



## Long Island Veterinary Specialists

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## Steroid Responsive Meningitis Arteritis – Beagles, Boxers, and Beyond, Part 1

Neil S. Mittelman, DVM, DACVIM (LAIM; Neurology)



Compared to other species, dogs rarely get infectious meningitis, encephalitis, or myelitis, but autoimmune/inflammatory causes of central nervous system dysfunction are common. Currently, our efforts as clinicians may be best suited to recognizing clinical signs and breed predilections to allow for expanded differential lists and allow for earlier diagnosis and treatment. Over the last several decades we have stopped naming these diseases after individual breeds (ex. yorkie encephalitis, pug encephalitis, Beagle pain syndrome, etc.), and this may have prevented misdiagnosis based on breed bias. We now recognize that even mixed breed dogs can get these conditions. While a complete discussion of all noninfectious inflammatory diseases of the canine central nervous system is beyond the scope of this article, a thorough discussion of Steroid Responsive Meningitis Arteritis (SRMA) is found below with emphasis on recognizing distinctive characteristics that separate it from other causes of meningitis. Part 1 of this article emphasizes recognition of clinical signs whereas part 2 of this article focuses on diagnostics and treatment. SRMA is an important condition for any veterinary practitioner to have on their differential list for fever of unknown origin as signs are often far less obvious than those of granulomatous meningoencephalitis or other meningoencephalitis of unknown origin.

# What is Steroid Responsive Meningitis Arteritis or SRMA?

Beagle Pain syndrome, necrotizing vasculitis, and sterile suppurative meningitis have all been used in the past to describe the same disorder now known as Steroid Responsive Meningitis Arteritis (SRMA). One of the most common inflammatory diseases of the central nervous system in dogs, SRMA is a systemic immune mediated disease. Although it is best known for inflammation of the spinal leptomeninges, the thin membranes of arachnoid and pia mater covering the spinal cord, as well as affecting the meningeal arteries, further inflammation has concurrently been detected in other vessels including those of the heart causing epicarditis, myocarditis, and even pericardial effusion despite not showing clinical signs of heart disease.

# **A NOTE FROM THE EDITOR** A Note from the Editor (Part 1)



To the reader....

Since the recent passing of my 90th birthday, I was asked to reflect on my 90 years. Thus, this two-part essay is going to be a bit different from what is usually written here as these are the highlights of 90 or so years I've spent on this earth.

### Part one:

I was born and have always lived on an island; born on the largest island in the Mediterranean, Sicily, I was brought to New York by my parents in early 1935 at age 2 1/2 and have lived on Long Island ever since. My parents were born at the turn of the (last) century, my father in 1906 in Brooklyn and my mother in 1910 in Santa Margarita di Belice in Sicily.



My earliest memories are of the days living in a cold water flat on Linden St. in the Bushwick section of Brooklyn, New York. For heat we had a coal burning stove in the kitchen and a gas water heater which barely produced enough hot water to take a bath. Food was kept cold in the "ice box" in the kitchen which was filled every few days by a large block of ice about eighteen inches square which fit in the upper part of the two compartment container. Food was kept on the shelves below and a pan was placed underneath that caught the water from the melting ice - - and had to be emptied daily. Years later when we moved into a "modern" two family house on Cornelia St. in the Ridgewood section of Queens, there was a lead pan on the floor where the icebox stood that had a hole in the back leading to a pipe that led into a sink in the basement eliminating the need to empty the pan. By that time almost everyone had a refrigerator and so the pans were no longer needed.



Our grandparent's siblings had a phone mounted on the wall, with a rotary dial and a "party line" which meant two or more families could use the phones...but not at the same time. We didn't get a phone till 1950 when we lived on Cornelia St.... in neighboring Ridgewood.

My mom worked in a sweatshop sewing pants and my father worked for his Uncle Vito during the early 1940s, the years of WW II. The Daily News was two cents and subway, bus and trolley rides were a nickel.

Cars fascinated me from the time I first arrived in the US in 1935 at just under age 3 and they still do. The first car that fascinated me was a 1936 Plymouth 4 door sedan, dark gray in color, that my grandfather's brother, "Zio Vito", bought in the summer of 1938 for his family. It was a "used" car and it was on display at the corner of Myrtle and Irving Avenues in the Bushwick section of Brooklyn. All cars then were standard shift, three on the floor or on the steering column...only in 1939 and the early forties did automatic transmissions arrive, the Hydra Matic. All cars then were standard shift, three on the floor or on the steering column...only in 1939 and the early forties did automatic transmissions arrive, the Hydra Matic.

Danny, Jimmy, Lenny, big Dominic and Geppy (Gaspare) were strapping youths who had handsome features and tanned muscled bodies, after all, they worked in their father's (and Uncle's) trucking company delivering flour sacks weighing about 130 pounds each to various macaroni makers like La Rosa which they, and my father, loaded onto trucks at the railroad yards in Brooklyn and N.J. and often had to carry up to the second floor storage areas at those plants.



# A Note from the Editor (Part 1) Continued from Page 2

New (but empty) flour sacks with one closed end inverted inwards towards the other were used as hoods and shoulder coverings to help minimize the flour that stuck to their sweat covered bodies. The brand name "Zerega" was stamped on them and they additionally served as very absorbent dish towels when cut down and hemmed! The trucks they were transported on were four cylinder Macks with pistons the size of garbage cans....not to mention chain drives, solid tires, kerosene headlights, and a hand crank to start them. Some even had Isinglass windows in the tarpaulin doors, but no heaters, and they rode on streets which were not all paved. That truck model is on display in the Smithsonian. Later on, balloon tires, heaters, electric starters and headlights, doors and a drive shaft which replaced the chain drive were available, but many of the old Macks were still in use before WW II, which then interrupted and changed all our lives.

In 1939 I was excited as a seven year old to go to Flushing Meadow (where the Mets now have a stadium) but which at that time housed the world's fair. I remember it as a magnificent display of what the future was supposed to bring, in fact General Motors sponsored something called "Futurama" and I distinctly recall the Westinghouse robot, the Trylon and Perisphere too. We went back for the 1964 World's Fair, this time I was with my wife Jane, Ninette was in a stroller and Nick (Dominic) was born a few months later....once again it was a magnificent display featuring the Unisphere which is still there. Following the path of many Italian immigrant children, I attended a local parish church and its parochial grammar school, St Brigid's, then Bishop Loughlin Memorial High School in Brooklyn. It was a Brooklyn Diocesan HS and it took two from each parish and there was no tuition. I took 12 cents to school daily to buy either a half pint of milk or a vanilla ice cream cup (seven cents)...the ice cream always won. I "brown bagged" my lunch from home...veal cutlet, meatball or salami sandwich on what we called american bread –" pane americanu". The nickel left was for the subway , trolley or bus ride to school as we only paid one way.

During my freshman year as a commuting student at Columbia College in NYC, a neighbor informed me that a 1946 Plymouth Special Deluxe Convertible was for sale in the neighborhood for \$800. The Plymouth was a beautiful "Sumac" red color and I excitedly told my father who, after a discussion with my mother, decided to show it to cousin Jimmy, who gave it his OK and so it was bought. What a spectacular first car!

I learned how to drive by first reading about shifting and clutch use in the Encyclopedia Britannica Junior at about 10 years of age, memorizing the steps, then watching my cousins shift while driving and by listening to another of my grandfather's brother's sons, Geppy demonstrate moving through gears synchronously in a 1938 Buick, a rather luxurious car.

In the early fifties, tires still had tubes and flats were hardly rare. We all learned how to fix them and carried patch kits and manual air pumps in the cars. Tires were often "recapped" and even "re-cut", so going 1000 miles flat free was a rarity. In the late forties and fifties, both my parents worked in sweatshops, my father in Manhattan for Ripley Clothes, and my mom about a mile or two away from home in Brooklyn. When I had early college classes, I would rush home by subway, get in the car and go pick her up from work; she was so grateful for the ride. Walking home, she said, saved money which added up to pay tuition for my brother and I. She not only walked but often shopped at the A&P on the way and carried the bags home. Picking her up also meant she could show her coworkers what all the sweat in those shops went for.

In 1953, the beloved Plymouth was traded for a Chrysler Windsor, a four door sedan that made it easier for mom to get in and out. It too had a clutch pedal but the Fluidmatic transmission allowed for minimal shifting.







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## Steroid Responsive Meningitis Arteritis – Beagles, Boxers, and Beyond, Part 1

### Continued from Front Cover

Echocardiogram, ECG, and Cardiac troponin I (CTnI) allowed for diagnosis of cardiac disease. Concurrent polyarthritis and panarteritis evident on post-mortem examination as necrotizing arteritis mostly affects small- to medium-sized vessels of the cervical spinal cord, mediastinum, and heart.

### **Risk Factors**

While meningoencephalitis of unknown etiology is most common in female toy to small breed dogs as young adults (often 3 years to 7 years), SRMA is more common in those from 6-18 months of age. Clinical signs and subsequent diagnosis have been reported from as young as 3 months to as old as 9 years. Frequently, no sex predilection has been observed. One recent study in Europe, however, showed a statistically significant higher occurrence in males (62.7%) vs. females (37.3%). This finding is interesting as other autoimmune conditions (ex. immune-mediated hemolytic anemia and thrombocytopenia) are more common in female and neutered dogs, and although occurrence or SRMA was more common in males relapse was significantly more common in females in that same study. It has been postulated in the past that androgens may protect from the development of immune-mediated disease. It is possible that endocrine imbalances due to heat cycle and stress factors may contribute to these relapses similarly to the development of diabetes mellitus in bitches.

Beagles, Bernese Mountain Dogs, Border Collies, Boxers, English Springer Spaniels, Jack Russell Terriers, Nova Scotia Duck Tolling Retrievers, Weimaraners, Whippets, Golden Retrievers, and German Shorthaired Pointer seem to be predisposed to SRMA. A recent study showed that Beagle and Boxer (fig.1) were affected significantly more often by SRMA than other canine breeds. Breed predisposition and age of onset is important to note as even in chondrodystrophic breeds, disk herniation a potential differential diagnosis is rare



**Figure 1:** Boxer with low head carriage due to cervical discomfort. Beagles and Boxers were the most common breeds affected by SRMA in one study.

at less than 1 year of age and would be even less common in many of the aforementioned large breed dogs.

### **Clinical Signs**

Both acute and chronic forms of SRMA have been described. In the acute form overt neurological deficits in gait or proprioception are uncommon; however, reluctance to walk and a stiff gait may be seen. Typical acute signs include fever, cervical hyperesthesia, and lethargy. Other signs reported include decreased appetite, kyphotic posture (likely associated with low head-carriage), and tremors. In one study only 65.6% of dogs were febrile on hospital admission with a rectal temperature >103°F (range 100.4°F-106.2°F). Thoracolumbar pain was also elicited on spinal palpation in 34.4% of dogs. Important differential diagnosis includes diskospondylitis, infectious and autoimmune causes of polyarthritis, bacterial meningitis, and other significant systemic infection. It is not uncommon for a young dog with a history of reluctance to move, fever, and elevated white blood cell count characterized by mature neutrophilia to initially be evaluated for fever of unknown origin and treated with broad spectrum antimicrobials without improvement prior to neurological evaluation. Severe discomfort due to intervertebral disk herniation and hyperpnea due to pain and/or anxiety can result in temperature elevation, so allowing the patient to relax as much as possible prior to checking the temperature is advised.

# Steroid Responsive Meningitis Arteritis – Beagles, Boxers, and Beyond Part, 1

### Continued from Page 5

Unlike other autoimmune causes of meningitis in dogs but consistent with its role in systemic vasculitis SRMA very commonly results in CBC abnormalities, which can aid in directing further testing. Cerebrospinal fluid abnormalities likewise often include neutrophilic pleocytosis (fig.2) and increased total protein, so the much less common condition of bacterial meningitis should be ruled out with imaging. I personally have treated a young Golden Retriever referred for possible SRMA, which after imaging and CSF analysis was diagnosed with focal meningitis in the cervical region secondary and subsequent infection due to trauma from chewing on a stick.

Accurate detailed history and general physical examination cannot be emphasized enough when dealing with puppies as nonspecific signs of fever and reluctance to walk could be due to many causes (ex. foreign body obstruction/perforation and subsequent peritonitis, other causes of sepsis, or a variety of conditions affecting the physes or other areas of the appendicular skeleton).

Concurrent autoimmune nonerosive polyarthritis may be more common than initially described. In one study 46% of dogs with autoimmune polyarthritis and spinal hyperesthesia had abnormal CSF analysis consistent with aseptic meningitis. The chronic form of SRMA is characterized by recurrent episodes of cervical and/or multifocal spinal hyperesthesia, paresis, and ataxia with deficits more typical of a myelopathy easily mistaken for multifocal intervertebral disk disease.

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# A Note from the Editor (Part 1 of 2) Continued from Page 3

During my junior year at Columbia, with the Korean War in a tenuous armistice, the US Army directed me to Whitehall St. in lower Manhattan, thence to Ft. Dix, N.J. for infantry training. It was still uncertain if things would heat up again, so on Dec 7, 1953, on the anniversary of Pearl Harbor, I became recruit "slick sleeve" Marino. While serving in Germany, I took a trip to northern Italy to visit relatives who lived in Padua (Padova) while on leave. They told me that American students were enrolled in the faulty of medicine at the university there, so I contacted a few and they encouraged me to apply through the Italian Consulate in N.Y. to study medicine in Italy. Upon returning to the states in September of 1955, I re enrolled at Columbia and graduated in the summer of '56. I had already applied through the consulate and was accepted.

I initially enrolled at the university of Padua, a graduate of which was Sir William Harvey (1602) who first described the circulatory system in detail. After two years I transferred to and graduated from the university of Bologna, the oldest existing medical school in the oldest existing university in the world; est. 1088 AD the "Alma Mater Studiorum."(The Nourishing Mother of Studies).

While there, it was hard to miss the incredible beauty of Italian cars and I vowed one day to own one. That comes later....

### Leonard J. Marino, MD, FAAP, LVT



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Michel Selmer, DVM MS, CTCVMP, CVMMP

# **Case Report: Strange Cause of Exophthalmos in a Young Dog**

John S. Sapienza, DVM, DACVO



"Mika", a one year old MaltiPoo castrated male dog presented with an apparently acute onset of periocular swelling and prominence of the left eye (Figure 1). Appetite and demeanor were normal. The ophthalmic evaluation demonstrated a normal Schirmer tear testing-OU, normal intraocular pressures -OU and a negative fluorescein corneal staining-OU. The third eyelid was elevated, and there was periocular swelling, diffusely, around the left eye which was visual. Pain could not be elicited upon retropulsion of the globe or opening the mouth, however, a lesion, a traumatic wound, was noted behind the last molar tooth.



**Figure 1:** *Clinical presentation. This young MaltiPoo presented with exophthalmos that was not painful upon globe retropulsion and not painful upon opening the mouth.* 

Indentation of the posterior sclera was not observed upon fundus evaluation. Our suspicions were that of an orbital abscess or cellulitis, but pain is usually prominent with these diseases of the orbit. Oral antibiotics for both aerobic and anaerobic infections were prescribed as well as an ophthalmic triple antibiotic ointment. Pain medications in the form of gabapentin were also advised. At the 10 days recheck examination, the owner reported that the dog was improved, but ophthalmic evaluation did not demonstrate any improvement at all with the exophthalmos. In fact, the swelling appeared worse, and a very ulcerated oral mass lesion was observed around the last premolar tooth on the left side of the maxilla.

A CT scan was advised in addition to potential retrobulbar cytology, biopsies, or drainage. The oral lesion would also be biopsied as deemed appropriate by the surgical department. The CT scan examination including a non-contrast series of the head extending from the nasal planum to the level of C2 was performed. Centered at the caudal ventral aspect of the left orbit was an exceptionally large 1.8 cm diameter soft tissue mass. This mass caused focal thinning and punctate lysis of the ventral aspect of the orbit and temporal bones. Rostrally, there was lysis of the ventral medial aspect of the left orbital bone and extension of the soft tissue component of the mass into the ventral aspect of the left nasal passage. Multifocal geographic to moth-eaten osseous lysis was present along the entirety of the left maxilla, extending to the level of the left maxillary canine tooth. Numerous left maxillary teeth were suspended within the soft tissue mass. The left eye was moderately to severely dorsolaterally displaced subsequent to the large retrobulbar mass (Figures 2a and 2b, Figure 3).



**Figure 2a:** *CT* scan scan of the patient demonstrating soft tissue mass in the ventral slot.



**Figure 2b:** *CT* scan demonstrating focal thinning and lysis of the ventral aspect of the orbit and temporal bones.

# **Case Report: Strange Cause of Exophthalmos in a Young Dog**

Continued from Page 8



**Figure 3:** *CT Scan - reconstruction demonstrating osseous lysis along the entirety of the left nasal maxilla.* 

CT scan conclusions: Large retrobulbar soft tissue mass. Neoplasia is prioritized.

Multifocal calvarial and orbital lysis on the left.

An oral biopsy of the mass surrounding the maxillary lesion was obtained and sent to a regional laboratory for histopathological analysis. The specimen contained portions of the mass that was composed of neoplastic round to polygonal and spindle-shaped cells arranged in sheets and streams. Atypia was prominent with 26 mitoses per high power fields. The microscopic interpretation was one of a poorly differentiated primitive malignant neoplasia with a possibility of an embryonal rhadomyosarcoma. Such neoplasms of the young dog can frequently metastasize. Regardless of the histogenesis, this is an aggressive malignancy with a high metastatic potential.

The patient was referred to an oncologist, but the overall prognosis was quite grave. This is an uncommon orbital neoplasm in young dogs and carries a grave prognosis with high likelihood of metastatic disease.

Any questions or concerns, please do not hesitate to contact us.

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Vials contain a prescribed dose up to 6.0 mCi (222 MBq) at the date and time to treat one dog.1 mL of suspension contains 2–4 mCi (74–148 MBq) of tin ( $^{11m}$ Sn) stannic colloid in ammonium salt at the date and time of end use.

#### PRODUCT DESCRIPTION

Synovetin  $OA^{\oplus}$  is a conversion electron therapeutic veterinary device comprising a colloidal, sterile suspension with a pH between 6.5 and 9.0 where at least 90% of the particles have a size between 1.5 µm and 20 µm (HORIBA light scatter instrument). The <sup>1170</sup>Sn emits monoenergetic conversion electrons (significant energies 127–158 keV; emission probability 113%) and imageable gamma radiation (159 keV, 86% abundant). Accompanying low-energy emissions are Auger electrons (<22 keV) and X-rays (<30 keV). The half-life of <sup>1170</sup>Sn is 14 days. 117mSn decays by isomeric transition to stable <sup>117</sup>Sn.

Excipients include ammonium carbonate ((NH,) 2CO.), ammonium chloride (NH,CI), ammonium iodide (NH,I), iodine (I.) and trace tin (Sn) salts.

#### MECHANISM OF ACTION

Synovetin OA® is a veterinary device consisting of a homogeneous tin colloid which emits discrete (<300 µm) low-energy conversion electrons confined to the joint space. The colonity is composed of microparticles (1.5 µm to 20 µm) that are retained in the joint space of the dog. The particles are absorbed and retained by synovicytes and macrophages in the synovium, resulting in apoptosis and reduction of inflammatory cells. Elimination of the pro-inflammatory cells reduces inflammation of the joint synovium, thereby reducing pain associated with synovitis. The data, including radiographic evidence, supports use in Grade 1, 2, and 3 osteoarthritis (OA) of the elbow joint.

#### CAUTION

Federal law restricts this device to sale by or on the order of a licensed veterinarian trained in the use of radioactive veterinary medical products. Use of this product is restricted to facilities with a compatible Radioactive Materials (RAM) license

#### INTENDED USE

Synovetin OA® is intended to reduce synovitis and associated pain of canine elbow joints afflicted with osteoarthritis.

#### WARNINGS

Do not exceed 6.0 mCi (222 MBq) of radiation activity per dog per treatment. Not for use in humans. Keep this and all medications out of reach of children. Consult a physician in case of accidental injection or ingestion by humans.

#### PRECAUTIONS

Injection should be performed only by a licensed veterinarian skilled in the delivery of intra-articular (IA) injections who is located at a facility that has a RAM license.

Rigorous aseptic technique must be ensured during injection

#### BOUTE OF ADMINISTRATION

Intra-articular injection. The product must NOT be administered by any other route. Confirmation of needle placement is recommended, whether by anatomical landmarks, fluoroscope, C-arm, ultrasound, or radiography,

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June 2022

EXN-SYN-190



#### DIRECTIONS FOR ADMINISTRATION

E S S S S

Dogs should be appropriately anesthetized or deeply sedated prior to administration to prevent vocalization and resistance to dosing. A 22-ga. needle can be used to inject Synovetin OA® directly into the elbow joint. Pain during and after treatment may occur Administration of non-steroidal anti-inflammatory agents at the labeled dose may help any post-treatment pain

#### FREQUENCY OF ADMINISTRATION

If needed, Synovetin OA® can be readministered to a previously treated elbow at least 12 months after the last treatment. DURATION OF EFFECT FROM ADMINISTRATION

Effectiveness has been shown to last up to 12 months following a single treatment of dogs with naturally occurring OA of the elbow MAXIMUM ANNUAL DOSE

Total radiation dose per joint should not exceed 3.0 mCi/joint, with the total body dose not exceeding 6.0 mCi (i.e., two elbow joints during a 12-month period).

#### ADVERSE REACTIONS

Dogs participating in clinical studies to evaluate safety and effectiveness (n=74 dogs, 97 elbow joints) exhibited no significant adverse reactions when administered Synovetin OA®. Discomfort in the treated elbow has been rarely reported in some dogs up to 72 hours after treatment. If adverse events are observed or suspected, please report them by calling Exubrion Therapeutics<sup>6</sup> Customer Service at 1-833-942-1247

#### POST-INJECTION CARE

Following administration of Synovetin OA®, the dog can recover with other post-operation animals in the general clinic population. Once the dog has fully recovered from anesthesia, it can be discharged to go home with the approval of the facility radiation safety officer or authorized user. All treatment site policies and license requirements should be observed.

#### **OWNER INSTRUCTIONS FOR POST-TREATMENT CARE**

When the level of radiation is determined to be below the established levels for release, the dog can be discharged. The dog will, however, retain a low level of radioactivity in the treated joint(s) for a short period of time. Specific written instructions based on the post-treatment radiation dosimetry for care and proximity to the treated dog will be provided by the radiation safety officer (RSD) or authorized user (AU) of a radioactive materials (RAM)-licensed veterinary hospital to the dog owner. These instructions include information on limiting proximity to the dog in the post-treatment period. If in the judgement of the veterinarian, the dog owners are not likely to comply with the release instructions, the product should not be administered. A RAM-licensed veterinary hospital RSO or AU should contact Exubrion Therapeutics® if there are specific questions. Apart from the proximity requirements to protect people there is no requirement for restraint of the dog itself, and it can resume its normal level of activity subject to the distance requirements.

#### MANUFACTURED BY Theragenics Corporation for Exubrion Therapeutics®

Manufacturer's contact information: Theragenics Corporation 5203 Bristol Industrial Way Buford, GA 30518 Customer Service Phone: 833-942-1247 info@exubrion.com

#### STORAGE INSTRUCTIONS

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## **DVM Video Sessions**



**24/7 video telehealth** services provided by experienced, US-based veterinarians that triage client-perceived pet emergencies. Connect in minutes, no software downloads or appointments needed, connect in minutes in 3 easy steps from any computer or mobile device.

### Maintain Veterinary Quality of Life



Eliminate the need for a veterinarian or technician to be on-call after-hours and overnights. This has shown to **substantially improve recruitment efforts** for new vets and technicians for clinic partners.

## Your Cases Stay Your Cases 🔁

VetTriage is a **seamless extension of your clinic**, and are recommended to follow-up with you, their primary veterinarian. A session summary is emailed to both your office and your client allowing you to reference their triage session and insert it into the medical records.

## No Cost to the Clinic

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VetTriage services are offered at **no cost to your clinic!** The client pays a small triage session fee to video chat with our veterinarians. Save money by eliminating the need for an after-hours answering service, whom are not medically trained and a source of frustration for the client.

### Cases are Triaged for Actual Emergencies

Nearly 80% of cases do not require a visit to the ER and the unnecessary expense associated with it. These cases are given advice and are re-directed back to the clinic for follow-up, diagnostics, and treatment. While actual emergencies are sent to the ER for immediate evaluation.

# Enhance Client Loyalty and Trust

Instill comfort in your current clientele that a reliable and experienced telehealth service is available during times of limited office hours and for emergency triage during after-hours, overnights, and holidays.

For more information contact our medical director Shadi Ireifej, DVM, DACVS at (845) 527-9812 or shadi.ireifej@vettriage.com





Where You Refer Your Patient First Makes All The Difference



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