



# HEMOPET/HEMOLIFE

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## IMMUNE-MEDIATED HEMATOLOGIC DISEASE AND BONE MARROW FAILURE

Immune-mediated hematologic disease is being reported with increasing frequency in animals and humans. In the dog this syndrome is often associated with bone marrow failure. Affected animals usually have one or more of the following signs: autoagglutinating red blood cells; Coombs positive hemolytic anemia; spherocytes; nonregenerative or poorly regenerative erythroid response; severe thrombocytopenia; profound leukopenia; other autoimmune diseases especially thyroiditis; active erythropoiesis, granulocytopenia or megakaryocytopenia with maturation arrest at the early stem cell level; and poor response to standard treatment protocols with corticosteroids and other immunosuppressive drugs. In many cases a recent stress (e.g. vaccination; drug; chemical or toxic exposure; surgery; hormonal influence; infection; injury) could be identified as a potential triggering event within the previous 30 days.

Our experiences with these cases indicate that:

1. Autoimmune thyroiditis/hypothyroidism is frequently present and/or affected dogs are often of breeds or cross-breeds susceptible to thyroid disease.
2. Aggressive and more sustained treatment with corticosteroids is needed. Suggested doses are: prednisone or prednisolone given at 2-3 mg/lb/day divided BID for 5-7 days, or dexamethasone equivalents at 0.25 – 0.35 mg/lb/day divided BID. Therapy is reduced weekly by ½ and maintained for at least six weeks. Alternate day steroid therapy may be needed for some time thereafter on a long-term, low level basis.
3. For severe cases, other immunosuppressive therapy is given. We prefer cyclosporine (Sandimmune, 100 mg/mL oral syrup) to cyclophosphamide (Cytosan) and give it at 10 mg/kg for 5 days, rest 2 days, then at 5 mg/kg for another 5 days. The lower dose is repeated after a 2 day rest on a 5 days on, 2 days off cycle as long as is needed (usually 2-3 courses of 5 days). This drug induces rapid T-cell suppression within about 48 hours and has been safe, effective, and well tolerated at these doses. CYCLOSPORINE CAN BE BITTER, so give with a little milk to reduce nausea potential. Neoral is the newer form, which is also well tolerated. In cases where sustained more potent immunosuppression is required for clinical stabilization, azathioprine (Imuran) should be instituted along with cyclosporine. Dose is 1 mg/lb/day for 7-10 days initially followed by a downward tapering over several weeks. Azathioprine may be needed every other day or less often, on a long-term basis. As azathioprine takes about 10 days to effectively suppress T-cells, clinical responsiveness will not occur immediately. Cyclosporine is therefore given concurrently in the early stages of the disease to provide rapid immunosuppression until the azathioprine takes hold. The goal of this immunosuppressive therapy is to stabilize the ongoing immune destructive process. The dosage guideline we use is adjusted to maintain the absolute lymphocyte count as about 1/3 of the normal range (750-1500/uL).

4. Those breeds most often affected in our case population are cocker spaniels, poodles (all varieties), golden retriever, Doberman pinschers, miniature schnauzers, akitas, beagles, rottweilers, lhasa apsos, German shepherds, shih tzus, terriers, and mixed breeds of these backgrounds. Any of the nearly 50 breeds predisposed to thyroid disease are at risk for an immune-mediated condition. Thyroid supplementation at 0.1 mg/10 lb given twice daily is essential for cases with concomitant thyroid disease and is helpful to stimulate the bone marrow whether or not thyroid tests indicate hypothyroidism. It also enhances platelet function.
5. Anabolic steroid (nandrolone decanoate, Deca Durabolin, 2-5 mg/kg given once a week for 4-6 doses) is given to stimulate the marrow.
6. Hematinics containing iron and vitamin B12 have been helpful.
7. In poorly responsive immune thrombocytopenias (ITP), an initial dose of vincristine (Oncovin, 0.01 mg/lb IV) may be helpful to release remaining platelet stores, and danazol (Danacrine, 2.5-5 mg/lb BID initially and then tapered to SID) has been effective along with steroids and thyroid for long-term maintenance.
8. The most severe cases with autoagglutinating red cells or profound thrombocytopenia may recover completely with the aggressive therapeutic approach outlined above, although a subset of these dogs convert to having a chronic low-grade nonresponsive anemia over the long term.
9. Cases with the best overall prognosis tend to be younger animals in which the underlying primary “trigger” of the immune-mediated disease was hypothyroidism, a drug which is withdrawn, or a recent vaccination/toxic exposure. Correction of the thyroid disease with serial monitoring of thyroid function to establish the appropriate maintenance dose of hormonal supplement is important.

## **SHELF-LIFE OF PACKED RED BLOOD CELLS**

A special nutrient solution (Adsol, Baxter Healthcare Corp.) is added to our units of canine packed red blood cells during preparation to preserve and extend the shelf-life from 28 to at least 42 days. The solution contains saline, dextrose, adenine, and mannitol. Post-transfusion viability studies in dogs have shown that 80% of the red cells in packed cell units remain viable for 37 days, whereas 75-80% are viable for up to 44 days in the presence of Adsol or equivalent nutrient solutions (Wardrop et al, J. Vet. Int. Med. 5, 1991, p. 148). Hemopet's units of packed red blood cells display a conservative expiration dating of 42 days from the time of collection.

If the units of packed you intend to transfuse are approaching the expiration date, most of the cells will still carry oxygen efficiently. However, a portion (20-25%) of these cells will be less viable or nonviable. Therefore, the dosage of packed cells to be transfused should be increased slightly to compensate for this reduction. For example: a dosage of 3-5 mL per pound of packed red blood cells is generally recommended to raise the PCV by 9 percentage points. If the red cell unit is within the first half of its shelf-life, 3 mL per pound should suffice. For older units, increasing the volume transfused to 5 mL per pound may be advisable.