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Brachyphalangy, an allele of extra-toes in the mouse

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1. INTRODUCTION

The semi-dominant gene for extra-toes (*Xt*, Johnson, 1967) in the mouse produces polydactyly when heterozygous and a complex lethal syndrome when homozygous. Brachphalangy (Xt^{bph}) is an allele with a similar but distinct phenotype.

2. ORIGIN

Brachyphalangy arose in a neutron irradiation experiment at the M.R.C. Radiobiological Research Unit at Harwell (Batchelor, Phillips & Searle, 1966) and was offered to the author late in 1964. Because of its similarity to *Xt*, tests for allelism and linkage were carried out.

3. GENETICS

Xt^{bph} is a semi-dominant gene with complete penetrance and a deficiency of homozygous abnormals at birth (Table 1). There is no deficiency before birth (Table 2). Indeed, there is a significant excess at Xt^{bph}/Xt^{bph} ($\chi^2_1 = 8{\cdot}02$) for which there is no obvious explanation.

Table 1. *Segregation of* Xt^{bph} *at birth*

Mating type	+/+	Xt^{bph}	Xt^{bph}/Xt^{bph}	Total	Litter size
(1) $Xt^{bph}/+ \times Xt^{bph}/+$	57	109	6	172	5·2
(2) $Xt^{bph}/+ \times +/+$ and $+/+ \times Xt^{bph}/+$	224	237	—	461	7·3

Table 2. *Segregation of* Xt^{bph} *in litters of embryos*

Age (days)	+/+	$Xt^{bph}/+$	Xt^{bph}/Xt^{bph}	Solid moles	Total	Litter size
9	40		16	9	65	8·1
10	27		9	3	39	7·8
11	41		19	6	66	7·3
12	41		22	8	71	7·9
13	19	52	29	4	104	8·0
14–18	19	63	36	0	118	6·9
Total	302		131	30	463	7·6

The only possible mating between mice carrying extra-toes and brachyphalangy is between heterozygotes (Table 3). Xt^{bph}/Xt^{bph} embryos resemble Xt/Xt but are more extreme with frequent exencephaly. Xt/Xt^{bph} are intermediate.

Xt is in linkage group XIV, the gene order being *cr–Xt–f–pe*, and the recombination between *Xt* and *cr* is about 1 % (Lyon, Morris, Searle & Butler, 1967). Xt^{bph} mice were tested for linkage with *cr* (Table 4): Xt^{bph} and *cr* are closely linked, with two recombinants out of 216 mice, again about 1 %.

Table 3. *Results of crosses between* Xt *and* Xt^{bph}

Pooled data of 25 litters of embryos aged 9–18 days.

Mating type	Normal or polydactylous	Presumed homozygous abnormals	Total
(1) $Xt^{bph}/+ \,♂ \times Xt/+ \,♀$	67	23	90
(2) $Xt/+ \,♂ \times Xt^{bph}/+ \,♀$	41	12	53
Total	108	35	143

Table 4. *Linkage of* Xt^{bph} *and* cr

Mating type	$\frac{Xt^{bph}+}{+\quad cr}$	$\frac{Xt^{bph}cr}{+\quad cr}$	$\frac{+\quad +}{+\quad cr}$	$\frac{+\quad cr}{+\quad cr}$	Total
		Coupling			
(1) $Xt^{bph}/+,+/cr♂ \times +/+, cr/cr ♀$	26	1	0	26	53
(2) $+/+,cr/cr♂ \times Xt^{bph}/+,+/cr ♀$	39	0	0	30	69
Total	65	1	0	56	122
		Repulsion			
(1) $Xt^{bph}/+,cr/+♂ \times +/+,cr/cr ♀$	1	35	35	0	71
(2) $+/+,cr/cr♂ \times Xt^{bph}/+,cr/+♀$	0	12	11	0	23
Total	1	47	46	0	94

4. HETEROZYGOTE

$Xt^{bph}/+$ mice are very constant in phenotype (Fig. 1). The hallux is thick and carries a broad claw. It is never doubled, but may be grooved longitudinally. The forefoot (Fig. 2) has a nubbin at the base of digit V. The pollex is broadened, and in extreme cases digit II may be flexed. In one family of the stock there is regular soft-tissue syndactylism between digits II, III and IV of the hindfoot and III and IV of the forefoot.

The sternum is regularly affected (Fig. 3), sometimes being so abnormal that individual sternebrae cannot be recognized; in other cases there are sternebral fusions. The interfrontal bone is present more often in $Xt^{bph}/+$ mice (9/13) than in normal litter-mates (5/13). Xt^{bph} produces belly spots on the genetic background of the crinkled stock, although no spots were seen on the original background.

(Of 66 $Xt^{bph}/+$ mice classified 30 had belly spots. None of their 56 normal litter-mates had one.)

$Xt^{bph}/+$ are heavier than their normal litter-mates at birth but not significantly so: 110 $Xt^{bph}/+$ mice had an average birth-weight of 1·506 g. Their 89 normal litter-mates averaged 1·462 g. ($t = 0{\cdot}75$, $P = 0{\cdot}5$.)

Some $Xt^{bph}/+$ foetuses have a transitional face bleb confined to the 13-day stage (Fig. 4, Table 5).

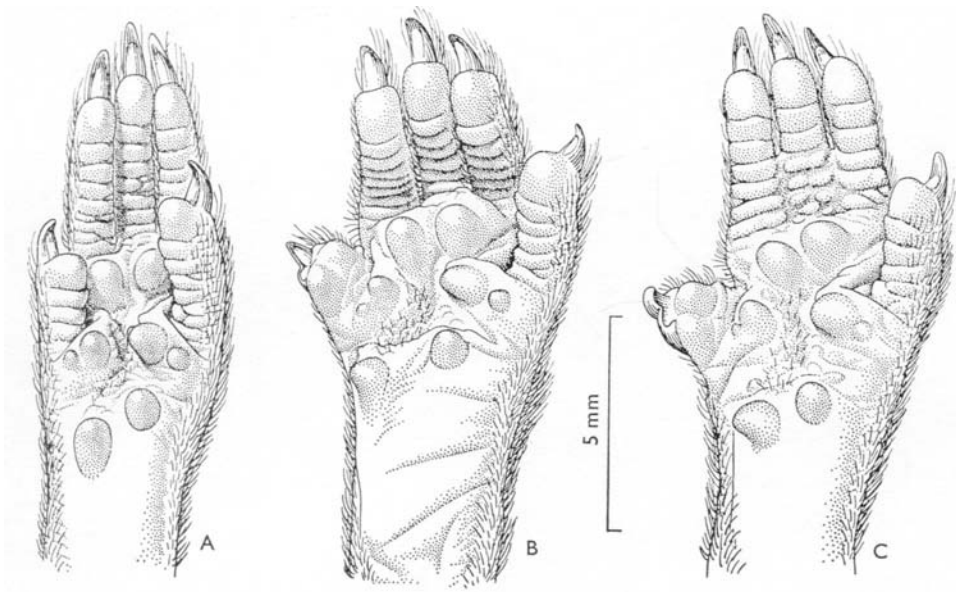

Fig. 1. Left hindfeet of adult mice, ventral view. A, normal; B, $Xt^{bph}/+$; C, $Xt^{bph}/+$ with soft-tissue syndactylism of digits II, III and IV.

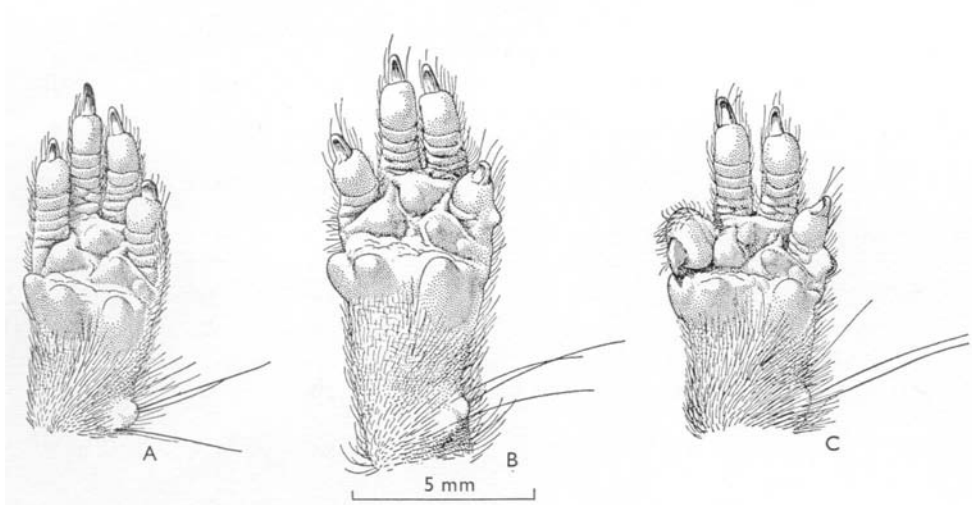

Fig. 2. Left forefeet of adult mice, ventral view. A, normal; B, C, $Xt^{bph}/+$.

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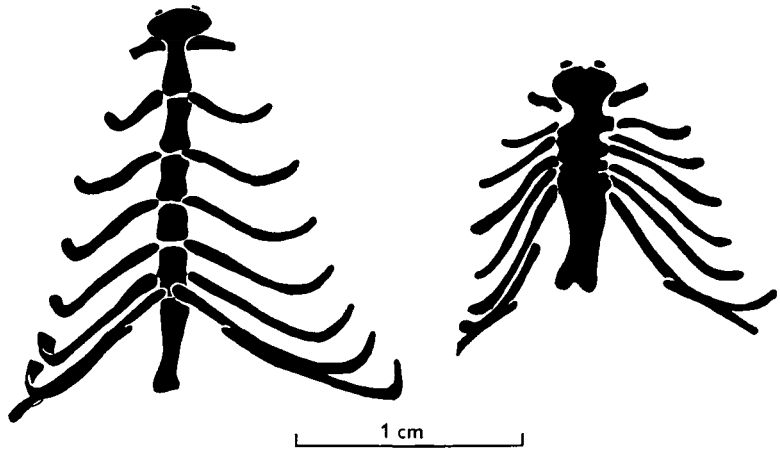

Fig. 3. Camera lucida drawings of alizarin clearance preparations of adult mice showing the sternum. Left, +/+ ; right, $Xt^{bph}/+$.

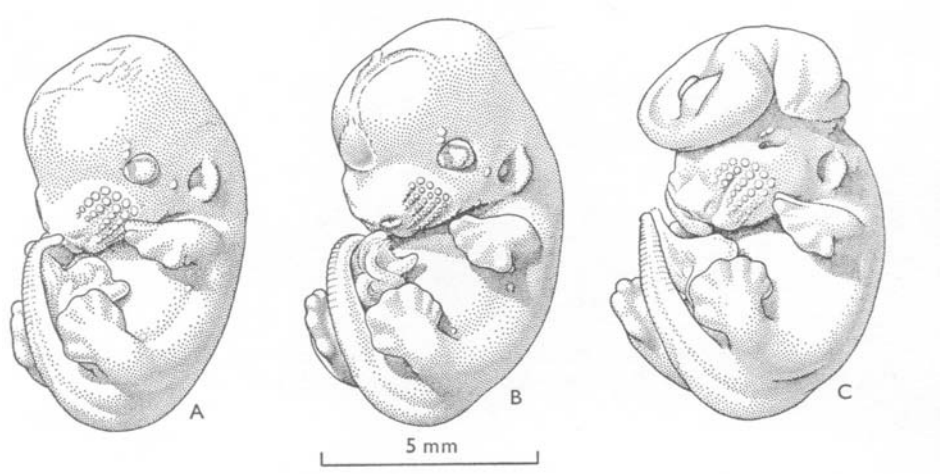

Fig. 4. Thirteen-day-old embryos from the Xt^{bph} stock. A, +/+ ; B, $Xt^{bph}/+$ with face bleb; C, Xt^{bph}/Xt^{bph}.

Table 5. *Face blebs in* 13*-day-old embryos from the* Xt^{bph} *stock*

Mating type	$Xt^{bph}/+$ Bleb	$Xt^{bph}/+$ No bleb	+/+ Bleb	+/+ No bleb	Total	$Xt^{bph}/+$ blebby (%)
(1) $Xt^{bph}/+ \delta \times Xt^{bph}/+ \varphi$	28	24	0	19	71	53·8
(2) $Xt^{bph}/+ \delta \times +/+ \varphi$	18	16	0	26	60	52·9
(3) $+/+ \delta \times Xt^{bph}/+ \varphi$	13	25	0	36	74	34·2
(4) $+/+ \delta \times +/+ \varphi$	—	—	0	54	54	—

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5. HOMOZYGOTE

Exencephaly occurs in $Xt/^{bph}$ embryos of all ages (Fig. 4). Of 115 such embryos examined at 10–18 days 65 were exencephalic. Oedema is more pronounced in $Xt/^{bph}/Xt^{bph}$ than in Xt/Xt and more blebs are present on the lower jaw, under the upper lip, in the external auditory meatus, on the cornea and often on the back of the head and between the digits of the feet. Unilateral or bilateral harelip may be present from 16 days onwards (3/16 embryos examined).

6. DISCUSSION

It is clear that Xt and Xt^{bph} are manifestations of the same genetic locus. In view of the consistent differences in phenotype observed (namely the morphology of the feet, the embryonic face bleb and the regular involvement of the sternum in the heterozygote, and the exencephaly and increased oedema of the homozygote) it is suggested that they are distinct alleles, and that the symbol Xt^{bph} is adopted for brachyphalangy.

Table 6. *Face blebs in the patch stock*

Mating type	Normal	Face bleb	Total	% with face bleb
(1) $Ph/+ \times Ph/+$	192	36	228	15·8
(2) $Ph/+ \times +/+$	123	40	163	24·5
(3) $+/+ \times Ph/+$	137	24	161	14·9

A central face bleb (at the same embryonic age) has been reported previously only in the patch (*Ph*) stock (Grüneberg & Truslove 1960). They rejected the 'attractive hypothesis' that the patch gene in the heterozygote was responsible for the bleb (*Ph/Ph* mice have a large central face bleb) because the calculated proportion of $Ph/+$ mice with face bleb was not constant in $Ph/+ \times Ph/+$ and $Ph/+ \times +/+$ matings (the $Ph/+$ mouse cannot be identified at 13 days). It was suggested that the face bleb was due to an independent genetic entity in the stock. The critical test of this alternative, the intercrossing of $+/+$ mice from the stock, was not performed.

By courtesy of Professor Grüneberg and Dr Truslove the original data was made available (Table 6). Reciprocal matings give different incidences of face blebs ($\chi^2_1 = 6{\cdot}19$). A similar but less marked difference was found in Xt^{bph} (Table 5). With this additional data it seems that the objection to the face bleb as part of the $Ph/+$ phenotype does not hold. The origin of the reciprocal differences is completely obscure: but as both genes produce blebs in the respective homozygotes it does not seem surprising that both should have a similar effect when heterozygous.

SUMMARY

Brachyphalangy ($Xt/^{bph}$) is an allele of extra-toes (Xt) in linkage group XIV of the mouse. The phenotypes of both heterozygote and homozygote are distinguishable from, but similar to, those of extra-toes.

The author is indebted to Mr A. J. Lee for Figs. 1–3.

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