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Normal Hematologic and Serum Biochemical Values of Cotton-Top Tamarins (*Saguinus oedipus*)

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We obtained whole-blood hematologic and serum biochemical values from 38 captive-bred cotton-top tamarins (*Saguinus oedipus*). Data were analyzed to determine the effect of sex on blood parameters. Significant differences between either the means or medians of male and female tamarins were found for creatinine, hematocrit, hemoglobin, RBC count, and PCV. These results establish baseline hematologic and serum biochemical values and provide a useful resource not previously available in the peer-reviewed literature for the clinical care of cotton-top tamarins, a critically endangered New World primate, in a captive setting.

Cotton-top tamarins, *Saguinus oedipus* (Linnaeus, 1758), are a callitrichid species found in seasonal deciduous rain forest and secondary growth forest in only a small area of northwest Columbia.[25] Listed as Critically Endangered in the *IUCN 2010 Red List of Threatened Species*, there are estimated to be fewer than 7500 cotton-top tamarins living in the wild[49] and approximately 2700 in captivity worldwide.[13] One recent study documented a 31% decrease between 1990 and 2000 in forested habitat within the historic distribution range of the cotton-top tamarin,[39] with a further decrease since 2000.[49] An estimated 20,000 to 30,000 cotton-top tamarins were imported to the United States for use in biomedical research between the late 1960s and 1973, when the species was declared endangered and legal importation ceased.[25,49] All of these data taken together provide some indication of the precipitous decline of the wild population.[49]

Cotton-top tamarins have many diverse uses in research, and their dwindling numbers belie their continued importance in research. Long used as an animal model of spontaneous ulcerative colitis and colonic adenocarcinoma,[10,12,31,54,58] given naturally high incidences of both diseases in captive and wild populations; numerous models of these diseases now exist in mice and rats.[32,33,57] Cotton-top tamarins continue to be used in cognitive behavioral research in the areas of cooperative rearing,[1,46,60] complex learning,[15,17,36] prosocial behavior and altruism,[14,23,51] reproduction and reproductive hormone analysis,[45,48,53,61,62] and other areas.[16,18,19,50,52] Cotton-top tamarins regularly give birth to twins and are natural bone marrow chimeras, due to placental vascular anastamoses,[42,43,56] making them useful in studies on the major histocompatibility complex and functions of the immune system.[2,9,41-43,56] Cotton-top tamarins have also been used as a model for the study of Epstein–Barr Virus[30] and have recently been suggested as a possible model for early Alzheimer disease.[35]

Hematologic and serum biochemical reference ranges for many other species of nonhuman primates have been published, including common marmosets,[59] rhesus macaques,[7,11] chimpanzees[27] and vervets,[47] as well as several species of tamarins, including, red-bellied tamarins[55] and white-footed tamarins.[20] In addition, limited whole-blood hematologic and serum biochemical reference ranges for cotton-top tamarins have been published. Studies done more than 40 y ago provide hematology and serum biochemistry data on cotton-top tamarins but lack information on whether sex plays a role in those values.[3,8] A later study examined the effects of sex on whole-blood hematologic but not serum biochemical values.[24] However, all 3 studies had limitations in scope, and 2 of the 3 studies identified the subjects as wild-caught, laboratory-housed animals, whereas the third did not specify the origin of the tamarins. The purpose of the present study was to establish comprehensive clinically relevant reference ranges for both hematologic and serum biochemical values for each sex of captive-bred and laboratory-housed cotton-top tamarins and to determine what effects sex may have on these values in this critically endangered species. Sex has been found to have an effect on the hematologic and serum biochemical values of other nonhuman primate species.[7,26,44,47]

Materials and Methods

All tamarins were housed at the University of Wisconsin Department of Psychology animal facility (Madison, WI) as pairs in cages measuring 1.8 × 1.0 × 2.3 m or as family groups in cages measuring 1.8 × 3.0 × 2.3 m. Cages were constructed of anodized aluminum with a urethane-coated mesh and contained tree branches, ropes, and other climbing structures. Food and water were presented on platforms more than 1 m above the floor. Rooms were maintained at 26 C° and were on a 12:12-h light:dark cycle. In rooms with multiple cages, cloth barriers prevented animals from seeing each other, but they had auditory and olfactory contact. Monkeys were fed a high-protein snack with vitamins at lights-on, a main meal (5040 New World Primate Diet, Purina Lab Diet, St Louis, MO, and Zupreem Marmoset Diet Canned, Premium Nutritional Products, Mission, KS) supplemented with fresh fruits and vegetables at midday, and a high-protein supplemental snack in late afternoon. Further details of husbandry are provided elsewhere.[21] The animal housing and procedures were approved by the College of Letters and Science Animal Care and Use Committee and complied with the USDA Animal Welfare Act[4] and Regulations,[5] Public Health Service Policy[40] and the *Guide for the Care and Use of Laboratory Animals*.[29]

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Table 1. Whole-blood hematologic values in adult cotton-top tamarins

	Unit	Female tamarins	Male tamarins
Total protein	g/dL	7.05 ± 0.38 (n = 18)	6.97 ± 0.46 (n = 15)
RBC[a]	$\times 10^6/\mu L$	6.13 ± 0.35 (n = 19)	6.42 ± 0.20 (n = 16)
Hgb[a]	g/dL	16.51 ± 1.06 (n = 19)	17.50 ± 0.85 (n = 16)
RBC Hgb[b]	g/dL	15.58 ± 1.04 (n = 18)	16.34 ± 0.75 (n = 15)
HCT[a,b]	%	49.21 ± 3.03 (n = 19)	52.19 ± 1.94 (n = 16)
PCV[a,b]	%	50.22 ± 3.00 (n = 18)	53.13 ± 1.92 (n = 15)
MCV	fL	79.03 ± 4.93 (n = 18)	81.33 ± 2.68 (n = 16)
MCH	pg	26.91 ± 1.16 (n = 19)	27.08 ± 1.33 (n = 16)
MCHC	g/dL	33.56 ± 0.77 (n = 19)	33.31 ± 1.16 (n = 16)
RBC distribution width	%	15.60 ± 0.70 (n = 19)	15.52 ± 0.52 (n = 16)
PLT	$\times 10^3/\mu L$	267.71 ± 63.98 (n = 17)	253.94 ± 57.19 (n = 16)
MPV	fL	13.28 ± 1.86 (n = 19)	13.19 ± 1.56 (n = 16)
WBC	$\times 10^3/\mu L$	7.41 ± 2.49 (n = 19)	5.92 ± 1.85 (n = 16)
Segmented neutrophils	$\times 10^3/\mu L$	3.42 ± 1.16 (n = 19)	2.88 ± 1.17 (n = 16)
Lymphocytes	$\times 10^3/\mu L$	2.96 ± 1.40 (n = 18)	2.37 ± 1.09 (n = 16)
Monocytes	$\times 10^3/\mu L$	0.36 ± 0.21 (n = 18)	0.38 ± 0.20 (n = 16)
Eosinophils	$\times 10^3/\mu L$	0.16 ± 0.14 (n = 18)	0.18 ± 0.14 (n = 16)
Basophils	$\times 10^3/\mu L$	0.07 ± 0.06 (n = 18)	0.06 ± 0.06 n = 16)
Nucleated RBC	$\times 10^3/\mu L$	0.02 ± 0.05 (n = 18)	0.04 ± 0.05 (n = 16)

Data are expressed as mean ± 1 SD.
[a]Significant ($P < 0.05$) difference in mean or median value between male and female cotton-top tamarins.
[b]Significant interaction between sex and age. HCT, PCV, and RBCHGB all decreased as female tamarins aged, but despite a significant interaction between sex and age, there was no significant correlation between age and HCT, PCV, or RBC HgB in male tamarins.

Blood samples were obtained as part of routine preshipment screenings for hematologic and blood serum chemistry testing from cotton-top tamarins ranging in age from 14 mo to 17 y, in a colony with an age range of newborn to 26 y of age at the time of the study; this 26-y-old animal is the oldest known cotton-top tamarin in captivity. Tamarins were fasted overnight: food was removed by 1700 the night before, and blood collection was performed at the start of the subsequent work day, approximately 16 h later. Tamarins were captured by net and sedated with ketamine hydrochloride (10 to 20 mg/kg IM). Blood was drawn from each animal's femoral vein by using 25-gauge needles and plastic microtainer blood collection tubes and was sent immediately to the Clinical Pathology Laboratory (Veterinary Medical Teaching Hospital, University of Wisconsin). Full physical exams and eyelid tuberculin skin testing were performed on all animals, and all were found to be healthy and free of tuberculosis. All colony animals were captive-bred, with known birth dates and pedigrees. Blood was collected from 41 animals, 38 of whom were included in the final data analysis.

Hematologic tests were performed by using an automated analyzer (Advia 120, Siemens Healthcare Diagnostics, Deerfield, IL), and serum biochemical tests were performed by using a clinical chemistry machine (Hitachi 912, Roche Diagnostics, Indianapolis, IN). Samples for serum fructosamine were sent to Marshfield Laboratories (Veterinary Division, Marshfield, WI) and analyzed by using a Modular Analytic System with FRUC kit (Roche Diagnostics).

Analyses were performed by using SAS software (version 9.2, SAS Institute, Cary, NC). The Kolmogorov–Smirnov test was used to determine whether data followed normal distribution. The review of test results suggested that a nonparametric Wilcoxon test was appropriate for some variables to test for sex differences in those measures violating the assumption of normality. Either a 2-sample t test or a Wilcoxon test was used to test whether there were sex-associated differences in all variables, except cholesterol. For cholesterol, the assumption of equal variances was violated, and the Satterthwaite t test was used instead of a 2-sample t test. ANCOVA was performed to determine whether data varied systematically as a function of age.

Age groups were defined as: infant, 0 to 7 mo (n = 0); juvenile, 8 to 14 mo (n = 2); subadult, 15 to 21 mo (n = 1); adult, older than 21 mo (n = 38). Given the small numbers of animals in the infant, juvenile, and subadult categories, we decided to exclude those data and perform the analyses by using data only from animals older than 21 mo (that is, sexually mature adults). Values that were 3 SD above or below the mean were considered outliers and excluded from data analysis.

Results

For both hematologic values (Table 1) and serum biochemical parameters (Table 2), data (mean ± 1 SD) were stratified by test performed and sex. Significant differences between either the mean or median for male and female tamarins were found for creatinine, hematocrit, hemoglobin, RBC count, and PCV (Tables 1 and 2).

Because reports from the analysis laboratory suggested that sample quality (5 of 38 samples analyzed for fructosamine and 3 of 41 samples for whole-blood hematology) might be a confounding factor, t tests were performed to determine whether there was interaction between sample artifacts and fructosamine (specimens reported as 'slightly hemolyzed' and 'lipemia') and independently between sample artifact ('slight hemolysis') and ALP, AST, and creatinine. No significant differences were found for any of these analyses.

Discussion

One of the limitations of working with cotton-top tamarins is their status as critically endangered in the wild and the relatively small captive populations in individual locations. Although the current colony was not particularly small (75 animals: 41

Table 2. Serum biochemical values in adult cotton-top tamarins

	Unit	Female tamarins	Male tamarins
Albumin	g/dL	4.06 ± 0.31 (*n* = 21)	3.97 ± 0.30 (*n* = 17)
Albumin:globulin ratio	—	1.74 ± 0.27 (*n* = 20)	1.80 ± 0.32 (*n* = 17)
ALP	U/L	116.19 ± 30.89 (*n* = 21)	96.29 ± 14.76 (*n* = 17)
ALT	U/L	44.43 ± 28.28 (*n* = 21)	44.71 ± 29.67 (*n* = 17)
AST	U/L	186.43 ± 68.16 (*n* = 21)	198.13 ± 76.41 (*n* = 16)
BUN	mg/dL	15.86 ± 3.35 (*n* = 21)	14.35 ± 2.89 (*n* = 17)
Calcium[b]	mg/dL	9.02 ± 0.50 (*n* = 21)	8.69 ± 0.59 (*n* = 17)
Chloride	mEq/L	106 ± 2.79 (*n* = 20)	104.40 ± 2.35 (*n* = 15)
Cholesterol[b]	mg/dL	134.67 ± 31.04 (*n* = 21)	153.94 ± 51.04 (*n* = 17)
Creatine kinase	U/L	865.25 ± 421 (*n* = 20)	772.47 ± 354.08 (*n* = 17)
CO_2	mEq/L	26.37 ± 2.67 (*n* = 19)	24.75 ± 3.38 (*n* = 16)
Creatinine[a]	mg/dL	0.33 ± 0.09 (*n* = 21)	0.41 ± 0.15 (*n* = 17)
Fructosamine	µmol/L	255.58 ± 47.62 (*n* = 19)	255.79 ± 53.62 (*n* = 14)
Globulin	g/dL	2.36 ± 0.27 (*n* = 20)	2.27 ± 0.34 (*n* = 17)
Glucose	mg/dL	262.95 ± 95.67 (*n* = 21)	266 ± 96.34 (*n* = 17)
Magnesium	mg/dL	1.97 ± 0.16 (*n* = 20)	2.03 ± 0.16 (*n* = 16)
Phosphorus	mg/dL	2.81 ± 0.67 (*n* = 21)	3.21 ± 0.64 (*n* = 16)
Potassium	mmol/L	4.04 ± 0.44 (*n* = 20)	4.25 ± 0.64 (*n* = 16)
Sodium	mmol/L	150.50 ± 2.12 (*n* = 20)	150.06 ± 2.54 (*n* = 16)
Total bilirubin	mg/dL	0.143 ± 0.0598 (*n* = 21)	0.15 ± 0.07 (*n* = 17)
Total protein	g/dL	6.41 ± 0.35 (*n* = 21)	6.24 ± 0.40 (*n* = 17)

Data are expressed as mean ± 1 SD.
[a]Significant ($P < 0.05$) difference in mean or median value between male and female cotton-top tamarins.
[b]Significant interaction between sex and age. Calcium decreased as male tamarins aged, and despite a significant interaction between sex and age, there was no significant correlation between age and calcium in female tamarins or between age and cholesterol in either male or female tamarins.

in this study, 38 in final data analysis), the requirements of the ongoing behavioral studies did not allow for earlier routine blood sampling of healthy animals. The unique circumstances of the closing of this colony and dissemination of tamarins to multiple locations (zoos, sanctuaries, and other behavioral research colonies) allowed for comprehensive preshipment health assessments without additional disruption of the animals' lives.

PCV, Hct, Hgb, RBC count, and creatinine were all lower in female than in male tamarins. However, the differences were small and were not clinically significant. Similar results have been reported by other authors.[26,44,47]

Most creatinine originates from nonenzymatic conversion of creatine that stores energy in muscle as phosphocreatine.[34] The higher levels reported with maturation and greater values in male than in female chimpanzees[28] and the positive correlation between serum creatinine and body weight in baboons[22] probably reflect the higher lean muscle mass in mature compared with younger and male compared with female animals of those species. A year-long analysis of the body weight of cotton-top tamarins by age found that female cotton-top tamarins are heavier than male tamarins, on average, and show greater variance in weights.[38] However, actual differences in mean weights between male and female tamarins were small (less than 10%) and consistent with the results of our current study, given the statistically significant but clinically negligible difference in mean creatinine levels that we found between male and female cotton-top tamarins.

We compared data from cotton-top tamarins in the current study with results from Old World (rhesus,[7] chimpanzees[27]) and New World (red-bellied tamarins,[55] white-footed tamarins,[20] and common marmosets[59]) species (Table 3) to identify clinically important differences in values. Total platelet and WBC counts in cotton-top tamarins were lower than values in red-lipped tamarins and white-footed tamarins, and although Hgb and Hct values were lower in cotton-top tamarins than in all rhesus monkeys, only male rhesus had higher WBC values. BUN, ALT, and cholesterol levels were higher in cotton-top tamarins than white-footed tamarins, ALP was higher than in red-lipped tamarins, and cholesterol and globulin were lower than rhesus values. AST was much higher in our cotton-top tamarins than in rhesus and chimpanzees, and phosphorus was much higher in marmosets. In addition, we compared values from the current study with the limited hematologic reference values from an earlier study in cotton-top tamarins,[23] and although platelets were higher in the previous study, all other available hematologic reference values were without clinically important differences. Interestingly, in the earlier study[23] hemoglobin, RBC count, and PCV levels were significantly lower in female than male cotton-top tamarins, as we showed in our colony.

We do not suggest an association between the whole-blood hematologic and serum biochemical values measured in the current study and in others.[7,20,27,55,59] However, although variations in hematologic and serum biochemical values can be found within and among species, most of the values we obtained are reasonable in the context of the nonhuman primate literature. In particular, values for the closely related common marmosets are especially similar to those here. The one exception to these similarities with other species is blood glucose.

Standard procedure for this behavioral research colony was to catch and examine tamarins only when they appeared ill. This meant, in practical terms, that many of the study subjects had never been handled by humans previously, and the remaining ones had only been caught and handled previously when they appeared or were in fact ill. It follows, then, that high mean glucose levels may have been transient and due to stress-induced hyperglycemia, perhaps even more so in the tamarins

Table 3. Serum glucose values (mg/dL) in adult Old and New World nonhuman primates

	Females	Males	Reference
Saguinus oedipus	167.28–358.62	169.66–362.34	Current study
Saguinus leucopus	100.1–240.1[a]	100.1–240.1[a]	20
Saguinus labiatus	101–187	110–200	55
Callithrix jacchus	140–244	124–220	59
Macaca mulatta	92–131	74–115	11
Pan troglodytes	52.8–114.5	59.7–128.5	27

Range reported is the mean ± 1 SD (except for *Pan troglodytes* [mean ± 2 SD]).
[a]Data reported are combined for male and female *S. leucopus*.

we evaluated than in others accustomed to being handled, at another captive colony, for example.

Blood glucose values for male and female white-footed tamarins (*S. leucopus*),[20] red-bellied tamarins (*S. labiatus*),[55] common marmosets (*Callithrix jacchus*),[59] rhesus macaques (*Macacca mulatta*),[11] and chimpanzees (*Pan troglodytes*)[27] are shown for comparison with those of male and female cotton-top tamarins from the current study (Table 3). Both *S. leucopus* and *C. jacchus* had large overlaps with *S. oedipus*, but none of the species compared were within 100 mg/dL of the high end of the cotton-top tamarin values (that is, values for *S. leucopus* and *C. jacchus* were lower overall). These values for cotton-top tamarins are certainly higher than expected, and although stress-induced hyperglycemia can lead to acute increases in plasma glucose in other species,[6] including humans,[37] this result suggests that further study is necessary to determine whether the reported values are repeatable in other colonies or are a result of unique conditions in this colony.

As mentioned previously, other studies have found differences in primate blood reference values by age. However, our results should be interpreted as valid only for adult cotton-top tamarins because animals classified as subadults and infants (that is, those younger than 21 mo) were excluded from the final data analysis due to the small numbers of nonadults in the study sample. Without any comprehensive published data available for blood hematological and serum biochemical values in critically endangered cotton-top tamarins, this study's data provide the clinician with useful reference ranges to which to refer in the assessment of clinical conditions.

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