Journal of the American Association for Laboratory Animal Science
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Vol 53, No 4
July 2014
Pages 336–343

# Hematologic and Serum Biochemical Values of 4 Species of *Peromyscus* Mice and Their Hybrids

**Charles E Wiedmeyer,[1] Janet P Crossland,[2] Monika Veres,[2] Michael J Dewey,[2,*] Michael R Felder,[2] Shayne C Barlow,[3] Paul B Vrana,[2] and Gabor Szalai[2]**

**Deer mice (*Peromyscus maniculatus*) and congeneric species are used in a wide variety of research applications, particularly studies of developmental, physiologic, and behavioral characteristics associated with habitat adaptation and speciation. Because peromyscine mice readily adapt to colony conditions, animals with traits of interest in the field are moved easily into the laboratory where they can be studied under controlled conditions. The purpose of this study was to determine the serum chemistry and hematologic parameters of 4 frequently used species from the *Peromyscus* Genetic Stock Center species (*P. californicus*, *P. leucopus*, *P. maniculatus*, and *P. polionotus*) and to determine quantitative differences in these parameters among species and between sexes. Triglyceride values were substantially higher in female compared with male mice in all 4 species. Similar cross-species differences in MCH were present. Overall there was considerable interspecific variation for most blood parameters, with little evidence for covariation of any 2 or more parameters. Because crosses of *P. maniculatus* and *P. polionotus* produce fertile offspring, segregation analyses can be applied to determine the genetic basis of any traits that differ between them, such as their 3.8- and 2.1-fold interspecific differences in cholesterol and triglyceride levels, respectively. The current data provide a set of baseline values useful for subsequent comparative studies of species experiencing different circumstances, whether due to natural variation or anthropogenic environmental degradation. To enable such comparisons, the raw data are downloadable from a site maintained by the Stock Center (http://ww2.biol.sc.edu/~peromyscus).**

**Abbreviations:** BW, *P. maniculatus bairdii*; IS, *P. californicus insignis*; LL, *P. leucopus*; PO, *P. polionotus subgriseus*.

Collectively peromyscine rodents are the most common, abundant, and speciose native North American mammals. Ranging from Alaska to Central America and from the Atlantic to the Pacific, they occur in a wide range of habitats, including sea-level wetlands, beaches, forests, prairies, and deserts and mountains of elevations to 14,000 ft.[23,24] As such, peromyscine rodents are uniquely positioned as models for studying the factors, genetic and otherwise, responsible for reproductive isolation and speciation. In addition, they are useful as models to study the factors enabling adaptive responses to changing environmental conditions, to other species, and to each other.[10,18,35] *Peromyscus maniculatus* (deer mice) and *P. leucopus* (white-footed mice) are the most familiar, widespread, and biologically best-known species. In addition, these particular species have drawn considerable public health interest owing to their roles as zoonotic reservoirs of infectious disease organisms,[41] notably hantavirus (*P. maniculatus*)[29] and the *Borrelia* spp. causing Lyme disease (*P. leucopus*).[27]

Peromyscines are reared in animal colonies incorporating caging, feeding, and maintenance regimens used for laboratory mice.[21] The stocks maintained by the *Peromyscus* Genetic Stock Center (http://stkctr.biol.sc.edu/) were all derived from wild-caught animals and bred by random mating to maintain genetic diversity. As such, they can be considered to be closely related genetically to their wild counterparts and possess allelic combinations maximizing the physiologic and behavioral traits undergirding the species' habitat adaptation. This situation contrasts with the standard inbred strains of laboratory mice, which are amalgams of genes derived from 3 or 4 different *Mus* spp.[6,16] and which lack wild natural counterparts. Random admixture of genes from different species may provide a means of unmasking gene effects that would otherwise go unnoticed, such as those being studied in collaborative cross strains.[8] Yet the results say little regarding the adaptive roles of such genes in wild populations and their corresponding phenotypes.

In the current report we present hematologic and biochemical comparisons of 4 species maintained by the Stock Center to determine the degree that species- and sex-associated factors affect various blood parameters. The phylogenetic relatedness of the 4 species is illustrated in Figure 1. The species examined were *P. californicus insignis* (IS), *P. leucopus* (LL), *P. maniculatus bairdii* (BW), and *P. polionotus subgriseus* (PO). Two of these (BW and PO) are interfertile sister species, whose offspring manifest disparate dysgenetic phenotypes depending on the parental sex.[9,12,51] Thus, PO females mated with BW males generate offspring manifesting lethal overgrowth and which rarely develop to term. Offspring of the reciprocal cross (BW females × PO males) are viable but undersized at birth and into adulthood. We determined the hematologic and chemical parameters of the BW × PO hybrids and compared the results with those of the parental stocks.

We undertook this study for 3 primary reasons: 1) to establish baseline values for commonly used stocks maintained by the Stock Center, thereby rendering them more useful and complementing their completed genome sequences (currently being assembled); 2) to compare species- and sex-associated differences in such values; and 3) to assess basic inheritance patterns of differences between the PO and BW stocks, which differ in numerous characteristics, including partner fidelity (PO and

*Received: 27 Aug 2013. Revision requested: 21 Oct 2013. Accepted: 11 Dec 2013.*
*[1]Veterinary Medical Diagnostic Laboratory and Department of Veterinary Pathobiology, College of Veterinary Medicine, University of Missouri, Columbia, Missouri; [2]Peromyscus Genetic Stock Center, Office of the Vice President for Research and [3]Department of Animal Resources, School of Medicine, University of South Carolina, Columbia, South Carolina.*
*[*]Corresponding author. Email: mjdewey@gmail.com*

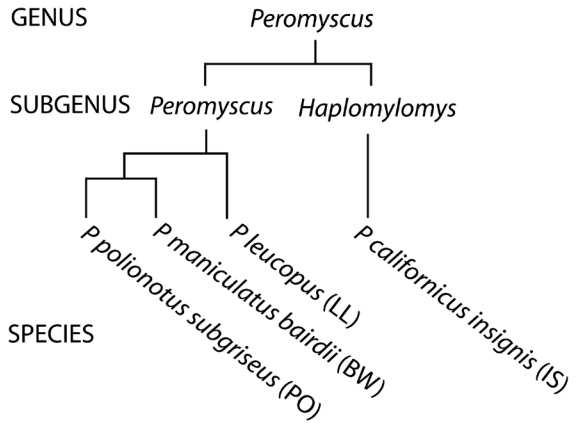


**Figure 1.** Evolutionary relationship and species designations (in parentheses) of the peromyscine species whose hematologic and serum biochemical parameters were profiled.

IS are monogamous species[10,14,19]), stress response and blood glucose homeostasis, repetitive behaviors, growth control, and various blood parameters documented in this study.

## Materials and Methods

**Animals.** All animals were obtained from the *Peromyscus* Genetic Stock Center and included 20 male and 20 female mice of each stock (age, 3 to 4 mo). The mice came from the following stocks: IS stock, derived from 60 ancestors collected between 1979 and 1987 in the mountains of Santa Monica, CA; LL stock, derived from 38 ancestors captured between 1982 and 1985 near Linville, NC; BW stock, descended from 40 ancestors caught in 1948 near Ann Arbor, MI; and PO Stock, derived from 21 ancestors caught in Ocala National Forest, FL. In addition, 10 male and 10 female hybrids obtained by mating BW female mice with PO male mice were analyzed.

Mice in the *Peromyscus* Genetic Stock Center are housed in a facility registered with the US Department of Agriculture and accredited by AAALAC. Animal procedures were in accordance with the USDA Animal Welfare Act[2] and *Guide for the Care and Use of Laboratory Animals*[19] and were reviewed and approved by the IACUC. Standard animal husbandry procedures were used throughout.[21] The mice were housed in polypropylene cages with aspen bedding, fed a standard commercial rodent diet (Rodent Diet W, Harlan Teklad, Madison, WI), and provided with filtered, UV-treated water ad libitum. All cages were changed weekly. Environmental conditions in the rooms included a 16:8-h light:dark cycle, temperature maintained at 18 to 23 °C, 50% to 70% relative humidity, and 15 air changes hourly.

The mice were monitored routinely for common rodent viruses (mouse hepatitis virus, Sendai virus, pneumonia virus of mice, reovirus 3, ectromelia, mouse parvovirus, epidemic diarrhea of mice, and lymphocytic choriomeningitis virus) and *Mycoplasma pulmonis*. In addition, mice were monitored for intestinal parasites by direct examination of cecal or colonic contents by fecal flotation and tape test of the perianal region. The presence of mites was determined by skin scrapes and hair-tuft examinations.

**Sample acquisition.** Animals were shipped from the *Peromyscus* Genetic Stock Center (Columbia, SC) to Comparative Clinical Pathology Services (Columbia, MO). After a 24-h acclimation period, the mice were euthanized by $CO_2$ overdose. Approximately 1.0 mL of whole blood was collected via cardiocentesis and placed in a tube containing lithium heparin, thoroughly mixed, and analyzed immediately.

**Hematologic analyses.** The CBC included red cell parameters (Hct, Hgb, RBC number, MCV, MCH, and MCHC), white cell parameters (WBC number and neutrophil, lymphocyte, monocyte, and eosinophil percentages and absolute counts), and platelet parameters (platelet number and mean platelet volume). Samples were analyzed by using an automated hematology instrument (Hemavet 950FS, Drew Scientific, Dallas, TX). Prior to CBC analysis, a blood smear was created, stained by using a Diff-Quik stain (Medical Solutions, Lakewood, NJ), and used to perform a manual WBC differential count and to assess RBC morphology and platelet clumping.

**Plasma biochemistry analyses.** After CBC analyses, the samples were centrifuged at 15,000 × *g* for 5 min to separate the plasma from the cells. The plasma was harvested and analyzed for plasma biochemical parameters (that is, glucose, BUN, creatinine, total protein, albumin, phosphorus, sodium, chloride, potassium, total $CO_2$, cholesterol, triglycerides, calcium, total bilirubin, ALP, ALT, and GGT) by using commercial assays (Beckman-Coulter, Brea, CA) on an automated clinical chemistry analyzer (model AU680, Beckman-Coulter). Globulins were calculated by subtracting albumin from total protein.

**Statistical analyses.** For the raw data available on the Stock Center website (http://ww2.biol.sc.edu/~peromyscus), 95% reference intervals were established by using a statistical program (version 11.6.0.0, MedCalc, Ostend, Belgium). The program calculates reference intervals according by using normal distribution and by using a nonparametric percentile method. Normal distribution was determined by using the D'Agostino–Pearson test, with significance set at a *P* value of less than 0.05. If the data failed to achieve normal distribution, a nonparametric statistical method was applied.

All comparisons were performed by using the statistical suite in the SAS Enterprise Guide (version 4.2, SAS Institute, Cary, NC). For interspecies comparisons, male and female values were pooled and the results analyzed by ANOVA. Statistical significance was inferred at a *P* value of less than 0.05. Interspecies comparisons of each parameter were derived from one-way ANOVA, coupled with Tukey tests to effect pairwise comparisons. The Enterprise Guide also was used to determine the significance of sex-associated differences and those between BW, PO, and their F1 hybrids (Figure 2) according to pairwise *t* tests. Equality of variances was evaluated by using the folded F statistic. If the assumption of equality of variances was not reasonable, the Satterthwaite approximation for degrees of freedom was used to determine *P* values.

## Results

Mean values and standard deviations for each hematologic and biochemical parameter, categorized by sex, for the 4 *Peromyscus* species and the BW × PO (female × male) hybrids are provided (Tables 1 and 2). Roughly half of the blood parameters among the pure species differed significantly between the sexes but usually with no apparent interspecific correlations. In a couple of cases, however, a consistent sex-associated difference was noted for all 4 species. Specifically, triglyceride concentrations were significantly higher in female than male mice; the ratios of the male:female means were: IS, 1:1.56; LL, 1:1.56; BW, 1:1.52; PO, 1:1.94. For interspecies comparisons, the male and female values from each were pooled and the results analyzed by one-way ANOVA (Tables 3 through 5); values that differed significantly among the species (determined by Tukey test) are so indicated.

Although BW and PO are closely related sister species (Figure 1), several blood values differed significantly between these species

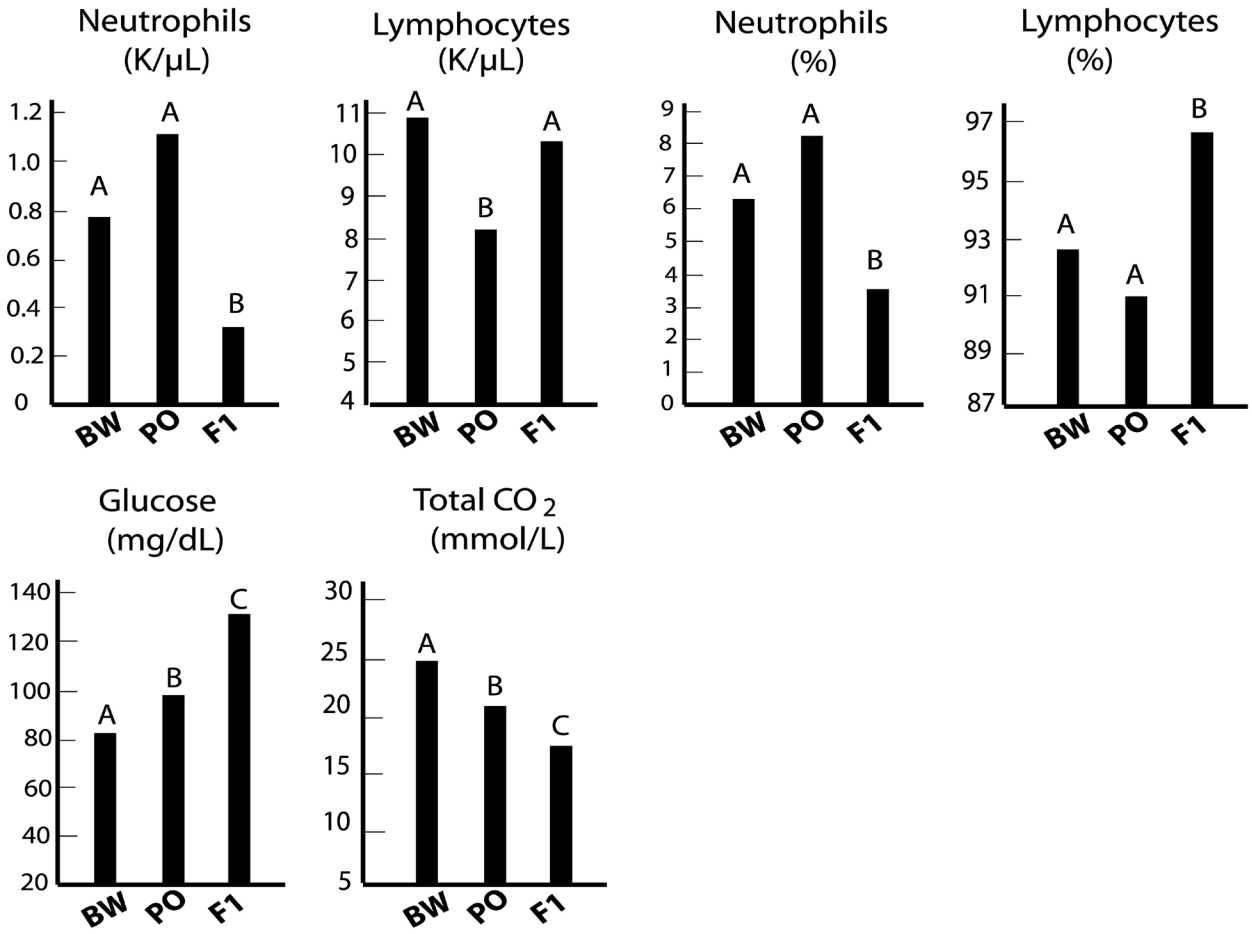


**Figure 2.** Hematologic and biochemical parameters in which the hybrid values lie outside those of either parent. Data derived from pooled male and female values (BW and PO, $n = 40$ each; (BW × PO)F1, $n = 20$. Values indicated with the same letter are considered to be in the same range; values with different letters are significantly different ($t$ test, $P < 0.05$).

(Tables 3 through 5). Furthermore, for most hematologic and biochemical parameters, the values for the (BW × PO) F1 hybrids fell close to or midway between those of the parental species (Tables 1 and 2). Exceptions to this pattern appeared among the values for the proportions of neutrophils and lymphocytes among WBC and the concentration of neutrophils (Figure 2). Glucose values were higher for hybrids than parental stocks, but blood $CO_2$ concentration was higher in BW and PO mice than in their hybrid progeny (Figure 2).

## Discussion

Despite peromyscine abundance, species richness, and diverse research applications, relatively few reports include blood chemical and cellular measurements.[5,52,53] One of the primary purposes of the current study was to assess the blood cell and biochemistry values of 4 of the most frequently studied species maintained by the *Peromyscus* Genetic Stock Center. Of these, both BW and LL continue to be studied for their roles as reservoir species for human infectious disease organisms, particularly hantavirus in BW,[1,39,40] and *Borrelia burgdorferi* (which is associated with Lyme disease) in LL.[3,36,46] In addition, both species are of interest for host–ectoparasite studies.[8,38] With a life span 3.5-fold longer than that of similar-sized *Mus* spp. mice, LL is an important model for longevity research.[26,42] For their ubiquity throughout the country, BW and LL routinely serve as sentinel species at sites, including superfund sites, experiencing high levels of chemical or radiation contamination.[14,17,34,45] Both PO and IS are monogamous species and the subjects of ongoing behavioral and physiologic partner-fidelity studies.[20,37,47] In addition, IS serves as a model of metabolic syndrome.[25] BW and its hybrids with PO are models for exploring the initial steps of speciation and the roles of genomic imprinting and other epigenetic processes therein.[43,48-50]

Each species presents with its own particular blood cellular and hematologic profile, with some interspecific overlap. There is little agreement, especially for the serum biochemistry, among the species set regarding which parameters display a female or male bias. Apart from that, many of those parameters demonstrated to be significantly different between sexes are based on small differences of questionable physiologic significance. Exceptions to this trend are the female biases for high serum triglycerides and high MCH in all 4 species (Tables 1 and 2). In addition, the 4 species are similar in that the neutrophil and monocyte counts, with no significant differences in proportions.

Interspecific total WBC counts differed significantly (IS = BW > LL = PO) and is driven by species-associated variation in lymphocyte counts (Table 3). At this level, these results fail to support a previously proposed theoretical paradigm[31,32] suggesting that polygamous species have more robust immune systems than do monogamous ones. This hypothesis was based on WBC and lymphocyte counts compared among 18 primate species segregated by partner fidelity; it assumes that immunologic potency is proportional to WBC numbers. Among the species in our current panel, IS and PO are documented to be monogamous, BW and LL polygamous;[4,11,15,20] their WBC counts

**Table 1.** Hematologic values

| | | IS | | LL | | BW | | PO | | BW × PO | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | F | M | F | M | F | M | F | M | F | M |
| WBC (K/μL) | Mean | 10.89 | 14.29 | 8.41 | 8.76 | 11.22 | 12.35 | 8.63 | 10.14 | 11.72 | 9.70 |
| | 1 SD | 2.90 | 4.76 | 2.72 | 2.40 | 3.88 | 3.72 | 1.58 | 3.06 | 3.12 | 2.54 |
| Neutrophils (%) | Mean | 6.00 | 9.53 | 4.26 | 7.75 | 4.00 | 8.55 | 6.75 | 9.75 | 2.10 | 4.00 |
| | 1 SD | 5.02 | 5.77 | 2.83 | 8.53 | 3.00 | 8.48 | 5.04 | 9.60 | 2.88 | 3.13 |
| | *n* | 19 | 19 | 19 | 20 | 19 | 20 | 20 | 20 | 10 | 10 |
| Lymphocytes (%) | Mean | 93.2 | 89.6 | 95.0 | 91.2 | 95.1 | 90.5 | 92.2 | 89.4 | 97.2 | 95.7 |
| | 1 SD | 5.2 | 6.0 | 4.3 | 8.8 | 3.7 | 8.6 | 5.5 | 10.1 | 3.2 | 3.3 |
| Monocytes (%) | Mean | 1.91 | 1.67 | 2.60 | 0.95 | 1.44 | 0.86 | 1.21 | 1.29 | 1.00 | 1.00 |
| | 1 SD | 0.94 | 0.82 | 3.05 | 0.83 | 0.73 | 0.86 | 0.43 | 0.49 | 0.63 | 0.00 |
| | *n* | 11 | 15 | 5 | 20 | 9 | 14 | 14 | 7 | 6 | 2 |
| Neutrophils (K/μL) | Mean | 0.62 | 1.43 | 0.35 | 0.66 | 0.47 | 1.05 | 0.58 | 1.68 | 0.22 | 0.42 |
| | 1 SD | 0.51 | 1.15 | 0.27 | 0.70 | 0.50 | 1.13 | 0.42 | 2.79 | 0.27 | 0.39 |
| | *n* | 19 | 19 | 19 | 20 | 19 | 20 | 20 | 20 | 9 | 10 |
| Lymphocytes (K/μL) | Mean | 10.18 | 12.75 | 8.02 | 8.00 | 10.64 | 11.21 | 7.96 | 8.91 | 11.45 | 9.26 |
| | 1 SD | 2.78 | 4.20 | 2.54 | 2.39 | 3.56 | 3.50 | 1.56 | 2.31 | 3.30 | 2.33 |
| Monocytes (K/μL) | Mean | 0.21 | 0.22 | 0.12 | 0.09 | 0.16 | 0.08 | 0.10 | 0.15 | 0.10 | 0.10 |
| | 1 SD | 0.08 | 0.14 | 0.04 | 0.08 | 0.07 | 0.07 | 0.04 | 0.09 | 0.08 | 0.04 |
| | *n* | 11 | 15 | 5 | 20 | 9 | 14 | 14 | 7 | 6 | 2 |
| RBC (M/μL) | Mean | 10.0 | 10.2 | 10.9 | 12.0 | 10.8 | 12.2 | 10.1 | 10.8 | 10.6 | 11.5 |
| | 1 SD | 0.7 | 0.9 | 1.0 | 0.8 | 0.9 | 0.7 | 0.6 | 0.5 | 0.7 | 0.8 |
| Hemoglobin (g/dL) | Mean | 15.0 | 14.3 | 14.3 | 13.0 | 13.2 | 13.2 | 13.9 | 14.0 | 14.1 | 14.6 |
| | 1 SD | 0.8 | 0.9 | 1.4 | 1.0 | 1.2 | 0.7 | 1.0 | 0.9 | 1.2 | 0.8 |
| Hematocrit (%) | Mean | 44.1 | 43.3 | 41.1 | 44.6 | 38.9 | 45.1 | 40.7 | 41.1 | 42.6 | 42.1 |
| | 1 SD | 2.5 | 2.6 | 3.9 | 3.3 | 4.0 | 2.7 | 2.3 | 2.4 | 3.8 | 2.4 |
| MCV (fL) | Mean | 44.3 | 42.8 | 37.5 | 37.2 | 36.1 | 37.2 | 40.1 | 38.1 | 40.4 | 36.5 |
| | 1 SD | 1.2 | 3.1 | 3.0 | 2.4 | 1.3 | 1.6 | 1.9 | 1.8 | 1.3 | 1.3 |
| MCH (pg) | Mean | 15.1 | 14.1 | 13.1 | 10.8 | 12.3 | 10.9 | 13.7 | 12.9 | 13.0 | 12.7 |
| | 1SD | 0.6 | 0.8 | 0.8 | 0.7 | 0.4 | 0.5 | 1.0 | 0.7 | 0.5 | 0.7 |
| MCHC (g/dL) | Mean | 34.1 | 33.1 | 34.9 | 29.1 | 34.0 | 29.3 | 34.1 | 34.0 | 33.0 | 34.6 |
| | 1SD | 0.9 | 1.0 | 2.1 | 0.5 | 0.7 | 0.9 | 1.4 | 1.3 | 1.3 | 1.4 |
| Platelets (M/μL) | Mean | 286 | 365 | 368 | 421 | 361 | 354 | 477 | 543 | 310 | 306 |
| | 1 SD | 125 | 168 | 131 | 145 | 162 | 117 | 178 | 188 | 58 | 134 |
| MPV (fL) | Mean | 5.53 | 5.01 | 4.83 | 4.61 | 4.60 | 4.55 | 5.48 | 5.23 | 4.95 | 6.87 |
| | 1 SD | 0.85 | 0.74 | 0.86 | 0.49 | 0.66 | 0.22 | 0.64 | 0.51 | 0.68 | 0.83 |

F, female; M, male.
Unless otherwise noted for specific parameters, $n = 20$ of each sex for pure species and $n = 10$ of each sex for the BW × PO hybrids.

and partner-fidelity profiles are obviously discordant. Among the RBC indices, the IS profile is the overall outlier among the 4 species. IS RBC counts are low, but the cells are 11% to 18% larger than those of the other species and contain 10% to 25% more Hgb. Phylogenetically IS is the most distantly related among the 4 species (Figure 1).

**Table 2.** Serum biochemical values

| | | IS | | LL | | BW | | PO | | BW × PO | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | F | M | F | M | F | M | F | M | F | M |
| Triglycerides (mg/dL) | Mean | 493 | 315 | 463 | 296 | 226 | 149 | 526 | 271 | 261 | 205 |
| | 1 SD | 233 | 236 | 214 | 114 | 56 | 61 | 253 | 113 | 127 | 100 |
| Cholesterol (mg/dL) | Mean | 146 | 165 | 114 | 100 | 78 | 97 | 390 | 283 | 179 | 181 |
| | 1 SD | 39 | 30 | 71 | 32 | 10 | 14 | 73 | 84 | 20 | 24 |
| Glucose (mg/dL) | Mean | 121 | 102 | 107 | 63 | 72 | 93 | 95 | 101 | 122 | 137 |
| | 1 SD | 25 | 41 | 26 | 27 | 24 | 25 | 26 | 31 | 39 | 34 |
| Total CO2 (mmol/L) | Mean | 23.5 | 24.0 | 19.4 | 19.1 | 21.5 | 28.2 | 21.5 | 22.0 | 16.2 | 18.7 |
| | 1 SD | 3.70 | 2.0 | 3.0 | 3.9 | 4.50 | 3.20 | 4.90 | 4.50 | 5.90 | 3.30 |
| BUN (mg/dL) | Mean | 33.8 | 36.6 | 23.6 | 24.1 | 33.4 | 30.3 | 41.4 | 38.3 | 37.1 | 33.0 |
| | 1 SD | 7.8 | 6.9 | 3.9 | 3.8 | 3.5 | 3.9 | 4.9 | 4.9 | 7.3 | 6.1 |
| Creatinine (mg/dL) | Mean | 0.22 | 0.22 | 0.21 | 0.23 | 0.20 | 0.20 | 0.25 | 0.22 | 0.24 | 0.21 |
| | 1 SD | 0.03 | 0.02 | 0.02 | 0.04 | 0.00 | 0.00 | 0.04 | 0.02 | 0.04 | 0.02 |
| Sodium (mmol/L) | Mean | 157 | 154 | 156 | 157 | 152 | 155 | 153 | 153 | 149 | 152 |
| | 1 SD | 6 | 2 | 6 | 5 | 2 | 4 | 4 | 3 | 9 | 1 |
| Potassium (mmol/L) | Mean | 7.88 | 7.99 | 6.78 | 7.27 | 6.10 | 6.97 | 5.68 | 6.44 | 6.62 | 6.72 |
| | 1 SD | 2.17 | 1.15 | 0.74 | 0.82 | 0.89 | 0.59 | 0.87 | 0.99 | 1.50 | 0.85 |
| Chloride (mmol/L) | Mean | 112 | 111 | 112 | 108 | 108 | 110 | 108 | 108 | 109 | 110 |
| | 1 SD | 4 | 2 | 4 | 2 | 2 | 5 | 3 | 3 | 3 | 2 |
| Calcium (mg/dL) | Mean | 10.4 | 10.7 | 11.0 | 10.9 | 10.2 | 10.0 | 11.5 | 11.3 | 11.7 | 10.9 |
| | 1 SD | 0.8 | 0.8 | 0.7 | 0.7 | 0.6 | 0.5 | 0.8 | 1.3 | 2.2 | 0.4 |
| Phosphorus (mg/dL) | Mean | 10.4 | 9.9 | 12.5 | 16.7 | 10.3 | 8.1 | 11.8 | 11.7 | 12.8 | 9.2 |
| | 1 SD | 3.5 | 2.3 | 2.2 | 2.4 | 2.4 | 1.4 | 1.8 | 2.1 | 2.7 | 1.0 |
| Total protein (g/dL) | Mean | 6.08 | 6.16 | 6.52 | 6.52 | 5.92 | 5.42 | 7.33 | 6.98 | 6.29 | 5.89 |
| | 1 SD | 0.43 | 0.36 | 0.42 | 0.44 | 0.35 | 0.36 | 0.47 | 0.52 | 0.24 | 0.34 |
| Albumin (g/dL) | Mean | 3.27 | 3.16 | 3.37 | 3.45 | 3.14 | 3.03 | 3.98 | 3.82 | 3.63 | 3.41 |
| | 1 SD | 0.23 | 0.15 | 0.37 | 0.21 | 0.21 | 0.19 | 0.23 | 0.27 | 0.21 | 0.15 |
| Globulins (g/dL) | Mean | 2.82 | 3.00 | 3.15 | 3.07 | 2.78 | 2.39 | 3.35 | 3.16 | 2.66 | 2.48 |
| | 1 SD | 0.24 | 0.25 | 0.26 | 0.26 | 0.24 | 0.33 | 0.32 | 0.37 | 0.20 | 0.23 |
| Total bilirubin (mg/dL) | Mean | 0.23 | 0.26 | 0.18 | 0.16 | 0.16 | 0.14 | 0.22 | 0.18 | 0.25 | 0.17 |
| | 1 SD | 0.05 | 0.08 | 0.05 | 0.05 | 0.05 | 0.05 | 0.04 | 0.04 | 0.07 | 0.05 |
| ALT (U/L) | Mean | 141 | 202 | 214 | 328 | 189 | 366 | 336 | 333 | 182 | 213 |
| | 1 SD | 62 | 190 | 209 | 146 | 96 | 225 | 206 | 151 | 71 | 131 |
| ALP (U/L) | Mean | 369 | 325 | 252 | 204 | 231 | 282 | 386 | 404 | 354 | 367 |
| | 1 SD | 48 | 59 | 53 | 41 | 38 | 101 | 66 | 56 | 68 | 32 |
| GGT (U/L) | Mean | 4.25 | 6.60 | nd | nd | 3.30 | 3.20 | 3.90 | 3.00 | 3.30 | 3.20 |
| | 1 SD | 1.64 | 4.00 | nd | nd | 0.80 | 0.70 | 2.66 | 0.00 | 0.64 | 0.40 |

F, female; M, male; nd, not determined.

**Table 3.** Interspecies comparisons of WBC parameters (mean [1 SD])

| Species | WBC (K/μL) | Lymphocytes (%) | Neutrophils (%) | Monocytes (%) | Lymphocytes (K/μL) | Neutrophils (K/μL) | Monocytes (K/μL) |
|---|---|---|---|---|---|---|---|
| IS | 12.6 (4.3)[a] | 91.4 (5.8) | 7.8 (5.6) | 1.77 (0.86) | 11.5 (3.7)[a] | 1.02 (0.97) | 0.21 (0.12) |
| LL | 8.6 (2.5)[b] | 93.1 (7.1) | 6.1 (6.6) | 1.28 (1.59) | 8.0 (2.4)[b] | 0.51 (0.55) | 0.09 (0.07) |
| BW | 11.8 (3.8)[a] | 92.8 (7.0) | 6.3 (6.7) | 1.09 (0.85) | 10.9 (3.5)[a] | 0.77 (0.92) | 0.11 (0.08) |
| PO | 9.3 (2.5)[b] | 90.8 (8.1) | 8.3 (7.1) | 1.24 (0.44) | 8.4 (2.0)[b] | 1.13 (2.04) | 0.12 (0.06) |

Data from male and female mice have been combined. Within a parameter, values with the same letter are considered to be within the same range; those with different letters are significantly different from each other according to Tukey tests ($P < 0.05$). The letter designations are size-ordered—a represents the largest values, and b, c, and d indicate successively smaller ones.

**Table 4.** Interspecies comparison of RBC parameters (mean [1 SD])

| Species | RBC (M/μL) | Hgb (g/dL) | Hct (%) | MCV (fL) | MCH (pg) | MCHC (g/dL) | Platelets (M/μL) | MPV (fL) |
|---|---|---|---|---|---|---|---|---|
| IS | 10.1 (0.8)[b] | 14.7 (0.9)[a] | 43.7 (2.6)[a] | 43.5 (2.4)[a] | 14.6 (0.9)[a] | 33.6 (1.1)[a] | 325 (151)[b] | 5.27 (0.83)[a] |
| LL | 11.5 (1.1)[a] | 13.7 (1.4)[b,c] | 42.8 (4.0)[a,b] | 37.5 (2.7)[c] | 12.0 (1.4)[c] | 32.0 (3.3)[b] | 394 (138)[b] | 4.71 (0.70)[b] |
| BW | 11.5 (1.1)[a] | 13.2 (1.0)[c] | 42.0 (4.6)[a,b] | 36.6 (1.5)[c] | 11.6 (0.8)[c] | 31.7 (2.5)[b] | 357 (139)[b] | 4.57 (0.48)[b] |
| PO | 10.5 (0.6)[b] | 13.9 (0.9)[b] | 40.9 (2.3)[b] | 39.1 (2.1)[b] | 13.3 (0.9)[b] | 34.0 (1.3)[a] | 510 (183)[a] | 5.35 (0.88)[a] |

Data from male and female mice have been combined. Within a parameter, values with the same letter are considered to be within the same range; those with different letters are significantly different from each other according to Tukey tests ($P < 0.05$). The letter designations are size-ordered—a represents the largest values, and b, c, and d indicate successively smaller ones.

**Table 5.** Interspecies comparison of serum chemical values (mean [1 SD])

| | Triglycerides (mg/dL) | Cholesterol (mg/dL) | Glucose (mg/dL) | Total $CO_2$ (mmol/L) | BUN (mg/dL) | Creatinine (mg/dL) | Sodium (mmol/L) | Potassium (mm/L) | Chloride (mm/L) |
|---|---|---|---|---|---|---|---|---|---|
| IS | 404 (254)[a] | 155.7 (36.6)[b] | 111.6 (35.6)[a] | 23.7 (3.0)[a,b] | 35.2 (7.6)[b] | 0.22 (0.03)[a] | 155.4 (5.3)[a,b] | 7.93 (1.76)[a] | 111.5 (3.4)[a] |
| LL | 380 (189)[a] | 107.6 (54.5)[c] | 84.7 (34.5)[b] | 19.3 (3.4)[c] | 23.8 (3.8)[d] | 0.22 (0.03)[a] | 156.6 (5.3)[a] | 7.02 (0.81)[b] | 109.7 (4.0)[b] |
| BW | 187 (69)[b] | 87.4 (15.6)[c] | 82.7 (26.7)[b] | 24.8 (5.1)[a] | 31.9 (4.0)[c] | 0.20 (0.00)[b] | 153.9 (3.7)[b] | 6.53 (0.87)[b,c] | 108.9 (3.7)[b,c] |
| PO | 398 (236)[a] | 336.6 (96.6)[a] | 97.8 (28.2)[a,b] | 21.7 (4.8)[b] | 40.0 (5.2)[a] | 0.23 (0.04)[a] | 152.9 (3.6)[b] | 6.06 (1.01)[c] | 107.7 (3.1)[c] |

| | Calcium (mg/dL) | Phosphorus (mg/dL) | Total protein (g/dL) | Albumin (g/dL) | Globulins (g/dL) | Total bilirubin (mg/dL) | ALT (U/L) | ALP (U/L) |
|---|---|---|---|---|---|---|---|---|
| IS | 10.52 (0.82)[b,c] | 10.1 (3.0) | 6.12 (0.40)[c] | 3.21 (0.20)[c] | 2.91 (0.26)[b] | 0.240 (0.071)[a] | 171 (147)[b] | 347 (59)[b] |
| LL | 10.94 (0.68)[a,b] | 14.5 (3.1) | 6.52 (0.42)[b] | 3.41 (0.30)[b] | 3.11 (0.26)[a] | 0.167 (0.052)[b,c] | 271 (187)[a,b] | 228 (53)[c] |
| BW | 10.09 (0.57)[c] | 9.2 (2.2) | 5.67 (0.43)[d] | 3.09 (0.21)[c] | 2.58 (0.35)[c] | 0.147 (0.050)[c] | 277 (193)[a] | 256 (79)[c] |
| PO | 11.40 (1.13)[a] | 11.7 (2.0) | 7.15 (0.53)[a] | 3.90 (0.26)[a] | 3.25 (0.36)[a] | 0.197 (0.048)[b] | 335 (183)[a] | 395 (62)[a] |

Data from male and female mice have been combined. For each parameter, values with the same letter are considered to be within the same range; those with different letters are significantly different from each other according to Tukey tests ($P < 0.05$). The letter designations are size-ordered—a represents the largest values, and b, c, and d indicate successively smaller ones.

Comparative values of BW and PO are of particular interest. These 2 sister species are interfertile and produce fertile hybrid offspring; they therefore are appropriate for genetic studies of BW–PO differences.[48] Furthermore, the molecular resources enabling detailed genetic and gene expression analyses have burgeoned in recent years.[13] Full sequencing of the BW (6-fold redundancy) and PO (2-fold) genomes is underway (http:/www.hgsc.bcm.edu/content/peromyscus-genome-project); the completed BW genome is currently undergoing annotation. The ability of BW × PO mating to produce fertile offspring enabled the construction of a complete linkage map composed of 185 type I (gene) markers and 155 type II (microsatellite) markers.[22] Furthermore, EST–transcriptome data from multiple tissues are available and steadily growing. In the current study, 2 traits draw particular attention for the degree of their BW–PO variation. PO cholesterol levels are almost 4-fold elevated over those of BW, and PO triglyceride levels are more than 2-fold higher than those of BW. Other BW–PO differences that might lend themselves to genetic analyses are total protein, albumin, globulins which all differ by 26% between the 2 species, and ALP which differs by 54% between the 2.

In Figure 2 are illustrated analytes whose (BW × PO) F1 hybrid values fell significantly outside (either greater than or less than) the values of the parental BW and PO stocks. These traits were the exceptions, in that most hybrid values fell close to or midway between the parental values. Accordingly, values for the number and proportion of neutrophils were lower in hybrids than the parental strains, and the proportion of lymphocytes—but not lymphocyte number—was greater in hybrid progeny than in the parents. This hybrid effect likely is centered on the reduced neutrophil concentration, which is responsible for the altered neutrophil and lymphocyte proportions. As noted earlier, (BW × PO) F1 hybrids manifest hybrid dysgenesis and are substantially smaller that either parent stock; whereas oversize embryos result from the reciprocal cross. Possibly the neutrophil effect is a manifestation at the cellular level of such dysgenesis. An alternate explanation is that multiple genes control a trait, with each species homozygous recessive for alternating ones.

In this scenario, hybrid values would lie outside of the parental values because the hybrids would be heterozygous for both genes. Similar phenomena have been observed regarding isoniazid sensitivity in inbred mice and their hybrids[44] and RBC osmotic fragility in inbred mice and their recombinant inbreds.[30] Additional segregation analyses are required to resolve these 2 possibilities. Similarly, among the serum biochemical traits, $CO_2$ concentration values were lower in hybrids than parents, whereas glucose values were higher in hybrids than parents. It is noteworthy that offspring of BW female ×PO male mice are viable but undersized at birth and into adulthood. Human infants that are born small for gestational age are likely to become diabetic with age.[28] The elevated glucose values in these hybrid offspring may be a reflection of this phenomenon. However, the hybrid values are more like that of PO mice in fasted glucose challenge tests;[33] therefore the interspecific differences in glucose homeostasis bear additional study as well.

The data presented provide the first comprehensive evaluation of the major blood cell and biochemical parameters of several *Peromyscus* species. This information serves as a useful baseline for comparisons with wild-caught specimens, to evaluate the extent to which there are similarities or differences associated with physiologic adaptation to various habitats (including contaminated sites), parasites, and microorganisms or to domestication and genetic drift. To facilitate utilization of this information, the raw data are available at http://ww2.biol.sc.edu/~peromyscus; these data can be downloaded and used for direct comparisons, as well as regression and correlation analyses.

## Acknowledgments

This work was partially funded by grants from the National Science Foundation (MCB-0517754) and NIH (P40 RR014279).

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