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BRIEF COMMUNICATION

Frequency of dog erythrocyte antigen 1.1 expression in dogs from Portugal

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Background: Dog erythrocyte antigen (DEA) 1.1 is the antigen considered most responsible for severe hemolysis owing to incompatible blood transfusions in previously sensitized dogs. Few reports describe the frequency of DEA 1.1 expression in European dogs, and there are no reports in dogs from Portugal.
Objective: The aims of this study were to identify the frequency of DEA 1.1 expression in Portuguese dogs, to examine the relationship between phenotypic traits and expression of this blood group, and to assess the risk of transfusing blood that is not typed or cross-matched.
Methods: Expression of DEA 1.1 was determined in 274 dogs using a migration gel test. Weight, sex, breed, and hair length and color were recorded for each dog. Results were analyzed by descriptive statistical analysis, probabilistic analysis, and χ^2-tests.
Results: Of 274 dogs, 56.9% were DEA 1.1-positive and 43.1% were DEA 1.1-negative. All Boxers, German Shepherds, and Dobermans were DEA 1.1-negative, whereas all Saint Bernards, 88.9% of Golden Retrievers, 88.2% of Rottweilers, and 61.4% of mixed breed dogs were DEA 1.1-positive. A significant relationship between DEA 1.1 expression and phenotypic traits was not found. The probability of sensitization of recipient dogs following first-time transfusion with blood that was not typed or cross-matched was 24.5%; the probability of an acute hemolytic reaction following a second transfusion with blood from any other donor in the absence of pretransfusion compatibility testing was 6%.
Conclusion: The frequency of DEA 1.1 expression in dogs in Portugal is high, and there is a potential risk of sensitization following transfusion with blood that is not typed or cross-matched. Breed-related frequencies may help predict DEA 1.1-positivity, but the best practice is to type and cross-match blood before transfusion.

Cell membranes of erythrocytes have species-specific antigens (glycolipids and glycoproteins) that constitute the basis for classification of blood groups.[1] There are 7 major antigens that have received international standardization in dogs; they are identified by the acronym dog erythrocyte antigen (DEA) followed by the numbers 1–8 (2 is not used),[1–3] and dogs may be classified as positive or negative for each antigen. The antigens that have been proven to cause acute hemolytic reactions in sensitized dogs are the 2 subtypes of DEA 1, DEA 1.1 and DEA 1.2.[1] To the authors' knowledge, no naturally occurring antibodies against these antigens have been identified.[4] Antibodies against DEA 1.1 or 1.2 are produced in a negative recipient 4–14 days after the first transfusion of RBCs positive for either DEA 1.1 or 1.2 and induces a delayed transfusion reaction that leads to premature and rapid destruction of transfused erythrocytes, thus decreasing the effectiveness of the transfusion.[1,5] If the dog receives subsequent transfusions of incompatible blood, the sensitized recipient may develop a severe acute hemolytic reaction.[1,5,6] DEA 1.1 is reported to have the most clinical relevance

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owing to its strong antigenicity, which is considered the strongest among all canine erythrocytic antigens.[5,6] Therefore, blood-typing of both donors and recipients for this antigen is highly recommended.

The aim of this study was to determine the frequency of DEA 1.1 in Portuguese dogs, estimate the risk of administering transfusions of untyped blood, provide criteria to aid selection of potential donors, and predict the presence of this antigen when typing of blood is not possible. In addition, we investigated the possibility of a relationship between some phenotypic traits and expression of DEA 1.1.

This prospective study determined the frequency of DEA 1.1 expression in 274 Portuguese dogs by analyzing blood-typing results for blood donors and recipients that were typed in 2008 and 2009. During blood collection, weight, sex, breed, and hair length and color were recorded. The weight of obese and cachectic animals was adjusted to estimate the normal weight based on breed and size. Length of fur was registered as short (< 1 cm), medium (1–3 cm), or long (> 3 cm). Hair color was defined as beige, white, brown, gray, or black. When hair color was ambiguous, data were not used. For each animal, 1 mL of blood was collected by jugular venipuncture into EDTA (K3E/EDTA 1 mL tubes, Aquisel SL, Abrera, Spain), stored refrigerated at 4–6°C, and processed within 24 hours of collection. DEA 1.1 expression was determined using a migration gel test (ID-Gel Test Canine DEA 1.1, DiaMed, Lisbon, Portugal) according to the manufacturer's instructions. Only results validated by negative controls were included. Results were analyzed by absolute and relative frequency analysis, joint probability, and χ^2-tests using SPSS Statistics 17.0 (IBM, Somers, NY, USA). Significance was set at $P < .05$.

Of 274 dogs, 118 (43.1%) were DEA 1.1-negative and 156 (56.9%) were DEA 1.1-positive (Table 1). There was high variability within and among breeds. All Boxers, German Shepherds, and Dobermans were DEA 1.1-negative, whereas all Saint Bernards were DEA 1.1-positive. Labrador Retrievers and Cocker Spaniels were predominantly DEA 1.1-negative (68.8% and 55.2%, respectively), whereas Golden Retrievers and Rottweilers were mostly DEA 1.1-positive (88.9% and 88.2%, respectively). To avoid skewed interpretation, all breeds represented by < 5 dogs were identified as "other." It should be noted that 5 Dobermans were related as were 5 Saint Bernards, which may have biased results for these breeds. In mixed breed dogs, the frequency of DEA 1.1 expression was 61.4%.

The probability of a dog becoming sensitized from first-time transfusion of blood that was not typed or

Table 1. Frequency of DEA 1.1 expression according to breed, probability of sensitization of a DEA 1.1-negative dog after a first-time transfusion of untyped blood, and probability of an acute hemolytic reaction during a second transfusion with blood from the same breed.

Breed	N	%	DEA 1.1+		DEA 1.1 −		Probability of Sensitization During First Transfusion (%)	Probability of Hemolytic Reaction During Second Transfusion (%)
			N	%	N	%		
Mixed breed	57	20.8	35	61.4	22	38.6	23.7	5.6
Great Dane	5	1.8	5	100.0	0	0.0	0	0
Saint Bernard	14	5.1	14	100.0	0	0.0	0	0
Golden Retriever	9	3.3	8	88.9	1	11.1	9.9	1
Rottweiler	17	6.2	15	88.2	2	11.8	10.4	1.1
Weimaraner	5	1.9	4	80.0	1	20.0	16	2.6
Poodle	7	2.6	4	57.1	3	42.9	24.5	6
Siberian Husky	7	2.6	4	57.1	3	42.9	24.5	6
Labrador Retriever	29	10.6	13	44.8	16	55.2	24.7	6.1
Cocker Spaniel	16	5.8	5	31.3	11	68.8	21.5	4.6
Boxer	13	4.7	0	0.0	13	100.0	0	0
Doberman	12	4.4	0	0.0	12	100.0	0	0
German Shepherd	10	3.6	0	0.0	10	100.0	0	0
Other*	73	26.6	49	67.1	24	32.9	22.1	4.9
Total	274	100	156	56.9	118	43.1	24.5†	6.0†

*Breeds represented by < 5 dogs.

†Probability of sensitization (following first-time transfusion) or an acute hemolytic reaction (following a second transfusion) relates to transfusion of blood from any other donor (regardless of breed) in the absence of pretransfusion compatibility testing.

Table 2. Summary of published frequencies of DEA 1.1 expression in dogs from several countries.

References	Location	Number of Dogs Tested	% DEA 1.1+	% DEA 1.1 −
Swisher and Young[10]	USA	332	45	55
Swisher et al[11]	USA	—	40	60
Suzuki et al[12]	USA	61	36	64
Wriesendorp et al[3]	USA	—	37 (Mixed breed)	63 (Mixed breed)
			43.4 (Beagle)	56.6 (Beagle)
			29 (Golden Retriever)	71 (Golden Retriever)
Ejima et al[19]	Japan	160 (Beagle)	39 (Beagle)	61 (Beagle)
		22 (Mixed breed)	73 (Mixed breed)	27 (Mixed breed)
Ejima et al[13]	Japan	545	44	56
Bucheler and Giger[14]	The Netherlands	31	38	62
Giger et al[5]	USA	224	33	67
Kohn et al[8]	Germany	88	52	48
Novais et al[7]	Brazil	150	51	49
Novais et al[18]	Brazil	150 (Mixed breed)	55 (Mixed breed)	45 (Mixed breed)
		50 (German Shepherd)	64 (German Shepherd)	36 (German Shepherd)
Van Der Merwe et al[16]	South Africa	233	47	53
Giger and Blais[6]	USA	—	33–45	55–67
DeLuca et al[9]	USA	84	54	46
Gracner et al[20]	Croatia	30 (Istrian Pointers)	67	33
Zubcic et al[21]	Croatia	95 (Croatian Sheepdogs)	90	10
Hale et al[15]	USA	9570	42	58

cross-matched was calculated using the following formula: %DEA 1.1-negative × %DEA 1.1-positive/100. The probability of the same dog developing an acute hemolytic reaction with a second incompatible transfusion using untyped blood from any other dog was calculated using the formula: %DEA 1.1-negative × %DEA 1.1-positive × %sensitization for the first transfusion/10,000. Results were reported for all dogs and for specific breeds (Table 2). Considering all dogs, the probability of a recipient becoming sensitized following first-time transfusion of blood that was not typed or cross-matched was 1 in 4 (24.5%), similar to the probability reported previously.[7] DEA 1.1 expression was detected in 82/139 (58.9%) female and 69/132 (52.3%) male dogs. There were no significant differences between sexes (P=.266). Statistical analysis failed to demonstrate a relationship between DEA 1.1 expression and the phenotypic traits examined.

The higher frequency of DEA 1.1-positive dogs in our study was similar to that previously reported in 3 other studies[7–9]; however, in studies of multiple breeds higher frequencies of DEA 1.1-negative dogs have been reported.[3,5,6,10–15] Although there are few reports of breed-specific frequencies of blood type, some comparisons between our results for groups of >10 animals of a single breed and those of other studies can be made. Similar to our findings, German Shepherds, Dobermans, and Boxers are predominantly DEA 1.1-negative, whereas Rottweilers are predominantly DEA 1.1-positive.[7,16,17] Conversely, frequencies reported in this study for Siberian Huskies, Great Danes, Labrador Retrievers, Poodles, German Shepherds, and Cocker Spaniels disagree with previously published data.[7,17,18] Diverse genetic pools of ancestors for a particular breed and different levels of inbreeding among countries may explain these differences. Mixed breed dogs had a higher frequency of DEA 1.1 expression in contrast to previous reports of lower frequencies of expression of this antigen in mixed breed dogs.[3,7,18] In some studies, sampling of low numbers of animals within a breed may have misrepresented the overall breed.[7,13] The probability of a recipient becoming sensitized after first-time transfusion of untyped blood was similar to that reported previously[7] and, along with the 6% probability of acute hemolytic reaction following a second incompatible transfusion, should not be dismissed as trivial.

In conclusion, this study, like others (Table 2), demonstrates that expression of DEA 1.1 varies geographically and within breeds. Also, despite the low probability of hemolysis after a second transfusion of untyped blood, the risk is not trivial and should not be ignored; therefore, we recommend blood-typing for DEA 1.1 and cross-matching before administering any blood transfusion as a best practice.

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