LIVS IN PLAIN VIEW

Long Island Veterinary Specialists

Where You Refer Your Patient First Makes All The Difference

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JULY/AUGUST 2021
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Management of Recurrent & Prolonged Seizures, *Part 1: Terminology & Pathophysiology*

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This newsletter is the first of several parts on the management of recurrent and prolonged seizures. Part 1 addresses terminology and the pathophysiology of seizures. Parts 2,3 and 4 address respectively cluster seizures (CS), status epilepticus (SE) and refractory status epilepticus (RSE).

Terminology:

The International veterinary epilepsy task force (IVETF) issued in 2015, several consensus proposals and a report on epilepsy terminology; a reminder is always helpful at the start of a discussion.

The term seizure refers to any sudden, short lasting and transient event. It does not imply that the event is epileptic in nature (i.e., no implication regarding possible repeated events or underlying cause, since epilepsy implies a recurring disorder as explained below).

Epilepsy is defined as an enduring (i.e. persistent/recurring) brain disorder triggering epileptic seizures, with at least two unprovoked epileptic seizures >24 h apart. Although it is often used to mean "idiopathic epilepsy" the two terms are not strictly synonymous as epilepsy can also be structural (see page 5).

Classification/Types of Epilepsy by etiology

Idiopathic epilepsy is understood as encompassing a group of conditions, which can be categorized into three sub-groups:

1. **Idiopathic epilepsy (genetic epilepsy)**: genetic background for epilepsy has been identified.
2. **Idiopathic epilepsy (suspected genetic epilepsy):** "a genetic influence supported by a high breed prevalence (>2 %), genealogical analysis and/or familial accumulation of epileptic individuals".
3. **Idiopathic epilepsy (epilepsy of unknown cause):** the etiology is yet unknown but without indication of structural epilepsy.

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Long Island Veterinary Specialists

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Dermatology Department

Who are we?

Our consulting board-certified dermatologists are experts in the diagnosis and treatment of your pets' dermatologic issues. You will receive a timely and accurate diagnosis and speak with specialists who have knowledge in the most up-to-date treatments and procedures. Our Dermatology Team will address all problems associated with your pet's specific skin and/or allergy diagnosis.

Conditions commonly seen by our Dermatology Department:

- Adverse drug reactions
- Allergic skin disease (atopy)
- Autoimmune skin disease
- Bacterial skin disease (pyoderma)
- Ear disease (otitis)
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- Flea allergy dermatitis
- Foot disease (pododermatitis)
- Fungal skin disease
- Genetic and congenital skin diseases
- Hair loss (alopecia)
- Hot spots (acute moist dermatitis)
- Immune-mediated dermatoses
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- Yeast infections

Services offered include:

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- Cytological evaluation
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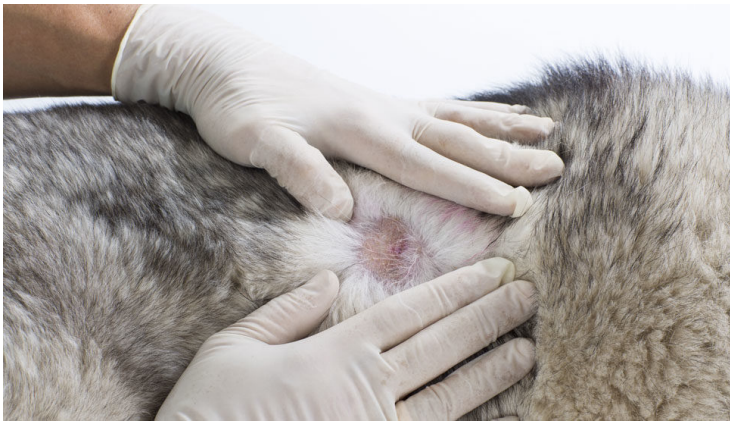
- Skin scrapings, cytological evaluations, skin biopsies



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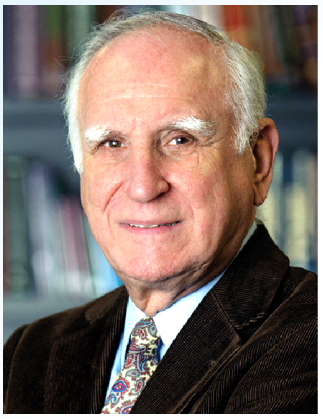
A NOTE FROM THE EDITOR



The warm, actually hot, days of summer hit in late June with temperatures approaching – even surpassing – 100 degrees. Even Olympic track and field trials were delayed into the evening hours as the readings in the stadiums reached 107 degrees.

When walking our dogs, we must keep in mind that it is feels hot enough to fry an egg outside, it probably is. When the air temperature is 86 degrees, the asphalt can reach a sizzling 135 degrees – and it can affect our canine companion's sensitive paw pads, causing burns, permanent damage, and scarring after just one minute of contact.

Rapids burns and blistering can occur at 150 degrees. Hot sidewalks, pavement and parking lots cannot only burn paws, they also reflect heat onto dogs' bodies, increasing their risk of deadly heatstroke.

If you wouldn't put your dog in a frying pan, please don't make him or her walk on hot pavement. Always test the pavement with your hand before setting out (too hot to touch is too hot for Spot), walk early in the morning or late at night when it's cooler, carry water, and take frequent breaks in shady spots, and never make dogs wear muzzles that restrict their breathing. Leaving pets and kids inside cards in the sun is cruel and dangerously life-threatening.

Construction at LIVS continues at a faster pace as COVID wanes on Long Island, however new variants are appearing, and caution is still being practiced. Although the CDC and NYS have relaxed their positions on mask wearing, LIVS will continue with its current policy of mask wearing until further notice. We believe social distancing, when possible, and mask wearing provides a safe environment for all team members.

In the news, besides the avalanche of political commentary, newer experiments using cells from animals and humans have emerged leaving much to be decided, and soon...as experiments strain the limits of what was once considered forbidden areas. A recent study on human cells in Petri dishes allowed growth of the tiny spheres until day 13 when all was halted. That's when the embryo starts to form a body plan deciding where the head will end up and when cells begin taking on special missions.

Recently, researchers created a human-pig hybrid. This creature is called a "chimera" – a name, as Merriam Webster says, is taken from a monster in Greek mythology that was part lion, goat, and serpent. The research was published in the journal *Cell* and reported in *National Geographic* and *ScienceDaily*. To create the chimera, researchers fertilized a pig embryo and then inserted human stem cells. The human cells were pluripotent stem cells, meaning they can develop into cells of any type. For example, given the right conditions, a pluripotent stem cell could develop into a neuron, a heart-muscle cell, or a skin cell.

Construction at LIVS is moving at a faster pace. Here, see the progress on the exterior of the hospital.

While construction continues, all our departments remain fully staffed to serve our patients all hours of every day and night.

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A NOTE FROM THE EDITOR

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So, the human stem cells combined with the pig cells, creating a single human-pig creature, albeit with many more pig cells than human cells. The researchers allowed the chimeras they created to gestate in a pig for three to four weeks before terminating them for further study.

The researchers' someday goal for this line of research is to end the need for organ donation. Say a patient suffers from kidney failure. If the chimera research sufficiently progressed, then a doctor could simply harvest cells from that patient and combine them with a pig embryo to make a sort of personal chimera. The chimera would then gestate, be born, and grow into adulthood, hopefully at the accelerated pace of pigs. If the research met our hopes, the now-adult chimera would have fully human organs of the same genetic makeup as our patient. The chimera's kidneys would then be harvested and transplanted to our patient, who could then expect a full recovery.

The immediate benefits over organ donation are obvious: no wait (and thus no patients dying on organ-donation waiting lists), much lower coordination costs (because the chimera's organs could be harvested at a predictable time and place), and no chance of organ rejection by the patient's body (since the organs would be genetically matched to the patient).

Imagine, though, pigs with human hearts or mice whose brains have a spark of human intelligence. In the latest advance, researchers in the U.S. and China announced recently that they made embryos that combined human and monkey cells for the first time.

So far, these human-monkey chimeras (pronounced ky-meer-uhs) are no more than bundles of budding cells in a lab dish, but the implications are far-reaching, ethics experts say. The use of primates so closely related to humans raises concerns about unintended consequences, animal welfare and the moral status of hybrid embryos, even if the scientific value of the work may be quite high.

But what if our researchers had announced the creation of a chimera comprising a single pig cell in an otherwise all-human-cell body. They then detailed their plan to gestate this mostly human chimera for nine months, mature it for 18 years, and then to promptly harvest its organs.

Such an announcement would not be warmly received. Indeed, I expect we would respond with condemnation. If this expectation were true, then it seems we should have answered the following question before we traveled down the chimera rabbit hole: how much of a human can a creature be, before it is a human?

Yet to draw this line, we cannot simply rely on the number of human cells in the chimera—as in, the more human cells the creature has, the more human it is. In other circumstances the mere number of cells in a creature doesn't make it more or less of what it is. A fertilized human egg is an individual human, despite the fact that this human is, for a short time, only one cell.

A seriously complex issue, and guidelines need to be created soon because science will create more of these chimeras, and we need to know where the science and morality take us.

We are pleased to be able to continue to extend hours for consultation in all our departments to serve our referring community and our clients more efficiently. Appointments can be made through our telephone receptionists at 516 501-1700.

We continue to welcome input and opinions which may be directed to the editor at *lmarino@livs.org*.

-**Leonard J. Marino, MD, FAAP, LVT**

Management of Recurrent & Prolonged Seizures, Part 1: Terminology & Pathophysiology

Continued from Front Cover

The most common type of seizures in dogs with Idiopathic epilepsy is focal seizures with secondary generalization (often in the form of facial focal twitching and ptyalism during the focal seizure, with tonic/tonic-clonic movements in lateral recumbency after generalization).

Structural epilepsy is defined as epileptic seizures due to an identified intracranial pathology such as neoplastic, inflammatory/infectious, cerebrovascular, traumatic, malformation, and degenerative diseases, confirmed by "diagnostic imaging, cerebrospinal fluid examination, DNA testing or postmortem findings".

Classification of seizures by etiology (i.e. underlying cause of the seizures):

Epileptic seizures are most commonly self-limiting manifestations (i.e., they will usually stop by themselves) of excessive synchronous, epileptic activity of neurons in the brain. The resulting signs are temporary, short episodes characterized by convulsions or focal motor, autonomic or behavioral features and due to abnormal excessive and/or synchronous epileptic neuronal activity in the brain.

A **reactive seizure** is a naturally occurring response from a normal brain (i.e. non-epileptic) to a transient disturbance in function resulting in changes in the brain humoral environment (metabolic or toxic in nature), which is reversible when the cause and brain environment is corrected.

Classification by seizure semiology (seizure type classification):

Focal epileptic seizures are "characterized by lateralized and/or regional signs (motor, autonomic or behavioral signs, alone or in combination). The ictal onset is consistent from one epileptic seizure to another. They may be discretely localized or more widely distributed. With focal epileptic seizures, the abnormal electrical activity arises in a localized group of neurons or network within one hemisphere. The clinical signs reflect the functions of the area or areas involved." Focal epileptic seizures can manifest with various clinical signs:

- **Motor** (characterized by abnormal motor activity: e.g. facial twitches, rhythmic blinking/twitching of facial muscles, repeated rhythmic jerks of one or several limbs and/or of the head)
- **Autonomic** (characterized by involvement of the autonomic nervous system, with often parasympathetic and epigastric components: e.g. mydriasis, ptyalism, vomiting)
- **Behavioral** (temporary and unexplainable/inappropriate behavior change: e.g. unusual clinginess/attention-seeking behavior, restlessness, unusual anxious/fearful behavior)

Focal epileptic seizures may remain focal (with only regional cerebral involvement and lateralized/regional clinical signs) or may undergo secondary generalization with bilateral cerebral involvement (propagation of the abnormal activity, initially limited to a localized network of neurons in one hemisphere, to larger cerebral area/networks involving both hemispheres). In the latter, clinical signs of focal seizure with motor, autonomic and/or behavioral signs (initially limited to one/several areas of the body) quickly changed into a convulsive stage with loss of consciousness and bilateral tonic, clonic or tonic-clonic activity.

Generalized epileptic seizures are "characterized by bilateral involvement (both sides of body and therefore both cerebral hemispheres involved)". They can occur de novo or from a focal epileptic seizure with secondary generalization. The latter is the most common form of seizures in dogs, although the initial focal onset can be extremely short and missed by the owners/clinician. The most common manifestations of generalized epileptic seizures in companion animals are tonic, clonic or tonic-clonic epileptic seizures. Generalized epilepti seizures can be **convulsive** (tonic, tonic-clonic, clonic, myoclonic) or **non-convulsive**. Generalized convulsive epileptic seizures include loss of consciousness (except myoclonic seizures) and are often accompanied with urination, defecation and ptyalism.

Generalized convulsive epileptic seizures can be: Tonic (with increased muscle contraction for seconds to minutes), Clonic (with involuntary contraction of groups of appendicular and/or axial muscles resulting in rhythmic movements), Tonic-clonic (with alternating tonic and clonic phases) **(see Figure 1)**, Myoclonic (with bilateral jerking movements).

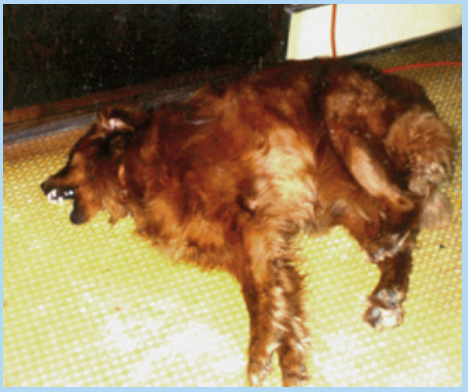

Fig. 1 - Dog with tonic-clonic generalized seizure. Note the lateral recumbency, loss of consciousness, and tonic component (from the Canine Epilepsy Network website: http://www.canine-epilepsy.net/basics/basics_index.html)

Non-convulsive generalized epileptic seizures are also called Atonic seizures, characterized by a sudden loss of muscle tone, involving limbs, trunk and/or head musculature (with possible collapse), with no previous myoclonic or tonic event.

The mechanisms underlying normal seizure initiation and termination are relevant to the treatment of seizures, and their abnormal repetition in cases of CS or absence of termination in cases of SE/RSE.

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Management of Recurrent & Prolonged Seizures, Part 1: Terminology & Pathophysiology

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Seizure initiation:

Epileptic seizures are the results of an excessively synchronous and sustained discharge from a group of neurons. Neuronal activity is dependent on the ionic milieu of the neurons (that is, the extracellular and intracellular concentrations of ions such as sodium and potassium influencing the transmembrane potential and the likelihood of depolarization). After depolarization, synaptic transmission may begin the spread of the discharge. The major inhibitory and excitatory pathways involved in synaptic transmission are respectively GABA-ergic (γ-aminobutyric acid), mediated mostly through GABA-a receptors, and Glutamatergic pathway, mediated mostly through NMDA receptors (N-methyl-D-aspartate).

Synchronization is the mechanism by which a network of neurons becomes involved in the initial discharge and is required for a seizure to occur. Different mechanisms are involved in synchronization such as growth of axon collaterals of excitatory neurons, increased number of glutamatergic interconnections, and increased number of GAP junctions (facilitating rapid synchronization by offering a low-resistance pathway). Generalization (or secondary generalization) is the mechanism whereby an initially focal onset seizure (that is, starting from a specific and limited area of the brain) generalizes and involves the entire cerebral cortex.

Seizure termination under normal circumstances:

Seizures are most commonly self-limiting events, which will terminate without therapeutic intervention. At the scale of a single neuron, the mechanisms of seizure termination involve calcium and sodium intracellular entry creating potassium efflux. The resulting changes in transcellular membrane ion gradients and cellular energy depletion are responsible for cessation of the neuronal discharge. At the scale of a network of neurons, the main mechanisms of seizure termination include synaptic inhibition by presynaptic release of the inhibitory neurotransmitter gamma amino-butyric acid (GABA), glutamate depletion (due to sustained burst creating depletion of the synaptic vesicles containing glutamate), acidification of the intra- and extracellular space (with resulting changes on transmembrane transport), and glial buffering of glutamate.

Parts 2, 3, and 4 will address respectively cluster seizures (CS), status epilepticus (SE) and refractory status epilepticus (RSE).

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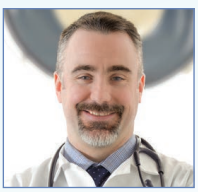

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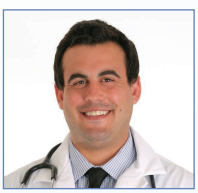

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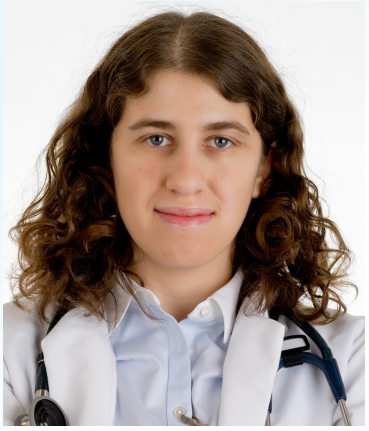
Hemoabdomen and Pericardial Effusion in Dogs: Basics of Diagnosis and Stabilization

Caroline Kramer, DVM, Emergency Staff Clinician



Hemoabdomen presentation is unfortunately a common emergency at veterinary hospitals. Generally, these patients are geriatric large breed dogs (with Golden Retrievers, Labrador Retrievers, German Shepherds being at particularly high risk, although all large breed dogs are at elevated risk and any dog is susceptible) with no related health history. Presentation typically includes a history of being completely apparently normal, or sometimes acting "off" for a few days, with an acute onset of lethargy, inappetence, vomiting, or collapse. Astute owners may notice pale or even white mucus membranes. Patient status on presentation depends on the interval since onset of signs and severity of initial bleed, but in most cases, they will be in some state of shock. Depending on the level of shock compensation and blood loss, mucus membrane color will range from normal to pale to sometimes white; pulses are often thready, or faint and the patient may present alert and ambulatory to laterally recumbent and dull to obtunded. Abdominal pain can usually be elicited during palpation on physical exam, and a palpable fluid wave can often be detected.

Although clinical suspicion alone can place a hemoabdomen high on the list of differential diagnoses, fluid analysis is necessary for a definitive diagnosis. Ideally, fluid should be obtained via ultrasound guided abdominocentesis. If there is a large amount of fluid, a blind tap can be attempted in the most centrally dependent area. Differentials for fluid in the abdomen include, but are not limited to, low oncotic pressure, hypoalbuminemia, right-sided congestive heart failure, portal hypertension, neoplasia, chylous effusion, sepsis, chemical peritonitis, and hemorrhagic effusion. One should confirm hemorrhagic effusion by placing the fluid in a white top tube and taking a PCV/TS. Hemorrhagic effusion will have a PCV/TS comparable to that of peripheral blood, and due to the consumption of clotting factors will not clot in a white top tube. Top differentials for internal bleeding include thrombocytopenia/coagulopathy, trauma, and a ruptured mass. Physical exam and history should identify the cause. Patients with thrombocytopenia or coagulopathy should have signs of bleeding into other body cavities, petechiation, ecchymoses, and/or bruising. Patients with traumatic causes of hemoabdomen should have a history and other signs of trauma.

These patients can decompensate quickly, especially in the case of trauma or rupture of an abdominal mass, so rapid stabilization is necessary. If possible, veterinarians should place an IV catheter and get rapid bloodwork; at the minimum, a PCV/TP should be taken to determine how much of a patient's declining status is due to fluid loss versus anemia from blood loss. However, PCV takes some time to catch up to the amount of blood loss after massive hemorrhage. During initial stabilization, administer crystalloid fluids in quarter shock bolus increments (20 mL/kg over 15-20 minutes) until blood pressure has stabilized to approximately 90-100 mmHg systolic, however, one needs to be cautious to avoid overzealous fluid administration, as this runs the risk of accelerating blood loss and causing exsanguination. Blood transfusions are often necessary, and ultimate treatment usually requires emergency exploratory surgery to identify and remove the source of hemorrhage.

Owners should be thoroughly informed on findings, possible differentials, and treatment before transport so they can make a fully informed decision on whether to proceed. Ruptured abdominal masses usually arise from the spleen or liver but can arise from any organ. They are often characterized as invariably neoplastic, but this is not the case. A common "rule of thumb" is that approximately ⅔ of splenic masses are neoplastic, and of those approximately ⅔ are particularly aggressive hemangiosarcomas. Recent studies, however, suggest that up to 50% of splenic masses are benign, and that a splenectomy will be curative. Regardless, treatment requires significant investment, and the outcome will usually not be known until biopsy results are received several days after surgery. Specialty veterinary facilities are well-equipped to manage post-surgery care, which includes monitoring for continuing hemorrhage and often blood transfusions, monitoring, and intervention for arrhythmias such as ventricular premature complexes which are common after splenectomy, and possible secondary effects of shock such as renal injury and DIC.

A related condition that has a similar presentation of acute collapse is that of pericardial effusion. These patients will also present with acute lethargy and collapse. On physical examination these patients will often be quiet and sometimes are recumbent. Ascites from right sided congestive heart failure secondary to compression of the right ventricle may be noted; this fluid should be a pure transudate. Heart sounds are often muffled due to the presence of fluid. An ECG will often show electrical alterans, or the rhythmic alteration in QRS complex amplitude secondary to the heart swinging back and forth in fluid. Thoracic ultrasound will show the heart surrounded by dark fluid. Take a look at enough of the heart to rule out pleural effusion.

One of the top differentials for pericardial effusion is hemorrhagic effusion secondary to hemangiosarcoma. Cardiac hemangiosarcoma is usually found on the right atrium or auricle.

Hemoabdomen and Pericardial Effusion in Dogs: Basics of Diagnosis and Stabilization

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Chemodectomas are less common tumors—though brachycephalic breeds are at higher risk—that arise on the aorta and cause pericardial effusion. Rarely, severe congestive heart failure with associated structural heart changes can cause rupture of the heart muscle and bleeding into the pericardial space. Sometimes pericardial effusion is idiopathic; no cause can be identified.

These patients can decompensate rapidly, and sudden death can occur without warning. As such, veterinarians should attempt pericardiocentesis before transporting or referring to a specialty hospital for further workup, especially if the patient is already in a state of shock or right-sided congestive heart failure. To perform a pericardiocentesis, clip and aseptically prepare the right ventral thorax between the 4th and 6th ribs, and locally anesthetize with lidocaine if possible. Place the needle cranial to the ribs to avoid injecting the intercostal vessels and nerves. Using the guidance of an ultrasound if possible, pierce the pericardial sac with a butterfly needle or catheter, according to user preference. Analyze the fluid much as one would abdominal effusion. Pericardial effusion may drain in time with the patient's heartbeat. The pericardial sac may slip off the needle and be unreachable as fluid is drained. However, in many cases, iatrogenic tearing of the pericardial sac during pericardiocentesis will cause flux to leak from the pericardial space into the pleural space. Although this is not ideal, this will relieve pressure on the heart and resolve cardiac tamponade. The amount of fluid that leaks into the pleural space is rarely enough to cause respiratory distress. Other complications can include arrhythmia from scratching the heart, piercing the lungs, and piercing the heart. Realistically, given that the alternative is cardiac tamponade and eventual sudden death, the benefits of pericardiocentesis usually outweigh the risks. After relieving pressure, perform additional basic stabilization as needed, then transfer to a specialty facility for advanced diagnostics and care.

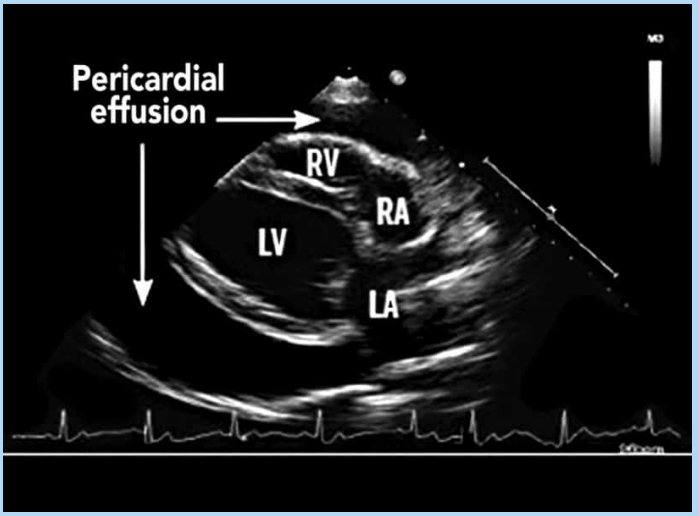

Fig. 1 - Echocardiogram of pericardial effusion. The dark space, which is fluid, surrounds the entire circumference of the heart. This does not occur with pleural effusion.

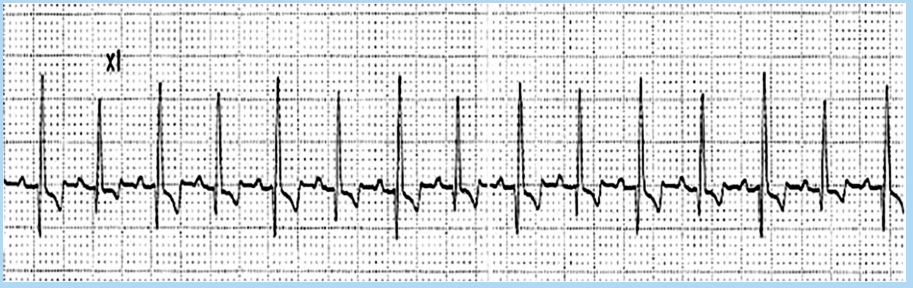

Fig. 2 - Electrical alterans secondary to pericardial effusion. The amplitude of each QRS complex alternates as the heart swings back and forth.

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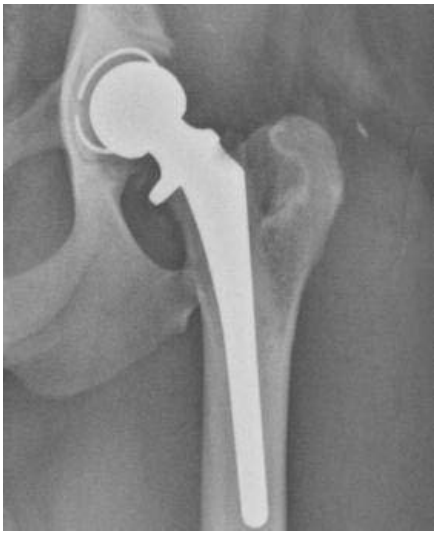
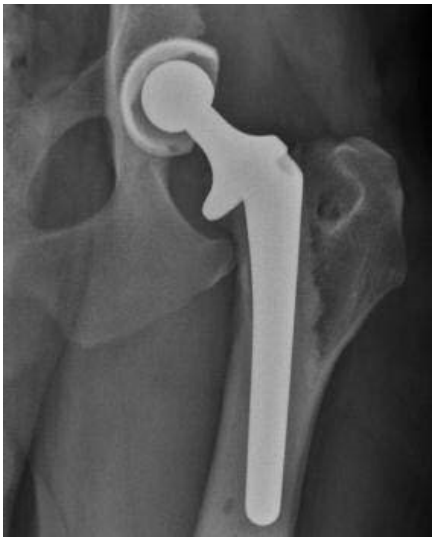
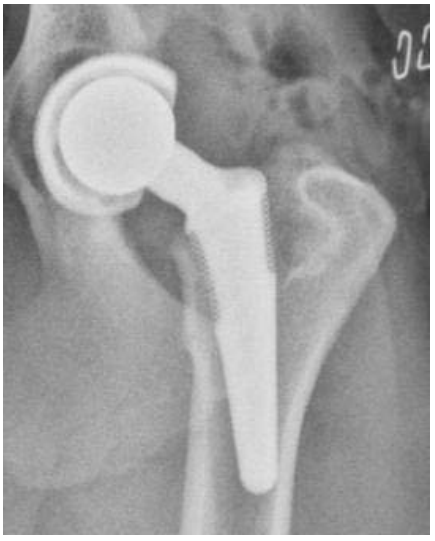
TOTAL HIP REPLACEMENT SURGERY AT LIVS



CEMENTED THR



HYBRID THR



CEMENTLESS THR

Total hip replacement (THR) is designed to eliminate the source of discomfort and restore range of motion by replacing the arthritic joint with an artificial hip joint prosthesis. THR surgery is a state-of-the-art procedure, very similar to the operation in humans. The arthritic femoral head and neck are removed and replaced with a metal head and stem (cobalt chrome metal). The arthritic socket is removed and replaced with a plastic cup (high molecular weight plastic). The metal head and plastic cup fit together like the original ball-and-socket joint, providing support and pain-free, mechanically sound movement almost immediately after surgery.

Dominic J. Marino, DVM
Dip. ACVS, Dip. ACCT, CCRP

Dr. Dominic J. Marino is one of the most experienced hip replacement surgeons in the country. He has performed over 2,000 THR procedures, in dogs, cats, and pot-bellied pigs. His areas of special interest include joint replacement surgery, brain surgery, and spine surgery. Dr. Marino has lectured nationally and internationally on these subjects.

To learn more about Total Hip Replacement procedures and other Hip Dysplasia treatment options, or to refer a case:

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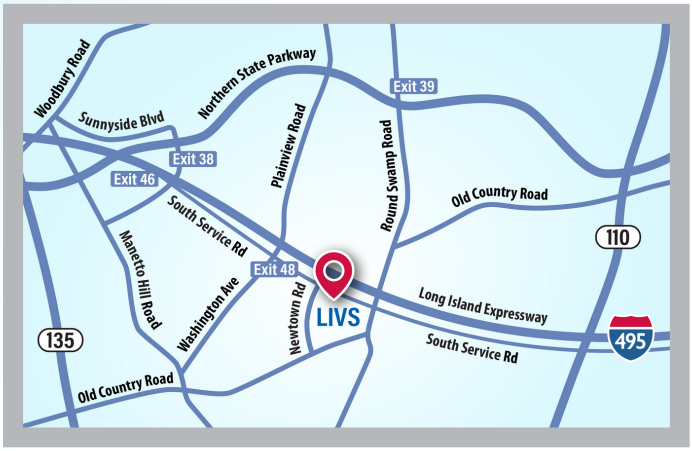

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