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Research Article

What does white blood cells tell us at the first clinic visit of the cat?

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ABSTRACT

Objectives: Interpretation of laboratory data is very important and based on comparison with reference intervals in routine practice. Leukocyte term includes all white blood cells and their precursors. These cells use blood circulation for going to the original tissues from their original locations. Total leukocyte count can be changed by various physiologic and pharmacologic reasons. In healthy cats, lymphocytes are the second most frequent leukocyte in the blood. Compared to middle-aged or old cats, young animals have higher absolute lymphocyte counts.

Materials and Methods: The medical records of cats referred to the Ankara University Small Animal Hospital for general examination between April 2016 and August 2017 were retrospectively reviewed. Complete blood count (CBC) data includes red blood cell (RBC) count, haemoglobin, haematocrit (HCT), mean cell volume (MCV), mean cell haemoglobin (MCH), mean cell haemoglobin concentration (MCHC), red blood cell distribution width, platelet count, white blood cell (WBC) count, neutrophils, lymphocytes, monocytes, eosinophils and basophils.

Results: Of 5292 cats, 191 cats at the age between 0 and 1 and with CBC data were included in the study. CBCs were obtained from all 191 cats at the first visit. The relationship of hematological data to the reference range is summarized in Table 2. It was observed that 25.7% of the cats had leucocyte counts below the reference interval and 3% had above the reference interval. Considering neutrophil counts, it is seen that 23.3% were lower and 4.5% were higher. According to the results of 191 hemogram tests, lymphocyte counts of 39 cats (19.3%) and monocyte counts of 9 cats (4,5%) were found to be low.

Discussion: This is a novel study that includes the results of detailed examination of breed and age distribution of complete blood count results at the first clinical visits of cats. According to our retrospective screening results, it is seen that the relation of monocyte numbers with age is statistically significant. ($p = 0.018$) The biggest difference between the two age groups in the study is the pre- and post-adolescence periods. It is important to precisely know the results of CBC test in the first visit to the clinic and to take the necessary precautions to eliminate the abnormal results before vaccination.

Keywords: Complete blood count, white blood cell, leucopenia, neutrophilia

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INTRODUCTION

Interpretation of laboratory data is very important and based on comparison with reference intervals in routine practice. Leukocyte term includes all white blood cells (WBC) and their precursors. These cells use blood circulation for going to the original tissues from their original locations. There are two main categories of granulocytes (or myelocytes) containing white blood cells, neutrophils, eosinophils and basophils, and agranulocytes containing lymphocytes and monocytes (Kerr, 2002). Many private veterinary practices have in-house high-quality automated hematology tools that can quickly achieve complete blood count (CBC) results (Harvey, 2017).

Total leukocyte count can be changed by various physiologic and pharmacologic reasons. Changes in the WBC count frequently parallel with the absolute neutrophil count, because neutrophils are the predominant blood leukocyte in cats (Weiss and Wardrop, 2011). Maturation of neutrophils can take approximately 3.5 – 6 days (Ettinger and Feldman, 2009).

Increased number of neutrophils in circulation or neutrophilia can occur in a number of ways (Harvey, 2017).

1- A shift of cells from the marginal to the circulating pool
2- Steroid effects
3- Response to infection
4- Masked granulocytosis
5- Neoplasia

Physiologic leukocytosis and Stress (Glucocorticoid - Induced) Leukogram are two distinct patterns of non-pathologic leukograms. Physiologic leukocytosis is generally seen in young, healthy cats that become excited or frightened by fear, excitement, restraint, venipuncture. Leukogram changes are temporary, taking about 20-30 minutes, with very rapid changes (Weiss and Wardrop, 2011). Endogenous or exogenous glucocorticoid elevations tend to cause mild to moderate leukocytosis with mature neutrophilia, lymphopenia and eosinopenia. 24 hours after a single 5 mg dose of prednisolone neutrophil values return to reference intervals (Ettinger and Feldman, 2009).

When immature neutrophils exceed 500 – 1000 bands/μL, left shift is considered clinically significant in the cats (Stockham and Scott, 2010). Septicemia, endotoxemia and severe inflammation of large-surface areas (e.g. peritonitis, pleuritis, pneumonia, gastroenteritis, placentitis) are reasons for degenerative left shift (Weiss and Wardrop, 2011).

If the size of the marginal pool is greater than normal and the circulating neutrophil numbers are not increased as in mild infections, this situation can be masked granulocytosis. If a leukemia is suspected, it can be difficult to differentiate from a marked neutrophilia, and a bone marrow biopsy therefore becomes essential (Kerr, 2002).

Viral infection (panleucopenia, Feline Immunodeficiency Virus (FIV)) are possible assumption for neutropenia in cats (Kerr, 2002). Several causes and various mechanisms can play a role in neutropenia. Increased tissue use or loss exceeding bone marrow production, decreased bone marrow production and sequestration of neutrophils or a single cause like endotoxemia can lead to neutropenia. (Weiss and Wardrop, 2011)

In healthy cats, lymphocytes are the second most frequent leukocyte in the blood. Compared to middle-aged or old cats, young animals have higher absolute lymphocyte counts. Young and healthy cats are especially prone to physiologic leukocytosis which is secondary to excitement or fear (Weiss and Wardrop, 2011). Lymphocytosis is also present in 20% of cats with glucocorticoid deficiency (Ettinger and Feldman, 2009). Lymphocytosis may also be seen in chronic antigenic stimulation and after a few days post–vaccination. Corticosteroid-induced redistribution of lymphocytes, viral infections, septicemia or endotoxemia, lymphocyte-rich thoracic effusions and some gastrointestinal diseases are the most frequent causes of lymphopenia (Weiss and Wardrop, 2011).

Hypersensitivity or inflammatory lesions, parasites, feline leukemia virus (FeLV)-associated eosinophilia, tumor-associated eosinophilia and miscellaneous conditions like hyperthyroidism and hypoadrenocorticism are some causes of eosinophilia (Ettinger and Feldman, 2009; Lapointe et al., 1997; Sellon et al., 1992; Tzounos et al., 2017). Eosinopenia is difficult to recognize clinically because the lower end of the reference interval for feline eosinophil counts is nearly 0 cells/μL.

It has been reported that 11 % of the leukograms of hospitalized cats have nonspecific monocytosis (Ettinger and Feldman, 2009). After acute and chronic inflammation, tissue destruction and trauma-related injuries, suppuration, necrosis, pyogranulomatous inflammation, hemolysis, hemorrhage, malignancy, and immune-mediated disorders cause neutrophilia. Like eosinopenia, monocytopenia is clinically unimportant in cats (Weiss and Wardrop, 2011).

MATERIALS AND METHODS

The medical records of cats referred to the Ankara University Small Animal Hospital for general examination between April 2016 and August 2017 were retrospectively reviewed. Only cats with

haematology profiles submitted to the diagnostic laboratory at our Central Diagnosis Laboratory were included in this study. Clinical data collected included sex, age and breed information.

		Frequency	Percent
WBC	Low	52	25,7
	Normal	144	71,3
	High	6	3,0
LYM	Low	39	19,3
	Normal	160	79,2
	High	3	1,5
MONO	Low	9	4,5
	Normal	115	56,9
	High	78	38,6
NEUT	Low	47	23,3
	Normal	146	72,3
	High	9	4,5
EOS	Low	24	11,9
	Normal	178	88,1

Table 2. Haemotological data and relationship between reference intervals for cats during first visit. WBC (white blood cells), LYM(Lymphocytes), MONO (Monocytes), NEUT (Neutrophils), EOS (Eosinophils)

Haematology was performed using an Exigo (Boule Diagnostics). CBC data includes red blood cell (RBC) count, haemoglobin, haematocrit (HCT), mean cell volume (MCV), mean cell haemoglobin (MCH), mean cell haemoglobin concentration (MCHC), red blood cell distribution width, platelet count, white blood cell (WBC) count, neutrophils, lymphocytes, monocytes, eosinophils, basophils. For this test, blood was taken and placed in an EDTA tube and analyzed the same day.

Statistical evaluation

Continuous variables were presented as mean, standard deviation, standard error, median, minimum and maximum, categorical variables as frequency and percentage. All blood parameters

were evaluated with Shapiro Wilk Test to check the normality assumption. Since all blood parameters violated the normality assumption, the differences were evaluated among sex, breed and age groups with Mann Whitney-U Test. Statistical analyzes were performed using SPSS version 14.01 (SPSS GmbH Software, Munich, Germany) and $p<0,05$ was considered to indicate a statistically significant difference.

RESULTS

Study population

Of 5292 cats, 191 cats at the age between 0 and 1 and with CBC data were included in the study (Table 3). 108 cats (56.5 %) were male and 83 were female (46.5 %). 54 cats (28.27%) were pedigree breeds including British Shorthair (n = 9), Scottish Fold (n = 22), Ankara (n=6), Exotic Shorthair (n=1), Siamese (n = 3), Persian (n = 4), Chinchilla (n=5), Bombay (n=2), Van (n=1) and Russian Blue (n=1). The mean age of the cats was 8.12 months (range 3–12 months).

			Cats (n)	Mean	SD	Standard Error	Median	Minimum	Maximum	*P* value
WBC	Gender	Female	108	9,21	5,93	0,57	8,20	0,60	39,80	0,664
		Male	83	8,52	4,43	0,49	8,10	0,40	22,40	
	Breed	Mixed	137	8,96	5,30	0,45	8,40	0,40	39,80	0,524
		Pedigree	54	8,79	5,43	0,74	7,40	1,50	29,20	
	Age	0-6 m	51	7,58	3,87	0,54	7,40	0,40	17,30	0,057
		7-12 m	140	9,40	5,70	0,48	8,50	0,60	39,80	
LYM	Gender	Female	108	2,28	1,57	0,15	1,90	0,30	8,60	0,824
		Male	83	2,26	1,64	0,18	1,70	0,20	8,40	
	Breed	Mixed	137	2,26	1,62	0,14	1,80	0,20	8,60	0,882
		Pedigree	54	2,30	1,53	0,21	1,90	0,20	6,50	
	Age	0-6 m	51	2,22	1,77	0,25	1,60	0,30	8,60	0,389
		7-12 m	140	2,29	1,54	0,13	1,90	0,20	8,40	
MONO	Gender	Female	108	0,97	0,66	0,06	0,80	0,10	3,00	0,918
		Male	83	1,11	0,96	0,11	0,70	0,00	4,90	
	Breed	Mixed	137	1,06	0,78	0,07	0,90	0,00	3,00	0,337
		Pedigree	54	0,97	0,88	0,12	0,70	0,00	4,90	
	Age	0-6 m	51	0,85	0,77	0,11	0,70	0,00	3,00	**0,018**
		7-12 m	140	1,10	0,82	0,07	0,90	0,00	4,90	
NEUT	Gender	Female	108	5,61	4,88	0,47	4,35	0,10	33,00	0,871
		Male	83	4,93	2,84	0,31	4,40	0,10	14,70	
	Breed	Mixed	137	5,34	4,14	0,35	4,50	0,10	33,00	0,563
		Pedigree	54	5,23	4,13	0,56	3,85	0,40	23,90	
	Age	0-6 m	51	4,32	2,33	0,33	4,10	0,10	9,50	0,128
		7-12 m	140	5,67	4,56	0,39	4,50	0,10	33,00	
EOS	Gender	Female	108	0,35	0,54	0,05	0,20	0,00	3,90	0,199
		Male	83	0,23	0,28	0,03	0,20	0,00	2,10	
	Breed	Mixed	137	0,30	0,45	0,04	0,20	0,00	3,90	0,584
		Pedigree	54	0,29	0,44	0,06	0,20	0,00	2,50	
	Age	0-6 m	51	0,18	0,14	0,02	0,20	0,00	0,60	0,129
		7-12 m	140	0,34	0,51	0,04	0,20	0,00	3,90	

Table 1. Haematological data for cats during first visit. WBC (white blood cells), LYM (Lymphocytes), MONO (Monocytes), NEUT (Neutrophils), EOS (Eosinophils)

Records of the cats without CBC or those not brought to the clinic the first time were excluded from the study. 51 cats (26.7%) were between 0-6 months, 140 (73.3%) were older than 6 months and younger than 1 year of age. There was no significant difference in the level of white blood cell counts except monocytes (p=0,018) (Table 1).

Complete Blood Count (CBC)

CBCs were available for all cats in first visit. The relationship of hematological data to the reference range is summarized in Table 2. It was observed that 25.7% of the cats had leucocyte counts below the reference interval and 3% was above the reference interval. Considering neutrophil counts, it is seen that 23.3% were lower and 4.5% were higher. According to the results of 191 hemogram tests, lymphocyte counts of 39 cats (19.3%) and monocyte counts of 9 cats (4.5%) were found to be low.

BREED	Frequency	Percentage
Mix	137	71,73
British Shorthair	9	4,71
Scottish Fold	22	11,52
Ankara	6	3,14
Exotic Shorthair	1	0,52
Siamese	3	1,57
Persian	4	2,09
Chinchilla	5	2,62
Bombay	2	1,05
Van	1	0,52
RB	1	0,52
Total	191	100,00

Table 3. Breed distribution of cats

DISCUSSION

This is a novel study that includes the results of detailed examination of breed and age distribution of complete blood count results at

the first clinical visits of cats. In the clinical examination of the puppies, WBC counts provide important information on the defense potential and inflammatory status of immune system. Infectious diseases can also be included in this diagnosis list. Since panleukopenia is one of the most common diseases among these, CBCs that are leukopenic outcome should be evaluated for this disease. Feline panleukopenia virus causes immunosuppression through cellular depletion by infecting lymphoid tissues. Lymphocyte migrates into tissues and as a result of lymphocytosis, lymphopenia arises (Stuetzer and Hartmann, 2014). 39 lymphopenic cases (19.3%) indicate that there is a probability of panleukopenia of approximately 2 out of every 5 cats brought to the clinic for the first time. Since not all cats infected with FPV develop clinical signs and immune status plays an important role in infection (Foley et al., 1999), leucocyte levels are very important for panleukopenia. Even lymphopenia and neutropenia are not consistently found, lymphopenia and severe neutropenia have been described in experimental infections (Dua et al., 1994). The most frequent hematologic abnormalities include anemia, neutropenia, lymphopenia and monocytosis (Hopper et al., 1989; Kohmoto et al., 1998; Shelton et al., 1990). The presence of neutropenia in 47 of the cases (23.3%) suggests that the possibility of feline immunodeficiency virus infection is not minimal. Monocytosis, which is statistically different between age groups, is also among the laboratory results of feline immunodeficiency virus infection.

It is known that most of the leukopenic patients do not have as much defense potential as the immune system. After bone marrow suppression, the earliest change in the blood is a neutropenia. It is seen that leukopenia and neutropenia data are close and parallel to each other in the obtained results. One of most likely causes of neutropenia is bone marrow suppression (Willard and Tvedten, 2011). Cases like feline leukemia virus, feline immunodeficiency virus, parvovirus, bone marrow toxicity, cancer chemotherapy, leukemia, myelonecrosis and immune mediated destruction of neutrophil should be considered in leukopenic patients.

Leukocytosis usually occurs with neutrophilia. The differential diagnosis of nutrophilic leukocytosis includes inflammation, stress/corticosteroids, exercise/epinephrine or leukemia. However, since they are less likely to be seen in 0-1-year-old cats, 3% of the cases have leukocytosis and 4.5 % have neutrophilia. In a study (Willard and Tvedten, 2011), of 232 CBC's with a leukocytosis, 226 (97.4 %) had neutophilia. The number of neutrophilic patients in our study was more than the number of patients with leukocytosis. The age group is considered to be effective in this difference.

Monocytosis is expected in diseases with a high need for macrophages. It is very rare that monocytosis is the only leukogram change in dogs with sepsis or bacterial endocarditis (Willard and Tvedten, 2011). Although macrophages are the "late" part of most inflammatory processes, monocytosis can occur during acute and chronic disease periods. Monocytosis also occurs in conditions such as suppuration, pyogranulamatous and granulomatous inflammation, necrosis, malignancy, hemolytic or hemorrhagic diseases and immune-mediated diseases.

According to our retrospective screening results, it is seen that the relation of monocyte numbers with age is statistically significant ($p = 0.018$). The biggest difference between the two age groups in the study is the pre- and post-adolescence periods. The absence of a difference in other leukocytes between these periods

may be explained by the increase in numbers in response to the macrophage requirement of monocytes or in normal circumstances, the higher monocyte count in circulation.

Conclusion

It is important to precisely know the results of the complete blood count test in the first visit to the clinic and to take the necessary precautions to eliminate the abnormal results before vaccination. A successful vaccination process and recovering this potentially hazardous 0-1-year-old period, a complete blood count test, especially for leukocyte counts, and assessing the results is very crucial for healthy cat pups.

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