



## Monthly Update

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December 2012

## PAMIDRONATE CASE STUDIES: PALLIATIVE OSTEOGENIC SARCOMA TREATMENT

**NEWER PALLIATIVE TREATMENTS:** Another more recent assumption was that in those dogs who were poor candidates for amputation because of age, size/weight, and/or other orthopedic diseases in their forelegs or rear legs (CHD OA, Untreated ACL's or Elbow OA) that perhaps palliative radiation was the only pain management option. It appears that **BISPHOSPHONATES** may be useful in the dogs with OS to manage pain.

**BISPHOSPHONATES: WHAT ARE THEY?** They are synthetic analogs of inorganic pyrophosphate. Bisphosphonates have been intensively investigated in human medicine as novel antineoplastic agents and randomly reported in veterinary medicine before 2005.<sup>18, 19</sup> At low concentrations, bisphosphonates inhibit bone resorption (osteoclast function) without inhibiting the process of bone mineralization, resulting in enhancement of bone density. Although there are several aminobisphosphonates commercially available, pamidronate has been used most extensively in human medicine for the management of tumor induced hypercalcemia, Paget's disease, osteolytic bone metastasis in breast cancer, osteolytic lesions of multiple myeloma, metastatic prostate cancer, and osteogenic sarcoma.<sup>15</sup> They increase bone mineral density (BMD) which in turn results in pain relief and prevention of pathologic micro fractures and catastrophic macro long bone fractures.

**PAMIDRONATE:** Is commercially available and recently became much less expensive. (\$194.85 for 10 ml bottle, 9mg/ml)

**PAMIDRONATE DOSAGE:** 1.0 mg/kg IV q28d as a 2-hour constant rate infusion (CRI). Higher doses; 3mgs./kg have been found to be nephro-toxic.<sup>15</sup> The 1mg/kg dose was empirically derived from clinical toxicity studies in the humans and thus used in the dog. The q28-30d interval was the conventional dosing intervals used in human patients with cancer.<sup>15</sup>

**ANCILLARY PALLIATIVE TREATMENT; NSAIDs:** Carprofen (Rimadyl) appears to be helpful in managing the pain associated secondary to OS as would be expected. The clinical association between the use of NSAIDs and delayed bone healing has led to increased concern regarding their routine use in human orthopedics because decreased blood supply to healing bone. A published report in the veterinary literature subjectively suggested rimadyl slowed the growth of OS. A recent study using Carprofen significantly down regulated vascular endothelial growth factor (VEGF) in vitro without significantly changing alkaline phosphatase.<sup>12</sup> No studies are available using the NSAID Deracoxib (Deramaxx), but because it's similar mechanism of action as Carprofen it appears to be helpful for OS pain management. One could interpret, due to down regulation of VEGF, that Carprofen slows the neovascularity to the tumor thus slowing its rate of growth. Tumors need an increased supply of oxygen to grow rapidly. Recognition of this has stimulated a lot of research in human medicine for methods of interrupting tumor neo-vascularity ie. VEGF.<sup>13</sup>

**PALLIATIVE TREATMENT PROTOCOL USING PAMIDRONATE AND CARPROFEN or DERACOXIB:** Pre-treatment complete blood panel; radiographs of the affected bone initially and monthly or bimonthly thereafter depending on the degree of lameness; standard three chest films initially and single view or standard three views monthly or bimonthly depending on clinical signs; monthly liver and kidney enzymes depending on clinical signs; Pamidronate 1mg/kg IV q28-30d as a CRI in 250 ml 0.9% sodium chloride.

*Continued next page*

## CT Corner



The CT CORNER this month demonstrates the value of it's use in the pretreatment decision process when dealing with Osteogenic Sarcomas.

**View video: William, male Doberman, Front Limb Lameness at:**

[http://www.youtube.com/watch?v=0VYiH6vot\\_U&feature=youtu.be](http://www.youtube.com/watch?v=0VYiH6vot_U&feature=youtu.be)

## Visit Our Newsletter Archive

Read our October newsletter article about the Pediatric Emergencies by visiting our newsletter archive:

<http://archive.constantcontact.com/fs032/1109892572426/archive/1110184841979.html>

CLINICAL EXPERIENCE / CASE STUDY EXAMPLES:

**CASE 1:** "Apollo"; Breed, Carnegie Corso, CM, DOB 4/26/04, WT. 148.3#s. Initial exam 4/26/11. Referred for left foreleg lameness, tentative diagnosis by RDVM, probable bone tumor. No radiographs provided due to his size and disposition-very aggressive! PE Supraspinatus muscle atrophy palpable, left distal radius swelling, mildly lame, palpable right elbow OA, hip status unknown.

Radiographs: Radius, probable OS. Chest, standard 3 views, normal.

RECOMMENDATIONS: Because of his size, ipsilateral elbow OA and age, ALK. PHOSP. 253 (normal 5-131) Monthly palliative medical treatment with Pamidronate was recommended along with weight loss by dietary management (T4 and FT4 were normal), and daily Rimadyl (100mgs bid, intentionally low dosed because of his obesity and attempt to avoid side effects with long term use along with a potential nephrotoxic/hepatotoxic drug, Pamidronate.

Lateral and AP Radiographs taken 4/26/10, Apollo.



6/1/11 Exam and Pamidronate injection. PE mildly lame, tumor is visibly larger. No radiographs were taken.

6/29/11 Exam and Pamidronate injection. PE now weight bearing with little or no limp. Tumor not appreciably larger. Chest radiograph normal. Lab values normal, even ALKP.



Exam 8/26/11 Fourth Pamidronate injection. PE minimally lame, normal Lab. values, chest radiograph normal. Owner elected 2 month interval for Pamidronate injection, previous injection 6/29/11.



Continuing Education Opportunities

All our lectures provide 2 hours of Continuing Education Credits. You can register online through our websites, Boston Veterinary Specialists ([www.bostonvetspecialists.com](http://www.bostonvetspecialists.com)) and Cape Cod Veterinary Specialists ([www.capecodvetspecialists.com](http://www.capecodvetspecialists.com)). A meal is provided during each lecture. Your technicians are welcome as well.

BVS:

**Dr. William Henry:**  
January 16, 2013,  
*"Osteogenic Sarcoma: Newer Treatment Options"*

**Dr. Catherine Briere:**  
March 6, 2013, "Hip Dysplasia"

**CCVS:**  
**Dr. Kimberly Bebar:**  
January 15, 2013, "Doc, Fluffy just stopped breathing!" Now what?: RECOVERing pets from cardiopulmonary arrest. Part I: an update on the new CPR guidelines.

February 12, 2013, "Doc, Fluffy just stopped breathing!" Now what?: RECOVERing pets from cardiopulmonary arrest. Part II: a CPR hands-on lab at CCVS. It is the first hands on lab at CCVS.

**Dr. Elizabeth Martin:**  
March 19, 2013, "Hospital hygiene and infection control"

**Dr. Katherine Westcott:**  
April 23, 2013, "Immune-mediated polyarthropathy (IMPA) in dogs"

**Dr. Louisa Rahilly:**  
May 21, 2013, "Steroids in veterinary medicine: Friend or Foe."

**Dr. Daniel Beaver:**  
June 4, 2013, "Hip Dysplasia"

Exam 10/11/11 He now weighs 125#s and is much more active. Actually was romping in the house today and became visibly lame. On PE weight bearing but mildly lame.



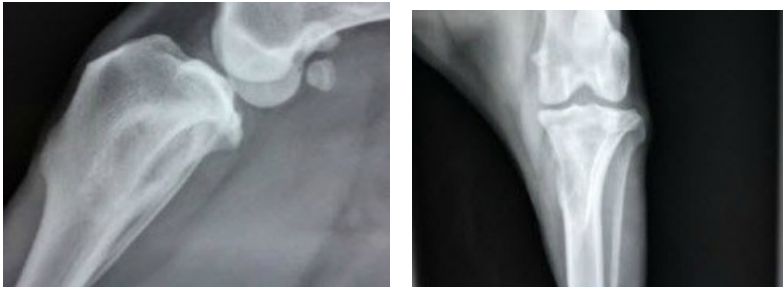
Lateral Radiograph, no visible fracture

Exam 11/7/11  
Seizure this morning followed by a second one within an hour and longer lasting. On PE he is ambulatory, weight bearing normally, but appears disoriented. The tumor has grown rapidly since the 10/11/11 exam. Chest radiograph is normal and the radius now has very dense mineralized bone. The owner declined CT exam for lung metastasis (if present we would assume CNS metastasis) and hospitalization for IV seizure control. He was euthanized. He had been ambulatory with minimal or no lameness for 6 1/2 months.



Radiograph, 11/7/11

**CASE 2:** Moët, Golden Retriever DOB 10/18/98, WT. 48.0#s; Exam 2/1/10; History: Right rear lameness, intermittent for the last week; hypothyroid, on Soloxine for 6 years; subaortic stenosis, on Enalapril for the last 4 years . PE not visibly lame today, mild to moderate right rear thigh muscle atrophy. Radiographic exam: Lytic bone lesion, proximal medial tibia, probable osteogenic sarcoma. Chest radiographs normal. Lab. work normal Rx: 2/2/10 Pamidronate 1mg/kg; Deramaxx 25 mgs. sid. Plan: Re-radiograph in one month.



DR Digital Radiographs 2/2/10  
1st Pamidronate Injection

4/22/10 Has not been lame since initiating 25 mg deramaxx sid. PE right thigh muscle mass almost equal to normal left thigh. Has had 3 Pamidronate Injections.



2/18/11 Has received Pamidronate monthly for a year. All Lab. values remain normal. She is never lame and has no muscle atrophy. Chest films remain normal (left radiograph).

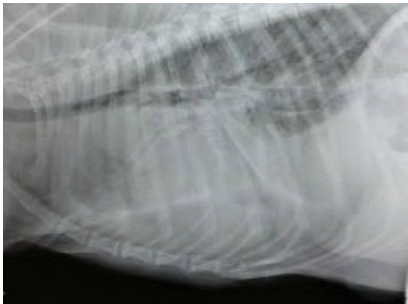


2/18/11 Normal Chest Radiograph



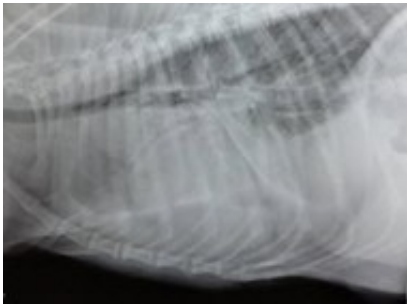
3/17/11 Collapsed after a short walk, pallor, cyanosis. Examined by a cardiologist, 450 ml fluid removed from the pericardial sac. Echocardiogram: suspected heart base tumor but too small to confirm. Cytology: Pericardial fluid contains many discrete cells having one to many nuclei and voluminous cytoplasm. The cytoplasmic edges suggest a brush border but none resemble typical mesothelial cells. These discrete cells are from a tumor but the cell line of origin can not be identified.

3/17/11 Pericardial Effusion



8/25/11 Suddenly collapsed again, pericardial fluid removed again, but continued to hemorrhage via a rent, intentionally done in hopes of allowing resorption of pericardial fluid, however she continued to hemorrhage.

8/25/11 Recurrent Pericardial Effusion



8/26/11 Euthanized, 13 years of age. Remained on 25 mgs. sid of deramaxx for the entire 18 months. Received Pamidronate monthly the first 12 months and every other month from 2/1/11 until she was euthanized. ALK. Phosp. remained normal throughout the 18 months. Continued normal weight bearing with no lameness and minimal atrophy. She was never allowed run free, off leash, during those 18 months.



Moët 8/26/11 Radiographs

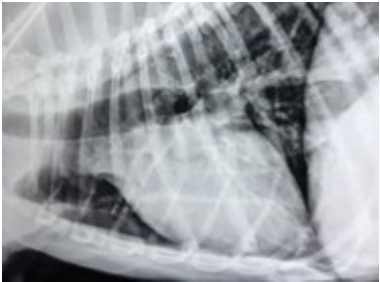


Histopathology Samples, Radiographed

Microscopic Findings: Osteosarcoma, fibroblastic, intermediate grade, right proximal tibia. Comment: Fibroblastic Osteosarcomas tend to grow more slowly and metastasize more slowly and may be less likely to metastasize than osteoblastic osteosarcomas.

**CASE 3:** Tonto, Retriever Mix Breed DOB 6/15/97 EXAM: 6/22/11 Wt. 34.1#'s Owner's Complaint: Left foreleg lameness, 2 weeks duration. PE: Elderly, very thin dog, with a mild, weight bearing lameness. Significant Supraspinatus and Infraspinatus muscle atrophy, however he has moderate generalized muscle atrophy. There is a palpable firm mass in the proximal left humerus. Lab. values all normal except ALKP 410 (normal range 5-131), FT4 48 (normal 8-40) T4 Normal, hypothyroid on Soloxine daily. Radiographic Exam: Probable Osteogenic Sarcoma. Standard Three Chest Radiographs, Normal

Monthly Pamidronate injections begun along with 25 rimadyl bid.



Normal Chest Radiographs 6/22/11



6/22/11 Radiographs

11/9/11 On PE he is not noticeably lame most of the time. The tumor is more easily palpated. Radiographically it is more visible because there is more periosteal cortical-cartilaginous proliferative tissue. His lung radiograph is normal. His ALK. Phosp. remains elevated 598 (normal range 5-131).



1/3/12 On PE Tonto appears very frail and has lost 5 #'s. Their other dog does chase him away from his food. He must be fed separately. The tumor is much larger. It is much more calcified, less bone lysis, and less likely to fracture. Surprisingly he weight bears with a mild limp. On his lateral chest radiograph he appeared to have a metastatic lesion but it was not visible on the other two radiographic views. His ALK. PHOS. is now 732 (normal range 5-131) and all other values are normal. The owner continues to decline CT scan and amputation. They will work at more calorie intake. He has always eaten mostly table food. He received his 6th Pamidronate injection, continues rimadyl 25mgs. bid and tramadol 50mgs bid was begun for pain.



2/29/12 Exam: On PE Tonto is now non-weight bearing. The tumor is much larger. Instead he drops down like a radial nerve paralysis injury. The tumor is very heavy, at least 2-3#'s, causing this gait abnormality. He weighs 29.5#'s but a portion of that is the tumor. His ALK. PHOS. continues to rise, now 876 (normal values 5-131). He is also now anemic, hemoglobin 8.8 and hematocrit 25.1. His limb was put in a Velpeau sling in hopes of helping his ambulating. Owner finally agreed to a CT scan prior to amputation. On 3/2/12 a CT scan was done and there was no metastatic disease. He had become weaker, stopped eating, and developed diarrhea, prior to the CT, so following his scan he was admitted to the critical care unit at CCVS. He became more anemic, was transfused in preparation for amputation, treated for his enteritis, regained his appetite, was making new RBCs indicated by an elevated reticulocyte count and was discharged 3 days later to see if he would maintain his improved condition. On 3/14/12 his Lab. values were nearly normal and had improved over all health. The owner consented to amputation. He was discharged 48 hours post-op. Histopathology: Osteosarcoma (19 mitoses in 10 400X field).

Radiographs: 3/2/12 Prior to CT. The tumor is massive, estimated 2-3#'s in weight. Lung Radiographs: No evidence of metastatic disease.



5/30/12 Exam: On PE appeared to have UTI, confirmed by C&S, Lab values normal except for ALK. PHOSP. 630 (normal values 5-131).

7/2/12 Exam: Anorexic, very weak, 22.9#'s, HCT 35%, BUN 20, hypothermic, owner elected euthanasia. Age 15 years, lived 13 months following his initial diagnosis with a tumor that had been present for a few months based on it's radiographic appearance at that time.

WHAT HAVE WE LEARNED?

- 1) ALL dogs with OS should not be euthanized because of a prognosis of impending pain from bone lysis resulting in micro fractures, and/or catastrophic pathologic long bone fractures, or severe pain (non-weight bearing), or early onset metastatic disease.
- 2) OS behave differently based on their histology.
- 3) OS pain can be modified with Pamidronate and NSAIDs
- 4) NSAIDs (rimadyl) down regulates VEGF, vascular endothelial growth factor, thus helping to slow the growth of the tumor. It should be prescribed for all OA dogs and monitored for tolerance both renal and liver.
- 5) Pamidronate appears to allow calcification of the affected bone and prevent bone lysis (osteoclast inhibition) in 6-8 weeks after initiating Pamidronate treatment.
- 6) Pamidronate gives us another option for OS treatment, especially in giant breeds who are poor amputation candidates and in elderly patients whose owner's will not consider amputation, or in dogs who have significant orthopedic disease in other limbs.
- 7) CT examination to determine metastatic lung disease is very accurate and inexpensive, thus very helpful when making decisions for treatment options. If owners want to go forward with either amputation alone, or amputation and chemotherapy, a CT should be done first.
- 8) Pamidronate is another option to palliative radiation, and appears to provide a comfortable weight bearing limb, for many months. If radiation is elected Pamidronate should be started before palliative radiation therapy.

CAN PAMIDRONATE BE COMBINED WITH PALLIATIVE RADIATION AND CHEMOTHERAPY? Based on one study the mean survival time (MST) was shortened when Pamidronate was given along with radiation and chemotherapy.<sup>14</sup> In another study when given 3-5 days before radiation and chemotherapy there was a synergistic effect.<sup>15</sup>

BETTER BISPHOSPHONATES? Zoledronate now used in human medicine more than Pamidronate BUT it is cost prohibitive at \$1093.53, our cost per bottle vs. Pamidronate \$194.34, our cost per bottle.

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DON'T GET HYPERTENSIVE OVER HYPOTENSION  
20

Blood pressure is the driving force for blood flow (perfusion) through capillaries that supply oxygen to organs and tissue beds of the body. Blood pressure is needed to propel blood through high resistance vascular beds, including those of the brain, heart, lungs and kidneys. Blood pressure values are expressed in millimeters of mercury (mm Hg) and as three measurements: systolic, mean and diastolic. The systolic pressure is the pressure generated when the left ventricle is fully contracted. Diastolic pressure is the pressure measured when the left ventricle relaxes. Mean arterial pressure (MAP) is calculated as one third the systolic pressure plus two thirds the diastolic pressure. Mean blood pressure determines the average rate at which blood flows through the systemic vessels. It is closer to diastolic than systolic because, during each pressure cycle, the pressure usually remains at systolic levels for a shorter time than at diastolic levels. Most times, under anesthesia, a patient's mean pressure is what the anesthetist focuses on. A mean arterial pressure of at least 60 mm Hg is needed to properly perfuse the heart, brain and kidneys.

Mean arterial blood pressures consistently below 60 mm Hg can lead to renal failure, decreased hepatic metabolism of drugs, worsening of hypoxemia, delayed recovery from anesthesia, neuromuscular complications and central nervous system abnormalities, including blindness after anesthesia. Prolonged hypotension (> than 15-30 minutes) can lead to nephron damage. Although the effects may not be immediately apparent since 65-75% of nephrons need to be damaged before renal disease becomes clinically observable, the effects may play a role in the onset of renal disease later in a pet's life. Severe untreated hypotension can lead to cardiac and respiratory arrest. Hypertension, or excessively high blood pressure, can lead to problems as well. Ideally, any animal under anesthesia should have regular blood pressure monitoring because most anesthetic drugs affect blood pressure in some way. Mean arterial blood pressure = cardiac output (CO) x systemic vascular resistance (SVR). Cardiac output is defined as the amount of blood pumped by the heart in a unit period of time. CO = Heart rate (HR) x stroke volume (SV = contractility). Systemic vascular resistance is the amount of resistance to flow through the vessels. Some vessels may be dilated, and therefore allow more flow at less resistance. Constriction of vessels may limit blood flow and require more pressure to get blood through. It's important to know that many of the drugs we use for anesthesia affect one or more of these systems in some way.

Pulse palpation: If no monitor is available, the manual palpation of an arterial pulse can give some indication of the state of the blood pressure. A palpable pulse pressure is the difference between the systolic and diastolic pressures. A difference of at least 30 mm Hg is necessary to palpate a strong pulse. Peripheral pulse palpation sites include the lingual, dorsal metatarsal, carpal, auricular and coccygeal. It is best to monitor the peripheral arteries because these pulses are lost at a much higher mean than the central (femoral) arteries. Potential cardiovascular abnormalities may be detected by regular palpation. Pulses should be assessed for strength, rate, and regularity and palpation should begin prior to induction so that differences in these can be tracked (monitor trends) from the very onset of anesthesia through recovery.

Blanching the mucous membranes with direct pressure should result in a refill time of less than 2 seconds. Delays in refill time can indicate intense vasoconstriction or hypotension.

Oscillometric devices work by picking up pulsation under an occlusion cuff placed over an artery. The cuff is connected to a monitor that can be programmed to measure blood pressure at specific intervals of time. These devices deliver systolic, mean and diastolic readings as well as the heart rate. Most have alarms that can be set to alert when readings are out of the accepted range. The cuff size should be approximately 40% of the circumference of the limb (or tail) around which it will be placed. Cuffs that are too large will lead to artificially low readings and too small a cuff will give false high readings. Ideally, cuffs should be placed on a limb that is close to heart level (the level of the right atrium is the zero mark for blood pressure). Limbs well above the heart may give artificially low readings. Legs hanging well below the heart will give false highs. The cuffs are usually marked with the proper placement over the artery. They must not be applied too tightly as this may occlude flow and cause inaccurate readings as well as swelling distal to the cuff. Poor pulse signals from poor flow (the rear limbs during a severe GDV or large abdominal mass), or any movement of the limb during a reading will interfere with the device and may cause it to fail or deliver an inaccurate reading. These devices do not usually work consistently or at all on very small patients, although there are some newer, veterinary specific monitors out that claim to work accurately on small animals.

Normal systolic blood pressures in the conscious patient are 100-160 mm Hg, normal diastolic pressures are 60-100 mm Hg and normal mean arterial blood pressure ranges are 80-120 mm Hg. Hypotension is classified as MAP of less than 60 mm Hg. It is important to be able to identify the cause of a blood pressure abnormality to know how to begin treatment for it. There are generally three things to consider when looking for causes of hypotension. Look for drugs or physiological/pathological factors that may reduce systemic vascular resistance (SVR), look at heart rate, and look for things that affect stroke volume (preload/contractility). As mentioned earlier, many of the drugs used in anesthesia cause some degree of hypotension, and less often, hypertension. Knowing the side effects of these drugs and how they work will help in determining treatment. Drugs that decrease SVR (and cause vasodilation) in a dose dependent manner include acepromazine, thiobarbiturates, propofol, isoflurane and sevoflurane. Other physiologic factors that may cause a decrease in blood volume or vascular tone include hemorrhage, inadequate volume administration or replacement, dehydration, shock, sepsis, anaphylaxis or severe hypercapnia (high CO<sub>2</sub>). Patients with acid/base abnormalities should be stabilized prior to anesthesia if possible to help reduce the possibility of hypotension. Drugs that can decrease heart rate include opioids, alpha 2 agonists, and the inhalant drugs isoflurane and sevoflurane. Patients with intracranial disease, hypothermic patients, and extremely fit pets may have low heart rates (bradycardia). Anesthetic drugs affecting the contractility of the heart include the inhalants, thiobarbiturates, propofol, and alpha 2 agonists. The inhalant drugs are potent vasodilators, with up to a 50% reduction in cardiac contractility at surgical planes of anesthesia as well. The other drugs' effect on contractility is more transient and less profound. Alpha 2 agonists and phenylephrine cause vasoconstriction of blood vessels which results in hypertension. The effects of hypertension from the alpha 2 agonists is transient, lasting only a few minutes before the vessels relax and hypotension can result. The dissociative drugs, Ketamine and Telazol have indirect positive effects on the cardiovascular system and thus increase heart rate, but this can cause a reduction in stroke volume. Patient positioning can affect blood pressure. Obese, bloated, or patients with large abdominal masses placed in dorsal recumbency may be hypotensive due to excessive pressure on the caudal vena cava. This pressure may compromise venous return and result in hypotension. The same can happen when positive pressure ventilation is used.

Certain disease states can cause hypertension including pheochromocytomas, pulmonic stenosis, heartworm disease, and hyperthyroidism. Ideally these patients will have their hypertension well controlled before surgery. The exception may be the pheochromocytoma patient whose hypertension may spike up during surgery when the tumor is manipulated. A nitroprusside CRI may be indicated for these patients. If a patient develops hypertension under anesthesia that is not related to a disease state, the cause is most likely related to inadequate anesthetic depth and/or inadequate analgesic administration. Adjusting anesthetic depth and providing additional pain medications should result in normotension.

Step one in developing a plan for treatment of hypotension is determining the cause. If the patient is otherwise normal and healthy, the anesthetic drugs are most likely the cause of hypotension. The effects of these drugs are dose related and therefore the best first treatment always involves reducing the dose of the drug, or reducing anesthetic depth. Anesthetic protocols that include appropriate analgesics, pre-operatively and peri-operatively will allow lower doses of all anesthetic drugs to be used, lowering the side effects of each drug as well. Any patient anesthetized with inhalant drugs and/or premedicated with acepromazine will have some degree of vasodilation. Intravenous fluid administration of crystalloids at a rate of 10 ml/kg/hr is recommended in any patient under anesthesia to help "fill the space" caused by vasodilation and to replace normal ongoing losses that occur for patients (with normal cardiovascular and renal function, patients with certain cardiac diseases may not be able to "handle" excessive fluid overload) under anesthesia. Fluid therapy is best begun before hypotension exists. For suspected hypovolemia a fluid bolus of "one hour's worth" the patient's maintenance rate may be given (i.e. 35 kg pet = 350 mls bolus, along with maintenance fluids). Reassess following the bolus. If the patient is instrumented with a Doppler monitor you may be able to hear the improvement and "stronger" flow. Blood loss should be replaced with 2-3 times the suspected amount of loss. One ml of blood loss should be replaced with 2-3 mls of crystalloid. Excessive hemorrhage may require replacement with colloids including Hetastarch and blood products.

If blood pressure fails to respond to these therapies, and surgical stimulation does not fix the problem, then pharmacologic intervention may be necessary. Pharmacologic agents stimulate the cardiovascular system through two primary mechanisms. Vaso-pressor effects increase MAP through changes in heart rate, myocardial contractility or affecting the tone of the vasculature. Inotropic effects increase contractility and cardiac output. The two most common drugs used for this purpose in dogs and cats are dopamine and dobutamine. Less commonly, ephedrine and phenylephrine can be used. In extreme circumstances, epinephrine and norepinephrine may be indicated. Before beginning dopamine or dobutamine therapy it is important to ensure proper vascular volume. Side effects of these drugs include tachycardia and possible arrhythmias. Tachycardia is more prevalent in hypovolemic patients or with overdose. ECGs should be monitored when beginning therapy. Therapy should be reduced or discontinued at any sign of side effects. The half life of both drugs is relatively short and side effects should diminish with the discontinuation of therapy. These drugs are given as a constant rate infusion with the dose varying from 0.5-20 mcg/kg/min. Infusions should be started slowly and increased to the desired effect while the heart rate and rhythm are monitored closely.

Blood pressure should be routinely measured on any patient undergoing general anesthesia. The best way to prevent hypotension is to detect changes in blood pressure as soon as they begin.

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