(NASA-CR-160401) SYSTEM PARAMETERS FOR ERYTHROPOIESIS CONTROL MODEL: COMPARISON OF NORMAL VALUES IN HUMAN AND MOUSE MODEL (General Electric Co.) 29 p HC A03/MF A01 CSCL 06C G3/51

N80-13759

Unclas 46339

160401

...D SYSTEMS DEPARTM...

GENERAL ELECTRIC

HOUSTON, TEXAS

TECHNICAL INFORMATION RELEASE

TIR 741-LSP-8024

FROM	TO
J. I. Leonard	J. A. Rummel, Ph.D./SE2

DATE	WORK ORDER REF	WORK STATEMENT PARA:	REFERENCE:
12-15-78		NAS9-15487	

SUBJECT System Parameters for Erythropoiesis Control Model: Comparison of Normal Values in Human and Mouse Model

The computer model for regulation of erythropoiesis, originally developed to represent human function, has been recently adapted to the mouse system. This was accomplished by altering the values of the system parameters describing fluid volumes, blood flows, metabolic rates, hematologic indices, etc. This report documents the values used in the mouse model and compares them to the original human model. In addition, the report summarizes the source documents and data used in obtaining the parameter values for the mouse and the rat. It is anticipated that a similar model for the rat will be implemented.

The capability of using models for two different species will greatly enhance the realism of the simulations and provide greater flexibility for spaceflight hypothesis testing. A companion report, TIR 741-LSP-8029, documents the validation of the mouse model and its utility in suggesting new experimental approaches.

The extensive literature search, summarized in the Appendices, which provided the basis for the new parameter values was conducted by Robert Chamberlain, a summer engineer trainee.

J. I. Leonard

Attachment
/db

CONCURRENCES

Counterpart:

Life Sciences Projects Unit Manager: DGFitzjerrel

Engrg. & Advanced Programs Subsection Mgr. CWFulcher

DISTRIBUTION

NASA/JSC:	GE/TSSD:
W. C. Alexander, Ph.D.	S. N. Brand
S. L. Kimzey, Ph.D.	D. J. Grounds
C. S. Leach, Ph.D.	R. Chamberlain
P. C. Rambaut, Sc.D.	V. Marks
	J. Leonard

Page No. 1 of 1

ASD 4028

SYSTEM PARAMETERS FOR ERYTHROPOIESIS CONTROL MODEL: COMPARISON OF NORMAL VALUES IN HUMAN AND MOUSE MODEL

Introduction

The computer model for erythropoietic control was adapted to the mouse system by altering system parameters originally given for the human to those which more realistically represent the mouse. Parameter values were obtained from a variety of literature sources as indicated in the Appendix* and in the Reference List. The immediate application of the mouse model was the study of the mouse as a potential experimental model for spaceflight. Data for the simulations were to be obtained from Dr. C.D.R. Dunn's experiments at the University of Tennessee Memorial Research Center and included studies of dehydration and hypoxia. The strain of mice used in these studies were C3H with approximate weight of 25 grams. Parameter values were chosen for this strain where possible. In certain cases, the literature values were superseded by values obtained directly from Dr. Dunn's studies. In a few cases mouse data were not available and data for the rat were substituted. Large variations in parameter values were usually observed as indicated in the Appendix, depending on mouse strain and investigator. The values finally chosen are, therefore, highly idealized.

Basic System Parameters

This report, in addition to documenting the source material, contains a comparison of system parameters for the mouse and human models as shown in Table I. Aside from the obvious differences expected in fluid volumes, blood flows and metabolic rates, larger differences were observed in the following: erythrocyte life span (126 d vs. 42.5 d)** erythropoietin

---

* The appendix also contains parameter values for the rat which were collected in anticipation of implementing a similar model for the study of that species.

** First and second numbers in parenthesis refers to human and mouse, respectively.

TABLE I

SYSTEM PARAMETERS FOR ERYTHROPOIESIS CONTROL MODEL

PARAMETER	MODEL SYMBOL	PARAMETER VALUE HUMAN	MOUSE	REF.	UNITS
* Red Cell Mass	RCM	2000	0.63	(10)	ml
* Plasma Volume	PV	3000	0.77	(10)	ml
Blood Volume	BV	5000	1.40	(10)	ml
Whole-Body Hematocrit	HCT	40.0	45.0	(10)	ml packed RBC / 100 ml blood
* Mean Corpuscular Hemoglobin Concentration	MCHC	0.375	0.300	(1)	gm Hb/ml RBC
Hemoglobin Concentration	-	15.0	13.5	(1,4)	gm Hb/100 ml blood
* O_2 Capacity of Blood	-	20.1	19.0	(4)	ml O_2/100 ml blood
O_2 Capacity of Hemoglobin	$CHBO_2$	1.34	1.41	(1,4)	ml O_2/gm Hb
* PO_2 tension at ½Hb Sat.	P50	27	39	(21)	mm Hg
* Arterial pO_2	PO2A	95	78	(12)	mm Hg
Arterial Hb Saturation	SO2A	.97	.99	(21)	percent
* Renal Metabolic Rate	MO2T	20	.04	(5)	ml O_2/min
* Renal Blood Flow	BF	1200	1.83	(16)	ml/min
* Normal Tissue pO_2	PO2T	20	20		mm Hg
* Erythropoietin Half-Life	EHL	12	3.25	(11)	hours
* Red Cell Life Span	-	126	42.5	(12)	days
* Erythrocyte Maturation Time	Z	4	3.5		days
* Normal RBC Production Rate	P	22	.0205	(12)	ml RBC/day
RBC Turnover Rate	RKC	1.1	3.26	(12)	percent/day

* Fundamental value from which other parameter values may be derived (see Table II)

TABLE II

RELATIONSHIPS USED TO DERIVE PARAMETERS IN MOUSE MODEL

1. Blood Volume $BV = RCM + PV = 0.63 + 0.77 = 1.4$ ml

2. Whole-Body Hematocrit

$HCT = RCM/BV = 0.63/1.4 = .45$ ml packed RBC/ml blood

3. Hemoglobin Concentration

$HB = HCT \times MCHC = 45 \times 0.3 = 13.5$ gm Hb/100 ml blood

4. O_2 Capacity of Hemoglobin:

$$CHBO_2 = \frac{O_2 \text{ concentration of blood}}{\text{Hb concentration of blood}} = \frac{19}{13.5} = 1.41 \text{ ml } O_2/\text{gm Hb}$$

5. Arterial Hb Saturation

SO2A = function (PO2A)

(see oxygen-hemoglobin dissociation curve, Figure 1)

6. RBC Turnover

RKC = turnover rate/100 = .693/RBC Half-Life

$= .693/42.5/2 = .0326 \text{ day}^{-1} = 3.26\%$ per day

Steady State Destruction Rate = RCM x RKC

$= 0.63 \times .0326 = .0205$ ml/day

half-life (12 hrs vs. 3.25 hrs) and normal arterial pO_2 (95 mm Hg vs. 78 mm Hg). The shorter life span of the mouse RBC implies a three-fold faster turnover of erythrocytes. That is, the daily rates of red cell production and destruction (as well as reticulocyte index) are about three times higher in the mouse than the human. Other parameters found to be more similar between the two species: hematocrit (40 vs. 45), mean corpuscular hemoglobin concentration (.375 vs .30) and maximum oxygen carrying capacity of hemoglobin (1.34 vs. 1.41).

Although the arterial pO_2 in the mouse is much lower than in the human, the oxygen saturation of hemoglobin of both species are nearly identical (97% vs. 99%). This is a result of the distinctly different oxygen-hemoglobin dissociation curves shown in Figure 1 and reflected in the different P50 values (26.7 vs. 39.0 mm Hg). The P50 differences implies that at the same level of tissue oxygen tension, oxygen is more easily unloaded in the mouse than in the human. It should be noted that the normal pO_2 of arterial blood assumed here (78 mm Hg) was obtained from rat data (Ref. 4 & 11) and has been used in a previous model validated for the mouse with reasonably good results (Ref. 20). No corresponding mouse data could be located.

Values for renal blood flow of the mouse was not available and data from rats were utilized (6 ml/min-gm tissue).

Scaled Parameters

Some parameters of the mouse model differ considerably from the human model due to scaling factors alone. That is, the values used in the model are given on an absolute basis for the whole animal rather than as a specific property in terms of "per gram of tissue." In terms of specific units the differences between the mouse and human system are much smaller as shown below.

TABLE III - ABSOLUTE VS. SPECIFIC PARAMETER VALUES

PARAMETER	ABSOLUTE UNITS HUMAN	ABSOLUTE UNITS MOUSE	SPECIFIC UNITS* HUMAN	SPECIFIC UNITS* MOUSE	
Red Cell Mass	2000	0.63 ml	28.6	25.2	ml/kg body wt.
Plasma Volume	3000	0.77 ml	42.9	30.8	ml/kg body wt.
Blood Volume	5000	1.40 ml	71.4	56.0	ml/kg body wt.
Renal Blood Flow	1200	1.83 ml/min	4.28	6.10	ml/min-gm tissue
Renal O_2 Consumption	20	0.04 ml/min	0.073	0.133	ml/min-gm tissue
Body O_2 Consumption	250	0.51 ml/min	0.00357	0.0255	ml/min-gm tissue

* Based on: Body Weight = 70 kg man and 25 gm mouse
Renal Mass = 280 gm (.4% BWt) in man and 0.3 gm (1.2% BWt) in mouse

Oxygen Balance

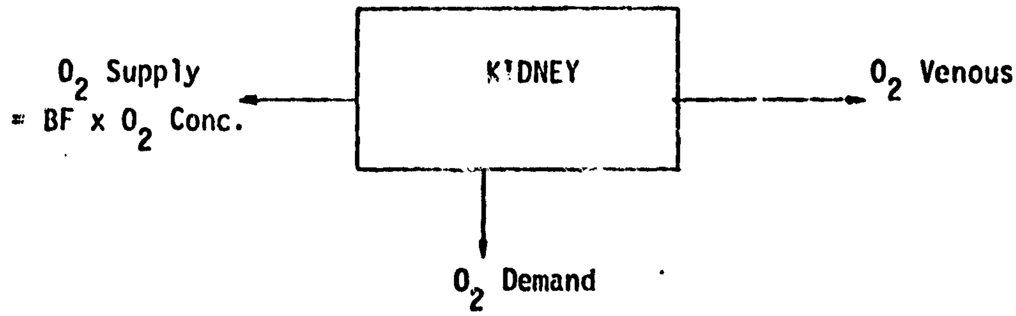
The balance of oxygen supply vs. oxygen demand is crucial to the feedback regulation of erythropoiesis. A parameter reflecting this complex balance is the tissue oxygen tension which is believed to govern the release of erythropoietin. The oxygen balances for the human and mouse systems as used in the model are given in Table IV.

Oxygen consumption per gm renal tissue in the mouse is about twice that for the human. (Overall total oxygen consumption per gm body weight is nearly seven times greater in the mouse.) This higher oxygen demand of the mouse is satisfied in two ways in the model: a) there is a 50% greater efficiency in oxygen extraction as indicated in Table IV. (Note that in both species the amount of oxygen delivered at rest is more than sufficient - i.e. roughly 10 times that required by the tissues.), b) there is a 30% higher blood oxygen supply per gm of tissue due to greater tissue blood flow in the mouse.

The resting tissue oxygen tension is arbitrarily assumed to be identical in both model systems; i.e., 20 mm Hg. The equation describing oxygen diffusivity to the tissues from venous capillaries is given in the steady-state as:

TABLE IV

OXYGEN BALANCE AT KIDNEY



		HUMAN	MOUSE
A.	<u>Oxygen Demand</u>	20	.04 ml O_2/min
		0.073	0.153 ml O_2/min-gm
B.	<u>Oxygen Supply Parameters</u>		
	PO_2, arterial	95	78 mm Hg
	SO_2, arterial	97.4	98.6 % saturation
	O_2 concentration	196	188 ml O_2/liter blood
	BF	1200	1.83 ml blood/min
	O_2 Supply Rate	235	.343 ml O_2/min
		.839	1 143 ml O_2/min-gm
C.	<u>Oxygen Venous Parameters</u>		
	PO_2, venous	56	57 mm Hg
	SO_2, venous	89	86 % saturation
	PO_2, tissue	20	20 mm Hg
D.	<u>Percent Oxygen Extraction</u>		
	$= \dfrac{O_2 \text{ Demand}}{O_2 \text{ Supply}}$	8.7%	13.4%

Net oxygen delivery = tissue oxygen consumption

$$= (pO_2,\text{vein} - pO_2,\text{ tissue}) \times K$$

where K = conductivity coefficient = O_2 Diffusivity x Capillary Surface Area

The ratio of K(man)/K(mouse) would be expected to reflect the surface area ratio between species if diffusivity were assumed similar in mouse and man. Therefore, if S = capillary surface area, then

$$\frac{S(\text{man})}{S(\text{mouse})} = \frac{K(\text{man})}{K(\text{mouse})} = \frac{O_2 \text{ consumption,man}}{O_2 \text{ consumption,mouse}} \times \frac{(pO_2,\text{vein} - pO_2,\text{tis}),\text{mouse}}{(pO_2,\text{vein} - pO_2,\text{tis}),\text{man}}$$

$$= \frac{20 \text{ ml/min}}{.04 \text{ ml/min}} \times \frac{(57.5 - 20)}{(56.4 - 20)} \text{ mm Hg} = 508$$

This is in good agreement with the surface area ratio of 650 of the glomerular derived from data in Ref. 5 (pg. 174) in the following way:

Let: R = glomerular radius = 37 μ (mouse) and 100 μ (man)

V = glomerular volume = 2.6 mm^3 (mouse) and 4600 mm^3 (man)

L = glomerular capillary length

S = glomerular capillary surface area

$$S = 2\pi R \times L \qquad \text{and } V = \pi R^2 \times L$$

Therefore, $S = 2\pi R \cdot V/\pi R^2 = 2V/R$

and

$$\frac{S(\text{man})}{S(\text{mouse})} = \frac{V(\text{man})}{V(\text{mouse})} \times \frac{R(\text{mouse})}{R(\text{man})}$$

$$= \frac{4600 \text{ mm}^3}{2.6 \text{ mm}^3} \times \frac{37\mu}{100\mu}$$

$$= 650$$

This agreement lends support to the general representation of the kidney in the computer model.

Functional Relationships

Three functional relationships are included in the computer model: a) oxygen-hemoglobin equilibrium curve (EC), b) erythropoietin release as a function of tissue pO_2, and c) erythrocyte production rate as a function of erythropoietin concentration. The first of these is shown in Figure 1 and will be described in detail below. The form of the function curves for erythropoietin and red cell release will be assumed identical in the mouse and human models (Figures 2 and 3). There is no reason at the present time to take issue with this assumption, particularly since the bone marrow function (Figure 3) was originally obtained from the mouse. These curves (as shown in Figures 2 and 3 and as used in the models) are represented in normalized form (i.e. % of control) so that any species may be represented. The gain factors, G_1 and G_2, representing the slope of the relationships, may be different between species. This is of little concern in the basic design of the model since these parameters will be adjusted during the simulation process and their actual values estimated by "fitting" the model output to the experimental data.

The equation describing the sigmoidal OEC is a form of the Hill equation and is shown in the insert of Figure 1. The two solid lines represent human and mouse blood, respectively, and were recently obtained from single blood samples in Dr. Dunn's laboratory. The value of P50 is explicitly stated in the equation so that shifts in oxygen-hemoglobin affinity may be easily described. The value of the exponent "K", found from the best fit of the mouse curve, also provides a good fit of the human curve as shown by the symbols in Figure 1. Thus, the only difference between the equation describing the human and mouse OEC is the value of P50. The dashed line in Figure 1 is a theoretical calculation of a P50 shift of +10 mm Hg from the standard mouse curve.

Simulations

A model representing the mouse system was implemented and verified as being substantially appropriate. The model presently exists on the UNIVAC 1110 and PDP 1140 systems at NASA/JSC as well as on the DEC facility at the University of Tennessee. Preliminary validation studies were performed and have been summarized in a companion report, TIR 741-LSP-8029.

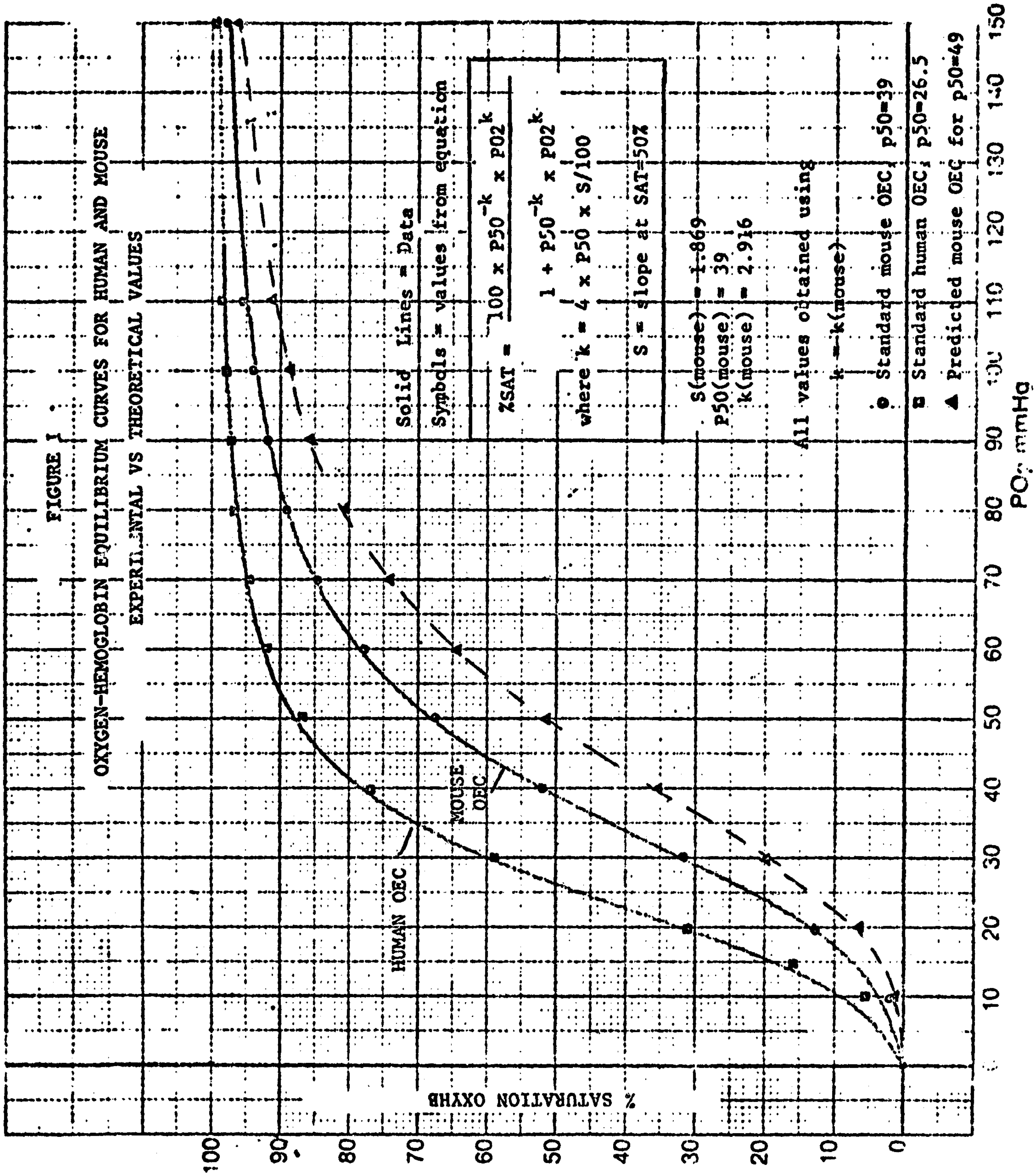
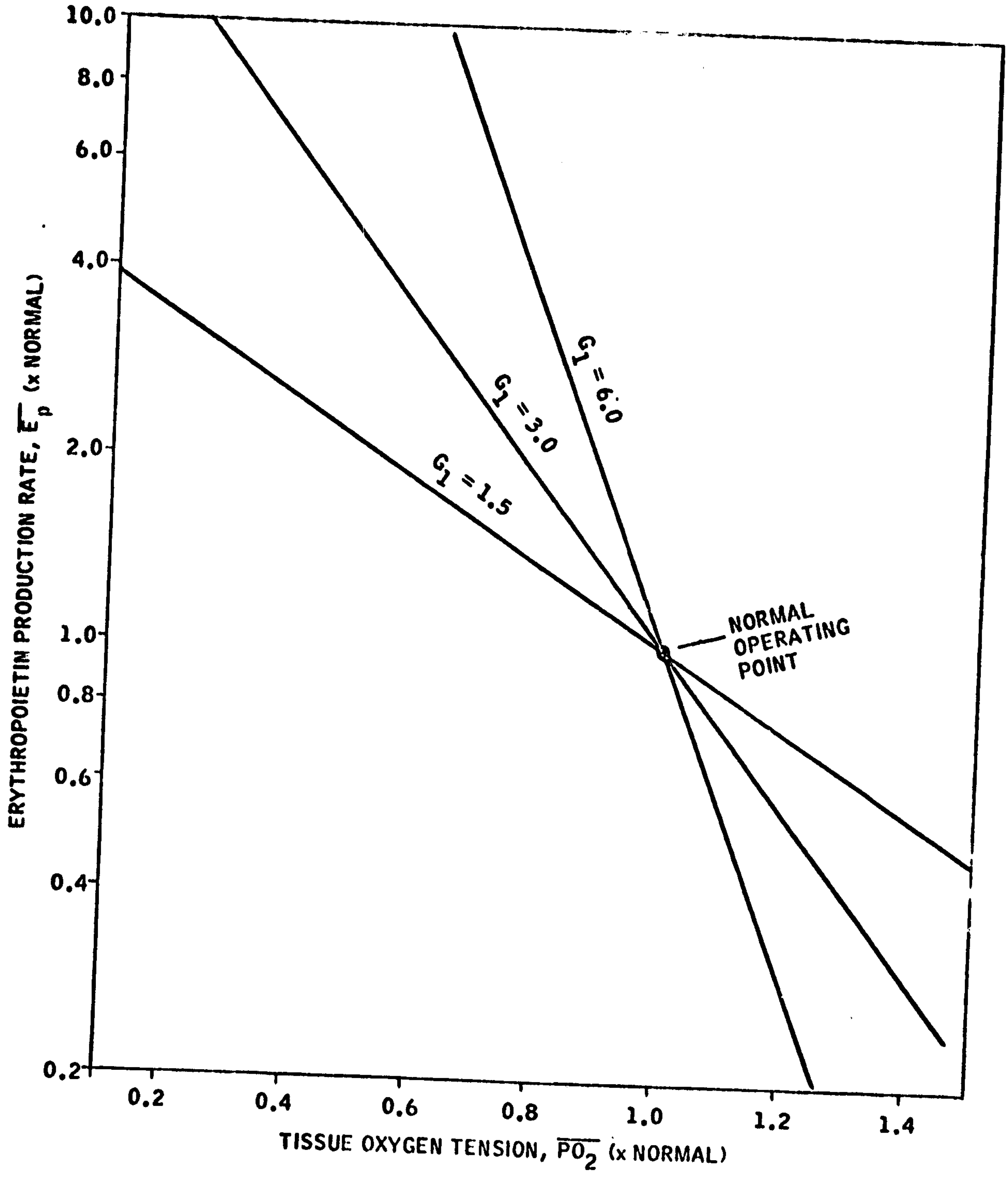


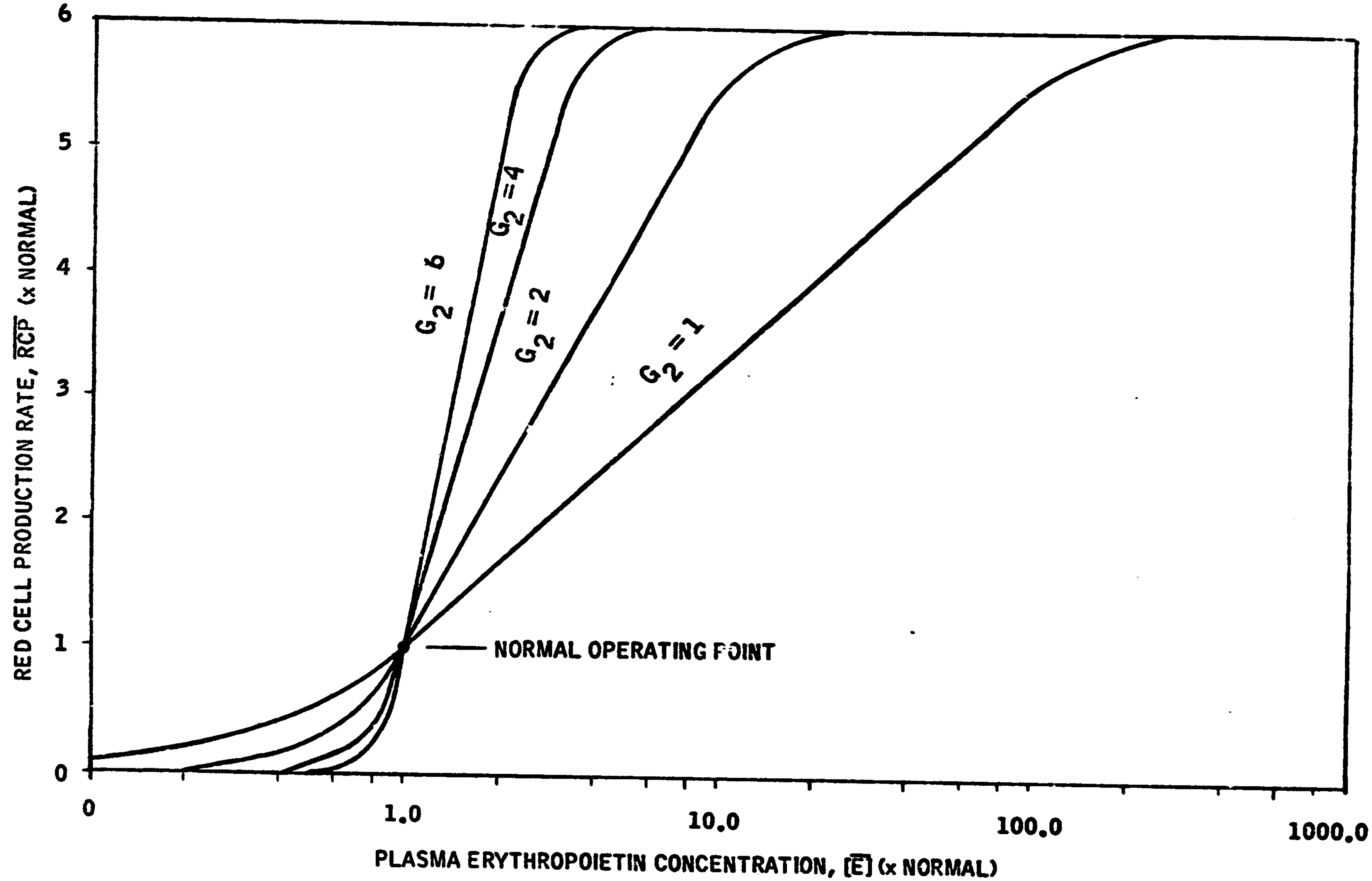
FIGURE I

OXYGEN-HEMOGLOBIN EQUILIBRIUM CURVES FOR HUMAN AND MOUSE
EXPERIMENTAL VS THEORETICAL VALUES



RENAL ERYTHROPOIETIN PRODUCTION RATE FUNCTION CURVES

FIGURE 2



BONE MARROW RED CELL PRODUCTION FUNCTION CURVES

FIGURE 3

REFERENCES

1. Green, Earl L.; Biology of the Laboratory Mouse; New York: McGraw-Hill, 1966; p. 351-372.

2. Goodman, Joan Wright and L. H. Smith. "Erythrocyte Life Span in Normal Mice and in Radiation Bone Marrow Chimeras." American Journal of Physiology, 200(4):764-770, 1961.

3. Schermer, Siegmund; Blood Morphology of Laboratory Animals; Philadelphia: F. A. Davis Co., 1967; p. 61-74.

4. Attman, Philip L., Dorothy S. Dittmer and Bethesda Maryland; Biology Data Book; Federation of American Societies for Experimental Biology, 1972; Volumes 1, 2, and 3.

5. Spector, William S.; Handbook of Biological Data; Philadelphia: W. B. Saunders Co., 1961.

6. Schmidt-Nielsen, Knut Stortebecker; Animal Physiology; Englewood Cliffs: Prentice-Hall, 1964.

7. Melby, E. C., Jr. and N. H. Altman; Handbook of Laboratory Animal Science; Cleveland: CRC Press, 1976.

8. Altland, P.D., et al. "Blood Gases and Acid-Base Values of Unanesthetized Rats Exposed to Hypoxia." American Journal of Physiology, 212(1): 142-148, 1967.

9. Mylrea, Kenneth C. and Peter H. Abbrecht." Hematologic Responses of Mice Subjected to Continuous Hypoxia." American Journal of Physiology, 218(4): 1145-1149, 1970.

10. Dunn, C.D. R. Private Communication. See also Effect of Dehydration on Erythropoiesis in Mice, Aviat. Space Environ. Med. 49: 990-993, 1978.

11. Abbrecht, Peter H. and Judith K. Littell. "Plasma Erythropoietin in Men and Mice During Acclimatization to Different Attitudes." Journal of Applied Physiology, 32(1): 54-58, 1972.

12. Abbrecht, Peter H. and Judith K. Littell. "Erythrocyte Life Span in Mice Acclimatized to Different Degrees of Hypoxia." Journal of Applied Physiology. 32(4): 443-445, 1972.

13. "Conference on Bone Marrow Transplantation and the Physiology of Hematopoietic Tissues." Experimental Hematology, no. 14. Paris, 1967.

14. Altland, P.D., et al. "Blood Gases and Acid-Base Values of Unanesthetized Rats Exposed to Hypoxia." American Journal of Physiology 212(1): 142-148, 1967.

REFERENCES (Continued)

15. Schermer, Siegmund; Blood Morphology of Laboratory Animals; Philadelphia: F. A. Davis Co., 1967; p. 41-60.

16. Arendshorst, William F. "Autoregulation of Blood Flow in the Rat Kidney." American Journal of Physiology 228(1): 127-133, 1975.

17. Heighley, Geoffrey. "Metabolic Fate of Erythropoietin." In Jacobsen, Leon O. and Margot Doyle's Erythropoiesis.

18. Jacobsen, Leon O. "Studies on the Production and Metabolism of Erythropoietin in Rat Liver and Kidney." In Jacobsen, Leon O.'s Erythropoiesis.

19. Kaneko, Jerry F. Comparative Erythrocyte Metabolism, Table I.

20. Mylrea, Kenneth C. and Peter H. Abbrecht. "Mathematical Analysis and Digital Simulation of the Control of Erythropoiesis." Journal of Theoretical Biology, 33: 279-297, 1971.

21. Ulrich, S., P. Hilpert, and H. Bartels. "Uber die Atmungrfunktion des Blutes von Spitzmausen wuBen Mausen und syrischen Goldhamstern." Pflugers Archiv. 277: 150-165, 1963.

APPENDIX

SYSTEM PARAMETERS FOR THE MOUSE[1]

STRAIN	RBC millions/mm^3	Hct. %	MCV,	Hb g/100 cc blood	Hb g/cc cells	Ret. %
A/J	9.42 ± 0.	42.5 ± 0.4	45.1 ± 1.4	12.9 ± 0.2	0.30	3.5
A/HeJ	9.48 ± 0.18	42.5 ± 0.5	44.8 ± 1.0	12.7 ± 0.2	.30	2.9
AKR/J	9.38 ± 0.24	45.6 ± 1.0	48.5 ± 1.6	13.9 ± 0.2	.30	2.3
BALB/e AnJ	10.14 ± 0.15	46.5 ± 0.8	45.9 ± 1.1	14.5 ± 0.2	.31	3.3
BALB/e J	10.51 ± 0.16	48.0 ± 0.7	45.7 ± 1.0	15.0 ± 0.2	.31	2.9
CBA/J	10.04 ± 0.27	45.0 ± 1.3	44.8 ± 1.8	13.5 ± 0.2	.31	2.6
C3H/J	8.79 ± 0.24	39.5 ± 0.7	44.9 ± 1.4	12.2 ± 0.4	.31	2.8
C3H/SeJ	9.63 ± 0.26	43.0 ± 1.0	44.7 ± 1.6	13.2 ± 0.3	.30	2.2
C57BL/6pJ	9.70 ± 0.15	43.4 ± 0.8	44.7 ± 1.0	13.0 ± 0.3	.30	2.5
C57BL/6J	9.66 ± 0.09	44.0 ± 0.4	45.5 ± 0.6	13.3 ± 0.2	.30	2.6
C57BR/edJ	10.54 ± 0.17	50.0 ± 0.5	47.4 ± 0.9	14.6 ± 0.2	.29	2.1
C576/HeJ	9.82 ± 0.20	50.6 ± 0.4	51.5 ± 1.1	14.9 ± 0.2	.29	2.6
DBA/1J	10.52 ± 0.27	43.8 ± 0.6	41.6 ± 1.2	13.2 ± 0.2	.30	1.5
DAB/WaJ	9.93 ± 0.27	43.0 ± 0.6	43.3 ± 1.1	12.5 ± 0.2	.29	2.6
DBA/2J	10.30 ± 0.25	42.6 ± 0.5	41.4 ± 1.1	12.7 ± 0.1	.30	3.1
I/J	10.27 ± 0.27	46.8 ± 0.7	45.6 ± 1.5	13.5 ± 0.1	.29	2.4
RHI/J	9.63 ± 0.25	44.5 ± 0.6	46.2 ± 1.3	13.7 ± 0.2	.31	2.8
ST/J	9.88 ± 0.19	44.1 ± 1.1	44.6 ± 1.4	1[illegible].1 ± 0.2	.31	2.1

MOUSE ERYTHROCYTES & HEMOGLOBIN

Author	#	RBC(millions)	Hb
Hirschfield 1897	6	5.2-9.15(7.06)	85-100(93.3)
Kabierski 1961	33	8.2-14 (10.7)	97.0
Levy 1926	55	5.5-13.98(9.8)	75-125 (97.1)
Klieneberger 1927	17	7.3-11.7 (9.7)	94-128 (116)
Haam 1931	20	8.16-11.46(9.42)	76-112 (94.2)
Albritton 1955	--	7.7-12.5(9.3)	10-19 (14.8) gm%
Schermer 1967	34	6.14-11.5(9)	70-103 (90)

RETICULOCYTE COUNT[3]

2.8 - 3.5% (Kunze)
3.2 - 8% (Isaacs)
1.8 - 1.9% (Schermer ——— larger values in juvenile mice)
40% at birth to 5% 6 weeks later (Seyfarth & Jurgens)
44$ at birth to 20% 14 days later (Kunze)

HCT. 41.5% (Albritton) (3)

Serum Viscosity 1.47 (Frank) 1.41 - 1.50 (3)

Specific Gravity of Blood 1.057 (Albritton) 1.052 - 1.062 (3)

ERYTHROCYTE AND HEMOGLOBIN VALUES

	RBC count million/ 1 blood	RBC packed volume ml/100 ml blood	RBC Volume μ^3	Hb g/100 ml blood	Hb g/100 ml RBC	RBC Hb Content pg	RBC Dimensions (6)
Musculus	9.3 (7.7 - 12.5)	41.5	49(48-51)	14.8(10-19	36 (33-39)	16(15.5-16.5)	6.0

RBC millions/mm^3	HCT ml/100 ml	Reticulocytes % of total RBC	RBC diam. μ [dry film]	RBC vol. cu μ	Blood (Hb) g/100 ml blood	RBC (Hb) g/100 ml RBC	RBC Hb content $\mu\mu$g	
9.3(7.7-12.5)	41.5	4.0	6.0	49(48-51)	14.8(10-19)	36 (33-39)	16 (15.5-16.5)	(5)

	RBC/mm^3 x 10^6	HB g/100 ml	PCV %	MCV cuμ	MCH $\mu\mu$g	MCHC %	Retics %	(7)
C57Bl/6xA 6	8.6	14.8	43	49	17	35	---	
Charles River	7.9	11.9	41	52	15	29	---	
C57Bl/6Jax	10.0 (9.9)	16.2 (13.4)	48 (45)	48 (45)	16 (13)	34 (30)	---	(2.5)
Strong CBA	9.0	15.3	---	---	17	---	---	
C57Bl	7.4	12.7	42	57	17	30	0.8	
Final Est.	8.6	14.2	45	51	17	33	2.0	

	HCT %	[Hb] g/100 ml	RBC count millions/mm^3	(9)
mouse	50	16.7	10.5	

HCT %	RBC (No. x 10^6/ μ l)	(10)
47.9 $\pm$ 0.7	9.5 $\pm$ 0.8	

OXYGEN

TENSION OF 1/2 SATURATION

pCO_2 mm Hg	pH	Temp. °C	Tension 1/2 sat mm Hg (5)
40	---	38	72

EHL

	RBC LIFESPAN	HALF-LIFE	RBC LIFESPAN AND/OR 1/2 LIFE PROCEDURE USED FOR DETERM.	
TE	40-43 days		C^{14}- labeled glycine or Hb precursor	
C3H	40-43 days		C^{14}- labeled glycine or Hb precursor	
(C57 BL x CBA) F_1	40-43 days		in vivo P^{32}-labeled duropropylfluorophorphate	
		20 days	transferred isologous normal C^{51}-labeled (Goodman & Smith)	
		25.6 days	transferred isologous C^{51}-labeled (Bernstein)	(1)
sev. inbred strains (avg.)	50-55 days	15-20 days	" " " "	
DBA/2		19.7 (18.5-- 20.8) days	" " " "	
BALB/C		16.6 (11.5 - 20.3) days	" " " "	
(BALB/C x A/JAX) F_1		15.0 (12.5 - 17.2) days	" " " "	
(C57BL/6 x DBA/2)F_1		19.0 (17.5 - 20.3) days	" " " "	
(C57L x A/JAX)F_1		17.6 (14.8 - 19.7) days	" " " "	(2)
(C57BL x 101)F_1		19.7 (16.1 - 21.7) days	" " " "	
(C3H x 101)F_1		18.4 (13.1 - 22.7) days	" " " "	
(101 x C3H)F_1		16.6 (14.1 - 19.4) days	" " " "	
Sprague-Dawley Rats	60 days	19 (15.8 - 20.5) days	" " " "	

RBC Life Span of about 20 days (Guess)[9]

ERYTHROPOIETIN HALF-LIFE (IN PLASMA)[11] => 3.25 Hours

Normal erythropoietin level = 0.02 units/ml (Int. Ref. Prep. units/ml) in plasma

Blood volume est. at 7% of total body weight

Maximum erythropoietin level = 0.3 units/ml in plasma at 14,500 ft (440 mm Hg)

ERYTHROCYTE LIFE SPAN[12]

Method used was intraperitoneal injection of 1 μ c of	46.9 days at 1 atm
raticactively labelled diuropropyl phorphorofluorodate	44.0 days at .7 atm
$\left[DF^{32}P\right]$ => very accurate at S.S.	39.2 days at .5 atm

Normal life span using ^{51}Cr dilution has been det. to be from 23-63 days;
19 days using the sulfhemoglobin method.

two other studies by Van Putten using $DF^{32}P$ => 40.7 and 44.6 days

DATA FOR CONSTRUCTING BLOOD OXYGEN DISSOCIATION CURVES(4)

	Blood or Blood Fraction	Solvent $\left[P_{CO_2}, \text{mm Hg}\right]$	pH	Temp. °C	P50 mm Hg	BOHR Effect	n $\left[\Delta \log P_{50}/^{\circ}C\right]$
Mus Musculus	Whole Blood	-----	7.40	37	52	----	----
		[40]	7.4	37	41.5	----	----
	Free Solution	0.03 M PO_4	6.8	37	34.2	----	----
		0.1 M PO_4	---	20	12.3	-0.93	2.4
		0.1 M PO_4	7.16	35	26.0	-0.96	2.80

MORPHOMETRIC PARAMETERS OF LUNG (4)

	#	Wt, kg	lung volume, ml	Alveolar surface, m^2	capillary surf, m^2
mouse	5	0.023 ± 0.002	0.74 ± 0.075	0.068 ± 0.009	0.059 ± 0.006

Capillary volume, ml	0.084 ± 0.009
Mean thickness of alveolar - capillary tissue barrier, μm	1.25 ± 0.08
Harmonic mean barrier thickness, μm	0.32 ± 0.0006
Minimal barrier thickness,	0.15
Harmonic Mean thickness of plasma layer, μm	0.11 ± 0.002
Maximal diffusion capacity of lung	0.147 ± 0.015
Ratio of capillary to alveolar surface	0.87
Capillary volume per alveolar surface, ml/m^2	1.23

Mus musculus

LUNG VENTILATION

Respiration Freq. breath/min.	Tidal Volume (ml)	Minute Volume (L) $\left[\begin{matrix}\text{(resp.freq.)}\\ \times\ \text{T.V.}\end{matrix}\right]$ (5)
163 (84 - 230)	0.15 (0.09-0.23)	0.023 (0.011 - 0.036)

TISSUE OXYGEN CONSUMPTION

Mouse	Med.	$-Q_{O_2}$	Tissue	Medium	$-Q_{O_2}$
			Mouse (concluded)		
Adrenal	A	6.0	Ovary	A	9.0
Brain cortex	D^1	32.9	Placenta, 0.4 mg	A	7.5
Cerebral cortex	E	11.0	10.9 - 13.7 mg	A	6.4
Embryo	B_1	10.4	Pituitary	A	8.0
Kidney cortex	D^1	46.1	Skin, newborn	B_1	6.1
Liver	B	8.8-13.8	Spleen	D^1	16.9
Liver	E_1	18.7			
Liver	D^1	23.1			
Lung	B_1	7.3- 8.0			
Lung	D^1	12.0			

A = Serum

B = Ringer Glucose

D = Ringer Phosphate Ca^{++} free

E = Ringer Solution

OXYGEN CONSUMPTION (4)

#	Body Wt. gm	Ambient Temp. °C	O_2 Consumption ml/gm hr	Deviation %
47	35.7	32	1.59	+ 4.6

OXYGEN CAPACITY AND BOHR EFFECT (4)

#	Method of Measurement	Temp. °C	P_{50} mm Hg	O_2 Capacity ml O_2/100 ml blood	BOHR Effect
31	micromanometric	37.0	34	19	0.63

Arterial PO_2 => 78 mm Hg (11,20)

Maximum O_2 capacity of Hb => calculated => 1.41 using 13.4 g Hb/100 ml blood (1) and 19 ml O_2/100 ml blood as oxygen capacity (4)

BODY TEMPERATURE [5]

	°C
Mouse, deer (Peromyscus leucopus)	37.4(33.6-41.2)
Mouse, deer (P. maniculatus)	37.9(35.7-40.1)
Mouse, house (Mus musculus)	36.5(35.2-37.9)
Mouse, jumping (Zapus hudsonicus)	37.3(35.3-39.3)
Mouse, meadow (Microtus pennsylvanicus)	39.3(34.7-43.1)
Mouse, pocket (Perognathus hispidus)	36.5(34.9-38.1)
Mouse, red-backed (Clethrionomus gapperi)	37.3(35.3-39.3)
Mouse, red-backed (C. rutilus)	38.3(36.6-40.0)

BLOOD PRESSURE mm Hg [5]

SYS	DIA
147 (133-160)	160 (102-110)

HEART RATE beats/min [5]

Mus musculus	600 (328-780)
Peromyscus rp. (deer)	534 (324-858)

BLOOD VOLUME [3]

2-2.5 ml (Isaacs) in a 25 gm mouse
7.6% of body weight (6.3-8.3) Welker
6.6% of body weight (5.4-8.3) Jolly & Lafond

PLASMA VOLUME [5]

57.4 ml/kg (dessication)

BLOOD INDICES ARE GREATLY INFLUENCED BY NATURE OF BLOOD SAMPLING, AGE [3]

	Venous blood from tail			Blood from femoral artery		
	RBC's	Hb (%)	WBC	RBC	Hb (%)	WBC
1	10.6	120	16,000	10.25	120	8,250
2	10.745	125	13,000	10.625	125	10,568
3	11.225	125	31,600	11.03	125	10,900
4	12.385	133	16,086	10.475	133	7,500
5	8.89	-	18,500	9.2	95	6,200
6	11.64	-	12,750	8.75	120	6,000
7	9.15	-	7,000	7.73	95	2,000

Erythrocyte counts are 1.3 million higher on the average if tail is immersed in warm water.[3]

	RANGE OF VARIATION	MEAN VALUE [3]
RBC	6-2 million	9 million
Reticulocytes	2-5%	3%
Hemoglobin	70-100%	90%

KIDNEY MEASUREMENTS(5)

	Body wt. (kg)	Wt. of 1 Kidney g	Wt. of 1 Kidney % body wt.	Radius (μ)	1000's/kidney	Glomerulus Vol/kidney cu mm	Glomerulus Vol/g Kidney cu mm
Mouse	0.02	0.12	0.61	37	12.4	2.6	21

Specific gravity of whole mouse blood is 1.057 (1.052 - 1.062) (5)

Spleen and bone marrow transit time => 3-4 days(1)

Renal mass = 0.12 g or 0.61% BW (5)

HEPATIC BLOOD FLOW (4)

Mouse	Anesthetized	Det. by ext. counting of head		(93-103)
		Single injection of colloidal $\left[{}^{198}Au.\right]$ gold	$63.0 \frac{ml*kg}{min}$ *body wt.	$102\ ml*min^{-1}*100g*liver^{-1}$
		ICG Injection		$35\ ml*min^{-1}*100\ g*liver^{-1}$

SYSTEM PARAMETERS FOR THE RAT[4]

RBC Count millions/μl blood	PCV RBC Packed Vol. ml/100 ml blood	RBC Vol. μ^3	(Hb) g/100 ml blood	g/100 ml RBC	RBC Hb Content pg	RBC Dimensions	μ
8.9 (7.2 - 9.6)	46 (39 - 53)	61 (57 - 65)	14.8(12.0-17.5)	32 (30 - 35)	17 (15 - 19)	7.5 (6.0 - 7.5)	

RBC millions/mm³	HCT ml/100 ml	Reticulocytes % of total RBC	RBC Diameter (Any film) μ	RBC Volume μ^3	Blood (Hb) 2/100 ml blood	Blood (Hb) 2/100 ml RBC	RBC Hb Content μμg
8.9 (7.2 - 9.6)	46 (39 - 53)	2.9 (0.6-4.9)	7.5(6.0-7.5)	61(57-65)	14.8(12-17.5)	32 (30-35)	17 (15-19)

	RBC/mm³ x 10^6	HGB g/100 ml	PCV %	MC. cu	MCH μμg	MCHC %	Retics % [7]
Chas.River	8.2	15.7	40	49	20	40	---
	7.5	15.4	38	52	21	40	---
Wistar	7.9	16.6	53	67	21	31	---
	7.5	16.4	52	70	22	31	---
	7.7	17.0	49	64	22	35	---
	7.2	16.7	48	67	23	35	---
Long-Evans	7.1	14.2	43	61	20	33	0.99
Mixed Stock	6.6	13.0	39	61	20	32	---
Sprague Dawley	6.1	13.5	40	65	22	34	---
Fischer Axenic	9.0	14.6	47	54	16	31	---
	8.0	13.8	44	58	17	31	---
	8.2	14.8	43	53	18	35	---
Final Est.	7.3	15.2	45	62	21	34	0.7

#	HCT %	Hb	determined by co method at sea level[14]
10	40.8	13.1 g/100 ml; 2.39 g total	
53	49.4	15.0 g/100 ml	RBC millions/μl / 9.1 ml

RBC/mm³	HTC %	Hb g% [13]
8.4 x 10^6 ± 2.5	43 ± 5.2	12.0 ± 0.52

RETICULOCYTES %

2.9 (0.6 - 4.9)	Albritton
2-5	Scherher
2.3	Hulse
3-5	Seyfarth

RBC DIAMETER μ

6.2 (5.7 - 7)	Klieneberger
6.8 (6.0 - 7.5)	Albritton

HEMOGLOBIN gm/100 ml[15]

16.5 (11.4-19.2)	Wirth
14.8 (12- 17.5)	Albritton
15.4	Hulse

HEMATOCRIT %

50	Ferris & Griffith
46 (39-53)	Albritton
50.5	Hulse

DATA FOR CONSTRUCTING BLOOD OXYGEN DISSOCIATION CURVES(14)

	Blood or Blood Fraction	Solvent (PCO_2, mmHg)	pH	Temp. °C	P_{50} mmHg	BOHR Effect	m $\Delta \log P_{50}/°C$
Rattus norvegicus	Whole Blood	40	7.4	37	38	---	---
Long-Evans	Whole Blood	35	-	37	49	---	---
	Free Solution	0.1 M PO_4	7.40	20	6.0	-0.78	---
White	Whole Blood	---	7.40	37	38	---	---
	Free Solution	0.03 M PO_4	7.2	37	19.7	---	---
Wild	Whole Blood	---	7.40	37	39	---	---
	Free Solution	0.03 M PO	7.2	37	20.3	---	---

	#	Method of Measurement	Temp. °C	P_{50} mmHg	O_2 Capacity ml O_2/100 ml blood	BOHR Effect
Rattus norvegicus, Wistar I	16	Micromanometric	37.0	35	23	---

Body Temp. °C	Sample Blood	Plasma pH (7.26-7.44)	Hb* mM/L	Cell Vol. %	CO_2 COMB Power mM/L	CO_2 Total mM/L	CO_2 Pressure mm Hg	H_2O g/L
38.2	Arterial	7.35	9.0	46	19.5	24 (20-28)	42	946

* Assumed [ ] of 20 mM Hb/L RBC; 1 mM (single Fe - atom structure, molecular weight 16,500) combines with 22.4 ml of O_2, S.T.P. when saturated.

* 1/2 sat (tension of 1/2 saturation) of rat in mm Hg at 37°C and pH of 7.4 is = 40

Tidal Vol. (ml)	Minute Vol. (L)
1.5 (1.4-1.6)	0.100 (0.075 - 0.130)

Respiratory Exchange Characteristics = RQ or CO_2/O_2 is 0.894 (0.754 - 1.072)

TISSUE OXYGEN CONSUMPTION(15)

1 atm 37°C

Tissue	Medium	$-QO_2$
32 Kidney	M	15.8
33 Kidney	N	38.0
34 Kidney	O	23.2
35 Kidney	L	23.1
36 Kidney	I	34.0
37 Kidney	K_1	26.0
38 Kidney Cortex	D	38.2
39 Liver	C	7.2
40 Liver	L	8.1
41 Liver	I	9.0
42 Liver	I	10.7
43 Liver	J_1	25.0
44 Liver	D	17.2
45 Liver fetus	A,B	7.1

cu mm O_2 per mg dry wt. tissue in one hour

A = Serum
B = Ringer
D = Ringer Phosphate
I = Lactate
J = Succinate
K = Pyruvate
L = Glucose
M = No substrate added
N = Alanine
O = Butyrate

Intravenously injected erythropoietin 1/2 life in plasma is 1 hour[17]

Long-Evans ♀ Rats

Erythropoietin 1/2 life is 1-5 hours

Half life of ESF in perfused Rat Liver is 3.5 hours

RBC Life span = 55 days[19]

Erythrocyte Life Span and Half Life[2]

Sprague-Dawley   60 days life span and 19 days half life

Rattus norvegicus body temperature of 37.3 (34.5-40.0)°C [5]

BLOOD VOLUME

Blood Volume = 5.29 ml/100 gm BW[18]

Blood Volume[15]

5-8% of body weight (Schulz and Von Kruger)

6.7 ml/100 gm body weight (Cartland & Koch)

HEPATIC BLOOD FLOW[14]

Rat	Normal	Single injection of colloidal	I - albumin	66.2 ml min^{-1} kg body wt^{-1}
	Normal	Thermoelectric		79 (75-92) ml. min^{-1} 100g $liver^{-1}$
	Anesthetized	Thermoelectric		42 ml min^{-1} 100 g $liver^{-1}$

KIDNEY FUNCTION[15]

S.A. = surface area = 0.18 sq. m in 0.2 kg rat

Effective renal blood flow	8 ml/min	221 ml/min per sq. m. S.A.
Effective renal plasma flow	4.4 ml/min	145 ml/min per sq. m. S.A.
Glomerular Filtration rate	1.7 ml/min	40 (23-96) ml/min per sq. m. S.A.
Filtration fraction GFR/ERPF [(% Plasma filtered)]	28	

PLASMA VOLUME ml/kg[15]

Very young	54.7 (49.6 - 59.8)	♂ 290-350g	45.1 (31-59)
Pubescent	65.0 (59.2 - 70.8)		
Adult	41.5 (29.5 - 53.5)		

Comparison of mean values for total blood flow (RBF) in one kidney in vivo by different techniques in nondiuretic rats (16)

Technique	RBF ml min	Mean AP mmHg [a]	Strain of Rat [b]	No. of Animals
Electromagnetic flow transducer	6.0 g KW[c]	114	SD	13
	6.1 g KW[d]	112	SD	6
PAH clearance	6.2/g KW[d]	112	SD	6
	5.4/g KW	112	W	6
	6.5/g KW[f,g]			28
	6.4/250 g BW[g,h,i]			124
	6.2/250 g BW		SD	7
	5.5	112	SD	9
	6.6	120	SD	8
	3.9/250 g BW[j,k]		W	10
	8.5/g KW		W	10
Microsphere	5.8		SD	11
Antiglomerular basement membrane Antibody	6.8/g KW		SD	14
	7.5		SD	6
	6.3	127	SD	6
K uptake	4.4/250 g BW			17
	7.1/250 g BW			23
RH uptake	3.6/g KW		W	
Macro puncture of superficial nephrons	4.8	130	MW	7
	4.8	122	MW	8
	3.9	109	MW	18
XE washout	4.2/g KW			28
	3.4/g KW	114	W	15
Renal venous outflow	3.5/250 g BWk		W	20
	3.9/250 g BWk		W	16
High frequency microcinematographic	3.1/250 g BWk		W	9

VISCOSITY OF BLOOD (15)

min	1.44
max	1.96
avg.	1.54

RENAL BLOOD FLOW (16)

Arterial pressure mmHg	Blood flow
>100	6 ml/min .g kidney wt.

EFFECT OF VARIATIONS IN ARTERIAL PRESSURE ON RENAL BLOOD FLOW AND RENAL VASCULAR RESISTANCE[16]

	PRESSURE RANGE										
	40-50	50-60	60-70	70-80	80-90	90-100	100-110	110-120	120-130	130-140	140-150
AP, mm Hg	45.3 ± 3.2	54.5 ± 2.0	64.6 ± 0.9	75.2 ± 1.0	84.9 ± 1.1	94.5 ± 1.2	104.7 ± 1.3	114.0 ± 1.4	123.1 ± 2.9	132.7 ± 1.5	144.4 ± 2.2
RBF, ml/min.g KW	2.82 ± 0.69	3.39 ± 0.65	4.29 ± 0.82	4.76 ± 1.05	5.24 ± 1.05	5.66 ± 0.91	5.90 ± 0.93	5.95 ± 0.82	6.05 ± 0.88	6.13 ± 0.80	6.14 ± 0.86
RVR, mmHg/ml. min.g KW	14.9 ± 2.9	15.1 ± 2.9	14.4 ± 2.9	15.5 ± 3.6	15.9 ± 3.7	16.2 ± 2.8	17.3 ± 3.1	18.8 ± 3.1	20.1 ± 3.2	21.2 ± 2.9	23.2 ± 3.2
No. of animals	9	12	12	13	13	13	13	13	13	12	5

Values are means ± 1 SD.

SPECIFIC GRAVITY OF BLOOD[5]

Whole	1.054 (1.046 - 1.061)
Plasma	1.023 (1.018 - 1.028)

HEPATIC BLOOD FLOW[4]

Basal thermoelectric 79 (75-92) ml/100g tissue per min.

ARTERIAL BLOOD PRESSURE mm Hg[4]

Sys.	Dias.
116 (88-130)	90 (60-100)

CAPILLARY BLOOD PRESSURE (MESENTERY) cm H_2O[4]

Arterial	Venous
30.0 (22.0 - 34.0)	17.0 (15.0 - 20.0)

CARDIAC OUTPUT (4)

	Body Wt. (kg)	S.A. (sq. m.)	Stroke Vol. ml/beat	L/min Cardiac Output	L/sq m/min Cardiac Index
Anesthetized	0.18	0.0[illegible]	1.3 - 2.0*	0.047 (0.015-0.079)	1.[illegible]

* .5 ml/kg = > animals 2.5-4 kg

HEART RATE Beats/min (4)

328 (261 - 600)

Cardiac Output = 286 ml/kg min
Heart Rate = 420 beats/min
Arterial Blood Pressure = 130

Arterial Oxygen Saturation = 91.3%

	Range of Variation	Mean (15)
RBC	5.5 - 10 million	8 million
Retics	2-5%	---
Hb%	80-129	100
Hb gm/100 ml	11.4 - 19.2	16.0

Max. O_2 Capacity of Hb is 1.55 (calculated)

Renal Mass is .37% BW

2.8 ± 0.1 ml RBC/100 gm BW

O_2 Capacity of Blood is 23 ml O_2/100 ml blood

MORPHOMETRIC PARAMETERS OF LUNG (4)

Number of Subjects	8
Body Wt., kg	0.14 ± 0.007
Lung Vol., ml	6.[illegible] ± 0.[illegible]
Alveolar surface, m^2	0.39 ± 0.02
Capillary surface, m^2	0.41 ± 0.02
Capillary Vol., ml	0.48 ± 0.02
Mean thickness of alveolar - capillary tissue barrier, μm	1.42 ± 0.07
Harmonic mean barrier thickness, μm	0.38 ± 0.02
Harmonic mean thickness of plasma layer, μm	0.18 ± 0.005
Minimal barrier thickness	0.15
Maximal diffusion capacity of lung	0.83 ± 0.03
Minimal diffusion capacity of lung	----
Ratio of capillary to alveolar surface	1.05
Capillary volume per alveolar surface	1.23

	#	Body wt.g	Temp. °C Body	Temp. °C Ambient	O_2 Consumption ml g^{-1} hr^{-1}	Deviation %
Rattus norvegicus	40	545	37.5	28	0.84	+15

MEASURED VALUES CALCULATED VALUES(14)

Rat No.	Hct	OXYGEN Capacity, mM	OXYGEN Content, mM	OXYGEN Satur., %	pH	(CO_2)b, mM	P_{CO_2}, mmHg	(HCO_3^-)p, mEq/liter	Buff. base, mEq/liter
1	50	8.2	7.8	95.1	7.39	21.4	43.5	25.8	50.0
2	45	8.5	8.2	96.5	7.39	18.6	36.0	21.6	45.0
3	45	9.4	8.2	87.2	7.41	20.4	38.0	24.0	47.7
4	42	8.1	7.2	88.9	7.42	20.7	37.0	23.8	47.7
5	44	8.4	7.7	91.7	7.42	17.7	32.8	20.1	44.0
6	42	8.3	7.3	88.0	7.33	19.0	[illegible]	21.6	46.5
7	46	8.6	8.0	93.0	7.41	21.2	40.0	25.0	50.0
8	46	8.9	8.2	92.1	7.39	19.1	37.4	22.3	46.0
9	45	9.1	8.1	89.0	7.39	20.9	40.0	23.9	46.7
Mean	45.0	8.6	7.9	91.3	7.40	19.9	38.0	23.1	47.1
± SD	2.4	0.44	0.39	3.19	.015	1.32	3.12	1.83	2.04
± SEM	0.80	0.15	0.13	1.06	.005	0.44	1.04	0.61	0.68

In this and subsequent tables, b = blood; p = plasma