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Evaluation of acid–base disorders in dogs and cats presenting to an emergency room. Part 1: Comparison of three methods of acid–base analysis

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Abstract

Objective – To compare the diagnostic performance of the traditional approach to acid–base analysis with the Stewart approach and a semiquantitative approach.
Design – Prospective cohort study.
Setting – University teaching hospital.
Animals – A total number of 84 dogs and 14 cats presenting to a university teaching hospital emergency room.
Procedures – All dogs and cats in which venous blood samples for acid–base, lactate, and serum biochemical analysis were all collected within 60 minutes of each other, over a 5-month enrollment period. Acid–base analysis was performed using the traditional approach, Stewart approach, and a semiquantitative approach.
Results – Traditional acid–base analysis identified respiratory acid–base abnormalities in 14/98 animals and metabolic acid–base abnormalities in 67/98. A mixed disorder of metabolic acidosis and respiratory alkalosis was most common occurring in 29/98 patients. The Stewart approach identified metabolic abnormalities in 82/98 patients; strong ion difference abnormalities were evident in 68/98 cases; an increased strong ion gap acidosis was identified in 49/98 cases; and changes in the quantity of weak acids in 25/98 cases. The semiquantitative approach identified abnormalities in all cases evaluated. Of the 14 patients with a primary respiratory acid–base abnormality, the Stewart approach identified metabolic abnormalities in 9 and the semiquantitative approach found abnormalities in all animals.
Conclusions and Clinical Relevance – The physicochemical approaches diagnosed more acid–base abnormalities in this population than the traditional approach although many of the abnormalities identified were small and of unknown clinical relevance. The physicochemical approaches may provide greater insight as to the underlying etiology of abnormalities, which maybe of particular relevance to cases with changes in albumin and/or phosphorus concentration.

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Keywords: Stewart approach, anion gap, strong ion difference

Introduction

Acid–base disorders are common in critically ill or injured human patients and have been found to have diagnostic and prognostic relevance.[1–4] Acid–base abnormalities may have similar significance in veterinary patients. Base excess (BE) was correlated with survival in canine blunt trauma patients and bicarbonate concentration has been inversely correlated with mortality in feline patients.[5–7] Correct

Abbreviations

AG	anion gap
A_{TOT}	total quantity of weak acids
BE	base excess
SID	strong ion difference
SIG	strong ion gap
XA	semiquantitative measure of unmeasured ions

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identification of acid–base disorders is likely to be a valuable tool in the effective recognition and treatment of metabolic derangements in critically ill and injured animals.

There are several different approaches to acid–base analysis described in the literature. The traditional approach is based on the Henderson–Hasselbalch equation and evaluates pH, P_{CO_2}, and bicarbonate, with the option to also consider BE and the anion gap (AG). Several authors have criticized the traditional approach for its inability to detect complex metabolic acid–base disturbances that are common in critically ill or injured patients.[8–11] Moreover, these traditional approaches typically offer little specific guidance to the clinician on how these complex disorders might be most effectively addressed.

An alternative approach to acid–base analysis uses physicochemical principles as described by Stewart, who defined acid–base balance with 3 variables: P_{CO_2}, strong ion difference (SID), and the total quantity of nonvolatile weak acids (A_{TOT}).[12] Strong ions are those that are fully dissociated at physiologic pH, and SID is the difference in quantity between the strong cations and strong anions measured in the plasma. The parameter A_{TOT} is a measure of the 2 main nonvolatile weak acids, albumin and phosphorus. Studies performed in human patients comparing the diagnostic performance of the Stewart approach with the traditional approach have yielded contradictory results.[9,13–15]

A third approach, developed by Fencl et al,[10] combines concepts from the Stewart physicochemical method with the BE, determined via traditional analysis.[10] This semiquantitative approach calculates the influence of individual contributors to the BE, including changes in free water, chloride, albumin, phosphorus, and lactate concentrations. This approach has been reported to allow the detection of acid–base abnormalities in patients considered to have a normal acid–base balance by traditional acid–base methods.[10,11,15]

Although there are several reports in the human literature comparing the performance of traditional versus the Stewart acid–base analytical approach, there is at present no consensus regarding which is superior.[9,13,16] There are no such investigations in the veterinary literature and very few evaluations of the diagnostic performance of the semiquantitative approach have been published in this setting. Our hypothesis was that there would be no difference between the diagnostic performance of these 3 approaches to acid–base analysis when applied to venous blood samples collected from dogs and cats on presentation to an emergency room. The secondary aim of this study was to describe the nature of acid–base abnormalities in this patient population.

Table 1: Venous acid–base and biochemical values of healthy dogs and cats used as a comparison group

Parameter	Dogs	Cats
Sodium (mmol/L; mEq/L)	144–152	148–156
Chloride (mmol/L; mEq/L)	111–121	115–126
Potassium (mmol/L; mEq/L)	3.6–4.7	3.4–4.7
Ionized calcium (mmol/L)	1.2–1.5	1.1–1.4
Albumin (g/L)	34–43	22–46
Albumin (g/dL)	3.4–4.3	2.2–4.6
Phosphorus (mmol/L)	0.8–1.7	1–2
Phosphorus (mg/dL)	2.6–5.2	3.2–6.3
pH	7.32–7.43	7.34–7.43
$PvCO_2$ (mmHg)	37–45	34–39
Bicarbonate (mmol/L; mEq/L)	18–26	20–23
Base excess (mmol/L; mEq/L)	−4 to −1	−5 to 0
Lactate (mmol/L)	<2.0	<2.0
Calculated acid–base values (mmol/L; mEq/L)		
Anion gap	8–16	16–20
SIDapparent	34–40	32–34
A_{TOT}	10–16	8–17
SIG	−6 to 4	−2 to 4
Free water effect	−1.0 to 1.0	−1.0 to 1.0
Chloride effect	−5 to 5	−4 to 5
Albumin effect	−2 to 2	−3 to 3
Phosphorus effect	−1 to 1	−1 to 1

A_{TOT}, total quantity of weak acids.

Materials and Methods

This prospective, observational study enrolled all dogs and cats presenting to the University of California, Davis, William R. Pritchard Veterinary Medical Teaching Hospital emergency service in which venous blood samples for acid–base, electrolyte, lactate, and serum biochemistry analysis were all collected within 60 minutes of each other, over a 5-month enrollment period. The timing and choice of blood sample type and diagnostic tests performed was at the clinician's discretion. Patients that qualified for enrollment were recorded on a data sheet by the emergency room clinician or technician at the time of blood sample collection. The patient signalment and primary clinical diagnoses were recorded.

Comparison values

Blood samples from 10 healthy dogs and 8 healthy cats were obtained for the purposes of comparison of acid–base, lactate, and electrolyte values (Table 1) on the ICU point of care machine with those obtained from clinical patients.[a] This range was derived from the mean ± 2 SDs. These animals were determined to be in good health on the basis of history, physical examination, packed cell volume, and total protein measurement. The standard reference values at the clinical pathological laboratories of the University of California, Davis determined from 100 healthy adult dogs and cats were used for the

Table 2: Formulas for calculated variables[9,17–19]

Parameter	Formula
Anion gap	$([Na^+] + [K^+]) - ([HCO_3^-] + [Cl^-])$
SIDapparent	$([Na^+] + [K^+] + [Ca^{2+}]) - [Cl^-]$
Albumin contribution	Measured albumin $\times$ $((0.123 \times pH) - 0.631) \times 10$
Phosphorus contribution	Measured phosphorus $\times$ $0.323 \times ((0.309 \times pH) - 0.469)$
A_{TOT}	Albumin contribution + Phosphorus contribution
SIDeffective	$[HCO^{3-}]$ + albumin contribution + phosphorus contribution
Strong ion gap	SID apparent − SID effective
Free water effect	$0.25([Na^+]$ − mid-normal $[Na^+])$
Dogs cats	$0.22([Na^+]$ − mid-normal $[Na^+])$
Corrected chloride	Measured $[Cl^-] \times$ (mid-normal $[Na^+]$/measured $[Na^+]$)
Chloride effect	Mid-normal $[Cl^-]$ − corrected $[Cl^-]$
Phosphate effect	0.58 (Mid-normal [phosphorus] − measured [phosphorus])
Albumin effect	3.7 (Mid-normal albumin − measured [albumin])
Lactate effect	$-1 \times$ [lactate]
Sum of effects	Free water effect + chloride effect + phosphate effect + albumin effect + lactate effect
Unmeasured anion effect	Base excess − sum of effects

Note: Mid-normal values were determined as the central value of the comparison range shown in Table 1. Albumin, g/dL; phosphorus, mg/dL; electrolytes and lactate, mmol/L. SID, strong ion difference; A_{TOT}, total quantity of weak acids.

phosphorus and albumin concentrations measured on a serum biochemistry panel. A comparison range for calculated acid–base values was determined from the normal values collected from apparently healthy dogs and cats (Table 2).[10,17–19]

Measurements

Heparinized blood samples for acid–base, lactate, and electrolyte values were measured immediately following sample collection on a point of care machine.[a] The majority of samples were collected as whole blood and immediately transferred to 125 μL heparinized clinitubes, purpose-made for the blood gas machine. Some of the samples were transferred to commercial heparinized tubes containing 50 units of heparin with a minimum volume of 1 mL of blood.

Blood samples for phosphorus and albumin concentrations were submitted to the hospital central diagnostic laboratory for analysis.[b] The results of the blood gas, lactate, and serum biochemistry tests were imported from the computer-based laboratory data bank to a spreadsheet for analysis.[c]

Calculated variables

Bicarbonate and BE were calculated by the analyzer using the Henderson–Hasselbalch and van Slyke equations, respectively.[17,20] The BE equation used was that recommended by the Clinical Laboratory Standards Institute (C46-A2). Table 2 lists the formulas used for all other calculated acid–base variables. The value for CO_2 solubility S_{CO_2} in plasma used by the blood gas machine[a] was 0.03 mmol/L/mmHg. The equation used for the determination of bicarbonate was

$$HCO_3 = S_{CO_2} \times P_{CO_2} \times 10^{(pH - pK'1)}$$

where the pK'_1 used was derived from the formula: $pK'_1 = 6.125 - \log[1 + 10^{(pH - 8.7)}]$.

Acid–base analysis

The metabolic acid–base diagnosis of each patient was determined using each of three different approaches, as outlined in the text boxes. The respiratory acid–base diagnosis utilized the criteria outlined for the traditional approach in textbox 1.

Statistics

Abnormal values for definitions of each acid–base disorder were considered as those that were 2 SDs above or below the mean of the comparison values. A reference range for AG, SIDapparent, SIDeffective, and SIG was determined from the normal values collected, for dogs and cats, respectively. A reference range for the semiquantitative parameters of free water effect, chloride effect, albumin effect, and phosphorus effect was determined by using the high and low value of the normal range for each variable.

Results are reported as median and range. Linear regression was used to evaluate the correlation between SID with BE.[d] A P value of <0.05 was considered significant.

Textbox 1: Diagnostic criteria for traditional acid–base analysis[18,19]

Dogs
1) Simple disturbances
  a. Metabolic acidosis: pH $<$ 7.32, HCO_3- $<$ 18 mmol/L,
  $PvCO_2 = 40 - (\Delta HCO_3$ x 0.7) $\pm$ 3
  b. Metabolic alkalosis: pH $>$ 7.43, HCO_3 $>$ 26 mmol/L,
  $PvCO_2 = 40 + (\Delta HCO_3$ x 0.7) $\pm$ 3
  ΔHCO_3 = Mid-normal HCO_3 [22 mmol/L]– Measured HCO_3
  c. Respiratory acidosis: pH $<$ 7.32, $PvCO_2$ $>$ 45 mmHg,
  $HCO_3 = 22 + (0.15\text{-}0.35$ x $\Delta PCO_2) \pm 2$
  d. Respiratory alkalosis: pH $>$ 7.43, $PvCO_2$ $<$ 37 mmHg,
  $HCO_3 = 22 - (0.25-0.55$ x $\Delta PCO_2) \pm 2$
  ΔPCO_2 = Mid-normal PCO_2 [41 mmHg] – Measured PCO_2
2) Mixed disturbances
  · Response in the secondary system not within predicted range
3) Metabolic acidosis further classified by anion gap
  a. Metabolic acidosis associated with increased AG: AG $>$ 16 mmol/L
  b. Metabolic acidosis not associated with increased AG: AG $\leq$ 16 mmol/L
Cats
1) Simple disturbances
  i. Metabolic acidosis: pH $<$ 7.34, HCO_3- $<$ 18 mmol/L
  j. Metabolic alkalosis: pH $>$ 7.43, HCO_3 $>$ 26 mmol/L
  k. Respiratory acidosis: pH $<$ 7.34, $PvCO_2$ $>$ 39 mmHg
  l. Respiratory alkalosis: pH $>$ 7.43, $PvCO_2$ $<$ 34 mmHg
2) Mixed disturbances
  Compensation was not calculated for cats, if abnormalities were present of both $PvCO_2$ and BE/HCO_3- it was reported as two co-existing abnormalities
3) Metabolic acidosis further classified by anion gap
  c. Metabolic acidosis associated with increased AG: AG $>$ 20 mmol/L
  b. Metabolic acidosis not associated with increased AG: AG $\leq$ 20 mmol/L

Textbox 2: Diagnostic criteria for Stewart acid-base analysis[18,21]

Dogs
1) Strong ion difference
  a.Increased SID metabolic alkalosis: SIDapp $>$ 45 mmol/L
  b. Decreased SID metabolic acidosis: SIDapp $<$ 32 mmol/L
2) Total weak acids
  a. Increased ATOT metabolic acidosis: A_{TOT} $>$ 11 mmol/L
  b. Decreased ATOT metabolic alkalosis: A_{TOT} $<$ 10 mmol/L
3) Unmeasured Anions:
  a. Increased SIG: SIG $>$ 7 mmol/L
Cats
1) Strong ion difference
  a. Increased SID metabolic alkalosis: SIDapp $>$ 44 mmol/L
  b. Decreased SID metabolic acidosis: SIDapp $<$ 40 mmol/L
2) Total weak acids
  a. Increased ATOT metabolic acidosis: A_{TOT} $>$ 17 mmol/L
  b. Decreased ATOT metabolic alkalosis: A_{TOT} $<$ 8 mmol/L
2) Total weak acids
  c. Increased ATOT metabolic acidosis: A_{TOT} $>$ 17 mmol/L
  d. Decreased ATOT metabolic alkalosis: A_{TOT} $<$ 8 mmol/L
3) Unmeasured Anions:
  b. Increased SIG: SIG $>$ 9 mmol/L

Textbox 3: Semi-quantitative Acid-base Analysis — Diagnostic Criteria[10,19,22]

Dogs
Free water effect:
  · Dilutional acidosis: Free water effect $<$ −1.25 mmol/L
  · Contraction alkalosis: Free water effect $>$ 1.0 mmol/L
Chloride effect:
  · Acidosis: Chloride effect $<$ −5.0 mmol/L
  · Alkalosis: Chloride effect $>$ 5.0 mmol/L
Albumin effect:
· Acidosis: Albumin effect $<$ −2.0 mmol/L
  · Alkalosis: Albumin effect $>$ 2.0 mmol/L
Phosphorus effect:
  · Acidosis: Phosphorus effect $<$ −1.0 mmol/L
  · Alkalosis: Phosphorus effect $>$ 1.0 mmol/L
Lactate effect:
  · Acidosis: Lactate effect $>$ −2.0 mmol/L
Cats
Free water effect:
  · Dilutional acidosis: Free water effect $<$ −1.0 mmol/L
  · Contraction alkalosis: Free water effect $>$ 0.7 mmol/L
Chloride effect:
  · Acidosis: Chloride effect $<$ −4.0 mmol/L
  · Alkalosis: Chloride effect $>$ 5.0 mmol/L
Albumin effect:
  · Acidosis: Albumin effect $<$ −3.0 mmol/L
  · Alkalosis: Albumin effect $>$ 3.0 mmol/L
Phosphorus effect:
  · Acidosis: Phosphorus effect $<$ −1.0 mmol/L
  · Alkalosis: Phosphorus effect $>$ 1.0 mmol/L
Lactate effect:
  · Acidosis: Lactate effect $>$ −2.0 mmol/L
Dogs and Cats
Unmeasured Ions (XA):
XA =BE – (Free water effect + chloride effect + albumin effect + phosphorus effect + lactate effect)
  a. Unmeasured acids: XA $<$ −0.5 mmol/L
  b. Unmeasured alkalis: XA $>$ 0.5 mmol/L

Results

A total of 98 animals were enrolled including 84 dogs and 14 cats. The acid–base, electrolyte, and lactate values for these animals are shown in Table 3 and the clinical diagnoses are shown in Table 4.

Traditional acid–base analysis revealed an abnormality in 82/98 cases with simple respiratory acid–base abnormalities in 14 of the cases evaluated, and a metabolic acid–base abnormality evident in 68 cases (Table 5). The most common abnormality was a mixed disorder of metabolic acidosis with a concurrent respiratory alkalosis, found in 29/98 of patients. A primary respiratory alkalosis was evident in 11 patients, a mixed disorder of metabolic alkalosis with respiratory alkalosis occurred in 6 patients making a total of 46/98 patients with respiratory alkalosis. A simple metabolic acidosis was uncommon (14/98), but overall 53/98 animals had a metabolic acidosis when those with mixed disorders were also considered. An increased AG metabolic acidosis was present in 34 patients, including both simple and mixed disorders.

The Stewart approach detected metabolic acid–base abnormalities in 82/98 patients. Changes in SID were evident in 68/98 cases; changes in A_{TOT} were found in

Table 3: Acid–base, electrolyte, and lactate values in 84 dogs and 14 cats presented to the emergency room

Parameter	Dogs median (range)	Cats median (range)
Sodium (mmol/L)	146 (131–162)	151 (141–194)
Potassium (mmol/L)	4.0 (2.3–9.3)	3.4 (2.6–8.3)
Ionized calcium (mmol/L)	1.16 (0.64–2.02)	1.19 (0.78–1.42)
Chloride (mmol/L)	115 (91–156)	121 (113–156)
Chloride corrected (mmol/L)	113 (97–123)	118 (115–124)
Albumin (g/dL)	3.1 (1.0–4.6)	3.0 (1.7–4.2)
Phosphorus (mg/dL)	4.8 (0.9–22.3)	5.9 (3.2–14.3)
pH	7.38 (7.118–7.510)	7.258 (7.167–7.386)
$PvCO_2$ (mmHg)	34 (18–51)	34 (25–51)
Bicarbonate (mmol/L)	20.6 (9.2–37.4)	16.4 (9–21.1)
BE (mmol/L)	−4.3 (−18.7 to 12.2)	−7.8 (−18 to −3.3)
Lactate (mmol/L)	2.1 (0.6–11.6)	1.9 (0.8–6.4)
Anion gap (mmol/L)	14 (9–32)	18 (12–26)
SIDapparent (mmol/L)	42 (32–54)	40 (34–49)
A_{TOT} (mmol/L)	11.9 (5.7–17.7)	13.4 (8.0–15.7)
SIDeffective (mmol/L)	32.3 (16.4–49.7)	28.3 (22.8–36.3)
SIG (mmol/L)	8.9 (0.9–25.1)	11.3 (1.6–22.5)
Free water effect (mmol/L)	−0.8 (−3.8 to 2.5)	−0.7 (−2.3 to 8.7)
Chloride effect (mmol/L)	−0.3 (−10.4 to 16.2)	3.7 (−2.2 to 7.1)
Albumin effect (mmol/L)	1.6 (−2.5 to 7.2)	0.9 (−2.2 to 4.3)
Phosphorus effect (mmol/L)	−0.1 (−10.2 to 2.2)	−0.6 (−5.4 to 0.9)
Lactate effect (mmol/L)	−2.1 (−11.6 to 0)	−1.9 (−6.4 to −0.8)
Sum of effects (mmol/L)	−2.5 (−11.8 to 13.3)	0.1 (−6.6 to 6.4)
XA (mmol/L)	−1.5 (−20.6 to 3.7)	−8.1 (−18.1 to −5.2)

A_{TOT}, total quantity of weak acids; BE, base excess.

Table 4: Clinical diagnosis of 84 dogs and 14 cats presented to an emergency room

Disease process	*N*
Neoplasia	18
Renal or urinary disease	14
Pulmonary disease	11
Sepsis	10
Gastrointestinal disease	9
IMHA and/or ITP	7
Neurological disease	6
Seizures	5
Trauma	4
Other	4
Hepatic disease	3
MODS	3
Pancreatitis	3
Heart failure	3
Endocrine disease	3

Patients can be represented in more than one category.
IMHA, immune-mediated hemolytic anemia; ITP, immune-mediated thrombocytopenia; MODS, multiple organ dysfunction syndrome.

Table 5: Traditional acid–base diagnosis of 84 dogs and 14 cats presented to an emergency room

Acid–base diagnosis	*N*
Normal acid–base balance	17
Simple disorders	31
Respiratory acidosis	3
Respiratory alkalosis	11
Metabolic acidosis with normal AG	6
Metabolic acidosis with elevated AG	8
Metabolic alkalosis	3
Mixed disorders	50
Metabolic acidosis and respiratory acidosis	10
Metabolic acidosis and respiratory alkalosis	29
Metabolic alkalosis and respiratory alkalosis	6
Metabolic alkalosis and respiratory acidosis	5

AG, anion gap.

25/98 cases, and an increased SIG acidosis was identified in 49/98 of cases (Table 6). The Stewart approach identified one or more acidotic processes in 34/98 cases, one or more alkalotic processes in 12/98 cases, and coexisting alkalotic and acidotic processes in 36/98 cases.

Of the 82/98 cases found to have an abnormal metabolic acid–base balance by the Stewart approach, 24 of these animals were considered to have a normal metabolic acid–base balance by the traditional approach (either normal acid–base or simple respiratory disorders). Of the 67/98 cases considered to have an abnormal metabolic acid–base balance by the traditional approach, 9 animals were considered normal by the Stewart approach. These two methods agreed that a

Table 6: Stewart approach to acid–base diagnosis of 84 dogs and 14 cats presented to an emergency room

Metabolic acid–base diagnosis	N
Normal	16
One or more acidotic processes	34
One or more alkalotic process	12
Both alkalotic and acidotic processes	36
Individual abnormalities identified	
Increased SID alkalosis	33
Decreased SID acidosis	35
Increased A_{TOT} acidosis	3
Decreased A_{TOT} alkalosis	22
Increased SIG acidosis	49

Note: Cases can have more than one acid–base abnormality. A_{TOT}, total quantity of weak acids; SID, strong ion difference.

Table 7: Semiquantitative approach to metabolic acid–base diagnosis of 84 dogs and 14 cats presented to an emergency room

Metabolic acid–base diagnosis	N
Normal	0
One or more acidotic processes	38
One or more alkalotic processes	6
Both alkalotic and acidotic processes	54
Individual abnormalities identified	
Increased free water acidosis	27
Decreased free water alkalosis	9
Decreased chloride assoc alkalosis	12
Increased chloride assoc acidosis	12
Increased albumin acidosis	1
Decreased albumin alkalosis	34
Increased phosphorus acidosis	20
Decreased phosphorus alkalosis	8
Increased lactate acidosis	50
Increased unmeasured anions	68
Increased unmeasured cations	17

Note: Cases can have more than one acid–base abnormality.

metabolic acid–base abnormality was present 66% of the time and disagreed 34% of the time.

The semiquantitative approach identified metabolic acid–base abnormalities in all cases evaluated. The most common abnormalities were increases in unmeasured anions (68/98), and elevations in lactate (50/98), abnormalities in free water (36/98), albumin (35/98), and chloride effect (24/98) (Table 7). The semiquantitative approach identified one or more acidotic processes in 38/98 patients, assuming increased unmeasured anions reflect an acidotic process, one or more alkalotic processes in 6/98 cases, and coexisting alkalotic and acidotic processes in 54/98 cases. The diagnosis made by the semiquantitative approach agreed with the Stewart approach in 31/98 cases (Table 8).

Of the 14 patients diagnosed with a primary respiratory acid–base abnormality via the traditional approach, the Stewart approach identified metabolic abnormalities in 9 animals and the semiquantitative approach found abnormalities in all animals.

The SIDapparent showed a moderate correlation with the BE ($R = 0.45$, $P < 0.001$).

Discussion

This study found that the Stewart approach, as used in this study, indicated the presence of metabolic acid–base abnormalities more frequently than the traditional approach, while the semiquantitative approach identified abnormalities in all patients evaluated. In addition, both the Stewart and semiquantitative approaches diagnosed coexisting alkalotic and acidotic processes in many patients. There is ongoing controversy regarding the best method by which to analyze acid–base disorders. The traditional approach has the advantage of simplicity and the ability to comment on metabolic compensatory responses to primary respiratory disorders. The proposed advantages of the physiochemical approaches (Stewart and semiquantitative) are a greater ability to detect patients with abnormal metabolic acid–base balance as well as a greater insight as to the underlying mechanisms of metabolic acid–base abnormalities.

The acid–base diagnosis for many of the individual patients in this study varied depending on the approach to acid–base analysis utilized. The Stewart approach, as used in this study identified abnormalities in 24 patients that were considered to have a normal metabolic acid–base balance by the traditional approach whereas the traditional approach identified an abnormal acid–base balance in 9 patients considered to be normal by the Stewart approach. Without a gold standard for comparison, the relative accuracy of these two approaches cannot be determined. The results of previous human studies have been varied with some showing the Stewart approach revealed more acid–base abnormalities than the traditional approach while other studies reported they performed similarly.[9,13,16,23] It has been suggested that in the absence of abnormalities in albumin concentration or multiple coexisting disease processes the traditional approach is likely to have equivalent diagnostic performance to the physicochemical approaches.[13,18,24] It is important to note that there are a variety of formulas that can be used for the Stewart type approach to acid–base analysis; other analytic methods such as Constable's simplified strong ion model may have provided different results than those reported here.[18]

The semiquantitative approach to acid–base analysis detected more acid–base abnormalities in this study than the traditional or Stewart approaches. This may reflect a greater diagnostic sensitivity or a greater likelihood of error. Compared to the traditional or Stewart approaches, the semiquantitative approach allows identification of

Table 8: Comparison of the acid–base diagnosis between the Stewart approach and the semiquantitative approach for 84 dogs and 14 cats presented to an emergency room

	Stewart: normal metabolic acid–base	Stewart: one or more acidotic processes	Stewart: one or more alkalotic processes	Stewart: both alkalotic and acidotic processes
Semiquantitative: one or more acidotic processes	6	9	10	13
Semiquantitative: one or more alkalotic processes	0	2	1	3
Semiquantitative both alkalotic and acidotic processes	11	16	6	21

Numbers represent number of animals.

multiple coexisting acid–base abnormalities in the same patient, even if they counteract each other.[10,11] This likely explains why the Stewart approach and semiquantitative approach disagreed more often than it agreed as illustrated in Table 8. It is important to note that many of the abnormalities identified with the semiquantitative approach in patients in the present study were minor in severity, although it is possible that recognition of these individual processes may aid in understanding complex disease states and direct therapy. Unlike traditional acid–base analysis, the physicochemical approaches require numerous calculations based upon measurement of electrolyte, albumin, and phosphorus concentrations in addition to routine blood gas evaluation. It remains to be determined if there are any clinical benefits to the increased costs and effort involved in physicochemical acid–base analysis.

It is generally accepted that compensatory changes occur in response to primary acid–base disorders in dogs in an effort to regulate arterial pH. It is interesting to note that in the present study, the Stewart approach identified metabolic abnormalities in 9 of the 14 dogs with primary respiratory acid–base abnormalities and the semiquantitative approach found metabolic abnormalities in all animals with primary respiratory disorders. All the physiochemical approaches to acid–base analysis evaluate metabolic changes without reference to concurrent respiratory acid–base disorders, raising the concern that they can misinterpret metabolic compensatory responses as primary metabolic abnormalities.[13] This needs to be considered when assessing the sensitivity of these approaches as such misdiagnosis would be misleading and could confuse the clinical assessment of patients.

In this group of emergency room patients, traditional analysis identified metabolic acidosis in 53/98 patients, most commonly as part of a mixed disorder. In a large retrospective study at the same institution, metabolic acidosis was evident in 49% of canine and feline patients and mixed acid–base disorders were also the most common form of metabolic acidosis identified.[25] Metabolic acidosis is considered the most frequent acid–base abnormality in human trauma and intensive care patients, but the frequency of occurrence of individual acid–base disorders is not well reported.[3,9] In comparison to the traditional approach, the Stewart approach identified acidotic processes in 70/98 patients (many had more than one acidotic process present). The semiquantitative approach identified acidotic process in 92/98 patients; many of them were small in magnitude and most patients had more than one acidotic process present.

Despite the conceptual differences, the BE should be quantitatively similar to the change in SID, if A_{TOT} remains normal.[20,23] Hence, it is not surprising that when BE and SID have been compared in previous studies they yield very similar results.[13,23,24] In the present study, the SID showed only moderate correlation with the BE. This is likely to be due to abnormalities in A_{TOT} evident in this population. The blood gas machine calculates BE using a human algorithm which may further disturb the correlation between BE and SID in animals. This highlights the necessity of evaluating all components of Stewart acid–base analysis in order to accurately assess clinical cases. Purely evaluating the SID alone, a method that is preferred by some, can lead to misdiagnosis.

Hypoalbuminemia is a common finding in critically ill or injured animals.[26] As albumin is a weak acid, hypoalbuminemia is a cause of metabolic alkalosis that is unrecognized by traditional acid–base analysis. In Stewart acid–base analysis, hypoalbuminemia is evident by a decreased A_{TOT}, present in 22/98 of the patients in this study, while the semiquantitative approach identified an alkalotic effect associated with hypoalbuminemia in 34/98 of cases. As A_{TOT} is a measure of both albumin and phosphorus effects, the presence of a concurrent hyperphosphatemia may mask the effect of hypoalbuminemia. Although the results of this study suggest that the semiquantitative approach is more

sensitive at detecting the acid–base impact of changes in albumin concentration, many of the changes detected were very small in quantity and the clinical significance remains to be determined. This study used the human formula for A_{TOT}. Although Constable developed a formula for A_{TOT} validated for healthy dog albumin, it does not account for changes in phosphorus concentration.[27] We elected to use the human formula as we expected a group of emergency room patients to commonly have abnormal phosphorus levels. It would be interesting to compare Constable's approach in a future study.

Each of the 3 acid–base approaches evaluated provide an estimate of the presence of unmeasured anions, an entity utilized most commonly to aid in the diagnosis of metabolic acidosis. The AG is an adjunct to the traditional approach of acid–base analysis and an elevated AG metabolic acidosis was found in 34/98 of the cases in this study. In comparison, the Stewart measure of unmeasured anions, SIG, was elevated in 49/98 of the patients. A vital difference between AG and SIG is the role of albumin. Albumin is the major anion that contributes to the normal AG in healthy patients. In patients with hypoalbuminemia, the AG is decreased such that it may fail to reveal the presence of unmeasured anions as may accumulate in some types of metabolic acidosis.[28–30] In contrast, SIG does not include albumin and as a consequence it is more sensitive to unmeasured anions than AG.[3,13] The semiquantitative parameter, XA identified ummeasured anions in 68/98 of patients, which may reflect a greater diagnostic sensitivity. The assessment of unmeasured anions is further investigated in part 2 of this study published elsewhere in this issue.[31]

The potential clinical benefit of the Stewart and semiquantitative approaches is the ability to determine underlying causes for metabolic acid–base abnormalities that may direct therapy. For instance, an increased SID metabolic alkalosis will likely benefit from the administration of low SID IV fluid such as 0.9% sodium chloride. Similarly, if the semiquantitative approach revealed a significant alkalotic effect attributable to a low chloride, the use of a high chloride fluid such as 0.9% sodium chloride may be indicated. In addition, both the Stewart and the semiquantitative approaches can quantify the impact of changes in albumin concentration on acid–base balance; this may allow a clinician to identify the cause of a metabolic acid–base abnormality that would otherwise remain "mysterious" if only traditional acid base analysis was performed. As the physicochemical approaches can identify coexisting metabolic acidotic and alkalotic processes in a patient, it is possible to determine acid–base abnormalities in animals with a normal BE and bicarbonate concentration.[15,32]

This study has several limitations. For accuracy it would have been ideal to evaluate all the measured parameters on the same blood sample. In this study, we allowed a 60 minute time interval for both the blood gas and biochemistry sample collection so we cannot rule out the possibility that fluid therapy given during the sample collection period may have impacted our results. The majority of samples in this study were collected simultaneously so the effect of this issue is likely to be minimal. Another limitation is the small number of cats included in this study. As such, these results should be applied to cats with caution. This study was performed in a tertiary referral institution, so the nature of the emergency room population included may not be representative of general clinical practice. Another limitation is the small number of dogs and cats used to determine the comparison acid–base values for this study. Although not ideal, this was considered preferable to using previously published normal acid–base values measured on different blood gas machines, often on small numbers of animals.

In conclusion, the Stewart and semiquantitative approaches appeared to have greater diagnostic ability than the traditional approach in this group of patients. Compared to the traditional approach, the Stewart and semiquantitative approaches are more complex and require a computer spreadsheet to use them effectively. They add another layer of complexity to an already challenging field, making acid–base less approachable for clinicians. Unfortunately, the clinical benefits of physicochemical acid–base analysis have yet to be determined. Future prospective studies are needed to determine the diagnostic and prognostic value of acid–base analysis in veterinary patients.

Footnotes

[a] ABL 705, Radiometer Medical A/S, Copenhagen, Denmark.
[b] Hitachi 717 chemistry analyzer, Roche Diagnostics, Indianapolis, IN.
[c] Microsoft Excel 2008, Microsoft Corp, Santa Rosa, CA.
[d] LogXact 8 for Windows, Cytel Software Corporation, Cambridge, MA.

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