

Supplementary Information 1: Inclusion Criteria and Pathogen-Specific Searches

Inclusion Criteria

1. Study presents primary data from dog(s) and cat(s) with spontaneous or experimentally induced disease. Reports of individual cases are suitable if they otherwise fulfil the inclusion criteria below.
2. Study is published as a complete report in a peer-reviewed journal; if written in a language other than English, it will be translated to assess suitability.
3. IMHA is diagnosed by the presence of a PCV or hematocrit <37% (dogs) or <27% (cats), or a hemoglobin concentration <12g/dL (dogs) or <9.5g/dL (cats), associated with the presence of antibodies directed against erythrocyte antigens, as indicated by one or more of the following criteria:
 - a. a positive saline agglutination test (dogs, cats);
 - b. a reciprocal titer of 5 or greater in a polyvalent Coombs' test or at least one reagent in a monovalent Coombs' test, at either 4°C or 37°C (or a 'positive' Coombs' test result) (dogs, cats);
 - c. the observation of significant spherocytosis (>1 spherocyte per high power field; or unquantified presence of spherocytes; dogs); in cats, wet mount preparations would be required to detect spherocytosis with any reliability;
 - d. ghost cells in the absence of oxidative damage (Heinz bodies), if examined in a fresh smear (cats);
 - e. flow cytometric confirmation of erythrocyte-bound IgM, IgG and/or C3 (dogs, cats); older papers may also apply the direct enzyme-linked anti-globulin test to detect IgG bound to erythrocytes (dogs, cats) or an enzyme-linked

immunosorbent assay to detect anti-erythrocyte antibodies in serum or plasma (dogs, cats).

Phagocytosis of erythrocytes or their precursors observed in a bone marrow, splenic or hepatic aspirate (dogs, cats) will be considered supportive, but not indicative, of immune-mediated disease in isolation, unless accompanied by remission of disease with immunosuppressive therapy in a patient with no evidence of hemophagocytic syndrome (i.e. bicytopenia or pancytopenia with >2% hemophagocytic macrophages in a bone marrow aspirate).

4. The dataset is independent: If the same group of animals is used in >1 study, only the study reporting data from the largest number of animals is included.

These criteria were all-inclusive for the purposes of data accrual. More rigorous diagnostic criteria for IMHA were subsequently developed by the Consensus Panel (Figure 2).

Pathogen-Specific Search Algorithms

Organisms identified in the manuscripts resulting from the original search were documented. Subsequent searches on PubMed to identify additional studies were made using the following search strings:

("Organism Genus"[MeSH Terms] OR "Organism genus"[All Fields]) AND cat[All Fields] AND ("anaemia"[All Fields] OR "anemia"[MeSH Terms] OR "anemia"[All Fields])

and

("Organism Genus"[MeSH Terms] OR "Organism Genus"[All Fields]) AND ("dogs"[MeSH Terms] OR "dogs"[All Fields] OR "dog"[All Fields]) AND ("anaemia"[All Fields] OR "anemia"[MeSH Terms] OR "anemia"[All Fields])

Papers were included if they met the following modified inclusion criteria to include studies that asked questions about mechanisms of IMHA induced by a given infection, but did not necessarily document IMHA in individual patients:

- Anemia as defined by the authors' laboratory reference interval for PCV, hematocrit or red blood cell number, or documentation of hemoglobin concentration less than 12g/dL, PCV less than 37% and red blood cell number less than 5.5×10^6 for dogs; or hemoglobin concentration <9.5 g/dL and PCV less than 27% for cats AND evidence of immune-mediated destruction (as defined by the inclusion criteria for IMHA above); OR mechanistic exploration of red cell membrane destruction in blood samples taken from an infected animal.