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Haemolytic anaemia in Basenji dogs
I. Genetic investigations

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Familial occurrence, comprising 20 individual cases of haemolytic anaemia, are on record among dogs of the Basenji breed in Denmark. Previous evidence suggests that the anaemia is caused by erythrocytic pyruvate kinase deficiency. The present report encompasses a genetic analysis based on pedigree information combined with segregation results. The latter are obtained by truncate selection through affected individuals. The results give strong support for simple, autosomal recessive inheritance. In the pedigree 33 individuals are heterozygous according to genetic criteria. The recessive gene has been traced through 15 generations which include individuals of importance for the breed in various countries.

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Dogs of the Basenji breed in Europe and the USA are descendants of individuals imported from their natural habitat of Central Africa (TUDOR-WILLIAMS 1976). From the USA are reports on familial occurrence of haemolytic anaemia (HA) among dogs of this breed. TASKER et al. (1969) have described the disease in three dogs and ERWIN (1969) has reported on eight additional cases. The latter author called attention to a similarity between the clinical and haematological manifestations of pyruvate kinase (PK) deficiency in man and the symptoms observed in the Basenji dogs. This was corroborated by SEARCY et al. (1971) who found decreased PK activity in the erythrocytes from seven anaemic Basenji dogs as compared with normal controls. On the other hand TENG (1974) found increased values in two anaemic dogs. Meanwhile TENG found that presumed heterozygous individuals exhibited lower PK activity than normal individuals, analogously with observations in man (TANAKA and VALENTINE 1968). This ostensible gene dosage effect was exploited in conjunction with segregation for the anaemia to assess the mode of inheritance (TENG 1974; BROWN and TENG 1975). However, it seems appropriate to investigate the two aspects of such procedure independently, i.e. to examine the two assumptions, (1) that the haemolytic anaemia in Basenji dogs is inherited as a simple, autosomal recessive trait, and (2) that this anaemia is due to pyruvate kinase deficiency. The first of these topics is subject to analysis in this report. In addition the aim is to reveal possible routes of gene transmission of importance for the occurrence of the disease among Basenjis in Denmark.

Material and methods

Animals. — The animal material which is illustrated in Fig. 1 includes a total of 22 HA dogs (12 males and 10 females). Two of these, i.e. A and B, were born in England in 1956/57 and the remaining 20 were born in Denmark during the period December 1967—December 1975. Most of the HA diagnoses were made by veterinary surgeons including the present author; two (i.e. A and B) were based on descriptions by TUDOR-WILLIAMS (1972). Information about the ancestry of each individual was obtained either from official

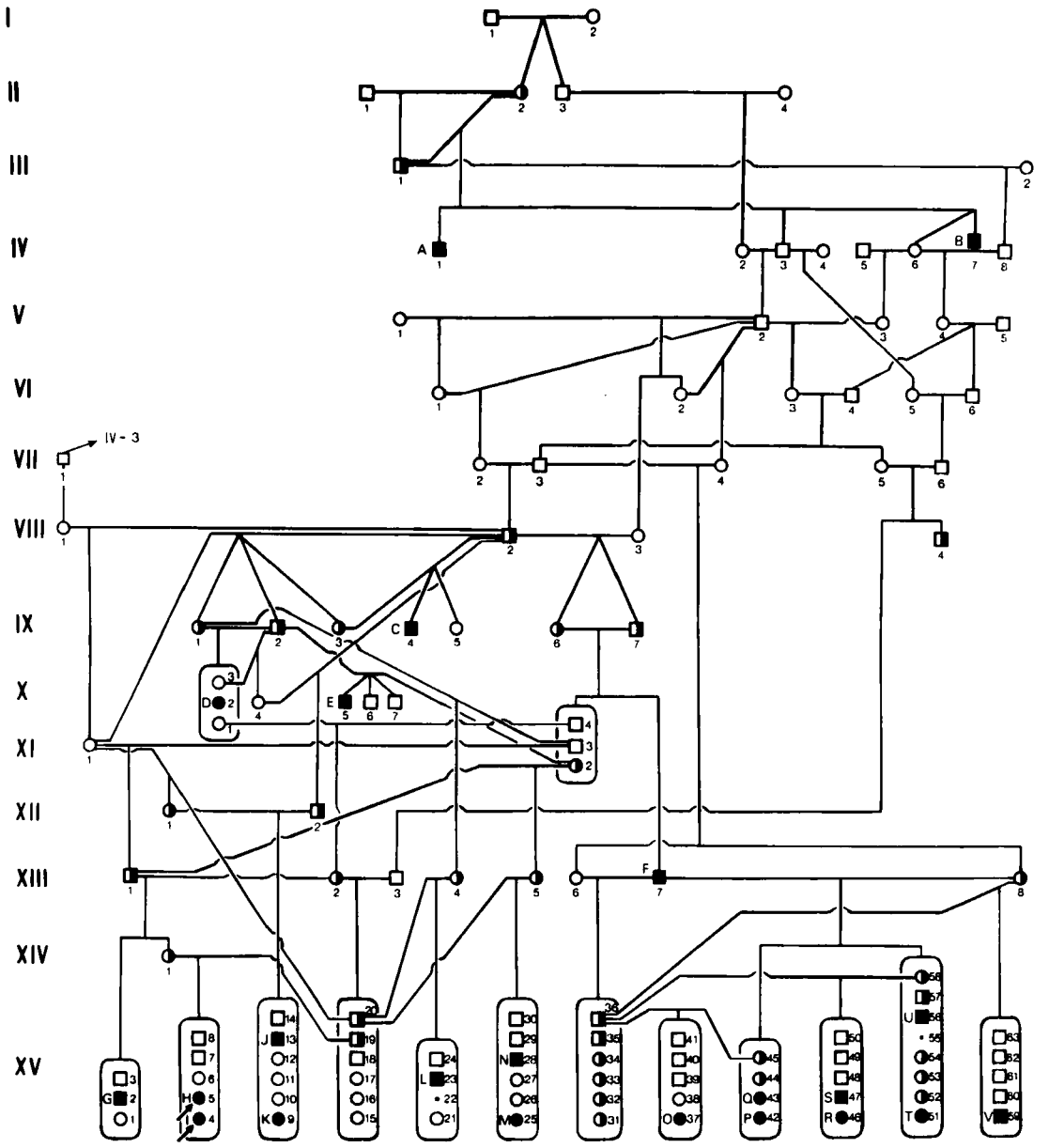

Fig. 1. Pedigree for Basenji dogs affected by haemolytic anaemia (HA). The proband litter includes two females, H and I, with HA. A total of 22 HA dogs and 33 heterozygous carriers are indicated by respective symbols. The criteria for heterozygosity are described in the text. Nos. XV-22 and XV-55 were stillborn females.

registration books provided by the owners and Danish Kennel Club, or from the book on Basenjis by TUDOR-WILLIAMS (1976). The total material includes individuals from fifteen generations.

Statistical procedures. — The material for statistical analysis comprises eleven litters with HA dogs illustrated in generations X and XV and ascertained by truncate selection, i.e. exclusively through affected individuals. The proband litter with the affected individuals H and I was omitted from statistical treatment. The remaining 10 litters were of two types. Eight had phenotypically normal parents and two, with the affected individuals P, Q, T, and U, had one

affected parent, i.e. the male F in generation XIII, whereas the other parent, XIII-8, was phenotypically normal. Hence, the appropriate test of simple, autosomal recessive inheritance is based on the 3:1 and 1:1 a priori segregation ratios corrected according to the ascertainment procedure, see e.g. ANDRESEN (1974).

The segregation results were subjected to a chi-square analysis (Table 1) as the material examined fulfills the requirement of being of fixed sample size. This material does not include the individuals A, B, C and E.

Table 1. Test of simple, autosomal recessive inheritance of haemolytic anaemia (HA) in Basenji dogs

Designation of sibship refers to the respective dwarf(s). The a priori expected ratios of 1:1 and 3:1 for two and eight sibships, respectively, are corrected according to the ascertainment procedure.

Sibship	Normal		Affected		Chi-square and probability
	Obs.	Exp.	Obs.	Exp.	
P, Q	2	1.867	2	2.133	
T, U	5	3.472	2	3.528	
Total	7	5.339	4	5.661	$\chi^2_{1df} = 1.00$; $P > 0.30$
D	2	1.703	1	1.297	
G	2	1.703	1	1.297	
J, K	4	4.175	2	1.825	
L	2	1.703	1	1.297	
M, N	4	4.175	2	1.825	
O	4	3.360	1	1.640	
R, S	3	3.360	2	1.640	
V	4	3.360	1	1.640	
Total	25	23.539	11	12.461	$\chi^2_{1df} = 0.26$; $P > 0.50$

Results and discussion

Simple Mendelian inheritance as well as polygenic inheritance of threshold characters is characterized by familial occurrence of the traits although the latter manifestation is not necessarily due to genetic causes. Therefore, previous observations of familial occurrence of haemolytic anaemia (HA) in dogs of the Basenji breed prompt genetic analysis of additional material relevant for testing the mode of inheritance. This material is presented in Fig. 1. The mating: XIII-7(F) × XIII-8 comprises an HA male mated with a phenotypically normal female. The result of this mating in two litters is 4 HA offspring (i.e. P, Q, T, and U) and 7 phenotypically normal offspring (Table 1). This segregation ratio does not significantly deviate from a 1:1 a priori expectation, irrespective of ascertainment procedure. Thus, if looked upon isolated the observed segregation in the two litters agree with dominant as well as recessive inheritance. However, among the remaining eight litters by phenotypically normal parents the ratio normal:affected offspring of 25:11 fits well with the expected ratio of 23.5:12.5 according to autosomal, recessive inheritance. In contrast, if the observed segregation ratio should reflect dominant inheritance the penetrance must be relatively low among the offspring and even lower among the adults.

The hypothesis of recessive inheritance is supported by the observation of two affected individuals, A and B, in generation IV and a high probability of gene transmission to the following generations via one or more members of that generation, i.e. the individuals IV-2, 3, 6, and 8. Since the HA individuals A and B are results of a mother (II-2)—son (III-1) mating one or both members of generation I must have carried the gene. Members of generations I—IV have influenced the Basenji breed in several countries. The breed history and the pedigree in Fig. 1 indicates that the recessive gene may have been imported to Denmark via members of generations V to VII. Since this gene can be traced to generation I, comprising merely two members, it is likely that the HA trait in Denmark is due to a two-allelic system, whereas cases of HA in the USA have been assumed to be due to the effect of multiple alleles (TENG 1974; BROWN and TENG 1975).

In the pedigree are indicated 33 individuals which must be heterozygous carriers according to the following criteria: (1) parents of offspring having HA except the parent XIII-7 (F), which had HA and, therefore, was doubly recessive, (2) all non-HA offspring by the latter mentioned male, and (3) one individual, VIII-4, which was heterozygous according to TENG (1974).

Basenjis with HA have reduced viability and usually die prior to the age of about three years. Still an HA dog may be vital enough to be a parent (cf. the male XIII-7(F), Fig. 1). This combined with a limited founder material and a perfect health of heterozygous carriers may have lead to a relatively high frequency of the recessive gene among Danish Basenjis. However, it is natural to relate a high frequency of this deleterious trait to the population genetic consequences of sickle cell anaemia in man, which occurs in the same geographic areas of Africa as the Basenjis. Meanwhile, a possible selective mechanism favouring heterozygous Basenjis within and outside their natural habitat remains to be investigated. It should be noticed, however, that the target in humans with

sickle cell anaemia is the haemoglobin molecule whereas the target in the Basenjis appears to be the erythrocytic pyruvate kinase; the hemoglobin of affected Basenjis seems unaltered.

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Literature cited

ANDRESEN, E. 1974. The effect of ascertainment by truncate selection on segregation ratios. — *1 World Congr. Genetics Applied to Livestock Production, Vol. 3, Madrid*, p. 111—114

BROWN, R. V. and TENG, YAO-SHENG 1975. Studies of inherited pyruvate kinase deficiency in the Basenji. — *J. Am. Vet. Med. Ass. 167*: 362—365

ERWIN, G. O. 1969. Familial nonspherocytic hemolytic anemia of Basenji dogs. — *J. Am. Vet. Med. Ass. 154*: 503—507

SEARCY, G. P., MILLER, D. R. and TASKER, J. B. 1971. Congenital hemolytic anemia in the Basenji dog due to erythrocyte pyruvate kinase deficiency. — *Can. J. Comp. Med. 35*: 67—70

TANAKA, K. R. and VALENTINE, W. N. 1968. Pyruvate kinase deficiency. — In *Hereditary Disorders of Erythrocyte Metabolism* (*Ed.* E. BEUTLER), *Grune and Stratton, New York*, p. 229—248

TASKER, J. B., SEVERIN, G. A., YOUNG, S. and GILLETTE, E. L. 1969. Familial anemia in the Basenji dog. — *J. Am. Vet. Med. Ass. 154*: 158—165

TENG, YAO-SHENG 1974. Congenital nonspherocytic hemolytic anemia due to pyruvate kinase deficiency. — *Thesis, Univ. Missouri, Columbia*

TUDOR-WILLIAMS, V. 1972. Observations on haemolytic anaemia. — *Am. Mag. "The Basenji", Sept.*

TUDOR-WILLIAMS, V. 1976. Basenjis The Barkless Dogs of Central Africa. — *David and Charles, London*