiotropic effect on other organs and crooking of vertebral colum is restricted in the part of coccygeal vertebral unlike other genetical tail-bending abnormalities in mice (cf.

GRÜNEBERG, 1952). The crooked genes are considered not to have any influence on viability of mice, because the crooked strain have easily been established after the selective matings for this character, and because any trace of viability depression has never been recognized during the course of selection and maintenance of this mutant strain. For instance, the mean litter sizes were calculated as 5.6±0.1(384 litters) in the high selection line and 5.8±0.1 (462 litters) in the low selection line; the mean litter size of the KK strain to which the crooked mice owed a majority of their genes was 5.2±0.8 (KONDO, HIMENO, IKOMA and KATSURAGI, 1953).

Next, examinations were carried out whether some environmental differences — litter size, maternal age and month of birth — could influence on the frequency of occurrence of crooked abnormality. All the litters in and after the llth generation of

Table 9. Frequency of occurrence of crooked individuals in the litters different in size

Litter size	Progeny of high selection line			Progeny of low selection line		
	Number of mice counted	Number of crooked mice	Percentage with its standard error	Number of mice counted	Number of crooked mice	Percentage with its standard error
1	5	5	100.0	6	1	16.6±15.1
2	28	26	92.8±4.8	20	5	25.0±9.6
3	100	97	97.0±1.7	138	48	34.7±4.0
4	219	211	96.3±1.2	258	111	43.0±3.0
5	225	217	96.4±1.2	328	106	32.2±2.5
6	360	340	94.4±1.2	377	121	32.0±2.4
7	372	360	96.7±0.9	452	170	37.6±2.2
8	267	253	94.7±1.3	241	81	33.6±3.0
9	158	149	94.3±1.8	252	96	38.0±3.0
10	75	73	97.3±1.8	115	35	30.4±4.2
11	47	46	97.8±2.1	81	30	37.0±5.3
12	34	34	100.0	23	5	21.7±8.5
13	12	12	100.0	44	16	36.3±7.2

Table 10. Frequency of occurrence of crooked individuals in mice born in different maternal ages

Maternal age in months	Progeny of high selection line			Progeny of low selection line		
	Number of mice counted	Number of crooked mice	Percentage with its standard error	Number of mice counted	Number of crooked mice	Percentage with its standard error
<3	300	285	95.0±1.2	328	129	39.3±2.6
3-4	455	439	96.4±0.8	436	163	37.3±2.3
4-5	250	245	98.0±0.8	269	92	34.2±2.8
5-6	250	235	94.1±1.4	344	121	35.2±2.5
6-7	231	216	93.5±1.6	291	84	28.8±2.6
7-8	189	180	95.2±1.5	215	82	38.1±3.3
8-9	80	74	92.5±2.9	116	37	31.8±4.3
9-10	47	46	97.8±2.1	123	38	30.8±4.1
10-11	34	31	91.2±4.8	87	30	34.4±5.0
11-12	17	17	100.0	31	11	35.4±8.5
12<	32	31	96.8±3.1	21	6	28.5±9.8

Table 11. Frequency of occurrence of crooked individuals in mice born in different months of the year

Month	Progeny of high selection line			Progeny of low selection line		
	Number of mice counted	Number of crooked mice	Percentage with its standard error	Number of mice counted	Number of crooked mice	Percentage with its standard error
January	123	113	91.8±2.3	172	44	25.5±3.3
February	136	132	97.0±1.4	164	45	27.4±3.4
March	204	194	95.0±1.5	190	71	37.3±3.5
April	203	193	95.0±1.5	235	85	36.1±3.1
May	191	181	94.7±1.6	271	101	37.2±2.9
June	174	168	96.5±1.3	215	95	44.1±3.3
July	216	205	94.9±1.4	267	91	34.0±2.8
August	123	121	98.3±1.1	155	74	47.7±8.0
September	85	83	97.6±1.6	120	35	29.1±4.1
October	178	166	93.2±1.8	233	81	34.7±3.1
November	115	113	98.2±1.2	168	53	31.5±3.5
December	163	155	95.0±1.7	123	39	31.7±4.1

high selection line and in and after the 1st generation of low selection line were totalled for these objectives, because both selection lines showed fairly constant frequencies of crooked-tail although in the low selection line a steady decline was observed as shown in Fig. 1. Variations of the crooked frequency in different litter sizes, in differerent maternal ages and in different months of parturition were shown in Tables 9, 10 and 11, respectively. From the tables it can be observed the frequency of occurrence of crooked-tail can not markedly be influenced by these three environmental variables; however, in the low selection line such a slight and inconsistent tendency is observed that the frequency is low in winter and high in summer.

DISCUSSION

Among many kinds of genetical tail abnormalities in mice already known, "Tail-kinks" and "Bent-tail", both of which have been reported by GRÜNEBERG (1955 a and b), are considered to be most resemble morphologically to Japanese crooked-tail. However, the former is controlled by the autosomal recessive gene (tk) and abnormality is not confined to the coccygeal vertebral portion; and the latter is expressed by a sex-linked dominant gene (Bn) and sometimes such pleiotropisms are observed as interfrontal bone, dyssymphysis posterior of the axis and foramen acetabuli perforans. The peculiarities of the Japanese crooked-tail are its multifactorial genetic basis and lack of pleiotropic effects. In that meaning the Japanese crooked-tail is considered to have a close similarity to a hereditary crooked toes in chickens which have been analysed genetically by HICKS and LERNER (1949). LERNER has named such genetic abnormalities with variable penetrance, which are controlled by multiple factors, "phenotypic deviant (phenodeviant)" in his book "Genetic Homeostasis" (1954).

The most classical cases of the phenodeviant are considered to be otocephaly and appearance of four toes in guinea pig (WRIGHT, 1934 a and b) and harelip in the house mouse (REED, 1936 a). WRIGHT (1934 c) made crosses between several inbred strains of guinea pigs differing in number of digits and succeeded in estimating minimum numbers of gene difference between these strains. On the other hand, REED (1936 b) considered in his genetic analysis of harelip in the mouse such a possibility that the character was controlled by from three to five pairs of cumulative genes and the abnormality was brought into expression when from two to three pairs of them became homozygous. Later on, CHASE (1951) suggested that a polydactyl character in the mouse was controlled by several hereditary factors none of which was major, from such evidences that the abnormality appeared sporadically in several inbred lines, that test crosses did not give 3: 1 or 1: 1 clear segregation ratio, and especially that the frequency of appearances of polydactyly increased markedly by successive backcross experiment. Further, it seems likely that several kinds of skeletal variation which GRÜNEBERG and his associates have called "quasi-continuous variation" (GRÜNEBERG, 1952; TRUSLOVE, 1952, 1954; DEOL, 1955; SEARLE, 1959) are also belonging principally to the same category of hereditary characters.

Now, on the basis of the consideration that Japanese crooked-tail would also be the same kind of genetic variant and REED's explanation (1936 b) be applicable to this case, the present authors tried to construct a mathematical theory so that we could gain an insight into the number of polygenes controlling expression of Japanese crooked-tail character. The mating system of the successive backcross experiment was used for constructing the theory. Assume that all the crooked polygenes are located on autosomes, segregate randomly (no linkage relation) to each other, give same effect to the character expression, and are completely recessive. Furthermore, let us assume that m pairs of such polygenes are homozygous in the high selection line after the 11 th selective generation, and that n ($m \geq n$) is the minimum number of polygenic loci being homozygous for the expression of crooked abnormality. Then, the mathematical expectations of the frequency of crooked phenotype up to the N th generation of the successive backcrosses are as follows:

$$E(q_1) = 1 - \frac{1}{2^m}\sum_{j=0}^{n-1} {}_1W_j, \qquad \text{in which} \qquad {}_1W_j = \binom{m}{j},$$

$$E(q_2) = 1 - \frac{1}{E(1-q_1)\cdot 2^m}\sum_{j=0}^{n-1} {}_2W_j, \qquad \text{in which} \qquad {}_2W_j = {}_1W_j \frac{1}{2^{m-j}}\sum_{i=0}^{n-1-j}\binom{m-j}{i},$$

$$E(q_3) = 1 - \frac{1}{E(1-q_1)\,E(1-q_2)\cdot 2^m}\sum_{j=0}^{n-1} {}_3W_j, \quad \text{in which } {}_3W_j = {}_2W_j \frac{1}{2^{m-j}}\sum_{i=0}^{n-1-j}\binom{m-j}{i},$$

.....

$$E(q_N) = 1 - \frac{1}{E(1-q_1)\,E(1-q_2)\cdots\cdots E(1-q_{N-1})\cdot 2^m}\sum_{j=0}^{n-1} {}_NW_j,$$

$$\text{in which } {}_NW_j = {}_{N-1}W_j \frac{j}{2^{m-j}}\sum_{i=0}^{n-1-j}\binom{m-j}{i}.$$

If the values of m and n are given, the series $E(q_1)$, $E(q_2)$, $\cdots\cdots$, $E(q_N)$ can be obtained by numerical calculations. Then the limiting value of this series, $E(q_\infty)$, can be given as

$$E(q_\infty) = 1 - \frac{1}{2^{m-n+1}},$$

and a numerical relationship between $m-n$ and $E(q_\infty)$ is as follows:

$m-n$	$E(q_\infty)$ in %
0	50.0
1	75.0
2	87.5
3	93.7
4	96.8
5	98.4

The $m-n$ represents a difference between maximum and minimum numbers of polygenes giving rise to crooked-tail. From the above numerical relationship it can be observed that the frequency of appearance of crooked individuals among the progeny of successive backcrosses approaches closely to 100% when the difference, $m-n$, be sufficiently large.

When we examine the results of successive backcross experiments (Table 7), it is clear that the limiting values of crooked frequency are above 90% in every cases. Therefore, $m-n$ must be 3 or more. This means that the number of crooked polygene loci segregating in successive backcross lines is at least 3 larger than the minimum number of fixed polygene loci for expression of the tail abnormality. It can be considered that in the high selection line, for example, 6 pairs of polygenic loci are fixed in which 2 or 3 pairs are necessary to fix for expression of the crooked-tail.

From such a mathematical consideration and from the result of "outcross, high-selection and between-line cross" experiment it can be considered that the existence of crooked polygenes have been of fairly ubiquitous nature in the Japanese Kasukabe group of mice. Explanations would also be given for the facts that a crooked strain was easily established by successive selective matings of crooked individuals from the Kasukabe group and that among the F_1 or backcross progeny of the regular outcrosses clear 3 : 1 or 1 : 1 segregation ratios could not be obtained. Failure of establishment of a line with zero or very low frequency of appearance of crooked abnormality from the 10th generation of high selection line would be explained by a presumption that a majority of the crooked polygenes had already been accumulated and fixed in that generation of the high selection line. Moreover, it can be considered that the sporadic appearances of crooked abnormality in Japanese strains of mice are a result of chance fixation of crooked polygenes being maintained and segregating in the strain.

SUMMARY

The Japanese crooked-tail which frequently appeared sporadically in the Japanese laboratory mice named Kasukabe group was analysed genetically. Sporadic appearance of this abnormality, a clear selection response to increasing frequency of appearance, and an easy establishment of crooked stock in which the frequency was always beyond 90%, made us assume that this genetic abnormality was controlled by a number of polygene pairs none of which had major effect. This assumption was confirmed by the results of experiments comprised of outcrossing the crooked strain with other strains and successive backcrosses of normal segregants to the crooked individuals from the crooked strain; in this mating experiment the frequency of occurrence of crooked abnormality increased markedly from generation to generation. Furthermore, the result of "outcross, high selection and between-line cross" experiments showed that the expression of crooked phenotype did not necessitate a complete accumulation of the polygenes responsible and that the polygenes were in general of recessive nature. From these observations the authors considered that the Japanese crooked-tail was a kind of genetic variation similar in its genetic basis to LERNER's "phenotypic deviants (phenodeviants)" and GRÜNEBEG's "quasi-continuous variations."

From the analysis of results of successive backcross experiment and mathematical formulation, it could be considered that the number of crooked polygene loci being maintained in the crooked strain and so segregating in successive backcross lines was at least 3 larger than the minimum number of polygene loci fixed for expression of the tail abnormality. This meant that the existence of crooked polygenes had been of fairly ubiquitous nature in the Japanese Kasukabe group of mice.

LITERATURE CITED

Chase, H. B., 1951 Inheritance of polydactyly in the mouse. Genetics **36**: 697–710

Deol, M.S, 1955 Genetical studies on the skeleton of the mouse. XIV. Minor variations of the skull. J. Genetics **53**: 498–514.

Grüneberg, H. 1952 Genetical studies on the skeleton of the mouse. IV. Quasi-continuous variations. J. Genetics **51**: 95–114.

Grüneberg, H., 1955a Genetical studies on the skeleton of the mouse. XVI. Tail-kinds. J. Genetics **53**: 536–550.

Grüneberg. H., 1955b Genetical studies on the skeleton of the mouse. XVII. Bent-tail. J. Genetics **53**: 551–562.

Grüneberg, H., 1952 "The Genetics of the Mouse". Martinus Nijhoff, The Hague.

Hicks, A. F., and I. M. Lerner, 1949 Hereditary crooked toes in chickens. Poultry Sci. **28**: 625–626.

Kondo, K., K. Himeno, H. Ikoma, and T. Katsuragi, 1953 The breeding in mouse. Bull. Nat. Inst. Agric. Sci., Series G **7**: 9–27.

Kondo, K. Nozawa, T. Tomita, and K. Esaki, 1957 Laboratory strains reared from Japanese native mice. Experimental Animals **6**: 107–112.

Lerner, I. M., 1954 "Genetic Homeostasis", John Wiley and Sons, New York.

Nozawa, K., and K. Kondo, 1956 Genetical study on a new type of crooked tail in Japanese laboratory mice. Proc. Japan Acad. **32**: 293–297.

Reed, S. C., 1936 a Harelip in the house mouse. I. Effects of the external and internal environment. Genetics **21**: 339-360.

Reed, S. C., 1936 b Harelip in the house mouse. II. Mendelian units concerned with harelip and application of the data to the human harelip problem. Genetics **21**: 361-374.

Searle, A. G., 1959 A study of variation in Singapore cats. J. Genetics **56**: 111-126.

Truslove, G. M., 1952 Genetical studies on the skeleton of the mouse. V. "Interfrontal" and "parted frontal". J. Genetics **51**: 115-122.

Truslove, G. M. 1954 Genetical studies on the skeleton of the mouse. XIII. Variations in the presphenoid. J. Genetics 52: 589-602.

Wright, S., 1934 a On the genetics of subnormal development of the head (otocephaly) in the guinea pig. Genetics **19**: 471-505.

Wright, S., 1934 b An analysis of variability in number of digits in an inbred strain of guinea pigs. Genetics **19**: 506-536.

Wright, S., 1934 c The results of crosses between inbred strains of guinea pigs, differing in number of digits. Genetics **19**: 537-551.