ACTA VETERINARIA INDONESIANA
P-ISSN 2337-3202, E-ISSN 2337-4373
Vol. 14, No. 5: 217-223, November 2025

Research

Hematological Profile of *Macaca nemestrina* Across Different Age Groups

Sri Wahyuni[1], Fitriya Nur Annisa Dewi[2,4], Anita Esfandiari[2*], Suryo Saputro[4], Huda Shalahudin Darusman[3,4]

[1]Veterinary Biomedical Science Graduate Study Program,
School of Veterinary Medicine and Biomedical Sciences, Bogor, Indonesia
[2]Division of Internal Medicine, School of Veterinary Medicine and
Biomedical Sciences, Bogor, Indonesia
[3]Division of Pharmacology and Toxicology, School of Veterinary Medicine and
Biomedical Sciences, Bogor, Indonesia
[4]Primate Research Center IPB University, Bogor, Indonesia
*Correspondence author: anitaes@apps.ipb.ac.id
Received: 23 January 2025, Accepted: 25 September 2025

ABSTRACT

Macaca nemestrina, also known as the pigtail macaque, plays a crucial role in drug development and serves as a highly valuable animal model for studying various human diseases due to its phenotypic similarities to humans, including those related to the aging process. Hematology is a critical component of clinical assessments for this spesies, serving both as a diagnostic tool to determine their health status and to characterize disease models, including degenerative and geriatric diseases. As anemia is a common phenomenon in the elderly, it is also important to determine whether *M. nemestrina* exhibit a similar condition with age. The aim of this study was to determine the hematological profiles of clinically healthy female *M. nemestrina* across young, adult, and elderly age groups, particularly related to anemia parameters. This study was conducted at the Primate Research Center, IPB University, Bogor, Indonesia. The animals were part of a breeding colony and were divided into three groups based on age: young (5–7 years), adult (12–14 years), and elderly (18–21 years). Following anesthesia with ketamine, a physical examination was performed to determine clinical status, and blood samples were collected for a complete blood count (CBC) evaluation using an automated analyzer. The results showed that total erythrocytes, hemoglobin concentration, hematocrit value, and mean corpuscular hemoglobin (MCH) were significantly different (P<0.05) in the elderly group compared to the other groups. Additionally, the red cell distribution width (RDW) percentage and leukocyte count differed significantly between the adult and elderly groups. The results showed that the erythrogram differs with age in clinically healthy *M. nemestrina*, suggesting the importance of determining appropriate baseline reference values in macaques of different ages.
Keywords: nonhuman primate, macaques, animal model, hemogram, anemia

ABSTRAK

Macaca nemestrina, yang juga dikenal sebagai monyet ekor babi, memiliki peran penting dalam pengembangan obat dan menjadi hewan model hewan untuk mempelajari berbagai penyakit manusia karena kemiripan fenotipiknya dengan manusia, termasuk proses penuaan. Hematologi merupakan komponen penting dalam penilaian klinis untuk spesies ini, berfungsi sebagai alat diagnostik untuk menentukan status kesehatan mereka maupun sebagai sarana untuk mengkarakterisasi model penyakit, termasuk penyakit degeneratif dan geriatri. Anemia sering terjadi pada orang lanjut usia, sehingga penting juga untuk mengetahui apakah *M. nemestrina* mengalami kondisi serupa seiring bertambahnya usia. Penelitian ini bertujuan untuk menentukan profil hematologi betina *M. nemestrina* yang sehat secara klinis pada kelompok usia muda, dewasa, dan lanjut usia, khususnya terkait parameter anemia. Penelitian ini dilakukan di Pusat Penelitian Primata, IPB University, Bogor, Indonesia. Hewan-hewan tersebut merupakan bagian dari koloni pembiakan dan dibagi menjadi tiga kelompok berdasarkan usia: muda (5–7 tahun), dewasa (12–14 tahun), dan lanjut usia (18–21 tahun). Setelah anestesi dengan ketamin, dilakukan pemeriksaan fisik untuk menentukan status klinis, dan sampel darah dikumpulkan untuk hitung darah lengkap (HDL dengan analis otomatis. Hasil menunjukkan bahwa jumlah sel darah merah total, konsentrasi hemoglobin, nilai hematokrit, dan rata-rata hemoglobin sel darah merah (MCH) secara signifikan berbeda (P<0.05) pada kelompok lanjut usia dibandingkan dengan kelompok lainnya. Selain itu, persentase lebar distribusi sel darah merah (RDW) dan jumlah leukosit berbeda secara signifikan antara kelompok dewasa dan lanjut usia. Hasil menunjukkan bahwa eritrogram berbeda berdasarkan usia pada M. nemestrina yang secara klinis sehat, menyarankan pentingnya menentukan nilai acuan dasar yang sesuai pada monyet dengan usia yang berbeda.
Kata kunci: primata non-manusia, monyet, model hewan, hemogram, anemia

INTRODUCTION

Nonhuman primates (NHPs), such as macaques, have contributed significantly to biomedical research (Dewi *et al.*, 2024). The species of macaques commonly used is *Macaca nemestrina,* which is used in research such as AIDS (Frenkel *et al.*, 2021), Dengue vaccine (Prabandari *et al.*, 2017), and COVID-19 vaccine (Melton *et al.*, 2021). *Macaca nemestrina* is frequently used as a model for replicating human diseases and plays a significant role in drug development due to its phenotypic similarities to humans, including anatomy, physiology, and immunology (Mattison and Vaughan, 2017). Nonhuman primates offer insights into various aspects of aging, including neurodegenerative diseases (Alldritt *et al.*, 2024), metabolic disorders (Li *et al.*, 2015), and hematological disorders such as anemia (Nascimento *et al.*, 2015).

Anemia is highly prevalent among elderly patients, affecting approximately 10% of this population. Its occurrence increases with advancing age and is strongly associated with age-related factors. Additionally, anemia serves as an independent predictor of mortality in elderly patients. It is crucial to note that anemia is a symptom rather than a standalone disease, necessitating investigation into its underlying causes (Abinizha, 2024). Based on the information regarding the increased risk of anemia with advancing age in humans, we aim to investigate whether a similar association exists in *M. nemestrina*. Hematological studies on *M. nemestrina* have been previously reported, but the data did not include age categorization (Kim *et al.*, 2024).

This study aims to identify the hematological profiles of clinically healthy *M. nemestrina* across young, adult, and elderly age groups, particularly related to anemia parameters. Age-based classification is essential for assessing physiological changes over time and ensuring a more accurate interpretation of health status based on appropriate reference values.

MATERIALS AND METHODS

Tools and Materials

The tools and materials used included a scale, stethoscope, thermometer, stopwatch, micropipette (Fortuna), Class II B2 Biological Safety Cabinet, centrifuge (Biobase), hematology analyzer MEK-6550®, vacutainer tubes containing tripotassium ethylene diamine tetraacetic acid (K3-EDTA), and disposable syringes.

Animals and Housing

The study was performed at the Research Animal Facility – Lodaya of the Primate Research Center at IPB University, an AAALAC International-accredited institution in Bogor, Indonesia (Gettayacamin *et al.*, 2018). We utilized clinically healthy *M. nemestrina* females aged 5 to 21 years. The animals were housed in a combination of semi-outdoor group corrals. Their diet consisted of monkey biscuits (from Charoen Pokphand Thailand and PT. Citra Ina Feedmill), supplemented with natural foods such as cassava, bananas, and guava. Feeding was conducted twice daily, with drinking water provided either ad libitum through water pipes in the enclosure. Structural environmental enrichment was provided in group enclosures to encourage natural behaviors. Routine health monitoring, including general check-ups and tuberculin skin tests, was performed every 3 to 6 months, alongside deworming and supportive care, such as vitamin supplementation and fluid rehydration.

Experimental Design

All procedures were approved by the IACUC of the Primate Research Center at Bogor Agricultural University (IPB University) with protocol approval number IPB PRC-23-B002. The study involved 15 females *Macaca nemestrina*, housed in group cages and divided into three age groups: young (5–7 years), adult (12–14 years), and elderly (18–21 years), with each group consisting of five individuals. The *M. nemestrina* were fasted for 12 hours before anesthesia. The animals were sedated using ketamine hydrochloride (Ilium Ketamil®) at a dose of 10 mg/kg of body weight, which was injected intramuscularly into the thigh. After the animal is sedated, a physical examination is peformed, paying attention to any clinical symptoms that may be present, such as injuries, hydration status, lung, and heart auscultation. Blood samples were collected from the femoral vein using a 3 mL syringe (Figure 1).

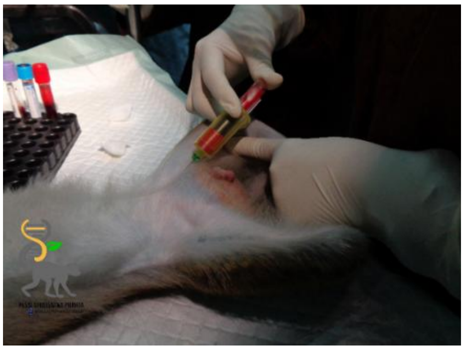

Figure 1. The process of blood collection from the femoral vein

All blood samples were stored in a cool box immediately after collection and transported to the laboratory under proper cold chain management. All animal-related activities are conducted by trained personnel who have received comprehensive training, including primates care and use, as well as biosafety and biosecurity.

Hematological Analysis

Whole blood was collected from the animals into K3-EDTA bottle and assayed for the erythrocyte count, hemoglobin (Hgb) levels, hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), total leukocyte count, platelet count, mean platelet volume (MPV), and platelet distribution width (PDW) using standard laboratory techniques (the automated hematology analyzer).

Statistical analysis

Data were expressed as means ± standard error of the mean (SEM), and normality was tested with the Shapiro-Wilk method. All variables showed $P > 0.05$, confirming a normal distribution and allowing the application of one-way analysis of variance (ANOVA) with Duncan's test. For variables that did not meet normality assumptions, the Mann-Whitney test was applied.

RESULTS

Clinical examination

Table 1 shows clinical examination data for all age groups of *M. nemestrina*. Although not statistically significant (P>0.05), an increasing trend was observed with age for body weight and respiratory rate. In contrast, heart rate shows a decreasing trend with age. Body temperature remains stable across the three age groups. All animals showed capillary refill time (CRT) of less than 2 seconds. Their oral mucosa appeared pink and moist, confirming the clinically healthy status of all animals examined.

Erythrocyte

Table 2 shows the results of erythrogram parameters in *M. nemestrina*. The erythrocyte count, Hgb, Hct, and MCH were significantly higher in the elderly age group than the others (P<0.05). Meanwhile, the RDW percentage differed significantly (P<0.05) only between the adult and elderly groups, which was higher in the elderly group.

Leukocyte

The level of leukocyte counts in the young, adult, and elderly age groups showed statistical significance (P<0.05). As shown in Table 3.

Table 1. Examination Results of *M. nemestrina* Across All Age Groups

No	Variable	Age Group		
		Young	Adult	Elderly
1.	Weight (Kg)	$8.40±1.44^a$	$9.72±1.61^a$	$9.76±4.30^a$
2.	Temperature (°C)	$39.32±0.56^a$	$38.94±0.48^a$	$39±0.82^a$
3.	Heart Rate (beats/minute)	$181.60±29.75^a$	$172.8±23.22^a$	$172±16^a$
4.	Respiration Rate (breaths/minute)	$35.2±7.69^a$	$38.4±10.43^a$	$44±10.20^a$

Note: Data are presented as mean with standard deviation (x ± SD). Identical superscript letters (a) indicate no significant differences (P>0.05) between groups.

Table 2. Mean Hematological Parameters (Erythrogram) in *M. nemestrina* Across All Age Groups

No	Parameters	Age Group		
		Young	Adult	Eldelry
1.	Erythrocyte (10^6/µl)	$4.414±0.19^b$	$4.416±0.32^b$	$5.194±0.21^a$
2.	Hb (g/dl)	$10.4±0.41^b$	$10.34±0.50^b$	$12.9±0.07^a$
3.	Hct (%)	$30.04±1.30^b$	$30.12±2.41^b$	$35.86±1.54^a$
4.	MCV (fl)	$68.04±0.55^a$	$68.36±1.33^a$	$69.02±1.06^a$
5.	MCH (pg)	$23.54±0.18^b$	$23.46±0.96^b$	$24.9±1.09^a$
6.	MCHC (g/dl)	$34.64 ±0.37^a$	$34.32 ± 1.56^a$	$36.04 ±1.68^a$
7.	RDW (%)	$12.62 ± 0.18^{ab}$	$12.36 ± 0.57^b$	$13.18 ± 0.54^a$

Note: Data are presented as mean with standard deviation ($\bar{x}$ ± SD). Identical superscript letters (*a* or *b*) indicate no significant differences (P > 0.05) between groups.

Platelet

Table 4 shows the examination of platelet parameters. An increasing trend is observed with age in platelet count; in contrast, MPV values show a decreasing trend with age, and platelet distribution remains stable across the three age groups, although not statistically significant (P>0.05).

Table 3. Mean Leukocyte Counts in *M. nemestrina* Across All Age Groups

Parameters	Age Group		
	Young	Adult	Eldelry
Leukocytes (10^3/µl)	7.82±2.56 ^{ab} (5.26 - 10.38)	13.5±7.93^{a} (5.57 - 21.43)	4.56±1.01^{b} (3.55 - 5.57)

Note: Data are presented as mean with standard deviation (x̄ ± SD). Identical superscript letters (*a* or *b*) indicate no significant differences (P > 0.05) between groups.

Table 4. Mean platelet count, MPV values, and PDW percentages in *M. nemestrina* across all age groups

No	Parameters	Age Group		
		Young	Adult	Eldelry
1.	Platelet (10^3/µl)	225 ± 61.55^{a} (163.45 - 286.55)	252 ± 34.79^{a} (217.21-286.79)	273 ± 26.81^{a} (246.19 - 299.81)
2.	MPV (fl)	9.18 ± 0.39^{a} (8.79 - 9.57)	9.12 ± 0.56^{a} (8.56 - 9.68)	8.84 ± 0.79^{a} (8.05 - 9.63)
3.	PDW (%)	13.38 ±0.44^{a} (12.94 - 13.82)	13.42 ± 0.77^{a} (12.65 - 14.19)	13.5 ± 0.54^{a} (12.96 - 14.04)

Note: Data are presented as mean with standard deviation (x̄ ± SD). Identical superscript letters (*a* or *b*) indicate no significant differences (P > 0.05) between groups.

DISCUSSION

Clinical examination

The present study showed that the female pigtail macaques examined were clinically healthy, with variables such as body weight, temperature, respiration, and heart rate that fell within the normal range (Fortman *et al*., 2018) and did not differ with age. There was a trend of body weight increase with age in female pigtail macaques. These changes may result in metabolic disturbances, which may occur due to increasing adiposity, insulin resistance, and dyslipidemia. These conditions contribute to weight gain and are common in primates, such as rhesus macaques (Vaughan and Mattison, 2016). Environmental factors, including diet and physical activity, are crucial in weight gain. Macaques experience changes in energy expenditure and activity levels with age, leading to increased body fat and reduced lean mass (Ramsey, 2000). The resulting body weight ranged from an average of 5 to 14 kg, consistent with the findings of Kim *et al*., (2024), who reported that *M. nemestrina* had weights ranging from 5.65 to 12.05 kg. The respiratory rate ranged from an average of 27 to 54 breaths per minute, consistent with the the findings of Fortman *et al*., (2018) on *Macaca fascicularis*, which reported respiratory rates ranging from 30 to 54 breaths per minute in healthy animals. A slight increase in respiratory rate with age may be linked to age-related physiological changes in the respiratory system, including alterations in the chest wall, diaphragm shape, and lung parenchyma. These changes may reduce the efficiency of lung ventilation, requiring an increased respiratory rate to meet oxygen demands.

This study found that the heart rate of female pigtail macaques ranged from an average of 149 to 196 beats per minute, consistent with the findings of Fortman *et al*., (2018) in *M. fascicularis*, which reported the rate ranging from 115 to 243 breaths per minute. As age increases, a decline in heart rate may be found, reflecting significant changes in cardiac function and the cardiovascular system's ability to adapt to various conditions (Chester and Rudolph, 2011). In this study, there was a trend of a mild decrease in heart rate with age, although it was not statistically significant. Elderly primates, there tend to be a decreased in physical activity and changes in social behavior, such as reduced social interactions, which can contribute to lower heart rates. This decline has also been observed in several primate species, including *Macaca tibetana*, where cardiovascular activity and social behavior decrease with age (Cysne *et al*., 2015).

Erythrocytes

The hematological parameters obtained in this study were compared with previous reference values for *M. nemestrina* reported by Kim *et al.,* (2024). Both studies were conducted in AAALAC International-accredited facilities, ensuring standardized housing and welfare conditions. However, specific details on climate and geographical location were not provided in the study by Kim *et al.* (2024). Nevertheless, environmental factors undoubtedly play a significant role in hematological outcomes, as variations in temperature, humidity, and geographical conditions can influence physiological responses. Despite these potential influences, our study found trends in erythrocyte parameters that were generally consistent with previous findings, with some variations observed across age groups.

Hematology examinations revealed that several erythrogram variables, including erythrocyte count, Hgb concentration, Hct, and MCH, increased with age, with a significant difference observed in the elderly age group ($P<0.05$). This phenomenon may be associated with the reproductive status of the animals, as the menstrual cycle like that in women occurs in young and adult female macaques (Hadzic *et al*., 2014). Menstruation leads to blood loss, directly decreasing erythrocyte count, Hgb concentration, Hct, and MCH. Additionally, estrogen produced during the ovarian cycle plays a role in hematopoiesis (Perigard *et al*., 2016). Prolonged menstrual phases can potentially induce iron deficiency anemia due to chronic blood loss (Turk *et al*., 2012). The elderly group in this study, aged 18–21 years, represents the reproductive senescence period in *M. nemestrina* (Caro *et al*., 1995). A limitation in our study, however, was the lack of data regarding the menstrual status of each animal, which warrants further study, such as those involving hormonal measurement. Another contributing factor to increased erythrocyte parameters could be stress, potentially related to the hierarchy of the animal colony. Macaques are animals that live in social groups with a hierarchy. Animal hierarchical status in the colony may affect the stress level (Toufexis *et al*., 2017). In female rhesus monkeys, a study has shown that stress elevates cortisol levels (Lee *et al*., 2018). Cortisol interacts with specific receptors on erythroid progenitor cells, facilitating their proliferation and differentiation into mature erythrocytes. This process involves upregulating erythroid transcription factors, such as Kruppel-like factor 1 (KLF1), which plays a key role in erythroid maturation (Voorhees *et al*., 2013). These parameters fall within the normal range reported by Kim *et al*., (2024), with erythrocyte count of 4.49–5.95 × 10^6/µL, Hgb 9.80–12.60 g/dL, Hct 32–44%, and MCH 19.40–23.60 pg. RBC counts are relatively stable in adult *M. fascicularis*, aged 4 to above 15 years (Ling *et al*., 2022).

Significant differences in RDW between the adult and elderly groups may result from disruptions in erythrocyte production and turnover (Dugdale and Badrick, 2018). In the elderly, increased apoptosis, particularly eryptosis, has been observed (Foller *et al*., 2008). One cause of eryptosis is oxidative stress, which activates Ca^{2+}-permeable cation channels, leading to elevated intracellular calcium levels and subsequent cell death (Bissinger *et al*., 2019). The RDW values in the elderly age group in this study align with a previous report (Kim *et al*., 2024) wherein RDW percentages range from 13.50 to 17.80%. A decrease in RDW indicates a more uniform red blood cell size, potentially reflecting less variability in erythrocyte production (Karal *et al*., 2023). In *M. fascicularis*, RDW values were reported to show no significant differences across all age groups (Ling *et al*., 2022).

Leukocyte

The higher leukocyte counts in adults may reflect the immune system's peak performance, marked by high leukocyte production to support immune responses and active leukocyte turnover to maintain balance and efficiency (He *et al.* 2018). In a previous report on *M. nemestrina*, leukocyte counts ranged between 0.60 and 4.90 × 10^3/µl (Kim *et al*., 2024). Based on this reference, the results of this study show higher leukocyte counts. Leukocyte counts in circulation are influenced by various intrinsic and extrinsic factors, including physiological effects, environmental conditions, and health status, such as infections, inflammation, stress, and chronic diseases (Chmielewski and Strzelec, 2018).

Platelet

The age-related increase in platelet counts is influenced by changes in hematopoietic stem cells (HSCs) (Aksoz *et al*., 2024). Aksoz *et al*. (2024) reported that the frequency of HSCs biased towards platelet production, known as platelet-biased HSCs (P-HSCs), increases with age, while HSCs with the potential to produce multiple blood cell types (multi-lineage HSCs) decrease. This finding contributes to the increased production of megakaryocytes and platelets in the bone marrow. Platelet counts align with the study on *M. nemestrina*, which reported counts ranging from 261 to 593 × 10^3/µl (Kim *et* al., 2024). In *M. fascicularis*, no significant differences were observed among age groups, with platelet counts remaining relatively stable across all groups (Ling *et al*., 2022).

This study found that the mean platelet volume (MPV) aligns with the study on *M. nemestrina* by Kim *et al*. (2024) which reported values ranging from 7.40 to 10.60 fL. Similarly, in *M. fascicularis*, MPV values were reported to be relatively stable without significant differences among age groups (Ling *et al.* 2022). This study did not find a statistical difference with age, although there may be an indication of a mild decline with increasing age. A reduction in MPV in nonhuman primates as they age is attributed to various physiological and hematological changes associated with aging. Firstly, hematopoietic activity decreases, including a reduction in the frequency and activity of hematopoietic progenitor cells such as CD34+, leading to diminished platelet production and size (Lee *et al*., 2005).

The hematological profile of female *Macaca nemestrina*, based on the age groups of young, adult, and elderly, showed differences in several variables. In clinically healthy animals, erythrocyte counts, hemoglobin levels, hematocrit values, and MCH were higher in the elderly than in the young and adult groups. The RDW percentage was higher in the elderly group than in the adult group, whereas the total leukocyte count showed the opposite trend.

ACKNOWLEDGMENTS

Our deepest gratitude goes to the Primate Research Center (PRC) of IPB University for providing the opportunity and support for this study. We would also like to extend our heartfelt thanks to all the staff of the Animal Research and Clinical Pathology Laboratory at PRC IPB University, especially Permanawati, DVM, Suzy Tomongo, DVM, Amelia Diyan S, DVM, and Adinda Darayani Azhar, S.KH, for their invaluable discussions and significant assistance throughout this research.

"The authors declare no conflicts of interest with any parties involved in this study."

REFERENCES

Abinizha S. 2024. Prevalence of Anemia in Geriatric Population. Int J Sci Res. 13:14–6. doi:10.36106/ijsr.

Aksöz M, Gafencu G-A, Stoilova B, Buono M, Zhang Y, Turkalj S, Meng Y, Jakobsen NA, Metzner M, Clark S-A, et al. 2024. Hematopoietic stem cell

Aksöz M, Gafencu G-A, Stoilova B, Buono M, Zhang Y, Turkalj S, Meng Y, Jakobsen NA, Metzner M, Clark S-A, et al. 2024. Hematopoietic stem cell heterogeneity and age-associated platelet bias are evolutionarily conserved. Sci Immunol. 9(98):1–59. doi:10.1126/sciimmunol.adk3469.

Alldritt S, Ramirez JSB, Vos de Wael R, Bethlehem R, Seidlitz J, Wang Z, Nenning K, Esper NB, Smallwood J, Franco AR, *et al.* 2024. Brain Charts for the Rhesus Macaque Lifespan. *BioRxiv*. 1(1):4–27. doi:10.1101/2024.08.28.610193.

Bissinger R, Bhuyan AAM, Qadri SM, Lang F. 2019. Oxidative stress, eryptosis and anemia: a pivotal mechanistic nexus in systemic diseases. *FEBS Journal*. 286(5):826–854. doi:10.1111/febs.14606.

Caro TM, Sellen DW, Parish A, Frank R, Brown DM, Voland E, Borgerhoff Muider M. 1995. Termination of Reproduction in Nonhuman and Human Female Primates. *Int J Primatol*. 16(2):205–219.

Chester JG, Rudolph JL. 2011. Vital Signs in Older Patients: Age-Related Changes. *J Am Med Dir Assoc*. 12(5):337–343. doi:10.1016/j.jamda.2010.04.009.

Chmielewski PP, Strzelec B. 2018. Elevated leukocyte count as a harbinger of systemic inflammation, disease progression, and poor prognosis: A review. *Folia Morphol*. 77(2):171–178. doi:10.5603/FM.a2017.0101.

Cysne LB, Andrade MCR, Goncalves MABG, Lopes CA de A, Ramos S, Zanini GM, Cabello EPH. 2015. Clinical, morphometric and hematological evaluation of captive Cynomolgus monkeys (Macaca fascicularis). *RESBCAL*. 3:36–44. www.poloprinter.com.br.

Dewi FN, Permanawati, Saputro S, Azhar AD, Putriyani W, Wyatt JD, Suparto IH, Darusman HS. 2024. Social Housing of Previously Single-Caged Adult Male Cynomolgus Macaques (Macaca fascicularis). *Vet Sci*. 11(11). doi:10.3390/vetsci11110538.

Dugdale AE, Badrick T. 2018. Red blood cell distribution width (RDW)—a mechanism for normal variation and changes in pathological states. *J Lab Precis Med*. 3:73–73. doi:10.21037/jlpm.2018.08.03.

Foller M, Huber SM, Lang F. 2008. Erythrocyte programmed cell death. *IUBMB Life*. 60(10):661–668. doi:10.1002/iub.106.

Fortman Jeffrey D, Hewett Terry A, Halliday Lisa C. 2018. *The Laboratory Nonhuman Primate Second Edition*. Ed ke-2. CRC-Press: Boca Raton London:47-49.

Frenkel LM, Kuller LR, Beck IA, Tsai CC, Joy JP, Mulvania TM, Hu SL, Montefiori DC, Anderson DM. 2021. Immunization by exposure to live virus (SIVmne/HIV-2287) during antiretroviral drug prophylaxis may reduce risk of subsequent viral challenge. *PLoS One*. 16 4 April. doi:10.1371/journal.pone.0240495.

Gettayacamin M, Grant R, Davun H, Heidrich JE, San S, Paramastri YA, Winoto IL, Sajuthi D, Meng GY, Mutalib AR, *et al.* 2018. Chapter 11 - Laws, Regulations, Guidelines, and Principles Pertaining to Laboratory Animals in Southeast Asia. Di dalam: Guillén J, editor. *Laboratory Animals (Second Edition)*. Academic Press:319–373.

Hadzic S V., Wang X, Dufour J, Doyle L, Marx PA, Lackner AA, Paulsen DB, Veazey RS. 2014. Comparison of the Vaginal environment of Macaca mulatta and Macaca nemestrina Throughout the Menstrual Cycle. *Am J Reprod Immunol*. 71(4):322–329. doi:10.1111/aji.12201.

He Z, Allers C, Sugimoto C, Ahmed N, Fujioka H, Kim W-K, Didier ES, Kuroda MJ. 2018. Rapid Turnover and High Production Rate of Myeloid Cells in Adult Rhesus Macaques with Compensations during Aging. *The JI*. 200(12):4059–4067. doi:10.4049/jimmunol.1800207.

Karal-ogly DD, Shumeev AN, Keburiya V V., Mintel M V., Rybtsov SA. 2023. Age-Related Changes in the Clustering of Blood Populations in Cynomolgus Monkeys Depend on Sex and Immune Status. *Life*. 13(2). doi:10.3390/life13020316.

Kim D, Derton A, Khalil G, Pan Y, Bachman S, Kelley K, García-Lerma G, Dobard CW, Daly MB. 2024. Defining blood hematology reference values in female pig-tailed macaques (Macaca nemestrina) using the Isolation Forest algorithm. *J Med Primatol*. 53(4). doi:10.1111/jmp.12723.

Lee CCI, Fletcher MD, Tarantal AF. 2005. Effect of age on the frequency, cell cycle, and lineage maturation of rhesus monkey (Macaca mulatta) CD34+ and hematopoietic progenitor cells. *Pediatr Res*. 58(2):315–322. doi:10.1203/01.PDR.0000169975.30339.32.

Lee YA, Obora T, Bondonny L, Toniolo A, Mivielle J, Yamaguchi Y, Kato A, Takita M, Goto Y. 2018. The Effects of Housing Density on Social Interactions and Their Correlations with Serotonin in Rodents and Primates. *Sci Rep*. 8(1). doi:10.1038/s41598-018-21353-6.

Li Linzhao, Liao G, Yang G, Lu Y, Du X, Liu J, Li Lan, Wang C, Li Li, Ren Y, *et al.* 2015. High-fat diet combined with low-dose streptozotocin injections induces metabolic syndrome in Macaca mulatta. *Endocrine*. 49(3):659–668. doi:10.1007/s12020-015-0542-9.

Ling X, Luo T, Huang Q, He Y, Lv L, Wang Y, Ma R, Chen J, He Jicun, Zhang J, *et al.* 2022. Establishment of Hematological and Serum Biochemical Parameters in 4,834 Healthy Cynomolgus Monkeys (Macaca fascicularis). *BIO Integration*. 3(4):151–160. doi:10.15212/bioi-2022-0011.

Mattison JA, Vaughan KL. 2017. An overview of nonhuman primates in aging research. *Exp Gerontol*. 94:41–45. doi:10.1016/j.exger.2016.12.005.

Melton A, Doyle-Meyers LA, Blair R V., Midkiff C, Melton HJ, Russell-Lodrigue K, Aye PP, Schiro F, Fahlberg M, Szeltner D, *et al.* 2021. The pigtail macaque (Macaca nemestrina) model of COVID-19 reproduces diverse clinical outcomes and reveals new and complex signatures of disease. *PLoS Pathog*. 17(12). doi:10.1371/journal.ppat.1010162.

Nascimento L, Andrade M, Goldschmidt B. 2015. Iron Depenia Anemia in Smelly Monkeys. *RESBCAL*. 3:109–118.

Perigard CJ, Parrula MCM, Larkin MH, Gleason CR. 2016. Impact of menstruation on select hematology and clinical chemistry variables in cynomolgus macaques. *Vet Clin Pathol*. 45(2):232–243. doi:10.1111/vcp.12350.

Prabandari SA, Arifin E, Saepuloh U, Pamungkas J. 2017. Dengue Virus Type 3 (DENV-3) Distribution in Tissues of Pig-tailed Macaque (Macaca nemestrina) Post Infection Using Immunohistochemistry Technique. *Int j sci: basic appl res*. 33(2):1–9. http://gssrr.org/index.php?journal=JournalOfBasicAndApplied.

Ramsey JJ LJKJW. 2000. Age and gender differences in body composition, energy expenditure, and glucoregulation of adult rhesus monkeys. *J Med Primatol*.(29):11–19.

Toufexis D, Bradley King S, Michopoulos V. 2017. Socially Housed Female Macaques: a Translational Model for the Interaction of Chronic Stress and Estrogen in Aging. *Curr Psychiatry Rep*. 19(11). doi:10.1007/s11920-017-0833-3.

Turk ML, Simoni R, Cacioppo L, Marini RP, Patterson M. 2012. Chronic Anemia and Effects of Iron Supplementation in a Research Colony of Adult Rhesus Macaques (Macaca mulatta). *Comp Med*. 62(2):137–141.

Vaughan KL, Mattison JA. 2016. Obesity and Aging in Humans and Nonhuman Primates: A Mini-Review. *Gerontology*. 62(6):611–617. doi:10.1159/000445800.

Voorhees JL, Powell ND, Moldovan L, Mo X, Eubank TD, Marsh CB. 2013. Chronic Restraint Stress Upregulates Erythropoiesis through Glucocorticoid Stimulation. *PLoS One*. 8(10). doi:10.1371/journal.pone.0077935.