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Sudden Acquired Retinal Degeneration Syndrome in Canine Patients

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Murray State University Honors College

HONORS THESIS

Certificate of Approval

Sudden Acquired Retinal Degeneration Syndrome in Canine Patients

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May 2024

Approved to fulfill the
requirements of HON 437

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Sudden Acquired Retinal Degeneration Syndrome in Canine Patients

Submitted in partial fulfillment
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for the Murray State University Honors Diploma

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Abstract

Sudden Acquired Retinal Degeneration Syndrome (SARDS) is a perplexing and debilitating ocular condition that affects canine patients primarily in the form of the sudden onset of total vision loss. Veterinary literature will be reviewed to discuss the basic anatomy of the canine eye and retina, as well as to investigate various diagnostic techniques to evaluate ophthalmic function and hypotheses of the pathogenesis of SARDS. The complexity of this disease and the absence of research leads to veterinarians and clients grappling with unanswered questions. This research surveys veterinarians to gain a perspective of the rareness of the disease, the most frequent symptoms potential SARDS patients present with, their deductive reasoning in which diagnostic testing to perform, and the difficulties encountered when communicating a SARDS diagnosis to clients.

Table of Contents

I. Abstract……...……....i

II. List of Figures…….iii

III. Introduction……1

IV. Background……3

i. Basic Anatomy of the Canine Eye……....……..3

ii. The Retina……....……..4

iii. Diagnostic Techniques…….…...……..7

iv. Hypotheses of Pathogenesis…….....11

V. Methods and Procedures……..…..…16

VI. Results……..….19

VII. Analysis……..……...29

VIII. Conclusion…….……....……34

IX. Works Cited…….…….…….36

X. Appendix A…….……...38

XI. Appendix B…….……...39

XII. Appendix C……45

List of Figures

I. Figure 1……..……..3

II. Figure 2……5

III. Figure 3……6

IV. Figure 4a……..……9

V. Figure 4b……10

VI. Figure 5……..19

VII. Figure 6……..20

VIII. Figure 7……..21

IX. Figure 8……..22

X. Figure 9……..……22

XI. Figure 10……23

XII. Figure 11……24

XIII. Figure 12……25

XIV. Figure 13……26

Introduction

In the recent history of veterinary medicine, Sudden Acquired Retinal Degeneration Syndrome (SARDS) has become a debilitating ocular condition affecting the canine population. Sudden Acquired Retinal Degeneration Syndrome was first described in canine patients in the United States of America in the early 1980s; when first documented, the condition was called ‘toxic metabolic retinopathy’ and also ‘silent retina syndrome’(Komáromy et al., 2016). This condition presents with the rapid onset of total and irreversible blindness. SARDS is a perplexing condition that leaves many dog owners wondering what they could have done differently to prevent their pets from losing their vision. The harsh reality of this disease process, which many owners have difficulty accepting, is that it is idiopathic in origin. The mechanism of the disorder is inadequately understood due to the lack of research, leading to no clearly defined clinical signs, as well as many hypothesized links to various endocrine diseases.

In a society that upholds the significance of canine companionship, clients depend heavily on their veterinarians to ensure the welfare of their beloved pets. The amount of unknown and hypotheses surrounding a SARDS diagnosis can negatively affect many clients' understanding of the diagnosis. There is an apparent necessity in veterinary medicine for a deeper understanding of SARDS to benefit not only the veterinary-client communication but also the welfare and quality of life of SARDS patients. This research aims to advance the understanding of Sudden Acquired Retinal Degeneration Syndrome by exploring the disease process, understanding clinical signs that the patients present with, and addressing hypothesized clinical signs and links to secondary endocrine diseases. It will also analyze the data obtained

from surveyed veterinarians, discussing clinical symptoms noted upon exam, the course of diagnostics testing and imaging performed, and the development of their long-term care plan.

Background

Basic Anatomy of the Canine Eye

The canine eye, while small, is very complex. Each structure holds an essential function within its delicate anatomy. Figure 1 below provides a diagram for a visual reference of the eye, as the functions of the major structures are provided to help the reader better understand the basic anatomy of the canine eye.

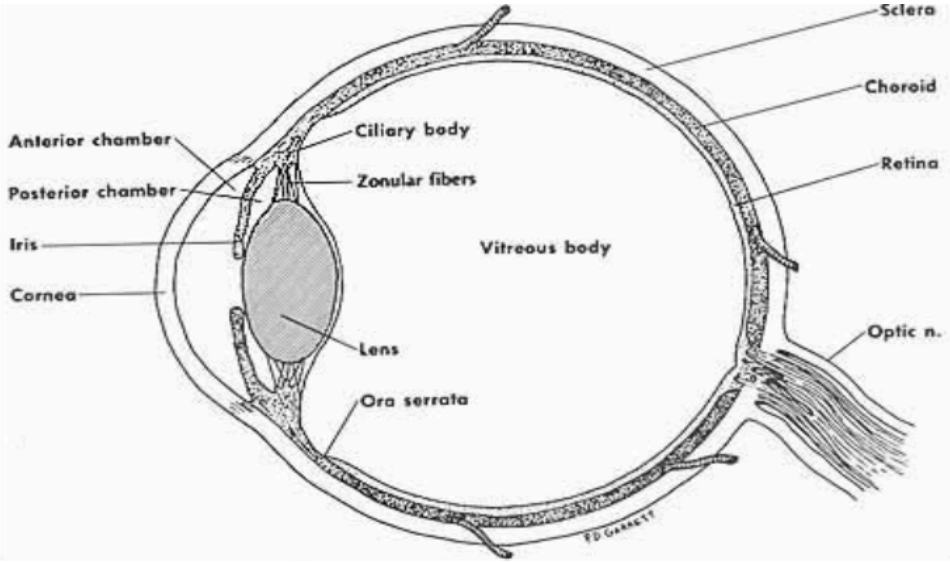

Figure 1. (Clarkson et al., 2019) University of Minnesota CVM schematic drawing of the canine eye on the sagittal plane.

The outer fibrous layer of the canine eye includes the cornea and the sclera. The cornea is the transparent convex cranial surface of the eye, in which the cornea is the first portion of the eye that light photons pass through (Gelatt, 2018). The sclera is the thick layer that surrounds the rest of the eye and is easily identifiable as the white portion of the eye. The middle vascular portion of the eye includes the choroid, ciliary body, zonule, iris, and pupil. The choroid is a highly

vascularized membrane characterized by a thin and pigmented layer. The ciliary body is the layer between the choroid and the iris; the ciliary body consists of the ciliary process and ciliary muscles. Ciliary muscles are small muscles that contract and relax the lens (Gelatt, 2018). The zonule is a suspensory apparatus between the ciliary body and the lens. The iris is a commonly known structure as it is the colored portion of the eye that surrounds the pupil. The pupil is the most central portion of the eye and is surrounded by the iris; once light passes through the cornea, it will pass through the pupil to reach the lens. The innermost nervous layers of the eye are the lens and the retina. The lens is a transparent structure located behind the iris; ciliary muscles can contract the lens to thicken it and allow it to focus on close objects. The ciliary muscles can also relax the lens, causing it to become thinner and focus on objects in the distance (Gelatt, 2018). The retina is multilayered and will be discussed in depth in the next section.

The Retina

The retina is the most complex of all ocular components and is housed in the inner nervous portion of the eye. The retina is comprised of 10 layers; in order from outside inward, the layers are retinal pigment epithelium, photoreceptor outer segments- rods and cones, outer limiting membrane, outer nuclear layer, outer plexiform layer, inner nuclear layer, inner plexiform layer, ganglion cell layer, nerve fiber layer, and inner limiting layer (Rachel et al., 2017). Figure 2 provides a closer look at the defined layers of the retina.

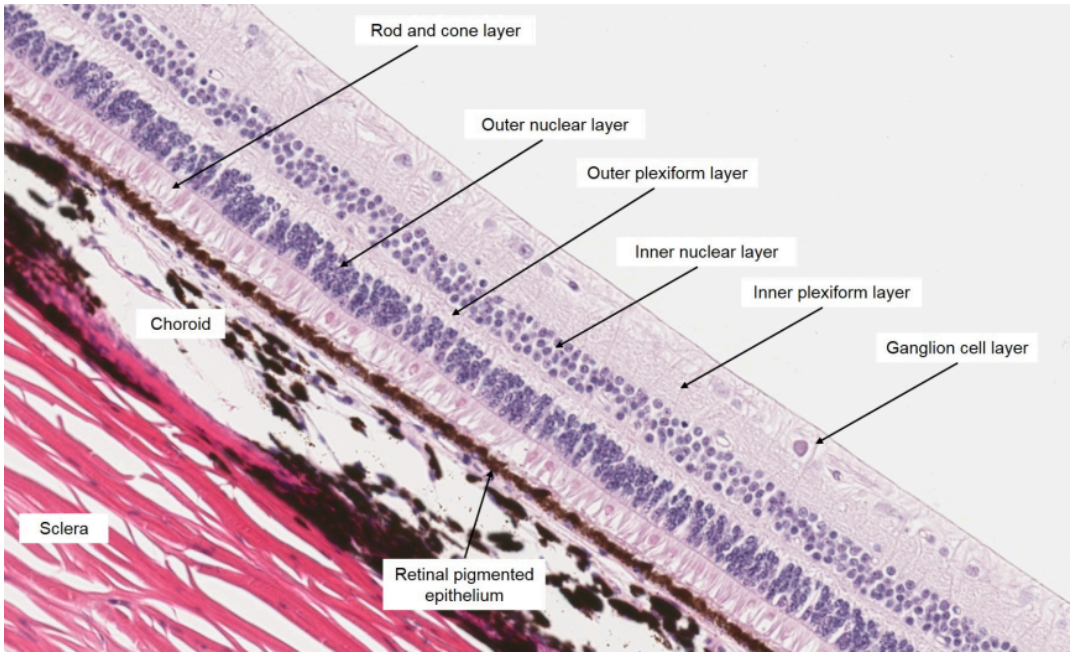

Figure 2. (Rachel et al., 2017) retinal histology.

The retina is a critical component in ocular function; light photons will first pass through the cornea and continue to pass through to the lens, focusing the light on the retina. Within the retina, many light photons are absorbed and converted into electrical impulses, which are modified and transmitted to the ganglion cells, eventually traveling to the optic nerve and proceeding toward the brain (Rachel et al., 2017). The photoreceptor layer of the retina, often referred to as the rod and cone layer, is the outer cells of the sensory retina. The photoreceptor layer is the layer of the retina in which light photons are converted into electrical impulses. The rod and cone cells within the photoreceptor layer help to interpret the light photons. The rod cells allow for vision in dim lighting with minimal details as they are highly light-sensitive and mostly inactive when adequate light is present (Rachel et al., 2017). The cone cells of the photoreceptors are just the opposite of the rod cells; the cone cells provide more detailed vision, including color vision, and are less light-sensitive (Rachel et al., 2017).

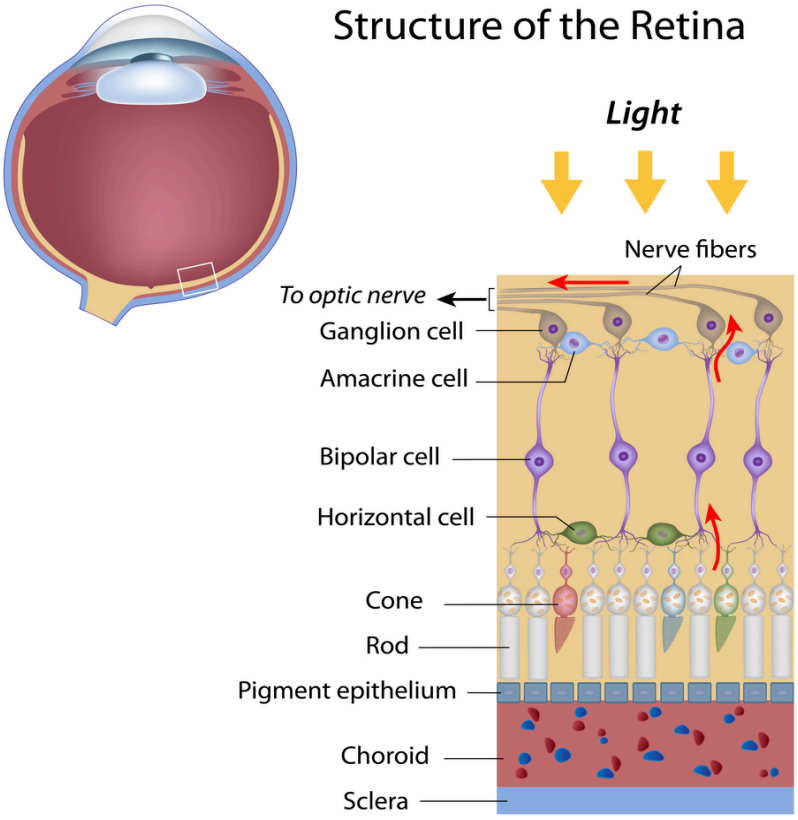

Figure 3 shows the process of light through the layers of the retina to the optic nerve (Lin & Tsai, 2022).

Figure 3 visually depicts how the light enters the retina and moves through the different layers. The figure shows specific cellular components of the different layers of the retina, which can be seen in Figure 2 above. In Figure 3, light is depicted by the yellow arrows, which will enter the retina and travel to the pigment epithelium and then to the rod and cone layer. Within the rod and cone layer, light is turned into electrical impulses, depicted by the red arrows representing the path to the optic nerve.

Diagnostic Techniques

There is a plethora of diagnostic tests that veterinarians will conduct to assess the ocular function of a canine patient. In the veterinary profession, the pricing of services and the cost of patient care have become determining factors in whether diagnostic ocular testing will be performed on the patient or not. Due to this, many clients opt to have the general practice veterinarian perform an ocular exam and ocular test in the clinic to rule out specific disease processes and use their deductive reasoning to arrive at a diagnosis. Rather than be referred to a specialty practice and pay for a more expensive but more conclusive diagnostic test.

General practice veterinarians can assess the ocular function of a canine eye in numerous ways. These ocular tests evaluate certain functions of the patient's eye. They can be done during a physical exam with little to no extra time or resources, and they allow the veterinarian to rule out many other ocular conditions. These ocular tests include intraocular pressure, Schirmer tear test, fluorescein stain test, menace test, maze test, and pupillary light response. Intraocular pressure is assessed using a tonometer to measure fluid pressure inside the anterior chamber of the eye. By obtaining a patient's intraocular pressure, veterinarians can help diagnose or eliminate various other ocular conditions. The Schirmer tear test evaluates the canine eye's tear production level. It can lead to a diagnosis of keratoconjunctivitis sicca, which can be diagnosed secondary to blindness in patients. The fluorescein stain test uses orange dye and blue light, allowing the veterinarian to assess the patient's cornea for any stain uptake that will signify scratches or abrasions that could hinder their ocular function. The menace test is a simple evaluation a veterinarian can perform to detect if the patient has the ability to see. The simplicity of this test makes it commonly done upon routine physical examinations. All the veterinarian

does is move their hand swiftly toward the patient's eye without touching the patient and observe the patient's reaction, which is a blink or recoil in a healthy patient. Similarly, the maze test also assesses the patient's visual ability; if the patient consistently has difficulty navigating the course and constantly bumps into objects, it implies the patient suffers from blindness or visual impairment.

The pupillary light response is typically performed on a general physical examination; this test consists of briefly shining a bright light into one of the patient's eyes, typically using an ophthalmoscope or a pen light. This will allow the examining veterinarian to observe the pupillary response; ideally, when a light is shined into the eye, the pupil will have a direct constriction, and the pupil in the other eye should have a consensual constriction. Performing the pupillary light response allows the veterinarian to assess if the visual pathway from the eye to the brain involving the optic nerve and muscles controlling the pupils is intact. However, there are numerous documented cases of diagnosed SARDS patients eliciting a direct and consensual pupillary constriction when high light intensities are used to perform the test. Many veterinarians with a suspected SARDS case will opt to perform a chromatic pupillary light response in which the pupillary light response is performed at low light intensities using red and blue wavelengths of light. Healthy patients should elicit the same pupillary response of direct and consensual constriction at high and low light intensity. No change should be observed in a healthy patient's pupillary response between a high-intensity pupillary light response test and a chromatic pupillary light response test. However, there has been a noted change in SARDS patients between the two tests. While SARDS patients have been documented to elicit a pupillary response at a high light intensity, no SARDS patients have elicited a pupillary response at very low light intensities (Grozdanic et al., 2007). SARDS patients tested with the chromatic pupillary

light response have only elicited a response to high-intensity blue light but not low-intensity red light, which demonstrates the loss of rod and cone cells within the photoreceptor layer of the retina (Grozdanic et al., 2007).

Electroretinography is a diagnostic tool used by veterinary ophthalmologists, and it is required to officially confirm a diagnosis of a suspected SARDS patient. An electroretinogram (ERG) plays a pivotal role in diagnosing a blind canine patient. This test can confirm or exclude a diagnosis of SARDS and can even help diagnose treatable central nervous system conditions in canine patients. An electroretinogram assesses the function of the retina by flashing a light in front of the eye; this light stimulates the retina to generate electrical impulses, which are recorded. The recorded electrical impulses are then amplified by the machine and transcribed into waveforms correlating to the retina's sensitivity to light and the overall function. Below are two electroretinograms obtained from adult canine patients.

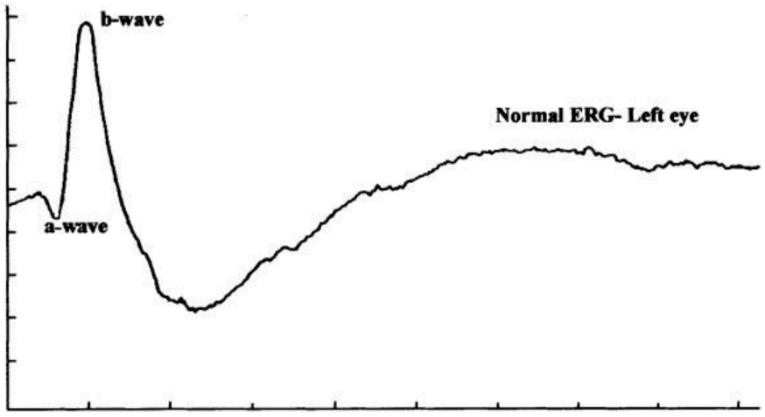

Figure 4a. (Cullen et al, 2002) Electroretinogram of an adult German shepherd cross with normal retinal function.

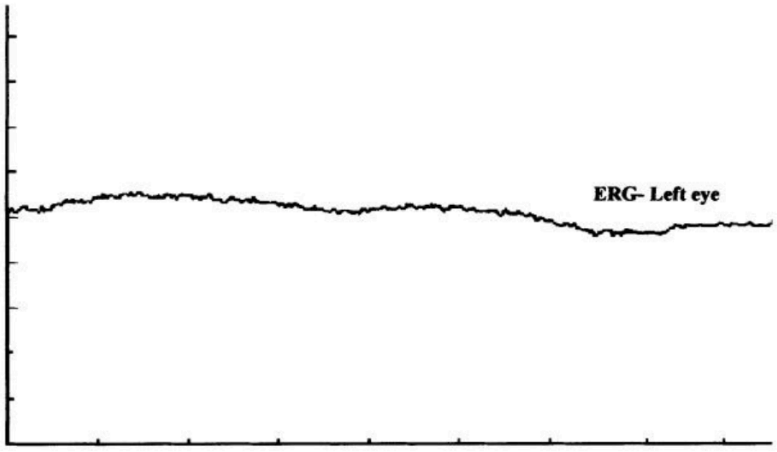

Figure 4b. (Cullen et al, 2002) Electroretinogram of an adult terrier cross with no retinal function.

Figure 4a shows an electroretinogram for a canine patient with normal retinal function. Note that the a-wave and b-wave waves represent the electrical impulses generated by the retina as a response to the stimulation of light, which was then amplified and transcribed by the diagnostic machine. It is important to note that both canines, the patient from Figure 4a and the patient from Figure 4b, were tested under the same conditions (Cullen et al., 2002). The lack of waves in the electroretinogram of Figure 4b represents the lack of electrical impulses generated by the retina; the relatively flat electroretinogram confirms the loss of photoreceptor cell layer function within the retina. Figure 4b was used to confirm a diagnosis of SARDS, as the patient experienced sudden blindness but had a normal appearance during an ophthalmoscope examination when the sudden blindness first occurred (Cullen et al., 2002).

Hypotheses of Pathogenesis

The unknown disease process of sudden acquired retinal degeneration syndrome has led to many hypotheses of what exactly is causing sudden retinal degeneration, resulting in total and incurable blindness. The lack of research surrounding the mechanism of SARDS has led to numerous hypotheses by board-certified veterinary ophthalmologists and within the veterinary profession. These hypotheses attempt to explain the only proven clinical sign of SARDS, which is sudden and irreversible blindness. While there is no known exact cause of SARDS, it is hypothesized that it could be caused by potential environmental factors, genetic predisposition, or linked to various endocrine diseases.

Theories have suggested that environmental factors could lead to the development of SARDS. This theory was first documented in 1984, shortly after the initial discovery of the disease process. Two different research studies published in the *Transactions of the American College of Veterinary Ophthalmologists* in 1984 and 1986 found a numerical trend of diagnosis of SARDS peaking in December and January in the northeastern region of the United States (Komáromy et al., 2016). However, a study published in the *Journal of the American Veterinary Medical Association* in 2013 has since found no correlation between the winter months and a peak in the diagnosis of SARDS in any other geographic region within the United States (Stuckey et al., 2013). While a seasonality correlation of diagnosis of SARDS was debunked, other theories suggest stressful environmental factors might play a role in the risk factors of developing SARDS. Environmental risk factors can include stressful situations for the canine, such as kennel stays, grooming appointments, household changes, or vaccinations. It has been proposed that these stressful situations could be responsible for glutamate excitotoxicity, which

results in the death of the photoreceptor layer of the retina (Komáromy et al., 2016). Glutamate excitotoxicity is a toxic action of excitatory neurotransmitters that, over a prolonged period, can ultimately cause neurotoxicity and lead to loss of neuronal function. A research study published in 1993 reported an increase in glutamate concentrations in samples obtained from the vitreous humor, located between the lens and the retina, in SARDS patients (Komáromy et al., 2016). However, the legitimacy of this amino acid analysis of the obtained samples is extensively questioned, as E. Dreyer, the co-author of the publication and laboratory lead, was convicted of scientific misconduct in the year 2000 (Komáromy et al., 2016). No other studies utilizing vitreous humor samples obtained from SARDS patients for amino acid analysis have been published in veterinary medical journals at the time of the composition of this thesis. There is no established link between SARDS patients and environmental risk factors. The seasonality and geographical region correlating to diagnosis have been disproven. The link between glutamate excitotoxicity and SARDS has only been demonstrated in one study in which the scientific integrity is questioned. As of the time of this thesis's composition, there is insufficient evidence to conclude that there is a correlation between the environment of a canine and the development of SARDS.

Predisposition to sudden acquired retinal degeneration syndrome in canine patients has been a widely discussed topic among veterinarians and researchers. Age predisposition is reported in multiple studies; the majority of SARDS patients are most commonly middle-aged to older, with the median age being reported as nine years old (Heller et al., 2017). Unlike age predisposition, gender predisposition for SARDS is not widely agreed upon. Many research studies that shift the focus to a general overview of SARDS, just like *Sudden acquired retinal degeneration syndrome (SARDS) - a review and proposed strategies toward a better*

understanding of pathogenesis, early diagnosis, and therapy report that female canine patients are overly represented in the diagnosis of SARDS, with the majority of the females being spayed. Other research studies that focus more specifically on the predispositions of SARDS, just as the study *Sudden acquired retinal degeneration in dogs: breed distribution of 495 canines* report that there is no statistical significance between male and female patients; therefore, there is no gender predisposition to SARDS in canines. According to veterinary literature, small-breed dogs under 25 pounds are most commonly diagnosed with SARDS, while larger-breed dogs over 50 pounds seem to be more infrequently diagnosed (Heller et al., 2017). Numerous SARDS research studies also report that mixed-breed dogs are most represented within diagnosed SARDS cases. While there are no official age, gender, or breed predispositions to a SARDS diagnosis, veterinary literature has agreed upon common trends occurring in diagnosed SARDS patients. These agreed-upon trends describe SARDS patients as most commonly middle-aged to older, small, mixed-breed canines.

Current research and hypotheses suggest a correlation between SARDS and abnormal endocrine function. These hypotheses are based on evaluating all of the symptoms exhibited by the patient. The primary reason for an owner seeking veterinary care for the studied potential SARDS patient is that the owner has noticed that their dog has become disoriented and has had difficulty navigating without bumping into objects within a short period of time. Along with the clinical sign of sudden blindness, clients have also reported other symptoms, which include lethargy, polyuria, polydipsia, and polyphagia. Veterinary research and literature suggest that while not every patient will demonstrate these systemic signs, many can or will develop them throughout their lifetime after a SARDS diagnosis; as many as 85% of SARDS patients will indicate at least one systemic sign (Komáromy et al., 2016) the presentation of these systemic

signs are concurrent with textbook clinical signs of various endocrine diseases. This leaves veterinarians to determine if the sudden blindness is related to an endocrine disease and if that is the reason for the presentation of the systemic signs. Due to the similarity of signs, a full comprehensive blood panel is typically run, including a complete blood count and a chemistry profile. Approximately 75% of SARDS patients that present with signs similar to those of the clinical signs of endocrine diseases receive abnormal results on their chemistry profile of elevated alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) which are all used to measure the function of the liver (Komáromy et al., 2016). Elevated liver enzymes, in combination with lethargy, polyuria, polydipsia, and polyphagia, are consistent with the clinical signs seen in the endocrine disease of hyperadrenocorticism.

Further tests have been conducted, ACTH stimulation test and dexamethasone suppression test, on SARDS patients that have presented with the clinical signs of hyperadrenocorticism. One study indicates that only about 20% of SARDS patients exhibiting the clinical signs were diagnosed with hyperadrenocorticism upon abnormal ACTH stimulation and dexamethasone suppression testing (Komáromy et al., 2016). Currently, there are only two documented cases of patients with a pre-existing condition of hyperadrenocorticism that developed SARDS. The relationship between SARDS and hyperadrenocorticism remains a topic of debate within the veterinary field. While some literature reports a high correlation with pre-existing SARDS patients often receiving a diagnosis of hyperadrenocorticism, recent veterinary literature identifies the similarities in presenting symptoms between SARDS and hyperadrenocorticism. However, these studies have not defined a causal link between the two diseases. Recent research has laid significant groundwork for studying SARDS and the potential

correlation to hyperadrenocorticism. Future research studies are warranted to investigate and find a link between hyperadrenocorticism and the pathogenesis of SARDS.

Methods and Procedures

The unknown surrounding sudden acquired retinal degeneration syndrome has constituted further research to evaluate the appearance of the disease process. This research strives to obtain valuable insight into SARDS on a larger scale by asking questions focused on the prevalence, clinical presentation, and diagnostic methods of generalized SARDS cases instead of individual patients due to the rarness of the disease. Detailing the methodology utilized in this research survey ensures complete transparency and reliability of the survey findings. This research survey targets veterinarians located in both urban and rural areas inside the continental United States. This research hypothesizes that the only clinical sign observed consistently will be sudden blindness, while other clinical symptoms observed will vary significantly. Furthermore, the anticipated responses will indicate that diagnostic techniques will vary drastically among veterinarians as obtaining a confirmed diagnosis of SARDS via electroretinogram will not be common. Additionally, this research anticipates that each veterinarian who has seen a SARDS diagnosis has their own way of communicating the diagnosis and long-term care plan to the client, as there are no set parameters or guidelines for a long-term care plan for a SARDS patient.

The Murray State Institutional Review Board approved the survey in February of 2024. The survey participants were made aware of their rights, that no personal or identifying patient data would be asked or gathered, and that all data collected would be confidential. Participants had to check a box acknowledging that they read and fully understood their rights outlined in the informed consent clause to be able to continue with the survey. The survey is estimated to take

approximately 10-15 minutes but could take less depending on the amount of SARDS cases that the veterinarian has seen. The survey consisted of 14 questions, a mixture of multiple choice, select all that apply and open-response questions. The select all that apply questions provided a space in which the participants could add any additional comments for that question; participants could also add any additional comments at the end of the survey. The informed consent clause and the survey questions are in the appendices.

The survey was distributed online via email as a Google Forms. The subject line to all of the emails read "Undergraduate Thesis Canine Research Survey" the email contained an approved research advertisement as well as it contained a link to the survey that was titled "Sudden Acquired Retinal Degeneration Syndrome in Canine Patients Research Survey". Emails were obtained randomly and distributed in two waves; in the initial wave, all email addresses obtained were from the American College of Veterinary Ophthalmologists website, specifically located in the "Find Ophthalmologists" section. All emails collected in the initial wave belonged to ophthalmologists or practices located within the continental United States. The survey was accessible to participants in the initial wave for six weeks. The second wave of participants were general practice veterinarians, and the survey was made available for only four weeks because a greater number of general practice veterinarians and clinics were emailed than veterinary ophthalmologists. Emails from general practice veterinarians were obtained randomly from all 48 continental states in both rural and urban areas by utilizing Google Maps and a Google search of "General practice veterinary clinics in *insert name of state here*". The number of general practice veterinarians and clinics emailed was one hundred and fifty-eight, while the number of veterinary ophthalmologists emailed was significantly lower at sixty-eight. There was a significantly larger amount of general practice veterinarians who received the survey email than

veterinary ophthalmologists; this was done purposefully because it was recognized that since the survey title indicated the subject matter, potential participants who have not seen a SARDS patient may choose not to respond.

Results

Despite the survey being distributed via email to two hundred and twenty-six veterinarians and veterinary practices, the survey received twenty-seven responses. Even though there was low participation in this survey, the number of participating veterinarians currently employed at a general practice versus a specialty practice was approximately equal, as Figure 5 below illustrates.

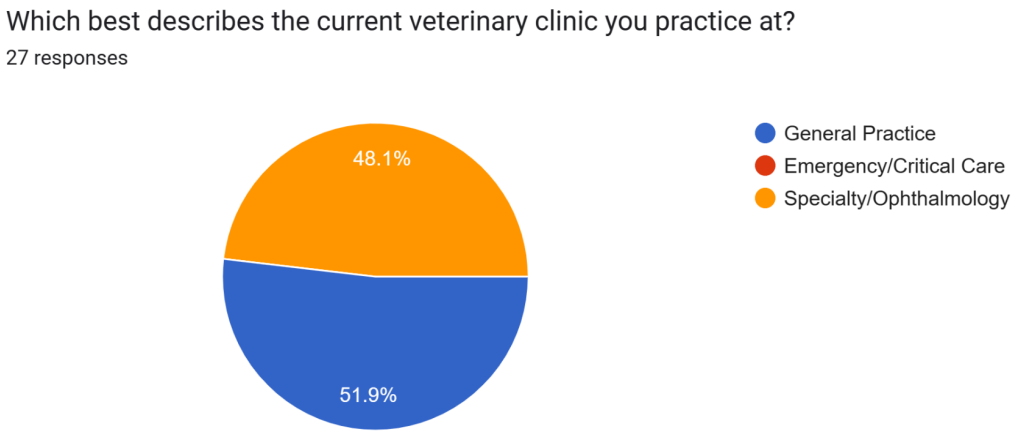

Figure 5. The pie chart reflects the distribution of participants within the veterinary medicine field based on the clinical setting in which they are employed.

The survey participants currently employed at a general practice versus a specialty/ophthalmology practice resulted in an approximately equal mixture. This mixture allows for the elimination of skewed results as the survey is not overly dominated by one particular classification of veterinary clinics in which the participants are employed.

Participants were prompted to select if they had ever been a veterinarian on a case regarding SARDS and to elaborate on their involvement with the cases. As seen in Figure 6, the majority, 48.1%, of participants had diagnosed at least one SARDS patient, followed by 22.2%

who had diagnosed and referred at least one SARDS patient, while only 7.4% have just referred at least one SARDS patient. An equal number of participants, 11.1%, have either never been involved in a SARDS case or have only been a primary veterinarian over a SARDS patient post-diagnosis.

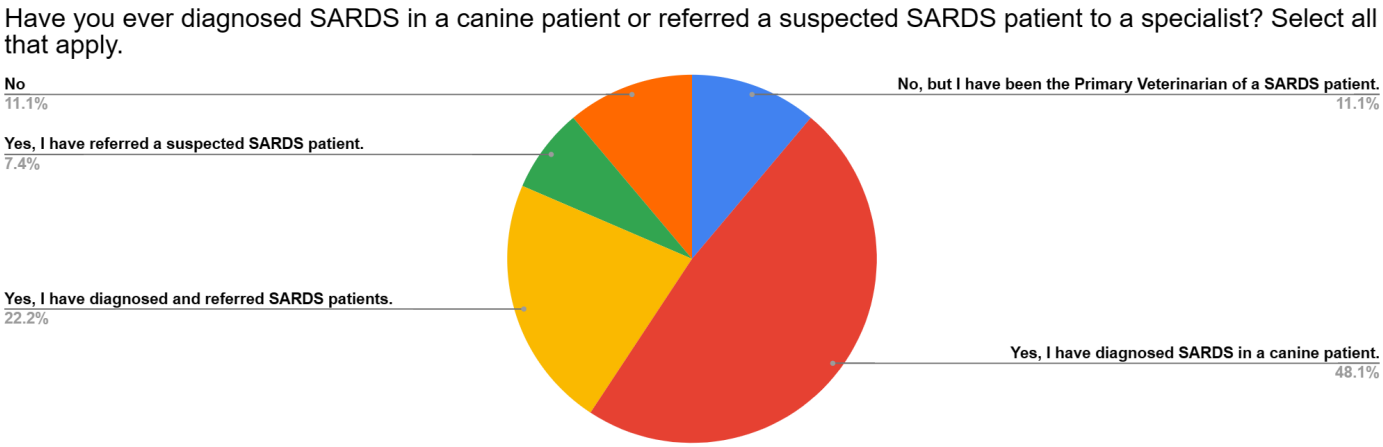

Figure 6. The pie chart reflects participant responses regarding if and how they have been involved in at least one case of a SARDS patient.

Participants were asked to elaborate on how long they have been practicing as veterinarians; the mean length of time the participants have been practicing is 19.24 years. The participants were asked to approximate the value of SARDS patients that they have personally diagnosed or referred, while the participants who have never seen a SARDS patient or have only been a primary veterinarian of a SARDS patient after diagnoses were instructed to leave the question blank. Figure 7 below shows a chart comparing how long each participant has been practicing veterinary medicine to the approximate value of SARDS cases in which they have been involved and their classification of the clinic in which they are employed.

How long have you been a practicing veterinarian?	Approximately how many SARDS patients have you diagnosed or referred?	Which best describes the current veterinary clinic you practice at?
13 years	2	General Practice
31 years	approx 5-6 per year of practice	Specialty/Ophthalmology
2.5 years	10	Specialty/Ophthalmology
14	40	Specialty/Ophthalmology
11 years	100	Specialty/Ophthalmology
11 years	80	Specialty/Ophthalmology
23 years	500 or more	Specialty/Ophthalmology
40 years	Maybe more than 20 cases, not sure	Specialty/Ophthalmology
11 years	30	Specialty/Ophthalmology
5 years		General Practice
7 years	a few dozen	Specialty/Ophthalmology
16 years	100 +	Specialty/Ophthalmology
12 years	hundreds	Specialty/Ophthalmology
25 years	10	General Practice
19 years	unknown. a bunch	General Practice
20 years		General Practice
11 years	50	Specialty/Ophthalmology
24 years		General Practice
12 years		General Practice
18yrs		General Practice
41 years	Two or three	General Practice
20 years		General Practice
42yrs	1	General Practice
15 years	6	General Practice
24 years		General Practice
31 years	less than 5	General Practice
21 years	Over 200	Specialty/Ophthalmology

Figure 7. The chart compares the number of years the participant has been practicing to how many SARDS cases they have diagnosed or referred. The blank spaces are participants who have only been a veterinarian of a SARDS patient post diagnosis or have never seen a SARDS patient. For clarity and transparency, the classification of the current clinic where the participant is employed was included.

It is important to note the larger volume of SARDS patients diagnosed and/or referred by a specialty/ophthalmology veterinarian versus a general practice veterinarian. Due to the rough approximation of SARDS patients diagnosed and/or referred by participants, no mean value of the amount of SARDS patients was determined.

This survey inquired about patients' clinical presentations upon examination, which prompted the veterinarian to suspect SARDS as a potential diagnosis. Additionally, the survey sought to gather the various diagnostic techniques performed to eliminate the possibility of other ophthalmic diseases.

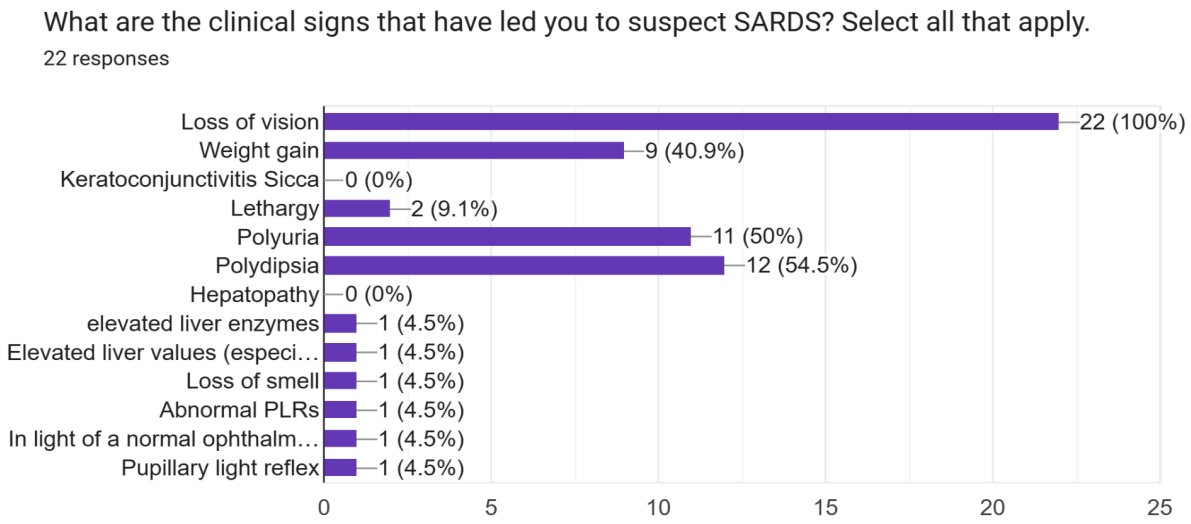

Figure 8. The above chart displays the percentage of clinical signs that patients have presented with to lead participants to suspect SARDS.

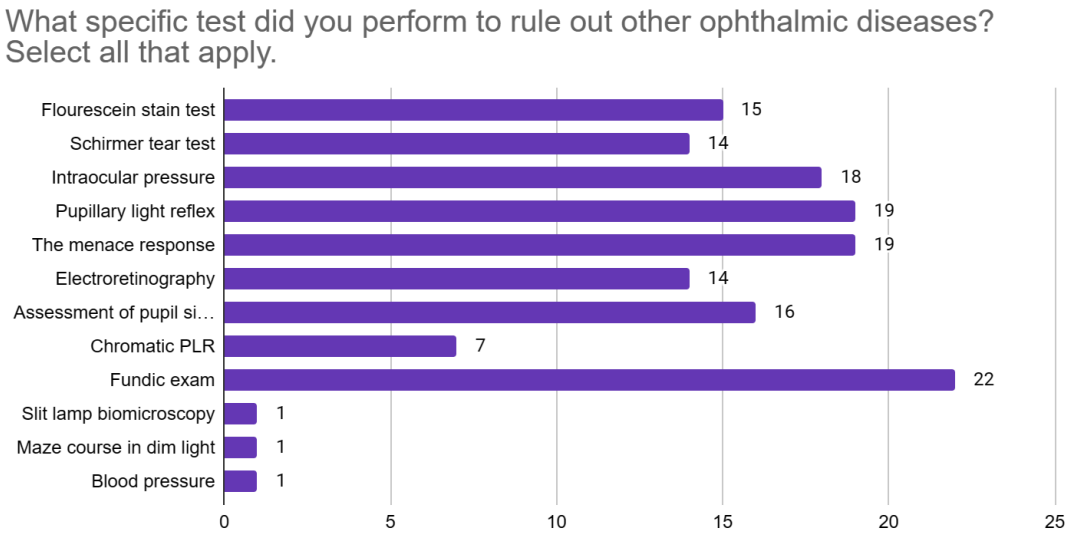

Figure 9. The above chart displays the various diagnostic techniques performed on potential SARDS by participants to rule out other ophthalmic diseases.

Figures 8 and 9 provide the data obtained from the survey. Figure 8 illustrates the most commonly seen clinical presentation of symptoms that lead veterinarians to suspect SARDS. Figure 9, which had 22 participants answer the question, represents the most frequently performed ophthalmic test to exclude other ophthalmic diseases and/or to confirm the diagnosis of SARDS.

The participants were asked in an open-response format, which did not require an answer to move forward with the survey if they performed any blood panels on patients in which concerns were raised, and if so, to please list the concerns. In many cases, the participants who responded stated that they let the primary or referring veterinarians do the bloodwork. All other responses stated concerns raised with the bloodwork. Nine responses stated that concerns had been raised on SARDS patients' bloodwork many times; the area of concern was the liver enzyme values. One value was especially noted by multiple participants, which was the elevated alkaline phosphatase values. The survey also inquired if the participants had ever performed diagnostic imaging on any diagnosed or potential SARDS patients. Figure 10 below demonstrates the distribution of answers.

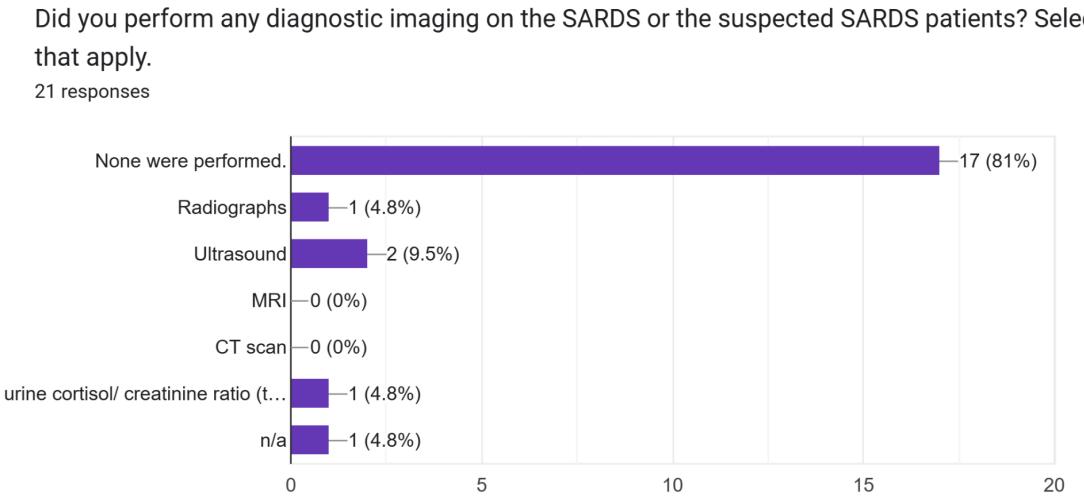

Figure 10. The bar graph above illustrates the amount and type of diagnostic imaging used.

After the question that Figure 10 illustrates was an open-response question asking if the participant performed any diagnostic imaging and, if so, were there findings that raised any concerns. One response noted that they found enlarged adrenal glands in a diagnosed SARDS patient via ultrasonography.

To further explore the potential correlation between SARDS and endocrine diseases, participants were asked if they had ever diagnosed an endocrine disease in a previously diagnosed SARDS patient.

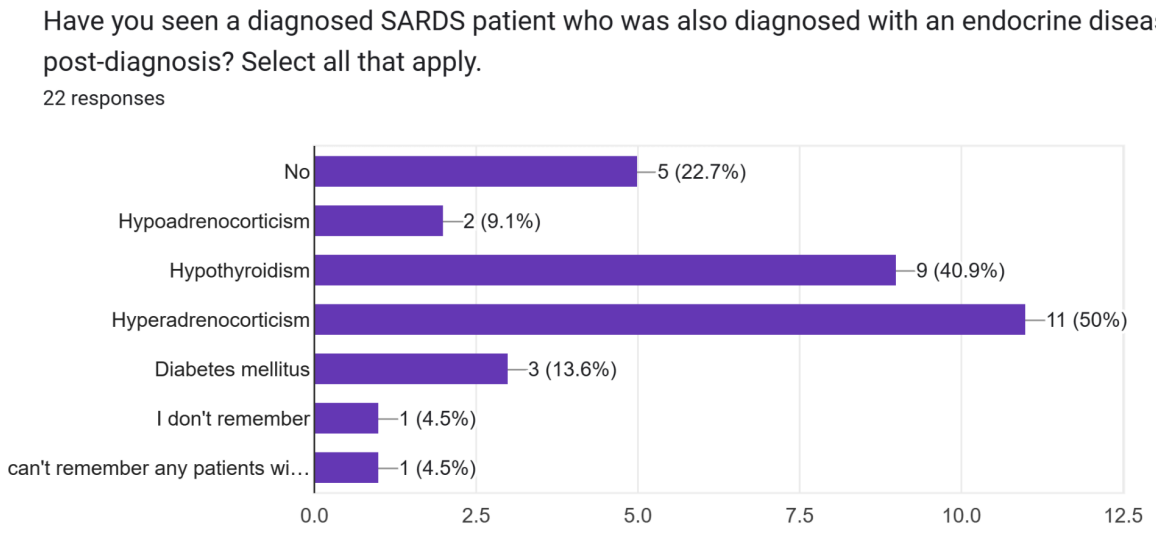

Figure 11. The bar chart above provides a visual representation of the distribution of answers regarding endocrine diseases in diagnosed SARDS patients.

The survey also aimed to explore the challenges and limitations that veterinarians have faced when diagnosing and developing a long-term care plan for SARDS patients. It also aims to gain insight into the barriers to communication and the difficulties of thoroughly explaining SARDS to clients.

Can you describe any challenges or limitations you've encountered in diagnosing or the long-term care of SARDS? How did you address them?

Owners not wanting to check ERG, so hard to make definitive diagnosis

availability of electroretinal imaging; referred to ophthalmologist

none that i can think of.

Difficulty helping SARDS patients adapt to acute loss of vision (+/- loss of other senses)
Significant limitations in treatment - no consistent/proven results w immunomodulation.

We see them too late, once retinas are too far gone for treatment.

No effective treatment

When we have suspected SARDS we typically complete our work up and try to refer to an ophthalmologist for confirmation. We discuss the challenges of having a blind pet and make suggestions as to care and safety measures we recommend.

The most significant challenge is having to debunk online information and treatments that have not been proven to be successful.

The long term care of SARDS patients largely dissipates with time as the patient becomes accustomed to being blind.

Inconsistent follow up. Once diagnosed they seldomly come for wellness follow up

Many owners are concerned about living with a blind pet, especially since the dogs seem quite stressed at first. Discussed how most dogs adapt well but it takes time/months. Stressed the importance of a consistent environment for the patient.

all are referred to ophthalmologist

Unremarkable in-house fundic exam usually results in a referral, but I'll refer to ophthalmology to confirm either way.

When treating with IVIG and immune suppression, difficulty maintaining vision as meds are backed down.

There is currently no reputable or efficacious treatment. No matter what certain ophthalmologists say.

Figure 12. Direct and unedited responses were received on Google Forms to this open-ended question. All spelling and grammatical errors are included for transparency.

How did you communicate and explain the diagnosis and/or long-term care of SARDS to the client?

Review of pathophysiology and anatomy of vision, explanation of causes of vision loss and explanation of specific signs in their pet /results of ERG/Chromatic PLR and how they explain the vision loss

discussed how to manage the environment for a blind dog.

SARDS is not treatable, although does not appear to be painful and does not seem to negatively impact lifespan. Focused on challenges with vision (+/- other sensory) loss and methods for clients to help their pet adapt while maintaining good QOL

In person and via informative handout

We explain what SARDS is to owners, that it is permanent, no treatment, but not painful. We provide a list of resources for visually impaired pets.

verbally and written handout

I only provide follow up care after the patient was diagnosed elsewhere.

Explaining SARDS to owners is perhaps the most difficult part of dealing with the disease, Since we don't have a specific cause and owners like answers. We like to refer these patients so we don't miss another potential cause of the vision loss. Most of our long term education centers around care and safety precautions for the blind pet. We do suggest yearly exams at the minimum to watch for any other possible ocular changes.

Gave information found from internet

We have numerous handouts that are provided to clients as well as we direct them to websites for help in having their pets adapt to the vision loss.

I discuss potential treatments to try (although nothing has been proven to treat SARDS), time required for adjustment to blindness, and thing that clients can do to help with the adjustments.

Lengthy talk in the exam room. Give advise for dealing with the blind patient.

Explained the condition, unknown cause but likely related to endocrine disease due to systemic side effects. Normal appearing eyes but suddenly blind. ERG needed to diagnose. Discussed blind dog care.

Explained to owner that this condition warrants a major lifestyle change. moving around the home and bumping into things could cause secondary trauma to animal. No off leash activity when outside.

That it is an immune mediated disease targeting the photoreceptors. That few patients recover vision with aggressive treatment. That single mode therapy will not work and that even with multiple modes of therapy, vision may return but might be lost again.

Clients need time to process. Having resources to help them adjust to living with a blind dog is recommended. Letting them know this disease process does not cause any ocular pain is important.

Figure 13. Direct and unedited responses were received on Google Forms to this open-ended question. All spelling and grammatical errors are included for transparency.

The survey also inquired about any generalized long-term care plans veterinarians used for diagnosed SARDS patients. This open-response question received fourteen responses in which all responses stated that the long-term care plan developed for a SARDS patient is adaptive care from the client while the canine is adjusting to life without vision. Of the fourteen responses, nine mentioned that the canine should receive follow-up care with a minimum of a yearly examination. Lastly, the final question asked in this survey was an open-response question for any additional comments the participant would like to add. This question received four total responses, two of which were comments to reach out for clarification of answers or any additional information needed. One response was a question asking if a board-certified veterinary ophthalmologist was involved in the research. Due to confidentiality, no participants' emails were collected, as stated in the informed consent clause. Consequently, there was no means to contact these three participants. The fourth response for transparency will be quoted directly as follows: “There is a plethora of incorrect information on the internet about the treatment of SARDS. Clients should be directed to the ACVO [American College of Veterinary Ophthalmologists] website for accurate information.”

Analysis

This research hypothesized that the only consistent clinical presentation that led veterinarians to suspect that the patient is potentially affected by SARDS was the sudden total loss of vision and that the rest of the clinical presentations would vary. Furthermore, diagnostic techniques used by veterinarians would vary widely, and the use of electroretinography to obtain a confirmed SARDS diagnosis would not be relatively common. Additionally, it was anticipated that the responses to this survey would demonstrate the barriers and difficulties of communicating a SARDS diagnosis and a long-term care plan for patients. The participants of this survey were veterinarians currently employed at either a general practice or a specialty/ophthalmology practice. This survey was widely sent out to veterinarians in all 48 states in the continental United States and emailed to board-certified veterinary ophthalmologists and general practices located in both urban and rural areas, totaling two hundred and twenty-six veterinary practices. The survey received twenty-seven responses, which the title of the survey, "Sudden Acquired Retinal Degeneration Syndrome in Canine Patients Research Survey," could have persuaded disinterest among potential participants of the survey if they had never diagnosed or referred and/or kept track of the amount of SARDS cases they have been involved in. While this survey received responses from only approximately 12% of the total potential participants this survey was disbursed to, the responses received were an approximately equal mixture of general practice and specialty/ophthalmology veterinarians. The mixture, depicted in Figure 5, allows for less probability of skewed results as responses from one group of veterinarians employed at a particular classification of the clinic will not be overly represented than the other. Participants were asked about their insolvency in SARDS cases; 48.1% of participants selected

that they had only diagnosed a SARDS patient. Conversely, 11.1% had never been involved in a SARDS case, and 11.1% of participants had only been the primary veterinarian of at least one SARDS case post-diagnosis. The distribution of participants' involvement in SARDS cases is illustrated in Figure 6, this data shows that the overwhelming majority of participants who completed this survey have had some sort of involvement in a SARDS case during their career. This also conveys that potential participants of the survey may have been persuaded not to complete the survey due to the rareness of the diseases. The rareness of the disease has been previously established in veterinary literature. However, this survey does not accurately depict the rareness of SARDS since 88.9% of participants have provided veterinary care for a SARDS or potential SARDS patient. Due to the lack of responses that indicate that they have not been a veterinarian to a SARDS patient, Figure 7 was created to illustrate the larger volume of SARDS patients seen by specialty/ophthamology veterinarians versus general practice veterinarians. For clarity and transparency, the length of time the participant has practiced veterinary medicine was also included to help demonstrate the infrequency of SARDS patients seen in general practice.

As hypothesized, the most consistent clinical presentation of patients that led to the suspicion of SARDS was loss of vision. Figure 8 shows that 100% of participants have noted the loss of vision, while 54.5% of participants noted polydipsia and 50% noted polyuria followed by weight gain, which was selected by 40.9 % of participants. Nine participants also noted that upon bloodwork of SARDS or potential SARDS patients, they had raised concerns with elevated liver enzyme values, especially elevated alkaline phosphatase. The clinical signs of polyuria, polydipsia, and weight gain, which is usually associated with polyphagia, paired with elevated liver enzymes, are common textbook clinical signs of hyperadrenocorticism. The link between SARDS and endocrine diseases, most commonly hyperadrenocorticism, is controversial and

debated within the veterinary community and veterinary literature. However, as shown in Figure 11, 50% of participants selected that they had treated at least one diagnosed SARDS patient who was diagnosed with hyperadrenocorticism post-SARDS diagnosis, which was followed by 40.9% who had treated at least one hypothyroidism patient post-SARDS diagnosis. Figure 10 shows the distribution of responses that performed diagnostic imaging on a diagnosed or potential SARDS patient. While the majority of responses show that no diagnostic images were performed, one participant who selected that they had used ultrasonography noted that enlarged adrenal glands were found upon ultrasound. There is no way to know if the patient was diagnosed with hyperadrenocorticism based on the survey; however, enlarged adrenal glands are concurrent with that disease. At the time this thesis was composed, no research was published on enlarged adrenal glands found via ultrasonography in SARDS patients.

As anticipated, the survey results demonstrated the various diagnostic tools to rule out other ophthalmic diseases; as seen in Figure 9, the only diagnostic tool that every participant selected was the fundic exam, which is necessary for any examination of a patient who has experienced vision loss. Following the fundic exam, nineteen responses indicated that participants also frequently performed the pupillary light response and the menace response test, while eighteen of the responses indicated that intraocular pressure is also frequently evaluated. As discussed previously in the diagnostic techniques section of the background, chromatic pupillary light response testing can be used to better determine if SARDS is a viable diagnosis option compared to conventional pupillary light response testing. Surprisingly, only seven out of twenty-two participants indicated that they had utilized chromatic pupillary light response testing to aid in eliminating other ophthalmic diseases in potential SARDS patients. Additionally, as mentioned in the diagnostic techniques section of the background, the only way to receive a

definitive confirmation of a SARDS diagnosis is to perform an electroretinogram and obtain results similar to those seen in Figure 4b, in which no retinal function is observed. Fourteen out of twenty-two responses indicated that they had performed electroretinography to diagnose or eliminate SARDS from a potential diagnosis. However, as participants mentioned in the open-response question, shown in Figure 12, there can be various difficulties surrounding obtaining a definitive confirmation of a SARDS diagnosis. These include the availability of electroretinography as well as clients not wanting to check the patient's electroretinogram for varius reasons including affordability. This opens up a discussion on the barriers to veterinary-client communication upon a SARDS diagnosis or the development of a long-term care plan. Figure 13 includes all responses received in an open-response question asking the participant to detail how they communicated with the client. Many participants included the importance of detailed communication with the client and providing written handouts about adjusting to life with a blind animal. Responses also stated that the most challenging part of communicating the diagnosis to the clients is that, at this time, there is no known cause of the disease. However, it has been reassuring to clients to know that their canine companion is in no pain and that a SARDS diagnosis does not negatively affect the animal's quality of life or lifespan. Responses included in Figure 13 also show the controversy surrounding the pathogenesis and treatment of SARDS. Some responses detail that they communicate to the client how SARDS could have manifested as an immune-mediated response and the possible aggressive treatments that have resulted in a few promising outcomes, concurrent with specific scientific journals and hypotheses. Other responses include how the participant communicates to the client that SARDS is an idiopathic disease with no treatment, concurrent with other research journals within veterinary literature. The unknown and controversy surrounding the pathogenesis

and potential treatment of SARDS within veterinary literature only constitutes further research to be conducted.

Conclusion

Veterinary professionals strive to educate and provide resources to further assist clients in adapting to life with a canine companion who has experienced sudden and total blindness. Unfortunately, the most confusing part of a SARDS diagnosis for clients, as indicated by the survey, is that veterinarians cannot provide clients with a treatment plan or explanation of the pathogenesis of SARDS. The unknown nature of SARDS has left veterinary literature and professionals with a multitude of unanswered questions. Various hypotheses have been proposed regarding the pathogenesis of SARDS and the numerous clinical symptoms that canine patients could potentially demonstrate along with sudden total blindness. However, the limited research available on SARDS has left many hypotheses unproven, and some research findings even conflict with these hypotheses. Thus, this complicates the understanding of SARDS even further.

Through a comprehensive literature review and analysis of data obtained from a research survey targeting veterinarians, this thesis has revealed the variation of clinical presentation of SARDS patients along with the multitude of diagnostics techniques used to evaluate ophthalmic function. The research survey highlights how infrequent SARDS patients are seen in general practice versus the amount seen in specialty/ophthalmology practices. Additionally, the research obtained data from the most frequently seen clinical symptoms, the multitude of ophthalmic tests performed and at what frequency, and veterinarians who have treated at least one SARDS patient who had developed an endocrine disease post-diagnosis. This research survey only collected a small amount of data but still demonstrates the most frequent approaches of veterinarians when dealing with a potential SARDS case, as well as the challenges and difficulties of communicating a SARDS diagnosis and long-term care plan to clients. In the future of veterinary medicine, it is

imperative to further investigate sudden acquired retinal degeneration syndrome through the collaboration of veterinarians, researchers, and clients. Further research must first address the need to establish evidence to uncover the pathogenesis of SARDS before the establishment of a treatment plan for patients.

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Appendix A

Online Research Participation Consent

Study title: Sudden Acquired Retinal Degeneration Syndrome in Canine Patients

Primary investigator: Morgan Powell

Faculty Advisor: Dr. Laura Ken Hoffman

You are being invited to participate in this survey as part of research for a Senior Honors Thesis conducted through Murray State University. This form contains information you will need to help you decide whether to be in this research study or not. Please read the form carefully and ask the study team member(s) questions about anything that is not clear.

Nature and Purpose of Project: This survey will be used to investigate Sudden Acquired Retinal Degeneration Syndrome in Canine Patients possibly being linked to other endocrine diseases, as well as the individual Veterinarian's diagnosis process.
Explanation of Procedures: This is a one-time online survey and should take approximately 10-15 minutes of your time.
Discomforts and Risks: There are no anticipated risks and/or discomforts for participants.
Benefits: Participation in this study will not benefit you directly, but will help the veterinary field gather more information to better diagnose and treat patients and formulate long-term care plans for the patient while working with the client.
Refusal/Withdrawal: Participation in this study is voluntary. You are free to leave questions blank or exit the survey at any time with no fear of repercussions. Please answer the questions honestly, there will be no judgment of answers perceived to be “right” or “wrong” by the investigator or involved parties.
Confidentiality: Your participation in this study is anonymous. Neither the researcher(s) nor anyone else will know if you have participated or how you responded. However, we are unable to guarantee the security of the computer on which you choose to enter your responses. Information (or data) you enter, and websites you visit online can be tracked, captured, corrupted, lost, or otherwise misused.

This research is overseen by Dr. Laura Ken Hoffman and Honors College Executive Director, Dr. Warren Edminster.

Any questions about the procedures or conduct of this research should be brought to the attention of the Faculty Advisor: Dr. Laura Ken Hoffman (lhoffman2@murraystate.edu)

If you have any questions about your rights as a research participant, you should contact the MSU IRB Coordinator at (270) 809-2916 or msu.irb@murraystate.edu.

Appendix B

Survey Questions

Sudden Acquired Retinal Degeneration Syndrome in Canine Patients Survey

This survey is part of Morgan Powell's Honors Senior Thesis for Murray State University.

* Indicates required question

1. By checking this box, you are acknowledging that you understand your rights below * (Informed consent document) AND that you are a licensed veterinarian.

You are being invited to participate in this survey as part of research for a Senior Honors Thesis conducted through Murray State University. This form contains information you will need to help you decide whether to be in this research study or not. Please read the form carefully and ask the study team member(s) questions about anything that is not clear.

This survey will be used to investigate Sudden Acquired Retinal Degeneration Syndrome in Canine Patients possibly being linked to other endocrine diseases, as well as the individual Veterinarian's diagnosis process. This is a one-time online survey and should take approximately 10-15 minutes of your time. There are no anticipated risks and/or discomforts for participants. Participation in this study will not benefit you directly, but will help the veterinary field gather more information to better diagnose and treat patients and formulate long-term care plans for the patient while working with the client. Participation in this study is voluntary. You are free to leave questions blank or exit the survey at any time with no fear of repercussions. Please answer the questions honestly, there will be no judgment of answers perceived to be “right” or “wrong” by the investigator or involved parties. Your participation in this study is anonymous. Neither the researcher(s) nor anyone else will know if you have participated or how you responded. However, we are unable to guarantee the security of the computer on which you choose to enter your responses. Information (or data) you enter, and websites you visit online can be tracked, captured, corrupted, lost, or otherwise misused.

Check all that apply.

☐ Yes, I have read and acknowledged the informed consent clause and wish to continue with the survey.

2. How long have you been a practicing veterinarian? *

_____

3. Which best describes the current veterinary clinic you practice at? *

Mark only one oval.

- ◯ General Practice
- ◯ Emergency/Critical Care
- ◯ Specialty/Ophthalmology
- ◯ Other: _____

4. Have you ever diagnosed SARDS in a canine patient or referred a suspected SARDS patient to a specialist? Select all that apply. *

Check all that apply.

- ☐ Yes, I have diagnosed SARDS in a canine patient.
- ☐ Yes, I have referred a suspected SARDS patient.
- ☐ Yes, I have diagnosed and referred SARDS patients.
- ☐ No, but I have been the Primary Veterinarian of a SARDS patient.
- ☐ No
- ☐ Other: _____

If you have diagnosed, referred, or treated a SARDS Patient please continue to this section. If you have NOT, then please submit the form. Thank You.

5. IF YES. Approximately how many SARDS patients have you diagnosed or referred?

_____

6. What are the clinical signs that have led you to suspect SARDS? Select all that apply.

Check all that apply.

- [ ] Loss of vision
- [ ] Weight gain
- [ ] Keratoconjunctivitis Sicca
- [ ] Lethargy
- [ ] Polyuria
- [ ] Polydipsia
- [ ] Hepatopathy
- [ ] Other: _____

7. What specific test did you perform to rule out other ophthalmic diseases? Select all that apply.

Check all that apply.

- [ ] Fluorescein stain test
- [ ] Schirmer tear test
- [ ] Intraocular pressure
- [ ] Pupillary light reflex
- [ ] The menace response
- [ ] Electroretinography
- [ ] Assessment of pupil size, shape, symmetry, and mobility
- [ ] Other: _____

8. Did you perform any blood panels on the patients in which the results raised a concern? If so, please list the values that raised a concern.

_____

_____

_____

_____

_____

9. Did you perform any diagnostic imaging on the SARDS or the suspected SARDS patients?
Select all that apply.

Check all that apply.

- [ ] None were performed.
- [ ] Radiographs
- [ ] Ultrasound
- [ ] MRI
- [ ] CT scan
- [ ] Other: _____

10. If yes, were there any findings on the diagnostic images that raised concerns?

_____

_____

_____

_____

_____

11. Have you seen a diagnosed SARDS patient who was also diagnosed with an endocrine disease post-diagnosis? Select all that apply.

Check all that apply.

- [ ] No
- [ ] Hypoadrenocorticism
- [ ] Hypothyroidism
- [ ] Hyperadrenocorticism
- [ ] Diabetes mellitus
- [ ] Other: _____

12. Can you describe any challenges or limitations you've encountered in diagnosing or the long-term care of SARDS?
How did you address them?

13. How did you communicate and explain the diagnosis and/or long-term care of SARDS to the client?

14. Do you have a general long-term care plan for diagnosed SARDS patients? If so, please provide a brief description.

15. Would you like to add any additional comments?

Appendix C

IRB approval

Institutional Review Board
328 Wells Hall
Murray, KY 42071-3318
(270)809-2916
Msu.irb@murraystate.edu

Date: 02/12/2024

Principal Investigator: Morgan Powell

Faculty Sponsor: Laura Hoffman

IRB Approver: Trent Wells

IRB Reference Number: 24-140

The IRB has completed its review of Exempt protocol Sudden Acquired Retinal Degeneration in Canine Patients. After review and consideration, the IRB has determined that the research as described in the protocol form, will be conducted in compliance with Murray State University Guidelines for the Protection of human participants.

The forms and materials approved for use in this research study are attached to the email containing this letter. These are the forms and materials that must be presented to the subjects. Use of any process or forms other than those approved by the IRB will be considered misconduct in research as stated in the MSU IRB procedures and Guidelines section 20.3.

Your stated data collection period is from 02/13/2024-02/13/2025

If data collection extends beyond this period, please submit a continuation to an approved protocol form detailing the new data collection period and the reason for the change.

This Exempt approval is valid until 02/13/2025.

If data collection and analysis extends beyond this date, the research project must be reviewed as a continuation project by the IRB prior to the end of the approval period, 02/13/2024. You must reapply for IRB approval by submitting a Project Update and Closure form (available at murraystate.edu/IRB). You must allow ample time for IRB processing and decision before your expiration date, or your research must stop until IRB approval is received. If the research project is completed by the end of the approval period, a Project Update and Closure form must be submitted for the IRB review so your protocol may be closed. It is your responsibility to submit the appropriate paperwork promptly.

This protocol is approved. You may begin data collection now.