

RETROSPECTIVE AND COMPARATIVE STUDY OF 42 CASES OF ANEMIA IN DOGS

Daniela Mihaela Neagu¹, Vlad Luca¹*, Răzvan Codea¹, Cristian Popovici¹,
Alexandra Biriș¹

¹University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca, Cluj-Napoca, Romania; *Corresponding author: dr.lucavlad@gmail.com

Abstract. Anemia is a common pathology in dogs, characterized by a decrease in red blood cells 16 or hematocrit concentration, leading to a reduction in the blood's ability to carry oxygen. Anemia in dogs is a multifactorial condition requiring a detailed diagnostic approach and treatment tailored to each individual case. A better understanding of the causes and treatments of anemia can significantly improve the quality of life of affected dogs and reduce the mortality associated with this condition. This thesis aims to explore the different causes based on scientific literature reviews and the analysis of clinical cases collected within the emergency hospital of the Faculty of Veterinary Medicine in Cluj-Napoca. Data were collected and interpreted to determine trends 24 and correlations between different types of anemia and their underlying causes. The results of the study revealed several causes of anemia, being classified as hemorrhages: by intoxication, trauma or postoperative hemorrhages; hemolysis: autoimmune, parasitic; and production deficits: mainly following chronic renal failure.

Keywords: anemia, red blood cells, dog, causes

INTRODUCTION

Hematology is concerned with blood cells such as red blood cells (erythrocytes), white blood cells (leukocytes) and platelets (thrombocytes). But also blood coagulation, hemostasis and coagulation factors. (Krafft M.P., 2001.)

The production of blood cells is called hematopoiesis, and is characterized by a succession of stages through which stem cells pass before becoming blood cells in their own right. Each cell line has its own regeneration: erythropoiesis for red blood cells, leukopoiesis for white blood cells and thrombocytopoiesis for platelets. Erythropoiesis leads to the formation of erythrocytes, a process that takes around 7 days. Under normal circumstances, the lifespan of erythrocytes in dogs is 110 days. Red blood cells are mainly used to transport oxygen. Their size enables them to pass through the blood capillaries and carry oxygen throughout the body (Felter, 2002) (Brakch Nouredine, Kessler Dagmar, 2011).

Anemia is the most common red blood cell disease. It is diagnosed in 31% of dogs over 8 years of age. They represent a considerable veterinary challenge, due to the diversity of their causes and their varied clinical implications. In addition to being a frequent pathology, anemia has a rather complex diagnosis due to the multitude of its etiologies. (Chikazawa, S., et M. D. Dunning, 2016). Anemia is defined as a lack of hemoglobin in the blood: less than 12g/dL. Hemoglobin is the protein that enables red blood cells to bind oxygen. Below 10g/dL, the dog is considered anemic. Anemia is linked to a lack of red blood cells, but since red blood cells are made up of hemoglobin, hemoglobinemia is reduced (Cervone and Deshuillers, 2023).

Thus, if the anemia is mild to moderate, the clinical picture may be virtually non-existent, but the more severe the anemia, the more obvious the symptoms. Pallor of the mucous membranes, intolerance to exertion, increased heart rate and respiratory rate to compensate for the lack of circulating hemoglobin. Occasionally, a heart murmur may appear (Bellier et Cordonnier 2010)(Balch, Andrea, et Andrew Mackin, 2007).

There are three main causes of anemia. These are hemorrhage: the loss of red blood cells; hemolysis: the destruction of red blood cells; and the lack of red blood cell production. Hemorrhage and hemolysis lead to regenerative anemia (peripheral origin), as the body reacts to the lack of red blood cells and produces new ones. Conversely, a production deficit indicates a non-regenerative phenomenon (central origin) (Deshuillier, 2024; Balch et Mackin, 2007).

The aim of this study is to carry out a retrospective incidence study of canine anemias by comparing data from the faculty's emergency hospital and the literature and to identify the typical subjects and types of anemia most often encountered in veterinary practice.

MATERIALS AND METHODS

Selection criteria

The biological material is based on dogs from the Faculty of Veterinary Medicine, Cluj-Napoca, from October 1, 2022 to June 1, 2024 (a period of 20 months). The study focuses on dogs of different sexes, ages and breeds.

The first selection of cases was based on all dogs mentioning anemia in the corresponding AtlasVet software file. At that time, we had 84 potential cases. In 27 dogs the diagnosis of anemia was not confirmed. We thus had 57 cases. The lack of a mandatory blood smear to diagnose anemia led to the exclusion of 15 more dogs from the study. Ainsi, l'étude compte finalement 42 cas. The non-biological equipment consists of the analysis machines and the microscope for examining the smears. The ABAXIS VetScan HM5 veterinary hematology analyzer provides a detailed blood count of all 22 parameters. Les examens ont été réalisés dans le département de Physiopathologie of the Faculty of Veterinary Medicine of UASMV.

Parameters studied

The parameters studied are the dog's age, sex, breed and hematological parameters. Red blood cell count, hematocrit, hemoglobin, GMV, MCHC and MCHR, as well as platelet count, white blood cell count and, when permitted by the smear report, percentage of reticulocytes and microhematocrit value.

Statistical analysis. All recorded data were subjected to analysis of variance (ANOVA) and then compared by Tukey's multiple range test ($P \leq 0.05$). The data shown are mean values \pm SE.

RESULTS AND DISCUSSIONS

Our study focuses on 42 cases with at least one blood count and one smear showing anemia. Of these 42 cases, 18 were females (42.9%) and 24 were males (57.1%) (Fig. 1).

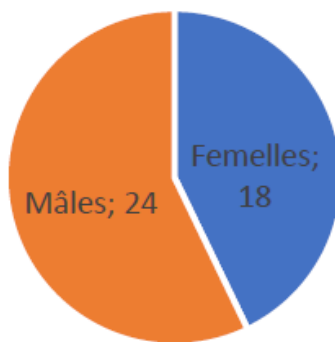


Fig. 1. Sex Prevalence in the study.

The mean age was 7.3 years, with the youngest case 12 weeks old and the oldest 17 years. The median age is 7.5 years.

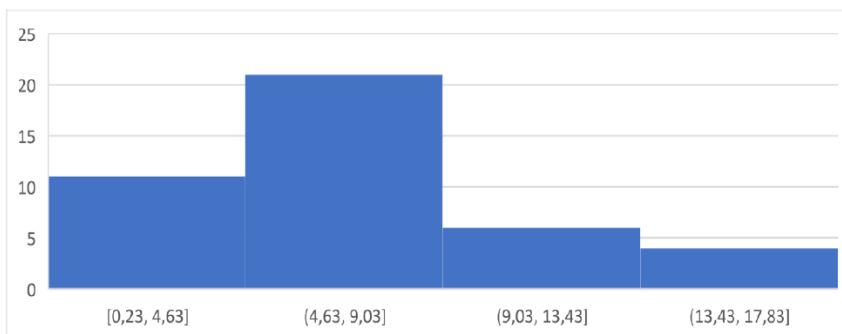


Fig. 2. Age prevalence in the study.

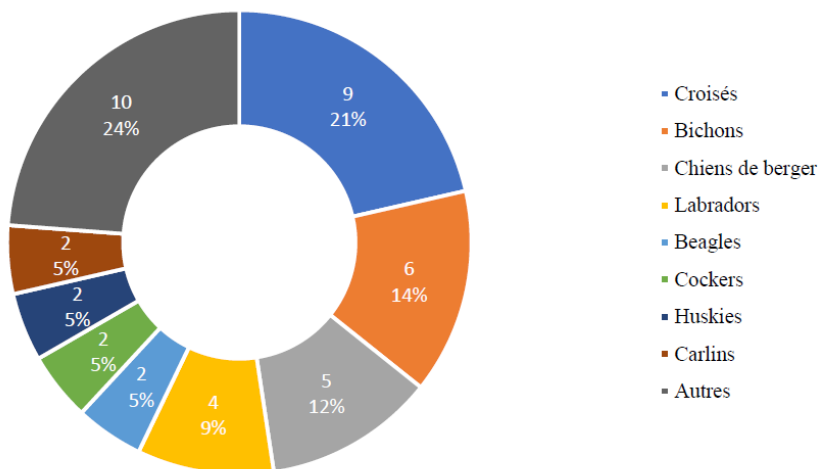


Fig. 3. Breed Prevalence in the study.

Regarding the breeds studied, we have 9 mixed breeds, 6 Bichons, 5 shepherd-type dogs (including 3 German Shepherds), 4 Labradors, 2 Beagles, 2 Cocker Spaniels, 2 Huskies, 2 Pugs, and other breeds that appear only once (Martin Cédric, 2004).

Basic Hematological Parameters

The patients studied had total red blood cell counts below the reference values of 5.5-8.5 million red cells per milliliter of blood. The average value obtained was 4 million red blood cells, with extremes of 1.1 million in a patient suspected of immune-mediated hemolytic anemia (female dog Rita) and 5.4 million in a patient with mild anemia (dog Max).

Hematocrit was the second parameter assessed, and most cases were below the norm. Only 6 animals (14%) were within the norm. These animals have rather mild anemias, as their red cell count is between 4.65 and 5.4 million. The lowest hematocrit value is 11.29%, corresponding to the animal cited in the previous paragraph (42). As hematocrit is an index directly related to red blood cell values, this correlation does not seem absurd. The average is 28.61%. (Maupas Hélène, 2003).

Hemoglobin was also taken into account. Once again, the majority of cases were below the norm. In fact, only 3 individuals are within the norms. The latter are already within the usual hematocrit values. The lowest value is 4g/dL, which again corresponds to the same dog suspected of autoimmune hemolytic anemia.

Platelets are also part of the studied parameters. Twenty (48%) of our cases are in thrombocytopenia (including three cases where values were so low that the device could not count them). Seven individuals had values above the normal range (McManus, P. M., et L. E. Craig, 2001).

Erythrocyte Indices Distribution

The erythrocyte indices are quite varied. Regarding the Mean Corpuscular Volume (MCV), most are within the normal range (80%), indicating normocytic anemia. Seven cases have values above the usual range, indicating macrocytic anemia, and one case is just below the normal range, indicating microcytic anemia (Brakch Noureddine, Kessler Dagmar, 2011).

The Mean Corpuscular Hemoglobin (MCH) represents the ratio between hemoglobin and the number of red blood cells. The average in this study is 23.2 pg. The Mean Corpuscular Hemoglobin Concentration (MCHC) corresponds to the ratio between hemoglobin and hematocrit. The average value of our cases is 32.3 g/dL. Both averages are within the reference intervals. However, some individuals fall outside these norms.

Fifteen individuals (36%) have increased MCH and/or MCHC values, indicating hyperchromic anemia. Thirteen individuals (31%) are considered to have hypochromic anemia, as their MCH and/or MCHC values are decreased. The remaining third of this study has normochromic anemia (Naigamwalla, D.Z., 2012).

To determine if the anemia was regenerative, we assessed the percentage of reticulocytes in 36 cases. Based on Fleishman's article (2012), anemias are considered non-regenerative if less than 1% reticulocytes are present. This scenario applies to 13 cases (36% of those with evaluated reticulocytes).

Anemias are considered mildly regenerative with reticulocyte percentages between 1% and 5%, which is the case for 14 individuals in this study (39%). Moderately regenerative anemia is identified with reticulocyte percentages between 5% and 20%, covering the remaining 9 cases (25%). In this study, we do not have any

marked regeneration cases with reticulocyte percentages over 20% (Renaud J.-B.,2016).

	Chiens	
Anémies non régénératives	13	36%
Anémies légèrement régénératives	14	39%
Anémies modérément régénératives	9	25%
Anémies fortement régénératives	0	0%

Fig. 4. Distribution of anemias according to the nature of their regeneration

Causes of Anemia in This Study

The classification of the patients included in the study was done in three categories: hemorrhagic anemia, hemolysis anemia and production deficiency anemia. In 5 cases, we were unable to determine the cause of the anemia. We are therefore basing our cause statistics on 37 cases.

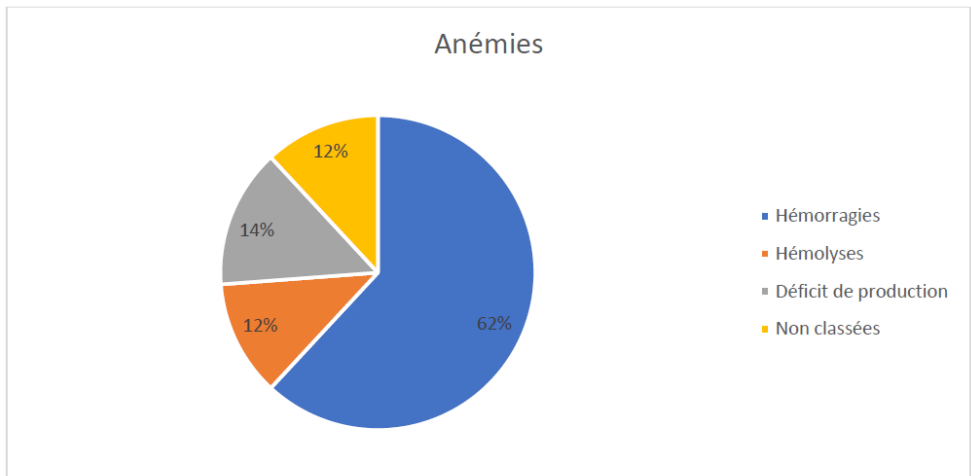


Fig. 5. Distribution of anemias by mechanism.

	GR	HT	HGB	VGM	TCM H	CCM H	RTC	μ H T	PLT	GB
Normes	5,5-8,5	37-55%	12-18	60-77	19,5-24,5	31-34			200-500	6-17
Total	4,00	28,61%	9,11	71,78	23,18	32,3	3,28%	24%	279,79	22,59
Hémorragies	4,20	29,66%	9,34	70,04	22,43	32,12	3,53%	26%	234,04	23,61
Hémolyses	2,58	20,30%	6,7	85,5	28,04	33,7	3,70%	16%	227	29,08
Déficit de production	4,27	30,05%	9,83	70,5	23,07	32,8	1,27%	27%	484,17	19,98

Fig. 6. Hematological values according to anemia mechanisms.

The table shows that erythrocyte values are below norms for red cell count, hematocrit and hemoglobin, validating the diagnosis of anemia. There is also an increase in white blood cells, which can be explained by various inflammatory reactions (Shih, Hong-Mou et al., 2018.) We note that anemia due to hemorrhage is lighter overall, since the number of red blood cells is 0.2 million higher. For hemolytic anemias, there is a clear inferiority of values: 1.42 million fewer red blood cells than the general average. Surprisingly, production-deficiency anemias have the highest values in this study (0.27 million red blood cells more than the general average).

Hematocrit levels are quite similar to red blood cell values, which is explained by the correlation between the two parameters. Once again, the values corroborate the diagnosis of anemia (Sugawara-Suda, Mei et al., 2023). Anemias due to bleeding and production deficiency are again rather subtle. And hemolysis is again well below the overall average (20.30% vs. 28.61%).

Les taux d'hémoglobine ont une nette diminution pour les hémolyses (6,7 g/dL) et des valeurs légèrement supérieures à la moyenne (9,11 g/dL) dans le cas des hémorragies (9,34 g/dL) et des déficits de production (9,83 g/dL). The average MCV and the trend previously observed are reversed. The MCV in cases of hemolysis (85.5 fL) is the highest value. In contrast, the MCV values for hemorrhagic anemias (70 fL) and anemias due to production deficits (70.5 fL) are slightly lower than the average value (71.78 fL), likely related to their more intense regeneration. (Vaqar, et al., 2024).

On remarque que les hémolyses (3,7% de réticulocytes) ont une tendance à régénérer légèrement plus que les hémorragies (3,53% de réticulocytes). Concernant les déficits de productions, rien d'étonnant à avoir moitié moins de régénération (1,27% de réticulocytes) étant donné la cause de l'anémie (Al-Naqshabendy, 2016).

In our study, we found 42 cases that could be interpreted. Males are slightly more represented. The literature does not indicate a predisposition for any particular sex regarding anemia in general. We also note that some breeds are more prevalent in our study, but given the small number of cases, we can question the accuracy of this prevalence. For instance, we have 6 Bichons, representing 14% of the study, which is quite significant. However, the Bichon is a popular breed in Romania due to its small size and docile nature, leading to a potential bias. The more common a breed is in the population, the more it will appear in varShepherd breeds are also omnipresent in this study, but they are already very common in the population. Nevertheless, among the 3 cases of immune-mediated hemolytic anemia (IMHA), we have a Cocker Spaniel, which is the breed most predisposed to this condition (Balch and Mackin, 2007).

As far as age is concerned, once again, anemia is not predisposing in the broadest sense. Hemorrhage following an MVA or poisoning, for example, can occur at any age. However, more specific cases, such as chronic renal failure, occur in older subjects. This was the case in our study: the median age of dogs with anemia due to renal pathology was 11 years.(Ambar, Neta, et Tricia Tovar, 2022). Similarly, AHMI tends to appear later in life, and in our study, the median age was 9 years. What's more, out of an already unrepresentative sample, 5 cases failed to find an etiological diagnosis. Incidences are therefore even less reliable.

This lack of diagnosis depends on the examinations carried out in the file. For those dogs whose anemia has not been classified, there is little information in the software or even in the physical file. The lack of complementary examinations makes it impossible to understand the pathological mechanisms leading to anemia. A

biochemistry, an ultrasound could have brought new information perhaps (Wysoke, J. M., 1990). Most anemias resulting from hemorrhages are microcytic and regenerative, which aligns with the literature. Indeed, during a hemorrhage, the body responds by rapidly producing new red blood cells, which results in slightly smaller red blood cells. Hemorrhagic anemias are the most interpretable in this study due to their higher frequency. In fact, the averages of each parameter for hemorrhages are close to the overall averages, given their significant proportion (62%).

With regard to anemia values following production deficits, such low values are rather surprising, given that regeneration is not efficient. But it's conceivable that this is just the beginning of the process and/or that these animals have received blood transfusions, keeping red blood cell and hematocrit values at the limit (Trudel Caroline, 2022). Platelets tend to be in the high range, unlike other types of anemia. Since there is no gap to close, as in the case of hemorrhages, the latter are not consumed. Diagnosing an anemic animal is not so complex, but determining the cause is even more so.

CONCLUSIONS

Anemia in dogs is a complex and multifactorial condition that requires a rigorous diagnostic approach and personalized treatment. Therefore, a comprehensive hematological evaluation and blood smear analysis are essential. This thesis has highlighted the various causes of anemia in dogs by reviewing the scientific literature and analyzing clinical cases from the Emergency Hospital of the Faculty of Veterinary Medicine in Cluj-Napoca. The collected data have allowed for the identification of significant trends and correlations between types of anemia and their underlying causes.

The results of our study revealed that anemias in dogs can be classified into three main categories: hemorrhages (caused by intoxications, trauma, or surgical interventions), hemolyses (of autoimmune or parasitic origin), and production deficits (often due to chronic renal insufficiencies). Each of these categories requires a specific therapeutic approach to optimize the chances of recovery and improve the quality of life for the affected animals.

In conclusion, a better understanding of the pathogenic mechanisms of anemia and the application of appropriate diagnostic and therapeutic protocols are essential for the effective management of this condition in dogs. Continued research in this field and ongoing training for veterinary practitioners are crucial for reducing the mortality associated with canine anemia and improving the care provided to our four-legged companions.

REFERENCES

1. Al-Naqshabendy, « Study of hematological and blood biochemical parameters in cats experimentally infected with *toxocara cati* ». *Assiut Veterinary Medical Journal* 62,2016, no 148: 35-38.
2. Ambar, Neta, et Tricia Tovar, « Suspected Hemolytic Anemia Secondary to Acute Zinc Toxicity after Ingestion of “Max Strength” (Zinc Oxide) Diaper Rash Cream ». *Journal of Veterinary Emergency and Critical Care (San Antonio, Tex, 2022, 32, no 1: 125-28.*
3. Balch, A., Mackin A., « Canine immune-mediated hemolytic anemia: Pathophysiology, clinical signs, and diagnosis ». *Compendium (Yardley, PA,) 29: 217-25.*

4. Bellier S., Nathalie Cordonnier, « Les valeurs usuelles en hématologie vétérinaire ». *Revue Francophone Des Laboratoires*, 2010, no 420: 27-42.
5. Brakch Noureddine, Kessler Dagmar, « FICHE TECHNIQUE MCV, MCH, MCHC », Centre Suisse de Contrôle de Qualité, 2011: 91-107.
6. Cervone M., Deshuillers P., « Mon analyseur voit rouge, que faire ? », 2023: 59-64.
7. Chikazawa, S., Dunning, M.D., « A Review of Anaemia of Inflammatory Disease in Dogs and Cats ». *The Journal of Small Animal Practice* 57, 2016, n° 7, 348-53.
8. Crichton R., « Iron Metabolism: From Molecular Mechanisms to Clinical Consequences. » John Wiley & Sons, 2016:567-74.
9. Gérard D., G. Fumagalli, F. Lierde, et Vincent Genty, « Érythroïèse et métabolisme du fer : interactions et applications biomédicales ». *Bio Tribune Magazine*, 2010, 34: 22-32.
10. Donzel Elise, 2007. « Les anémies et les thrombopénies auto-immunes chez les carnivores domestiques : étude bibliographique »
11. Eschbach, Joseph W, 1989 « The Anemia of Chronic Renal Failure: Pathophysiology and the Effects of Recombinant Erythropoietin ». *Kidney International* 35, 1989, no 1: 134-48.
12. Feldman, B. F., P. Handagama, et A. A. Lubberink, « Splenectomy as Adjunctive Therapy for Immune-Mediated Thrombocytopenia and Hemolytic Anemia in the Dog ». *Journal of the American Veterinary Medical Association* 187, 1985, n° 6:1205-1210.
13. Felter Marlène, « Modifications de l'hémogramme au cours des maladies et affections accompagnées d'anémie chez le chien », 2002:45-52.
14. Fleischman, Wendy, « Anemia : Determining the Cause », 2012: 147-155.
15. Galati Pamela, Sandy Walsh, Patty Lathan, 2019 « Diagnosis and Management of Hypoadrenocorticism in Dogs ». *Today's Veterinary Practice*, 25 juin 2019.
16. Gaston-Carrère Sophie, 2009. « Intervalles de référence hématologiques chez l'espèce canine avec l'analyseur XT-2000iV (Sysmex) », 2009:35-42.
17. Géraud Marion, « Les syndromes hématologiques d'origine toxique chez les carnivores domestiques : Etude clinique et synthèse bibliographique », 2007:112-119.
18. Haddam, A. E. M., et D. Meskine, « Les anomalies hématologiques dans l'hypothyroïdie ». *Annales d'Endocrinologie*, 34ème Congrès de la Société Française d'Endocrinologie SFE Poitiers 2017, 78, 2017, no 4: 349.
19. Hayaoui Nour El Houda, KADDOUR Kolée Amira Bouchra, « Etude des Anémies chez le Chien (Variations de l'Hémogramme Rouge) », 2018:678-690.
20. Jauzein, 2018 « EPO et dopage ». *Planet-Vie*, 12 décembre 2018.
21. King, L. G., U. Giger, D. Diserens, et L. A. Nagode, « Anemia of Chronic Renal Failure in Dogs ». *Journal of Veterinary Internal Medicine* 6, 1992, no 5: 264-70.
22. Krafft, Marie-Pierre, « Les émulsions de fluorocarbures (PFC) : Des transporteurs d'oxygène injectables efficaces et facilement détectables ». *Revue Française des Laboratoires* 2001, 2001, n° 331: 55-59.
23. Liu, Jui-Ming, Ren-Jun Hsu, Fung-Wei Chang, Feng-Hsiang Chiu, Chia-Lun Yeh, Chun-Fa Huang, Shu-Ting Chang, Hung-Chang Lee, Hsin Chi, et Chien-Yu Lin, 2017 « Increased risk of pernicious anemia following scabies: a nationwide population-based matched-cohort study ». *Therapeutics and Clinical Risk Management* 13 (13 septembre 2017): 1205-11.
24. Martin C., « Les ehrlichioses du chien : étude bibliographique, diagnostic et comparaison de trois kits de diagnostic sérologique rapide de l'ehrlichiose monocytaire », 2004: 398-405.
25. Maupas Hélène, « Les plaquettes sanguines chez le chien : physiologie et perturbations au cours des affections tumorales. Etude bibliographique », 2003: 89-94.

26. McManus, P. M., et L. E. Craig, 2001 « Correlation between Leukocytosis and Necropsy Findings in Dogs with Immune-Mediated Hemolytic Anemia: 34 Cases (1994-1999) ». *Journal of the American Veterinary Medical Association* 218, 2001, no 8: 2003,1308-13.
27. Mount, et Feldman, « Mechanism of Diphacinone Rodenticide Toxicosis in the Dog and Its Therapeutic Implications ». *American Journal of Veterinary Research* 44, 1983, no 11: 198-200.
28. Naigamwalla, Dinaz Z., Jinelle A. Webb, et Urs Giger, « Iron Deficiency Anemia ». *The Canadian Veterinary Journal = La Revue Veterinaire Canadienne* 53, 2012, no 3 (mars 2012): 250-256.
29. Thrall N.R. « Hemolytic anemia, spherocytosis, and thrombocytopenia associated with honey bee envenomation in a dog », 2019: 157-179.
30. Renaud J.-B., « Prévalence des hémopathogènes vectorisés lors d'anémie chez le chien », 2016:124-129.
31. Scafidi, Jason M., Razie Amraei, et Vikas Gupta, « Histology, Howell Jolly Bodies ». In *StatPearls*. Treasure Island (FL), 2024: StatPearls Publishing.
32. Shih, Hong-Mou, Chih-Jen Wu, et Shuei-Liong Lin, « Physiology and pathophysiology of renal erythropoietin-producing cells ». *Journal of the Formosan Medical Association* 117, 2018, no 11: 955-63.
33. Sugawara-Suda, Mei, Keitaro Morishita, Yuto Iwanaga, Jumpei Yamazaki, Yumiko Kagawa, Nozomu Yokoyama, Noboru Sasaki, Hiroshi Ohta, Kensuke Nakamura, et Mitsuyoshi Takiguchi, 2023 « Investigation of the Therapeutic Effects, Predictors, and Complications of Long-Term Immunosuppressive Therapy in Dogs with Precursor-Targeted Immune-Mediated Anemia ». *The Journal of Veterinary Medical Science* 85, no 7, 2023: 695-701.
34. Swann, James W., Oliver A. Garden, Claire L. Fellman, Barbara Glanemann, Robert Goggs, Dana N. LeVine, Andrew J. Mackin, et Nathaniel T. Whitley, « ACVIM Consensus Statement on the Treatment of Immune-Mediated Hemolytic Anemia in Dogs ». *Journal of Veterinary Internal Medicine* 33, 2019, no 3: 1141-72.
35. Trudel Caroline, « Investigation de l'état hypercoagulable chez le chien grâce à la génération de thrombine modifiée par l'ajout d'anticoagulants», 2022.
36. Vaqar, Sarosh, et Karen B. Shackelford, « Pernicious Anemia ». In *StatPearls*. Treasure Island (FL), 2024: StatPearls Publishing.
37. Wysoke, J. M., P. Bland van-den Berg, et C. Marshall, « Bee Sting-Induced Haemolysis, Spherocytosis and Neural Dysfunction in Three Dogs ». *Journal of the South African Veterinary Association* 61, 1990, no 1: 29-32.