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Hematology and Serum Chemistry Values of Sooty Mangabeys (*Cercocebus atys*): Comparison with Rhesus Monkeys

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Abstract

Background—The sooty mangabey is a vulnerable West African species that naturally harbors simian immunodeficiency virus (SIV) without pathological symptoms. We present normative hematology and serum chemistry values for this species.

Methods—Hematology analytes from 136 females and 96 males and serum chemistry analytes from 57 females and 26 males were studied.

Results—Values of several analytes fell outside published reference ranges in the rhesus monkey, a laboratory standard for Old World primates. Erythrocyte-related parameters were higher in mangabeys than in rhesus monkeys, while platelet counts were lower. Mangabeys also had higher gamma-glutamyltransferase levels and lower urea nitrogen levels. Males had higher erythrocyte-associated values in males than females. Albumin, globulin, albumin/globulin ratio, calcium, and creatinine, changed with age in patterns similar to those reported for the rhesus monkey.

Conclusions—The unique blood profile of the mangabey should be taken into account in clinical and experimental studies of this species.

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Conflict of Interest Statement

The authors declare that they have no competing interests.

Keywords

primate; monkey; blood values; age; sex

INTRODUCTION

Hematology and serum chemistry values are fundamental to medical diagnosis and treatment of disease and can vary over the life span. Standard values for these variables have been established for humans and nonhuman primates, including chimpanzees and rhesus monkeys [3–5, 8, 11, 13, 16, 19]. Although values of some clinical parameters have been published as part of experimental reports in sooty mangabeys [9, 15] and clinical values have been reported on a small number of white-crowned mangabeys [10], but normative values of sooty mangabey are lacking.

Because sooty mangabeys are a vulnerable species (source: International Union for Conservation of Nature) captive specimens are maintained with minimal disruption for their entire lifespan. This offers the unique opportunity to establish normative clinical blood values, including age-related changes. In addition, establishment of reference ranges will facilitate studies of AIDS pathogenesis and treatment, as the sooty mangabey serves as a unique and important animal model in AIDS research. This species is a natural host of simian immunodeficiency virus (SIV) [18, 20], but does not develop clinical signs of AIDS [9, 15].

To define normative hematology and serum chemistry values and study their variation over the life span of the sooty mangabey, we used data from specimens collected at annual animal health monitoring surveys performed in the YNPRC sooty mangabey colony, which is the only captive colony of this species. The parameters included 15 hematology and 24 blood chemistry variables (Table 1), providing normative values and describing sex differences and age-related patterns.

METHODS

This study was undertaken at YNPRC and all procedures and care of animals were approved by the Emory Institutional Animal Care and Use Committee (IACUC). It adhered to the Principles for the Ethical Treatment of Nonhuman Primates promulgated by the American Society of Primatologists.

Animals

All of the 232 sooty mangabeys used in this study were born at the Field Station of the YNPRC and were descendants of a founding group of 22 individuals, which was established in 1968. About 90% of the animals were housed in large social indoor/outdoor compounds; the remaining were housed individually or in pairs in standard indoor cages. All mangabeys were fed a standard monkey chow diet (Purina LabDiet 5037, St Louis, MO) supplemented daily with fresh fruit or vegetables as part of the animal enrichment program at the YNPRC. Blood collections were performed during annual surveys, conducted as part of YNPRC

health monitoring. Hematology and serum chemistry data reported herein were derived from these blood samples collected between 1990 and 2011.

Blood sample collection

After an overnight fast, sooty mangabeys were sedated with either ketamine (10 mg/kg) or Telazol (tiletamine/zolazepam) (3 to 5 mg/kg). Blood samples were collected from the femoral vein into EDTA and serum separator blood tubes. Serum chemistry samples were centrifuged and separated into a conical tube without additive and stored at 4° C until submission to the pathology laboratory. Serum samples were analyzed within 24 h.

Hematology and serum chemistry values

Total RBC and WBC counts, hematocrit and hemoglobin levels were determined by using automated Sysmex (Long Grove, IL) hematology analyzers (before 1992: Sysmex S800, 1992 to 1998: model K1000; 1998 to 2012: model XS-1000i. Serum chemistry analyses were performed by commercial laboratories (SmithKline Beecham, Decatur GA until 1998, Antech Diagnostics from 1998 until 2000). For the samples collected after 2010, the analyses were done by the YNPRC clinical pathology laboratory using an AMS Liasys Chemistry Analyzer (Analyzer Medical System SRL). Although different instruments were used in sequence, introduction of each new instrument included extensive validation between the old and new instrument platforms on paired sample analyses. The units for each analyte and the abbreviation used in this paper are listed in Table 1.

Statistical analysis

Analysis of hematology data—A total of 990 samples from 232 sooty mangabeys (96 males, 136 females), were used for the hematology analysis. For the 15 hematology analytes, there was an average of 4.4 samples for each sooty mangabey. To develop a table of normative values and ranges, we calculated the mean age of each mangabey when the blood samples were collected from that animal. Mangabeys were then assigned to the following age bins: infant to juvenile (0 to 5 y), young adults (5 to 10 y), middle-aged adults (10 to 20 y), and old adults (20+ y). Thus, each mangabey contributed one data point for each analyte, namely its average age and average analyte value during the study. These values were then averaged to provide means and standard deviations for each analyte and for each age group. Values for females and males were summarized separately. This method of data summary is useful as an initial step in mixed effects analysis of longitudinal data [6].

Analysis of serum chemistry data—Data from 83 mangabeys were used, with one sample per animal. Normative tables for the serum chemistry analytes were produced in the same way as for the hematology values. However, since there was only one sample available for each mangabey, average ages and average analyte values were not computed.

Linear mixed effects (LME) modeling was used to describe the influence of sex and age on the value of each hematology and serum chemistry analyte. The LME module within the Splus statistical package (TIBCO Spotfire S+ 8.1 for Windows) was used to compute best-fitting models in which sex, age, and age² were included as fixed effects (i.e. as predictor variables), as were the interactions of sex with age. Each individual's intercept and slope

were initially considered as random effects in the models, but one or both of these terms were eliminated if they did not improve model fit, as indicated by a reduction of the Akaike Information Criterion (AIC). We followed the LME modeling approach described by Pinheiro and Bates [12]. We confirmed appropriateness of the computed models as recommended by these authors. This approach to longitudinal data analysis is commonly called growth curve analysis [p 30, reference 12]. Examples of growth curve analysis, similar to the models we used, but programmed in the open-source R language can be found at <http://www.danmirman.org/gca>. The final model for each analyte included any remaining random effects and any coefficients for fixed effects that differed significantly from 0. These coefficients permitted us to determine whether the value of each analyte differed between males and females, and whether there was a significant linear or curvilinear (quadratic) change with age. Differences between the sexes in the rate of change in analyte values with age were indicated by significant Sex x Age interaction coefficient.

We computed a separate model for each hematology and serum chemistry. Since there were approximately 50 models computed, we considered a raw p-value of 0.001 to be statistically significant. (This corresponds approximately to a Bonferroni-corrected value of 0.05) The reported p-values in Tables 4 and 7 are without adjustment for multiple testing.

RESULTS

Hematology

Averages by Age Group and Sex—Tables 2 and 3 provide the mean value and standard deviation (SD) of each hematology analyte by age groups for female and male sooty mangabeys, respectively. For example, Table 2 shows that 8 females between the ages of 0 and 5 y were studied. They had a mean RBC value of 5.3 (with SD of 0.15). Means and SDs for the remaining hematology variables and age groups can be identified in a similar manner in Table 2 (females) and Table 3 (males). The rightmost column of Table 2, designated “Rhesus comparison” shows rows of 4 symbols comparing the mean analyte values for each age group with normal ranges for rhesus monkeys as provided in a standard veterinary formulary. Each symbol indicates whether the mean value for the respective age group was within ($\approx$), above ($\uparrow$), or below ($\downarrow$) the range for age and sex matched rhesus monkeys. A dash (—) in this column indicates that a standard value was not included in the formulary [7]. Thus, RBC values were within the rhesus range only for females aged 0 to 5 y, but below the rhesus range for the remaining 3 older groups. HCT, HGB, MCV, and MCH values were (with the exception of HCT in the oldest group) above the ranges considered normal in rhesus monkeys, while PLAT counts were below the rhesus range for all age groups. Although total leucocyte counts (WBC) were higher for the 3 oldest groups than in rhesus, the differentiated counts were, where available (SEG, LYMPH, MONO, EOS), within the rhesus range. In males (Table 3) there were fewer differences from rhesus than in females. The differences noted in male mangabeys were also seen in females, with male mangabeys having higher MCV and MCH and lower PLAT values in all age groups than male rhesus. Higher HGB values were observed in the 10 to 20 y group.

Longitudinal Analysis—Table 4 lists the intercepts, coefficients, and significance values for the linear mixed effects regression models. These parameters were based upon models in which age was “centered”; that is, each mangabey’s age was recoded as the deviation from the mean age of the sample. Sex was coded as 0 (female) or 1 (male). When the Sex x Age coefficient was significant, we subsequently ran separate regression models for the two sexes. These separate models (for RBC, HCT, HGB, MCV, MCH, and PLAT) are presented in Supporting Material. The models for females and males for RBC are shown graphically in Figure 1a, in which the sex difference in the patterns of curvilinear change with age, as described above, are evident.

Plots of the remaining hematology analytes are not shown, but the general pattern of their levels over the life span can be inferred from the parameters in Table 4. Thus, in addition to RBC, males also had significantly higher values HCT and HGB as indicated by significant positive coefficients for sex in the models for these variables. On the other hand, females had significantly higher values for PLAT, WBC and LYMPH, as indicated by significant negative coefficients for these analytes.

Age-related changes can be described as increases in average value across the life span, as indicated by significant positive regression coefficients for age, or as decreases in average value, as indicated by negative coefficients for these terms. Changes that are not uniform across the life span (e.g., maturational changes which may slow or reverse in direction after puberty) are represented by a significant age² parameter in the regression model. Only two of these variables had significant, monotonic changes with age that were not associated with significant curvilinearity. These were MCHC and BAND counts, of which MCHC decreased significantly, and BAND increased significantly across the life span.

Among the variables which had significant curvilinearity, only males showed significant curvilinear changes across their life span; this trend was not significant in females. RBC, HCT, HGB, MCV, and MCH values increased markedly in early maturation, whereas the number of PLAT and LYMPH decreased rapidly in the first years of life of the males. Finally, WBC, SEG, MONO, EOS and BASO did not change significantly across the life span, as indicated by non-significant coefficients associated with age.

Serum Chemistry

Averages by Age Group and Sex—Tables 5 and 6 contain the mean values and SD for each of the serum chemistry analytes for female and male mangabeys, respectively. For example, from Table 5 it can be gleaned that 15 females between the ages of 5 and 10 y were studied. The value for GLUC of 57 mg/dL (SD = 10) was the unweighted mean of the individual GLUC values obtained from the 15 female mangabeys in this age group. Means and SDs for the remaining serum chemistry analytes can be similarly located in Table 5 (females) and Table 6 (males). Tables 5 and 6 each contains a column in which the means of each serum chemistry analyte from mangabeys are compared with normal ranges for the rhesus monkey. Table 5 shows that female mangabeys had average values outside the normal range of rhesus monkeys for 16 of the 18 serum chemistry analytes for which rhesus formulary ranges are available. GLUC was elevated relative to rhesus in the two groups above 10 years of age, while BUN was decreased in all of the age ranges. CREAT was

lower than rhesus values in the youngest and oldest age groups. The electrolyte PHOS was lower in the 5 to 10y and 10 to 20 y female mangabey groups than in rhesus; the remaining electrolytes (SOD, POTAS, CHLOR) showed an irregular pattern of differences. CPK was higher than the rhesus norms for all but the oldest age group, while several analytes associated with liver function (ALT, ALK PHOS, AST, BILI, GGTP, and ALBU) differed with an irregular age pattern from the rhesus norms.

Table 6 shows that, for males, GGTP was consistently higher than in rhesus, while BUN was consistently lower. GLUC was also elevated in the youngest and the two oldest groups. BILI was elevated in all but the youngest age group (which contained only 1 animal) and AST was elevated in the 5 to 10 y group. ALBU was somewhat elevated in the single male in the 0 to 5 age range. Similar to hematology values, male sooty mangabeys displayed less divergence from rhesus than females; differences were found in only 6 of the 18 analytes for which formulary values were available.

Regression Analysis—The intercepts, coefficients, and significance values for the regression model of serum chemistry analytes are given in Table 7. As seen with hematology data, ages entered into models were deviations from the mean age (14 y) for the sample. Thus, according to the regression model, the mean for GLUC for females at the age of 14 y was 97.42 mg/dL. The mean for males was 9.94 mg/dL, which was higher than that of females, and there also was a significant increase of about 6.18 mg/dL each year. This general pattern of lower values for females than males and a general increasing trend with age were consistent with the data shown in Tables 5 and 6.

Other patterns were also evident. CREAT was related to sex, with males having significantly higher values on average than did females, but was uninfluenced by age; GLUC, SOD, POTAS, ALT TRIGLYC, and ALBU were significantly influenced by age, but not by sex.

Plots of ALBU and CALC are displayed as examples of how the values in Table 7 can be used to depict best-fitting estimates of blood chemistry variables. Figure 1b shows values and best fitting lines for ALBU. The lines were constructed from the parameters given for ALBU in Table 7. The significant term for sex indicates an overall difference between males and females. The significant negative coefficient for age (-0.07) shows that ALBU tends to decline with age. The Sex x Age interaction is reflected in the different slopes for the two sexes. Because there is no Age² effect, a straight line is the best estimate for each sex. The best-fitting line for CALC (Figure 1c) shows congruent lines for the two sexes because the coefficient for sex was not significant. The line has a negative slope, as indicated by the negative value of the Age coefficient (-0.03).

DISCUSSION

This study is the first presentation of normative hematology and serum chemistry values for the sooty mangabey, filling a critical need for accurate clinical reference ranges for health monitoring, disease diagnosis and treatment in this species. Our results clearly demonstrate a marked contrast between the mangabey and the rhesus monkey for a number of these measures. These differences are important, because the rhesus monkey is often considered a

reference species for Old World nonhuman primates in general. As shown in Tables 2 and 3, female mangabeys showed average levels outside of normal rhesus ranges for 8 of the 12 hematology measures for which standard ranges are provided in the Primate Formulary of the Association of Primate Veterinarians [7]. These include all 6 of the measures associated with erythrocytes and hemoglobin. RBC was lower for all of the adult age groups than the minimum rhesus values of $5.46 \times 10^6/\mu\text{g}$ for adult females and $5.85 \times 10^6/\mu\text{g}$ for geriatric females. Four other associated values (HCT, HGB, MCV, MCH) were higher in female mangabeys than the maximums provided for rhesus. WBC was also higher than rhesus ranges for the 3 adult groups of mangabeys, while PLAT was lower for all age groups. Male mangabeys also showed higher levels of MCV and MCH, and lower PLAT than rhesus in all age ranges but generally had fewer differences from rhesus than females for these parameters. The deviance of the mangabey hematology pattern from that of rhesus does not simply represent measurement variance, since two large studies on hematology of rhesus monkeys report virtually all of the analytes to be within range of the formulary [8, 16, 17]. Another macaque species, *M. radiata*, also has a pattern of hematology values entirely within rhesus formulary norms. These findings are difficult to compare definitively with findings on white-crowned mangabeys [10], because that particular study comprised only 7 females. However, this study reported lower RBC and higher MCV than the formulary values for rhesus, consistent with our findings, whereas HCT, MCH, and MCHC were within the rhesus range in that study.

It is clear from Table 5 that female sooty mangabeys differ dramatically from rhesus monkeys in serum chemistry measures as well, with two or more of the age groups falling outside the rhesus formulary ranges for most of the analytes. A detailed analysis of the functional significance of these differences is beyond the scope of this discussion, but examination of the patterns of differences with rhesus reveals that analytes associated with the pancreas (e.g. GLUC), kidney (e.g. BUN, CREAT, PHOS, SOD, POTAS, GGTP), and liver (e.g. ALT, ALKPPOS, AST, BILI) were present at different levels in the mangabey than in the rhesus monkey. As seen with hematology variables, male mangabeys displayed fewer differences from rhesus than females, with differences in the adult age groups (older than 5 y) only in GLUC, BUN, BILI, and GGTP. We submit that the differences in hematology and serum chemistry between our mangabey sample reported herein and the formulary ranges in rhesus monkeys do not result merely from experimental variation; two independent studies on rhesus [8, 16, 17] and one on bonnet macaques [10] showed nearly all serum chemistry analytes to be within the formulary ranges. In addition, the study of white-crowned mangabeys showed elevated GLUC, and decreased POTAS, as observed in our study, although a number of the other differences we observed were absent.

Male mangabeys had significantly higher average levels of several analytes associated with erythrocytes (RBC, HCT, and HGB) than females as indicated by positive and significant ($P < 0.001$) regression terms for sex for these variables (Table 4). This sex differences were not unexpected, as they have been reported in standard tables for several species, including humans [1], rhesus monkeys [7], and other primate species [2]. It has been suggested that, in the human, lower hemoglobin and iron binding protein (ferritin) may result from iron deficiency caused in part by menstrual blood loss [14]; the same mechanism may explain

lower erythrocyte-related hematology values in menstruating nonhuman primates as well. Among the remaining hematological measures, PLAT, WBC, and LYMPH were lower in males than in females, as indicated by significant ($P < 0.001$) negative terms for these measures.

Many hematology and chemistry analytes change with age in the mangabey. While an exhaustive comparison of age effects in the present data with other age related analyses of blood analytes is beyond the scope of this paper, there are several consistent age-related changes in the mangabey that can readily be compared with findings in rhesus or other primates. The most obvious ones are the erythrocyte-related measures. We found significant curvilinear effects of age for RBC, HCT, HGB, MCV, and MCH, indicating an increase in these measures through mid-life (about 12 – 15 y) for males and declines thereafter. Separate analyses for males and females (Table S1) reveal that the curvilinear pattern was present in both sexes only for RBC, while females show small rectilinear increases in HCT, HGB, and MCV, and a small decline in MCH. This pattern contrasted with the finding in rhesus [17] that RBC, HCT, and HGB showed a rectilinear and monotonic increase throughout the life span for both sexes, while MCV and MCH showed monotonic rectilinear decreases. Interestingly, the mangabey pattern of early life increases in HCT, HGB, MCV, and MCH (but not RBC) with decreases in later life (as indicated by Age² terms in Table 4) was very similar to the downward concave curvilinear pattern reported for chimpanzees [5].

In addition to the hematology analytes identified above as changing with age, Smucny and colleagues identify in 9 serum chemistry measures that varied significantly with age in the rhesus [17]. Mangabeys displayed similar changes in 6 of these: ALBU, A/G RATIO, CALC, CREAT, and PROT decreased with age, while GLOB increased with age in both studies. In contrast to the findings of Smucny et al, we did not observe significant changes in BUN, ALKPHOS, or B/C RATIO.

Conclusion

The sooty mangabey has a profile of clinical hematology and serum chemistry measures that contrast markedly with that of the rhesus monkey. The differences from macaques we have described may represent a good reference for other members of the genus *Cercocebus* in general, since the only other publication of hematology and serum chemistry values from another species of mangabey (*C. torquatus*, the white-crowned mangabey) showed similarities with the sooty mangabey [10]. The averages and standard deviations presented here provide a more accurate reference for clinical management of this species than the norms of rhesus monkeys. On the other hand, the formulary of reference values for rhesus closely match reported values for another macaque species [11].

Our findings raise a number of questions for future study. First among these is whether the unusual blood characteristics of the sooty mangabey are related to their status as hosts or non-carriers of SIV, and whether the resistance to SIV is somehow related to the unusual patterns of blood factors, a question we are now investigating. Another question of interest is whether the unusually high levels of GLUC seen here indicate a particularly susceptibility to diabetes in this species, that is often observed with increasing age in this species (Jones,

Sharma, and Cohen, in preparation). Likewise, the unusually high GGTP levels should also be investigated to determine whether they are associated with high rates of liver disease.

Finally, because the mangabey is maintained with minimal experimental intervention, due to its protected status, it provides a model which can be used in future studies of aging. The data we have provided on aging of hematology and serum chemistry analytes must be considered preliminary, since we do not have longitudinal data for the serum chemistry measures we present. However, the age-related changes we report for these measures were consistent with some of those reported in rhesus monkey [17] and chimpanzee [5], suggesting that they be potential biomarkers for aging.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Values and best-fitting lines for selected hematology and serum chemistry analytes of sooty mangabeys. (a) Red Blood Cells (RBC; parameters used to plot curves for this measure are provided in Supporting Material, Table S1, see text) (b) Albumin (ALBU), and (c) Calcium (CALC).

Table 1

List of analytes, their abbreviations, and their conventional units of measurement.

Variable	Abbreviation	Unit
<u>Hematology</u>		
Red blood cells	RBC	$10^6/\mu\text{L}$
Hematocrit	HCT	%
Hemoglobin	HGB	g/dL
Mean corpuscular volume	MCV	fL
Mean corpuscular hemoglobin	MCH	pg
Mean corpuscular hemoglobin conc.	MCHC	g/dL
Platelets	PLAT	$10^3/\mu\text{L}$
White blood cells	WBC	$10^3/\mu\text{L}$
Segmented neutrophils	SEG	$10^3/\mu\text{L}$
Banded neutrophils	BAND	$10^3/\mu\text{L}$
Lymphocytes	LYMPH	$10^3/\mu\text{L}$
Monocytes	MONO	$10^3/\mu\text{L}$
Eosinophils	EOS	$10^3/\mu\text{L}$
Basophils	BASO	$10^3/\mu\text{L}$
Atypical lymphocytes	AL	$10^3/\mu\text{L}$
<u>Blood Chemistry</u>		
Glucose	GLUC	mg/dL
Blood urea nitrogen	BUN	mg/dL
Creatinine	CREAT	mg/dL
Calcium	CALC	mg/dL
Phosphorus	PHOS	mg/dL
Sodium	SOD	mmol/L
Potassium	POTAS	mmol/L
Magnesium	MAGNE	mEq/L
Chloride	CHLOR	mmol/L
Creatine phosphokinase	CPK	IU/L
Serum glutamic oxalacetic transaminase ¹	AST	IU/L
Alkaline phosphatase	ALKPHOS	IU/L
Serum glutamic pyruvic transaminase ²	ALT	IU/L
Amylase	AMY	IU/L
Lipase	LIPAS	IU/L
Bilirubin	BILI	mg/dL
Gamma-glutamyltransferase	GGTP	IU/L
Triglycerides	TRIGLYC	mg/dL
Cholesterol	CHOLEST	mg/dL

Variable	Abbreviation	Unit
Total Protein	PROT	g/dL
Albumin	ALBU	g/dL
Globulin	GLOB	g/dL
Albumin/Globulin ratio	A/G RATIO	
BUN/Creatinine ratio	B/C RATIO	

¹ Formerly serum glutamic oxalacetic transaminase (SGOT)

² Formerly serum glutamic pyruvic transaminase (SGPT)

Mean value and standard deviation (SD) of 15 hematology analytes of 136 female sooty mangabeys, by age groups. The four symbols in the rehsus comparison column indicate, for the four age groups, whether means are within ($\approx$), above, ($\uparrow$), or below ($\downarrow$) normal ranges for rhesus monkeys. Analytes for which no comparison was possible are indicated by a dash (—).

Table 2

Age (y)	0 to 5	5 to 10	10 to 20	>20	Rhesus comparison
N	8	41	72	15	
Mean age (y)	4.23	7.6	13.98	23.4	
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	
RBC	5.3 $\pm$ 0.1	5.1 $\pm$ 0.3	5.2 $\pm$ 0.4	5.0 $\pm$ 0.6	$\approx$ $\downarrow\downarrow\downarrow$
HCT	43.5 $\pm$ 2.7	43.6 $\pm$ 3.1	43.0 $\pm$ 3.3	43.1 $\pm$ 4.5	$\uparrow\uparrow\uparrow \approx$
HGB	13.7 $\pm$ 0.7	13.9 $\pm$ 0.9	13.5 $\pm$ 1.1	13.5 $\pm$ 1.4	$\uparrow\uparrow\downarrow$
MCV	82.6 $\pm$ 3.5	84.4 $\pm$ 2.5	83.3 $\pm$ 2.8	86.1 $\pm$ 3.0	$\uparrow\uparrow\uparrow$
MCH	26.1 $\pm$ 1.0	27.1 $\pm$ 0.8	26.2 $\pm$ 1.1	26.9 $\pm$ 1.2	$\uparrow\uparrow\uparrow$
MCHC	31.6 $\pm$ 0.6	32.2 $\pm$ 0.8	31.5 $\pm$ 0.9	31.3 $\pm$ 0.9	$\downarrow \approx \approx \downarrow$
PLAT	232.4 $\pm$ 43.2	225.7 $\pm$ 49.3	256.0 $\pm$ 93.7	241.6 $\pm$ 44.9	$\downarrow\downarrow\downarrow$
WBC	11314.4 $\pm$ 4939.9	10638.7 $\pm$ 3118.2	10685.1 $\pm$ 3759.4	11517.5 $\pm$ 3261.6	$\approx$ $\uparrow\uparrow\uparrow$
SEG	6321.1 $\pm$ 4232.7	5420.0 $\pm$ 2628.2	5048.2 $\pm$ 2342.3	6016.9 $\pm$ 2054.0	$\approx \approx \approx \approx$
BAND	332.9 $\pm$ 809.3	189.1 $\pm$ 399.4	150.3 $\pm$ 278.2	134.3 $\pm$ 202.1	—
LYMPH	4132.2 $\pm$ 501.6	4458.7 $\pm$ 931.1	4927.2 $\pm$ 2402.3	4912.4 $\pm$ 2166.5	$\approx \approx \approx \approx$
MONO	357.8 $\pm$ 217.6	365.1 $\pm$ 199.6	358.8 $\pm$ 205.9	298.8 $\pm$ 236.2	$\approx \approx \approx \approx$
EOS	139.2 $\pm$ 127.8	154.7 $\pm$ 125.3	145.8 $\pm$ 182.5	114.0 $\pm$ 73.4	$\approx \approx \approx \approx$
BASO	31.3 $\pm$ 34.6	50.5 $\pm$ 43.0	53.6 $\pm$ 60.9	41.1 $\pm$ 48.1	—
AL	0.0 $\pm$ 0.0	0.6 $\pm$ 3.7	1.1 $\pm$ 7.6	0.0 $\pm$ 0.0	—

Table 3

Mean value and standard deviation (SD) of 15 hematology analytes of 96 male sooty mangabeys, by age groups. The four symbols in the rehusus comparison column indicate, for the four age groups, whether means are within ($\approx$), above, ($\uparrow$), or below ($\downarrow$). Analytes for which no comparison was possible are indicated by a dash (—).

Age (y)	0 to 5	5 to 10	10 to 20	>20	Rhesus comparison
N	6	40	45	5	
Mean age (y)	3.36	7.53	14.76	21.46	
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	
RBC	5.4 $\pm$ 0.3	5.6 $\pm$ 0.4	5.8 $\pm$ 0.4	5.7 $\pm$ 1.1	$\approx \approx \approx \approx$
HCT	43.8 $\pm$ 1.7	46.9 $\pm$ 3.0	49.2 $\pm$ 3.1	49.9 $\pm$ 9.4	$\uparrow \approx \approx \uparrow$
HGB	13.7 $\pm$ 0.6	14.9 $\pm$ 0.9	15.6 $\pm$ 1.1	15.3 $\pm$ 2.8	$\uparrow \approx \uparrow \uparrow$
MCV	81.2 $\pm$ 4.0	84.3 $\pm$ 2.5	85.3 $\pm$ 3.4	87.5 $\pm$ 4.4	$\uparrow \uparrow \uparrow$
MCH	25.4 $\pm$ 1.4	26.8 $\pm$ 0.9	27.0 $\pm$ 1.1	26.7 $\pm$ 0.5	$\uparrow \uparrow \uparrow$
MCHC	31.3 $\pm$ 0.5	31.8 $\pm$ 0.7	31.7 $\pm$ 0.9	30.8 $\pm$ 0.9	$\downarrow \approx \approx \approx$
PLAT	271.3 $\pm$ 37.0	219.4 $\pm$ 50.2	209.6 $\pm$ 46.9	178.4 $\pm$ 37.7	$\downarrow \downarrow \downarrow$
WBC	8823.6 $\pm$ 1529.3	9862.9 $\pm$ 3030.5	8001.3 $\pm$ 2595.2	9411.1 $\pm$ 5673.4	$\approx \approx \approx \approx$
SEG	3620.8 $\pm$ 1793.5	5680.7 $\pm$ 3033.7	4191.9 $\pm$ 2279.3	4996.8 $\pm$ 3406.1	$\approx \approx \approx \approx$
BAND	117.4 $\pm$ 203.4	97.6 $\pm$ 141.0	148.0 $\pm$ 204.8	69.9 $\pm$ 107.4	—
LYMPH	4607.7 $\pm$ 861.2	3565.8 $\pm$ 760.1	3203.4 $\pm$ 1095.9	3856.9 $\pm$ 1918.6	$\approx \approx \approx \approx$
MONO	331.5 $\pm$ 133.0	356.7 $\pm$ 226.8	329.1 $\pm$ 136.5	287.7 $\pm$ 246.5	$\approx \approx \approx \approx$
EOS	116.0 $\pm$ 50.2	110.1 $\pm$ 108.8	90.8 $\pm$ 70.8	136.2 $\pm$ 104.2	$\approx \approx \approx \approx$
BASO	30.2 $\pm$ 37.6	52.0 $\pm$ 52.1	38.3 $\pm$ 39.4	63.7 $\pm$ 100.2	—
AL	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	—

Table 4

Parameters (intercepts and coefficients) and significance levels (*p-values in italics*) for linear mixed effects models of 15 hematology analytes of sooty mangabeys.

Variable	Intercept	Sex	Age	Age ²	Sex x Age
RBC *	5.20 <i>0.0001</i>	0.62 <i>0.0001</i>	0.02 <i>0.0036</i>	-0.002 <i>0.0001</i>	0.04 <i>0.0001</i>
HCT *	43.69 <i>0.0001</i>	5.90 <i>0.0001</i>	0.15 <i>0.0046</i>	-0.02 <i>0.0001</i>	0.45 <i>0.0001</i>
HGB *	13.86 <i>0.0001</i>	1.86 <i>0.0001</i>	0.03 <i>0.0674</i>	-0.01 <i>0.0001</i>	0.15 <i>0.0001</i>
MCV *	84.06 <i>0.0001</i>	1.17 <i>0.0043</i>	0.10 <i>0.0005</i>	-0.01 <i>0.0006</i>	
MCH *	26.72 <i>0.0001</i>	0.32 <i>0.0215</i>	-0.02 <i>0.0861</i>	-0.01 <i>0.0001</i>	0.06 <i>0.0088</i>
MCHC	31.70 <i>0.0001</i>	-0.03 <i>0.7611</i>	-0.04 <i>0.0001</i>		
PLAT *	231.5 <i>0.0001</i>	-30.0 <i>0.0003</i>	1.7 <i>0.0287</i>	0.3 <i>0.0001</i>	-6.4 <i>0.0001</i>
WBC	4.00 <i>0.0001</i>	-0.09 <i>0.0001</i>	-0.002 <i>0.1705</i>		
SEG	5358 <i>0.0001</i>	-695 <i>0.0435</i>	4 <i>0.8677</i>		
BAND	-1.54 <i>0.0001</i>	-0.03 <i>0.8839</i>	0.08 <i>0.0001</i>		
LYMPH	4584	-1452	-91	6	

Variable	Intercept	Sex	Age	Age ²	Sex x Age
	0.0001	0.0001	0.0001	0.0007	
MONO	365	-29	3		
	0.0001	0.2124	0.1072		
EOS	147	-49	-4		
	0.0001	0.0064	0.0102		
BASO	50.6	-8.1	-0.3		
	0.0001	0.1585	0.5743		
AL	0.9	0.1	-0.2		
	0.2723	0.8393	0.258		

* We subsequently analyzed females and males with separate models (see Supplementary Material); only males showed significant quadratic changes with age.

Mean value and standard deviation (SD) of 24 serum chemistry analytes of 57 female sooty mangabeys, by age groups. The four symbols in the rhesus comparison column indicate, for the four age groups, whether means are within ($\approx$), above ($\uparrow$), or below ($\downarrow$). Analytes for which no comparison was possible are indicated by a dash (—).

Table 5

Age (y)	0 to 5*	5 to 10	10 to 20	>20	Rhesus comparison
N	1	15	35	6	
Mean age (y)	4.5	8.24	15.16	25.41	
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	
GLUC	66.0 $\pm$ n/a	57.2 $\pm$ 10.4	107.8 $\pm$ 58.6	156.5 $\pm$ 54.0	$\approx \approx \uparrow \uparrow$
BUN	12.0 $\pm$ n/a	12.1 $\pm$ 2.9	9.7 $\pm$ 2.5	10.3 $\pm$ 1.2	$\downarrow \downarrow \downarrow$
CREAT	0.7 $\pm$ n/a	1.0 $\pm$ 0.1	0.8 $\pm$ 0.2	0.8 $\pm$ 0.1	$\downarrow \approx \approx \downarrow$
CALC	9.8 $\pm$ n/a	9.5 $\pm$ 0.3	9.3 $\pm$ 0.5	9.2 $\pm$ 0.6	$\approx \approx \approx \approx$
PHOS	3.9 $\pm$ n/a	3.0 $\pm$ 1.1	2.9 $\pm$ 1.0	3.6 $\pm$ 1.3	$\approx \downarrow \approx$
SOD	153.0 $\pm$ n/a	149.7 $\pm$ 1.8	146.4 $\pm$ 5.1	141.5 $\pm$ 6.7	$\uparrow \approx \approx \downarrow$
POTAS	4.7 $\pm$ n/a	4.7 $\pm$ 0.8	4.0 $\pm$ 0.6	3.7 $\pm$ 0.5	$\approx \approx \downarrow \downarrow$
MAGN	1.9 $\pm$ n/a	1.8 $\pm$ 0.1	1.8 $\pm$ 0.2	1.7 $\pm$ 0.1	—
CHLOR	114.0 $\pm$ n/a	110.9 $\pm$ 2.4	109.0 $\pm$ 3.6	108.3 $\pm$ 2.6	$\approx \downarrow \approx$
CPK	1730.0 $\pm$ n/a	2002.0 $\pm$ 2295.7	1072.8 $\pm$ 825.7	908.5 $\pm$ 336.0	$\uparrow \uparrow \uparrow \approx$
AST	74.0 $\pm$ n/a	71.8 $\pm$ 23.4	48.1 $\pm$ 16.4	38.8 $\pm$ 10.1	$\uparrow \uparrow \downarrow$
ALKPPOS	319.0 $\pm$ n/a	137.3 $\pm$ 32.3	164.6 $\pm$ 170.0	243.2 $\pm$ 188.8	$\uparrow \approx \approx \uparrow$
ALT	24.0 $\pm$ n/a	34.2 $\pm$ 13.3	38.2 $\pm$ 21.7	22.7 $\pm$ 6.0	$\downarrow \approx \approx \downarrow$
AMY	109.0 $\pm$ n/a	151.5 $\pm$ 108.9	137.4 $\pm$ 45.6	82.2 $\pm$ 24.1	—
LIP	48.0 $\pm$ n/a	72.1 $\pm$ 70.2	65.2 $\pm$ 40.5	26.0 $\pm$ 7.8	—

Age (y)	0 to 5 *	5 to 10	10 to 20	>20	Rhesus comparison
N	1	15	35	6	
Mean age (y)	4.5	8.24	15.16	25.41	
BILI	0.6 ± n/a	0.4 ± 0.2	0.3 ± 0.1	0.4 ± 0.3	↑↑ ≈ ↑
GGTP	210.0 ± n/a	263.3 ± 207.4	190.3 ± 137.9	169.5 ± 122.0	↑↑↑↑
TRIGLYC	37.0 ± n/a	46.9 ± 9.5	79.0 ± 51.4	158.0 ± 157.8	≈ ≈ ≈ ≈
CHOLEST	141.0 ± n/a	142.8 ± 23.7	148.9 ± 37.4	140.8 ± 39.4	↓ ↓ ≈ ≈
PROT	6.5 ± n/a	7.1 ± 0.3	7.2 ± 0.6	7.1 ± 0.7	↓ ↓ ≈ ≈
ALBU	4.7 ± n/a	4.9 ± 0.3	4.2 ± 0.7	3.8 ± 0.8	≈ ↑ ≈ ≈
GLOB	1.8 ± n/a	2.2 ± 0.3	3.0 ± 0.6	3.3 ± 0.5	—
A/G RATIO	2.6 ± n/a	2.2 ± 0.4	1.5 ± 0.4	1.2 ± 0.4	—
B/C RATIO	17.0 ± n/a	12.5 ± 2.6	12.6 ± 3.6	13.8 ± 2.4	—

* There is only one female in 0 to 5 category with age 4.5 years.

Mean value and standard deviation (SD) of 24 serum chemistry analytes of 26 male sooty mangabeys, by age groups. The four symbols in the rehsus comparison column indicate, for the four age groups, whether means are within ($\approx$), above ($\uparrow$), or below ($\downarrow$). Analytes for which no comparison was possible are indicated by a dash (—).

Table 6

Age (y)	0 to 5*	5 to 10	10 to 20	>20	Rhesus comparison
N	1	7	15	3	
Mean age (y)	4.7	7.3	15.4	22.4	
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	
GLUC	97.0 $\pm$ n/a	60.5 $\pm$ 16.0	129.2 $\pm$ 108.0	109.3 $\pm$ 25.7	$\uparrow \approx \uparrow \uparrow$
BUN	16.0 $\pm$ n/a	12.4 $\pm$ 4.2	12.5 $\pm$ 3.8	10.7 $\pm$ 2.5	$\downarrow \downarrow \downarrow$
CREAT	0.8 $\pm$ n/a	1.1 $\pm$ 0.1	1.0 $\pm$ 0.2	1.0 $\pm$ 0.2	$\approx \approx \approx \approx$
CALC	9.5 $\pm$ n/a	9.6 $\pm$ 0.3	9.3 $\pm$ 0.4	9.1 $\pm$ 0.8	$\approx \approx \approx \approx$
PHOS	5.2 $\pm$ n/a	3.4 $\pm$ 0.8	2.9 $\pm$ 1.2	2.9 $\pm$ 0.4	$\approx \approx \approx \approx$
SOD	149.0 $\pm$ n/a	152.1 $\pm$ 6.4	148.6 $\pm$ 6.4	144.3 $\pm$ 6.7	$\approx \approx \approx \approx$
POTAS	4.4 $\pm$ n/a	4.9 $\pm$ 0.7	4.5 $\pm$ 1.1	3.5 $\pm$ 0.2	$\approx \approx \approx \approx$
MAGN	1.5 $\pm$ n/a	1.8 $\pm$ 0.2	1.8 $\pm$ 0.3	1.7 $\pm$ 0.3	
CHLOR	107.0 $\pm$ n/a	109.7 $\pm$ 6.2	107.0 $\pm$ 4.3	106.3 $\pm$ 1.5	$\approx \approx \approx \approx$
CPK	1771.0 $\pm$ n/a	1656.3 $\pm$ 1250.3	1031.3 $\pm$ 728.5	860.0 $\pm$ 225.2	$\approx \approx \approx \approx$
AST	64.0 $\pm$ n/a	73.1 $\pm$ 23.2	65.8 $\pm$ 22.1	30.3 $\pm$ 8.1	$\approx \uparrow \approx \approx$
ALKPPOS	540.0 $\pm$ n/a	174.6 $\pm$ 132.7	113.4 $\pm$ 59.5	75.7 $\pm$ 11.0	$\approx \approx \approx \approx$
ALT	24.0 $\pm$ n/a	33.3 $\pm$ 17.4	44.4 $\pm$ 35.1	19.0 $\pm$ 3.0	$\approx \approx \approx \approx$
AMY	176.0 $\pm$ n/a	118.4 $\pm$ 23.8	103.5 $\pm$ 26.4	114.3 $\pm$ 21.9	
LIP	55.0 $\pm$ n/a	39.7 $\pm$ 21.4	137.1 $\pm$ 113.4	41.0 $\pm$ 2.8	

Age (y)	0 to 5 *	5 to 10	10 to 20	>20	Rhesus comparison
N	1	7	15	3	
Mean age (y)	4.7	7.3	15.4	22.4	
BILI	0.3 ± n/a	0.5 ± 0.2	0.4 ± 0.1	0.5 ± 0.4	≈ ↑↑↑
GGTP	135.0 ± n/a	194.5 ± 150.2	110.5 ± 65.2	180.7 ± 211.6	↑↑↑↑
TRIGLYC	45.0 ± n/a	59.9 ± 23.4	102.9 ± 71.7	92.7 ± 26.6	≈ ≈ ≈ ≈
CHOLEST	154.0 ± n/a	145.6 ± 32.0	139.3 ± 25.6	182.0 ± 22.6	≈ ≈ ≈ ≈
PROT	7.0 ± n/a	6.9 ± 0.3	7.0 ± 0.5	7.2 ± 0.7	≈ ≈ ≈ ≈
ALBU	5.1 ± n/a	4.8 ± 0.3	4.7 ± 0.3	4.7 ± 0.2	↑ ≈ ≈ ≈
GLOB	1.9 ± n/a	2.1 ± 0.4	2.3 ± 0.4	2.5 ± 0.6	—
A/G RATIO	2.7 ± n/a	2.4 ± 0.6	2.1 ± 0.4	2.0 ± 0.3	—
B/C RATIO	20.0 ± n/a	11.9 ± 4.3	13.1 ± 5.9	11.2 ± 4.0	—

* There is only one male (4.7 years of age) in the 0 to 5 category.

Table 7

Parameters (intercepts and coefficients) and significance levels (*p-values in italics*) for regression models of 24 serum chemistry analytes.

Variable	Intercept	Sex	Age	Age ²	Sex x Age
GLUC	97.42 <i>0.0000</i>	9.94 <i>0.4868</i>	6.18 <i>0.0000</i>		
BUN	10.48 <i>0.0000</i>	1.88 <i>0.0106</i>	-0.09 <i>0.1567</i>		
CREAT	0.84 <i>0.0000</i>	0.17 <i>0.0000</i>	-0.01 <i>0.0049</i>		
CALC	9.34 <i>0.0000</i>	0.01 <i>0.9190</i>	-0.03 <i>0.0077</i>		
PHOS	2.82 <i>0.0000</i>	0.08 <i>0.7524</i>	-0.01 <i>0.6294</i>	0.0076 <i>0.01</i>	
SOD	146.96 <i>0.0000</i>	1.99 <i>0.0970</i>	-0.48 <i>0.0000</i>		
POTAS	4.17 <i>0.0000</i>	0.32 <i>0.0759</i>	-0.07 <i>0.0000</i>		
MAGN	1.77 <i>0.0000</i>	0.02 <i>0.7523</i>	0.002 <i>0.6431</i>		
CHLOR	109.58 <i>0.0000</i>	-1.98 <i>0.0232</i>	-0.21 <i>0.0049</i>		
CPK	1325.01 <i>0.0000</i>	-132.40 <i>0.6489</i>	-56.87 <i>0.0261</i>		
AST	54.28 <i>0.0000</i>	8.76 <i>0.0556</i>	-2.08 <i>0.0000</i>		
ALKPPOS	147.67	-26.64	-2.14	0.73	

Variable	Intercept	Sex	Age	Age ²	Sex x Age
	0.0000	0.4204	0.4928	0.06	
ALT	38.95	2.75	0.93	-0.1348	
	0.0000	0.5995	0.0631	0.03	
AMY	135.45	-24.69	-2.81		
	0.0000	0.0724	0.0191		
LIP	65.34	36.40	1.67		
	0.0000	0.0352	0.3059		
BILI	0.37	0.05	-0.005		
	0.0000	0.2764	0.2177		
GGTP	208.88	-68.56	-5.04		
	0.0000	0.0500	0.0952		
TRIGLYC	76.69	12.89	6.05		
	0.0000	0.3524	0.0000		
CHOLEST	146.19	0.41	0.51		
	0.0000	0.9578	0.4440		
PROT	7.13	-0.15	0.01		
	0.0000	0.2270	0.5022		
ALBU	4.36	0.36	-0.07	0.0468	
	0.0000	0.0038	0.0000	0.0424	
GLOB	2.88	-0.50	0.09	-0.0038	-0.0594
	0.0000	0.0000	0.0000	0.002	0.0035
A/G RATIO	1.58	0.47	-0.09	0.0039	0.0468
	0.0000	0.0000	0.0000	0.0009	0.012
B/C RATIO	12.33	0.10	0.03		
	0.0000	0.9148	0.7321		