Use of different immunosuppressive protocols for treatment of immune mediated haemolytic anaemia in dog and cat

There are many protocols described in the literature for different immune-mediated diseases: three examples are provided here. It is vitally important that the diagnosis of immune-mediated disease is confirmed before undertaking any of these protocols.

Protocol 1: Canine immune-mediated haemolytic anaemia and immune-mediated thrombocytopenia

Induction

Immunosuppression: Prednisolone: 40 mg/m^2 p.o. q24h (<10 kg body weight, 2 mg/kg p.o. q24h) and azathioprine (2 mg/kg p.o. q24h) are preferred to prednisolone on its own**.** Dexamethasone (0.3–0.5 mg/kg i.v. q24h) may be substituted for prednisolone if the patient is unable to tolerate oral medications. Mycophenolate mofetil (MMF) (7–10 mg/kg i.v. q12h) can be substituted for azathioprine if:

- Patient is unable to tolerate oral medications
- Patient has historical evidence of a rapid (>10% in 24 hours) fall in haematocrit prior to presentation
- Patient has gross evidence of spontaneous agglutination (as documented by a haematologist)
- Patient has evidence of intravascular haemolysis (haemoglobinuria, haemoglobinaemia)
- Patient has evidence of pancreatitis on biochemistry or physical examination.

Once patient is able to tolerate oral medications, then substitute prednisolone for dexamethasone and switch to oral dosing of mycophenolate mofetil (10 mg/kg p.o. q12h) or, if preferred, azathioprine at the above doses.

Antithrombotics: Aspirin (0.5 mg/kg p.o. q24h unless thrombocytopenic) may improve survival in dogs. If active GI ulceration, renal disease, or the patient is intolerant of oral medications, then low molecular weight heparin (100 IU s.c. q12h) can be used. There are no studies currently on clopidogrel, but this may be appropriate. Heparin should be administered (concurrently with aspirin unless there are any contraindications) if there is clinical evidence of thromboembolic disease. Discontinue on remission.

Antibiotics: Not required unless there is a documented infection, known risk of infection (e.g. GI barrier compromise, previous endocarditis) or known exposure to ticks.

Gastrointestinal protection: In general not required. Sucralfate is optional, but if given should be given 2 hours before other medications. In cases with known or suspected GI bleeding (particularly cases with immune-mediated thrombocytopenia), effective suppression of gastric acid secretion is required. Current evidence suggests that only famotidine and omeprazole will provide this. The practice of administering ranitidine etc. to every animal receiving high doses of steroids is not necessary and likely ineffective.

Relapse and rescue

If a mild relapse (e.g. a fall in PCV of <5% without any clinical signs of anaemia) occurs following documented remission, this may be treated by re-instigating the drug dosages used at the last visit when the patient was in remission. Severe relapses should be treated by re-instigation of induction doses of all drugs used initially. If this is ineffective (i.e. no response (increase in haemocrit by <5% despite ongoing regenerative response) within 6 days), or if rescue is to be attempted during initial induction phase of treatment (due to progressive deterioration), then ciclosporin (5–7.5 mg/kg p.o. q24h) may be beneficial. If there is no response to the ciclosporin within 5 days and/or the patient continues to deteriorate over that time or if the patient is not tolerant to oral medications, then **consider immunoglobulin** (0.5–1.0 g/kg i.v. over 6–8 hours). Note that immunoglobulin is best utilized for acute deteriorations. In the non-acute setting, or if long-term control is necessary in a patient that has previously failed all other orally administered drugs, then consider leflunomide (4 mg/kg p.o. q24h).

Decreasing doses

Maintain on induction doses until remission (normal PCV with no evidence of ongoing immune activation) is achieved assuming no suspected/known side effects to the drug(s).

Week	Glucocorticoid	Azathioprine/MMF	Immunosuppressant 3 (if used)	GI protectants (if used)
Remission	1 mg/kg q24h	UC	UC	UC
2	0.5 mg/kg q24h	UC	UC	STOP
4	0.5 mg/kg every other day	UC	STOP	
6	0.25 mg/kg every other day	UC		
8	STOP	50% dose reduction		
10		UC		
12		UC		

UC = Dose unchanged.

General notes:
Haematology to be rechecked at each visit (including weeks 14 and 18) and remission confirmed prior to each dose reduction.
Liver parameters should be rechecked at remission and weeks 4 and 8 (if on azathioprine).

Protocol 2: Feline immune-mediated haemolytic anaemia

Induction
Immunosuppression: Prednisolone: 2 mg/kg p.o. q12h and either of the following:

- Chlorambucil: >4 kg body weight, 2 mg p.o. q48h; <4 kg body weight, 2 mg p.o. q72h
- Mycophenolic acid (MPA): 10 mg/kg p.o. q12h
- **See Appendix I for safety and handling of chemotherapeutic agents.**

Mycophenolic acid is preferred if:

- Patient has historical evidence of a rapid (>10% in 24 hours) fall in haematocrit prior to presentation
- Patient has gross evidence of spontaneous agglutination (as documented by a haematologist)
- Patient has evidence of intravascular haemolysis (haemoglobinuria, haemoglobinaemia).

If the patient is unable to tolerate oral medications, then dexamethasone (0.6–1.0 mg/kg i.v. q24h) may be substituted for prednisolone and mycophenolate mofetil (MMF) (7–10 mg/kg i.v. q12h) may be substituted for mycophenolic acid.

Antithrombotics: Avoid in cats as there is no evidence of efficacy and risk of side effects.

Antibiotics: Not required unless there is a documented infection, known risk of infection (e.g. GI barrier compromise, previous endocarditis) or known exposure to ticks.

Gastrointestinal protection: Not required unless GI bleeding has been diagnosed. Effective suppression of gastric acid production is then required. Current evidence suggests that only famotidine and omeprazole will provide this. The practice of administering ranitidine etc. to every animal receiving high doses of steroids is not necessary and likely ineffective.

Relapse and rescue
See Protocol 1: Canine immune-mediated haemolytic anaemia and immune-mediated thrombocytopenia for details.

Decreasing doses
See Protocol 1: Canine immune-mediated haemolytic anaemia and immune-mediated thrombocytopenia for details.
(Note: reports of feline immune-mediated thrombocytopenia are too rare to provide a protocol for treatment, but it is likely that a similar approach should be adopted.)