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NORMAL PHYSIOLOGICAL VALUES FOR CONSCIOUS PIGS USED IN BIOMEDICAL RESEARCH

J.P. Hannon, C.A. Bossone,
and
C.E. Wade

DIVISION OF MILITARY TRAUMA RESEARCH

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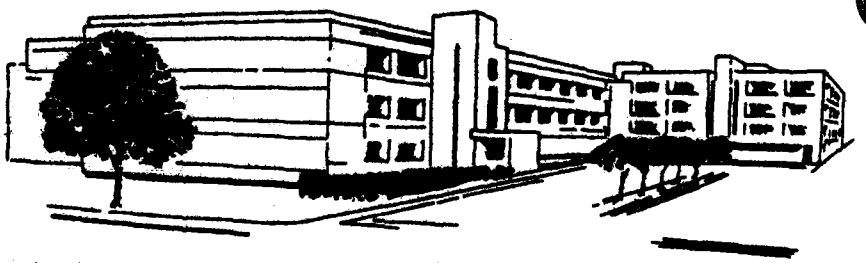

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Normal Physiological Values for Conscious Pigs Used in Biomedical Research,Hannon,J.P., et al

In conducting the research described in this report, the investigation adhered to the "Guide for the Care and Use of Laboratory Animals," as promulgated by the Committee on Revision of the Guide for Laboratory Animal Facilities and Care, Institute of Laboratory Animal Resources, National Research Council.

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Although the domestic pig is rapidly becoming an animal of choice in certain areas of biomedical research requiring a large animal model, effective utilization of the species is often encumbered by a lack of reference values for common functional variables. To address this problem, normal data for over 100 physiologic or related variables were collected from conscious chronically instrumented animals that were maintained under near basal conditions. Included were measurements of body composition, fluid volumes, blood physical and biochemical characteristics, blood gas and acid-base status, plasma hormone levels, energy metabolism, renal function, hemodynamics and pulmonary function. Most porcine values were similar to those collected under comparable conditions from humans.

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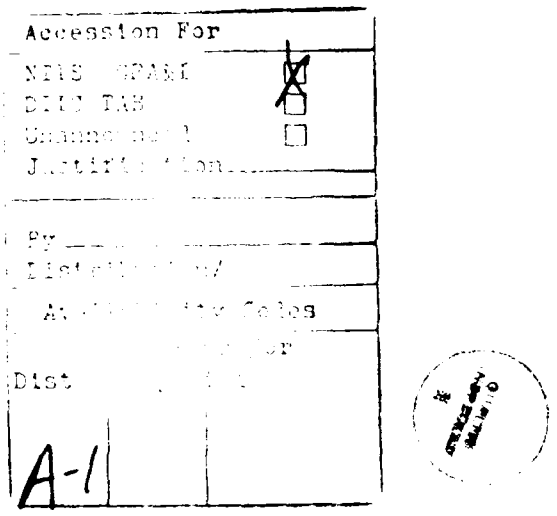
ABSTRACT

Although the domestic pig is rapidly becoming an animal of choice in certain areas of biomedical research requiring a large animal model, effective utilization of the species is often encumbered by a lack of reference values for common functional variables. To address this problem, normal data for over 100 physiologic or related variables were collected from conscious chronically instrumented animals that were maintained under near basal conditions. Included were measurements of body composition, fluid volumes, blood physical and biochemical characteristics, blood gas and acid-base status, plasma hormone levels, energy metabolism, renal function, hemodynamics and pulmonary function. Most porcine values were similar to those collected under comparable conditions from humans. Compared to adult man, however, pigs had higher values for extracellular space, plasma volume, arterial pH, plasma bicarbonate, cardiac output, arterial pressure, expired ventilation, heat production, and core temperature, and lower values for red cell volume, hemoglobin level, plasma osmotic and oncotic pressure, arterial O_2 content, renal blood flow, and glomerular filtration rate. Many of these deviations were due to immaturity. Nevertheless, we have found pigs to be an excellent large animal model for a variety of functional studies.



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NORMAL PHYSIOLOGICAL VALUES FOR CONSCIOUS PIGS USED IN BIOMEDICAL RESEARCH

John P. Hannon, Carol A. Bossone, and Charles E. Wade

INTRODUCTION

Over the past 10 to 15 years swine have become increasingly popular as a large animal model for biomedical research. Two recent symposia (1,2) and an entire issue of Laboratory Animal Science (3) have been devoted to the subject. In large measure, this popularity stems from the many anatomical and functional similarities of swine and humans, the ready availability of animals with predetermined characteristics, and the amenability of pigs to a wide variety of experimental procedures. At the present time, however, these attributes are frequently compromised by a paucity of reference data on the functional and related characteristics of conscious pigs.

Until recently, most porcine research has been directly or indirectly concerned with the commercial aspects of meat production, and results obtained in such studies are often of limited utility to the biomedical scientist. An investigator, for example, might desire reference data describing ventilatory functions of conscious swine, but a search of the scientific literature shows that these measurements are rarely made. Available reports on normal values for swine have been concerned almost exclusively with hematological or blood chemical characteristics (4-9). In fact, we are aware of only two reviews (10,11) of limited scope that summarize normal values for the functional characteristics of conscious swine, and even in these instances the authors note a lack of consistency in published data. Normal values summarized in these reviews are derived almost entirely from control measurements associated with a variety of subsequent experimental procedures. Diverse conditions attending these experiments probably account for most of the inconsistencies noted by reviewers (10,11).

In the present report we provide reference data for many common physiological, biochemical and related variables that characterize the normal resting pig. These data were collected during the course of a wide range of biomedical studies conducted over the past 15 years, but in all instances the measurements were taken from conscious, chronically instrumented animals maintained under precisely defined experimental conditions. Values so obtained have

shown reasonably good consistency not only from one experiment to the next but from year to year as well.

MATERIALS AND METHODS

The data reported here were collected as control values from conscious pigs that were prepared for study under experimental conditions defined as follows:

B/In: Basal, Intact
B/Sp: Basal, Splenectomized
R/In: Restrained, Intact
R/Sp: Restrained, Splenectomized

In most instances, the same experimental variables were measured under two or more of the foregoing conditions. However, to simplify data presentation in the tables that follow, only one condition will be specified for each variable. Those conditions that significantly altered the magnitude of an experimental variable will be addressed specifically. Significant differences ($P \leq 0.05$) were determined by analyses of variance.

All measurements were made on immature (20 to 25 kg) Yorkshire/Duroc cross swine, both barrows and gilts, obtained from a commercial breeder (J.G. Boswell, Corcoran, CA). They were maintained in a common indoor holding area at Letterman Army Institute of Research until utilized for study 2 to 4 weeks after arrival. Food (Purina Pig Chow, Ralston Purina, St Louis, MO.) and water were provided ad libitum. Seven to 10 days before study, after an overnight fast, each pig received an intramuscular preanesthetic injection of 0.8 mg/kg atropine sulfate, 2.2 mg/kg ketamine HCl, and 2.2 mg/kg xylazine. Halothane anesthesia was induced by face mask and maintained with an endotracheal catheter. As described elsewhere (10), polyvinylidine catheters were chronically implanted in the carotid artery and in some instances in the pulmonary artery. In two categories of animals (In/Sp, R/Sp) a celiotomy was performed and the spleen removed according to standard techniques. In the other two categories (B/In, R/In) either a sham operation was performed or the abdominal cavity was left undisturbed. An in situ isolated kidney preparation, as described by Loveday et al. (12), was used to assess renal function in a group of R/Sp pigs. All animals were allowed 8 to 10 days to recover from surgery before any experimental measurements were made. Pigs subjected to restraint were trained 60 minutes daily to lie quietly in a modified Pavlov sling with a respiratory mask in place. This training was initiated 3 days before, and reinstituted

2 days after surgical preparation; total training ranged from 8 to 10 days.

On the day of experimental use, each pig, after an overnight fast, was brought into a quiet laboratory in a portable, 60 x 120 cm, transport cage and was provided with waste paper or fabric bedding material. For 2 categories of animals (B/In, B/Sp), the pig was allowed to voluntarily assume a recumbent position and remain so for at least 30 minutes before experimental measurements were initiated. Control values were then obtained in duplicate or triplicate at 10 minute intervals. For the other 2 categories (R/In, R/Sp), the pig was transferred from the transport cage to the Pavlov sling and the respiratory mask was secured over the snout. The pig was then allowed to rest until minimal values for total body O_2 consumption were maintained for at least 10 minutes; this rest period ranged from 30 to 90 minutes. Thereafter, control values in duplicate or triplicate were taken, again at 10 minute intervals.

Conventional procedures were used in collecting the data reported here, and in most instances technical details are contained in previous reports. Included are the techniques used to assess body physical characteristics (porcinometry), body composition and fluid compartment volumes (13,14), blood gas and acid-base values (15), most blood chemical and physical characteristics (16), some plasma hormone levels (17), and most hemodynamic, ventilatory and metabolic variables (18,19). Plasma free fatty acid concentrations were determined with an HPLC procedure developed in our laboratory. Plasma concentrations of aldosterone, cortisol, total T_3, total T_4, free T_4, insulin and glucagon were determined with radioimmunoassay kits from Diagnostic Products (Los Angeles, CA). ACTH was measured with radioimmunoassay kits obtained from Nicholes Institute (Los Angeles, CA), beta endorphin with radioimmunoassay kits from Immunonuclear Corp. (Stillwater, MN), renin activity by radioimmunoassay for angiotensin I with kits from New England Nuclear (Boston, MA), and vasopressin by a radioimmunoassay procedure developed in our laboratory using lysine vasopressin as a standard. Plasma catecholamine (epinephrine and norepinephrine) concentrations were measured by electrochemical detection after chemical extraction and separation by HPLC (20).

The tables that follow also contain a number of physiological variables that were calculated using conventional procedures. These included mean arterial pressure, stroke volume, pulse pressure, left and right

ventricular work, systemic and pulmonary vascular resistance, alveolar ventilation, alveolar ventilation/perfusion ratio, arterial O_2 transport, tissue O_2 extraction ratio, pulmonary shunt fraction, and the arteriovenous difference in O_2 content (19-21).

Technical details concerning these calculations are contained in the physiological reference literature (21-22).

RESULTS

Typical values for the physical characteristics, body composition and compartmental fluid volumes of near-basal pigs are summarized in Tables 1 and 2. These data show that the spleen of intact animals sequesters 20 to 25% of total body red cells. Comparison data from intact and splenectomized animals revealed no significant differences in total circulating blood volume. Basal intact (B/In) pigs, however, had lower circulating red cell volumes (16.2 $\pm$ 1.39 ml/kg, N=20) and higher circulating plasma volumes (52.1 $\pm$ 3.42 ml/kg, N=20) than splenectomized pigs (B/Sp, Table 2). Though small, these differences were significant. Extracellular volume was significantly greater when the measurement was based on the dilution of $^{22}NaCl$ as compared to the dilution of ^{51}Cr-EDTA. Values obtained from dilution of $^{35}SO_4$, ^{3}H-inulin or ^{14}C-sucrose were essentially the same as those obtained with ^{51}Cr-EDTA (13).

Hematocrit and hemoglobin levels were significantly affected by the condition of the animal at the time of measurement. Compared to B/In pigs (Table 3), the hematocrit level of B/Sp pigs was 29.0 $\pm$ 2.37% (N=25), R/In pigs 32 $\pm$ 2.46% (N=14), and Sp/R pigs 31.5 $\pm$ 3.35% (N=15). Differences in hemoglobin levels for each of these animal groups paralleled the differences in hematocrit. The low recorded values for plasma oncotic pressure of swine reflected a low plasma protein concentration, a condition that applied to all of the treatment groups.

Significantly higher arterial PO_2 values were obtained in B/Sp pigs (86.7 $\pm$ 6.35 mmHg, N=12) than those recorded here for B/In pigs (Table 4); values obtained in R/In (N=12) and R/Sp (N=22) were intermediate to these extremes. Low values for arterial O_2 capacity and O_2 content of porcine arterial blood were attributable to low hemoglobin levels. Significant differences, however, were detected when the mixed venous PO_2 of R/Sp pigs (Table 4) was compared to that of R/In pigs (46.8 $\pm$ 2.49 mmHg, N=16) and when the A-V

difference in O_2 content was compared in R/Sp pigs and R/In pigs (4.7 ± 0.68 ml/dl, N=13).

The 7.48 ± 0.033 mean value for arterial pH in B/In animals (Table 5) was significantly greater than the average value (7.43 ± 0.053) recorded in B/Sp (N=12) animals; R/In (N=12) and R/Sp (N=22) values were intermediate to these extremes. Similar significant differences were seen in measurements of arterial PCO_2 and bicarbonate concentration. Mean values for arterial PCO_2 ranged from 39.6 ± 2.30 in B/Sp animals (N=36) to 42.6 ± 2.66 mmHg in R/Sp animals (N=22). Mean values for arterial bicarbonate were 27.2 ± 3.67 and 30.2 ± 3.05 mEq/L in the B/Sp (N=12) and R/Sp (N=22) groups respectively. Significant between-group differences in mixed venous acid-base values included pH which ranged from 7.36 ± 0.042 in R/In (N=16) to 7.42 ± 0.024 in R/Sp animals (Table 5), and mixed venous PCO_2 which ranged from 48.5 ± 3.20 mmHg in R/Sp pigs (Table 3) to 53.0 ± 5.28 mmHg in R/In pigs (N=15). Mixed venous bicarbonate values were essentially the same in all groups.

Except for free fatty acids, the arterial plasma concentrations of most electrolytes and metabolites were measured under all four experimental conditions, and no significant between-group variations were observed. The values summarized in Tables 6 and 7, therefore, are representative of the resting pig as defined here. Plasma free fatty acid levels were measured only in B/In animals.

Hormone concentrations of arterial plasma (Table 8) were determined under most of the experimental conditions, but significant differences between groups were few, largely because of the high coefficients of variance that characterized the control measurements of all groups. Significant differences included higher ACTH (53.2 ± 18.1 pg/ml, N=17) and epinephrine (142 ± 74.8 pg/ml, N=23) concentrations in R/Sp pigs, and lower cortisol concentrations in B/Sp pigs (2.9 ± 0.81 ug/ml, N=8) compared to the values recorded in B/In pigs (Table 8).

Except for heart rate and arterial pressure, most hemodynamic variables were measured while the animals were resting in a Pavlov sling (Table 9). Under such conditions, no significant between-group differences were observed. Similarly, no significant differences were noted when heart rates and arterial pressures were compared in restrained and unrestrained animals.

All ventilatory and metabolic variables were measured under conditions of sling restraint, and under such

conditions two significant between-group differences were recorded. Respiratory rate and O_2 consumption were slightly higher in R/In pigs (24 $\pm$ 3.6 breaths/min and 7.6 $\pm$ 1.46 ml/min/kg, N=15) than in R/Sp pigs (Tables 10,11). Tidal volume was slightly lower in R/In than in R/Sp animals, but the difference was not significant.

Resting rectal temperature values were essentially the same under all conditions of measurement, the mean and S.D. indicated in Table 11 being typical. Skin temperatures, on the other hand, can be quite variable depending on the measurement site and environmental conditions at the time of measurement. The values summarized in Table 11 were obtained from the dorsal surface of the neck at a room temperature of 22 C.

Various renal functions (Table 12) were only measured in splenectomized pigs under conditions of physical restraint, hence no between-group comparisons could be made.

DISCUSSION

Most of the normal values recorded here are quantitatively similar to those reported for children studied under comparable, near-basal conditions. There are, however, certain species differences which should be recognized since they can influence the outcome or interpretation of experimental studies based on a porcine model. Many of these differences are attributable to age or body mass, but some represent unique characteristics of humans or pigs. In evaluating the validity of data from either species, special attention should be paid to the introduction of confounding variables, often unrecognized, that can influence the magnitude of recorded measurements; wherever possible these variables should be identified and their effects described.

In terms of age and body size, the immature domestic pigs used in our studies are typical of those used in many other investigations employing a porcine model. The maturity factor is clearly evident in some of the body composition and body fluid data recorded here. Our animals exhibited distinctly lower hematocrit and hemoglobin values than those reported for either younger or older pigs (23), or humans of any age (24); porcine growth is characterized by a distinct nadir in hematocrit and hemoglobin values at two to three months of age (23). Depressed hemoglobin levels were directly responsible for the low arterial values for O_2 capacity and O_2 content recorded here. These

immature pigs also exhibited a lower circulating red cell volume and a higher plasma volume, relative to total body mass, than either younger or older pigs (13,14), or humans (25).

Unlike normal man (26), swine possess a contractile spleen that sequesters 20 to 25% of the total red cell mass under basal conditions (12). These red cells are readily mobilized by experimental or incidental conditions, e.g. restraint of the naive animal (12,17), that lead to sympathoadrenal activation. As a consequence, splenectomized swine are often used for human-oriented experiment, particularly when variable mobilization of sequestered red cells becomes an unacceptable, or confounding, variable. Studies of hemorrhagic hypotension are an example of such use (16).

The high values for extracellular water, and to a lesser extent total body water, recorded in our pigs also appear attributable, at least in part, to immaturity. The porcine values for functional extracellular space were 40 to 50% higher, and the total body water values were marginally higher, than those reported for young adult men of similar lean body mass (24,27). In both pigs (14) and humans (25) the water fraction of lean body mass decreases with age, and at least in humans (25), the extracellular fraction of total body water also decreases with age. At comparable ages of maturity, however, porcine values for extracellular space and the water fraction of lean body mass seem to be distinctly greater than those observed in humans.

With certain notable exceptions, the physical and chemical characteristics of human and porcine blood are quite similar. Exceptions include the difference in arterial O_2 content mentioned above, as well as slightly lower arterial O_2 saturation, and distinctly lower values for mixed venous O_2 content and O_2 saturation in pigs as compared to humans. The lower O_2 saturation values in pigs are largely attributable to species differences in hemoglobin-oxygen affinity. Thus, the oxyhemoglobin dissociation curve for porcine blood is displaced to the right of the human curve (28). This displacement, and its effect on saturation, is further accentuated by a higher normal body temperature in pigs as compared to humans (29). Other deviations from human characteristics include higher values for arterial pH and plasma bicarbonate concentration, and slightly lower values for buffer base concentration in blood obtained from young pigs (15). These species differences can lead to serious measurement errors if the

blood gas and acid-base status of porcine blood is evaluated in an instrument calibrated for human blood (15).

Most of the plasma hormone levels recorded here are similar to those reported for resting humans (30), but in both species subtle changes in experimental conditions or manipulations can readily lead to elevated values. Mild restraint of the naive pig, for example, produces an immediate increase in the plasma concentrations of epinephrine and norepinephrine, and more slowly evolving increases in the concentrations of ACTH, cortisol, vasopression, aldosterone, and plasma renin activity (17). Resting hormone concentrations in pigs, as in other species, show a high degree of variance with standard deviations nearly as large as, and in one instance (plasma renin activity) larger than, mean values. In most experimental settings, this variability does not pose a serious problem since the experimental variable, if it affects endocrine activity at all, usually produces a major change in plasma hormone concentration. Mild restraint, for example, can lead to a three-fold (17) and severe hemorrhage to a hundred-fold increase in plasma catecholamine concentrations (31).

Reported values for the cardiovascular functions of supposedly resting pigs vary considerably, both within and between studies (11). This disparity, presumably, is attributable to variations in experimental conditions or technique. Data collected under near-basal conditions, as in the studies reported here, usually show reasonably low coefficients of variance. Exceptions include certain calculated variables such as ventricular work, vascular resistance and pulmonary shunt fraction.

Perhaps the most distinguishing feature of porcine cardiovascular function is a distinctly high cardiac output compared to that seen in humans under similar experimental conditions. The average value for the near basal pig, about 150 ml/kg, is twice that of the near basal man, about 70 ml/kg (30). In part, the elevated value in pigs is achieved through a higher heart rate and in part by a higher stroke volume. The elevated output seen in pigs presumably reflects a compensation directed at supplying adequate oxygen to the body tissues. As indicated above, the blood of immature pigs has a low hemoglobin level and O_2 capacity, about half that of human blood, and to assure equivalent O_2 delivery (the product of cardiac output and O_2 content) twice the cardiac output is needed. The elevated cardiac output of immature pigs, as might be anticipated, caused deviations in certain other experimental variables relative

to those commonly seen in humans. Specifically, porcine values for left and right ventricular work exceed those measured in man, and porcine values for systemic and pulmonary artery resistance are lower than those measured in man. Central venous pressure was the only other porcine variable that was distinctly different from that recorded in normal man; values in pigs are about twice those seen in humans (30). Despite these differences in basal characteristics, hemodynamic responses of pigs to experimental variables such as hemorrhage (16,18,19,32) and exercise (33) are remarkably similar to those reported for man (30,32).

The porcine values for renal blood flow and renal plasma flow recorded here are marginally higher than those of adult humans, perhaps reflecting the above indicated species differences in cardiac output. Fractional flows (i.e. % of cardiac output) seen in pigs are about one-half those seen in men (30), while most other measures of renal function are essentially the same in the two species. It should be recognized, however, that certain of these variables can be readily altered by diet, particularly water and electrolyte intake, or other experimental conditions. Total body dehydration, for example, will lead to a conservation of body water (reduced urine production) and a conservation of body sodium (reduced sodium excretion). High salt intake, on the other hand, will increase sodium excretion, but will only marginally affect water excretion.

The metabolic rate of immature pigs, although higher than that of adult man, is comparable to that of children of equivalent weight. A 20 kg child has a heat production of about 32 calories/min/kg (24), a value not too different from the porcine value of 38.7 calories/min/kg reported here. The slightly higher value in pigs could be due in part to their higher normal body temperature (38.5 C versus 37 C for humans). It should be noted in this regard, that swine, in contrast to humans, have essentially no capacity to regulate body temperature by sweating, and increases in metabolic rate are often accompanied by an increase in body temperature and heat content (unpublished observations).

Despite the foregoing limitations, the immature pig is rapidly becoming established as an animal of choice for a wide range of biomedical endeavors (1-3). Species peculiarities, however, need to be documented and recognized before utility of the pig as an experimental animal for physiologic studies can be fully realized. Hopefully, the data on normal values reported here will contribute to this goal. Additional data of other functional entities are obviously needed.

REFERENCES

1. Tumbleson ME ed. Swine in Biomedical Research; vols 1-3. New York: Plenum Press, 1986.

2. Stanton HC, Mersmann HJ, eds. Swine in Cardiovascular Research; vols 1-2. Boca Raton, FL: CRC Press, 1986.

3. Laboratory Animal Science 1986;36(No 4).

4. Parsons AH, Wells RE. Serum biochemistry of healthy Yukatan miniature pigs. Lab Anim Sci 1986;36:428-430.

5. Radin MJ, Weiser MG, Fettman MJ. Hematologic and serum biochemical values for Yukatan miniature swine. Lab Anima Sci 1986;36:425-427.

6. Schmidt DA, Tumbleson ME, Swine hematology. In: Tumbleson ME ed. Swine in Biomedical Research; vol 2. New York: Plenum Press, 1986:767-782.

7. Tumbleson ME, Schmidt DA, Swine clinical chemistry. In: Tumbleson ME ed. Swine in Biomedical Research; vol 2. New York: Plenum Press, 1986; 783-807.

8. Pond WG, Houpt KA. The Biology of The Pig. Ithaca, NY: Comstock Press, 1978.

9. Wilson GDA, Harvey DG, Snook CR. A review of factors affecting blood biochemistry in the pig. Br Vet J 1972; 128:596-610.

10. Von Engelhardt W, Swine cardiovascular physiology - a review. In: Bustad LK, McClellan RO eds. Swine in Biomedical Research. Seattle, WA,: Frayn Printing, 1966;307-329.

11. Hannon JP, Hemodynamic characteristics of conscious swine: a review. In: Tumbleson ME ed, Swine in Biomedical Research; vol 3. New York: Plenum Press, 1986:1341-1352.

12. Loveday JA, Gonzaludo GA, Sondeen JL, et al. Renal hemodynamics and function in conscious swine: surgical preparation of a single kidney. FASEB J 1989;3:A1018.

13. Hannon JP, Bossone CA, Rodkey WG. Splenic red cell sequestration and blood volume measurements in conscious pigs. Am J Physiol 1985;248:R293-R301.

14. Bossone CA, Hannon JP. A multi-isotope procedure for simultaneously estimating the volume of body fluid compartments of swine. In: Tumbleson ME ed. Swine in Biomedical Research; vol 1. New York: Plenum Press, 1986:49-60.

15. Hannon JP. Construction of acid-base alignment nomograms to estimate buffer base and base excess concentrations in arterial blood from immature pigs. Am J Vet Res 1984;45:1918-1923.

16. Hannon JP, Skala JH. Physiologic aspects of porcine hemorrhage. V. Arterial metabolite, electrolyte, and enzyme alterations during spontaneous recovery from 30 and 50 percent blood volume loss in the conscious animal. Presidio of San Francisco, California: Letterman Army Institute of Research, 1982; Institute Report No. 115.

17. Wade CE, Hannon JP, Bossone CA, et al. Cardiovascular and hormonal responses of conscious pigs during physical restraint. In: Tumbleson ME ed. Swine in Biomedical Research; vol 3. New York: Plenum Press, 1986;1395-1404.

18. Hannon JP, Wade CE, Bossone CA, et al. Oxygen delivery and demand in conscious pigs subjected to fixed-volume hemorrhage and resuscitated with 7.5% NaCl in 6% dextran. Circ Shock (in press).

19. Wade CA, Hannon JP, Bossone CA, et al. Resuscitation of conscious pigs following hemorrhage: comparative effects of small volume resuscitation. Circ Shock (in press).

20. Davis GC, Kissinger PT, Shoup RE. Strategies for determination of serum or plasma norepinephrine by reverse-phase liquid chromatography. Anal Chem 1981;53:156-159.

21. Handbook of Physiology, Sect 2: Circulation, vols I-III. Washington, DC: American Physiological Society, 1965.

22. Handbook of Physiology, Sect 3: Respiration, vol I. Washington, DC: American Physiological Society, 1964.

23. Miller ER, Ullrey DE, Ackermann I, et al. Swine hematology from birth to maturity. II. Erythrocyte population, size and hemoglobin concentration. J Anim Sci 1961;20:890-897.

24. Altman PL, Dittmer DS. Biology Data Book; 2nd ed. vol III. Bethesda, MD: Federation of American Societies for Experimental Biology, 1974.

25. Forbes GB. Human Body Composition. Growth, Aging, Nutrition, and Activity. New York: Springer-Verlag, 1987.

26. Ebert RV, Stead EA, Jr. Demonstration that in normal man no reserves of blood are mobilized by exercise, epinephrine, and hemorrhage. Am J Med Sci 1941;201:655-664.

27. Elkinton JR, Danowski TS. The Body Fluids, Baltimore, MD: Williams and Wilkins, 1955.

28. Bartels H, Harms H. Sauerstoffdissoziationskurven des blutes von saugetieren (mensch, kanichen, meerschweinchen, hund, katze, schwein, rind und schaf). Pflugers Arch 1959;268:334-365.

29. Wilford DC, Hill EP. Temperature corrections for blood gas values. In: Tumbleson ME ed. Swine in Biomedical Research. Vol 3. New York: Pleum Press, 1986;1473-1478.

30. Ganong WF. Review of Medical Physiology; 8th ed. Los Altos, CA: Lange Medical Publications, 1977.

31. Wade CE, Bossone CA. Hunt MM, et al. Cardiovascular, hormonal, and metabolic responses to resuscitation with volumes of hypertonic solutions following hemorrhage. Fed Proc 1987;46:205.

32. Hannon JP, Bossone CA. The conscious pig as a large animal model for studies of hemorrhagic hypotension. In: Tumbleson ME ed. Swine in Biomedical Research. New York: Plenum Press, 1986:1413-1412.

33. McKirnen MD, White FC, Guth BD, et al. Cardiovascular and metabolic responses to acute and chronic exercise in swine. In Tumbleson ME ed. Swine in Biomedical Research. New York: Plenum Press, 1986:1379-1394.

TABLE 1: BODY COMPOSITION

Measurement	Cond	N	Mean	S.D.	Range
Body Weight (kg)	B/Sp	12	21.3	1.91	17.7 - 24.1
Shoulder Height (cm)	B/Sp	12	43.6	2.05	40.0 - 46.0
Poll - Tail Length (cm)	B/Sp	12	72.4	4.82	63.5 - 81.0
Neck Circumference (cm)	B/Sp	12	54.2	3.31	51.0 - 63.5
Chest Circumference (cm)	B/Sp	12	60.0	2.61	56.0 - 64.0
Belly Circumference (cm)	B/Sp	12	59.7	3.25	55.0 - 64.0
Back Fat Thickness (cm)	B/Sp	12	6.3	0.61	5.7 - 7.5
Total Body Fat (g/kg)	B/Sp	11	178	29.8	136 - 225
Lean Body Mass (g/kg)	B/Sp	11	822	29.8	775 - 864
Fat-Free Dry Mass (g/kg)	B/Sp	11	182	6.6	172 - 192

TABLE 2: BODY FLUID VOLUMES

Measurement	Cond	N	Mean	S.D.	Range
$^{3}H_2O$ Space (ml H_2O/kg)	B/Sp	11	639	23.2	603 - 672
^{51}Cr-Space (ml H_2O/kg)	B/Sp	9	246	36.8	192 - 307
^{22}Na-Space (ml H_2O/kg)	B/Sp	11	303	12.7	286 - 330
Interstitial Space (ml H_2O/kg)	B/Sp	7	172	38.7	127 - 234
Circ. Red Cell Volume (ml/kg)	B/Sp	20	17.8	1.64	15.0 - 21.6
Splenic Red Cell Volume (ml/kg)	B/In	8	4.5	0.89	3.7 - 5.6
Circ. Plasma Volume (ml/kg)	B/Sp	20	49.6	3.12	42.4 - 54.5
Circ. Blood Volume (ml/kg)	B/Sp	20	67.3	3.67	58.1 - 73.9

TABLE 3: BLOOD PHYSICAL CHARACTERISTICS

Measurement	Cond	N	Mean	S.D.	Range
Hematocrit (%)	B/In	69	27.0	3.13	23.5 - 33.0
Hemoglobin (g/dl)	B/In	26	8.5	0.75	7.3 - 10.2
Hemoglobin/Hematocrit Ratio	B/In	26	0.32	0.016	0.27 - 0.36
Packed Cell Trapped Plasma (%)	R/In	12	2.8	1.26	1.2 - 5.0
Plasma Osmolality (mOsm/kg H_2O	B/In	15	270	9.3	260 - 293
Plasma Oncotic Pressure (mmHg)	B/In	23	17.0	1.72	12.7 - 19.7
Plasma Water (g/dl)	R/In	6	95.0	0.73	94.0 - 95.9
Plasma Albumin (g/dl)	B/In	40	25.4	2.02	21.6 - 28.0
Plasma Globulin (g/dl)	B/In	40	32.2	4.43	27.1 - 41.2
Albumin/Globulin Ratio	B/In	24	0.89	0.188	0.51 - 1.31

TABLE 4: BLOOD OXYGENATION

Measurement	Cond	N	Mean	S.D.	Range
Arterial PO_2 (mmHg)	B/In	36	82	4.2	73 - 92
Arterial HbO_2 (%)	B/In	18	94	0.7	92 - 95
Arterial O_2 Capacity ml/dl)	R/Sp	21	13.1	1.04	10.1 - 14.2
Arterial O_2 Content (ml/dl)	R/Sp	21	12.4	1.62	8.7 - 15.1
Art ‹ial Carboxyhemoglobin (%)	B/In	18	4	0.4	4 - 5
Arterial Methemoglobin (%)	B/In	18	1	0.3	0.6 - 1.8
Mixed Venous PO_2 (mmHg)	R/Sp	22	41	3.3	32 - 45
Mixed Venous HbO_2 (%)	R/Sp	22	60	5.7	48 - 71
Mixed Venous O_2 Content (ml/dl)	R/Sp	20	8.0	1.27	5.3 - 10.8
Art. -Ven.O_2 Cont. Diff. (ml/dl)	R/Sp	26	4.3	0.43	3.4 - 5.7

TABLE 5: BLOOD ACID-BASE STATUS

Measurement	Cond	N	Mean	S.D.	Range
Arterial pH	B/In	36	7.48	0.033	7.40 - 7.53
Arterial PCO_2 (mmHg)	B/In	36	40	2.3	35 - 44
Arterial Plasma HCO_3 (mEq/L)	B/In	36	29	2.2	22 - 33
Arterial Buffer Base (mEq/L)	B/In	40	45	3.3	40 - 52
Mixed Venous pH	R/Sp	23	7.42	0.024	7.38 - 7.48
Mixed Venous PCO_2 (mmHg)	R/Sp	22	49	3.2	44 - 55
Mixed Venous Plasma HCO_3 (mEq/L)	R/Sp	14	31	2.1	28 - 35

TABLE 6: ARTERIAL PLASMA ELECTROLYTES

Measurement	Cond	N	Mean	S.D.	Range
Sodium (mEq/L)	B/In	35	138	3.49	129 - 143
Potassium (mEq/L)	B/In	35	4.4	0.37	3.9 - 4.1
Magnesium (mEq/L)	B/In	17	1.4	0.18	1.2 - 1.9
Calcium (mEq/L)	R/In	15	4.8	0.29	4.5 - 5.6
Chloride (mEq/L)	B/In	17	106	7.8	93 - 126
Bicarbonate (mEq/L)	B/In	36	29	2.2	22 - 33
Phosphate (mEq/L)	B/In	17	4.0	0.58	3.1 - 5.1
Albuminate (mEq/L)	B/In	40	7.6	0.80	6.2 - 9.2
Globulinate (mEq/L)	B/In	40	6.1	0.90	4.8 - 7.8

TABLE 7: ARTERIAL PLASMA METABOLITES

Measurement	Cond	N	Mean	S.D.	Range
Glucose (mM/L)	B/In	33	4.6	0.66	2.6 - 6.5
Lactate (mM/L)	B/In	33	1.0	0.26	0.5 - 1.5
Urea (mM/L)	B/In	17	3.2	1.15	2.0 - 5.4
Creatinine (uM/L)	B/In	17	89	19.5	62 - 131
Lauric Acid (uM/L)	B/In	18	6	0.59	5 - 7
Myristic Acid (uM/L)	B/In	18	11	2.67	7 - 16
Palmitic Acid (uM/L)	B/In	18	147	66.0	147 - 249
Palmitoleic Acid (uM/L)	B/In	18	30	8.9	9 - 43
Stearic Acid (uM/L)	B/In	18	121	38.2	58 - 108
Oleic Acid (uM/L)	B/In	18	244	100.6	89 - 394
Linoleic Acid (uM/L)	B/In	18	115	32.2	46 - 169
Arachadonic Acid (uM/L)	B/In	18	42	3.3	14 - 64
Total Free Fatty Acids (mM/L)	B/In	18	0.8	0.07	0.1 - 1.1

TABLE 8: PLASMA HORMONE CONCENTRATIONS

Measurement	Cond	N	Mean	S.D.	Range
ACTH (pg/ml)	B/In	17	34	23.5	11 - 96
B-Endorphin (pg/ml)	B/In	8	56	20.2	33 - 90
Cortisol (ug/dl)	B/In	18	4.3	1.43	1.8 - 7.9
Aldosterone (ng/dl)	B/In	17	3.4	2.89	1.6 - 6.1
Total T3 (ng/dl)	R/In	14	28	5.2	22 - 40
Total T4 (ug/dl)	R/In	14	2.6	0.50	1.8 - 3.5
Free T4 (ng/dl)	R/In	14	0.32	0.055	0.20 - 0.39
Insulin (ug/dl)	B/In	18	4.2	2.98	1.0 - 11.0
Glucagon (pg/ml)	B/In	18	237	73.9	156 - 407
Glucagon/Insulin Ratio ($x10^6$)	B/In	18	56	76.9	24 - 333
Vasopressin (pg/ml)	B/In	17	1.0	0.33	0.5 - 1.9
Renin Activity (ng/ml/min)	B/In	18	1.24	1.450	0.12 - 6.24
Epinephrine (pg/ml)	B/In	15	69	45.8	20 - 132
Norepinephrine (pg/ml)	B/In	17	179	90.0	53 - 332

TABLE 9: HEMODYNAMICS

Measurement	Cond	N	Mean	S.D.	Range
Cardiac Output (ml/kg)	R/Sp	15	147	22.4	123 - 188
Heart Rate (beats/min)	R/Sp	15	105	10.6	90 - 107
Stroke Volume (ml/beat/kg)	R/Sp	15	1.34	0.258	1.03 - 1.87
Mean Arterial Pressure (mmHg)	B/In	44	102	9.3	86 - 123
Systolic Pressure (mmHg)	B/In	28	127	7.9	112 - 139
Diastolic Pressure (mmHg)	B/In	28	86	7.1	72 - 98
Pulse Pressure (mmHg)	B/In	28	41	1.2	22 - 33
Central Venous Pressure (mmHg)	R/Sp	15	8.7	4.10	1.0 - 15.4
Mean Pulm. Art. Press. (mmHg)	R/Sp	15	16	4.2	11 - 24
Left Vent. Work (g.M/min/kg)	R/Sp	15	216	50.4	142 - 306
Right Vent. Work (g.M/min/kg)	R/Sp	15	34	12.6	18 - 61
Syst. Vasc. Res. (mmHg/ml/min/kg)	R/Sp	15	0.77	0.442	0.53 - 1.65
Pulm. Vasc. Res. (mmHg/ml/min/kg)	R/Sp	15	0.11	0.012	0.06 - 0.21
Pulm. Shunt Fraction (%)	R/Sp	15	4.8	2.45	1.6 - 8.3

TABLE 10: VENTILATION

Measurement	Cond	N	Mean	S.D.	Range
Expiratory Ventilation (ml/min/kg)	R/Sp	22	198	41.9	104 - 262
Ventilatory Rate (breaths/min)	R/Sp	22	20	2.9	16 - 25
Tidal Volume (ml/breath/kg)	R/Sp	22	10.1	2.08	5.9 - 14.5
Alveolar Vent. (ml/min/kg)	R/Sp	22	110	23.2	67 - 152
Alveolar Vent./ Perfusion Ratio	R/Sp	22	0.71	0.110	0.52 - 0.99
Alv. - Art. O_2 Diff. (mmHg)	R/Sp	13	8.9	0.87	5.5 - 14.0

TABLE 11: BIOENERGETICS

Measurement	Cond	N	Mean	S.D.	Range
Rectal Temperature (°C)	R/Sp	35	38.5	0.65	37.0 - 39.6
Skin Temperature (°C)	R/Sp	16	34.2	1.80	31.6 - 37.3
Heat Production (cal/min/kg)	R/Sp	22	38.7	4.14	31.6 - 45.3
O_2 Consumption (ml/min/kg)	R/Sp	22	6.6	1.27	4.4 - 9.2
CO_2 Production (ml/min/kg)	R/Sp	22	5.5	1.25	3.4 - 7.6
Respiratory Exchange Ratio	R/Sp	22	0.81	0.067	0.67 - 0.96
Arterial O_2 Delivery (ml/min/kg)	R/Sp	9	19.8	1.43	14.2 - 26.5
Tissue O_2 Extraction Ratio	R/Sp	9	0.36	0.009	0.33 - 0.39

TABLE 12: RENAL FUNCTION

Measurement	Cond	N	Mean	S.D.	Range
Renal Blood Flow (ml/min/kg)	R/Sp	17	24	8.0	12 - 43
Renal Blood Flow (% Card. Out.)	R/Sp	19	11.4	2.08	4.4 - 13.7
Renal Vasc. Res. (mmHg/ml/min/kg)	R/Sp	16	4.3	1.43	1.8 - 7.9
Renal Plasma Flow (ml/min/kg)	R/Sp	17	16.7	5.98	7.7 - 32.2
Glom. Filt. Rate (ml/min/kg)	R/Sp	19	2.4	0.92	1.0 - 4.5
Filtration Fraction (%)	R/Sp	19	15.3	5.89	4.2 - 29.4
Urine Flow (ml/min/kg)	R/Sp	19	0.05	0.051	0.01 - 0.15
Urine Osmolality (mOsm/kg H_2O)	R/Sp	19	253	126.9	115 - 546
Free Water Clearance (ul/min/kg)	R/Sp	19	50	2.7	10 - 130
Osmotic Clearance (ul/min/kg)	R/Sp	19	40	16.5	15 - 79
Sodium Clearance (ul/min/kg)	R/Sp	19	16	12.5	2 - 58
Potassium Clearance (ul/min/kg)	R/Sp	19	263	198.8	16 - 70
Urinary Na Excretion (uEq/min/kg)	R/Sp	19	2.29	1.781	0.25 - 8.13
Fractional Na Excretion (%)	R/Wp	19	12.4	9.60	1.9 - 31.1
Urinary K Excretion (uEq/min/kg)	R/Sp	19	1.28	1.020	0.09 - 3.31
Fractional K Excretion (%)	R/Sp	19	7.7	6.48	1.6 - 24.4

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