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Genetics of the Alaskan Malmute chondrodysplasia syndrome

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THE Alaskan Malmute purebred was formally recognized by the American Kennel Club in 1935[9]. Registry for a breed base had to be reopened again in 1947[5] because many dogs were killed during World War II. The breed base then consisted of about 30 dogs.

Actually, considerable selective breeding had preceded this date; therefore these animals could not be considered as a random sample of their panmictic predecessors. Subsequent intensive inbreeding disclosed a chondrodysplasic genetic trait given the trivial name dwarf. The gross phenotypic effect is somewhat rachitic (Figures 1 and 2), due mainly to anomalous bone morphology. Most notably affected are the forelegs, which show an enlargement of the carpal joints, turned out feet, and a bowing of the radius and ulna (Figure 3). Radiographic and histological examination have shown that the epiphyseal plates are wide and irregular, and aberrant differentiation is evident throughout the growing region[8]. The dwarf syndrome is clinically distinct from all previously noted dysplasias[1, 4, 6, 7]. Current

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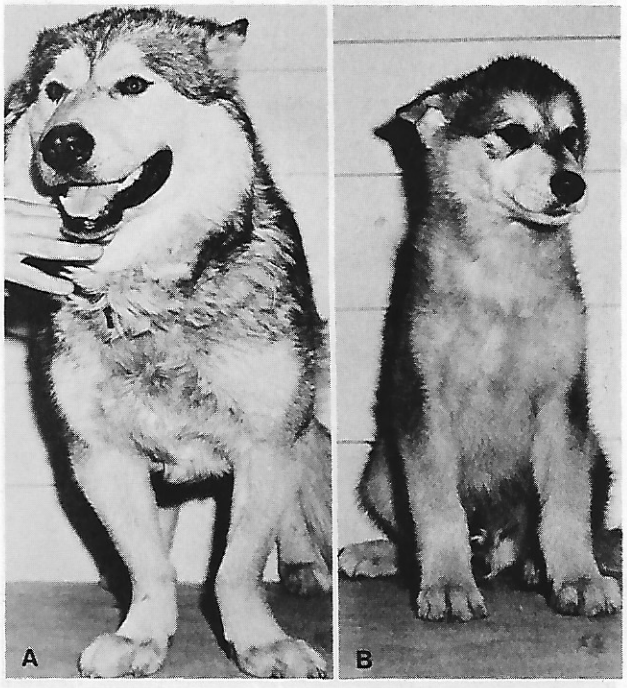


FIGURE 1—An affected dwarf (left) and normal Malmute (right).

investigations are now in progress to determine the biochemical basis of this lesion in the development sequence[2].

Although previous pedigree data were in agreement with an autosomal recessive inheritance of the dwarf gene[3], no crosses were made to preclude other possibilities, viz., multiple or interacting genes, sex linkage, modifier genes, lethal genes, and incomplete dominance or penetrance. This study was undertaken to elucidate the mode of inheritance of the dwarf gene.

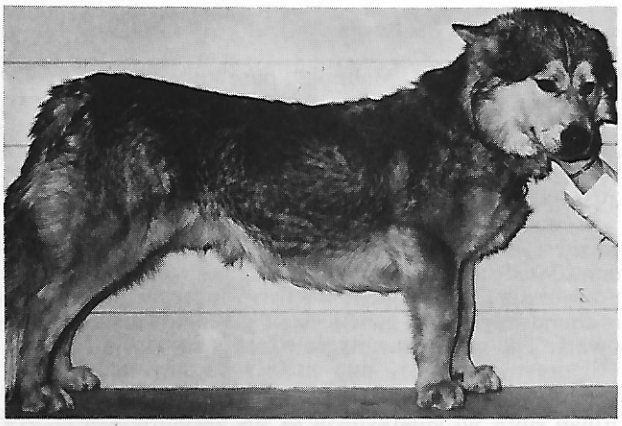
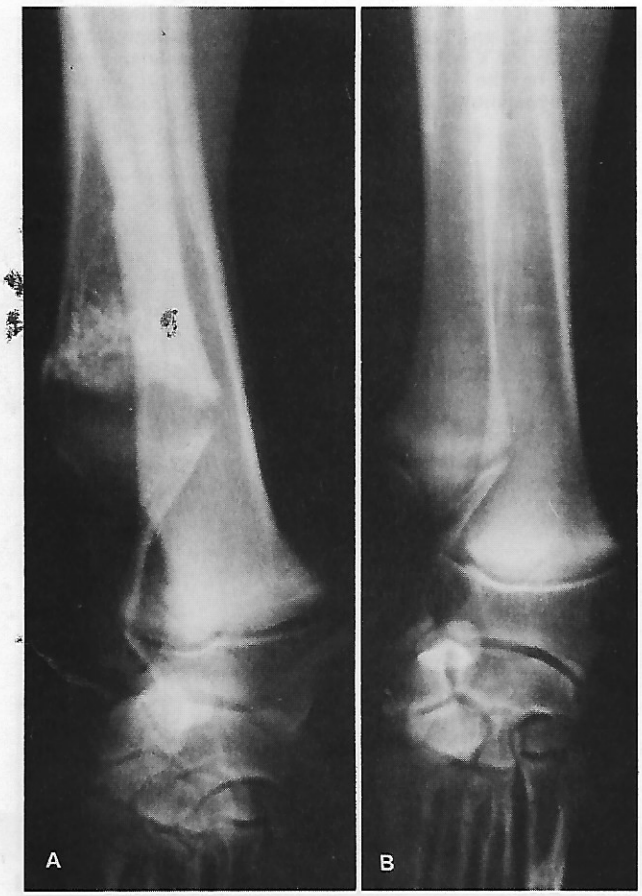


FIGURE 2—An affected dwarf Malmute.

FIGURE 3—Radiograph of deformed foreleg in an affected male dwarf pup at 4½ months of age (left) and normal male littermate (right).



Materials and Methods

A description of the test animals used in each cross is given in Table I and the crossing format in Table II. The animals used in the class 1 crosses are all phenotypically normal purebreds that were crossed by the breeders in their kennels. They constitute complete litter descriptions from 10 matings that produced dwarfs. Except where noted, the remaining crosses were done at the Guelph clinic.

Table I. Description of test animals

Test animal No.	Phenotype	Background
n 100 through n 190	normal ♂ and ♀	all purebred registered Malmutes out of the original M'Loot and Hinman stocks*
d 210	♂ dwarf	out of n 100 × n 105
d 220	♀ dwarf	related to known carrier 4 generations back
d 230	♀ dwarf	out of n 130 × n 135
n 310	♂ normal	out of n 120 × n 125
d 320	♀ dwarf	out of n 100 × n 155
n 330	♂ normal	grandson of n 160
d 340	♀ dwarf	similar to n 330
d 410	♂ dwarf	out of n 100 × sister of n 155
n 420	♀ normal	similar to n 230
n 510	♂ normal	similar to n 220

* The third Malmute stock (Kotzebue) has never produced dwarfs except when crossed to Hinman and M'Loot stocks and then inbred

Table II. Crosses performed

Class	Stud phenotype		Bitch phenotype
1 (a) to (j) putative carrier by carrier crosses	normal	×	normal
2 (a) and (b)	dwarf	×	dwarf
3 (a) and (b) putative carrier stud	normal	×	dwarf
4 putative carrier bitch	dwarf	×	normal
5 stud has dwarfs in each parental line and has dwarf sibs putative normal genotype in dwarf background	normal	×	dwarf

Artificial insemination proved somewhat unreliable so all matings were natural, albeit some mechanical problems were encountered with the dwarf stud and normal bitch crosses. The pups not being used for further test matings were euthanized after 25 days when a conclusive radiological identification on the dwarf phenotype was completed.

The results of all crosses and the probabilities for likely phenotypic ratios are reported in Table III.

Results and Discussion

It is reasonable to suppose that penetrance is complete because, although there is some variation in the expression of dwarfness, no clear-cut intermediate phenotype was discovered in any of the progeny used in this study. It should be noted that in the putative heterozygotes, e.g., n320, no discrete parameter was noted that would assist the breeder in identifying carriers. It follows that multigene modes of inheritance would be restricted to those with two viable progeny types.

Table III. Cross results

Cross	Test animal	Progeny				
		Normal ♂	Normal ♀	Dwarf ♂	Dwarf ♀	Stillborn
1 (a)	n 100 n 105	2	4	1	1	2
1 (b)	n 100 n 112	1	1	0	1	2
1 (c)	n 120 n 125	5	5	1	0	0
1 (d)	n 130 n 135	0	4	4	1	1
1 (e)	n 140 n 125	5	4	2	0	1
1 (f)	n 100 n 155	2	2	0	3†	0
1 (g)	n 160 n 165	5	0	1	0	0
1 (h)	n 170 n 175	2	2	2	1	0
1 (i)	n 180 n 185	4	2	1	0	0
Totals		26	25	12	7	6
$\chi^2 = 0.17$ $P = 0.67$ for 3:1 normals to dwarfs $\chi^2 = 1.19$ $P = 0.27$ for 2:1 normals to dwarfs $\chi^2 = 7.82$ $P = 0.005$ for 9:7 normals to dwarfs $\chi^2 = .41$ $P = 0.5$ for 9:4 normals to dwarfs						
2 (a)	d 210 d 220	0	0	4	0	2
2 (b)	d 210 d 230	0	0	2	5	0
Totals		0	0	6	5	2
$\chi^2 = 0$ $P = 1.0$ for 0:1 normals to dwarfs $\chi^2 = 5.51$ $P = 0.017$ for 1:2 normals to dwarfs						
3 (a)	d 310 n 320	3	1	1	0	0
(b)*	n 330 d 340	3	2	2	1	0
4	n 410 d 420	1	1	1	3	0
Totals		7	4	4	4	0
$\chi^2 = 0.474$ $P = .45$ for 1:1 normals to dwarfs $\chi^2 = 0.726$ $P = .38$ for 2:1 normals to dwarfs						
5*	n 510 d 220	3	3	0	0	0
$\chi^2 = 24$ $P = <0.001$ for 1:1 normal to dwarfs						

* Cross and whelping done at breader's kennel
† One pup was karyotypic ♂ and phenotypic ♀

Modes of inheritance involving lethals and lethal modifier genes are discounted because they imply a reduction in litter size that was not noted. The mean litter size of 30 randomly selected litters out of normal parents was 7.70 pups compared to 7.78 for carrier × carrier crosses. The mean litter size of carrier × dwarf and dwarf × dwarf crosses was 6.3 and 5.5, respectively, although the data were scanty and no allowance was made for characteristically smaller first whelpings as was the case in all class 2, 3, and 4 crosses.

Other statistically acceptable multigene modes such as dominant epistasis or closely linked genes give ratios indistinguishable from the single autosomal recessive mode and cannot be precluded using normal facilities and a reasonable number of dogs. These modes do, however, involve a considerable number of additional assumptions not required by the single autosomal recessive mode of inheritance. The single autosomal mode of inheritance consistently demonstrated the highest probability and involved the fewest assumptions.

A dwarf backcross to one of the putative heterozygote progeny from the class 5 cross was unsuccessful and will be attempted again when similar pedigrees can be found.

Summary

Several crosses were performed to determine the mode of inheritance of a chondrodysplasia gene associated with anomalous bone development in Alaskan Malmutes. The condition was given the name of dwarf. All phenotypic ratios noted in the progeny were consistent with and gave the highest probability for the single autosomal recessive mode of inheritance.

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