



VIRGINIA VETERINARY NOTES

VIRGINIA-MARYLAND REGIONAL COLLEGE OF VETERINARY MEDICINE

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THOUGHT FOR THE MONTH

We make a living by what we get,
but we make a life by what we give.

--Winston Churchill

PRACTICAL TRANSFUSION MEDICINE FOR SMALL ANIMAL PRACTICE

INTRODUCTION - Transfusion of whole blood and blood components is a frequent necessity in veterinary practice. Separation of blood into its cellular components allows for more efficient and specific replacement of the patient's needs as well as reducing the likelihood of transfusion reactions resulting from unnecessary cellular or plasma protein administration.

NECESSARY EQUIPMENT - Transfusion medicine does not necessitate much extra equipment. Anticoagulant plastic bags (see fresh whole blood below), transfer tubes, and transfer bags are required. A simple squeeze device may be purchased or fabricated. This is necessary to separate blood components. The only critical piece of equipment not readily available in veterinary clinical practices is a blood bag centrifuge. Most blood banks and human hospitals have centrifuges and, when asked, will readily centrifuge veterinary blood products. The separation of cryoprecipitate (see below) requires an ultrafreezer which is also available at blood banks and hospitals.

DEVELOPING A CORE OF CANINE DONORS is easy if all your good clients with large mild tempered and young dogs are asked: 1) could we type your dog? and 2) if she/he is the right type could he/she become a donor? The ideal canine donor should be screened for brucellosis, borreliosis, ehrlichiosis, Rocky Mountain Spotted Fever, dirofilariasis, and babesiosis. The ideal canine blood type is dog erythrocyte antigen (DEA) I.1, 1.2, and 7 negative. All potential blood and blood product recipients (dog, cat, horse) should minimally have major and minor crossmatches. The importance of crossmatching cannot be overemphasized. Patients never having had transfusions are subject to serious and perhaps lethal transfusion reactions!

Feline donors should be screened for FIV and FeLV, hemobartonellosis, and have low or negative antibody titers to corona viruses and toxoplasmosis. There is no universal feline blood donor. All feline recipients should have major and minor crossmatches. Stormont Laboratories, 1237 Beamer St. Woodland, California 95695 will type canine and feline EDTA blood.

CROSSMATCH PROTOCOL - **MAJOR**: 1) mix 0.2 ml of DONOR EDTA (or Citrated) packed red cells with 4.8 mls of 0.9% saline. 2) place 0.1 ml of this suspension in each of 3 test tubes. 3) add 0.1 ml of RECIPIENT serum to each tube. 4) incubate for 15 minutes - one tube at room temperature, one at 4.C and one at 37.C. 5) centrifuge all 3 tubes for 1 minute and evaluate each for agglutination and or hemolysis, either of which indicate incompatibility. **MINOR**: Repeat the above but substitute recipient red cells and donor serum.

BLOOD COMPONENTS that have the greatest demand in small animal practice are whole blood, packed red blood cells, whole plasma, and its derivatives. Plasma products can be further classified as fresh, fresh-frozen (that is frozen immediately after plasma is freshly harvested from fresh blood), stored (whole blood can generally be stored with minimal precautions while retaining red blood cell viability for periods up to four weeks in normal refrigerator temperatures), platelet rich plasma, and cryoprecipitate (a product of fresh frozen plasma).

Fresh Whole Blood: Indications for the use of fresh whole blood are hemorrhagic shock, anemia, excessive surgical hemorrhage, nonimmune hemolytic anemia, and in some circumstances associated with immune-mediated hemolytic anemia. Stored

whole blood has the same indications as fresh whole blood. When stored at 1 to 6°C in plastic bags containing CPD-A1 (Citrate-to chelate calcium and prevent coagulation; Phosphate and Dextrose to maintain red blood cell glycolysis and thus the ability to pick up and deliver oxygen; and Adenine to maintain ATP production and thus the ability of the red blood cell to deform and traverse the microcapillary beds), whole blood has an effective shelf life of four weeks. However, blood older than several weeks and stored in CPD-A1 plastic bags requires twenty-four hours or more, within the patient, before normal oxygen pickup and delivery returns to normal.

Packed Red Blood Cells: The major indication for packed red blood cells is replacement for all types of needs not requiring plasma. Basically, the correct treatment for anemia not associated with volume depletion is packed red blood cells. Only when hemorrhagic shock is extant or pending is fresh whole blood indicated. Packed red blood cell administration is indicated when volume overload is a potential hazard or complication. Fluid balance and oncotic pressure are maintained easily by crystalloids given, when necessary, along with packed red blood cells. Packed red cells have a useful shelf life of several weeks or even longer depending upon the clinical situation for which it will be utilized.

Fresh Plasma: The primary indication for fresh plasma administration is hemostatic (clotting factor) deficits. Fresh plasma is taken off of the cell pack after centrifugation within three to four hours and either used within twenty-four hours or frozen within six hours of blood collection.

Stored Plasma: The indications for stored plasma are volume expansion (shock and burn patients), hypoproteinemia, and general supportive therapy in severely ill individuals. When retrieved from blood collected and stored at 1 to 6°C in plastic bags containing CPD-A1, plasma may be frozen for more than one year, thawed, and administered to the appropriate patient. When stored plasma is not frozen it has a useful shelf life of four weeks in the situations indicated above. It cannot, however, be used in patients with clotting factor deficiencies because of the extremely short half-inactivation times of coagulation proteins.

Fresh Frozen Plasma: Fresh frozen plasma is harvested within six hours of blood collection and is frozen at -70 to -80°C for optimal preservation of clotting proteins. It is also useful in treating septicemic patients and patients with disseminated intravascular coagulation. Some clinicians feel that fresh or freshly frozen plasma aids in the amelioration of some cancers and the side effects from neoplasia.

Platelet-Rich Plasma: Platelet-rich plasma is indicated in cases of thrombocytopenia with active bleeding such as immune-mediated thrombocytopenia, ehrlichiosis, bone marrow suppression and platelet dysfunctional states (thrombocytopathies).

Cryoprecipitate: Cryoprecipitate is produced from fresh frozen plasma and is rich in coagulation factor VIII, fibrinogen, and fibronectin. In human medicine it is almost always a part of the therapy directed against sepsis, disseminated intravascular coagulation, hemophilia A, severe burns and von Willebrand's disease.

Super Plasma: Super plasma is obtained from whole blood of a donor pretreated with DDAVP (D-amino, D-arginine vasopressin). One hour before anticipated blood collection, the donor is administered DDAVP (1 g/kg subcutaneously). The DDAVP serendipitously activates and, perhaps, increases von Willebrand's factor in most dogs. Super plasma is the ideal treatment for von Willebrand's related problems such as parvoviral enteritis in those breeds markedly affected by von Willebrand's disease (a few examples are Doberman Pinschers and Rottweilers), hypothyroidism in Dobermans and enostosis in growing large breed dogs. It is also useful in treating fading puppy syndrome which is associated with von Willebrand's disease. --Bernard Feldman, DVM, PhD, Virginia-Maryland Regional College of Veterinary Medicine, Blacksburg, VA.

RABIES IN VIRGINIA

"Although the total number of rabies cases in Virginia is declining, the potential for exposure to rabies is not," said Dr. Suzanne R. Jenkins, assistant state epidemiologist for the Department of Health. Health officials are concerned about human exposure to rabies because the area of the outbreak is spreading. Also, many sections of the state reporting rabies cases have large human populations.

"It is normal for the number of rabies cases to decline after an initial peak," said Jenkins. "This is because the disease kills many animals and others may develop natural protection after exposure, leaving fewer susceptible animals. Once raccoon rabies has been in an area, it will not disappear. Therefore, people and pets are always at risk in that area, even if no new cases are reported."

To date, 127 rabies cases have been reported in Virginia this year. That compares to 172 cases reported for the same time period in 1989. In 1990, 65 percent of the cases reported occurred in raccoons.

The raccoon rabies outbreak began in 1977 in the northwest region of the state and has spread to the south and east. The counties of Matthews and Lunenburg and the city of Colonial Heights reported their first cases in 1990. Seven new communities reported rabid raccoons in 1989. They include the counties of Dinwiddie, Gloucester, Chesapeake, Prince Edward and Prince George, and the cities of Newport News and Petersburg.

"Most human rabies exposures come from domestic animals," said Jenkins. This year, six rabid cats and one rabid dog have been reported. In 1989, there were 12 rabid cats reported and one rabid dog.

Vaccination of dogs and cats provides a barrier between rabid wildlife and people. Virginia law requires inoculations for domesticated cats as well as dogs before the animals reach 4 months of age. The vaccines should be administered by a licensed veterinarian and kept up-to-date.

On the average, two persons die of rabies in the United States each year. The last human rabies case in Virginia was in 1953. In 1989, at least 226 state residents required treatment after exposure to rabid animals. Treatment consists of an injection of globulin and rabies vaccine followed by four more injections of vaccine over a four week period. Treatment should be given as soon as possible following exposure. --As reported in VDH Public Health News, August 1990, Virginia Department of Health, Richmond, VA.

FELINE DYSAUTONOMIA

Feline dysautonomia, also called Key-Gaskell syndrome, dilated pupil syndrome, and feline autonomic polygangliopathy, is a relatively new disease in cats. It was first reported in 1982 in the United Kingdom by Key and Gaskell. Up until 1988, this syndrome was only recognized in the United Kingdom, Ireland, Sweden, and Norway. In 1988, cases were reported to have occurred in cats in the United States.

Dysautonomia is a disturbance of the systemic autonomic innervation with a marked reduction in the number of neurons in the autonomic ganglia, resulting in complete autonomic denervation of the eye and other organs. Dysautonomia is reported to occur in man, horses, dogs, and cats. In man, the syndrome has been related to a number of different causes including diabetes mellitus, paraneoplastic syndrome, genetic defects, CNS lesions, chronic renal failure, drug reactions, and heavy metal toxicoses. In animals, the cause(s) of dysautonomia remain obscure despite extensive virologic, toxicologic, histologic, and epidemiologic studies. The sudden increase in the incidence of this disease in cats around 1982 suggested an environmental toxin or infectious agent as the cause. In two epidemiologic surveys, 140 cases were reviewed and no age or sex predilection, similarities in environment or management, or evidence to support an infectious cause were found.

CLINICAL SIGNS

The time of development for the classical clinical signs of dysautonomia is variable and ranges from rare, peracute cases to chronic ones with a more gradual onset of signs over several weeks. Initially, the cat may present for what seems to be the early stages of an upper respiratory infection or may show a transient fever with diarrhea. The CBC, chemistry panel, and urinalysis are typically normal. Most cats are FeLV negative. The signs seen are all related to dysfunctioning of the autonomic nervous system. A list of the most common clinical signs are as follows:

- Dilated, unresponsive pupils
- Protrusion of the third eyelids
- Blepharospasms
- KCS (STT <10 mm/min and as low as 0-2 mm/min)
- Dry crusted nose
- Dry oral mucous membranes and oral cavity
- Anorexia, lethargy
- Megaesophagus and difficulty swallowing
- Vomiting and/or regurgitation
- Slowed gastric emptying (seen with a Barium swallow)
- Fecal and urinary incontinence
- Constipation
- Bradycardia (<120 bpm and as low as 90 bpm)
- Distended bladder (which is easily expressed)

Seventy to ninety percent of the cases will have decreased tear production, bilateral mydriasis, and bilateral prolapsed third eyelids. The fundic examination is usually normal and there are no visual deficits. Some cats may have decreased to absent PLR's. In some dysautonomic cats that have been recovered, normal PLR's, D-shaped pupils will develop, with the flat border of the pupil consistently on the nasal side. This indicates selective loss of the malar nerve or regrowth of the nasal nerve.

DIAGNOSIS

Protrusion of the third eyelids with dilated, unresponsive pupils and vision that is not impaired, along with some the other clinical signs is almost pathognomonic for dysautonomia. This syndrome may at first be confused with an upper respiratory infection, intestinal obstruction, or Horner's syndrome, depending on the presenting complaints, but later in the disease the above clinical signs help differentiate dysautonomia from other differentials.

Pharmacological testing can also be used to demonstrate denervation hypersensitivity of both the sympathetic and parasympathetic systems. When a muscle or effector organ is chronically denervated, the threshold of response is lowered; this phenomenon is known as denervation hypersensitivity. Pharmacologic testing of the sympathetic and parasympathetic denervation is described below.

A) PARASYMPATHETIC DENERVATION

1. Instill one drop of 0.1% pilocarpine into the eyes and measure the pupillary diameter every five minutes. If denervation is present, immediate miosis can be expected when compared to a normal cat. Therefore, it is concluded that the iris sphincter muscle is hypersensitive to cholinergic stimulation.
2. Instill one drop of 0.6% echothiophate iodide into the eyes. Miosis will occur in normal cats. Because echothiophate iodide does not induce miosis in the dysautonomic eye, the mydriasis in dysautonomia must be attributable to postganglionic-parasympathetic denervation.

B) SYMPATHETIC DENERVATION

Instill one drop of 1:10,000 epinephrine into the eyes. The third eyelid will retract in the denervated eye because of hypersensitivity of the orbital smooth muscle to epinephrine.

Another diagnostic tool that can be used is histopathologic evaluation of the autonomic nervous system. Histopathological lesions are confined to the autonomic ganglia, all of which (sympathetic and parasympathetic) are affected to a similar degree. These lesions consist of severe neuronal degeneration and abnormal neuropile. Major abnormalities are found in the peripheral and central nervous system.

TREATMENT

A major problem in the management of dysautonomic cats, particularly in the early stages of the condition, is providing adequate fluid intake, electrolyte balance, and nutrition. Most affected cats are anorexic and have diffuse esophageal and gastrointestinal motility disorders. Total parenteral nutrition via a stomach tube or nasogastric tube is usually required. Steroids or Valium may be used to increase the cat's appetite, but are generally not useful. For cats that lack adequate gastric motility, metoclopramide may be beneficial. Prophylactic antibiotics may be required if megaesophagus is present and secondary aspiration pneumonia is a concern.

Parasympathomimetics such as bethanecol per os or physostigmine or pilocarpine eyedrops may be helpful if constipation or urinary retention is a problem. Complications with the use of these agents include hyperesthesia, muscular fasciculations, abdominal cramps, and diarrhea. These side effects can be countered with atropine.

If KCS is present, topical wetting agents may be instilled in the eyes three to six times a day, or ophthalmic preparations of cyclosporine may be used. The problems associated with the dilated pupils and prolapsed third eyelids usually are not specifically treated, as they don't interfere with vision or cause any discomfort to the cat.

PROGNOSIS

The owner of a dysautonomic cat should always be given a poor prognosis for full recovery of the cat. Twenty to forty percent will recover, but the initial severity does not appear to be particularly useful in assessing the eventual outcome. The cat's general condition and response to treatment are more reliable indicators for prognostication. The likely time for recovery is two to twelve months, but some cats will have residual signs such as dilated pupils and intermittent regurgitation for life. --Lori Staley, Denise M. Lindley, DVM, MS, Diplomate, ACVO, Sheryl G. Krohne, DVM, MS. *Purdue Veterinary Notes*, No. 169, October 1990. Purdue University, West Lafayette, IN.

CONTINUING EDUCATION OPPORTUNITIES SPRING 1991 VIRGINIA-MARYLAND REGIONAL COLLEGE OF VETERINARY MEDICINE

<u>Date</u>	<u>Program</u>	<u>Location</u>	<u>Contact Hours</u>
*March 15-16 *	Clinical Hemoatology/Cytology	Blacksburg	10
March 22-23	Small Animal Thoracic Radiology	Blacksburg	10
March 28 *	Small Animal Medicine Update	Charlottesville	4
April 12-13 *	Gastrointestinal Endoscopy (Basic)	Blacksburg	9
April 19-20	Orthopedic Surgery - Canine Forelimb	Blacksburg	10
April 27	Food Animal Practitioners Workshop	Staunton	6

*These courses are limited enrollment and feature hands on laboratories.

Note: Program brochures are mailed six-eight weeks prior to the course date. For course information or assistance, please contact:

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EASTERN STATES CONFERENCE

The seventh annual Eastern States Veterinary Conference takes place January 12-17, 1991 at the Marriott World Center in Orlando, Florida.

VIRGINIA ASSOCIATION WINTER MEETING

The Virginia Veterinary Medical Association annual convention will be held February 21-24, 1991 at the Homestead in Hot Springs.

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