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Thrombocytopenia in the Canine Patient

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DoveLewis Annual Conference Speaker Notes

Identifying Thrombocytopenia

Clinical signs: Petechia, ecchymoses, gingival bleeding, scleral hemorrhage, hyphema, epistaxis, hematuria and melena are common. Depending on degree of blood loss, the patient may also display signs of anemia or hypovolemia such as tachycardia or weakness. Many patients have no outward manifestations despite thrombocytopenia. Spontaneous bleeding occurs only with severe thrombocytopenia (<35,000plt/μL) unless platelet dysfunction or concurrent coagulopathies are present.

Platelet count: Difficult or prolonged venipuncture can lead to platelet clumping or even macroscopic blood clot formation. Blood samples should be immediately transferred into an EDTA containing blood tube. All automated platelet counts should be confirmed with a manual blood film. An estimated platelet count is calculated by averaging the platelets in the monolayer in ten fields at 100x (oil), and multiplying by 15,000.

Pseudothrombocytopenia: In 0.1% of humans, EDTA induces persistent platelet clumping. In the presence of EDTA, previously hidden platelet surface antigens are exposed, allowing antibody-mediated platelet aggregation to occur. Because the antigens are not available on the platelet surface in the absence of EDTA, this is a strictly in vitro phenomenon. Anticoagulation with citrate can give more accurate platelet counts in these patients, but can alter platelet indices and lead to more platelet clumping in normal patients, so EDTA remains the anticoagulant of choice for routine evaluation.

Breed variations in platelet count: 30-50% of Cavalier King Charles Spaniels have a beta tubulin mutation causing macrothrombocytopenia. A similar mutation has been described in Norfolk and Cairn Terriers, and asymptomatic macrothrombocytopenia has been reported in a Beagle. These dogs are not at increased risk for hemorrhage. Greyhounds may have platelet counts as low as 100,000 plt/μL, which is normal for the breed. Polish Ogar and Dogue de Bourdeaux have also been reported to have platelet counts below normal reference ranges.

The normal life cycle of the platelet: Platelets are produced by the bone marrow in response to thrombopoietin, which is produced in the liver and kidneys. Platelets contain receptors that allow the internalization and breakdown of thrombopoietin. With low platelet mass, less thrombopoeitin is internalized and plasma levels of thrombopoeitin rise,

stimulating platelet production. Platelets are released when mature megakaryocytes fragment, releasing thousands of platelets. The average platelet lifespan in the dog is 5-7 days. Senescent platelets are removed from circulation by the mononuclear phagocyte system (MPS) in the liver and spleen.

Causes of Thrombocytopenia

Infectious Diseases:
Bacterial, fungal, parasitic and viral infections can all lead to thrombocytopenia.

- Viral infections can cause direct platelet injury or trigger an immune-mediated process.
- Endotoxin released by gram negative bacteria causes endothelial injury, triggers coagulation while gram positive infections can lead to exotoxin-mediated platelet injury.
- Rickettsial infection can cause decreased production of platelets, increased consumption and destruction. Some degree of immune-mediated destruction plays a role in Ehrlichia, Anaplasma phagocytophilum and Rickettsia rickettsii infections. E. canis will also impair platelet function, which likely contributes to the bleeding propensity in this population. Coinfection is common; diagnosis of one infection should prompt further testing.
- Infection with Ehrlichia platys results in a cyclic thrombocytopenia, and an immune-mediated process is postulated.
- Thrombocytopenia occurs commonly in bartonellosis, and moderate to severe thrombocytopenia is a consistent feature of babesiosis.
- Leptospirosis: Thrombocytopenia occurs in 1/3 of dogs with leptospirosis, and occurs at a higher rate with Pomona serovar infection.
- Other infections: 30% of dogs with Leishmania suffer from thrombocytopenia, which is at least in part immune-mediated. ITP has also been reported secondary to Angiostrongylus infection in a dog.
- Hemolytic uremic syndrome (HUS): Consists of microangiopathic hemolytic anemia, thrombocytopenia and azotemia associated with gastroenteritis has been reported in dogs. Although HUS is reported to be commonly caused by E. coli O157:H7 in humans, this was not the case in a series of 3 dogs reported in 1993.

Non-infectious Causes of Thrombocytopenia:

Congenital Thrombocytopenias:

- Gray collie cyclic hematopoiesis syndrome is an autosomal recessive disorder of stem cell maturation resulting in cyclic decreases in neutrophils, platelets and red blood cells. This syndrome is rare and often fatal early in life due to infection.
- May-Hegglin anomaly was recently identified in a pug, and results in a macrothrombocytopenia that causes significant. May-Hegglin anomaly (MHA) can be differentiated from other macrocytopenias by cytoplasmic neutrophilic inclusions.

Heat injury: In severe hyperthermia, platelet aggregation occurs due to direct platelet injury. Human platelets begin to show hyperaggregability above 43C. GI hemorrhage,

vasculitis and DIC can all further contribute to exacerbation of thrombocytopenia. In a retrospective study of 54 dogs undergoing treatment for heat stroke, 62% were thrombocytopenic on hospital admission, and 83% developed thrombocytopenia during treatment. Although DIC was a risk factor for death, thrombocytopenia alone did not increase the risk of death.

Envenomation:

- Viper envenomation can cause thrombocytopenia and impaired platelet function. Platelet counts typically improve with the administration of antivenin.
- ITP is a rare complication of bee sting in humans. A recent case report detailed suspected ITP attributed to Africanized bee envenomation in a dog. Thrombocytopenia resolved in this patient with immunosuppressive treatment.

Immune-mediated thrombocytopenia: Immune-mediated thrombocytopenia has been referred to by a variety of descriptors and acronyms. In 2009, an international working group made recommendations for standard terminology, diagnosis and treatment of immune-mediated thrombocytopenia in humans. The working group authors endorsed the term "immune thrombocytopenia", preserving the acronym of ITP in order to maintain a link with prior publications. Immune-mediated platelet destruction occurs via Fc-mediated phagocytosis by the monocyte macrophage phagocytic system primarily in the spleen, and to a lesser degree the liver. ITP can be a primary, or idiopathic process, or can occur secondary to drug administration, toxin or underlying disease such as neoplasia or infection. Multiple myeloma, lymphoma, histiocytic sarcoma, and rarely, solid tumors have been implicated as causes of secondary ITP.

Post-transfusion purpura is an extremely rare complication of transfusion in humans with an estimated incidence <0.1 per 100,000 red blood cell units. Immune-mediated destruction of a patient's platelet occurs after sensitization to platelet antigens present in transfusion products. Although no viable platelets remain in most stored blood products, antigens may still be present in stored whole blood, packed red blood cells and plasma in addition to platelet transfusion products. Post-transfusion purpura has been reported in one hemophiliac dog that received repeated transfusions of fresh whole blood and plasma. Thrombocytopenia developed one week after transfusion and resolved with a tapered dose of prednisolone.

Vaccination with the MMR combo vaccine has been associated with ITP in children. Serious bleeding is rare and the disease is self-limiting. Given the risk for ITP triggered by natural infection, the American Society of Hematology guidelines recommend MMR vaccination for all children with ITP that have insufficient titers even in cases suspected to triggered ITP from vaccination. Vaccine-associated ITP is often considered as a differential in veterinary patients with ITP. Although there has been one report of severe thrombocytopenia associated with modified-live distemper vaccination in a dog, a retrospective study designed to investigate recent vaccination in thrombocytopenic dogs failed to find a temporal association. Although decisions about vaccination protocols should be individualized to a given patient, their immune status and their environment, evidence to support withholding vaccines in dogs and cats suffering from ITP is lacking.

Drug-related

- Idiosyncratic drug hypersensitivity reactions resulting in immune-mediated thrombocytopenia have been described in dogs treated with sulfonamides, beta-lactam antibiotics, amiodarone and gold.

- Heparin-induced thrombocytopenia has been well-described in humans and documented in horses but has not been documented in other animals.

Diagnostic Workup

The diagnosis of primary ITP is one of exclusion. In humans, a platelet count of $<100{,}000$ and the absence of known underlying disease is sufficient for a diagnosis of idiopathic ITP. In veterinary medicine, consensus guidelines are lacking, however, severe thrombocytopenia in the absence of identified underlying disease is often the only criteria for diagnosis. CBC should be performed to look for concurrent cytopenias and blood film should be evaluated to confirm and characterize the thrombocytopenia. Chemistry profile and urinalysis should be performed, and PT/aPTT should be performed to screen for primary or consumptive factor deficiency consistent with DIC, anticoagulant rodenticide toxicity or hepatic dysfunction. Imaging of the thoracic and abdominal cavities should be performed to identify organomegaly or neoplasia. Relevant infectious disease testing should be performed.

Bone marrow sampling is considered to be safe even in severely thrombocytopenic patients. A recent retrospective review of bone marrow cytology in thrombocytopenic patients suggested that evaluation of the bone marrow is unlikely to yield diagnostic information in patients with severe thrombocytopenia, and is more likely to be useful in patients with moderate thrombocytopenia. If multiple cytopenias are present or if neoplasia is high on the differential list, bone marrow should be evaluated regardless of the degree of thrombocytopenia.

Although anti-platelet antibody testing is ideal for diagnosis of ITP, testing is fraught with difficulty. Platelet surface-associated IgG (PSAIgG) measurement by flow cytometry is the gold standard for demonstrating the presence of anti-platelet antibodies in dogs. Unfortunately, few institutions have on site facilities for testing, and PSAIgG levels rise with >4h storage, making transportation of samples problematic. Furthermore, PSAIgG can be present without immune-mediated disease, making the presence supportive of but not conclusive for a diagnosis of ITP. Because of the shortfalls of autoantibody testing, ITP remains a clinical diagnosis.

Treatment of ITP

Corticosteroids: The mainstay of treatment of ITP, often used as a single immunosuppressive agent. Corticosteroids inhibit Fc-mediated clearance of platelets by the monocyte macrophage system, decrease Fc receptor expression and decrease Ab production. In one study, treatment with prednisone led to a median time to platelet count increase $>40{,}000$ plt/μL within 7 days.

Vincristine: A vinca alkyloid that increases platelet count by accelerating platelet release from bone marrow and clearance of circulating platelets by suppressing phagocytosis by the MMPS. Adding vincristine at a single dose of 0.02mg/kg IV has been demonstrated to reduce the time to platelet count >40,000 plt/μL to a median of 5 days. Although vincristine has been shown to decrease platelet function in dogs with lymphoma, platelet dysfunction does not appear to occur in healthy dogs. Extravasation of vincristine will cause severe tissue damage. In thrombocytopenic patients that may have undergone repeated venipuncture and associated bruising, great care should be taken in choosing an appropriate blood vessel. Side effects are most commonly loss of appetite, vomiting, diarrhea. Peripheral neuropathies are rarely reported. Bone marrow suppression has not been documented at the 0.02mg/kg dose.

IVIG: Consists of pooled, purified immunoglobulins from multiple human donors. Donor IgG is thought to create a blockade of the recipient's monocyte Fc receptors, inhibiting phagocytosis of antibody-coated platelets. Donor IgG molecules can also bind directly to circulating antiplatelet antibodies, speeding clearance from circulation. Complement and Fas ligand blockade and inhibition of cytokine release are additional effects of IVIG that may decrease platelet clearance. Recent veterinary studies evaluating human IVIG in dogs with ITP show a potential role for hIVIG in treatment of ITP. A case series of five transfusion-dependent dogs with ITP described a rapid response to treatment in four of the five dogs. A prospective, blinded study of hIVIG plus standard treatment with steroids vs. steroid alone in 18 dogs with ITP showed a median response time of 3.5 days in the hIVIG group compared to 7.5 days in the steroid only group. Duration of hospitalization was dramatically lower, which made total cost of treatment between the groups comparable despite the high cost of hIVIG. Another study examined hIVIG + steroid vs. vincristine + steroid and found no benefit in the hIVIG + CS protocol compare to the vincristine + CS protocol. A similar time to response of 2.5 days was found in both groups. Although one might draw the conclusion that hIVIG added cost without a therapeutic benefit compared to vincristine, it is worthwhile to note that treatment with hIVIG has resulted in relatively rapid increases in platelet counts across studies. Although hIVIG can be of benefit in treatment of ITP, hIVIG is not completely benign. HIVIG is a foreign protein for dogs and anaphylactic and delayed type hypersensitivity reactions are possible.

Administration of hIVIG to healthy dogs results in a prothrombotic, inflammatory state. Conclusive evidence is lacking in dogs, but thromboembolism is a reported complication of hIVIG in humans.

Cyclosporine: Immunomodulatory drug that blocks the actions of calcineurin, which permits the transcription of the activation factors for T-lymphocytes. Side effects are primarily vomiting, anorexia and diarrhea. Gingival hyperplasia, hepatotoxicity, hirsutism, opportunistic infection, lymphoproliferative disorders and papillomatosis have also been reported. Despite microemulsion formulation, drug absorption varies. Starting dose is often 5mg/kg PO BID on an empty stomach; dose is then titrated to achieve therapeutic serum levels or adjusted based on clinical response. Because of the variable half-life of cyclosporine, it may take weeks or more before steady state is achieved for a given patient. Cyclosporine is metabolized by cytochrome P450 so care must be taken to avoid drug interactions.

Azathioprine: A pro-drug that must be metabolized to 6-mercaptopurine by the liver and other tissues. Breed variations in metabolism may have important implications in toxicity. Giant Schnauzers have a decreased rate of metabolism. Metabolism is increased in Alaskan Malamutes. The metabolites of azathioprine are competitive purine inhibitors, interfering with DNA and RNA synthesis. The effects are greatest in lymphocytes, which lack the ability for de novo purine synthesis. Azathioprine takes up to 4 weeks to take effect, so its usefulness is limited in the acute stages of treatment; it is used commonly to allow more rapid weaning of corticosteroids. Major side effects of azathioprine include delayed onset reversible myelosuppression, GI upset, hepatic necrosis and pancreatitis. Liver enzymes should be periodically monitored along with CBC. A recent retrospective study identified a rate of liver enzyme elevations consistent with hepatotoxicosis in 15% of dogs receiving azathioprine. Starting dose for azathioprine is 2mg/kg QD, rapidly tapered to 1mg/kg EOD.

Leflunomide: A pro-drug whose active metabolites inhibit pyrimidine synthesis. Reports of veterinary use are limited, but a recent retrospective study from CSU demonstrated response to treatment in patients with immune-mediated disease at a 2mg/kg/day dose rather than the commonly prescribed 3-4mg/kg/day. Of the 7 dogs with IMT included in the study, 4 responded to leflunomide within 1-3 weeks, but 3 had no response. Side effects included lethargy, diarrhea, liver enzyme elevations, unexplained bleeding and thrombocytopenia. Side effects were more common in dogs that received higher doses. A single case report of a diabetic dog with Evan's syndrome responded to treatment with leflunomide and a single dose of hIVIG.

Mycophenolate mofetil: A pro-drug whose metabolites inhibit purine synthesis. A recent case series reported five dogs that responded to single agent therapy with MMF. All five dogs achieved complete remission, median time to response of 3 days, 2 dogs with signs of GI upset and no reports of relapse. A similar case series in five dogs with IMHA demonstrated severe treatment-limiting GI side effects in 4/5 dogs, while in a series of 30 dogs with IMHA receiving MMF, only 5 dogs developed diarrhea. Despite promising results presented in this case series, clinicians should be cautious given the high incidence of dose-limiting side effects.

Splenectomy: The American Society of Hematology guidelines recommend splenectomy as second-line treatment in adult humans with ITP that do not respond to corticosteroid therapy. Expected response rate is 70-80%. Splenectomy in a small number of dogs with ITP has been reported in various retrospective studies with some dogs responding favorably, however no prospective studies have been performed in dogs.

Thrombopoetin receptor agonists: Romiplostin (Nplate™) and eltrembopag (Revolade™) are thrombopoetin receptor agonists that are licensed for use in human ITP. Both have been demonstrated to increase platelet count in healthy humans and those suffering from ITP. Romiplostin is a parenterally administered drug that targets the extracellular domain of the thrombopoeitin receptors on megakarycytes, while eltrembopag targets the transmembrane domain. Dogs and humans share homology in the extracellular domain, however there is greater variability in the transmembrane domain, making romiplostin more likely to be effective in our canine patients. A single pilot study has been performed in Germany,

where 5 dogs suffering from ITP refractory to first line therapy showed an increase in platelet count after romiplostin administration.

Prognosis

Prognosis for primary immune-mediated thrombocytopenia in dogs is generally favorable.

- **Short-term:** Median time to platelet recovery has been reported to range from 2.5-7 days depending on treatment protocol. Early studies reported survival as low as 30%, but recent studies show survival to discharge from hospital as high as 84-97%. The presence of significant GI hemorrhage (as evidenced by elevated BUN or melena at the time of diagnosis) was associated with a significantly decreased survival in one retrospective study. Evan's syndrome (concurrent IMHA + ITP) carries a more guarded prognosis than ITP, with a survival rate of 75% in one retrospective study of 12 cases.
- **Long-term:** As with many disease processes in veterinary medicine, there is a paucity of information regarding long-term follow up in dogs IMT. Rates of relapse in studies reporting long term follow up range from 26-39%. Recently a retrospective study was published that included 45 dogs with a minimum of one year follow up. This study reported a 31% relapse rate, and importantly identified that 50% of the dogs that suffered one relapse went on to relapse again. Most dogs that relapsed were still receiving some immunosuppressive therapy at the time of relapse.
- **Prognostic indicators:** It has been repeatedly demonstrated that platelet number alone does not predict mortality or need for transfusion in dogs with IMT. One retrospective study showed increased mortality in patients with melena or an elevated BUN, suggesting that GI hemorrhage may influence prognosis. A novel immune thrombocytopenia bleeding severity scoring system was recently developed (DOGiBAT) that assigns a point for nine potential sites of hemorrhage. The DOGiBAT score at the time of hospital admission was significantly correlated with the need for transfusion and length of hospital stay, potentially offering providers valuable information about the likely cost of care when owners are making decisions as to whether or not to pursue treatment. The DOGiBAT score was not significantly associated with survival to discharge from the hospital.

TABLE 1 Novel canine daily bleeding score assessment tool, DOGiBAT, developed for canine ITP

Site	Bleeding grade 0	1	2
Skin	No	Petechiae/ecchymoses single site	Petechiae/ecchymoses >1 anatomic site
Catheter/venipuncture/ other cutaneous bleed	No	Self-limiting and <5 minutes	>5 minutes and/or intervention to control
Oral mucosa	No	Petechiae	Frank hemorrhage
Intraocular	No	Funduscopic	Hyphema
Epistaxis	No	Unilateral and <5 minutes	Bilateral or >5 minutes
Gastrointestinal	Occult blood (–); (Hema-chek™, Siemans Healthcare Diagnostics Inc., Tarrytown, New York)	Occult blood (+); (Hema-chek™, Siemans Healthcare Diagnostics Inc.)	Hematemesis, hematochezia, melena
Urinary	No	Microscopic (dipstick)	Macroscopic
Pulmonary hemorrhage (suspected/observed)	No	N/A	Yes
Intracranial hemorrhage (suspected/observed)	No	N/A	Yes

Each anatomic site receives a grade of 0 (none), 1 (mild), or 2 (severe), as detailed above. The grades at each site are totaled to give a maximal DOGiBAT of 18.

- **Complications:** May include pulmonary hemorrhage, neurologic signs, or blood loss requiring transfusion. In two recent studies, 37% of dogs undergoing treatment for ITP required transfusion. Neurologic signs occurred in 5 out of 73 dogs (7%) in one retrospective study, and were transient in 4 of the 5 affected dogs. Other complications reported in this study included aspiration pneumonia, ARDS, pancreatitis, neutropenia attributed to vincristine administration, and glaucoma secondary to hyphema. Thrombosis was diagnosed in two dogs, with one dog suffering from splenic thrombosis and one dog suffering from portal vein thrombosis.
  Although an early study of platelet function in dogs with ITP showed decreased platelet activation, a small pilot study in five dogs with ITP found thromboelastographic changes consistent with hypercoagulability in all dogs when platelet counts rose to >40,000plt/μL. Given the increased activation of immature platelets that are commonly found in ITP and the tendency of both prednisone and IVIG to promote hypercoagulable states, clinicians should be alert to subtle signs of thrombotic disease in dogs recovering from ITP.

- **Bleeding risk:** Unpredictable, and many patients with extremely low platelet counts will not demonstrate clinical significant bleeding. In addition to mechanical plugging of vascular defects, platelets stabilize endothelial integrity during inflammation. Spontaneous bleeding in thrombocytopenic patients may reflect inflammation and subsequent endothelial dysfunction rather than simple leaking of blood through unplugged defects in the endothelium. In addition to the possible confounding effects of varying degrees on inflammation in dogs with ITP, breed differences in platelet function may also play a role in the risk of hemorrhage for a given patient.
- A study evaluating the use of thromboelastography to predict bleeding in dogs undergoing total body irradiation documented platelet counts <30,000 plt/μL during

all observed bleeding events. This study supports the commonly cited threshold of a platelet count <30,000 plt/μL putting a dog at risk for spontaneous hemorrhage.

Platelet Transfusions

Indications: Prophylactic platelet transfusion for humans with thrombocytopenia remains controversial. In 2003, Abrams-Ogg proposed prophylactic platelet transfusion triggers for dogs and cats extrapolated from contemporaneous human guidelines. A trigger of 10,000 plt/μL in dogs and 5,000 plt/μL in cats was recommended. Since then, human studies have supported a lower transfusion trigger with some authors suggesting a trigger as low as 5,000-10,000plt/μL in patients without additional risk factors, and some support of withholding prophylactic platelet transfusion entirely unless clinical hemorrhage was present. There have been no studies evaluating platelet transfusion triggers in dogs.

Platelet transfusion for ITP is not generally recommended due to the rapid clearance of transfused platelets. However, in the case of intracranial hemorrhage or life-threatening hemorrhage, transfusion may help to provide emergency hemostasis even without a measureable increase in platelet number. Other indications for transfusion include planned surgical intervention in dogs with severe thrombocytopenia or thrombocytopathia.

Sources of platelets: Fresh whole blood will provide platelets when stored at room temperature and used within 8 hours of collection. Platelets can be directly harvested from donor dogs via plateletpheresis, or platelet-rich plasma (PRP) or platelet concentrate (PC) can be prepared from whole blood by centrifuge. PRP and PC must be stored under continuous agitation at room temperature and used within five days of collection. Cryopreserved and lyophilized platelets offer a source of platelets with a longer shelf life at the cost of decreased platelet lifespan and function compared to fresh platelets. In vitro and in vivo studies on cryopreserved platelets have shown decreased platelet survival and impaired aggregation compared to fresh platelets. A recent retrospective study demonstrated a numerical rise in platelet number for dogs receiving cryopreserved platelets, but no decreased in clinical bleeding. The study was small and retrospective in nature with a large number of ITP patients, so the jury is still out on this product. Both cryopreserved and lyophilized platelets are commercially available and offer greater flexibility for use due to their relatively long half-life.

Platelet transfusion dose: 10mL/kg of fresh whole blood is expected to raise the platelet count by ~10k/μL. 1 U/10 kg of fresh platelet concentrate is expected to raise a dog's platelet count by a maximum of about 40k/μL. Platelet rich plasma should cause a similar rise in platelet count per unit, albeit with a much larger accompanying volume. This degree of rise in platelet count is thought to be adequate to stop active hemorrhage. Due to the decreased survival and responsiveness of cryopreserved platelets, a higher dose of cryopreserved platelets is often recommended.

The Surgical Hemoabdomen

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DoveLewis Annual Conference Speaker Notes

Hemoabdomen is an acute, immediately life-threatening condition affecting dogs and cats. If not recognized and treated swiftly and effectively, it will result in the demise of our patients. When presented with a patient acutely hemorrhaging into its abdomen, effective and timely triage, stabilization, and definitive surgical treatment, followed by recognition and aggressive management of post-operative complications, are required for maximizing outcome in these patients. This lecture will focus on triage and stabilization of patients, diagnosis, timing of surgical intervention, post-operative care and common complications. Surgical treatment of traumatic and nontraumatic hemoabdomen originating from the liver and spleen will be discussed.

Patients suffering from acute blood loss into the abdomen are not uncommon in the emergency practice setting. Clinical signs may be reported as acute or more insidious in onset. An episode of recent trauma may precede presentation in some patients, but often they have more obscure histories ranging from anorexia, depression, lethargy and gastrointestinal signs, to acute weakness and collapse. Sometimes, progressive abdominal distension or pale mucous membranes will be noted by the patient's caregiver. In cases of nontraumatic spontaneous hemoabdomen, the signalment is often the older, large breed canine, but this condition can affect smaller canines and cats as well.

Presenting clinical signs at triage often include weakness and recumbency, pale mucous membranes, tachycardia with or without pulse deficits or a heart murmur. Tachypnea, a distended abdomen with a fluid wave, or a palpable abdominal mass is often identified. Hypotension, hypothermia and low oxygen saturation are often recorded.
Initial stabilization for any patient presenting with these signs should include oxygen supplementation, immediate venous access, IV fluid support, and pain management. Because these patients are often very unstable, pain medications should be used at low starting doses and titrated to control pain without causing deterioration in the patient's vital parameters. Reversal agents as well as emergency resuscitation drugs should be on hand at all times. ECG, pulse oximetry and blood pressure monitoring should be instituted and heat support should be provided.

Once initial stabilization is started, further diagnostics can commence. Some form of stat panel including electrolytes, kidney values, lactate and PCV/TS should be performed along with blood gas analysis if available. A coagulogram and platelet count should be performed on any patient with evidence of significant hemorrhage. Blood can be saved for a full CBC

and serum chemistry to be performed later along with blood typing and cross match if needed. Abdominal and thoracic FAST scan should be performed to confirm intraabdominal hemorrhage and obtain a peritoneal fluid sample for analysis, as well as evaluate for evidence of masses or organ trauma. A PCV similar or higher than the patient's peripheral PCV confirms acute hemorrhage. If no mass or organ trauma is noted on abdominal ultrasound with significant effusion, a differential diagnosis of rodenticide or other anticoagulant toxicity or coagulation factor deficiency should be considered. If hemorrhage appears to be originating from mass, thoracic radiographs and full abdominal ultrasound should be performed once the patient is stabilized to evaluate for metastasis. Echocardiography is also recommended if there is any evidence of pericardial effusion or other heart shape abnormality on radiographs (or t-FAST).

Medical treatment for acute abdominal hemorrhage includes restoration of circulating fluid volume, correction of anemia and coagulopathy. Addressing electrolyte or blood gas derangements and improving oxygen saturation, normalizing heart rhythm, blood pressure and body temperature are also very important. Fluid resuscitation requires a judicious combination of crystalloids, colloids and blood products. There is no cook book recipe and therapy must be tailored to meet the individual needs of the patient and titrated according to the patient's clinical response. In general, low volume resuscitation with colloids such as hetastarch, hypertonic saline and blood products is of more benefit than multiple high-volume shock doses of crystalloids. These can cause rapid hemodilution of remaining red cells, coagulation factors and albumin as well as cause rapid elevation in blood pressure that promotes a recurrence of active bleeding. A rule of thumb for initiation of transfusion at a PCV of 20% has been stated but in reality, patients with acute non-compensated bleeds often benefit from a transfusion when their hematocrits are still within the normal range. Mucous membrane color, tachycardia, tachypnea, hypotension and other indicators of uncompensated hemorrhage often dictate immediate administration of blood products in these patients. Patients with coagulopathy should be administered fresh frozen plasma as part of their treatment to replenish factor supply, especially if surgery is to be pursued. Lyophilized platelets are beneficial in patients with clinically significant thrombocytopenia or those about to undergo surgery.

With appropriate stabilization and fluid resuscitation, vital signs and electrolyte and acid base disturbances should improve. Lactate and venous blood gases can be serially monitored along with oxygen saturation, blood pressure, heart rate and rhythm to determine whether efforts to stabilize the patient are working. If persistent hypotension exists in the face of adequate fluid resuscitation, vasopressor therapy can be initiated. Tachyarrhythmias are often a sequela of hemorrhagic shock and may require treatment with lidocaine boluses or in CRI form especially if rate is persistently over 160 bpm, if the rhythm is multiform or if R on T phenomenon is present.

Deciding when to take a patient with abdominal hemorrhage to surgery can be challenging. Adequate stabilization takes time but there is an end point where the patient is not improving and definitive surgical treatment is necessary. While many patients stabilize rapidly with volume resuscitation, pain control and blood products, others with bleeding from multiple sources or large masses may not respond to aggressive measures. Ideally, prior to surgery a patient will have a heart rate below 160 bpm with improvement in pulse quality and rhythm, a blood pressure of 100 systolic or higher, a PCV of $>24\%$, and

improvement in mucous membrane color. Often when these points are reached, the patient will also become more alert and interactive. A patient that cannot reach these endpoints within a few hours or continues to deteriorate despite of aggressive resuscitation needs to go to surgery.

Anesthesia in critical patients is challenging and requires a multimodal approach to in order to limit further deterioration in clinical status. Patients should have two intravenous catheters to allow for simultaneous administration of fluids, blood and other medications. ECG and oxygen saturation via pulse oximetry is monitored. An arterial line for sampling and direct blood pressure monitoring is ideal, or indirect blood pressure and end tidal C02 monitoring should be used. Inhalant anesthetics should be minimized while oxygen delivery and ventilation maximized. Antiarrhythmic agents such as lidocaine may be required as well as vasopressors such as dopamine, dobutamine or norepinephrine. Emergency drugs and calculated doses for patient weight should on hand at all times. (For an excellent review of anesthetic methods in the ER please refer to Dr. Kate Earl's lecture- available on atdove.org)

Diseases or injury to the liver or spleen are common causes of surgical hemoabdomen. Traumatic hemoabdomen is a result of automobile associated injury or falls and most cases respond well to medical therapy. Capsular fissures in the liver and splenic fracture or vessel avulsion are among the more common causes for organ hemorrhage secondary to blunt trauma. Occasionally, massive hemorrhage occurs and emergency operation is required to save the patient. Autotransfusion can be used before and during surgery to maintain these patients until the hemorrhage is controlled. Vascular occlusion methods such as the Pringle maneuver and aortic and caval occlusion can provide temporary attenuation of hemorrhage to allow identification and control of the source of hemorrhage. Partial or complete splenectomy and or liver lobectomy may be required. Capsulorraphy is only indicated in cases of minor injury to the spleen or as an adjunct in liver trauma. In cases of diffuse fracture where damaged liver must remain in the patient, hemostatic agents, absorbable mesh and omentum may be used together to surround and help seal fissures and control hemorrhage. Alternately the liver can be packed off with laparotomy sponges and the abdomen temporarily closed in patients that cannot tolerate prolonged surgery for multiple lobectomies. Approximately 36 hours later reoperation is performed to remove the packing and perform any necessary resection or repair.

Rupture of splenic and hepatic neoplasia is by far the most common cause of intraabdominal hemorrhage treated surgically at our hospital. Ruptured splenic masses require complete splenectomy; partial splenectomy is never indicated for neoplasia. In cases of liver neoplasia, cessation of bleeding requires partial or complete liver lobectomy to control hemorrhage. Splenectomy can be performed along the hilus (hilar splenectomy) or at more proximal branch points (5 clamp method). Similarly, several techniques are effective for performing an emergent liver lobectomy. A variety of surgical instruments and materials are available to the ER surgeon to maximize efficiency and hemostasis for the emergency patient. These materials and techniques will be discussed in detail in the lecture.

Postoperative management of patients recovering from surgical management of hemoabdomen requires intensive care. Oxygen supplementation, active warming,

continuous ECG monitoring and treatment of arrhythmias, as well as frequent monitoring of attitude and vital signs are indicated. Fluid resuscitation and correction of anemia and hypoproteinemia continues in the post-operative phase. Patients who have had a significant episode of hemorrhagic shock are at risk for worsening arrhythmias, ileus, and derangements such as DIC and thromboembolic disease as well as SIRS or MODS. Malignant neoplasia also increases the chance of a patient developing these complications as well as recurrent hemorrhage, especially in patients with residual gross disease or distant metastasis.

Prognosis is variable and largely dependent on the cause of the hemorrhage in patients treated surgically for hemoabdomen, but timely intervention and aggressive and definitive treatment of hemorrhagic shock and its sequela maximize the chances for survival in these patients.

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Spontaneous Hemoperitoneum; Uh oh, not the spleen or liver

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DoveLewis Annual Conference Speaker Notes

Hemoperitoneum (or hemoabdomen) is a common presentation for patients coming to our emergency hospital. These patients are typically categorized into traumatic or spontaneous cases to aid in creating a diagnostic and management plan. The spontaneous hemoperitoneum cases can be further sorted into spleen or liver, and everything else. These notes compliment Dr. Magee's lecture covering the spleen and liver as the primary source of hemorrhage. My lecture will cover both traumatic and spontaneous cases of hemoperitoneum in dogs and cats.

Every vet in this room has probably shared the same feeling of mind-numbing dread when opening an abdomen that was advertised as a simple splenic tumor which turns out to be anything but simple. Your first hint is when you need to feel around in the bloody soup just to *find* the spleen. Then you gently slide it up and out of the abdomen only to discover no giant purple cavitary mass or hematoma, but rather a skinny pale lavender tongue of a spleen that might fit into a cat rather than the Golden Retriever over which you are hovering.

Next step is to grope cranially and run your fingers over each lobe of the liver, as you run the suction to improve your visibility. Uh oh, now the cold sweat is seriously collecting between your shoulder blades. Not spleen and not liver…now what? Finding the source and assessing your ability to stop active hemorrhage is the next phase of your exploratory surgery. Table 1 shows a list of the reported origins of hemorrhage for spontaneous hemoperitoneum in dogs from a recent retrospective study of two university hospitals. Their paper clearly demonstrates that hemorrhage can arise from nearly anywhere in the abdomen and it is to your patient's benefit to have a strategy for next steps.

Anatomic source of spontaneous hemoperitoneum in 637 dogs (diagnosed at surgery, necropsy or ultrasound examination)	*Vet Surgery* 2018:47:1031-1038 J Fleming et al. Number of cases (%)
Spleen	368 (57.8)
Liver	115 (18.1)
Retroperitoneum	22 (3.5)
Adrenal	10 (1.6)
Kidney	9 (1.4)
Body wall	3 (0.5)

Mesentery	4 (0.6)
Prostate	3 (0.5)
Lymph nodes	1 (0.2)
Pancreas	1 (0.2)
Stomach	1 (0.2)
Urinary bladder	1 (0.2)
Multiple sources	62 (9.7)
No source identified	37 (5.8)

To begin with, get another set of hands to scrub in. Nearly everything else that could be a source of hemorrhage in the abdomen will require adequate retraction to *see*, let alone *solve*. Second, get some good retractors and some vascular clamps. You may already have a set of Balfours holding open your abdomen. Ask for some malleable retractors and either an Army-Navy set or blunt Senns depending upon the size of your patient. Malleables are useful in that they can retract even when not held by an assistant. Use lap sponges to pack off the abdomen in whatever systematic approach is best for you. My personal rotation (after looking at the spleen and liver) is left kidney and left adrenal, right kidney and right adrenal, pancreas (both arms and angle), cranial mesenteric artery and associated lymph nodes, stomach, small intestine, large intestine, urinary bladder, prostate/uterus/cervix and finally retroperitoneum. Along the way I'm also feeling and/or looking at every inch of the body wall and diaphragm.

Is the blood welling too quickly to allow you this quick explore? From the animal's right side, lift the stomach and duodenum with your right hand, and use the fingers of your left hand to compress the aorta and caudal vena cava against the spine between the renal arteries and the caudal border of the liver. With your fingers, this aortic occlusion is less precise than a Rummel tourniquet but is quick and may at least help you identify an abdominal quadrant as the source of hemorrhage. If you are compressing the aorta cranial to the renal arteries and blood is still welling, you have probably isolated hemorrhage to the liver, gall bladder and stomach. Controlling hemorrhage at this point may require rapid access through the diaphragm to digitally compress aorta and cranial vena cava just cranial to the diaphragm. This is definitely a last ditch effort and is not often rewarded with survival of the patient.

The reality of surgical hemoperitoneum not of splenic or hepatic origin is often a guarded to grim prognosis for patients. The exceptions are generally those of traumatic cause such as a crushing or avulsion injury to a kidney or a slipped ligature from a spay procedure. The literature abounds with retrospective studies examining dogs and cats with hemoperitoneum, however these studies are inevitably skewed toward splenic and hepatic cases, leaving hemorrhage from other organs represented by only a handful of animals from which to draw conclusions. To complicate matters further, the perceived guarded prognosis for hemoperitoneum in general, and non-splenic in particular, tends to shift clients toward humane euthanasia earlier for both quality of life and financial reasons creating a self-fulfilling prophecy of early mortality.

It is important to remind yourself going into surgery for hemoperitneum that you rarely can tell a benign lesion from a malignant tumor. Of course you may have a suspicion based on lesion appearance and other case details, or you may find numerous abdominal lesions which is strongly supportive of a malignant process. However much of the time you will need to perform surgery as if it is a malignant process but keep hope alive for the rare benign mass.

The most common canine renal neoplasias attributed to spontaneous hemoperitoneum are renal cell carcinoma, transitional cell carcinoma or papilloma, hemangiosarcoma, lymphoma and nephroblastoma. Unilateral nephrectomy is the treatment of choice, assuming a functional contralateral kidney. Ranges of median survival time are shown in Table 2. As with HSA in other organs, renal hemangiosarcoma with hemoperitoneum significantly shortens median survival time. Benign diagnoses for hemorrhage originating from a renal mass is quite rare and includes renal adenoma and renal or perirenal cysts. In cats, lymphoma is the most common renal tumor and is rarely associated with hemoperitoneum.

Primary renal malignancies	Median survival times
Renal carcinomas	16 months (range 0-59)
Renal sarcoma	9 months (range 0-70)
Renal nephroblastoma	6 months (0-6)
Renal hemangiosarcoma	278 days (0-1005)
Renal hemangiosarcoma with hemoperitoneum	62 days

The most common primary adrenal neoplasms in dogs are adrenocortical tumors (carcinomas and adenomas) and pheochromocytoma. Both tumor types can result in spontaneous hemoperitoneum requiring emergency adrenalectomy, although adrenocortical carcinoma is much more likely a diagnosis. One retrospective study found a median survival time for dogs with acute adrenal hemorrhage was 208 days (range 1-1020) and a perioperative mortality rate of 50%.

Retroperitoneal masses resulting in spontaneous hemoperitoneum (following hemoretroperitoneum) are most commonly hemangiosarcoma and are generally difficult to remove surgically due to poorly defined margins. Other reported retroperitoneal tumors in dogs include osteosarcoma, leiomyosarcoma, peripheral nerve sheath tumor and hemangiopericytoma, though none of these are as likely to be associated with spontaneous hemoperitoneum. Published survival data suggests a median of 38 days (range 2-498 days) with surgery and chemotherapy or radiation. The difficulty in achieving complete resection and high metastatic rate associated with this tumor type (HSA) are suspected to be the cause of the short survival times.

The most common primary prostatic tumor in dogs is adenocarcinoma, but this rarely is associated with hemoperitoneum. A dog with spontaneous hemoabdomen arising from a prostatic mass is most likely to be hemangiosarcoma. Surgical prostatic ablation for bleeding tumor is not recommended due to the grim prognosis. Of note, however large clots often lodge in the caudal abdomen or just within the pelvic canal with

hemoperitoneum. Take care not to assume a clot near the prostate is *arising from* the prostate (either during ultrasound exam or surgical exploration).

Other reported sites of neoplastic origin for spontaneous hemoperitoneum in the dog include the body wall, mesentery/omentum, lymph nodes, pancreas, stomach and urinary bladder. The rarity of cases for these locations makes predicting tumor diagnosis and thus prognosis impossible. In our hospital, primary tumors found in the mesentery/omentum, abdominal lymph nodes and arising from the body wall have thus far been diagnosed as hemangiosarcoma when histopathology was submitted.

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Surviving or Not Surviving Sepsis: That is the Question

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DoveLewis Annual Conference Speaker Notes

What is the Surviving Sepsis Campaign?

In the recognition that sepsis was and continues to be big human healthcare problem, affecting millions of people annually associated with high mortality, the surviving sepsis campaign working group was formed to evaluate the evidence and publish clinical recommendations for the management of human septic patients. This consensus committee produce the Surviving Sepsis Campaign (SSC) guidelines a set of recommendations qualified by the strength of evidence in support of that recommendation. The original SCC guidelines were published in 2004 with revisions in 2008, 2012 and the most recent revision in 2016(1).

In the 2016 SSC guidelines there was a departure from the alphanumeric grading of the prior to guidelines. Table 1 represents the comparison of the current descriptive grading recommendations compared to previous numerical grading scheme. The statements in the 2016 SCC guidelines are given the descriptive grade "Strong" or "Weak" depending on the quality of evidence in support of that recommendation. Similar to other consensus statements in which published evidence is graded, well designed and unbiased randomized controlled trials (RCTs) are considered high quality of evidence, whereas observation studies or lower quality RCTs are considered moderate to low quality of evidence, with expert opinion considered to be very low quality of evidence. In the 2016 guidelines the statement "We recommend" is a "Strong" recommendation and the statement "We suggest" is a weak recommendation. In addition, the guidelines provide room for Best Practice Statements (BPS) representing strong recommendations with unequivocal benefit or harm but in which the evidence is difficult to grade.

Table 1: 2016 SCC guidelines grading terminology compared to previous guideline grades.

	2016 Descriptor	2012 Grade
Strength	Strong Weak	1 2
Quality	High Moderate Low Very Low	A B C D

Ungraded strong recommendation	Best Practice Statement (BPS)	Ungraded

The SCC guidelines were further distilled into "Sepsis Bundles" (2) which are easy to follow checklists intended to effect behavioral change that would be simple and result in uniform application of the SCC guidelines. Improved survival in human septic patients has been demonstrated with implementation of and compliance with these "Sepsis Bundles".

Why do we care about SSC guidelines in veterinary medicine?

Sepsis is an important clinical entity in dogs and cats associated with high mortality rate. Incidence of sepsis in dogs has been reported as 4.2% of hospital admissions(3) and sepsis in cats occurs in 6.2% of hospital admissions(4) in a veterinary teaching hospital. Septic dogs have a 55% mortality (3). Septic cats have a 33% (4) mortality rate.

Challenges of translating SCC guidelines to small animal medicine:

One of the major challenges in translating SCC guidelines to small animal medicine is that we are not certain we are diagnosing or treating the same condition. Clinical experience says that sepsis in cats is not the same as sepsis in dogs so it is a reasonable assumption that human sepsis is not the same entity as in our veterinary species. Access to advanced invasive monitoring is often not readily available in veterinary medicine. Access to prolonged organ support such as mechanical ventilation for respiratory failure or dialysis therapy for renal failure is a rarity in veterinary medicine. Finally client financial limitations and access to euthanasia affect our ability to fully utilize some of the recommendations within the SCC guidelines.

Utility of SCC guidelines:

Despite the acknowledged limitations of the SCC guidelines in veterinary medicine- if implementation of actionable protocols that improve diagnosis or treatment, and potentially improve outcomes can be achieved without a high outlay of cost then this incremental change is worthwhile in our septic patients. Additionally the questions raised by SCC guidelines can be a stepping stone for clinical research in our veterinary populations. Compared to the human literature the veterinary literature on sepsis is comparatively sparse.

A new definition of Sepsis:

The 2016 SCC guidelines were the first to incorporate new definitions of sepsis and septic shock (5). ***Sepsis*** is defined as "Life-threatening organ dysfunction caused by dys-regulated host response to infection." ***Septic shock*** is a subset of "Sepsis with profound circulatory, cellular and metabolic abnormalities associated with a greater risk of mortality" than sepsis alone.

The previous SCC guidelines definition of sepsis has been extrapolated to dogs and is the common criteria used in the veterinary literature to identify septic patients. These criteria

include infection plus meeting at least 2 of following SIRs (systemic inflammatory response syndrome) criteria:

1. Hypo or hyperthermia defined as: Temp < 100.6 or > 102.6
2. Tachycardia: HR>120
3. Tachypnea: RR>20
4. Leukopenia, leukocytosis or left shift: WBC < 6000/ul or WBC > 16,000/ul or >3% bands

The previous definition of sepsis has always been fraught with non-specificity and an overemphasis on the inflammatory response or SIRs criteria. The new definitions highlight the improved understanding of pathophysiology of sepsis activating pro and anti-inflammatory mechanisms as well as highlighting the life-threatening syndrome resulting from altered host response.

One advantage of the SIRs definition was an easy clinical application. In the new Sepsis definitions Sequential Organ Failure Assessment Score (SOFA) has been used to replace the SIRs criteria in identifying patients with infection who might be septic (6). The SOFA score is an additive score taking into account derangements in the respiratory, cardiovascular, hepatic, renal, neurologic and coagulation systems based on defined laboratory and clinical measurements. A higher SOFA score corresponds to increasing level of organ dysfunction and SOFA had good predictive validity for evaluation of mortality in septic patients.

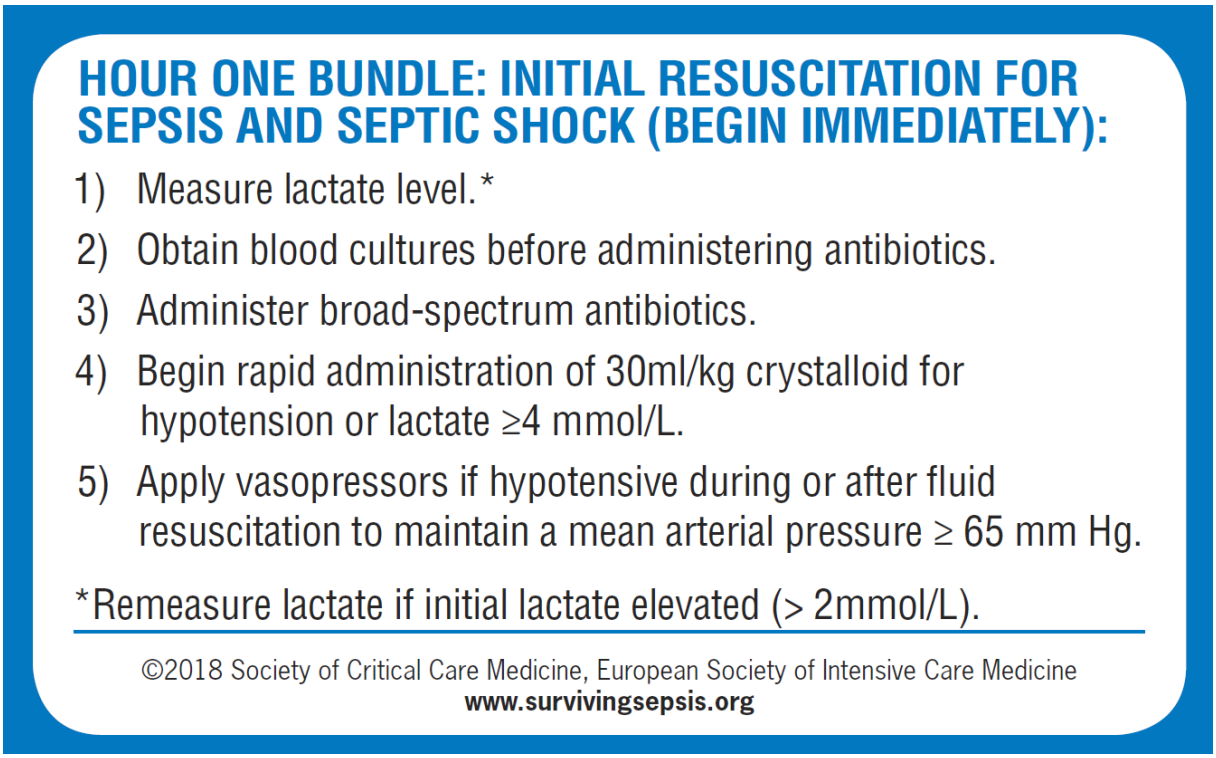
There are no published studies evaluating the ability of SOFA to discriminate between septic and non-septic veterinary patients. A study by Conti-Patara (7)evaluating the changes in perfusion parameters in dogs with severe sepsis and septic shock effectively reported the use of SOFA parameters to define “severe sepsis”. In that study patients with “severe sepsis” were defined as having infection plus meeting SIRs criteria plus having one or more measures of organ dysfunction (including doppler BP<90, PaO2:FiO2 <300, oliguria, increase in creatinine >1.8mg/dl, thrombocytopenia <200,000/ul, hyperbilirubinemia > 0.25mg/dL, increase in lactate > 2.5mmol/L).

Early assessment of SOFA is difficult to apply in all patients because it requires lab testing (chemistries including bilirubin, creatinine, arterial blood gases, urine output) which may not be immediately available. With this limitation in mind the quick SOFA (qSOFA) was developed simplifying the assessment of risk of sepsis in humans outside of an ICU setting. qSOFA relies on three parameters (tachypnea RR>22, hypotension BP<100, mentation change measured by Glasgow coma score <13) . qSOFA is additive with score of 0-3. qSOFA equal to 2 or 3 had 3 and 14 fold increase in hospital mortality compared to patients with a qSOFA of 1. qSOFA also needs to be validated in veterinary species but may prove to be an easily clinically applied assessment of whether our patients with infection may be septic.

Hopefully as the new definition of sepsis becomes more widely recognized our veterinary literature in the future will apply this uniform definition of sepsis to allow better interpretation of results of clinical studies in septic veterinary populations.

SCC Bundle (1)(2)(8)**:**

The 1 hour Surviving Sepsis Bundle a tool to guide the diagnosis, treatment and resuscitation of septic patients in an easy to access format. The 1 hour bundle is intended to highlight simultaneous action on all these points however acknowledging that achievement of the resuscitation goals may occur over a longer period of time. Additionally the bullet points within the bundle are qualified by more specific recommendations within the guidelines.



Beyond the SCC Bundle:

SCC Bundle recommendation: Measure Lactate and Remeasure lactate if initial lactate was elevated

- SCC guideline statement- We **suggest** guiding resuscitation to normalize lactate in patients with elevated lactate levels as a marker of tissue hypoperfusion (weak recommendation with low quality of evidence)

Veterinary sepsis literature for lactate:

Cortellini, S, etal (9). Plasma lactate concentration in septic peritonitis: A retrospective study of 83 dogs (2007-2012). J Emer Crit Care 2015; 23(3): 388-395

- Plasma lactate on admission >2.5mmol/L was associated mortality
- Admission lactate > 4mmol/L had 36% sensitivity and 92% specificity for nonsurvival

- Inability to normalize lactate within 6 hours of admission was 76% sensitive and 100% specific for nonsurvival.
- Persistent post op hyperlactatemia had a sensitivity of 92% and specificity of 100% for nonsurvival

Conti-Patara A, et al. Changes in tissue perfusion parameters in dogs with severe sepsis/septic shock in response to goal directed hemodynamic optimization at admission to ICU and the relation to outcome. J Vet Emer Crit Care. 2012;22(4):409–18

- Nonsurvivors had higher lactate concentration on admission to ICU than survivors

LACTATE conclusion: Agree with the SCC bundle recommendations- if lactate is available using normalization of lactate as a resuscitation target in veterinary species seems reasonable.

SCC Bundle Recommendations: Obtain blood cultures before administering antibiotics and administer broad spectrum antibiotics.

SCC Guideline Statements (antimicrobials):

- We **recommend** that appropriate routine microbiologic cultures (including blood) be obtained before starting antimicrobial therapy in patients with suspected sepsis and septic shock **if doing so results in no substantial delay in the start of antimicrobials.** (BPS)
- We **suggest** empiric combination therapy (using at least two antibiotics of different antimicrobial classes) aimed at the most likely bacterial pathogen(s) for the initial management of septic shock (weak recommendation with low quality of evidence)

Veterinary Antibiotic Literature for Sepsis:

Abelson A, etal (10). Positive impact of an emergency department protocol on time to antimicrobial administration in dogs with septic peritonitis. J Vet Emer Crit Care 2013; 23(5): 551-556.

- Development of an emergency department antimicrobial protocol significantly decreased the time to administration of antibiotics (Median time 6 hours in the PRE protocol group and Median time 1 hour in the POST protocol group).
- The collection of samples post antimicrobial administration did not increase the incidence of negative cultures
- Although the protocol improved the time to administration of antimicrobial no significant improvement in survival was noted between early antimicrobial administration v. delayed antimicrobial administration.

Dickinson A, etal (11). Impact of appropriate empiric anti-microbial therapy on outcome of dogs with septic peritonitis. J Vet Emer Crit Care 2015; 25(1): 152-159

- Appropriate antimicrobial administration chosen in only 52% of patients.
- Appropriate versus inappropriate empiric antimicrobial administration did not affect outcomes.

ANTIBIOTIC conclusion: Although the veterinary literature is inconclusive with regard to the outcome benefit of appropriate and early antibiotic administration. The speaker recommends early and broad antimicrobial administration in septic patients. These antimicrobials should target the most likely organisms based on location of infection. In addition, I recommend following the SCC guidelines to deescalate antimicrobial therapy once a pathogen is identified (BPS) and to initiate source control where feasible (BPS) including removal of access devices.

SCC Bundle: Rapid administration of 30ml/kg crystalloid for hypotension or hyperlactatemia and vasopressors if hypotensive with fluids to keep MAP>65mmHg.

SCC Guideline Statements (Resuscitation and pressors):

- We **recommend** that in the resuscitation from sepsis-induced hypoperfusion, at least 30ml/kg of intravenous crystalloid fluid be given within the first 3 hours. (strong recommendation; low quality of evidence)
- We **recommend** that following initial fluid resuscitation, additional fluids be guided by frequent reassessment of hemodynamic status. (BPS)
- We **recommend** crystalloids as the fluid of choice for initial resuscitation and subsequent intravascular volume replacement in patients with sepsis or septic shock. (strong recommendation; moderate quality of evidence)
- We **recommend** initial target mean arterial pressure of 65mmHg in patients with septic shock requiring vasopressors. (strong recommendation; moderate quality of evidence)

Veterinary Septic Resuscitation Literature:

Conti-Patara A, et al. Changes in tissue perfusion parameters in dogs with severe sepsis/septic shock in response to goal directed hemodynamic optimization at admission to ICU and the relation to outcome. J Vet Emer Crit Care. 2012;22(4):409–18

- Primarily descriptive of the application of a resuscitation protocol for early goal directed therapy. Resuscitation protocol in this study was administration of 40ml/kg/hr of crystalloid (0.9% NaCl) over 3 hours, if hypotension remained then administration of 20-30ml/kg of HES, followed by dopamine 5-15ug/kg/min infusion.
- Non-survivors required more crystalloids
- Non-survivors required more vasopressors
- HES requirement between survivors and non-survivors was not reported

RESUSCITATION conclusion: There is a paucity of veterinary literature from which to draw on to guide resuscitation guidelines in veterinary sepsis. Due to the increasing volume of human literature against the use of HES and synthetic colloids, I recommend crystalloids as the primary resuscitation fluid and the earlier use of pressors with preference for norephinephrine administered to a resuscitation endpoint of MAP=65mmHg and clinical improvements in perfusion parameters. If available improvements in central venous oxygen saturation, lactate and base excess can be used as resuscitation targets.

SCC Guideline Statements (Nutrition):

- We **suggest** the early initiation of enteral feeding rather than a complete fast or only IV glucose in critically ill patients with sepsis or septic shock who can be fed enterally. (Weak recommendation; low quality of evidence)
- We **suggest** either early trophic/hypocaloric or early full enteral feeding in critically ill patients with sepsis or septic shock; if trophic/hypocaloric feeding is the initial strategy, then feeds should be advanced according to patient tolerance. (Weak recommendation; moderate quality of evidence)

Veterinary literature for nutrition in sepsis:

Lui D, etal (12). Early Nutritional support is associated with decreased length of hospitalization in dogs with septic peritonitis: A retrospective study of 45 cases (2000-2009)

- Early nutrition (within 24hours of surgery) was associated with a decreased length of hospitalization compared to septic patients receiving nutrition more than 24hours after surgery
- There was no difference in LOH between IV and enteral nutrition

NUTRITION Conclusion: The above retrospective supports the initiation of early nutrition in veterinary septic patients. Veterinary literature in other patients with critical illness support the initiation of early enteral nutrition.

SCC Guidelines Statements (Setting Goals of Care):

- We **recommend** that goals of care and prognosis be discussed with patients and families. (BPS)
- We **recommend** that the goals of care be incorporated into treatment and end-of-life care planning, utilizing palliative care principles where appropriate. (Strong recommendation; moderate quality of evidence)
- We **suggest** that goals of care be addressed as early as feasible, but no later than within 72 hours of ICU admission. (Weak recommendation; low quality of evidence)

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Common Arrhythmias in Small Animal Patients

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DoveLewis Annual Conference Speaker Notes

Introduction

Cardiac arrhythmias are common in veterinary patients and are associated with alterations in autonomic tone, drug exposure, electrolyte abnormalities, trauma, myocardial hypoxia/inflammation, or primary cardiac disease.

In many cases, rhythm disturbances are secondary to systemic disease and do not require antiarrhythmic therapy. Other arrhythmias, particularly those that arise from primary cardiac disease, are hemodynamically significant and require aggressive intervention.

Dogs and cats with hemodynamically significant arrhythmias may present with depressed mentation, collapse, syncope, congestive heart failure, or exercise intolerance. Decreased cardiac output can also sometimes cause non-specific symptoms such as lethargy, vomiting, or inappetence.

A rhythm disturbance may be the first hint of significant cardiac or systemic disease, giving the veterinarian the opportunity to intervene before clinical signs develop.

Physical examination finding consistent with an arrhythmia include bradycardia, tachycardia, an irregular rhythm, or pulse deficits.

Recognition and characterization of the rhythm diagnosis with electrocardiography is essential for successful management.

Atrial fibrillation and ventricular arrhythmias are the most common arrhythmias seen in patients with structural heart disease

Why do we care about tachyarrhythmias?

Tachyarrhythmias such as sinus tachycardia, and supraventricular or ventricular premature complexes, are common in patients with high sympathetic tone, pain, trauma or systemic disease. These rhythms associated with non-cardiac illness are less likely to cause clinical signs.

The most malignant arrhythmias typically occur in patients with significant underlying cardiac disease, such as cardiomyopathy, valvular disease, or myocarditis and can cause clinical signs of weakness, lethargy, collapse, or congestive heart failure.

Decreased cardiac output results from very fast ventricular rates, so generally heart rates must be greater than 220 bpm in dogs and 260 bpm in cats to become acutely hemodynamically significant.

Aside from a marker of cardiac or systemic disease, concerning consequences of tachyarrhythmias are 1) rapid rates that cause a drop in cardiac output, resulting in syncope or weakness, and 2) prolonged rapid rates result in cardiac remodeling and heart failure (tachycardiomyopathy).

- **Atrial fibrillation (AF)**
    - The features of atrial fibrillation are easily recognized, since that is virtually the only differential for an irregular rhythm with no P waves.
    - Structural heart disease is responsible for most cases of small animal AF
        - Dilated cardiomyopathy
        - Chronic valvular disease
        - Arrhythmogenic right ventricular cardiomyopathy
        - Patent ductus arteriosus
        - Feline cardiomyopathies (hypertrophic, restrictive, unclassified)
    - Large and giant breed dogs can develop lone AF due to elevated vagal tone in the absence of significant structural heart disease
    - Treatment of AF
        - Atrial fibrillation rarely requires emergency antiarrhythmic therapy, but since the ventricular rate is usually fast, treatment is indicated in the chronic term.
        - Treatment for volume overload should be initiated before the AF is addressed in patients with congestion
        - Rhythm control
        - Cardioversion back to sinus rhythm is not performed in many patients due to the underlying structural disease
        - Rate control is most common therapy
            - Slow conduction through the AV node to control the heart rate
                - Diltiazem
                - Diltiazem and digoxin
                - Atenolol
            - Goal is average heart rate 80 to 120 bpm as measured on 24 hour Holter monitor
- **Ventricular arrhythmias**
    - Diagnostic approach to single ventricular premature complexes:
        - In breeds with a high incidence of primary cardiac causes of arrhythmias, i.e. boxers, bulldogs and dobermans, single VPCs, while unlikely to cause clinical signs, raise suspicion for cardiomyopathy. Echocardiogram, 24-hour Holter monitor, and potentially thoracic radiographs are the next step in these patients.

        - In other breeds with less risk of genetic cardiomyopathy, non-cardiac causes are most common. A reasonable next step may be CBC, blood chemistry, infectious disease titers, serum cardiac troponin I, abdominal ultrasound, and thoracic radiographs. A systemic cause of inflammation is often found in these patients and the rhythm will normalize with resolution of the underlying cause.
    - Accelerated idioventricular rhythm
        - A sustained ventricular rhythm at normal heart rates (100 - 180bpm) is likely to be caused by significant systemic disease. These are most commonly seen in the critical patient, secondary to neoplasia, trauma, or acute abdomen. Since the heart rate is not rapid enough to cause hemodynamic compromise, specific antiarrhythmic therapy is rarely needed.
    - Ventricular tachycardia
        - The diagnosis of ventricular tachycardia (VT) is based on more than 3 wide QRS complexes in a row, not associated with P waves, at very rapid heart rates, usually > 250bpm. This rhythm is usually a result of primary cardiac disease such as cardiomyopathy, congenital disease causing hypertrophy, or myocarditis.
        - Diagnostics to assess the severity, need for treatment, and malignancy of the rhythm include echocardiogram, 24 hour Holter monitor, cardiac troponin I, and possibly thoracic radiographs.
        - Antiarrhythmic therapy is generally reserved for VT causing clinical signs of syncope, weakness, or congestive heart failure; or if the rhythm is sustained on Holter monitor which could potentially cause tachycardiomyopathy.
        - Emergency treatment is only necessary for patients presenting with cardiogenic shock caused by sustained rapid VT. Lidocaine is usually effective and safe in dogs to terminate this rhythm. A constant rate infusion is needed while oral therapy achieves therapeutic levels.
        - Oral antiarrhythmics for VT:
            - Sotalol
            - Mexiletine
            - Sotalol and mexiletine
            - Amiodarone
        - After starting medical therapy, a 24 hour Holter monitor is indicated to ensure adequate rhythm control.