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Factors Affecting Hematologic and Serum Biochemical Parameters in Healthy Common Marmosets (*Callithrix jacchus*)

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Physiologic changes during development, aging, and pregnancy may affect clinical parameters. Previously available reference values have been based on samples that may include wild and captive marmosets, with little representation of geriatric or pregnant animals. Establishing reference values under various conditions would support better recognition of pathologic conditions in marmosets. One hundred and forty-seven (70 males and 77 females) healthy marmosets from a research colony were included in this study. Exclusion criteria were abnormal physical exam findings at the time of blood sampling, chronic medications, or clinical or pathologic evidence of disease. Reference intervals were calculated for serum chemistry and hematology. Using metadata, samples were classified based on age, sex, colony source and pregnancy status. Multiple tests indicated significant differences with varying effect sizes, indicating that developing reference intervals based on metadata can be useful. Across all the comparisons, medium or large effect sizes were observed most frequently in blood urea nitrogen (BUN), calcium, total protein, alkaline phosphatase (ALP), weight and serum albumin. We report normative clinical pathologic data for captive common marmosets through all life stages and reproductive status. Significant differences were observed in most parameters when stratifying data based on age, sex, colony source, or pregnancy, suggesting that developing reference intervals considering this information is important for clinicians.

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Introduction

Common marmosets (*Callithrix jacchus*) are a New World nonhuman primate (NHP) species that is experiencing a resurgence in popularity as a model species for biomedical research.[20] Due in part to their small size and increased fecundity compared with larger, Old World species such as macaques, use of marmosets in neuroscience, aging research, toxicology, and other areas of biomedical research has increased over the past 15 y. Despite their recent popularity, however, references for normal clinicopathological parameters in marmosets are limited, making captive management of the species more challenging. Existing published references are outdated or based on a small number of animals.[8,16,21-23,32] Furthermore, earlier studies focused on adult marmosets, but underrepresented geriatric animals (>8 y) or did not include pregnant animals. An increase in the number of publications in the 1980s reflected an initial interest in the species as a model for biomedical research. While these publications established an important baseline for current and future work, early studies used both wild-caught and laboratory-bred marmosets to characterize the animal model.[22,23,32] In the past 30 y, the establishment of captive breeding programs and changes in dietary and husbandry practices have potentially changed the baseline biologic parameters in captive-born animals and necessitate updates in the clinical chemistry and hematology reference ranges.

In addition to physical examinations, one of the most important tools for evaluating the health of any animal, including marmosets, is a panel of blood tests including hematology and serum biochemistry values. This hematology panel (complete blood count, CBC), serum chemistry panel, and urinalysis are often called the "minimum database" in veterinary medicine. While some parameters are tightly controlled physiologically and exhibit minimal variation, others show significant variation across species. In some mammalian species, including humans, well-defined differences in some hematologic and clinical chemistry parameters distinguish juveniles, adults, and geriatric individuals, as well as males and females.[7] Therefore, defining reference ranges for clinical chemistry and hematology measures in healthy, captive, common marmosets is critical to clinical interpretation of laboratory test results in both healthy and diseased states. Appropriate interpretation of clinical chemistry and hematology measures throughout various life stages and between sexes in "healthy" animals allows more nuanced and accurate interpretation of diagnostic tests within a colony, and potentially across marmoset colonies, especially for institutions with insufficient animals to generate internal reference ranges. Reference interval data are crucial to aid clinicians in identifying and selecting subjects for future biomedical research projects and selection of animals for breeding colonies[4,5,10] Furthermore, additional insights on marmoset physiology and its differences compared with humans and other model organisms will allow better interpretation of values and the marmosets' translational usefulness.

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This study describes the clinical chemistry and hematology reference ranges documented in male and female marmosets housed at MIT, including juvenile, adult, and geriatric animals, as well as both pregnant and non-pregnant females. Using clinical chemistries and complete blood counts performed at our institution, we retrospectively analyzed and determined the reference value distributions and reference intervals for hematology and serum biochemistry tests from 147 common marmosets aged 0.5 to 12.4 y. To generate reference intervals, we evaluated samples from a well-characterized group of clinically healthy subjects and reported the middle 95% of values of this healthy population. In addition to calculating reference values for healthy marmosets, we investigated how factors, including age, sex, pregnancy, and colony source, which roughly reflects genetic diversity, affect those reference values. The aims of the study were 1) to provide reference intervals for clinical chemistry and hematology according to age category and sex from a large and heterogenous cohort of indoor-housed healthy common marmosets and 2) to describe how values for these parameters differ due to reproductive status.

Materials and Methods

Subjects. One hundred and 47 common marmosets (*Callithrix jacchus*) housed at the Massachusetts Institute of Technology in Cambridge, MA were used for this study. These marmosets were originally from 5 different source colonies designated as N, B, G, C, and E. Source N was established at MIT in 2014, source C in 2016, B in 2017, E in 2018 and G in 2019. Of these 147 animals, 70 were male and 77 were female. Colony N had 63 marmosets (28 female and 35 males), colony B had 23 (11 females and 12 males), colony G had 33 (26 female and 7 male), colony C had 20 (8 female and 12 male), and colony E had 8 (4 female and 4 male). All animals were laboratory-bred at MIT or the source institution with the possible exception of a single animal from source B. This animal was received by MIT from another institution after having been purchased from a commercial primate vendor by that institution. During the time of data collection, no interbreeding or co-mingling of animals from different sources had occurred. The marmosets ranged in age from 0.53 y to 12.40 y (mean, 3.83 y and median 2.48 y) at the time of sampling. The 25th percentile was 1.55 y and the 75th percentile was 6.10 y. Exclusion criteria included abnormal physical exam findings at the time of blood collection, chronic medications, or clinical or pathologic evidence of disease. Exclusion criteria were determined by comprehensive record review, such that animals having any significant abnormal physical exam findings at any point in their clinical history were excluded from our analysis. Significant abnormal physical exam findings included evidence of systemic disease, such as thickened intestines on abdominal palpation or abnormal body condition score (less than 2.5/5 or greater than 4/5). Focal alopecia, localized dental disease, or previous or current minor trauma (for example superficial scrapes) did not warrant exclusion. Retrospective examination of medical records allowed categorization by age at the time of sampling (juvenile/subadult less than 2 y, adult 2 to 8 y, geriatric greater than 8 y), sex, colony source, and pregnancy status. Pregnancy and gestational age were determined by ultrasonographic findings at the time of sampling and/or parturition dates.[14] All animals were housed in 2 vivaria at MIT, an AAALAC International accredited institution. Vivarium A housed approximately 40 to 50 animals over the course of the study, while vivarium B housed numbers ranging from 32 to close to 200 animals over the dates included in our analysis. Both vivaria were managed identically with respect to environmental parameters, diet, biosecurity, and other aspects of the animal care program as described below. All marmosets included in this study were on an animal use protocol approved by the MIT Institutional Animal Care and Use Committee (IACUC).

The animal holding room temperature was maintained at 74 ± 2°F with a relative humidity of 30% to 70% and a minimum of 10 complete non-recirculated air exchanges per hour. A 12:12h light:dark cycle was maintained. Marmosets were housed in pairs or family groups in cages composed of stainless-steel bars and polycarbonate perches with the following dimensions: 30″ W x 32″ D x 67″ H. Each cage had a nest box made of polycarbonate attached the outside of the cage. Other enrichment fixtures present in the cages included hammocks, hanging toys, and manzanita wood branches. Foraging enrichment in the form of dried acacia gum-filled branches and forage board were provided weekly. Cages were removed for sanitization on a biweekly rotation.

All animals received a base diet of biscuits (Teklad New World Primate Diet 8794). In addition to the base diet, a cafeteria-style supplemental offering of fruits and vegetables (for example grapes, oranges, bananas, carrots, green beans, sweet potatoes) and additional protein sources including hard-boiled eggs, yogurt, cottage cheese or ZuPreem canned Marmoset Diet (Premium Nutritional Products, Mission, KS) were supplied in a daily rotation.

Sample collection. On a semiannual basis, physical exams were performed on all colony animals. Marmosets were screened for potentially pathogenic bacteria (including *Mycobacterium tuberculosis*, *Salmonella* spp., *Shigella* spp, β-hemolytic *E.coli*, *Klebsiella* spp., and *Campylobacter* spp.) and parasites (including *Enterobius* spp., *Entamoeba* spp., *Giardia* spp., *Taenia* spp., and *Cryptosporidium* spp.). All animals derived from progenitor stock that were negative for squirrel monkey cytomegalovirus, Saimiriine herpesvirus 1, Saimiriine herpesvirus 2, and measles virus. Complete blood count and serum chemistry analysis were performed on a semiannual to annual basis and during diagnostic workup of clinical cases, importation, or quarantine. Hematology analysis was performed by the MIT Division of Comparative Medicine (DCM) diagnostic laboratory using a HemaVet 950 veterinary hematology analyzer (Drew Scientific, Oxford, CT). A background check and control samples from the manufacturer were run before each batch of samples was analyzed or after reagents were changed. Serum chemistry analysis was performed by Idexx Laboratories (Westbrook, ME). All animals were fasted the morning of blood collection (approximately 2 to 5 h) and sedated with an intramuscular injection of ketamine (20 to 40 mg/kg) or alfaxalone (5 to 10 mg/kg). Blood samples (1 to 2 mL) were collected by venipuncture of the femoral or saphenous vein into microvolume EDTA and serum separator blood tubes (Sarstedt, Newton, NC). The EDTA-treated blood samples were processed on the same day by our in-house diagnostic laboratory. Serum-separator blood tubes were processed same-day by centrifugation at 1000 × g for 25 min before aliquoting the serum. After initial processing, serum samples were submitted to Idexx for biochemical analysis. Serum chemistry and complete blood counts (CBC) data were collected from the clinical records of the MIT colony between 2015 to 2019. Longitudinal serum chemistry samples were collected from individual animals, with each marmoset having 1 to 13 samples (mean, 3.7) collected over this period.

CBCs were also collected, and individual animals had 0 to 10 samples (mean, 1.9) collected over the course of the study. Medical records were used to identify pregnant individuals based on ultrasound examination and/or parturition dates.

Clinical chemistry values that were routinely measured include albumin, alkaline phosphatase (ALP), alanine aminotransferase (ALT or serum glutamic-pyruvic transaminase (SGPT)), amylase, aspartate aminotransferase (AST), bilirubin (direct, indirect and total), γ glutamyl transferase (GGT), globulin, lipase, total protein, creatine kinase (CK), cholesterol, blood urea nitrogen (BUN), total serum calcium, chloride, creatinine, glucose, phosphorus, potassium, sodium, and bicarbonate (total CO2). The ratios of albumin to globulin (A:G ratio), BUN to creatinine (B:C ratio) and sodium to potassium (NA:K ratio) were computed, as well as the anion gap.

CBCs were used to measure the levels of 3 basic blood cells: white blood cells, red blood cells and platelets. Hematology values collected were red blood cells (RBC), hemoglobin (HGB), hematocrit (HCT), packed cell volume (PCV), mean corpuscular volume (MCV), red blood cell distribution width (RDW), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), white blood cells (WBC), neutrophils (NEUT), bands, platelets (PLT), mean platelet volume (MPV) and percentages and counts for neutrophils, lymphocytes, monocytes, eosinophils and basophils.

Statistical analysis. Statistical analysis was performed using Microsoft Excel and R (version 3.6.3) with packages dplyr and effsize. Weight, serum chemistry, and CBC data collected from 2015 to 2019 were used in this analysis. The first step of the analysis was to remove outliers from the dataset using the interquartile range (IQR) method. Briefly, the 1st (Q1) and 3rd (Q3) quartiles were defined as the medians of the lower and upper half of each dataset, respectively. The IQR was the difference between Q3 and Q1. For each parameter, samples that were measured outside of the range between $Q1-1.5\times IQR$ and $Q3+1.5\times IQR$ were removed from the dataset for the calculation of the reference intervals. For hematologic and clinical chemistry parameters, an average of 4.7% of observations were removed as outliers. After removing outliers, reference intervals were defined using data from nonpregnant, clinically healthy marmosets from the colony. Reference intervals were defined as the middle 95% of the data for each parameter and were calculated as the range determined by the mean ± 2 × standard deviation (SD). The 90% confidence intervals (CI) of the standard reference range were calculated as $margin\ of\ error = z^* \times \frac{standard\ deviation}{\sqrt{n}}$. To determine a 95% CI, the value of z* is 1.96 and the value of n was the number of tests available for the given parameter. When the lower limits and CI were negative numbers, the values were converted to zeros.

Nonparametric, Kruskal-Wallis tests were applied to determine statistically significant differences between groups. Subsequently, statistically significant Kruskal-Wallis tests ($P < 0.05$) were analyzed using paired samples Wilcoxon tests. Multiple testing correction was carried out using the Benjamini-Hochberg correction. Effect size was determined using Cohen's d defined as $d = \frac{\mu_1 - \mu_2}{SD}$ and calculated using the effsize package. Effect sizes were grouped from 0.0 to 0.2, 0.2 to 0.5, 0.5 to 0.8 and greater than 0.8, and were considered "negligible," "small," "medium," and "large" respectively. Comparisons between subsets of healthy marmosets used data with outliers removed. However, comparisons involving pregnant marmosets used the complete dataset without exclusion of outliers, with the exception of values determined to be errors in data entry.

Results

Reference ranges for blood analytes in healthy marmosets. From 2015 to 2019, we identified 580 samples with a weight measurement and either serum chemistry analysis or CBC that were collected from 147 (70 males and 77 females) clinically healthy marmosets as determined by clinical assessments and medical records. Reference intervals for the MIT colony were determined from these 147 individuals (Table 1). 47.76% of samples from healthy marmosets were collected from adults, followed by 39.66% from juvenile animals and 12.59% from geriatric animals. Ages ranged from 0.53 to 12.4 y of age. Sex- and age-specific reference intervals for blood analytes were determined (Table 2, Table 3, and Table 4).

Effect of age and sex. Twenty-three parameters were significantly different between male and female marmosets but 17 had a negligible or small effect between sexes (Table 2). The 6 remaining parameters having a medium effect (d = 0.5-0.8) were indirect bilirubin, total bilirubin, RBC, hematocrit, packed cell volume (PCV) and hemoglobin.

Based on both age and sex, we observed significant differences between juveniles/subadults and adults, as well as geriatric animals and adults (Table 3 and Table 4). 23 of 50 tests were significantly different between male juveniles/subadults and adult male animals with 10 parameters having a medium effect (A:G ratio, chloride, phosphorus, lymphocyte #, lymphocyte %, MPV, monocyte #, neutrophil %, PLT, RDW) and 3 parameters having a large effect (d > 0.8) (weight, ALP, eosinophil #). Geriatric males were significantly different from adult males in 13 tests, with a high number of tests having a large effect (n = 10 (albumin, A:G ratio, cholesterol, globulin, lipase, phosphorus, total CO2, lymphocyte %, MCV, neutrophil %)) or medium (n = 3 (BUN, calcium, lymphocyte #)). Fewer differences were observed between age groups in females with 8 significant differences observed between juvenile and adult females and 16 between geriatric and adult females. Comparing juvenile and adult females, 6 differences had a medium effect (A:G ratio, BUN, calcium, creatinine, phosphorus, RBC) and only 1 had a large effect (ALP). Geriatric females differed from adult females in 10 tests with medium effect (calcium, chloride, GGT, total

Table 1. Demographics of healthy marmosets used to determine reference intervals

		Animals	Samples
Sex			
	Male	70	294
	Female	77	286
Source			
	B	23	107
	C	20	68
	E	8	23
	G	33	58
	N	63	324
Age#			
	2 and under		230
	2 to 8		277
	Over 8		73

Individual animal numbers not reported as individual animals contributed to multiple age brackets over duration of collection

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Table 2. Clinical Pathology Reference Ranges for Common Marmosets by Sex

		Male reference interval					Female reference interval						
	Units	Range	Median	Samples (n)	Lower 95% CI	Upper 95% CI	Range	Median	Samples (n)	Lower 95% CI	Upper 95% CI	Significance (M compared with F)	Effect Size
Weight	g	302.5-516.1	406.0	167	294.4 - 310.6	508 - 524.2	323.3-526.4	424.0	176	315.8 - 330.8	518.9 - 533.9	**	–0.3 (S)
Alanine aminotransferase (ALT)	U/L	0.0-20.3	6	254	0 - 0	19.5 - 21	0.0-22.8	8	231	0 - 0	21.9 - 23.6	***	–0.3 (S)
Albumin	g/dL	3.1-5.0	4.1	274	3.1 - 3.2	4.9 - 5.1	3.1-5.2	4.2	259	3 - 3.2	5.1 - 5.2	*	–0.2 (N)
Albumin/Globulin (A:G) ratio		1.3-2.6	1.9	176	1.2 - 1.3	2.6 - 2.7	1.2-2.7	1.9	148	1.2 - 1.3	2.6 - 2.8		
Alkaline Phosphatase (ALP)	U/L	13.3-148.6	75	266	9.2 - 17.3	144.5 - 152.6	11.5-132.9	69	243	7.7 - 15.3	129.1 - 136.7	**	0.3 (S)
Amylase	U/L	129.4-319.2	219	241	123.4 - 135.4	313.2 - 325.2	146.5-317.1	230	189	140.4 - 152.6	311.1 - 323.2		
Anion Gap	mM/L	17.8-31.2	25	82	17 - 18.5	30.5 - 31.9	18.6-30.1	24	77	17.9 - 19.2	29.5 - 30.7		
Aspartate aminotransferase (AST)	U/L	60.6-177.9	116	210	56.6 - 64.5	174 - 181.9	47.9-175.6	107.5	208	43.6 - 52.3	171.2 - 179.9	**	0.2 (S)
Blood urea nitrogen (BUN)	mg/dL	12.7-31.5	22	276	12.2 - 13.3	31 - 32.1	10.2-31.1	20	255	9.6 - 10.8	30.5 - 31.8	***	0.3 (S)
BUN/Creatinine (B:C) ratio		0.0-153.2	75	112	0 - 0	145.4 - 161	0.0-159.0	70	93	0 - 0	150.4 - 167.5		
Calcium	mg/dL	8.5-11.0	9.75	274	8.4 - 8.6	10.9 - 11.1	8.6-11.3	10	257	8.5 - 8.6	11.2 - 11.4	**	–0.3 (S)
Chloride	mM/L	100.1-112.2	106	141	99.6 - 100.6	111.7 - 112.7	101.1-113.4	108	128	100.5 - 101.6	112.9 - 113.9	**	–0.3 (S)
Cholesterol	mg/dL	90.3-234.0	161.5	176	85 - 95.6	228.7 - 239.3	38.2-245.5	134	149	29.9 - 46.5	237.2 - 253.8	***	0.5 (S)
Creatine Kinase (CK)	U/L	0.0-905.6	182	101	0 - 0	849.3 - 962	0.0-922.6	219	86	0 - 0	861.8 - 983.5		
Creatinine	mg/dL	0.1-0.4	0.3	147	0.1 - 0.1	0.4 - 0.4	0.1-0.4	0.2	131	0 - 0.1	0.4 - 0.4	***	0.5 (S)
Direct Bilirubin	mg/dL	0.00-0.00	0.00	101	0 - 0	0 - 0	0.00-0.00	0.00	94	0 - 0	0 - 0		
Gammaglutamyl transferase (GGT)	U/L	0.0-12.6	4	237	0 - 0	12.1 - 13	0.0-14.4	6	175	0 - 0	13.8 - 15	**	–0.3 (S)
Globulin	g/dL	1.5-2.7	2.1	271	1.5 - 1.6	2.6 - 2.7	1.6-2.7	2.1	257	1.6 - 1.6	2.7 - 2.7		
Glucose	mg/dL	29.5-238.0	126.5	262	23.2 - 35.8	231.7 - 244.3	25.2-233.1	118.5	250	18.7 - 31.6	226.6 - 239.5		
Indirect Bilirubin	mg/dL	0.02-0.26	0.10	119	0 - 0	0.2 - 0.3	0.01-0.20	0.10	104	0 - 0	0.2 - 0.2	***	0.6 (M)
Lipase	U/L	11.7-49.8	30	174	10.3 - 13.1	48.4 - 51.2	11.0-46.4	28	139	9.5 - 12.5	44.9 - 47.9		
Phosphorus	mg/dL	1.8-5.2	3.4	249	1.7 - 1.9	5.1 - 5.3	2.1-5.5	3.7	201	2 - 2.2	5.4 - 5.6	***	–0.4 (S)
Potassium	mM/L	2.3-3.9	3.1	136	2.2 - 2.4	3.9 - 4	2.3-3.9	3.1	127	2.3 - 2.4	3.9 - 4		
Sodium	mM/L	146.5-155.4	151	135	146.2 - 146.9	155 - 155.7	145.8-154.5	150	129	145.4 - 146.2	154.1 - 154.9	**	0.4 (S)
Sodium/Potassium (Na:K) ratio		33.1-61.9	48	88	31.6 - 34.6	60.4 - 63.4	34.4-60.8	48	86	33.1 - 35.8	59.4 - 62.2		
Total Bilirubin	mg/dL	0.04-0.25	0.10	252	0 - 0	0.2 - 0.3	0.03-0.20	0.10	205	0 - 0	0.2 - 0.2	***	0.6 (M)
Total CO2 (Bicarbonate)	mM/L	14.6-30.8	23	111	13.8 - 15.3	30.1 - 31.6	14.6-28.1	22	91	13.9 - 15.3	27.4 - 28.8	**	0.4 (S)
Total Protein	g/dL	5.0-7.3	6.2	272	4.9 - 5.1	7.3 - 7.4	5.0-7.5	6.3	261	5 - 5.1	7.4 - 7.6	*	–0.2 (N)
Bands	x10^3/µL	0.0-5.2	1	29	0 - 0	4.6 - 5.8	0.0-4.6	1	22	0 - 0	4 - 5.3		
Basophil #	x10^3/µL	0.0-0.0	0	92	0 - 0	0 - 0	0.0-0.0	0	81	0 - 0	0 - 0		
Basophil %	%	0.0-0.5	0.2	89	0 - 0	0.4 - 0.5	0.0-0.6	0.1	79	0 - 0	0.5 - 0.6		
Eosinophil #	x10^3/µL	0.0-0.3	0.1	89	0 - 0	0.2 - 0.3	0.0-0.2	0.1	90	0 - 0	0.2 - 0.3		
Eosinophil %	%	0.3-4.3	2.2	90	0.1 - 0.5	4.1 - 4.5	0.2-3.7	1.8	88	0 - 0.4	3.5 - 3.9	*	0.4 (S)
Hematocrit (HCT)	%	33.8-47.3	40.3	137	33.2 - 34.4	46.8 - 47.9	31.0-45.5	37.9	123	30.4 - 31.6	44.9 - 46.2	***	0.6 (M)
Hemoglobin (Hgb)	g/dL	12.1-16.4	14.2	137	11.9 - 12.3	16.2 - 16.5	10.9-16.1	13.35	124	10.7 - 11.2	15.9 - 16.3	***	0.6 (M)
Lymphocyte #	x10^3/µL	0.0-4.9	2.1	91	0 - 0.1	4.7 - 5.2	0.0-5.2	2.25	88	0 - 0.2	5 - 5.5		
Lymphocyte %	%	15.6-78.1	47.4	93	12.5 - 18.8	74.9 - 81.2	12.1-84.7	49.25	92	8.3 - 15.8	81 - 88.4		

(*continued*)

Table 2. (Continued)

		Male reference interval					Female reference interval						
	Units	Range	Median	Samples (n)	Lower 95% CI	Upper 95% CI	Range	Median	Samples (n)	Lower 95% CI	Upper 95% CI	Significance (M compared with F)	Effect Size
Mean corpuscular hemoglobin (MCH)	pg	17.0-22.6	19.8	139	16.8 - 17.2	22.4 - 22.9	16.8-23.2	19.9	127	16.5 - 17.1	22.9 - 23.4		
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	31.3-39.3	35.4	137	30.9 - 31.6	39 - 39.6	30.6-39.7	35.3	128	30.2 - 31	39.3 - 40.1		
Mean corpuscular volume (MCV)	fL	49.9-62.5	56.5	139	49.4 - 50.5	62 - 63	49.8-63.7	56.25	124	49.1 - 50.4	63.1 - 64.4		
Mean platelet volume (MPV)	fL	7.1-13.3	10.1	142	6.9 - 7.4	13 - 13.5	6.9-12.9	9.8	131	6.6 - 7.1	12.7 - 13.2		
Monocyte #	x10^3/µL	0.0-0.3	0.1	83	0 - 0	0.3 - 0.3	0.0-0.3	0.1	87	0 - 0	0.3 - 0.3		
Monocyte %	%	0.0-7.2	2.8	87	0 - 0	6.8 - 7.6	0.0-5.4	2.3	89	0 - 0.2	5.1 - 5.7	*	0.4 (S)
Neutrophil #	x10^3/µL	0.0-5.0	2	90	0 - 0.1	4.7 - 5.3	0.0-5.6	2.1	88	0 - 0	5.3 - 5.9		
Neutrophil %	%	13.5-79.6	45.5	93	10.1 - 16.8	76.3 - 83	11.1-79.3	43	92	7.6 - 14.6	75.8 - 82.8		
Platelet count (PLT)	x10^3/µL	193.6-686.3	436	142	173.3 - 213.9	666 - 706.6	129.3-756.8	425	126	101.9 - 156.7	729.4 - 784.2		
Red blood cell count (RBC)	x10^6/µL	5.8-8.5	7.25	139	5.7 - 5.9	8.4 - 8.6	5.4-8.2	6.81	123	5.2 - 5.5	8.1 - 8.4	***	0.5 (M)
Red cell distribution width (RDW)	%	14.3-19.6	16.65	138	14.1 - 14.5	19.4 - 19.9	14.3-19.2	16.5	125	14.1 - 14.6	19 - 19.5		
Packed Cell Volume (PCV)	%	39.5-55.6	48	140	38.8 - 40.2	55 - 56.3	38.3-52.9	45	137	37.7 - 38.9	52.3 - 53.5	***	0.5 (M)
White blood cell count (WBC)	x10^3/µL	1.4-8.9	4.8	141	1.1 - 1.7	8.6 - 9.2	1.5-8.7	4.8	121	1.2 - 1.8	8.3 - 9		

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

N = negligible, S = small, M = medium, L = large

Table 3. Clinical Pathology Reference Intervals by Age in Male Marmosets.

Analyte	Unit	Age	Range	Median	Samples, n	Lower 95% CI	Upper 95% CI	*P* value compared with male adults	Effect Size
Weight	g	Juvenile/subadult	272.5-476.9	363	45	257.5 - 287.4	462 - 491.9	0.00E+00	−1.0 (L)
Weight	g	Adult	323.9-521.4	420	109	314.6 - 333.1	512.1 - 530.6		
Weight	g	Geriatric	341.6-493.1	401	13	321.1 - 362.2	472.5 - 513.7		
Alanine aminotransferase (ALT)	U/L	Juvenile/subadult	0.0-20.6	6	100	0 - 0	19.4 - 21.9		
Alanine aminotransferase (ALT)	U/L	Adult	0.0-19.8	6.5	138	0 - 0	18.8 - 20.8		
Alanine aminotransferase (ALT)	U/L	Geriatric	0.0-21.8	4.5	16	0 - 0	18.2 - 25.4		
Albumin	g/dL	Juvenile/subadult	3.3-5.1	4.3	105	3.2 - 3.4	5 - 5.2	3.90E-03	0.4 (S)
Albumin	g/dL	Adult	3.1-4.9	4.1	153	3.1 - 3.2	4.8 - 5		
Albumin	g/dL	Geriatric	2.7-4.4	3.5	16	2.5 - 2.9	4.2 - 4.6	1.00E-04	−1.1 (L)
Albumin/Globulin (A:G) ratio		Juvenile/subadult	1.5-2.7	2.1	66	1.4 - 1.6	2.6 - 2.8	1.00E-04	0.7 (M)
Albumin/Globulin (A:G) ratio		Adult	1.2-2.5	1.8	103	1.2 - 1.3	2.5 - 2.6		
Albumin/Globulin (A:G) ratio		Geriatric	1.1-1.8	1.6	7	1 - 1.3	1.7 - 2	1.30E-03	−1.2 (L)
Alkaline Phosphatase (ALP)	U/L	Juvenile/subadult	37.5-170.3	101	96	30.9 - 44.2	163.6 - 176.9	0.00E+00	1.2 (L)
Alkaline Phosphatase (ALP)	U/L	Adult	14.0-121.9	64	154	9.8 - 18.3	117.7 - 126.2		
Alkaline Phosphatase (ALP)	U/L	Geriatric	25.0-109.8	64.5	16	14.6 - 35.4	99.5 - 120.2		
Amylase	U/L	Juvenile/subadult	140.3-307.8	214	91	131.7 - 148.9	299.2 - 316.4		
Amylase	U/L	Adult	121.5-329.7	225	137	112.8 - 130.3	321 - 338.4		
Amylase	U/L	Geriatric	157.5-267.0	203	13	142.6 - 172.4	252.1 - 281.8		

(*continued*)

Table 3. (Continued)

Analyte	Unit	Age	Range	Median	Samples, n	Lower 95% CI	Upper 95% CI	*P* value compared with male adults	Effect Size
Anion Gap	mM/L	Juvenile/subadult	19.3-32.2	25	36	18.3 - 20.4	31.1 - 33.2		
Anion Gap	mM/L	Adult	17.2-30.0	24	41	16.2 - 18.2	29 - 31		
Anion Gap	mM/L	Geriatric	18.1-26.7	23	5	16.2 - 20	24.8 - 28.6		
Aspartate aminotransferase (AST)	U/L	Juvenile/subadult	67.8-176.1	119	88	62.1 - 73.5	170.5 - 181.8		
Aspartate aminotransferase (AST)	U/L	Adult	55.5-178.2	114	110	49.8 - 61.3	172.5 - 184		
Aspartate aminotransferase (AST)	U/L	Geriatric	59.5-182.7	118	12	42.1 - 76.9	165.3 - 200.1		
Blood Urea Nitrogen (BUN)	mg/dL	Juvenile/subadult	13.5-32.1	23	104	12.6 - 14.4	31.2 - 33		
Blood Urea Nitrogen (BUN)	mg/dL	Adult	12.9-31.1	22	156	12.2 - 13.6	30.4 - 31.9		
Blood Urea Nitrogen (BUN)	mg/dL	Geriatric	9.1-28.8	19.5	16	6.6 - 11.5	26.4 - 31.2	3.58E-02	−0.7 (M)
BUN/Creatinine (B:C) ratio		Juvenile/subadult	0.0-135.2	70	49	0 - 0	124.6 - 145.8		
BUN/Creatinine (B:C) ratio		Adult	0.0-164.7	80	58	0 - 0	153.3 - 176.2		
BUN/Creatinine (B:C) ratio		Geriatric	32.3-143.7	95	5	7.9 - 56.7	119.3 - 168.1		
Calcium	mg/dL	Juvenile/subadult	8.7-11.2	9.9	105	8.6 - 8.8	11.1 - 11.3	3.00E-03	0.4 (S)
Calcium	mg/dL	Adult	8.5-10.8	9.7	153	8.4 - 8.6	10.7 - 10.9		
Calcium	mg/dL	Geriatric	8.2-10.2	9.15	16	8 - 8.5	10 - 10.5	3.00E-03	−0.8 (M)
Chloride	mM/L	Juvenile/subadult	99.4-111.1	105	53	98.6 - 100.2	110.3 - 111.9	1.60E-03	−0.6 (M)
Chloride	mM/L	Adult	101.5-112.4	107	81	100.9 - 102.1	111.8 - 113		
Chloride	mM/L	Geriatric	95.9-112.7	106	7	92.8 - 99	109.6 - 115.8		
Cholesterol	mg/dL	Juvenile/subadult	89.9-239.9	167.5	68	81 - 98.9	231 - 248.8		
Cholesterol	mg/dL	Adult	92.1-221.7	157	101	85.8 - 98.4	215.4 - 228		
Cholesterol	mg/dL	Geriatric	153.1-267.7	224	7	131.9 - 174.4	246.5 - 288.9	1.20E-03	1.7 (L)
Creatine Kinase (CK)	U/L	Juvenile/subadult	0.0-838.4	201	47	0 - 0	762.5 - 914.2		
Creatine Kinase (CK)	U/L	Adult	0.0-987.7	180.5	50	0 - 0	900.9 - 1074.5		
Creatine Kinase (CK)	U/L	Geriatric	63.3-211.7	130	4	27 - 99.7	175.3 - 248		
Creatinine	mg/dL	Juvenile/subadult	0.2-0.4	0.3	54	0.1 - 0.2	0.4 - 0.4		
Creatinine	mg/dL	Adult	0.1-0.4	0.3	86	0.1 - 0.1	0.4 - 0.4		
Creatinine	mg/dL	Geriatric	0.1-0.3	0.2	7	0.1 - 0.2	0.3 - 0.3		
Direct Bilirubin	mg/dL	Juvenile/subadult	0.0-0.0	0	42	0 - 0	0 - 0		
Direct Bilirubin	mg/dL	Adult	0.0-0.0	0	54	0 - 0	0 - 0		
Direct Bilirubin	mg/dL	Geriatric	0.0-0.0	0	5	0 - 0	0 - 0		
Gammaglutamyl transferase (GGT)	U/L	Juvenile/subadult	0.0-13.5	3	87	0 - 0	12.6 - 14.4		
Gammaglutamyl transferase (GGT)	U/L	Adult	0.0-11.7	5	137	0 - 0	11.1 - 12.2		
Gammaglutamyl transferase (GGT)	U/L	Geriatric	0.3-13.7	5	13	0 - 2.1	11.9 - 15.6		
Globulin	g/dL	Juvenile/subadult	1.5-2.6	2	104	1.4 - 1.5	2.5 - 2.6	1.35E-02	−0.4 (S)
Globulin	g/dL	Adult	1.6-2.7	2.1	151	1.5 - 1.6	2.6 - 2.7		
Globulin	g/dL	Geriatric	2.0-2.9	2.35	16	1.9 - 2.1	2.8 - 3	3.00E-04	1.1 (L)
Glucose	mg/dL	Juvenile/subadult	31.0-254.0	132.5	100	20 - 41.9	243.1 - 265		
Glucose	mg/dL	Adult	33.4-223.6	122.5	146	25.7 - 41.1	215.9 - 231.3		
Glucose	mg/dL	Geriatric	5.8-247.1	109.5	16	0 - 35.3	217.5 - 276.7		

(*continued*)

Table 3. (Continued)

Analyte	Unit	Age	Range	Median	Samples, n	Lower 95% CI	Upper 95% CI	*P* value compared with male adults	Effect Size
Indirect Bilirubin	mg/dL	Juvenile/subadult	0.0-0.3	0.2	51	0 - 0.1	0.3 - 0.3	3.10E-02	0.5 (S)
Indirect Bilirubin	mg/dL	Adult	0.0-0.2	0.1	63	0 - 0	0.2 - 0.3		
Indirect Bilirubin	mg/dL	Geriatric	0.0-0.2	0.1	5	0 - 0.1	0.2 - 0.2		
Lipase	IU/L	Juvenile/subadult	10.3-48.2	28	71	8.1 - 12.5	46 - 50.4	3.81E-02	−0.4 (S)
Lipase	IU/L	Adult	13.8-51.5	31	93	11.9 - 15.7	49.5 - 53.4		
Lipase	IU/L	Geriatric	14.9-33.5	25.5	10	12 - 17.8	30.6 - 36.4	2.48E-02	−0.9 (L)
Phosphorus	mg/dL	Juvenile/subadult	2.0-5.5	3.8	92	1.9 - 2.2	5.3 - 5.6	1.00E-04	0.6 (M)
Phosphorus	mg/dL	Adult	1.8-4.8	3.2	145	1.7 - 1.9	4.6 - 4.9		
Phosphorus	mg/dL	Geriatric	1.9-6.0	3.6	12	1.3 - 2.5	5.4 - 6.6	4.56E-02	0.9 (L)
Potassium	mM/L	Juvenile/subadult	2.2-4.0	3.1	50	2.1 - 2.3	3.8 - 4.1		
Potassium	mM/L	Adult	2.3-3.9	3.1	80	2.3 - 2.4	3.9 - 4		
Potassium	mM/L	Geriatric	2.3-3.8	3	6	2 - 2.6	3.5 - 4.1		
Sodium	mM/L	Juvenile/subadult	145.7-155.0	150	50	145 - 146.3	154.3 - 155.6		
Sodium	mM/L	Adult	147.2-155.4	151	79	146.7 - 147.7	155 - 155.9		
Sodium	mM/L	Geriatric	147.5-155.5	151	6	146 - 149.1	153.9 - 157		
Sodium/Potassium (Na:K) ratio		Juvenile/subadult	32.2-62.3	45.5	36	29.7 - 34.6	59.8 - 64.7		
Sodium/Potassium (Na:K) ratio		Adult	33.6-61.5	48	48	31.7 - 35.6	59.6 - 63.5		
Sodium/Potassium (Na:K) ratio		Geriatric	36.9-61.1	49.5	4	31 - 42.8	55.2 - 67		
Total Bilirubin	mg/dL	Juvenile/subadult	0.1-0.3	0.2	93	0 - 0.1	0.3 - 0.3	3.60E-03	0.4 (S)
Total Bilirubin	mg/dL	Adult	0.0-0.2	0.1	146	0 - 0	0.2 - 0.2		
Total Bilirubin	mg/dL	Geriatric	0.0-0.2	0.1	13	0 - 0.1	0.2 - 0.2		
Total CO2 (Bicarbonate)	mM/L	Juvenile/subadult	14.3-28.8	22	48	13.3 - 15.3	27.8 - 29.8	3.39E-02	−0.5 (S)
Total CO2 (Bicarbonate)	mM/L	Adult	14.9-31.7	24	58	13.8 - 16	30.7 - 32.8		
Total CO2 (Bicarbonate)	mM/L	Geriatric	25.3-28.3	27	5	24.6 - 26	27.6 - 29	3.39E-02	0.9 (L)
Total Protein	g/dL	Juvenile/subadult	5.0-7.4	6.25	104	4.9 - 5.1	7.3 - 7.6		
Total Protein	g/dL	Adult	5.0-7.3	6.2	152	4.9 - 5.1	7.2 - 7.4		
Total Protein	g/dL	Geriatric	5.0-7.0	5.85	16	4.8 - 5.2	6.7 - 7.2		
Bands	x10^3/µL	Juvenile/subadult	0.0-4.7	1	11	0 - 0	3.9 - 5.6		
Bands	x10^3/µL	Adult	0.0-5.4	2	18	0 - 0	4.6 - 6.2		
Bands	x10^3/µL	Geriatric			0				
Basophil #	x10^3/µL	Juvenile/subadult	0.0-0.0	0	35	0 - 0	0 - 0		
Basophil #	x10^3/µL	Adult	0.0-0.0	0	49	0 - 0	0 - 0		
Basophil #	x10^3/µL	Geriatric	0.0-0.0	0	8	0 - 0	0 - 0		
Basophil %	%	Juvenile/subadult	0.0-0.5	0.2	34	0 - 0	0.4 - 0.5		
Basophil %	%	Adult	0.0-0.5	0.1	47	0 - 0	0.4 - 0.5		
Basophil %	%	Geriatric	0.0-0.4	0.15	8	0 - 0	0.3 - 0.5		
Eosinophil #	x10^3/µL	Juvenile/subadult	0.0-0.3	0.2	33	0 - 0.1	0.3 - 0.3	2.20E-03	1.0 (L)
Eosinophil #	x10^3/µL	Adult	0.0-0.2	0.1	48	0 - 0	0.2 - 0.2		
Eosinophil #	x10^3/µL	Geriatric	0.0-0.2	0.1	8	0 - 0	0.1 - 0.2		

(*continued*)

Table 3. (Continued)

Analyte	Unit	Age	Range	Median	Samples, n	Lower 95% CI	Upper 95% CI	*P* value compared with male adults	Effect Size
Eosinophil %	%	Juvenile/subadult	0.7-4.7	2.5	33	0.3 - 1	4.4 - 5.1		
Eosinophil %	%	Adult	0.2-4.1	2.1	49	0 - 0.5	3.9 - 4.4		
Eosinophil %	%	Geriatric	0.7-2.3	1.45	8	0.5 - 1	2 - 2.5		
Hematocrit (HCT)	%	Juvenile/subadult	34.6-47.7	41	53	33.8 - 35.5	46.8 - 48.5		
Hematocrit (HCT)	%	Adult	33.5-47.3	40.25	76	32.7 - 34.3	46.5 - 48.1		
Hematocrit (HCT)	%	Geriatric	34.5-41.6	38.65	8	33.3 - 35.7	40.4 - 42.9		
Hemoglobin (Hgb)	g/dL	Juvenile/subadult	12.2-16.8	14.5	53	11.9 - 12.5	16.5 - 17.1		
Hemoglobin (Hgb)	g/dL	Adult	12.1-16.1	14.15	76	11.9 - 12.3	15.9 - 16.4		
Hemoglobin (Hgb)	g/dL	Geriatric	12.8-14.6	13.45	8	12.5 - 13.1	14.3 - 14.9		
Lymphocyte #	x10^3/µL	Juvenile/subadult	0.6-5.5	2.85	34	0.2 - 1	5.1 - 5.9	5.90E-03	0.7 (M)
Lymphocyte #	x10^3/µL	Adult	0.0-4.5	1.8	49	0 - 0.1	4.2 - 4.8		
Lymphocyte #	x10^3/µL	Geriatric	0.4-2.1	1.1	8	0.2 - 0.7	1.8 - 2.3	3.70E-02	−0.8 (M)
Lymphocyte %	%	Juvenile/subadult	22.1-83.6	54.8	35	17 - 27.2	78.5 - 88.7	2.48E-02	0.5 (M)
Lymphocyte %	%	Adult	18.2-72.7	46.45	50	14.4 - 22	69 - 76.5		
Lymphocyte %	%	Geriatric	4.4-54.3	30.35	8	0 - 13	45.7 - 63	1.70E-02	−1.2 (L)
Mean corpuscular hemoglobin (MCH)	pg	Juvenile/subadult	17.1-22.4	19.9	53	16.7 - 17.4	22.1 - 22.8		
Mean corpuscular hemoglobin (MCH)	pg	Adult	17.0-22.9	19.9	78	16.6 - 17.3	22.6 - 23.2		
Mean corpuscular hemoglobin (MCH)	pg	Geriatric	17.6-20.4	19.15	8	17.1 - 18.1	19.9 - 20.9		
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	Juvenile/subadult	31.9-38.7	35.35	52	31.4 - 32.4	38.3 - 39.2		
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	Adult	30.8-39.6	35.4	77	30.4 - 31.3	39.1 - 40		
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	Geriatric	32.1-39.9	35.9	8	30.8 - 33.5	38.5 - 41.2		
Mean corpuscular volume (MCV)	fL	Juvenile/subadult	50.8-61.6	56.2	54	50.1 - 51.6	60.9 - 62.3		
Mean corpuscular volume (MCV)	fL	Adult	49.8-63.3	56.8	77	49.1 - 50.6	62.6 - 64.1		
Mean corpuscular volume (MCV)	fL	Geriatric	50.6-55.2	53	8	49.9 - 51.4	54.4 - 56	3.20E-03	−1.1 (L)
Mean platelet volume (MPV)	fL	Juvenile/subadult	7.4-14.2	10.6	54	6.9 - 7.8	13.7 - 14.7	2.95E-02	0.6 (M)
Mean platelet volume (MPV)	fL	Adult	7.3-12.5	9.75	80	7 - 7.6	12.2 - 12.7		
Mean platelet volume (MPV)	fL	Geriatric	7.0-11.3	8.75	8	6.3 - 7.8	10.5 - 12		
Monocyte #	x10^3/µL	Juvenile/subadult	0.0-0.3	0.2	29	0 - 0.1	0.3 - 0.4	2.00E-02	0.7 (M)
Monocyte #	x10^3/µL	Adult	0.0-0.3	0.1	46	0 - 0	0.3 - 0.3		
Monocyte #	x10^3/µL	Geriatric	0.0-0.2	0.1	8	0 - 0	0.1 - 0.2		
Monocyte %	%	Juvenile/subadult	0.0-7.6	3.5	31	0 - 0.6	6.9 - 8.3		
Monocyte %	%	Adult	0.0-7.0	2.75	48	0 - 0	6.5 - 7.6		
Monocyte %	%	Geriatric	0.0-5.2	1.95	8	0 - 0.5	4.2 - 6.2		
Neutrophil #	x10^3/µL	Juvenile/subadult	0.0-5.2	2	35	0 - 0.1	4.7 - 5.6		
Neutrophil #	x10^3/µL	Adult	0.2-4.3	1.9	48	0 - 0.5	4 - 4.6		
Neutrophil #	x10^3/µL	Geriatric	0.0-7.2	2.1	7	0 - 0.6	5.7 - 8.7		
Neutrophil %	%	Juvenile/subadult	7.8-70.5	36.2	35	2.6 - 13	65.3 - 75.7	1.03E-02	−0.6 (M)

(*continued*)

Table 3. (Continued)

Analyte	Unit	Age	Range	Median	Samples, n	Lower 95% CI	Upper 95% CI	*P* value compared with male adults	Effect Size
Neutrophil %	%	Adult	20.2-76.8	45.85	50	16.3 - 24.1	72.9 - 80.8		
Neutrophil %	%	Geriatric	39.5-93.9	66.15	8	30.1 - 48.9	84.5 - 103.4	1.03E-02	1.3 (L)
Platelet count (PLT)	x10^3/µL	Juvenile/subadult	39.9-57.5	49	57	38.8 - 41	56.3 - 58.6	2.83E-02	0.4 (S)
Platelet count (PLT)	x10^3/µL	Adult	40.0-54.0	47	76	39.2 - 40.8	53.2 - 54.8		
Platelet count (PLT)	x10^3/µL	Geriatric	38.2-50.4	44	7	35.9 - 40.4	48.1 - 52.7		
Red blood cell count (RBC)	x10^6/µL	Juvenile/subadult	156.7-643.0	395	54	124.2 - 189.1	610.6 - 675.5	2.93E-02	−0.5 (M)
Red blood cell count (RBC)	x10^6/µL	Adult	226.7-692.9	455	80	201.1 - 252.2	667.3 - 718.4		
Red blood cell count (RBC)	x10^6/µL	Geriatric	278.6-745.9	514	8	197.6 - 359.5	665 - 826.9		
Red cell distribution width (RDW)	%	Juvenile/subadult	6.1-8.6	7.37	53	5.9 - 6.3	8.4 - 8.7	5.00E-02	0.4 (S)
Red cell distribution width (RDW)	%	Adult	5.6-8.4	7.13	78	5.5 - 5.8	8.3 - 8.6		
Red cell distribution width (RDW)	%	Geriatric	6.7-7.7	7.305	8	6.5 - 6.9	7.5 - 7.8		
Packed Cell Volume (PCV)	%	Juvenile/subadult	14.7-20.3	17.4	54	14.3 - 15.1	20 - 20.7	1.70E-03	0.7 (M)
Packed Cell Volume (PCV)	%	Adult	14.2-19.0	16.25	76	13.9 - 14.5	18.7 - 19.3		
Packed Cell Volume (PCV)	%	Geriatric	15.0-18.2	16.4	8	14.5 - 15.6	17.7 - 18.8		
White blood cell count (WBC)	x10^3/µL	Juvenile/subadult	1.7-9.4	5.45	54	1.2 - 2.3	8.9 - 9.9	4.31E-02	0.4 (S)
White blood cell count (WBC)	x10^3/µL	Adult	1.5-8.3	4.55	80	1.1 - 1.8	7.9 - 8.7		
White blood cell count (WBC)	x10^3/µL	Geriatric	0.0-9.4	3.3	7	0 - 1.6	7.6 - 11.2		

N = negligible, S = small, M = medium, L = large

Table 4. Clinical Pathology Reference Intervals by Age in Female Marmosets.

Analyte	Unit	Age	Range	Median	Samples, n	Lower 95% CI	Upper 95% CI	*P* value compared with female adults	Effect Size
Weight	g	Juvenile/subadult	294.7-521.7	408	52	279.3 - 310.1	506.3 - 537.2		
Weight	g	Adult	327.0-532.6	427	79	315.6 - 338.3	521.3 - 543.9		
Weight	g	Geriatric	364.7-506.0	438	45	354.3 - 375	495.7 - 516.4		
Alanine aminotransferase (ALT)	U/L	Juvenile/subadult	0.0-25.3	7.5	102	0 - 0	23.9 - 26.8		
Alanine aminotransferase (ALT)	U/L	Adult	0.0-21.6	7	87	0 - 0	20.3 - 22.9		
Alanine aminotransferase (ALT)	U/L	Geriatric	1.7-17.2	8.5	42	0.5 - 2.8	16.1 - 18.4		
Albumin	g/dL	Juvenile/subadult	3.6-5.2	4.4	110	3.5 - 3.6	5.1 - 5.2	3.40E-03	0.4 (S)
Albumin	g/dL	Adult	3.3-5.1	4.2	100	3.2 - 3.4	5 - 5.2		
Albumin	g/dL	Geriatric	2.7-4.5	3.6	49	2.5 - 2.8	4.4 - 4.7	0.00E+00	−1.3 (L)
Albumin/Globulin (A:G) ratio		Juvenile/subadult	1.5-2.8	2.2	48	1.5 - 1.6	2.7 - 2.9	1.50E-03	0.6 (M)
Albumin/Globulin (A:G) ratio		Adult	1.4-2.6	1.9	65	1.3 - 1.4	2.5 - 2.7		
Albumin/Globulin (A:G) ratio		Geriatric	1.1-2.1	1.6	35	1 - 1.2	2.1 - 2.2	0.00E+00	−1.3 (L)
Alkaline Phosphatase (ALP)	U/L	Juvenile/subadult	34.7-153.8	88	93	28.6 - 40.7	147.7 - 159.9	0.00E+00	1.3 (L)
Alkaline Phosphatase (ALP)	U/L	Adult	13.1-104.9	54	102	8.7 - 17.6	100.5 - 109.4		
Alkaline Phosphatase (ALP)	U/L	Geriatric	22.6-92.3	52.5	48	17.6 - 27.5	87.4 - 97.3		
Amylase	U/L	Juvenile/subadult	159.6-316.4	237	55	149.2 - 169.9	306 - 326.7		
Amylase	U/L	Adult	147.0-309.2	229	91	138.7 - 155.4	300.9 - 317.6		

(*continued*)

Table 4. (Continued)

Analyte	Unit	Age	Range	Median	Samples, n	Lower 95% CI	Upper 95% CI	*P* value compared with female adults	Effect Size
Amylase	U/L	Geriatric	132.4-331.3	218	43	117.5 - 147.2	316.4 - 346.2		
Anion Gap	mM/L	Juvenile/subadult	17.8-30.5	25	20	16.4 - 19.2	29.1 - 31.9		
Anion Gap	mM/L	Adult	18.4-29.6	23	30	17.4 - 19.4	28.6 - 30.6		
Anion Gap	mM/L	Geriatric	19.6-30.1	24	27	18.6 - 20.6	29.1 - 31.1		
Aspartate aminotransferase (AST)	U/L	Juvenile/subadult	46.4-175.5	106.5	94	39.9 - 52.9	169 - 182		
Aspartate aminotransferase (AST)	U/L	Adult	45.6-177.6	107	73	38 - 53.2	170 - 185.2		
Aspartate aminotransferase (AST)	U/L	Geriatric	56.1-171.5	108	41	47.3 - 65	162.7 - 180.3		
Blood Urea Nitrogen (BUN)	mg/dL	Juvenile/subadult	12.8-32.7	22	106	11.8 - 13.7	31.8 - 33.7	0.00E+00	0.8 (M)
Blood Urea Nitrogen (BUN)	mg/dL	Adult	9.7-28.5	20	101	8.8 - 10.7	27.5 - 29.4		
Blood Urea Nitrogen (BUN)	mg/dL	Geriatric	8.8-29.9	19	48	7.3 - 10.3	28.4 - 31.4		
BUN/Creatinine (B:C) ratio		Juvenile/subadult	2.0-144.9	70	32	0 - 14.4	132.5 - 157.3		
BUN/Creatinine (B:C) ratio		Adult	0.0-159.9	70	33	0 - 0	144.1 - 175.7		
BUN/Creatinine (B:C) ratio		Geriatric	0.7-168.3	66.7	28	0 - 16.2	152.8 - 183.8		
Calcium	mg/dL	Juvenile/subadult	9.1-11.4	10.2	108	9 - 9.2	11.3 - 11.5	2.00E-04	0.6 (M)
Calcium	mg/dL	Adult	8.5-11.2	9.9	100	8.4 - 8.7	11.1 - 11.3		
Calcium	mg/dL	Geriatric	8.3-10.4	9.3	49	8.2 - 8.5	10.3 - 10.6	0.00E+00	−0.8 (M)
Chloride	mM/L	Juvenile/subadult	100.1-112.3	107	39	99.2 - 101.1	111.4 - 113.3		
Chloride	mM/L	Adult	100.9-113.0	107	54	100.1 - 101.7	112.2 - 113.8		
Chloride	mM/L	Geriatric	103.5-114.0	109	35	102.7 - 104.4	113.1 - 114.8	8.80E-03	0.6 (M)
Cholesterol	mg/dL	Juvenile/subadult	57.2-210.1	129.5	48	46.3 - 68	199.3 - 220.9		
Cholesterol	mg/dL	Adult	32.8-224.9	118	66	21.3 - 44.4	213.3 - 236.5		
Cholesterol	mg/dL	Geriatric	60.9-294.1	186	35	41.5 - 80.2	274.8 - 313.4	3.00E-04	0.9 (L)
Creatine Kinase (CK)	U/L	Juvenile/subadult	0.0-753.1	254	25	0 - 0	668.2 - 838.1		
Creatine Kinase (CK)	U/L	Adult	0.0-909.6	197	37	0 - 0	814.5 - 1004.7		
Creatine Kinase (CK)	U/L	Geriatric	0.0-1071.5	264	24	0 - 0	940.6 - 1202.5		
Creatinine	mg/dL	Juvenile/subadult	0.1-0.4	0.3	45	0.1 - 0.1	0.4 - 0.4	3.26E-02	0.5 (M)
Creatinine	mg/dL	Adult	0.1-0.4	0.2	54	0 - 0.1	0.3 - 0.4		
Creatinine	mg/dL	Geriatric	0.0-0.4	0.2	32	0 - 0.1	0.4 - 0.5		
Direct Bilirubin	mg/dL	Juvenile/subadult	0.0-0.0	0	31	0 - 0	0 - 0		
Direct Bilirubin	mg/dL	Adult	0.0-0.0	0	33	0 - 0	0 - 0		
Direct Bilirubin	mg/dL	Geriatric	0.0-0.0	0	30	0 - 0	0 - 0		
Gammaglutamyl transferase (GGT)	U/L	Juvenile/subadult	0.0-14.8	6	55	0 - 0	13.7 - 15.9		
Gammaglutamyl transferase (GGT)	U/L	Adult	0.0-13.5	4	77	0 - 0	12.6 - 14.4		
Gammaglutamyl transferase (GGT)	U/L	Geriatric	1.5-14.3	7	43	0.6 - 2.5	13.3 - 15.2	6.00E-04	0.6 (M)
Globulin	g/dL	Juvenile/subadult	1.6-2.6	2.1	111	1.5 - 1.6	2.6 - 2.7		
Globulin	g/dL	Adult	1.6-2.7	2.1	98	1.5 - 1.6	2.7 - 2.8		
Globulin	g/dL	Geriatric	1.7-2.7	2.1	48	1.7 - 1.8	2.6 - 2.8		
Glucose	mg/dL	Juvenile/subadult	31.3-229.9	120	105	21.8 - 40.8	220.4 - 239.4		
Glucose	mg/dL	Adult	23.5-248.7	125	96	12.2 - 34.8	237.4 - 259.9		

(*continued*)

Table 4. (Continued)

Analyte	Unit	Age	Range	Median	Samples, n	Lower 95% CI	Upper 95% CI	*P* value compared with female adults	Effect Size
Glucose	mg/dL	Geriatric	24.9-199.6	107	49	12.7 - 37.1	187.3 - 211.8		
Indirect Bilirubin	mg/dL	Juvenile/subadult	0.0-0.2	0.1	34	0 - 0	0.2 - 0.2		
Indirect Bilirubin	mg/dL	Adult	0.0-0.2	0.1	40	0 - 0	0.2 - 0.2		
Indirect Bilirubin	mg/dL	Geriatric	0.0-0.2	0.1	30	0 - 0	0.2 - 0.2		
Lipase	IU/L	Juvenile/subadult	11.6-46.7	28	37	8.8 - 14.4	43.9 - 49.6		
Lipase	IU/L	Adult	9.4-45.9	26	65	7.2 - 11.7	43.7 - 48.1		
Lipase	IU/L	Geriatric	13.7-46.4	28	37	11.1 - 16.4	43.8 - 49.1		
Phosphorus	mg/dL	Juvenile/subadult	2.5-5.6	4.1	61	2.3 - 2.7	5.4 - 5.8	9.00E-04	0.5 (M)
Phosphorus	mg/dL	Adult	1.9-5.4	3.6	94	1.7 - 2.1	5.2 - 5.5		
Phosphorus	mg/dL	Geriatric	2.1-5.5	3.6	46	1.8 - 2.3	5.2 - 5.7		
Potassium	mM/L	Juvenile/subadult	2.2-3.9	3	38	2.1 - 2.4	3.8 - 4.1		
Potassium	mM/L	Adult	2.4-3.9	3.2	53	2.3 - 2.5	3.8 - 4		
Potassium	mM/L	Geriatric	2.3-3.9	3.1	36	2.2 - 2.5	3.8 - 4		
Sodium	mM/L	Juvenile/subadult	145.9-154.0	150	39	145.3 - 146.5	153.3 - 154.6		
Sodium	mM/L	Adult	145.8-154.3	150	54	145.2 - 146.3	153.8 - 154.9		
Sodium	mM/L	Geriatric	146.0-155.2	151	36	145.2 - 146.7	154.5 - 156		
Sodium/Potassium (Na:K) ratio		Juvenile/subadult	34.7-62.4	50	27	32 - 37.3	59.8 - 65		
Sodium/Potassium (Na:K) ratio		Adult	33.4-57.5	46	31	31.3 - 35.5	55.4 - 59.6		
Sodium/Potassium (Na:K) ratio		Geriatric	36.8-61.6	49	28	34.5 - 39.1	59.3 - 63.9		
Total Bilirubin	mg/dL	Juvenile/subadult	0.0-0.2	0.1	64	0 - 0	0.2 - 0.2		
Total Bilirubin	mg/dL	Adult	0.0-0.2	0.1	95	0 - 0	0.2 - 0.2		
Total Bilirubin	mg/dL	Geriatric	0.0-0.2	0.1	46	0 - 0	0.2 - 0.2	1.05E-02	−0.5 (M)
Total CO2 (Bicarbonate)	mM/L	Juvenile/subadult	16.1-28.3	22	26	14.9 - 17.2	27.1 - 29.5		
Total CO2 (Bicarbonate)	mM/L	Adult	15.9-27.9	22	36	14.9 - 16.9	26.9 - 28.9		
Total CO2 (Bicarbonate)	mM/L	Geriatric	12.7-27.1	20	29	11.4 - 14	25.8 - 28.4	3.39E-02	−0.6 (M)
Total Protein	g/dL	Juvenile/subadult	5.3-7.6	6.5	111	5.2 - 5.4	7.5 - 7.7		
Total Protein	g/dL	Adult	5.1-7.5	6.4	100	5 - 5.3	7.4 - 7.6		
Total Protein	g/dL	Geriatric	4.8-6.9	5.9	50	4.6 - 4.9	6.7 - 7	0.00E+00	−0.9 (L)
Bands	x10^3/µL	Juvenile/subadult	0.0-5.7	1	6	0 - 0	4.2 - 7.3		
Bands	x10^3/µL	Adult	0.0-4.5	1	8	0 - 0	3.5 - 5.5		
Bands	x10^3/µL	Geriatric	0.0-3.7	1	8	0 - 0	3 - 4.5		
Basophil #	x10^3/µL	Juvenile/subadult	0.0-0.0	0	26	0 - 0	0 - 0		
Basophil #	x10^3/µL	Adult	0.0-0.0	0	32	0 - 0	0 - 0		
Basophil #	x10^3/µL	Geriatric	0.0-0.0	0	23	0 - 0	0 - 0		
Basophil %	%	Juvenile/subadult	0.0-0.6	0.1	27	0 - 0	0.5 - 0.6		
Basophil %	%	Adult	0.0-0.6	0.1	29	0 - 0	0.5 - 0.7		
Basophil %	%	Geriatric	0.0-0.5	0.2	23	0 - 0	0.4 - 0.5		
Eosinophil #	x10^3/µL	Juvenile/subadult	0.0-0.2	0.1	26	0 - 0	0.2 - 0.2		
Eosinophil #	x10^3/µL	Adult	0.0-0.3	0.1	40	0 - 0	0.3 - 0.3		

(*continued*)

Table 4. (Continued)

Analyte	Unit	Age	Range	Median	Samples, n	Lower 95% CI	Upper 95% CI	*P* value compared with female adults	Effect Size
Eosinophil #	x10^3/µL	Geriatric	0.0-0.2	0.1	24	0 - 0	0.2 - 0.3		
Eosinophil %	%	Juvenile/subadult	0.3-3.6	1.7	26	0 - 0.6	3.3 - 3.9		
Eosinophil %	%	Adult	0.4-3.8	1.95	38	0.1 - 0.6	3.5 - 4		
Eosinophil %	%	Geriatric	0.0-3.7	1.5	24	0 - 0.2	3.3 - 4		
Hematocrit (HCT)	%	Juvenile/subadult	32.4-45.1	39.45	38	31.3 - 33.4	44.1 - 46.2		
Hematocrit (HCT)	%	Adult	31.3-44.0	37.5	53	30.4 - 32.1	43.2 - 44.9		
Hematocrit (HCT)	%	Geriatric	29.6-47.8	38.65	32	28 - 31.2	46.2 - 49.4		
Hemoglobin (Hgb)	g/dL	Juvenile/subadult	11.7-15.9	13.8	39	11.4 - 12.1	15.6 - 16.2		
Hemoglobin (Hgb)	g/dL	Adult	10.9-15.8	13.2	51	10.6 - 11.2	15.5 - 16.1		
Hemoglobin (Hgb)	g/dL	Geriatric	10.3-16.6	13.2	34	9.8 - 10.8	16 - 17.1		
Lymphocyte #	x10^3/µL	Juvenile/subadult	0.3-5.3	2.6	27	0 - 0.7	4.8 - 5.8		
Lymphocyte #	x10^3/µL	Adult	0.0-4.9	2.2	37	0 - 0.4	4.5 - 5.3		
Lymphocyte #	x10^3/µL	Geriatric	0.0-5.5	2.05	24	0 - 0.3	4.9 - 6.1		
Lymphocyte %	%	Juvenile/subadult	19.9-91.8	57	28	13.3 - 26.6	85.2 - 98.5		
Lymphocyte %	%	Adult	14.4-81.8	45.95	40	9.2 - 19.6	76.6 - 87.1		
Lymphocyte %	%	Geriatric	6.7-73.5	31.75	24	0 - 13.3	66.8 - 80.1		
Mean corpuscular hemoglobin (MCH)	pg	Juvenile/subadult	16.1-23.0	19.35	38	15.6 - 16.7	22.5 - 23.6		
Mean corpuscular hemoglobin (MCH)	pg	Adult	16.8-23.0	19.9	53	16.4 - 17.2	22.5 - 23.4		
Mean corpuscular hemoglobin (MCH)	pg	Geriatric	17.8-23.2	20.75	36	17.3 - 18.2	22.8 - 23.7		
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	Juvenile/subadult	31.0-39.5	35.05	38	30.4 - 31.7	38.8 - 40.1		
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	Adult	31.5-39.5	35.7	54	31 - 32	39 - 40		
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	Geriatric	29.2-39.7	34.55	36	28.3 - 30.1	38.8 - 40.6		
Mean corpuscular volume (MCV)	fL	Juvenile/subadult	49.5-61.9	55.5	39	48.5 - 50.5	61 - 62.9		
Mean corpuscular volume (MCV)	fL	Adult	50.1-62.2	55.5	51	49.2 - 50.9	61.4 - 63.1		
Mean corpuscular volume (MCV)	fL	Geriatric	51.5-66.2	58.5	34	50.3 - 52.8	64.9 - 67.4	2.60E-03	0.8 (L)
Mean platelet volume (MPV)	fL	Juvenile/subadult	7.4-12.3	9.8	38	7 - 7.8	11.9 - 12.7		
Mean platelet volume (MPV)	fL	Adult	7.2-13.2	10.05	56	6.8 - 7.6	12.8 - 13.5		
Mean platelet volume (MPV)	fL	Geriatric	6.2-12.9	9.5	37	5.7 - 6.7	12.4 - 13.5		
Monocyte #	x10^3/µL	Juvenile/subadult	0.0-0.3	0.1	26	0 - 0	0.2 - 0.3		
Monocyte #	x10^3/µL	Adult	0.0-0.3	0.2	37	0 - 0	0.3 - 0.3		
Monocyte #	x10^3/µL	Geriatric	0.0-0.3	0.1	24	0 - 0	0.2 - 0.3		
Monocyte %	%	Juvenile/subadult	0.2-4.8	2.25	26	0 - 0.7	4.4 - 5.3		
Monocyte %	%	Adult	0.1-6.0	2.7	39	0 - 0.5	5.6 - 6.5		
Monocyte %	%	Geriatric	0.0-4.6	1.9	24	0 - 0.2	4.1 - 5.1		
Neutrophil #	x10^3/µL	Juvenile/subadult	0.0-4.7	1.75	28	0 - 0	4.2 - 5.1		
Neutrophil #	x10^3/µL	Adult	0.0-5.3	1.9	37	0 - 0	4.9 - 5.8		
Neutrophil #	x10^3/µL	Geriatric	0.7-6.3	3.1	23	0.1 - 1.2	5.7 - 6.9	4.40E-03	0.8 (M)

(*continued*)

Table 4. (Continued)

Analyte	Unit	Age	Range	Median	Samples, n	Lower 95% CI	Upper 95% CI	*P* value compared with female adults	Effect Size
Neutrophil %	%	Juvenile/subadult	6.3-66.6	35.65	28	0.7 - 11.9	61 - 72.2		
Neutrophil %	%	Adult	14.4-75.5	47.4	40	9.7 - 19.2	70.8 - 80.2		
Neutrophil %	%	Geriatric	23.7-87.9	60.65	24	17.3 - 30.1	81.5 - 94.4	2.22E-02	0.7 (M)
Platelet count (PLT)	x10^3/µL	Juvenile/subadult	39.0-53.2	45.5	68	38.1 - 39.8	52.4 - 54.1		
Platelet count (PLT)	x10^3/µL	Adult	38.6-52.8	45	54	37.6 - 39.5	51.9 - 53.8		
Platelet count (PLT)	x10^3/µL	Geriatric	36.9-49.0	43	15	35.4 - 38.4	47.4 - 50.5	2.75E-02	–0.8 (M)
Red blood cell count (RBC)	x10^6/µL	Juvenile/subadult	157.5-587.3	359	38	123.3 - 191.7	553.2 - 621.5		
Red blood cell count (RBC)	x10^6/µL	Adult	130.7-711.9	404.5	54	91.9 - 169.4	673.2 - 750.7		
Red blood cell count (RBC)	x10^6/µL	Geriatric	236.7-876.3	595.5	34	182.9 - 290.4	822.6 - 930.1	8.00E-04	0.9 (L)
Red cell distribution width (RDW)	%	Juvenile/subadult	5.9-8.3	7.005	38	5.7 - 6	8.1 - 8.5	4.53E-02	0.6 (M)
Red cell distribution width (RDW)	%	Adult	5.3-8.1	6.72	51	5.1 - 5.5	7.9 - 8.3		
Red cell distribution width (RDW)	%	Geriatric	5.1-8.2	6.725	34	4.9 - 5.4	7.9 - 8.4		
Packed Cell Volume (PCV)	%	Juvenile/subadult	14.2-20.2	16.7	37	13.7 - 14.6	19.7 - 20.6		
Packed Cell Volume (PCV)	%	Adult	14.8-19.0	16.65	52	14.5 - 15.1	18.7 - 19.3		
Packed Cell Volume (PCV)	%	Geriatric	14.4-18.3	16.15	36	14.1 - 14.7	17.9 - 18.6	3.96E-02	–0.5 (M)
White blood cell count (WBC)	x10^3/µL	Juvenile/subadult	1.7-8.2	4.8	38	1.2 - 2.2	7.7 - 8.7		
White blood cell count (WBC)	x10^3/µL	Adult	0.8-8.4	4.15	48	0.3 - 1.4	7.8 - 8.9		
White blood cell count (WBC)	x10^3/µL	Geriatric	2.7-9.0	5.8	35	2.2 - 3.3	8.5 - 9.5	7.70E-03	0.7 (M)

N = negligible, S = small, M = medium, L = large

bilirubin, total CO2, neutrophil #, neutrophil %, RDW, packed cell volume (PCV), WBC) and 6 with a large effect (albumin, A:G ratio, total protein, cholesterol, PLT, MCV).

Effect of colony of origin. Given the MIT colony was populated with marmosets imported from different research colonies, we evaluated whether differences in blood analytes could be detected between sources of origin by comparing individuals that had not been cohoused with animals from other sources. As sources E and G were imported after N and C and had fewer tests performed, we selected 9 tests (ALP, AST, ALT, albumin, total protein, globulin, BUN, glucose, and calcium) that had at least 20 samples in healthy animals from each source. A total of 45 comparisons were statistically different when using source to define subsets, with 38 comparisons having medium or large effects. Of these, 26 comparisons involved marmosets from source G, followed by marmosets from source N (21), C (16), B (15) and E (12). Of the 26 comparisons involving marmosets from source G, 19 had a large effect while 5 had a medium effect (Figure 1a). Age differences between sources were as follows: B, mean 3.7 ± 2.3 y; C, 5.3 ± 1.9 y; E, 5.7 ± 3.0 y; G, 1.3 ± 0.2 y; and N, 4.5± 3.3 y. Because source G animals had a strong representation of females (79%) and juveniles (100%), we repeated our statistical analysis using only juvenile females from each source and found that 17 of 20 statistically significant comparisons still involved source G with all comparisons having a medium or large effect (Figure 1b).

Hematology and serum chemistry values of healthy, nonpregnant and pregnant marmosets. To determine the effects of pregnancy on hematologic and serum chemistry values, healthy, nonpregnant females were compared with samples from pregnant, healthy females. No differences were observed between the pregnant and nonpregnant cohorts based on age ($p = 0.16$). The median age of the nonpregnant cohort was 2.5 y old, while the median age of the pregnant marmosets was 2.9 y of age. The means and standard deviations in blood parameters for pregnant and nonpregnant marmosets are presented in Table 5. Statistically significant differences between pregnant and nonpregnant animals were seen in weight, ALT, ALP, anion gap, BUN, calcium, cholesterol, lipase, total CO2, neutrophil number, neutrophil %, and RDW (Table 5). Tests with medium to large effects included anion gap, BUN, cholesterol, total CO2, neutrophil number, neutrophil % and RDW. Further analysis comparing values from nonpregnant marmosets with samples from pregnant marmosets divided into 3 trimesters and a postpartum period of 50 d after parturition found differences in clinical chemistry and hematology values between nonpregnant animals and animals in all stages of pregnancy, but the strongest effects occurred in animals that were in either the 2nd or 3rd trimester (Table 6). Significant changes between nonpregnant samples and samples from the 2nd trimester marmosets included increases in anion gap and decreases in BUN and cholesterol. Samples from the 3rd trimester differed from nonpregnant samples with increases in weight and RDW, and decreased ALP. Compared with nonpregnant animals, marmosets within the 50-d window postpartum had lower amylase and lipase levels (Table 6).

Discussion

Our study presents reference ranges for blood chemistry and hematology values measured in a captive colony of common marmosets as compared with previous publications[8,16,21-23,32] and including animals of all life stages. To our knowledge, this report is the first to document the normal changes to blood chemistry and hematology values encountered during preg-

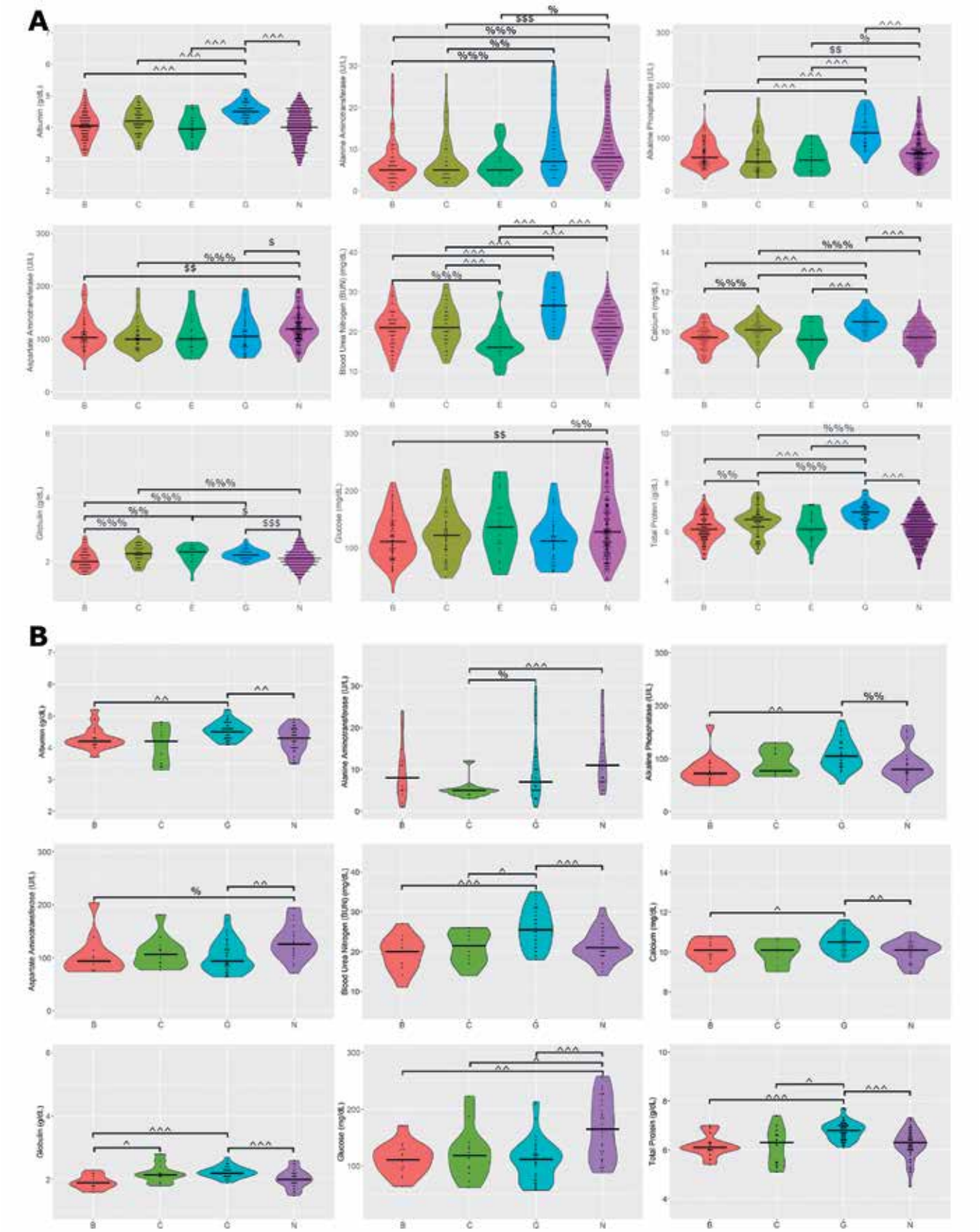

Figure 1. Comparison of 9 blood parameters between different marmoset sources are represented using violin plots, the shaded areas of which help to visualize the full distribution of the data and identify multimodal distributions. Dots represent individual samples, and the median is represented by the solid black bar. a) Comparison between 5 sources using healthy male and female animals, b) Comparison between 4 sources using healthy juvenile female animals. Legend for significance as follows. Negligible effect: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. Small effect: \$ $P < 0.05$, \$\$ $P < 0.01$, \$\$\$ $P < 0.001$. Medium effect: % $P < 0.05$, %% $P < 0.01$, %%% $P < 0.001$. Large effect: ^ $P < 0.05$, ^^ $P < 0.01$, ^^^ $P < 0.001$

Table 5. Comparison of Clinical Pathology Values in Healthy Pregnant and Non-Pregnant Females

		Non-Pregnant			Pregnant				
Parameter	Units	n	Mean ± SD.	Median	n	Mean ± SD.	Median	Significance	Effect Size
Weight	g	182	430.5 ± 58.8	426.5	29	459.5 ± 58.6	450	0.015	−0.49 (S)
Alanine aminotransferase (ALT)	U/L	264	16.9 ± 23.5	9	42	10 ± 15.5	7	0.005	0.31 (S)
Albumin	g/dL	264	4.1 ± 0.6	4.2	41	4 ± 0.4	4		
Albumin/Globulin (A:G) ratio		152	2.9 ± 12.2	1.9	25	1.9 ± 0.3	1.9		
Alkaline Phosphatase (ALP)	U/L	263	84.8 ± 54.7	71	42	60.8 ± 22.8	52.5	0.003	0.46 (S)
Amylase	U/L	193	234.2 ± 50.6	231	34	228.9 ± 37.7	223.5		
Anion Gap	mM/L	79	23.9 ± 3.8	24	14	29.6 ± 6.6	28	0.001	−1.3 (L)
Aspartate aminotransferase (AST)	U/L	214	115.2 ± 37.5	108	34	106.7 ± 26.6	100		
Blood Urea Nitrogen (BUN)	mg/dL	262	21.1 ± 6	21	42	18 ± 4.4	17.5	0	0.55 (M)
BUN/Creatinine (B:C) ratio		103	89.6 ± 61.7	73.3	17	78.1 ± 50.7	63.3		
Calcium	mg/dL	263	9.8 ± 1.1	10	41	9.6 ± 0.6	9.6	0.007	0.24 (S)
Chloride	mM/L	130	106.7 ± 6	108	21	106.8 ± 2.5	107		
Cholesterol	mg/dL	152	146.8 ± 63.4	134	24	102.3 ± 27.2	106	0	0.74 (M)
Creatine Kinase (CK)	U/L	95	470 ± 480.6	263	16	529.4 ± 658.3	287.5		
Creatinine	mg/dL	154	0.2 ± 0.1	0.2	24	0.2 ± 0.1	0.25		
Direct Bilirubin	mg/dL	104	0 ± 0	0	16	0 ± 0	0		
Gammaglutamyl transferase (GGT)	U/L	197	12.9 ± 32.9	6	34	9 ± 11.1	4		
Globulin	g/dL	262	2.1 ± 0.3	2.1	42	2.2 ± 0.4	2.1		
Glucose	mg/dL	261	138.2 ± 67.3	120	41	151 ± 77.5	121		
Indirect Bilirubin	mg/dL	104	0.1 ± 0	0.1	16	0.1 ± 0	0.1		
Lipase	IU/L	144	30.1 ± 11.3	28	27	27.5 ± 13.8	25	0.047	0.22 (S)
Phosphorus	mg/dL	206	3.8 ± 1	3.7	35	3.7 ± 0.9	3.5		
Potassium	mM/L	130	3.2 ± 0.5	3.1	21	3.3 ± 0.6	3.2		
Sodium	mM/L	132	148.4 ± 14.6	150	22	149.9 ± 2.8	149.5		
Sodium/Potassium (Na:K) ratio		87	47.1 ± 8.2	48	15	45.2 ± 8.1	46		
Total Bilirubin	mg/dL	207	0.1 ± 0.4	0.1	35	0.1 ± 0	0.1		
Total CO2 (Bicarbonate)	mM/L	95	21 ± 5.1	22	16	18 ± 5.3	18	0.037	0.58 (M)
Total Protein	g/dL	263	6.3 ± 0.7	6.3	42	6.2 ± 0.6	6.05		
Bands	x10^3/µL	24	2.2 ± 2.5	1	8	3.6 ± 2.8	2.5		
Basophil #	x10^3/µL	92	0 ± 0	0	14	0 ± 0.1	0		
Basophil %	%	92	0.3 ± 0.5	0.2	14	0.5 ± 0.8	0.2		
Eosinophil #	x10^3/µL	92	0.1 ± 0.1	0.1	14	0.3 ± 0.3	0.1		
Eosinophil %	%	92	2.4 ± 3.3	1.8	14	2.5 ± 1.5	2.25		
Hematocrit (HCT)	%	131	38.7 ± 5.4	37.9	22	39.7 ± 9.2	39.6		
Hemoglobin (Hgb)	g/dL	131	13.6 ± 1.7	13.4	22	14 ± 2.2	13.45		
Lymphocyte #	x10^3/µL	92	2.8 ± 1.6	2.3	14	2.9 ± 2.1	2.15		
Lymphocyte %	%	92	48.4 ± 18.2	49.25	14	38 ± 12.9	37.6		
Mean corpuscular hemoglobin (MCH)	pg	132	19.7 ± 3	19.9	22	19.3 ± 2.7	19.65		
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	131	34.8 ± 4.3	35.3	22	34.2 ± 2.6	34.6		
Mean corpuscular volume (MCV)	fL	131	56.7 ± 6	56.3	22	57.7 ± 4.2	56.85		
Mean platelet volume (MPV)	fL	132	9.9 ± 1.6	9.8	22	10.3 ± 1.6	10.3		
Monocyte #	x10^3/µL	92	0.2 ± 0.2	0.1	14	0.3 ± 0.3	0.2		
Monocyte %	%	92	3.2 ± 3.9	2.3	14	3 ± 1.8	2.8		
Neutrophil #	x10^3/µL	92	2.8 ± 2	2.15	14	4.5 ± 3	3.9	0.013	−0.78 (M)
Neutrophil %	%	92	45.2 ± 17	43	14	56 ± 12.1	55.3	0.025	−0.65 (M)
Platelet count (PLT)	x10^3/µL	142	45.1 ± 4.5	45	17	46 ± 5.1	46		
Red blood cell count (RBC)	x10^6/µL	132	445.9 ± 189.2	425	22	481.6 ± 137.8	467		
Red cell distribution width (RDW)	%	132	6.7 ± 1.1	6.77	22	7.2 ± 1.2	6.915		
Packed Cell Volume (PCV)	%	131	16.8 ± 2.1	16.5	22	18.4 ± 2.5	17.85	0.014	−0.73 (M)
White blood cell count (WBC)	x10^3/µL	132	5.8 ± 3	4.9	22	6.9 ± 4.7	5.6		

Table 6. Significant Clinical Pathology Values by Trimester in Pregnant Marmosets

Parameter	Mean ± SD.(# of samples)					*P* value (effect size)			
						Not pregnant compared with			
	Not pregnant	1st trimester	2nd trimester	3rd trimester	Postpartum	1st	2nd	3rd	Postpartum
Weight	430.5 ± 58.9 (171)	432.6 ± 48.4 (10)	448 ± 26.9 (11)	508.9 ± 70.7 (8)	430.7 ± 57.9 (11)			0.032 (large)	
Alkaline Phosphatase (ALP)	85 ± 55 (254)	68.8 ± 21.5 (19)	59.7 ± 23.9 (15)	43.6 ± 11.2 (8)	77.4 ± 45.2 (9)			0.01 (medium)	
Amylase	236.7 ± 49.3 (184)	237.7 ± 38.6 (17)	228 ± 33.1 (11)	205.5 ± 32.8 (6)	183.1 ± 50 (9)				0.044 (large)
Anion Gap	24.1 ± 3.6 (74)	30.8 ± 8.1 (6)	29.4 ± 4.9 (7)	24 ± 0 (1)	21.8 ± 5.4 (5)		0.016 (large)		
Blood Urea Nitrogen (BUN)	21.2 ± 6 (253)	19.8 ± 3.7 (19)	16.4 ± 3.9 (15)	16.5 ± 5.3 (8)	20 ± 4.8 (9)		0.009 (large)		
Cholesterol	147.3 ± 62.8 (146)	125.4 ± 16.6 (8)	84.5 ± 23 (12)	109.8 ± 15.6 (4)	134.5 ± 74 (6)		0.001 (large)		
Lipase	30.9 ± 11.1 (135)	27.9 ± 11.4 (15)	28 ± 19.6 (8)	25 ± 4.4 (4)	17.9 ± 6.8 (9)				0.003 (large)
Neutrophil #	2.6 ± 1.8 (87)	8 ± 3.2 (4)	2.9 ± 1.1 (6)	3.6 ± 1.8 (4)	6 ± 3.1 (5)	0.026 (large)			
Red cell distribution width (RDW)	16.8 ± 2.1 (125)	18.7 ± 3.2 (9)	17.8 ± 2.3 (8)	18.8 ± 0.8 (5)	17.8 ± 0.9 (6)			0.047 (large)	

nancy in common marmosets, and one of only a few publications to evaluate these changes in NHP.[3,12,13,29] In addition we explore the effects of age, sex, and source colony in the data presented. Understanding how these factors may affect clinical parameters is critical to correctly interpret these values for clinical health and reproductive management and research studies.

Based on sex alone, we found that hematocrit, hemoglobin, RBC, PCV, indirect bilirubin and total bilirubin were higher in males than in females with a medium effect. In contrast, previous analyses of the effect of sex on red blood cell indices have yielded differing results. Two studies[21,22] found no significant differences in any hematology parameters measured between adult males and females, though they did not include all the RBC indices we evaluated. In contrast, a group that also analyzed hemoglobin, MCV, MCH, and MCHC reported significantly higher MCV and MCH in females than in males.[16] Our study found higher RBC, hematocrit, packed cell volume and hemoglobin levels in males. The reason for these differences is unknown, but the previous study analyzed only 54 samples, while our analysis included 580 unique sampling points. In addition, higher red blood cell indices (RBC, Hgb, Hct, and PCV) have been reported in male compared with female cotton top tamarins *(Saguinus oedipus)*.[27] Sex-based differences in bilirubin have not been previously reported in marmosets. The finding of significantly higher cholesterol in males is consistent with several previous reports,[16,22,32] indicating this is likely a true physiologic difference, although its clinical significance is unknown. In our analysis, cholesterol had a large *P* value but an effect size of 0.46, so it marginally missed the cut off for a medium effect. We did not evaluate LDL (low density lipoprotein) cholesterol or triglycerides specifically, but these have also been reported as significantly higher in both male marmosets[16,32] and human males.[6]

In both male and female animals, we observed a large decrease in ALP in adult animals compared with juveniles. The increase in ALP activity in juveniles has been previously observed in many species, including dogs, cats, macaques, and African green monkeys.[5,17,27,30] It is the result of bone iso-enzyme activity in young, rapidly growing animals. This difference was found in our study, as well as by others,[8,32] indicating that marmosets follow the pattern seen in other species. Decreases in A:G ratio and phosphorus were also observed in adult animals of both sexes in the current study.

Stronger effects on clinical parameters were observed in geriatric animals. Both sexes of geriatric marmosets had lower albumin, A:G ratios and total serum calcium than did adult animals. Given that the A:G ratio and total serum calcium measurements are mathematically affected by the albumin levels, these observations are likely the result of the primary finding of lower serum albumin in geriatric animals. Ionized calcium was not measured in this study. Another report also made this observation when characterizing aging phenotypes.[25] That study found that age and serum albumin were negatively correlated over a range of 2 to 14 y. As serum albumin concentration is an important diagnostic indicator of GI disease in marmosets,[2] the finding that serum albumin concentrations are significantly lower in healthy geriatric animals than adults has important clinical implications. Clinicians should consider using a different reference range or a different diagnostic cut-off value for low albumin in geriatric animals than adults for GI disease, and take into account other indicators of GI disease in addition to albumin concentrations when making a clinical diagnosis of GI disease in geriatric animals. One study[2] reported that less than 3.5 mg/dL of albumin was a good biomarker for GI disease in

marmosets, along with body weight, but our data indicate that an albumin below 3.5 mg/dL may be normal for the geriatric age group. In contrast, cholesterol and neutrophil percentages were higher in the geriatric animals. These findings have not been previously reported, as most of the literature on normal clinical pathology values in marmosets has limited representation of geriatric animals. While pathology and phenotypes of aged marmosets have been examined,[18] only a few clinical pathology parameters have been evaluated.[25]

Recent publications have examined the effects on the microbiome of importing new marmosets into colonies and have found that distinctive microbiota are retained, even after one year of standardization of husbandry and diet.[7,26] These observations led us to determine whether differences in hematology or serum chemistry could be related to the original source of the marmosets imported into our research colony. To date, the MIT marmoset research colony includes animals imported from 5 sources including 3 different countries. The most recently imported marmosets (source G) had more significant differences than did animals from the other 4 sources in the MIT colony. Of 9 tests evaluated, 8 of them (albumin, ALP, ALT, total protein, calcium, globulin, glucose and BUN) were significantly different and had medium to large effect sizes when comparing source G with at least one of the other colonies (Figure 1a). At the time of sampling, animals from source G had been on site for less than 1 y and the cohort consisted predominantly of juvenile females. As we had previously noted age- and sex-specific differences, we reanalyzed the comparison between sources using only juvenile females from 4 sources, as source E did not have enough appropriate samples. Even when focusing on juvenile females, we found that all 9 tests were still significantly different between source G and at least one of the other cohorts (Figure 1b). Although animals from various sources were not equally distributed between the 2 vivaria that housed marmosets, we believe it is unlikely that unintended differences in environment and housing contributed to differences related to source colony. Both vivaria are managed with the same environmental parameters, husbandry, diet, biosecurity level, and other aspects of the animal care program. However, our study did not specifically control for or evaluate effects of housing location. Further longitudinal studies will be required to determine if blood parameters eventually converge with values found for marmosets from other sources at MIT or if the genetics of animals in source G might affect basal levels of these analytes.

Multiple measures changed during pregnancy and the postpartum period in marmosets, but analysis by trimester showed a few parameters were consistently altered. BUN was significantly lower in pregnant animals, specifically in the 2nd trimester. Lower BUN has been reported during pregnancy in other species, including African green monkeys, baboons and rabbits.[5,12,24] As in African green monkeys, changes in creatinine were not observed.[5] The decrease in BUN in humans occurs due to a dramatically increased glomerular filtration rate (GFR) that helps to process the large increases in plasma volume that accompany pregnancy.[9] Presumably, the same mechanism operates in other species, including marmosets. In humans, both BUN and creatinine levels decrease; this was not observed in marmosets. Similarly, a decrease in cholesterol was observed in pregnant marmosets, which is consistent with observations made in rhesus macaques, baboons, and squirrel monkeys.[5,12,24,29]

As blood volume increases with pregnancy, humans commonly develop decreases in total protein, albumin, calcium, hemoglobin, hematocrit, and RBC.[9,15,28,31] Of these parameters, pregnant marmosets showed decreases in calcium, as also occurs in other NHP,[5,12] but they showed no changes in the levels of total protein, albumin, hemoglobin, hematocrit, and RBC. Decreased hemoglobin, hematocrit and RBC are commonly observed in humans, NHP and other mammalian species.[3,5,12,15,24] While weight was significantly higher in pregnant animals, the effect size was small when comparing all stages of pregnancy with nonpregnant animals. A large effect size was only observed when comparing animals in their 3rd trimester with nonpregnant animals. This is consistent with the relatively slow placental and embryonic development of marmosets, normalized by gestation, as compared with humans and other primates.[20] We speculate that this slower pace of development may limit the scale of physiologic changes during pregnancy as compared with other primates, as indicated by the fewer and smaller scale differences in hematology and serum chemistry parameters that we found between pregnant and nonpregnant marmosets. This may reflect an adaptation in callitrichids that facilitates increased fecundity and shorter interbirth intervals than those observed in other primates.

Pregnant marmosets showed decreased ALP levels with a small effect; however, these changes were more pronounced during the 3rd trimester, where changes in ALP levels had a large effect. In humans, ALP normally increases due to placental production,[31] a change seen in great apes, but not in other primate species.[11] Differences in liver enzyme activities are commonly observed during pregnancy in multiple species.[3,5,12,15,24] Increased numbers of neutrophils were observed during the first trimester in pregnant marmosets. Increasing neutrophil and monocyte counts have been reported during pregnancy in humans,[1,19] but increases in these leukocytes were observed during the entire pregnancy. This was not the case in our study, potentially due to smaller number of samples available in the 2nd and 3rd trimesters, as current protocols in our institution attempt to reduce handling and testing during the later stages of pregnancy.

Although the mixed population of animals used in this study may increase variability in the data and reference ranges determined, it also provides a better understanding of the normal distribution of values in common marmosets. We view the variability in different animal holding rooms located in 2 different vivaria as minimal, given that the physical design criteria and management practices are consistent between vivaria, and both meet defined AAALAC standards. In addition, large sample sizes resulted in many statistically significant differences that may not be biologically relevant, necessitating additional analysis of effect size. While the large colony size allowed us to analyze a significant number of samples, we did encounter smaller sample sizes in analyses including pregnant marmosets and geriatric animals.

Due to the retrospective nature of this study and the colony population, the sample size of the various groups or categories differed (for example geriatric males compared with adult males). Similarly, the number of samples from individual animals was affected by factors such as the animal's residence time at the MIT colony or clinical requirements (for example, additional exams during quarantine). For example, marmosets from colony N were sampled 5.1 times on average, as this was the first colony to arrive at MIT. In contrast, marmosets from colony G were sampled approximately 1.75 times on average as these had been recently imported. While our analysis evaluated the entire colony and highlighted different relative contributions due to sex, age and source colony, future longitudinal studies will be necessary to corroborate differences observed and rule

out bias introduced through sampling in the current study. Sample sizes (n) are provided for each calculated parameter in the tables.

We have demonstrated that animal source, age, and sex can impact normal clinical chemistry and hematology references ranges. Other factors such as the laboratory performing analyses, diet, and management practices may also affect normative values. For these reasons, we recommend that institutions consider generating internal reference ranges for their colonies to most accurately determine what is "normal" at any given institution. Generation of internal reference ranges requires a significant amount of time to collect samples and analyze data, considerable expense, and sufficient sample sizes for statistical analyses. Because these resources may not be available for every colony, we encourage other institutions with the appropriate resources to calculate and publish their own normative values for this species.

In conclusion, we have provided extensive reference intervals for hematology and clinical chemistry values in common marmosets at our institution Statistical analysis identified multiple parameters with significant differences, but not all recorded differences should be viewed as clinically relevant. Effect sizes were computed to help clinicians determine the relative importance of significant changes, and the normative data are important for investigators and veterinarians using common marmosets with different health statuses, ages, and genetic backgrounds. As diagnoses and therapy often rely on hematology and clinical chemistry, the data presented should provide additional resources for evaluation and interpretation of the health of common marmosets.

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