Effect of general anesthesia and minor surgical trauma on urine and serum measurements in horses

Zara E. Watson, BVSc; Eugene P. Steffey, VMD, PhD; Linda M. VanHoogmoed, DVM, PhD; Jack R. Snyder, DVM, PhD

Objective—To characterize the effect of general anesthesia and minor surgery on renal function in horses.

Animals—9 mares with a mean (± SE) age and body weight of 9 ± 2 years and 492 ± 17 kg, respectively.

Procedure—The day before anesthesia, urine was collected (catheterization) for 3 hours to quantitate baseline values, and serum biochemical analysis was performed. The following day, xylazine (1.1 mg/kg, IV) was administered, and general anesthesia was induced 5 minutes later with diazepam (0.04 mg/kg, IV) and ketamine (2.2 mg/kg, IV). During 2 hours of anesthesia with isoflurane, $Paco_2$ was maintained between 48 and 52 mm Hg, and mean arterial blood pressure was between 70 and 80 mm Hg. Blood and urine were collected at 30, 60, and 120 minutes during and at 1 hour after anesthesia.

Results—Baseline urine flow was 0.92 ± 0.17 ml/kg/h and significantly increased at 30 and 60 minutes after xylazine administration (2.14 ± 0.59 and 2.86 ± 0.97 ml/kg/h respectively) but returned to baseline values by the end of anesthesia. Serum glucose concentration increased from 12 ± 4 to 167 ± 8 mg/dl at 30 minutes. Glucosuria was not observed.

Conclusions and Clinical Relevance—Transient hyperglycemia and an increase in rine production accompanies a commonly used anesthetic technique for horses. The increase in urine flow is not trivial and should be considered in anesthetic management decisions. With the exception of serum glucose concentration and urine production, the effect of general anesthesia on indices of renal function in clinically normal horses is likely of little consequence in most horses admitted for elective surgical procedures. (*Am J Vet Res* 2002;63:1061–1065)

Anesthesia and surgical trauma may adversely affect renal function.[1] Previous laboratory studies[2-4] of inhalation anesthesia in horses have consistently identified transient increases in **serum urea nitrogen (SUN)**, **creatinine (Cr)**, and **inorganic phosphate (iPO_4)** concentrations immediately after prolonged anesthesia. Although these changes were considered minor, their consistent development confirms the influence of anesthesia on renal function in horses. However, these studies[2-4] differ in a number of ways from contemporary clinical anesthetic management of horses. For example, in previous studies[2-4] horses were subjected to more than 5 hours of anesthesia that was induced and maintained by a single drug; no attempts were made to support cardiovascular function, and no associated surgical manipulations were performed. In contrast, under clinical conditions in private and university-based practices in the United States, general anesthesia is commonly induced and maintained with a drug regimen that usually includes an α_2-agonist such as xylazine hydrochloride and ketamine hydrochloride (with or without supplementary drugs such as diazepam or guaifenesin). Xylazine in particular is known to cause direct and indirect changes in renal function in awake[5] and anesthetized[6-9] horses. The purpose of the study reported here was to characterize the effect of general anesthesia and minor surgery on renal function and serum biochemical variables in horses.

Received Aug 29, 2001.
Accepted Dec 17, 2001.
From the Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California, Davis, CA 95616.
Supported by funds from contributions by private donors.
Address correspondence to Dr. Watson.

Materials and Methods

Horses—Nine sexually intact mares were studied. Mean (± SE) age and body weight was 9 ± 2 years and 492 ± 17 kg, respectively. Horses included 3 Quarter Horses, 4 Thoroughbreds, 1 warmblood horse, and 1 crossbred Quarter Horse. All horses were clinically normal. Our study was performed in conjunction with a separate study on determination of amikacin concentrations in the tibiotarsal joint after minor surgical preparation and infusion (under general anesthesia) via different routes of local entry.[10] Blood concentrations of amikacin were judged too low to be a confounding influence on the presently reported study of urine formation. All horses were owned by the Center for Equine Health, University of California-Davis, and the Campus Animal Use and Care Administrative Advisory Committee approved the study.

Study conditions—Baseline data were collected the afternoon prior to surgery, commencing between 12:00 and 2:00 PM. All horses served as their own control. Horses were restrained in stocks, the tail bandaged, and the perineum washed and disinfected. Urethral catheterization was performed without sedation by use of a 28-F 30-ml balloon Foley catheter. The catheter was lubricated sparingly with sterile lidocaine jelly and inserted manually by use of sterile technique. The urinary bladder was drained of all urine by air displacement technique, after which the catheter was connected to a sterile closed-system collector. Urine was collected passively (continuous) by gravity and actively (at specific collection times) by syringe. Urine samples from both collection modes were combined, measured, and recorded every 60 minutes for 3 hours. An aliquot of the total urine collected was saved for later analysis. Venous blood was also obtained after 2 hours of urine collection, and serum was harvested for same day analysis. The urinary catheter was removed after 3 hours. Fresh water and free-choice hay were available during this urine collection period.

Anesthesia—Horses were handled in a similar manner to usual equine patients. Between 7:00 and 8:00 AM on the morning following the collection of baseline urine and blood samples, horses were prepared for general anesthesia and surgery. Food, but not water, was withheld for up to 10 hours before anesthetic induction. A 14-gauge 13-cm-long catheter with injection port attached was percutaneously positioned in the right external jugular vein. The urinary bladder was again aseptically catheterized and drained of urine. Immediately after draining the bladder, xylazine (1.1 mg/kg, IV) was administered, and the time of injection considered time zero for later reference to anesthesia-related sample collection. Anesthesia was induced with diazepam (0.04 mg/kg, IV) and ketamine (2.2 mg/kg, IV) 5 minutes after xylazine administration. Following recumbency, orotracheal intubation was performed with an appropriately sized, cuffed large animal tracheal tube. Horses were positioned in dorsal recumbency (required for the surgical procedure) on a waterbed-covered large animal surgery table[a] and moved to the surgery room. General anesthesia was maintained with isoflurane delivered in O_2 via a large animal circle breathing circuit that included components for mechanical ventilation.[b] Ventilation was spontaneous for approximately the first 15 minutes of anesthesia. Following application of anesthetic and vital organ monitoring instrumentation, intermittent positive-pressure ventilation was started (18 to 22 cm H_2O), and the respiratory frequency was adjusted to maintain $PaCO_2$ at approximately 50 mm Hg (range, 48 to 52 mm Hg). Oxygen flow rates were usually set at 8 L/min for the first 10 to 15 minutes and then adjusted downward to 4 L/min for the duration of general anesthesia. Inspired concentration of isoflurane was adjusted to suit anesthetic requirements and surgical needs of each horse. End-tidal isoflurane and CO_2 concentrations were continuously monitored from the circuit end of the endotracheal tube via a gas analyzing system[11,12,c] or appropriate infrared analyzers.[d,e] Multiple secondary gas standards were used to verify accuracy of the anesthetic analyzer system or to calibrate the other analyzers. A thermistor probe was positioned in the nasopharynx to measure body temperature during general anesthesia.

Arterial blood pressure (systolic, diastolic) was monitored via a 20-gauge catheter percutaneously placed in the right facial artery. The catheter was connected to a calibrated strain gauge positioned level with the sternum and connected to a cardiovascular monitor.[f] Mean arterial pressure was determined by the monitor from measured systolic and diastolic arterial blood pressure signals. A base-apex ECG was monitored (heart rate and rhythm), and wave forms for ECG and blood pressure were displayed on an oscilloscope. The blood pressure and heart rate were manually recorded every 5 minutes along with frequency. All horses received lactated Ringer's solution (10 ml/kg/h, IV). A mean arterial blood pressure of 70 to 80 mm Hg was desired, and efforts to maintain mean arterial blood pressure in this range included administration of dobutamine and adjustment of anesthetic dose.

Arterial blood samples were collected anaerobically in heparinized syringes, usually every 30 minutes during anesthesia, and analyzed[g] for pH, Pa_{O_2}, and Pa_{CO_2}. Arterial blood was analyzed at 37 C, but the reported results were corrected to the horse's body temperature recorded at the time of blood sample collection.

Postanesthetic period—At the conclusion of anesthesia, the anesthetic breathing circuit was disconnected from the endotracheal tube, and horses were placed in lateral recumbency in a padded large animal recovery stall adjoining the surgery room. During lateral recumbency, O_2 was insufflated (15 L/min) via the endotracheal tube. Tracheal intubation was maintained until the horse stood and was chewing on the tube (immediately or at least within a few moments of standing). The urinary catheter was removed after obtaining samples at 1 hour after disconnection of the anesthetic-breathing circuit from the endotracheal tube (1 hour after anesthesia). All horses received phenylbutazone (4.4 mg/kg, IV) 10 minutes after discontinuation of inhalation anesthesia.

Blood and urine analysis—Baseline measurements were made as described. In addition, urine volume was measured 30, 60, 90, and 120 minutes during general anesthesia and at 1 hour after anesthesia. Aliquot samples of urine from each period were collected for routine urinalysis and biochemical analyses that included quantitative assessment of **sodium (Na)**, **potassium (K)**, **chloride (Cl)**, **total calcium (Ca)**, Cr, glucose, and protein concentrations and **γ-glutamyltransferase (GGT)** activity. Venous blood samples were obtained for quantitative analysis of serum Na, K, Cl, Ca, iPO_4, Cr, SUN, and glucose concentrations at the same times that urine samples were collected.

Statistical methods—Descriptive statistics were summarized for grouped data. Data are expressed as mean (± SE) values unless otherwise indicated. Time trends on raw and log-transformed data were tested by repeated measures ANOVA. The post hoc comparisons were done by use of contrast decomposition against the baseline value. For all other measurements, a mixed model analysis was used, and the post hoc comparisons were done on the basis of least squares means by use of a Tukey-Kramer adjustment. A value of $P < 0.05$ was considered significant.

Results

General management—Urethral catheterization was usually performed easily in all horses. Two horses required administration of 10 ml of 2% lidocaine into the caudal epidural space to eliminate excessive straining throughout the period of gathering baseline data. Anesthetic induction was smooth and intubation performed easily. Three horses required an additional dose of ketamine (300 mg, IV) to facilitate transportation to the surgery room. All horses received dobutamine at some point throughout the course of anesthesia for hemodynamic support; the mean infusion rate was 1.5 µg/kg/min (range, 0.75 to 3 µg/kg/min). General anesthesia was maintained with a mean end-tidal isoflurane

Table 1—Mean (± SE) urine variables in 9 horses before, during, and after general anesthesia

Variables	Baseline	Anesthesia (min) 30	60	120	1 h after anesthesia
Volume (ml/kg/h)	0.92 ± 0.17	2.14 ± 0.59	2.86 ± 0.97*	1.06 ± 0.26	0.76 ± 0.16
Specific gravity	1.032 ± 0.002	1.022 ± 0.003*	1.016 ± 0.004*	1.019 ± 0.003*	1.024 ± 0.002*
GGT (U/L)	18 ± 5	30 ± 6	23 ± 7	28 ± 5	23 ± 4
GGT:Cr (U/g)	10 ± 2	21 ± 4*	34 ± 14*	24 ± 4*	23 ± 4*

*Values differ significantly ($P < 0.05$) from baseline.
GGT = γ-Glutamyltransferase. Cr = Creatinine. GGT:Cr = Ratio of urine GGT activity to urine Cr concentration.

concentration of 1.7% (range, 1.6 to 1.85%) for the 2-hour period. A mean peak inspiratory pressure, measured at the distal end of the endotracheal tube, was 21 cm H_2O (range, 20 to 30 cm H_2O), and the frequency averaged 7 breaths/min (range, 3 to 17 breaths/min). The PaO_2 was > 200 mm Hg during anesthetic maintenance. Recovery from general anesthesia was uneventful for all horses. Eight of the 9 horses were standing at the time of collection of the postanesthetic samples. The mean time to standing was 40 minutes (range, 21 to 72 minutes).

Urine volume and specific gravity—Baseline urine flow was 0.92 ± 0.17 ml/kg/h (**Table 1**). Urine flow significantly increased by 1 hour of anesthesia to 2.86 ± 0.97 ml/kg/h and then decreased to baseline during the subsequent monitoring period (**Fig 1**). Of the 9 horses, 3 horses had urine flow at 1 hour of anesthesia equal to or less than the mean baseline urine flow (compared with mean values for these 3 horses as well as mean values for all 9 horses) and were referred to as nonresponders, 3 horses had a mild increase in flow from baseline for this period (mild responders), and 3 horses had a major increase in flow (major responders). Mean urine flow during the first 60 minutes of anesthesia for these 3 groups of horses was 0.71 ml/kg/h (40% decrease from baseline values; range, 0.55 to 0.93 ml/kg/h), 1.44 ml/kg/h (95% increase; range, 1.13 to 1.57 ml/kg/h), and 5.35 ml/kg/h (728% increase; range 4.92 to 6.08 ml/kg/h) for the nonresponders, mild responders, and major responders, respectively (**Fig 2**).

Urine specific gravity was decreased from baseline at all measurement points (Table 1). In general, specific gravity decreased from baseline to a minimum value by 60 minutes of anesthesia and then progressively increased toward (but not reaching) the baseline value by the end of study.

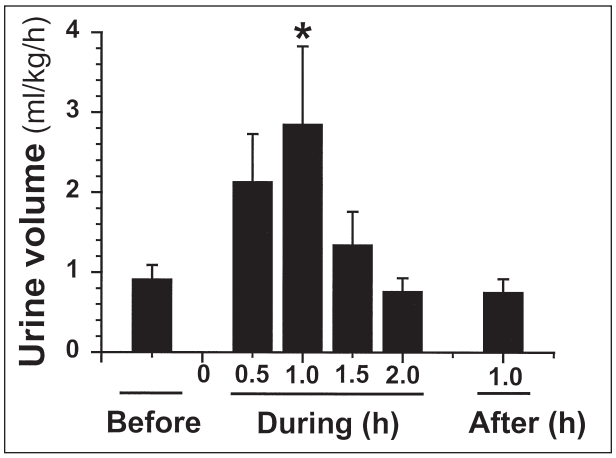

Figure 1—Mean (± SE) urine volume before, during, and after 2 hours of general anesthesia and minor surgery in 9 horses. *Significant difference ($P < 0.05$) from baseline (before anesthesia).

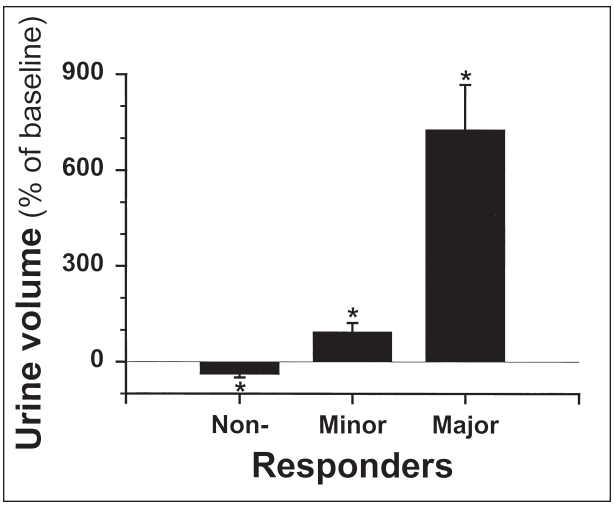

Figure 2—Mean (± SE) percent change in urine volume measured from 0 to 60 minutes after anesthetic induction, compared with baseline values (before anesthesia, horizontal line) in 9 horses. Of the 9 horses, 3 had urine flow equal to or less than the mean baseline urine flow (nonresponders), 3 horses had a mild increase in urine flow from baseline (minor responders), and 3 had a major increase in urine flow (major responders). *Significant ($P < 0.05$) difference from baseline values.

Table 2—Mean (± SE) urine and serum analytes in 9 mares before, during, and after general anesthesia

Analytes	Baseline	Anesthesia (min) 30	60	120	1 hour after anesthesia
Serum Na (mmol/L)	139 ± 1	137 ± 1*	138 ± 1	138 ± 1	138 ± 1
Serum K (mmol/L)	3.5 ± 0.2	3.8 ± 0.1	3.5 ± 0.1	3.4 ± 0.1	4.2 ± 0.2*
Serum Cl (mmol/L)	95 ± 1	95 ± 1	95 ± 1	95 ± 1	94 ± 1
Serum Ca (mg/dl)	12.4 ± 0.2	10.9 ± 0.1*	10.6 ± 0.1*	10.3 ± 0.1*	10.6 ± 0.1*
Serum iPO_4 (mg/dl)	2.9 ± 0.2	3.5 ± 0.3*	3.7 ± 0.3*	3.9 ± 0.3*	4.6 ± 0.3*
Serum Cr (mg/dl)	1.2 ± 0.1	1.1 ± 0.1*	1.1 ± 0.1*	1.1 ± 0.1*	1.5 ± 0.1*
SUN (mg/dl)	23 ± 1	20 ± 1*	19 ± 1*	19 ± 1*	20 ± 1*
Serum glucose (mg/dl)	121 ± 4	167 ± 8*	144 ± 6	138 ± 11	144 ± 13
Urine Na (mmol/L)	64 ± 14	76 ± 14	93 ± 20	95 ± 14	95 ± 15
Urine K (mmol/L)	257 ± 23	562 ± 395	91 ± 34*	152 ± 33	197 ± 22
Urine Cl (mmol/L)	138 ± 8	102 ± 17	87 ± 21*	121 ± 16	132 ± 9
Urine Ca (mg/dl)	414 ± 161	66 ± 17*	24 ± 7*	34 ± 5*	37 ± 8*
Urine iPO_4 (mg/dl)	0.2 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.5 ± 0.2	0.5 ± 0.3
Urine Cr (mg/dl)	178 ± 15	150 ± 28	86 ± 26*	126 ± 22	179 ± 29
Urine glucose (mg/dl)	4 ± 1	8 ± 4	12 ± 7	14 ± 5†	17 ± 6†

†Mean values determined on the basis of data from 8 horses.
iPO_4 = Inorganic phosphate. SUN = Serum urea nitrogen.
See Table 1 for remainder of key.

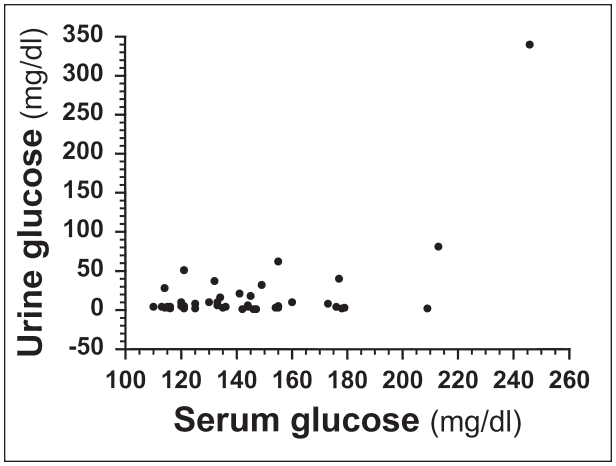

Figure 3—Results of time-paired serum and urine glucose measurements from 9 horses under general anesthesia. Five time-matched pairs of measurements were obtained from each horse at 30, 60, 90, and 120 minutes during general anesthesia and at 1 hour after anesthesia.

Table 3—Mean (± SE) urine glucose and protein concentrations in 9 horses before, during, and after general anesthesia

		Anesthesia (min)			
Variables	Baseline	30	60	120	1 hour after anesthesia
Glucose (mg/dl)	3.8 ± 0.4	7.7 ± 4.1	12 ± 6.5	21 ± 8.5	17 ± 5.9*
Protein (mg/dl)	27.7 ± 1.8	25.7 ± 4.3	21.8 ± 6.4	41 ± 6.8	53 ± 19.3

*Mean value determined on the basis of data from 8 horses as the result of laboratory error.

Blood and urine analytes—Except for isolated points, serum and urine concentrations of Na, K, and Cl did not change (**Table 2**). Serum Ca, Cr, and SUN concentrations significantly decreased during anesthesia. With the exception of serum Cr concentration, these changes persisted during the 1-hour period after anesthesia. A small but significant increase in serum Cr concentration was observed after anesthesia. Urine Ca concentration decreased during anesthesia, and the ratio of urine GGT activity to urine Cr concentration increased slightly at all points during and following anesthesia. The serum iPO_4 concentration was significantly increased during and following anesthesia.

Serum glucose concentration increased significantly by 30 minutes of anesthesia and then decreased toward baseline over time (Table 1). Except for 2 horses, glucose concentration in urine was negligible (**Fig 3**). Anesthetic induced variation in urine protein concentration was also negligible (**Table 3**).

Discussion

Renal disease is often considered of low natural occurrence in horses. However, an increasing number of drugs and therapeutic measures applied to equine patients may have serious and irreversible consequences on normal physiologic functions.

Detection of renal dysfunction in horses can be difficult. Consequently, many problems may go unnoticed and resolve spontaneously, whereas others are not diagnosed until later in the developmental process. It is generally appreciated that drugs and events associated with general anesthesia may temporarily disrupt normal renal function. If the initiating insult is severe or occurs in horses with increased susceptibility, ischemic or nephrotoxic renal injury may result.[1] Accordingly, results of the nature reported here are of benefit for later reference.

The purpose of our study was to provide baseline information on the effect of general anesthesia and minor surgery on the quantity and quality of urine in horses. Results of our study reveal changes in selected serum and urine analytes from clinically normal horses subjected to 2 hours of general anesthesia and minor surgical intervention.

In our study, alterations in serum Na, K, Cl, Cr, and SUN concentrations from baseline measurements were significant, but these changes were small in magnitude and judged to be of no major clinical importance. Similarly, changes in urine GGT activity were significant but also small in magnitude and not of clinical importance. The γ-glutamyltransferase is an enzyme found in high concentrations in the kidney (especially proximal tubular cells) and some other tissues of horses.[13,14] An increase in urine GGT activity is a sensitive, specific, and early indicator of acute renal injury.[14-16] Baseline values for urine GGT activity and urine GGT activity indexed to urine Cr concentration from our study are within the reported reference range for horses.[15,17] Therefore, our baseline values provide additional independent reference values for horses.

In the horses of our study, serum Ca concentration decreased and iPO_4 concentration increased within 30 minutes of anesthetic induction; these changes continued throughout 1 hour after anesthesia. The observed changes between baseline measurements and those 1 hour after anesthesia are similar to reports[2-4] of other clinically normal horses anesthetized only with an inhalation agent in the absence of modifying factors such as anesthetic adjuvant drugs, surgical stress, or both. These findings imply transient alteration in renal function; however, the mechanism remains unexplained. Results of our study indicate that changes in serum Ca and iPO_4 concentrations develop early in the course of anesthesia.

The most prominent results of our study were an anesthesia-related increase in serum glucose concentration, an increase in urine volume, and an associated decrease in urine specific gravity. These changes are likely caused by xylazine, with perhaps a reduced magnitude of change imposed by other conditions of general anesthesia.

Xylazine induces hyperglycemia in awake and anesthetized horses,[5,9,18-20] and these changes are largely a result of a decrease in serum concentration of insulin.[18-20] Results of our study are in qualitative agreement with previous reports[9,19] of hyperglycemia. They are also in close quantitative agreement with results from ketamine-anesthetized horses studied by Tranquilli et al,[19] but serum glucose concentrations in our study are less (about 40%) than that recently published by Steffey et al[12] in horses anesthetized for a prolonged period only with isoflurane.[9] The underlying mechanism of this discrepancy is unresolved; however, confounding effects of anesthetic adjuvant

drugs (eg, influence on renal blood flow) in the study by Tranquilli et al[19] and our study are relative to another study[9] that used prolonged anesthesia with isoflurane.

Xylazine transiently increases urine production in awake and anesthetized equids.[5,6,21] Likely, the increased urine flow measured in our study was caused by actions of xylazine. Similar to findings from an earlier study from this laboratory,[9] the significant increase in urine flow observed in our study of anesthetized horses was almost 40% less than that found previously in awake horses given a similar dose of xylazine.[5] This information adds further indirect evidence that general anesthesia influences (reduces) the diuretic effect of xylazine.

The increased urine flow found in our study is of interest for a number of reasons. First, these results highlight that increased urine output likely will be associated with anesthetic protocols designed for horses that include xylazine (or other α_2-adrenergic agonists such as detomidine) and that this should be considered in overall patient management.[9,21] Second, although xylazine administration resulted in hyperglycemia, glucose was not detected in substantial quantities in urine (Table 2). This lends further evidence that in horses, unlike for example cattle,[22] the increased urine flow does not reflect a prominent osmotic diuretic effect of glucose.[5,7,21] Glucosuria occurs when the renal tubular maximum for reabsorption from filtrate is exceeded. This may occur as a result of hyperglycemia or because tubular glucose reabsorptive capacity is reduced. The renal threshold for glucose is generally considered to be 160 to 180 mg/dl in horses.[23] In our study, none of the blood glucose concentrations below 160 mg/dl or between 160 and 180 mg/dl were associated with abnormal glucose concentrations in urine. Only 2 horses had a blood glucose concentration in excess of 180 mg/dl at any time during our study (Fig 3), and only 1 of these horses had a remarkably high serum concentration (at 2 time points) of glucose. Interestingly, this horse was 1 of 3 horses referred to as minor responders with reference to urine volume. These data raise the question as to the accuracy of the commonly accepted range of blood glucose concentrations of 160 to 180 mg/dl as the renal threshold for horses. Although difficult to trace from the literature, it appears that this long-held standard for horses was extrapolated from work in other species and a study[24] of 9 horses. Further investigations are necessary to confirm or refute this commonly accepted quantitative benchmark.

[a]Kimsey Welding, Woodland, Calif.
[b]JD Medical, Phoenix, Ariz.
[c]Poet IQ, Criticare Systems, Waukesha, Wis.
[d]LB-2 anesthetic analyzer, Sensormedics Corp, Anaheim, Calif.
[e]LB-2 CO_2 analyzer, Sensormedics Corp, Anaheim, Calif.
[f]Model #90603A-11, Spacelabs, Redmond, Wash.
[g]ABL 330, Radiometer America, Cleveland, Ohio, or ABL 510, Radiometer, Copenhagen, Denmark.

References

1. Sladen RN. Renal physiology. In: Miller RD, ed. *Anesthesia*. Philadelphia: Churchill Livingstone Inc, 2000;663–693.
2. Steffey EP, Zinkl J, Howland D Jr. Minimal changes in blood cell counts and biochemical values associated with prolonged isoflurane anesthesia of horses. *Am J Vet Res* 1979;40:1646–1648.
3. Steffey EP, Farver T, Zinkl J, et al. Alterations in horse blood cell count and biochemical values after halothane anesthesia. *Am J Vet Res* 1980;41:934–939.
4. Steffey EP, Giri SN, Dunlop CI, et al. Biochemical and haematological changes following prolonged halothane anaesthesia in horses. *Res Vet Sci* 1993;55:338–345.
5. Thurmon JC, Steffey EP, Zinkl JG, et al. Xylazine causes transient dose-related hyperglycemia and increased urine volumes in mares. *Am J Vet Res* 1984;45:224–227.
6. Gasthuys F, Vandenhende C, de Moor A. Study of some ionary parameters in horse serum and urine during halothane anaesthesia with xylazine premedication. *J Vet Med* 1986;33:791–800.
7. Gasthuys F, Terpstra P, Vandenhende C, et al. Hyperglycaemia and dieresis during sedation with detomidine in the horse. *Zentralbl Vetinarmed [A]* 1987;34:641–649.
8. Gasthuys F, Vandenhende C, de Moor A. Biochemical changes in blood and urine during halothane anaesthesia with detomidine premedication in the horse. *Zentralbl Veterinarmed [A]* 1988;35:655–665.
9. Steffey EP, Pascoe PJ, Woliner MJ, et al. Effects of xylazine hydrochloride during isoflurane-induced anesthesia in horses. *Am J Vet Res* 2000;61:1225–1231.
10. Scheuch BC, VanHoogmoed LM, Wilson WD, et al. Comparison of intraosseous or infravaneous vein infusion to deliver amikacin sulfate to the tibiotarsal joint of a horse. *Am J Vet Res* 2002;63:374–380.
11. Ozanne GM, Young WG, Mazze WJ, et al. Multipatient anesthetic mass spectrometry: rapid analysis of data stored in long catheters. *Anesthesiology* 1981;55:62–70.
12. Steffey EP, Woliner MJ, Young WG, et al, Two years' experience with a multi-station, multi-anesthetic and respiratory gas analysis system (MARGAS), in *Proceedings*. 4th Int Congr Vet Anaesth 1991;83–85.
13. Rico AG, Braun JP, Benard P, et al. Tissue distribution and blood levels of gamma-glutamyl transferase in the horse. *Equine Vet J* 1977;9:100–101.
14. Braun JP, Benard P, Burgat V, et al. Gamma glutamyl transferase in domestic animals. *Vet Res Commun* 1983;6:77–90.
15. Adams R, McClure JJ, Gossett KA, et al. Evaluation of a technique for measurement of g-glutamyltranspeptidase in equine urine. *Am J Vet Res* 1985;46:147–150.
16. Bayly WM, Brobst DF, Elfers RS, et al. Serum and urinary biochemistry and enzyme changes in ponies with acute renal failure. *Cornell Vet* 1986;76:306–317.
17. Brobst DF, Carroll RJ, Bayly WM. Urinary enzyme concentrations in healthy horses. *Cornell Vet* 1986;76:299–306.
18. Thurmon JC, Neff-Davis CA, Davis LE, et al. Xylazine hydrochloride-induced hyperglycemia and hypoinsulinemia in thoroughbred horses. *J Vet Pharmacol Ther* 1982;5:241–245.
19. Tranquilli WJ, Thurmon JC, Neff-Davis CA, et al. Hyperglycemia and hypoinsulinemia during xylazine-ketamine anesthesia in thoroughbred horses. *Am J Vet Res* 1984;45:11–14.
20. Greene SA, Thurmon JC, Tranquilli WJ, et al. Effect of yohimbine on xylazine-induced hypoinsulinemia and hyperglycemia in mares. *Am J Vet Res* 1987;48:676–678.
21. Trim CM, Hanson RR. Effects of xylazine on renal function and plasma glucose in ponies. *Vet Rec* 1986;118:65–68.
22. Thurmon JC, Nelson DR, Hartsfield SM, et al. Effects of xylazine hydrochloride on urine in cattle. *Aust Vet J* 1978;54:178–180.
23. Carlson GP. Clinical chemistry tests. In: Smith BP, ed. *Large animal internal medicine*. St Louis: Mosby Year Book Inc, 1996;441–469.
24. Link RP. Glucose tolerance in horses. *J Am Vet Med Assoc* 1940;97:261–262.