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Value of the Anion Gap in Clinical Diagnosis and Laboratory Evaluation

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We report the incidence of normal (50.4%), increased (46.7%), and decreased (2.9%) anion gap among hospitalized patients in a retrospective study. The mean and range of increased anion gaps were 25 and 19–28 mmol/L. Values exceeding 30 mmol/L were uncommon and may indicate either acidosis or laboratory error. The most common causes of the increased anion gap among patients were chronic renal failure, congestive heart failure, malignant neoplasm, and diabetes mellitus. Increased anion gap in this study may be due to excess acids along with decreases in sodium, chloride, and carbon dioxide. The mean and range of decreased anion gap were 6 and 3–8 mmol/L. Anion-gap values <3 mmol/L were uncommon (one of 500 cases), and a high incidence of such values may indicate laboratory error. Nephrotic syndrome, liver cirrhosis, intestinal obstruction, and severe hemorrhage were the common disorders associated with decreased anion gap, which resulted from hypoalbuminemia and hyponatremia. Although most patients with decreased anion gap had hypoalbuminemia, hypoalbuminemic patients did not necessarily have decreased anion gap.

Additional Keyphrases: *quality control · hypoalbuminemia · hyponatremia · diseases in which the anion gap is affected*

If all of the cations and anions in human serum are considered together, the result is electrical neutrality. However, only sodium, potassium, chloride, and bicarbonate are the major electrolytes routinely measured in the clinical laboratory, and so an imbalance must occur as the result of incomplete measurement. The term "anion gap" is, therefore, used arbitrarily *(1–3)* to describe the difference between the sum of the measured cations and anions, $(Na^+ + K^+) - (Cl^- + HCO_3^-)$ or $Na^+ - (Cl^- + HCO_3^-)$. Oh and Carroll *(1)* clearly define the anion gap and represent it as the difference in concentration between the unmeasured anions and unmeasured cations, which can be estimated from the known values of the measured electrolytes (Na^+, K^+, Cl^-, and HCO_3^-). Normally, the anion gap ranges in healthy individuals from 8 to 16 *(2)* or 9 to 17 *(3, 4)* mmol/L. An anion gap below or above these intervals is considered a decreased or increased anion gap, respectively.

Theoretically, an increased anion gap may occur as the result of: *(a)* decreased unmeasured cations, as in hypokalemia, hypocalcemia, and hypomagnesemia; *(b)* increased unmeasured anions, as in organic and inorganic acid excess, transient hyperalbuminemia, and intoxication with methanol or salicylate; *(c)* laboratory error with falsely increased sodium or falsely decreased chloride or bicarbonate *(1)*. The anion gap can be decreased as the result of: *(a)* increased unmeasured cations, as in hyperkalemia, hypermagnesemia, hypercalcemia, or the accumulation of IgG in multiple myeloma; *(b)* decreased unmeasured anions, as in hypoalbuminemia; and *(c)* laboratory error from falsely decreased sodium or falsely increased chloride or bicarbonate *(1)*.

The concept of anion gap is not new, and its value in clinical diagnosis and for laboratory quality control is widely reported in the literature *(1–9)*. However, applications of laboratory and clinical data to either support or reject the concept are very few. We retrospectively studied the incidence of abnormal anion gap and the associated diseases to find whether it has any benefit for clinical diagnosis or laboratory evaluation.

Materials and Methods

We measured serum electrolytes (Na, K, Cl, and HCO_3) with the basic AutoAnalyzer incorporating the flame photometer III (Technicon Instruments Corp., Tarrytown, NY 10591). We used commercial sera (General Diagnostics, Warner-Lambert Co., Morris Plains, NJ 07590) as the quality-control samples.

We determined normal values of serum electrolytes in 150 men and women (ages 18 to 80 years), apparently healthy volunteers, and persons who came to the hospital for a routine health check-up. From these data we estimated the normal range as the 5 and 95 percentile values by a nonparametric percentile estimation method *(10)*.

Values for the anion gap were retrospectively calculated from 7466 sets of electrolytes, requested daily in our routine laboratory during January to December 1977; we used the formula $Na^+ - (Cl^- + HCO_3^-)$. Results were compared with those determined for the normal population.

We sorted the abnormal anion gaps according to whether they were increased or decreased. Because there was a high incidence of increased anion gap (3485 samples), we traced the history of patients with increased anion gap from the first 15 samples (952 sets) of each day requested during July to December 1977.

Results and Discussion

Table 1 shows the precision of individual electrolyte measurements of a mid-range concentration commercial control serum. Day-to-day variables observed in each month were tabulated as standard deviation (SD) and variance (CV). The overall analytical variables were acceptable. Our precision was similar to that of Witte et al. *(4)*. Our normal reference intervals for sodium, potassium, chloride, and bicarbonate (respectively, 135–143, 3.8–5.0, 98–108, and 19–25 mmol/L) were similar to those reported (respectively, 134–145, 3.4–5.1, 98–108, and 22–26 mmol/L) by Bold and Wilding *(11)*. The reference interval for the anion gap (5 and 95 percentiles) in this study was 9–18 mmol/L, which was similar to the range of 9–17 mmol/L found by Thomas et al. *(3)* among blood donors and by Witte et al. *(4)* among volunteers.

This study included only the sets of electrolytes requested in the routine laboratory. Both inpatients and outpatients were included. Although we do not know the exact number of patients in each group, from 455 medical records found, 88 were outpatients and 367 were inpatients. The incidence of normal and abnormal anion gap in both groups was almost equal (Table 2). The incidence of an increased anion

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Table 1. Precision of Electrolyte Measurements during 1977[a]

	Concn, mmol/L		
	SD	SE	CV, %
Na^+	1.8	0.5	1.3
K^+	0.1	0.03	2.0
Cl^-	1.7	0.5	1.7
HCO_3^-	1.3	0.4	5.7

[a] Pooled data (n = 264) over 12 months for commercial control serum containing 140 mmol of Na, 5.1 mmol of K, 100 mmol of Cl, and 22 mmol of HCO_3 per liter.

Table 3. Incidence of Increased Anion Gap

Anion gap, mmol/L	No.	%	Cumulative %
19–21	1492	42.9	42.9
22–24	990	28.5	71.4
25–27	551	15.9	87.3
28–30	234	6.7	94.0
31–33	111	3.2	97.2
34–36	43	1.2	98.4
37–39	27	0.8	99.2
40–42	9	0.3	99.5
43–45	7	0.2	99.7
46–67	10	0.3	100.0

gap (46.7%) was much greater than the decreased anion gaps (about 3%). The average finding of normal, increased, and decreased anion gap among 30 electrolyte samples determined daily were 15, 14, and 1 cases (respective ranges of 0–35, 0–36, 0–8 cases) (Table 2). The range of anion gap values among patients (5 and 95 percentiles) was 11–26 mmol/L, which was similar to that found by Thomas et al. (10–25 mmol/L) among 3920 hospitalized patients (*3*) and by Goldstein et al. (8–25 mmol/L) among 39 360 patients *(12)*.

The most frequently found value for *increased* anion gap was 19–21 mmol/L (42.9%) (Table 3). The central 90% range among the increased anion gap values was 19–28 mmol/L. Values of 40 mmol/L or more were rarely found (0.8%). The increased anion gap among 369 patients whose charts were available for study ranged from 19 to 40 mmol/L (central 90%, 19–30 mmol/L). There were many different diseases among these patients, and we tabulated only eight disease systems with high incidence of increased anion gap (Table 4). Diseases with low incidence (fewer than 20 cases) were grouped as miscellaneous. Diseases of the urinary system had the highest incidence (22.5%) of increased anion gap, especially those with chronic renal failure, which involved as much as 13%. Patients with chronic renal failure may accumulate inorganic acids such as sulfate and phosphate. Increases in unmeasured anion would produce an increased anion gap, and in patients with renal failure the central 90% ranged from 9 to 30 mmol/L. Moreover, the patients with chronic renal failure had lower than normal values for bicarbonate (94%), sodium (63.8%), and chloride (61.7%) (Table 5). Vomiting, chronic diarrhea, and loss of sodium and chloride through urine as the result of uremia *(13)* may be the causes of these abnormalities. Chronic renal failure (26.3%), congestive heart failure (36.8%), diabetes mellitus (31.5%), and diarrhea (5.3%) were the associated diseases in 19 patients with urinary tract infection who also had increased anion gap.

The central 90% range of anion gap value among the five diseases most commonly associated with increased anion gap (Table 5) was 19–30 mmol/L. Most of the hypertensive patients in this study also had other associated disorders such as chronic renal failure, congestive heart failure, diabetes mellitus, and malignant neoplasm. Therefore, the increased anion gap in our study was mostly due to the accumulation of inorganic and organic acids. According to Table 5, hypernatremia (0–6.6%) was not the common cause of increased anion gap. In contrast, hyponatremia (33.3–63.8%), hypochloremia (50–73.7%), and low carbon dioxide (44–93.6%) were more commonly found in patients with an increased anion gap.

Table 6 shows the incidence of findings of *decreased* anion gap, arranged in descending order from 8 mmol/L to −6 mmol/L. The central 90% range of the decreased gap lay

Table 4. Underlying Diseases in 369 Patients with Increased Anion Gap

	No. of cases[a]			
Disease	Adults	Children	Total	% of total
Urinary system	72	11	83	22.5
Chronic renal failure	45	3	48	13.0
Urinary tract infection	16	3	19	5.2
Others	11	5	16	4.3
Heart	58	4	62	16.8
Congestive heart failure	35	3	38	10.3
Acute myocardial infarction	8	0	8	2.2
Cardiomyopathy	7	0	7	1.9
Others	8	1	9	2.4
Malignant neoplasms	57	4	61	16.5
Liver	9	0	9	2.4
Bronchus and lung	8	0	8	2.2
Others	40	4	44	11.9
Endocrine system	39	6	45	12.2
Diabetes mellitus	31	1	32	8.8
Others	8	5	13	3.5
Liver, gall bladder, and pancreas	41	3	44	11.9
Cirrhosis of liver	17	0	17	4.6
Others	24	3	27	7.3
Hypertensive disease	30	0	30	8.1
Blood and blood-forming organs	22	1	23	6.2
Respiratory system	21	2	23	6.2
Chronic obstructive lung disease	11	0	11	3.0
Others	10	2	12	3.2
Miscellaneous	112	19	131	35.5
Total	452	50	502	

[a] Some patients had more than one disease.

Table 2. Incidence of Normal and Abnormal Anion Gap Found in Routine Work Daily and during 1977

	Cases/day			Cases/year	
	Range	Mean	%	No.	%
Total specimens	10–48	30	100.0	7477	100.0
Normal anion gap	0–35	15	50.0	3746	50.4
Abnormal anion gap	0–36	15	50.0	3702	49.6
Increased anion gap	0–36	14	46.7	3845	46.7
Decreased anion gap	0–8	1	3.3	217	2.9

Table 5. Anion Gap and Electrolytes in Diseases Commonly Associated with Increased Anion Gap

	Chronic renal failure		Congestive heart failure		Malignant neoplasms		Diabetes mellitus		Hypertension	
Results, mmol/L	No.	%	No.	%	No.	%	No.	%	No.	%
Anion gap										
19–21	22	46.8	18	47.4	38	62.3	18	56.3	12	40
22–24	11	23.4	11	28.9	13	21.3	5	15.6	12	40
25–27	4	8.5	7	18.4	6	9.8	5	15.6	5	16.7
28–30	8	17.0	1	2.6	3	4.9	2	6.3		
31–33	1	2.1			1	1.6	1	3.1	1	3.1
34–36	1	2.1	1	2.6			1	3.1		
37–39										
40–42	1	2.1								
Total	48	100	38	100	61	100	32	100	30	100
Electrolytes										
Na^+ <135	30	63.8	18	47.4	28	45.9	18	56.3	10	33.3
Na^+ >143	2	4.3	0	0	4	6.6	0	0	0	0
K^+ <3.8	13	27.7	11	28.9	26	42.6	4	12.5	11	36.7
K^+ >5.0	14	29.8	5	13.2	6	9.8	7	21.9	3	10
Cl^- <98	29	61.7	28	73.7	38	62.3	23	71.9	15	50
Cl^- >108	3	6.4	0	0	0	0	1	3.1	3	10
CO_2 <19	44	93.6	20	52.6	27	44.3	23	71.9	16	53.3
CO_2 >25	0	0	1	2.6	4	6.6	1	3.1	3	10

Table 6. Incidence of Decreased Anion Gap

Anion gap, mmol/L	No. cases	%	Cumulative %
8	73	33.6	33.6
7	42	19.4	53.0
6	41	19.0	72.0
5	17	7.9	79.9
4	16	7.4	87.3
3	10	4.6	91.9
2	1	0.5	92.4
1	6	2.8	95.2
0	2	0.9	96.1
Between −1 and −6	9	4.1	100.2

Table 7. Underlying Diseases in Patients with Decreased Anion Gap and Hypoalbuminemia (Serum Albumin <25 g/L)

	No. of cases			
Diseases	Adult	Children	Total	% of total
Kidney diseases				
Nephrotic syndrome	13	4	17	32.7
Chronic renal failure	2	1	3	5.8
Malignant neoplasm of kidney	1	0	1	1.9
Liver diseases				
Cirrhosis	13	0	13	25.0
Liver abscess	6	0	6	11.5
Intestinal obstruction	7	0	7	13.5
Chronic diarrhea and anemia	0	1	1	1.9
Severe hemorrhage	3	1	4	7.7

between 3 and 8 mmol/L. The occurrence of the negative anion gap in this study was only 0.12% (nine of 7466 cases), which was lower than the value of 2% found by others *(4, 7–9)*. However, patient populations differed among these studies: patients in the other studies had asymptomatic plasma cell dyscrasias *(7)* and multiple myeloma *(4, 8, 9)*, whereas ours were general patients. The lowest anion gap value among patients with asymptomatic plasma cell dyscrasias was −1 mmol/L *(7)*; among the multiple myeloma patients it was 1 mmol/L *(4, 9)* and −4 mmol/L *(8)*. Witte et al. *(4)* found that the anion gap value among 46 patients with multiple myeloma ranged from 1 to 16 mmol/L (mean 7.5 mmol/L). Recently, Goldstein et al. *(12)* also found a low incidence of decreased anion gap (0.8%) among 67 740 sets of electrolytes obtained from 39 360 patients.

Of the 217 samples with decreased anion gap, only 86 patients' charts were available for the study. Of these, 52 patients had serum albumin <25 g/L. Their underlying diseases (Table 7) were most commonly nephrotic syndrome (17 cases, or 32.7%) and liver cirrhosis (13 cases, or 25%). Table 8 indicates the frequency of decreased anion gap and serum electrolyte values in 52 hypoalbuminemic patients. Values of anion gap were 8 and 7 mmol/L in 55.8% (29 cases) of these patients, 76.9% (40 cases) of whom had hyponatremia. In contrast, only 5.8% and 21.2% had high chloride and bicarbonate values. Hyponatremia was also seen in 70% of patients who had normal serum albumin with decreased anion gap. We conclude that the main causes of decreased anion gap in this study were hypoalbuminemia and hyponatremia. Laboratory error also played an important role in this study. The values of sodium (<2 SD) and chloride (>2 SD) in the control samples were not within acceptable limits (±2 SD) on the day the samples with anion gap value of −2, −5 and −6 mmol/L (Table 8) were tested. Therefore, these three negative anion gap values were due to hypoalbuminemia, hyponatremia, and under- and overestimation of sodium and chloride, respectively.

Although determinations of arterial blood gases (and of serum bicarbonate, lactate, and ketones) are the most reliable means to diagnose metabolic acidosis, many laboratories, especially in the developing countries, have no blood-gases instrument. Therefore, metabolic acidosis is usually diagnosed from the patient's history, physical examination, and concentration of serum bicarbonate. According to Gabow et al. *(6)*, an increased anion gap of less than 30 mmol/L predicts the presence of organic acidosis less accurately than values of 30 mmol/L or more. Therefore the magnitude of the increased anion gap is another factor contributing to the accuracy of the clinical diagnosis of metabolic acidosis. In our study, values >30 mmol/L were uncommon (2.8%). Therefore, an anion gap exceeding 30 mmol/L will suggest the presence of metabolic acidosis, provided the laboratory performance is reliable. However, more prospective data are needed to confirm or reject this suggestion.

A patient with a decreased anion gap should be suspected

Table 8. Value of Anion Gap and Electrolytes Concentration in Patients with Decreased Anion Gap and Hypoalbuminemia (52 cases)

Results, mmol/L	No. of cases									
	Kidney diseases			Liver diseases		GI obstruction	Diarrhea	Hemorrhage	Total	% of total
	NS	CRF	Tumor	Cirrhosis	Abscess					
Anion gap										
8	5	1	1	5	3	1	0	2	18	34.6
7	5	0	0	3	2	1	0	0	11	21.2
6	0	1	0	1	1	0	1	1	5	9.6
5	1	0	0	1	0	1	0	1	4	7.7
4	2	0	0	0	0	0	0	0	2	3.8
3	2	0	0	1	0	2	0	0	5	9.6
1	0	1	0	0	0	1	0	0	2	3.8
−2	1	0	0	0	0	1	0	0	2	3.8
−5	0	0	0	1	0	0	0	0	1	1.9
−6	1	0	0	1	0	0	0	0	2	3.8
Total	17	3	1	13	6	7	1	4	52	100.0
Electrolytes										
Na^+ <135	11	2	1	9	6	6	1	3	40	76.9
Na^+ >143	0	0	0	0	0	0	0	0	0	0
K^+ <3.8	1	0	0	4	3	1	0	2	11	21.2
K^+ >5.0	2	0	0	0	0	0	0	0	2	3.8
Cl^- <98	5	1	1	4	2	1	1	1	16	30.8
Cl^- >108	3	0	0	0	0	0	0	0	3	5.8
CO_2 <19	5	1	0	4	0	1	1	1	13	25.0
CO_2 >25	3	0	0	3	2	2	0	1	11	21.2

NS, nephrotic syndrome; CRF, chronic renal failure; GI, gastrointestinal.

of having hypoalbuminemia and hyponatremia, although not all hypoalbuminemic patients have a decreased anion gap. In our additional study on 238 samples with serum albumin of less than 25 g/L, 61.3%, 34.5% and 3.8% of the anion gap values were normal, increased, and decreased, respectively.

Clinicians and laboratorians have different ways of judging the reliability of laboratory results. Clinicians relate laboratory results with clinical findings and may have little concern with the quality-control system of the laboratory. Therefore, unexpected laboratory results that cannot be explained by clinical findings are often designated as laboratory errors. In contrast, the laboratorians may rely exclusively on the results of quality-control procedures with little attention to clinical findings on the patients. The difference in judging laboratory results may be related to the inconvenience with which the clinicians can obtain quality-control data and with which the laboratorians can obtain detailed clinical findings. Anion gap values, however, can be used by clinicians as one of the guidelines to judge the reliability of laboratory performance. For example, given the rarity of a decreased anion-gap, especially in patients with normal serum albumin, if laboratory reports show a high incidence of markedly decreased anion gap (<3 mmol/L), one should question the quality control system of the laboratory. On the contrary, if the laboratory results appear to be reliable, one should check serum albumin and gamma-globulin to see whether the patients have hypoalbuminemia or hypergammaglobulinemia. Increased anion gap is common in hospitalized patients, but a markedly increased anion gap (more than 30 mmol/L), which indicates organic acidosis (*6*), is uncommon. One should check the laboratory control system if markedly increased anion gap is frequently reported from the laboratory.

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Addendum

Ed. note: A reviewer of this paper offers the following comment.

On the Significance of the Expression, "Anion Gap"

Not until the mid-1950s did pH equipment become generally available in the routine laboratory. Thus, in the 1940s when Gamble introduced his graphic representation of acid–base composition of blood, a major objective was to estimate

Table 1A. Anion Gap Observed in Five Acutely Ill Patients

mEq/L					
Na^+	Cl^-	Total CO_2	Anion gap	pH	Diagnosis
120	112	10	−2	7.15	Diabetic coma (organic acidemia)
139	94	31.1	+13.9	7.52	Status asthmaticus treated with $NaHCO_3$ (metabolic alkalemia)
140	102	53	−15	7.10	Mechanical obstruction in trachea (respiratory acidemia)
141	103	18	+20	7.56	Hyperventilation due to apprehension (respiratory alkalemia)
134	92	23.5	+18.5	7.04	Asthmatic attack untreated (organic acidemia & respiratory acidemia)

the "base deficit" or "base excess," and suggest a rough measure of the blood pH. Gamble added the cation concentrations (Na^+, K^+, Ca^{2+}, Mg^{2+}), and balanced the sum against the sum of the anions (HCO_3^-, Cl^-, proteinate, PO_4^{3-}, SO_4^{2-}, and organic acids).

When the flame photometer became available at the end of the 1940s, and Na^+ could now be determined conveniently, laboratories were asked to draw "Gamblegrams," balancing anions and cations. This soon degenerated into adding concentrations of Na^+ and K^+ and comparing them with the sum of the Cl^- and HCO_3^- concentrations, these being readily determined. Subsequently, as used in the preceding paper and others, the K^+ was dropped, and the formula became: anion gap = $Na^+ - Cl^- - HCO_3^-$. In the healthy individual, Na^+ = 140, Cl^- = 103, and HCO_3^- = 25 mEq/L, as approximate mean values, and the anion gap is thus about 12 mmol/L. Variations of this value were then claimed to be a measure of the organic acids and proteinate and to give some idea of the blood pH.

When the pH meter became generally available, it became apparent that the anion gap was not a reliable measure of base deficit and blood pH, and that high, low, or normal anion-gap values could accompany any of the conditions of acidemia, alkalemia, or normal pH values. Table 1A shows a few examples from my experience. The CO_2 values were determined by microgasometer, Na^+ with the flame photometer, and Cl^- amperometrically. The fourth and fifth patients had similar anion gaps, but one is in alkalemia, the other in acidemia. The second patient has a normal anion gap and is in alkalemia.

The concept of anion gap was revived during the 1970s—at least partly motivated by the desire for a simple procedure to estimate lactate, lactate acidemia having gained prominence as a major problem in medicine. This revival was also stimulated by the widespread use of computers in automated equipment, which could readily add a calculated parameter. The term "anion gap," however, has no significant meaning, because lactate, proteinate, sulfate, phosphate, acetoacetate, hydroxybutyrate, and others are all anions. Thus, there is no anion gap, if electrical neutrality is to be maintained. Further, the addition of total Cl^- to HCO_3^- (total CO_2), anions having different activity coefficients, especially at their different concentrations, is not acceptable chemical practice.

The paper of Lolekha and Lolekha is representative of the better papers on the anion gap. Let us examine their data to see whether the calculation of this value is a significant aid in the diagnosis and management of patients.

Method of Assay

In the AutoAnalyzer, separated plasma or serum from blood taken in an evacuated container is placed in the cups of the turntable and sits exposed to the air for as long as 40 min. In most patients' serum, especially those with respiratory acidosis, CO_2 is lost rapidly. For example, the third patient listed in Table 1A had a small metal object lodged in the trachea, which resulted in CO_2 retention. If this serum were analyzed after waiting on the turntable, the CO_2 value would be less than if it had been measured from a syringe without delay after sampling. Thus a respiratory acidosis, which should show a low to negative anion gap, would be missed. The data of Lolekha and Lolekha illustrate this point: only 3% of the cases had a decreased anion gap, and *only nine of 7466 cases had a negative anion gap.* Thus, in effect, this procedure abolished respiratory acidosis.

Reasons for Calculating Anion Gap

The reasons for calculating the anion gap are given under three headings in the preceding paper. In all three the authors suggest that an abnormal anion gap may be used in quality control to uncover aberrant Na^+, Cl^-, or HCO_3^- values that result from laboratory error. This is a poor argument. The use in the laboratory of an effective quality-control program for the different analyses is more desirable.

In their first major point, they note an increased anion gap in 47% of the cases. Many are undoubtedly due to technical handling of the specimen, as discussed above. The authors also point out that CO_2 values were reduced by as much as 44–94% of the normal value. The most common disorders associated with this change are heart disease, neoplasm, and diabetes mellitus. In addition, they note a *decrease* in Na^+, Cl^-, and CO_2 and then suggest an accumulation of *inorganic* and organic acid as the cause. It is difficult to follow this argument, especially in the light of Table 1.

In their second point they state that decreased anion gap was rarely found in routine analysis of electrolytes. This has been commented on above. The authors then claim that a major cause of the decreased anion gap is hypoalbuminemia, but subsequently modify this by saying that hypoalbuminemia was not a consistent cause of decreased anion gap.

From the arguments of Lolekha and Lolekha, we need to conclude that the calculation of the anion gap has very little practical value, and that the patient would better be served if his physician receives a report of the values obtained for the electrolytes, blood pH, protein, and other data pertinent to the management of the patient. Lactate values, measured directly, are preferable to estimates of their value from the anion gap. *A most serious objection is that the anion gap values may serve to misinterpret the patient's condition* (see Table 1A).

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