The principles of therapy for immune-mediated hemolytic anemia (IMHA) and immune-mediated thrombocytopenia (ITP) include:

- Treating the underlying disease, where applicable
- Inhibiting red blood cell and platelet phagocytosis
- Decreasing auto-antibody production
- Monitoring for, and potentially undertaking prophylactic therapy for, complications
- Providing supportive care

**Immunosuppressive Therapy**

Immunosuppressants work by a variety of methods to decrease phagocytosis of red blood cells or platelets by the mononuclear phagocyte system and to decrease anti-erythrocyte and anti-platelet production by lymphoid tissue. For either IMHA or ITP, it is important to prepare the owners for months of therapy, typically >6 months. Medications are tapered slowly, usually by decreasing the dose by 25% (of the initial dose) every 2-4 weeks. Some patients may require life-long therapy.

**Prednisolone: 2 mg/kg PO q 24 hr; Dexamethasone: 0.25 mg/kg IV q 24 hr**

- Indicated for: IMHA & ITP
- Mechanisms of action: reduces Fc-mediated phagocytosis of red blood cells and platelets by macrophages & reduces antibody production
- Pros: rapid onset of immunosuppression & inexpensive
- Cons: iatrogenic Cushing’s disease, gastrointestinal ulceration & prothrombotic

**Azathioprine: 2 mg/kg PO q 24 hr**

- Indicated for: IMHA & ITP
- Mechanisms of action: reduces lymphocyte number & reduces antibody production
- Pros: retrospective studies in IMHA suggest a beneficial response over prednisone alone & relatively inexpensive
- Cons: slow onset of immunosuppression, hepatotoxicity, acute pancreatitis, myelosuppression (so profound in cats, that its use in this species is not recommended)

**Cyclosporine (CyA): 3-5 mg/kg PO q12 hr**

- Indicated for: IMHA & ITP
- Mechanisms of action: reduces lymphocyte proliferation & reduces antibody production
- Pros: rapid onset of immunosuppression & relatively low rate of severe side-effects (self-limiting GI side-effects, gingival hyperplasia)
• Cons: expensive, highly variable oral bioavailability, theoretically should not be used in diabetic patients & retrospective studies have not necessarily found an improvement in outcome

**Mycophenolate mofetil (MMF): 10-20 mg/kg PO q 12 hr**

- Indicated for: IMHA & ITP
- Mechanism of action: reduces lymphocyte proliferation
- Pros: rapid onset of immunosuppression & relatively low rate of severe side-effects (diarrhea)
- Cons: expensive (but less than CyA) & retrospective studies have not necessarily found an improvement in outcome

**Splenectomy**

- Indicated for: IMHA & ITP
- Mechanisms of action: removes a major site of extravascular hemolysis and antibody production
- Pros: one small study looked at proactive splenectomy early in the course of treatment for IMHA and found increased survival
- Cons: expensive, invasive, anemic patients may be poor candidates for anesthesia, thrombocytopenic patients may be poor candidates for surgery

**Liposomal clodronate**

- Indicated for: IMHA
- Mechanisms of action: causes apoptosis of macrophages thereby inhibiting phagocytosis of red blood cells
- Pros: no adverse effects noted in pilot study
- Cons: no significant improvement in survival time

**Human Intravenous Immuglobulin (hIVIG): 0.5 g/kg IV once**

- Indicated for: ITP
- Mechanisms of action: thought to block Fc-mediated phagocytosis of platelets by macrophages & possibly reduces antibodies
- Pros: significantly faster recovery compared to prednisone alone documented in a randomized, double-blind, placebo-controlled trial
- Cons: expensive, availability & potential for allergic reaction

**Vincristine: 0.02 mg/kg IV once**

- Indicated for: ITP
- Mechanisms of action: encourages early platelet release by the bone marrow & reduces phagocytosis by macrophages
- Pros: significantly faster recovery compared to prednisone alone documented in a non-randomized, unmaskested trial
- Cons: myelosupression

**Melatonin: 3-6 mg/kg PO q 12 hr**
• Indicated for: ITP
• Mechanisms of action: ?
• Pros: inexpensive & relatively low rate of severe side-effects (drowsiness)
• Cons: use is entirely anecdotal

**Leflunomide: 4 mg/kg PO q 12 hr**
• Indicated for: ITP? (Anecdotally appears more useful for immune-mediated polyarthritis than for IMHA or ITP)
• Mechanism of action: reduces lymphocyte proliferation
• Pros: rapid onset of immunosuppression & case report of 2 dogs with ITP that improved with leflunomide monotherapy
• Cons: expensive (but less than CyA), hepatotoxicity, myelosuppression, cutaneous vasculitis

**Cyclophosphamide** – No longer recommended as studies suggested increased morbidity and increased incidence of serious adverse effects.

**Danazol** – No longer recommended as studies suggested it was not efficacious.

**Thromboprophylactic Therapy**
Thromboembolism is a major complication of IMHA and a major cause of mortality. Not only does the disease inherently cause hypercoagulability, but our mainstay therapy – glucocorticoids – also contribute. Dogs with ITP are likely also prothrombotic, but their thrombocytopenia is likely “self-treating” their risk.

**Aspirin: 0.5 mg/kg PO q 24 hr**
• Indicated for: IMHA
• Mechanism of action: inhibits platelet aggregation
• Pros: inexpensive
• Cons: potential for GI side-effects (extremely rare at this dose)

**Clopidogrel: 2 mg/kg PO q 24 hr**
• Indicated for: IMHA
• Mechanism of action: inhibits platelet aggregation
• Pros: well tolerated
• Cons: expensive

**Heparin** – Unfractionated heparin is no longer recommended due to unpredictable bioavailability, expense associated with monitoring & lack of evidence of improved survival. While low molecular weight heparin may surmount some of these problems, the effective dose is currently unknown and their expense is unrealistic for most patients.