

## HEREDITARY OSTEOPETROSIS IN *ABERDEEN-ANGUS* CALVES

### II. — GENETICAL ASPECTS (1)

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### SUMMARY

Evidence is presented to indicate that congenital osteopetrosis in 3 herds of *Aberdeen-Angus* cattle may be inherited as a recessive autosomal trait.

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### INTRODUCTION

A premature stillborn purebred *Aberdeen-Angus* calf with a short lower jaw and protruding tongue was the first of 23 such calves born in three herds during the 1960's. Detailed pathologic examination revealed osteopetrosis, a disturbed relationship between bone formation and resorption (LEIPOLD *et al.*, 1971). A similar pathologic condition was described in 2 other herds of the same breed (THOMPSON, 1966; LEIPOLD *et al.*, 1970). To be presented here is the evidence pertinent to the inheritance of bovine osteopetrosis.

### I. — MATERIALS AND METHODS

The abnormal calves were reported in conjunction with a previously described long-term study of the nature and causes of congenital defects in animals (HUSTON and WEARDEN, 1958;

(1) This research was part of the North Central U. S. Regional Dairy Cattle Breeding Project NC-2.

LEIPOLD and HUSTON, 1968 *a*). Pertinent information was secured by personal visits to the farms and by mail inquiries.

Genetic analyses follow the rationale described by MORTON (1962) for man, with certain simple modifications for differences in cattle family structure. Usually full-sib families of cattle are very small and relatively infrequent while three-fourths-sib families are large and frequent. A three-fourths-sib family often includes several full-sib families. Furthermore, several three-fourths sib families may be part of a larger paternal half-sib family. For a recessive trait, a single proband in a three-fourths-sib family identifies the common parent but cannot indicate which of the parents of the other parent (usually the proband's maternal grandparents) contributed a recessive allele. A second proband usually identifies that common grandparent. Thus, examination of three-fourths-sib families with two or more affected calves provides a basis for testing segregation ratios, after appropriate adjustment for exclusion of families containing fewer than two affected progeny. However, when several three-fourths-sib families all are part of a half sib family, a sub-family containing a single affected progeny furnishes useful information.

The conditional probability of each offspring being affected was computed under specified assumptions. These were summed and compared with the observed number by an approximate  $\chi^2$  statistic (LEIPOLD and HUSTON, 1968 *b*). Complete ascertainment was assumed.

## II. — RESULTS

### A. — Herd I

In this artificially inseminated herd of about 950 registered and grade *Angus* cows calving annually, the herdsman thought the first osteopetrotic calf (fig. 1, no. 1) may have been born in the early 1960's. In the calving season from September

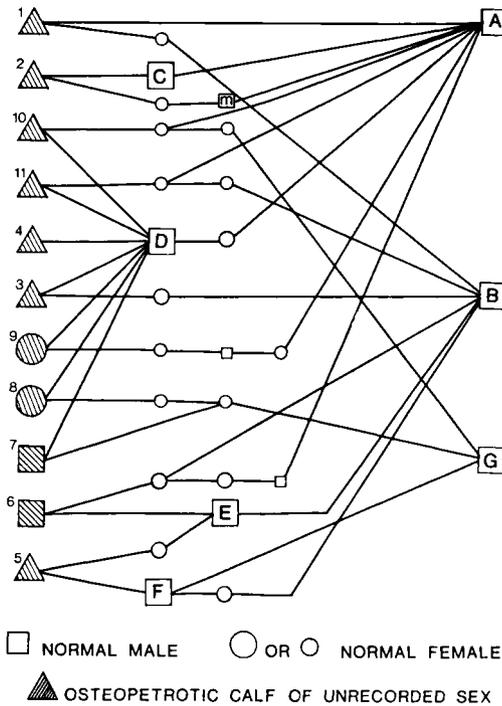


FIG. 1. — Close relationships among eleven osteopetrotic calves of Herd I  
Étroites relations de parenté entre les onze veaux ostéopétroriques du troupeau I

1966 through March 1967, no abnormalities were noted. In the calving season a year later, 5 abnormalities (fig. 1, nos. 2 to 6) occurred among 939 calves. At last report in the next year, 5 more have been born (fig. 1, nos. 7 to 11).

As reported elsewhere (LEIPOLD *et al.*, 1971), 7 of the 11 calves' average gestation was 262 days. All but one were born dead ; the single live calf was carried 268 days and killed shortly after birth. Close relationships among the calves are shown in figure 1. Of the 4 calves of recorded sex, two were males and two, females. All calves but nos. 4, 7 and his maternal half-niece 8 were related through both parents to either bulls A or B.

In pedigrees containing 6 ancestral generations, bulls A and B had 3 common ancestors, two of which were father and son. The coancestry of A and B through that ancestral pair was .007 ; through the remaining common ancestor, .001.

Though 4 affected calves descended from bull G, none of his several thousand progeny was affected.

Matings of suspected heterozygous bulls A through F with each other's daughters during the calving years 1965-1966 to 1967-1968 are shown in table 1. In 1968-1969 Bull D was bred to 45 daughters of A ; 2 abnormalities had been reported in the early part of the calving season.

B. — Herd II

Bull D from Herd I sired in 2 years 4 abnormalities among 70 progeny in this herd of about 350 registered and grade *Angus* cows. Pedigrees of two were available and show the following relationships (fig. 2). Another calf was from an unrelated dam.

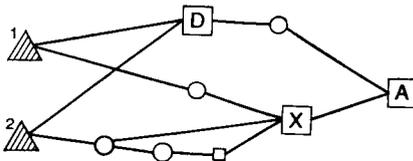


FIG. 2. — Relationships between two calves in Herd II  
Relations de parenté entre deux veaux du troupeau II

C. — Herd III

In this herd of 80-95 grade *Angus* cows, 8 abnormal calves were born, most 3 to 6 weeks premature. Seven sired by Bull Y were born in 1968 and one by a registered bull of unknown ancestry was born in 1969. From 1965 to 1967, Bull Y mated to 35 to 45 cows yearly produced normal calves. In 1968, he produced the abnormal calves. Some of Bull Y's mates likely were daughters of a previous herd sire who sired no abnormalities when mated to ten of his own daughters. Bull Y was collaterally related to both Bulls A and B in Herd I.

The sire of the other abnormal calf produced 29 other normal calves.

III. — DISCUSSION

The data of Herd I provide the most precise evidence concerning inheritance. Because normal parents produced only a few abnormal progeny and many normal progeny, the trait seems to behave as a recessive trait.

The 50 matings in table 1 yield evidence appropriate for testing a recessive hypothesis. The probability of each of the 50 matings yielding an affected offspring was computed under the following conditions. Affected animal no. 1 (fig. 1) was excluded as a proband because the herdsman's recollection of that calf was uncertain. Affected animals 2 to 6 were included in table 1 and served as probands as follows : no. 2 for ancestors C and A ; no. 3, ancestors D, A, B ; no. 5 ancestors F, E ; no. 6, ancestors E and B. For families involving A or B, only those compound families with two or more affected were included. For families involving E, only those having 1 affected from daughters of B ; or 2 affected, one each sired by D or F, or two sired by F, were included. For families involving F, only those with one or more affected were included. The single proband families involving affected animals nos. 2 and 4 were included as probands though they contribute no information to the segregation ratio.

TABLE 1

*Progeny of suspected heterozygous Bulls from each other's Daughters.  
Fall 1965 through spring 1968*

*Descendance des taureaux suspects d'hétérozygotie  
et croisés à leurs filles réciproques, 1965 à 1968*

Matings	Normal	Abnormal	Total
A × Daughters of B .....	18	0	18
C × Daughters of B .....	4	0	4
D × Daughters of B .....	5	1 (# 3)	6
E × Daughters of B .....	5	1 (# 6)	6
F × Daughters of B .....	2	0	2
D × Daughters of A .....	9	0	9
D × Daughters of E .....	1	0	1
F × Daughters of E .....	1	1 (# 5)	2
D × Dam of # 4 .....	0	1 (# 4)	1
C × Daughters of <i>m</i> .....	0	1 (# 2)	1
	45	5	50

Under those conditions, the expected number of abnormal animals in table 1 was 9. Only 5 were reported, leaving a deficiency of 4 affected animals ( $\chi^2 = 2.50$ ,  $.20 > P > .10$ .) The deficiency may have resulted from sampling, incomplete ascertainment or incomplete penetrance.

Other evidence is consistent with recessive inheritance. Bulls A and B were related and thus might have received copies of the same mutant gene. Though the dams of animals no. 4 and no. 7 were thought to have been related to ancestors of A and B, their recessive genes could have been identical in state rather than by descent, a circumstance requiring a somewhat higher frequency of the gene in the breed or an older mutation.

The evidence in Herd II accords suitably also, except for the single « unrelated » dam. She could have received her copy of the mutant gene from the same ancestral source as animals of Herd I since that source could have been a more remote ancestor than appeared in the owner's pedigree.

The limited evidence from Herd III also accords with recessive inheritance. The coancestries of Bull Y with Bulls A and B were .011 and .004 respectively. The cases from Saskatchewan, Canada (LEIPOLD *et al.*, 1970), descended from a son of bull A and were produced by sire-daughter matings.

Because the deficiency in number of affected calves in table I was fairly large, evidence of embryonic death was sought in breeding records. The number of inseminations/conception for mates producing abnormal calves was slightly, but not significantly, higher than characteristic for the herd. The affected calves also were calved somewhat, but not significantly, later in the season than characteristic for the herd. However, available evidence is inadequate to achieve greater resolution on this point.

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## RÉSUMÉ

### OSTÉOPÉTROSE HÉRÉDITAIRE EN RACE ABERDEEN-ANGUS. II. - ASPECT GÉNÉTIQUE

Selon toute évidence l'ostéopétrose congénitale observée dans trois troupeaux de bovins *Aberdeen-Angus* a un déterminisme héréditaire autosomal récessif.

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