



Hemolytic Anemia Origins

The History and African Origins of Congenital Hemolytic Anemia in the Basenji

BY JAMES E. JOHANNES

In the late 1960s, Basenjis suffering from anemia began to show up at vet hospitals. Tests for toxins and parasites were negative and the same condition occurred in littermates on several occasions (1,2). Basenjis afflicted with this disease exhibited low energy, slow or stunted growth, increased sensitivity to cold, pallor in gums or skin, upset digestion or lack of appetite, and fainting after exertion (3, 5). Most of the afflicted Basenjis died before two or three years of age (1, 4, 5).

A few Basenjis with this disease showed up at the Veterinary Clinic at Colorado State University. This sparked interest in studies on this disease (1, 5). The studies determined that the hemolytic anemia disease showed a deficiency in pyruvate kinase (PK) similar to what occurs in humans (1). Pyruvate kinase is an enzyme carried by red blood cells. It is necessary for the metabolic process within the red blood cells to produce energy. The deficiency in pyruvate kinase causes the red blood cells to die early causing the bone marrow to produce more red blood cells at a faster rate. Eventually, only immature red blood cells are released before finally the bone marrow stops producing red blood cells and the Basenji dies (5).

In 1969, Dr. Russell Brown started to study diseases in the Basenji. He estimated the incidence of the gene for hemolytic anemia to be more than 20% in the American Basenjis tested (7). Teng Yao-Sheng, a student of Dr. Brown, found that presumed heterozygous individuals (carriers) exhibited lower PK activity than normal individuals, the same as observed in humans (8, 9). A biochemical test was available to test PK enzyme activity, but it could give questionable results and Dr. Brown found that errors did occur (10, 11). He stated that, "Many, but not all, major breeders submitted blood samples for their dogs for testing. Biochemical tests for pyruvate kinase activity indicated the presence of the defective pyruvate kinase gene. Soon, many breeders refused stud service to untested bitches, or refused to breed their bitches to males that had not tested clear of the disorder. By 1975, the incidence of the gene causing hemolytic anemia was less than one percent in pups born that year" (7). Removing afflicted animals, as well as carriers for this disease, from the breeding pool may have contributed to a bottleneck in the Basenji population and possibly caused an increase in the expression of Fanconi syndrome. In 1977, a Danish study provided evidence that hemolytic anemia disease is inherited as a simple autosomal recessive in the Basenji (6). It was not until 1995 that a genetic test became available for pyruvate kinase deficiency (10). Currently, genetic testing for Hemolytic Anemia is only required for Native Stock imported from Africa. Breeders should still consider testing for this disease because the previous biochemical test missed carriers and in 2003 a carrier was found (12).

Veronica Tudor-Williams believed that the disease came out of the original Blean dogs first imported to England in the 1930s and was possibly produced due to inbreeding (13). It is more likely this disease is of African origin and is probably prevalent in the landrace the Basenjis originated from (11). Dr. Brown proposed that "HA

probably arose as the result of many mutations and maintained itself, even increased in frequency in Africa, because it probably gave the Basenji protection against various parasites." (11). A 2008 study on humans indicated that those homozygous (afflicted) for PK deficiency were given higher protection than those heterozygous (carriers) from Malaria (14). A study on African Americans suggested that the frequency of the heterozygote allele for PK deficiency was 2.4 times more common in Africans than in Caucasians (15). Researchers recently sequenced 19 Nigerian dog's genome and found that they carry the gene ADGRE1, which might be responsible for providing host immunity for the dogs to Malaria. This gene is also found in humans and is implicated in providing protection from Malaria in humans (16). Convergent evolution in both humans and dogs resulted in protective biologic mechanisms to Malaria. Basenjis are not the only African domestic animal to have this Hemolytic Anemia. The Abyssinian cat is thought to have originated from cats brought back from North Africa by British Soldiers (17). The Abyssinian, Somalia (an offshoot of the Abyssinian), and domestic shorthairs are prone to PK deficiency as well (18).

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