My take on RR IVA

Clayton Heathcock; May 1, 2018

Introduction

I am writing this review of the Rhodesian Ridgeback Inherited Ventricular Arrhythmia ("RR IVA") research and DNA test for the benefit of concerned Rhodesian Ridgeback breeders who may not have the background or the time to review and digest what has been published in both the scientific literature and on social media about the subject. My reason for doing this is that I think many in the RR community are making breeding decisions that may not be in the best long-term interests of the breed.

I have a concern – not only as a breeder, but as a scientist – that people in the RR community are not sufficiently informed about the North Carolina State University (NCSU) DNA test. Breeders are flocking to use this test, thinking that the results will provide guidance for future breeding decisions. However, little information has been provided about how the test was devised or what the test results actually mean. Consequently, in my opinion, we must not rush to hasty conclusions about using this DNA test in making breeding decisions, because the scientific investigation of RR IVA is in its infant stages. Much more research is needed, and this additional research has to be vetted and accepted by peer-review scientists and published in the scientific literature following accepted protocol. Only then can breeders make truly informed breeding decisions.

Background

1. "RR IVA" means "Rhodesian Ridgeback Inherited Ventricular Arrhythmia." The name was first applied by Dr. Kathryn Meurs of the College of Veterinary Medicine at North Carolina State University.[1] Dr. Meurs was approached in 2014 by a breeder who reported four instances of sudden death of young Rhodesian Ridgebacks between 7 and 12 months of age, with no apparent cause (hereinafter "Sudden Death Dogs"). The four dogs were closely related,

[1] (a) Meurs, K. M. *et al.*, "Ventricular arrhythmias in Rhodesian Ridgebacks with a family history of sudden death and results of a pedigree analysis for potential inheritance patterns," *JAVMA*, **2016**, *248*, 1135-1138. (b) See also Meurs webinar: https://mymediasite.online.ncsu.edu/online/Play/ff848277440346afacbaa6a5238cb4641d

including two littermates, and this alone is strong evidence for a hereditary cause behind the tragic deaths found in this RR family. Dr. Meurs and her coworkers collected pedigree information for the deceased dogs and examined 21 closely related dogs, including littermates and parents when available. A substantial number of these closely related dogs displayed a particular cardiac arrhythmia, and it was reasonable to hypothesize that the Sudden Death Dogs likely also had this arrhythmia and that this was related to the sudden death.

2. Before going further, I will briefly describe what is meant by arrhythmia and how arrhythmia is detected and quantitated. 'The heartbeat is normally controlled by the electrical system of the heart, . . . [which] consists of the sinoatrial (SA) node, the atrioventricular (AV) node and special tissues in the ventricles that conduct electricity."[2] "Arrhythmias are abnormalities of the heartbeat. There are several types of arrhythmia, and they are classified by . . . where they begin in the heart (the atria, AV node, or the ventricles). . . . . Generally speaking, . . . those that come from the ventricles are called ventricular arrhythmias."[3]

3. The type of arrhythmia that is the focus in RR IVA manifests itself by numerous premature ventricular contractions (PVCs) (ref. 1). PVCs are heartbeats that occur earlier than they should in the normal heart rhythm. They are relatively common, both in people and in dogs. A juvenile Rhodesian Ridgeback has on the order of 100,000 heartbeats in 24 hours and the occurrence of fewer than 50 PVCs is generally considered normal.[4]

4. An accepted experimental method used to detect cardiac arrhythmias is called a 24-hour ambulatory electrocardiogram (ECG), which employs a monitor attached to the thorax of the dog by electrodes. The dog wears the monitor for 24 hours and a continuous electrocardiogram is recorded. Evaluation of the ECG trace can be carried out by a trained technician, either manually or by using a computer analysis, to identify PVC events. The

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[2] https://www.medicinenet.com/premature_ventricular_contractions/article.htm

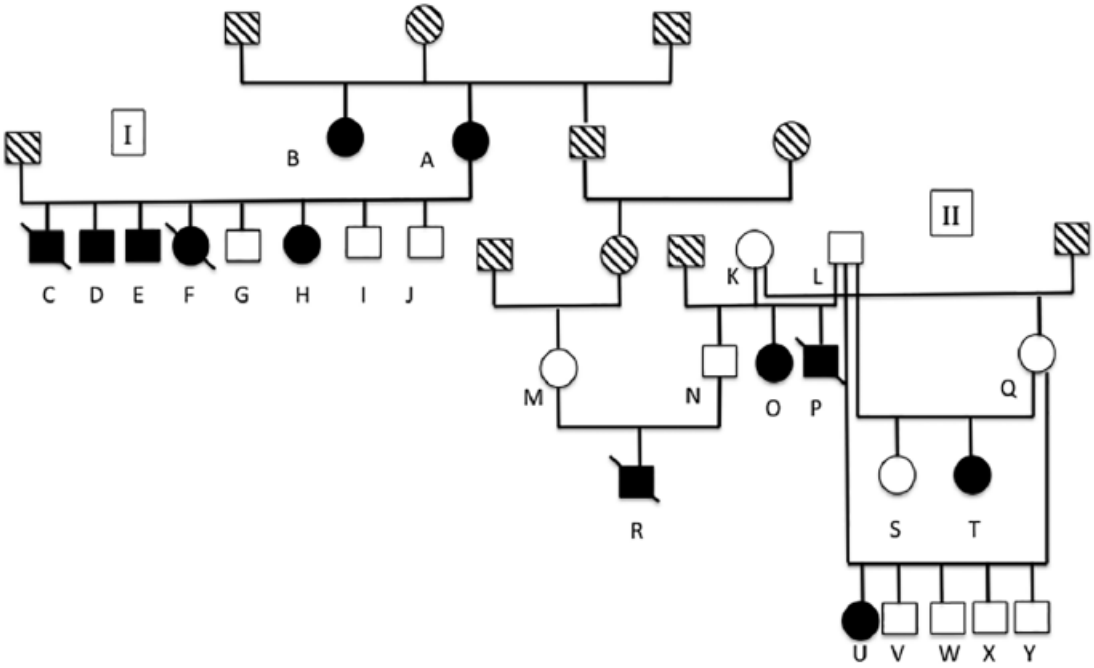
[3] https://www.emedicinehealth.com/heart_rhythm_disorders/article_em.htm#what_is_an_arrhythmia_heart_rhythm_disorder

[4] Meurs, K. M., *et al.*, "Familial Ventricular Arrhythmias in Boxers," *J. Vet. Intern. Med.*, **1999**, *13*, 437-439.

recording device is called a "Holter monitor," after the name of the scientist who invented it. Holter monitors are commonly used to evaluate cardiac function in humans as well as in dogs.[5]

5. PVCs can occur as singlets (one occurrence), doublets (two occurrences – also called couplets), triplets or longer runs. This terminology refers to whether the irregular heartbeat is followed by a normal run of heartbeats (PVC singlet) or as a sequence of multiple consecutive irregular beats (doublets, triplets, etc). Three or more consecutive PVCs before the normal heart rhythm resumes is called ventricular tachycardia (VT).[6] Multiple PVCs, especially VT, are considered more serious than singlet PVCs, as described later (paragraph 11 below).

6. The four Sudden Death Dogs that prompted the Meurs investigation were from two related families, I and II, stemming from a bitch bred to two different stud dogs, as illustrated by the following pedigree graphic, taken from the 2016 Meurs article:[7]



[5] A **Holter monitor** is a battery-operated portable device that measures and records your heart's activity (ECG) continuously for 24 to 48 hours or longer depending on the type of monitoring used. The device is the size of a small camera. It has wires with silver dollar-sized electrodes that attach to your skin. http://www.heart.org/HEARTORG/Conditions/HeartAttack/DiagnosingaHeartAttack/Holter-Monitor_UCM_446437_Article.jsp#.WeelZkzMw7w

[6] https://en.wikipedia.org/wiki/Ventricular_tachycardia "Three or more beats in a row on an ECG that originate from the ventricle at a rate of more than 100 beats per minute constitute a ventricular tachycardia."

[7] The tree depicted as Figure 1 in the 2016 Meurs article is slightly incorrect, as one generation is omitted in the family II part of the tree. For the corrected tree see the Appendix. This corrected tree was constructed by the author on the basis of interviews with the breeders of the various depicted dogs.

In this family tree gender is depicted as a round figure for females and a square figure for males. The 12 solid black symbols represent dogs identified as affected (8 who had frequent or complex PVCs, and the 4 Sudden Death Dogs depicted with a line through the symbol), the 13 solid white symbols represent dogs deemed to have normal cardiac electrical function, and the 10 diagonally shaded symbols represent dogs that were not available for evaluation.

In Family I, the two Sudden Death Dogs (male C and female F) died within 11 days at the age of 7 months. All six littermates of the two deceased dogs were evaluated by 24-hour ambulatory ECG (Holter monitor test) at 8 months of age. Three littermates were found to have frequent ventricular irregularities (male D: 1,240 PVCs/24 hours [all singlets], male E: 5,335 PVCs/24 hours [singlets and doublets] and female H: 8,700 PVCs/24 hours [singlets with ventricular tachycardia]. The other three littermates (males G, I and J) had no detectable PVCs. The dam (female A) was Holter-monitored at 6 years of age, with reported results of 90 PVCs (singlets with ventricular tachycardia), which exceeded the 50 PVC top of the normal range.

Family II included five parents (males N and L and females K, M and Q) and all five of these dogs were determined, after Holter-monitoring, to be within the normal range of PVCs. These included male N and female M (parents of the Sudden Death Dog R) and male L and female K (parents of the Sudden Death Dog P). In this family II, three females were identified as affected (O: 803 PVCs/24 hours (all singlets), T: 792 PVCs/24 hours (singlets with one triplet) and U: 3,913 PVCs/24 hours (singlets, doublets, triplets and ventricular tachycardia). Five other dogs in Family II (female S and males V, W, X and Y) were found to be in the normal range of PVCs.

7. The definition of "affected" used by Meurs in the NCSU publication and webinar is based mainly on the number of PVCs; only secondary attention seems to be given to the complexity of PVCs (*i.e.* triplets or longer runs that are associated with ventricular tachycardia).[8] However, the one graphic illustrating the disease in Dr. Meurs' 2016 article and webinar shows ventricular tachycardia with a run of 6 consecutive PVCs in a 13-month old Rhodesian

[8] Meurs *et al.* state that "Holter-monitor data was evaluated for presence of abnormal pauses, bradyarrhythmias, or tachyarrhythmias that could be associated with a fatal cardiac event. The number of VPCs/24 hours and their complexity (eg, single monomorphic VPCs [singlets]; bigeminy; trigeminy; couplets; triplets; R-on-T phenomenon; or ventricular tachycardia) were tabulated. However, this data was not presented in the publication. (ref. 1a)

Ridgeback (this appears to be female H in the foregoing family tree, who also had 8,913 PVCs/24 hours).

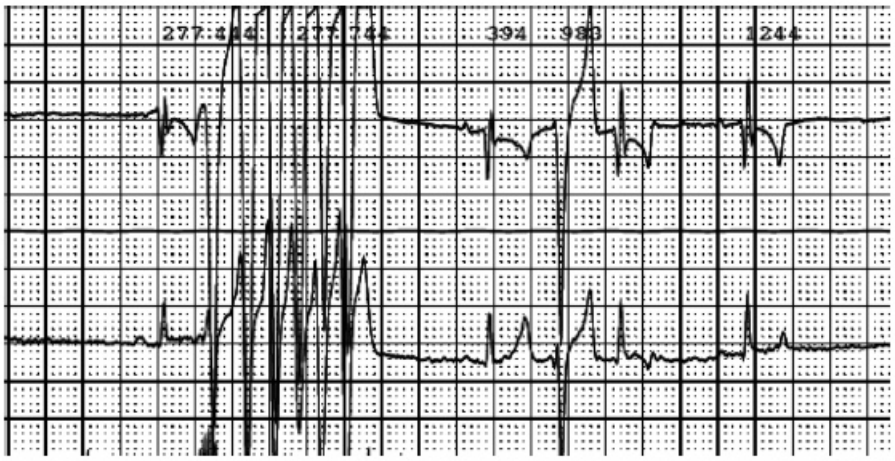


Figure 2—Representative ECG tracings (leads II and III) obtained from a 13-month-old Rhodesian Ridgeback with VPCs. Notice the short run of ventricular tachycardia and a single VPC. Paper speed, 25 mm/s; 1 cm = 1 mV.

8. Dr. Meurs has concluded that RRs with RR IVA have the following characteristics:
   a) Affected dogs exhibit an abnormally large number of PVCs when tested by 24-hour ambulatory ECG (Holter test). Dogs with more than 50 PVCs in the 24-hour test are considered to be affected.[9]
   b) The condition is normally found in juvenile RRs and Dr. Meurs hypothesized that most affected RRs normally outgrow the condition by the age of 36 months.[10] The age of onset has not been determined, but is generally believed to develop between the ages of 4-36 months. One puppy has been identified with RR IVA at 4 months of age. Dr. Meurs and her associates are currently studying this aspect.[11]
   c) Dr Meurs presumes that the Sudden Death Dogs had ventricular arrhythmia. This is a hypothesis, since (to my knowledge) no reported RR who suddenly died at a young age was previously tested by ambulatory ECG. However, as described above, littermates and other close relatives of these Sudden Death Dogs were found to display an abnormally large

[9] Meurs 2016, at 1136: "If a ventricular arrhythmia was present, it was interpreted as a normal finding if there were < 50 VPCs/24 hours and all were single beats." See also Meurs, K. M., *et al*. Use of ambulatory electro-cardiography for detection of ventricular premature complexes in healthy dogs. *J Am Vet Med Assoc* **2001**, *218,* 1291–1292.
[10] Note that bitch A in the foregoing family tree is an exception to this generalization, as she was found to still have an abnormally large number of PVCs and even ventricular tachycardia at 6 years of age.
[11] https://cvm.ncsu.edu/research/clinical-trials/list/?ID=462191

number of PVCs. This provides support for the hypothesis that the sudden deaths may be associated with ventricular arrhythmia or ventricular tachycardia.

9. There seems to be an assumption in the Ridgeback community[12] that the frequent VPCs are more common in Rhodesian Ridgebacks than in other breeds of dogs,[13] and this may turn out to be the case. However, as yet, I am not aware of a publication that discloses data to fully support this generalization. In a 2001 article, Dr. Meurs and coworkers reported the use of Holter monitoring to evaluate healthy dogs for PVCs.[14] This study concluded that "healthy mature dogs have infrequent VPC in a 24-hour period . . . " Although this study included 28 dogs representing 12 breeds and 22 mixed-breed dogs, little information about the ages of the dogs except that there was at least one as young as 1-year old and they were generally considered to be "mature" with an average age of 5 years. Therefore, this study does not appear to give information that can be compared with the juvenile arrhythmia seen in Rhodesian Ridgebacks.

10. Extensive studies of Inherited Ventricular Arrhythmia and sudden death in German Shepherd Dogs have been published[15] and, to date, the described characteristics of GSD IVA strongly correlate with some characteristics of RR IVA. The detailed GSD IVA studies included as the main analytical technique 24-hour ambulatory ECGs (Holter tests). A 2009 review of GSD IVA contained the following preamble:[16]

> "Spontaneous ventricular arrhythmia (VA) and sudden death occur in young German Shepherd Dogs (GSDs). The disorder ranges in severity from infrequent and non-life-threatening single premature ventricular complexes (PVCs) to multiple episodes of rapid polymorphic ventricular tachycardia (VT). Dogs with VT are most likely to die suddenly. No other clinical indicators of abnormality are apparent, and pathological examination of the hearts of dogs that die suddenly reveal morphologically normal hearts. A window of vulnerability for the presence of VA and sudden death exists between approximately 3 and 18 months of age, with peak affectedness occurring at approximately 6–7 months of age. Affected dogs rarely have VA after ~24 months of age, and when they do, it is infrequent.

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[12] https://www.facebook.com/groups/1346498062074178

[13] This assumption is also implicit in the name "inherited Rhodesian Ridgeback ventricular arrhythmia."

[14] Meurs, K. M. *et al.*, "Use of ambulatory electrocardiography for detection of ventricular premature complexes in healthy dogs," *JAVMA*, **2001**, *218*, 1291-1292.

[15] (a) N. S. Moïse, *et al.*, "Inherited Ventricular Arrhythmias and Sudden Death in German Shepherd Dogs," *JACC*, **1994**, *24*, 233-243. (b) N. S. Moïse, *et al.*, "Age dependence of the development of ventricular arrhythmias in a canine model of sudden cardiac death," *Cardio. Res.*, **1997**, 483-492. (c) N. S. Moïse, "Inherited arrhythmias in the dog: potential experimental models of cardiac disease," *Cardio. Res.*, **1999**, 37-46.

[16] J. Cruickshank, *et al.*, "Genetic Analysis of Ventricular Arrhythmia in Young German Shepherd Dogs," *J. Vet. Intern. Med.*, **2009**, *23*, 264-270.

The trait of VT is most commonly observed in dogs lying at rest and during rapid eye movement sleep. Because of the age and behavioral dependence of the expression of this disease, extensive observation via 24-hour ambulatory ECG monitoring (Holter monitoring) is often required to ascertain disease presence and its severity."

11. An important conclusion that emerged from the GSD study is that sudden death only occurred in dogs with rapid polymorphic ventricular tachycardia (VT) (ref. 13a). The following figure, taken from Moïse's 1994 article on GSD IVA, shows a portion of the ECG traces of five GSDs that died suddenly during the study:

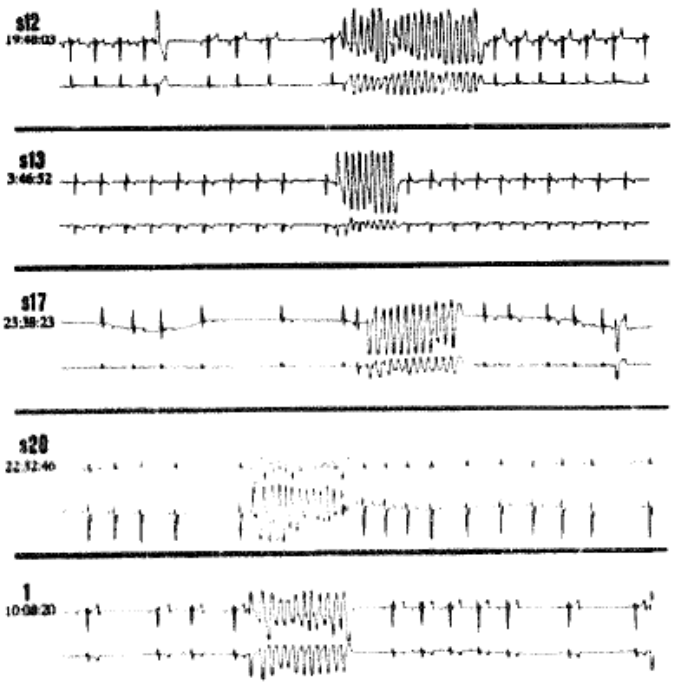


Figure 1. Electrocardiographic recordings from five German shepherd dogs (dogs s12, s13, s17, s28, 1) that died suddenly. Each of these dogs had multiple runs of rapid polymorphic ventricular tachycardia of at least six consecutive ventricular complexes with a rate ≥480 beats/min. Most frequently, the ventricular tachycardia was preceded by a long RR interval.

It is notable that each of these dogs had runs of six or more consecutive ventricular contractions with a heart rate of >480 beats per minute. However, it was noted that ". . . the presence of VT is not an exact surrogate for sudden death [since] . . . 50% of dogs that had VT survived the first 2 years of life and subsequently lived a normal lifespan without cardiac compromise such as heart failure or syncope [fainting]." (ref. 14).

In contrast to the GSD IVA studies, to date (and to my knowledge), there was no previous ECG data on any of the Sudden Death Dogs. Accordingly, we do not know if those Sudden Death Dogs were affected by simple ventricular arrhythmia or, like the GSDs documented in the Moïse study, had rapid polymorphic ventricular tachycardia (VT), or if some other unidentified issue was related to their deaths.

It should be noted that GSDs, including GSDs that exhibit juvenile ventricular arrhythmia, have been subjected to the NCSU DNA test and found not to have the mutation that has been identified in Rhodesian Ridgebacks.[17]

The RR IVA DNA Test

12. In her webinar, Dr. Meurs announced the availability of a DNA test that is intended to be predictive of dogs that are disposed to RR IVA. The test is marketed by NCSU at a cost of $70 per test.[18] Results are given as "negative", "positive heterozygous", or "positive homozygous". These three results mean that the dog has 0, 1, or 2 copies of an abnormal DNA marker at a particular allele. Although NCSU does not disclose results to anyone except the owner of the tested dog, a community initiative[19] resulted in a tabulation of results from 244 dogs, and is believed to provide a reasonable estimate of the prevalence of the abnormal marker. The data from this survey is as follows:

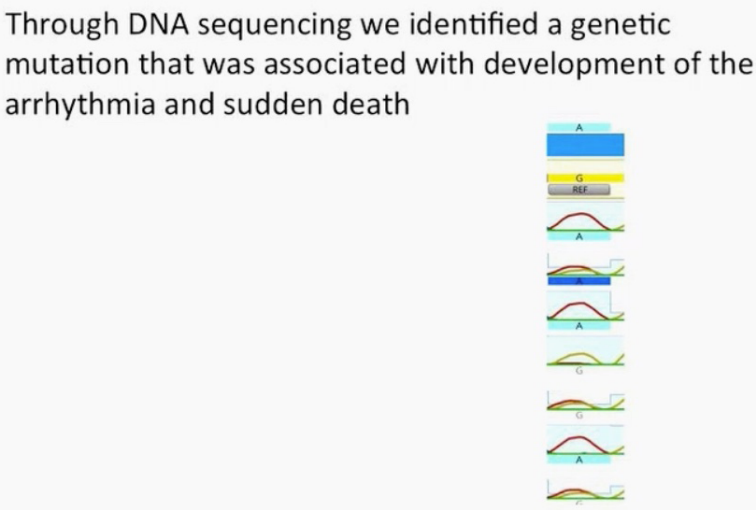
Negative	Positive Heterozygous	Positive Homozygous	Total
43	117	84	244
17.6%	48.0%	34.4%	

13. As yet, there has been no publication that describes details of how this DNA test was devised and validated. The test is said to be diagnostic for identifying dogs that are positive (either heterozygous or homozygous) and, therefore are "at risk for the disease" (ref. 6).

14. In her webinar, Dr. Meurs illustrated results from seven dogs, four affected and three non-affected. Although the details were not explicitly described, the following graphic, taken from

[17] Meurs, K. M., private communication.
[18] https://cvm.ncsu.edu/genetics/rhodesian-ridgeback-inherited-arrhythmia-rr-iva/
[19] Information was solicited and tabulated in 2017 by the author from participants in the Facebook page devoted to Rhodesian Ridgeback Inherited Ventricular Arrhythmia.

Dr. Meurs' webinar (ref. 1b) shows that at a given position the four affected dogs had "A" and three unaffected dogs had "G."



This was presumably done by whole genome sequencing of the seven subject dogs. To date, no information has been provided with regard to what criterion was applied to define "affected". Presumably it was DNA samples from dogs found to exhibit the ventricular arrhythmia, probably from from members of the extended family summarized in Figure I of the 2016 Meurs article.

15. Since the overwhelming majority of RRs tested are positive on the test (83%, or approximately 5 out of 6), the DNA test itself is not particularly useful for making breeding decisions, especially since the test is based on risk factors versus genetic certainty for the disease. It would be disastrous for the breed if breeders were to eliminate 5 out of every 6 dogs from our ridgeback gene pool solely because the dogs are positive on the RR IVA DNA test.

16. There is some limited data on the correlation of the RR IVA DNA test with Holter monitor results. In the fall of 2017 the author conducted a survey using the Facebook Rhodesian Ridgeback IVA page. The survey gathered DNA and Holter test results and produced the following result for dogs under 36 months of age:

    - NEG 100% clear
    - HET+ 78% clear, 22% affected
    - HOMO+ 76% clear, 24% affected

A somewhat less granular summary is found in Appendix B.

17. This limited correlation of DNA and Holter test data is consistent with a model wherein there are two different DNA mutations, each of which is necessary but not sufficient to cause the arrhythmia. If two mutations are necessary for the arrhythmia to exist, a DNA test that measures only one of the mutations would have false positives but not false negatives. This is what the data to date show – 0% false negatives and about 77% false positives. One problem is that many more Holter tests have been carried out on dogs that are DNA positive than on dogs that are DNA negative. Recall that there are about 5 times as many DNA positives as DNA negatives (83% positive, 17% negative). People whose dogs test negative on the DNA test are understandably less prone to put out the effort and expense to do the Holter monitor test. The author and several colleagues are attempting to locate and test more DNA negative dogs to further validate the significance of a negative DNA test.

18. Finally, I would like to express a note of caution about the level of anxiety, worry and fear that seems to be occurring in some quarters on social media.
    a) First, while the sudden death of any young dog is admittedly tragic, we must avoid the instinct to panic. To the extent the NCSU DNA test indicates a malfunctioning gene that is responsible for ventricular arrhythmia, we can conclude that the lethality of this particular genetic defect is low. This conclusion is based on the following analysis:
        - 83% of RRs so far are positive for this particular mutation on the DNA test, which Dr. Meurs equates to 83% of the ridgeback population being at risk for ventricular arrhythmia.
        - There are about 750 Ridgeback litters registered per year; at an average litter size of 7, the number of puppies born each year in registered litters would be about 5,250.
        - About 23% of the DNA-positive dogs show arrhythmia on a Holter test.
        - It follows that each year approximately 1000[20] Rhodesian Ridgebacks have ventricular arrhythmia as juveniles, which is not detected because, there are no obvious symptoms and most juveniles outgrow the condition by the age of 3.
        - Although there is no comprehensive data for sudden cardiac deaths in juvenile ridgebacks, there are anecdotal reports of about two dozen sudden deaths over the last

[20] Estimated as follows: 5250 x 0.83 x 0.23 = 1002.

20 years. Although this number may be under representing, it is far less than the thousands of RR puppies who should – at least statistically according to the DNA test – have juvenile arrhythmia.

- Finally, the very fact that the identified genetic mutation is so widespread in the general population underscores the low probability of lethality in the general ridgeback population.

19. I think (and this is speculation on my part) that there are degrees of risk for a dog identified as having VA by ECG test. In most cases, I believe it is benign, but in rare sudden death cases there is some other system failure – perhaps genetic in nature – as yet unidentified. It is this modifier or other genetic mutation that should be sought.

20. How do we apply the information available through the existing NCSU DNA test and/or Holter tests? It should be noted that so far, almost two years after the 2016 Meurs JAVMA article, hundreds of RRs have been tested by the NCSU DNA test and/or by the Holter test. To my knowledge, none of the RRs tested by either of these methods has died suddenly.

21. It is important for breeders to recognize that the characteristics of the existing DNA test are different from other genetic tests with which Ridgeback breeders are familiar. For example, both DM and EOAD operate in a recessive fashion. The DNA tests that have been created to identify associated mutations show a dog to be clear, carrier or at-risk. In both DM and EOAD, the dogs that are positive homozygous (2 abnormal genes) may be affected and it is rare for carriers (heterozygous; 1 abnormal copy of the gene) to actually have the disease. Therefore, for these two particular tests, breeders have a clear breeding strategy – do not mate two carriers. Furthermore, the majority of Ridgebacks are clear in both DM and EOAD, so it is not difficult for breeders to find clear dogs that also show excellent breeding characteristics. Accordingly, the genetic diversity of the ridgeback pool is easier to maintain. In contrast, VA in ridgebacks may occur for both heterozygous (1 abnormal gene) and homozygous (2 abnormal genes) dogs. Instead of following recessive genetics, as described for DM and EOAD tests, this RR IVA DNA test suggests a dominant mode of inheritance with "incomplete penetrance," which is far more complicated. Incomplete penetrance means that some dogs that have the DNA mutation associated with the disease actually have the disease, but others do not.

Another way to describe this situation is that the RR IVA test has a large number (about 75%) of false positives – test results that do not correctly predict that the subject dog actually has ventricular arrhythmia when tested. As explained above in ¶17, this may be because the test identifies only one of two DNA mutations that are necessary for the arrhythmia.

22. Holter monitoring is a different matter because it actually identifies arrhythmia in dogs (within the normal or abnormal range). This test measures an actual physical condition – there is no issue of incomplete penetrance or false positive results; PVCs are either above the normal range or not. Consequently, the Holter test gives a much richer set of data than the DNA test, which has only three possible results – negative, positive heterozygous or positive homozygous.

    There is a suggestion that a negative DNA result might be meaningful and actionable, since there have not as yet been any demonstrated false negatives (at least to my knowledge). However, this generalization is based on only nine dogs and much more data is needed to provide confidence that a negative DNA test is definitive. On the other hand, a positive DNA test, either heterozygous or homozygous, is inconclusive since there is only about one chance in three that a dog with a positive DNA will actually have ventricular arrhythmia at a level considered "affected".

    Furthermore, a given dog can have a wide range of PVCs, from zero to many thousands per 24 hours and the PVCs can be singlets or complex, including ventricular tachycardia. Moreover, dogs with <50 PVCs/24 hours are considered "unaffected" or "normal" while those with >50 PVCs/24 hours are considered "affected". Of course, this is just an arbitrary cutoff – it seems obvious that a dog that has a few hundred PVC/24 hours would be less at risk than one with thousands of PVCs.

23. As a practical matter, we must recognize that in most cases information about the presence and degree of ventricular arrhythmia will not be available to a breeder, unless the dog to be bred was Holter-tested during the susceptible age range. Unfortunately, the vast majority of breeding candidates have not been tested during the juvenile age range and, if affected with VA, have likely outgrown the arrhythmia by the time he or she is ready to be bred. Going

forward, we need to continue to gather information that will let us understand the risk factors for sudden death of young RRs. For that reason, I recommend that breeders continue to Holter-test as many juveniles as possible over the susceptible age range of 6-15 months and make the results available in a database to be established.

24. Although, to my knowledge there has not yet been a sudden cardiac death of a young Ridgeback previously Holter-tested, or whose parents or other ancestors were Holter-tested, this will probably happen at some time in the future. When this occurs, DNA profiling of this young dog, and its parents and littermates, might be instrumental in developing a DNA test which is actually predictive of sudden death ventricular arrhythmia in juvenile ridgebacks. As of this date, however, according to publications, there is no such conclusive DNA test for predicting sudden deaths in ridgebacks.

25. Finally, I am not opposed to breeding dogs who demonstrated ventricular arrhythmia (but not ventricular tachycardia) as juveniles, provided, however, that the dog was was determined by Holter testing to be normal by age 2-3 years. In addition, I think it is incumbent on the breeder who breeds a dog (male or female) who had abnormal Holter results as a juvenile, to examine all of the puppies by Holter test at the age of 9 months of age.

26. I would recommend caution in breeding parents or littermates of Juvenile Sudden Death Dogs.

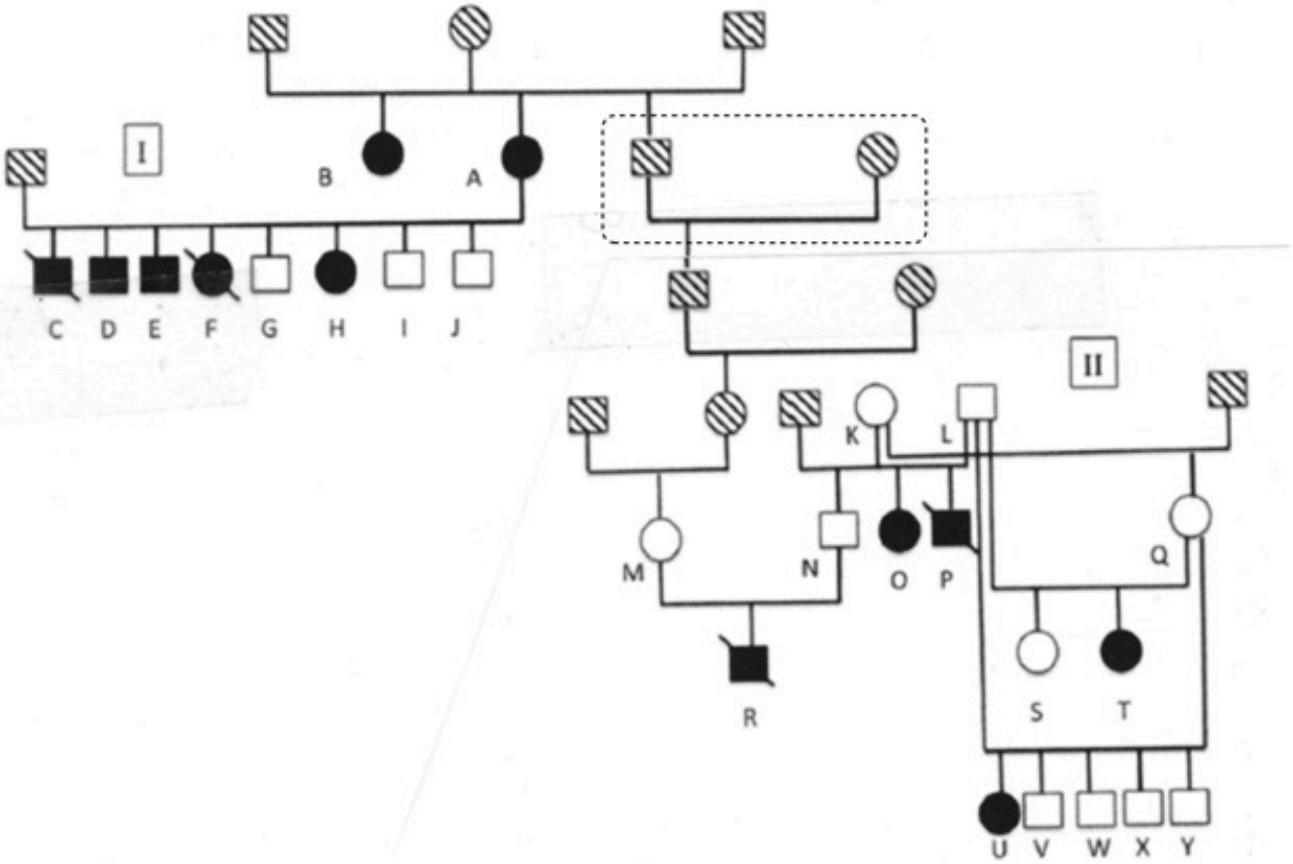
Conclusions:

- Ventricular arrhythmia, as measured by Holter testing, seems to be common in young Rhodesian Ridgebacks.
- A very small fraction of juvenile dogs have died suddenly – presumably from ventricular arrhythmia or tachycardia. The vast majority of juvenile ridgebacks testing positive for VA by Holter testing outgrow the condition. At present, the actual risk of sudden cardiac death to juveniles who manifest the ventricular arrhythmia appears to be rather low.
- Much more data must still be collected on the time course of the condition – ages at which the ventricular arrhythmia begins and declines, and I endorse the NCSU program to collect this valuable data.

- The RR IVA DNA test that is being marketed by NCSU – which does not definitively predict ventricular arrhythmia nor predict sudden cardiac death – is of little use for making breeding decisions for the general ridgeback population. There clearly are missing aspects – modifiers or other mutations – that need to be identified to unequivocally identify those dogs that carry the "sudden cardiac death" gene or gene cocktail.

APPENDIX A

One generation is missing from the family tree depicted in Figure 1 of the 2016 Meurs article. The correct tree is shown below. The omitted generation is indicated by the dashed box.



APPENDIX B

- Neg: 9 dogs age 7-36 mos; all normal (0-1 PVC)

- Het+: 29 dogs age 5-36 mos
    - 22 with <50 PVCs
    - 2 with 50-2000 PVCs
    - 5 with > 2000 PVCs

- Homo+: 37 dogs age 5-36 mos
    - 29 with <50 PVCs
    - 7 with 50-2000 PVCs
    - 1 with >2000 PVCs