Acid-Base Disorders and ABGs

Kenneth Christopher, MD, SM
Associate Physician
Renal Division
Brigham and Women's Hospital
Assistant Professor in Medicine
Harvard Medical School

Conflict of Interest Disclosure Slide

- I have no financial relationships with commercial entities producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients relevant to the content I am presenting.

Overview

- Acid-Base Disorders
- Interpretation
- Anion Gap
- The Delta Ratio
- Urinary Anion Gap
- Osmolar Gap

Acid Base

The maintenance of a normal pH in the face of the 70,000,000 nmol of hydrogen ion generated daily depends on…

- buffers
- on the mechanisms for eliminating CO_2 through the lungs
- the ability to eliminate acid in the urine.

Metabolic Alkalosis

- Metabolic alkalosis is a common disorder.
- Alkalosis is more likely in those who require nasogastric feeding compared with oral feeding.
- An inadequate metabolic response to chronic hypercapnia has been associated with increased mortality.

Initiation of Metabolic Alkalosis

Gain of alkali

Exogenous source (IV $NaHCO_3$ infusion, citrate in transfused blood pheresis or renal replacement)

Endogenous source (metabolism of ketoanions to produce bicarbonate)

Loss of H+

Kidneys (diuretics)

Gut (vomiting, Gastric suction)

Maintenance of Metabolic Alkalosis

Chloride depletion

Loss of gastric acid and diuretic use account for 90% of clinical cases of metabolic alkalosis

Loop / Thiazide Diuretics (Urinary chloride losses are greater than Urine bicarbonate losses). Seen only in volume depleted (high aldosterone) patients with low dietary chloride intake ('salt restricted' diet)

Potassium depletion

Bicarbonate reabsorption in both the proximal and distal tubules is increased in the presence of potassium depletion.

Primary hyperaldosteronism

Cushing’s syndrome – high dose corticosteroids

Urinary Chloride in Metabolic Alkalosis

If the cause is not apparent then Urine Cl can be helpful

Urine Cl- < 10 mmol/l

Volume depletion (increased proximal tubular reabsorption of HCO_3)

Responsive to IV NaCl (replaces chloride and volume)

Cause: Vomiting (90% of cases), Prior thiazide diuretic use

Urine Cl- > 20 mmol/l

Volume expansion and hypokalaemia

Not responsive to IV NaCl

Cause: Excess aldosterone, severe K+ deficiency, Current diuretic therapy

Metabolic Alkalosis

Compensation

Hypoventilation causes a compensatory rise in arterial pCO_2

Magnitude of the response has generally been found to be quite variable.

Expected $pCO_2 = 0.7\ [HCO_3] + 20\ mmHg \pm 5$

Correction

Treat underlying disorder

Repletion of chloride, potassium and volume will improve renal bicarbonate excretion

Major Effects of Metabolic Alkalosis

Respiratory Effects

Respiratory depression via both central and peripheral chemoreceptors.

Cardiovascular Effects

Decreases oxygen delivery to the tissues by exerting a vasoconstrictor effect and by impairing hemoglobin's ability to release oxygen.

Alkalosis-induced tissue hypoxemia can adversely affect cerebral, coronary, and peripheral circulation.

An inadequate metabolic response to chronic hypercapnia has been associated with increased mortality.

Acetazolamide

- Carbonic anhydrase inhibitors hinder renal acidification causing the kidney to partially correct the metabolic alkalosis.
- Only rarely does the plasma HCO_3 concentration return to normal.

- A potential problem associated with use of carbonic anhydrase inhibitors in patients with lung disease is a worsening of hypercapnia.
- Carbonic anhydrase inhibition can prevent red cell uptake of CO_2 in peripheral tissues and can prevent CO_2 release in the lung.

Metabolic Acidosis

- Metabolic acidosis is a disorder that reduces the extracellular bicarbonate concentration.
- Accumulation of excess acids that consume bicarbonate
  - Generates a high anion gap (AG) acidosis because the excess acids contribute an organic anion to the circulation as well as a hydrogen ion.
- Gastrointestinal or renal loss of bicarbonate salts.
  - Non gap acidosis.

Metabolic Acidosis

- The kidney's role in regulating acid-base balance includes
  - Reclamation of filtered HCO_3 and
  - Regeneration of HCO_3 consumed by net acid production.
- Quantitatively, the most important urinary buffer is the NH_3/NH_4^+ (Ammonia/Ammonium) system. $H^+ + NH_3 \rightarrow NH_4^+$
- The rate of NH_3 production and excretion can be varied according to physiologic needs.
- Under normal circumstances, urine excretion of NH_4^+ accounts for more than half of the net acid excreted per day.
- Acidosis and hypokalemia stimulate NH_4^+ excretion.
- Alkalosis and hyperkalemia diminish NH_4^+ excretion.

Non gap / Hyperchloremic Metabolic Acidosis

Renal Causes

- Renal tubular acidosis
- Carbonic anhydrase inhibitors

GI Causes

- Severe diarrhea
- Uretero-enterostomy or Obstructed ileal conduit
- Drainage of pancreatic or biliary secretions
- Small bowel fistula

Other Causes

- Recovery from ketoacidosis
- Addition of HCl, NH_4Cl

Urinary Anion Gap

- Useful for Non gap (or hyperchloraemic) acidosis that is not obvious

- Only Na+, K+ and Cl- are commonly measured in urine so the other charged species are the unmeasured anions (UA) and cations (UC).

- Urinary Anion Gap = (UA - UC) = [Na+]+ [K+] - [Cl-]
- Urinary Anion Gap (UAG) provides a rough index of urinary ammonium (NH_4^+) excretion.
- With normal kidney function and acidosis, urine NH_4Cl should increase driving the UAG negative.
- A negative UAG = GI loss of bicarbonate (diarrhea) “neGUTive”
- A positive UAG = impaired renal distal acidification (RTA).

Anion Gap

- Anions associated with:
  - endogenous organic acidosis (lactate, beta-hydroxybutyrate, and acetoacetate)
  - Exogenous poisons (formate, glycolate, salicylate)
  - Renal failure (sulfate, phosphate, and other anions)
- Negative charges on plasma albumin are a large component of the unmeasured anions that make up the calculated AG.
- Hypoalbuminemia will lead to an underestimate of the size of the AG and potentially to the failure to recognize a clinically important high AG acidosis.
- A “corrected anion gap” avoids this problem: For every 1 g/dl decrease in serum albumin below 4.4 g/dl, 2.5 mEq/L is added to the calculated AG.

Anion Gap

An elevated Anion Gap always strongly suggests a Metabolic Acidosis

AG 20-30: high chance of metabolic acidosis

AG > 30: metabolic acidosis is certainly present

Delta/Delta

Delta Ratio Assessment Guidelines in patients with a metabolic acidosis

< 0.4	Hyperchloremic non gap acidosis
0.4 - 0.8	Combined high AG and non gap acidosis
1 to 2	Typical pattern in high AG metabolic acidosis
> 2	Either a co-existing Metabolic Alkalosis or a co-existing Chronic Respiratory Acidosis

Delta/Delta

Increase in Anion Gap / Decrease in bicarbonate

If one molecule of metabolic acid (HA) is added to the ECF and dissociates, the one H+ released will be buffered by one molecule of HCO_3- to produce CO_2 and H_2O.

The net effect will be an increase in unmeasured anions by the one acid anion A- (ie anion gap increases by one) and a decrease in the bicarbonate by one.

Significant intracellular buffering with extracellular retention of the unmeasured acid anion (A-) will cause the value of the delta ratio to be greater than one in a high AG metabolic acidosis.

Delta/Delta example

"Normal" AG 10 Normal HCO_3 24

Case 1
Anion gap 20 HCO_3 17
Delta AG/ Delta HCO_3 = 20-10/24-17 = 1.42 -> uncomplicated high-AG acidosis

Case 2
Anion gap 20 HCO_3 12
Delta AG/ Delta HCO_3 = 20-10/24-12 = 0.08 -> less HCO_3 than expected
High AG acidosis with additional nongap acidosis

Case 3
Anion gap 20 HCO_3 20
Delta AG/ Delta HCO_3 = 20-10/24-20 = 2.5 -> more HCO_3 than expected
High AG acidosis with additional metabolic alkalosis or additional compensated respiratory acidosis

Delta/Delta

Increase in Anion Gap / Decrease in bicarbonate

< 0.4
Hyperchloraemic nongap acidosis

0.4 - 0.8
Combined High AG and nongap acidosis
acidosis associated with renal failure Delta/Delta < 1

Less HCO_3 present than expected by increase in AG

1 to 2
Usual for uncomplicated high-AG acidosis
Lactic acidosis, DKA

> 2
Pre-existing elevated HCO_3 level so consider:
concurrent metabolic alkalosis, or
pre-existing compensated respiratory acidosis

More HCO_3 present than expected by increase in AG

Osmolar gap

The osmolar gap is the difference between the measured osmolality and the calculated osmolarity.

Measured Osmolality is measured in the lab via an osmometer

Calculated Osmolarity = (2 x [Na+]) + glucose/18 + BUN/2.8 + ethanol/4.6

Osmolar gap

Screening test for detecting abnormal low molecular weight solutes

methanol	(Osm gap + high AG)
ethylene glycol	(Osm gap + high AG)
ethanol	(Osm gap + normal AG)
acetone	(Osm gap + normal AG)
isopropyl ethanol	(Osm gap + normal AG)
propylene glycol	(Osm gap + high AG, vehicle in Ativan IV)

osmolar gap > 10 mOsm/l is often stated to be abnormal

osmolar gap≥ 25 is suggestive of methanol or ethylene glycol ingestion

Major Effects of Metabolic Acidosis

Respiratory Effects

- Hyperventilation - compensatory response
- Shift of oxyhaemoglobin dissociation curve to the right
- Decreased 2,3 DPG levels in red cells (shifting back to the left)

Cardiovascular Effects

- Depression of myocardial contractility
- Sympathetic overactivity
- Resistance to the effects of catecholamines
- Peripheral arteriolar vasodilatation

Respiratory Acidosis

An adult at rest produces 200mls of CO_2 per minute

Increased production of CO_2 leads to a respiratory acidosis if ventilation remains constant.

Increases in pCO_2 very promptly results in a large increase in ventilation maintaining the at pCO_2 40 mmHg.

Respiratory Acidosis

Inadequate Alveolar Ventilation (most common)

- Central Respiratory Depression & Other CNS Problems
- Inadequate mechanical ventilation
- Nerve or Muscle Disorders
- Lung or Chest Wall Defects
- Airway Disorders (obstruction)

Over-production of Carbon Dioxide

- Hypercatabolism (Malignant Hyperthermia)

Increased Intake of Carbon Dioxide

- Rebreathing of CO_2-containing expired gas
- Insufflation of CO_2 into body cavity (laparoscopic surgery)

Respiratory Acidosis

Hypercapnea

- Stimulation of ventilation via both central and peripheral chemoreceptors
- Cerebral vasodilation increasing cerebral blood flow and intracranial pressure
- Central depression at very high levels of pCO_2
- Stimulation of the sympathetic nervous system resulting in tachycardia, peripheral vasoconstriction and sweating
- Peripheral vasodilation by direct effect on vessels

Respiratory Acidosis

The compensatory response to an acute respiratory acidosis is limited to buffering rapidly inside red blood cells via carbonic anhydrase and hemoglobin

$CO_2 + H_2O <-> H_2CO_3 <-> H+ + HCO_3-$

With continuation of the acidosis, the kidneys respond by retaining bicarbonate.

The renal response begins by 6 - 12 hours and is maximal at 3 - 4 days.

- Increased HCO_3 production
- Increased NH_3 production to 'buffer' the H+ to increase urinary excretion of NH_4Cl

The pCO_2 quickly returns to normal with restoration of adequate alveolar ventilation

Respiratory Acidosis

The pCO_2 quickly returns to normal with restoration of adequate alveolar ventilation

The correction of the elevated bicarbonate (renal compensation) associated with chronic respiratory acidosis may not be rapid.

Return of plasma bicarbonate to normal requires renal excretion of the excess bicarbonate.

Certain abnormal conditions the excretion is impaired and the bicarbonate level remains elevated.

The persistence of elevated bicarbonate despite resolution of the chronic respiratory acidosis is referred to by some as ‘post-hypercapnic alkalosis’

Respiratory Alkalosis

A respiratory alkalosis is a primary acid-base disorder in which arterial pCO_2 falls to a level lower than expected

A respiratory alkalosis is due to increased alveolar ventilation

The low arterial pCO_2 will be sensed by the central and peripheral chemoreceptors and the hyperventilation will be inhibited unless the patient's ventilation is controlled

Consequences:

- decreased cerebral blood flow
- decrease in myocardial contractility
- shift of the oxygen dissociation curve to the left

Respiratory Alkalosis

Central Causes

Head Injury, Stroke

Anxiety, Pain, fear, Drugs (salicylate intoxication)

progesterone during pregnancy, cytokines during sepsis

Hypoxemia

peripheral chemoreceptors stimulate respiration

Pulmonary Causes (act via intrapulmonary receptors)

Pneumonia, Asthma, Pulmonary Embolism, Pulmonary edema

Iatrogenic

Excessive controlled ventilation

Respiratory Alkalosis

Acute

The buffering is by intracellular proteins

slight decrease in HCO_3-

Renal compensation has insufficient time to respond

The lower limit of 'compensation' is 18mmol/l

Chronic

Renal loss of bicarbonate causes a further fall in plasma bicarbonate

This maximal response takes 2 to 3 days to reach.

The limit of compensation is a [HCO_3-] of 12 to 15 mmol/l.

Respiratory Alkalosis

A patient cannot have both a respiratory alkalosis and a respiratory acidosis

Hyperventilation is used to acutely decrease intracranial pressure as the onset is rapid.

The effect on cerebral blood flow is time-limited as equilibration of bicarbonate across the blood-brain barrier occurs over 4 to 6 hours and cerebral blood flow and intracranial pressure return towards normal

Acid-Base Interpretation

1. Clinical stem (vomiting/ nasogastric suction / diarrhea)
2. pH: <7.40 Acidemia or >7.40 Alkalemia

   pH=7.40 can occur with mixed acid base disorders
3. Pattern of HCO_3 and pCO_2 (primary disorder)
4. Is compensation appropriate?
5. Is Anion Gap (AG) present?
6. If AG then Delta/Delta and Osmolar Gap
7. Hints in other investigations (urine ketones)

Rules for Acid-Base Disorders

Acute Respiratory Acidosis
Expected HCO_3= 24 +1[(Actual pCO_2-40)/10]

Chronic Respiratory Acidosis
Expected HCO_3 = 24 +4[(Actual pCO_2-40)/10]

Acute Respiratory Alkalosis
Expected HCO_3 = 24 -2[(40-Actual pCO_2)/10]

Chronic Respiratory Alkalosis
Expected HCO_3 = 24 -5[(40-Actual pCO_2)/10]

Metabolic Alkalosis
Expected pCO2 = 0.7 [HCO3] + 20

Metabolic Acidosis
Expected pCO2 = 1.5 [HCO3] + 8

Hints

High anion gap

Metabolic acidosis

Hypokalaemia and/or hypochloraemia

Metabolic alkalosis

Hyperchloraemia

Normal anion gap acidosis

Elevated creatinine and urea

Uremia acidosis or prerenal renal failure

Hyperglycaemia

DKA or hyperosmolar non-ketotic syndrome

Summary Slide

1. Clinical stem
2. pH
3. Pattern of HCO_3 and pCO_2 (primary disorder)
4. Is compensation appropriate?
5. Is Anion Gap (AG) present?
6. If AG then Delta/Delta and Osmolar Gap
7. Hints in other investigations

Respiratory Acidosis and Alkalosis cannot occur together

More than one metabolic acid-base disorder can be present at one time

Urine AG for Non gap acidosis [NeGUTive]

Urinary Chloride in Metabolic Alkalosis

Board Question 1

A 58 year old diabetic woman on insulin was found down nearly unresponsive. Reported to be sick for several days. Past history of CHF. Medications included insulin, digoxin and a thiazide diuretic.

Lytes: K+ 2.8, HCO_3 18, glucose 70, anion gap 31

Arterial Blood Gases pH 7.40, pCO_2 34, pO_2 84

Q: Acid base disorder present is:

A: No acid-base disorder is present

B: High Anion Gap Metabolic Acidosis

C: High Anion Gap Metabolic Acidosis and respiratory alkalosis

D: High Anion Gap Metabolic Acidosis and metabolic alkalosis

E: High Anion Gap Metabolic Acidosis, non gap acidosis and metabolic alkalosis

Board Answer 1

HCO_3 18, anion gap 31, pH 7.40, pCO_2 34, diabetic on thiazide

Q: Acid base disorder present is:

D: High Anion Gap Metabolic Acidosis and metabolic alkalosis

1. Clinical stem (diabetes, obtundation)
2. pH: 7.40 can occur with mixed acid base disorders
3. Pattern of HCO_3 and pCO_2 (primary metabolic acidosis AG+)
4. Is compensation appropriate? expected pCO2 is ((1.5 x 18) + 8) = 35
5. Is Anion Gap (AG) present? yes
6. Delta/Delta and Osmolar Gap

   Delta/Delta = (34-10)/(24-18) = 4 ∴ more HCO_3 than expected = metabolic alkalosis probably from thiazide

   Not enough information for Osmolar Gap
7. Hints in other investigations (urine ketones, serum Osm)

Board Question 2

A 35 yr old healthy female presented with confusion and abdominal pain 8 hours following exercise. RR 22/min.

There was no evidence of intoxication. EtOH=0

Lytes: Na+ 135, K+ 3.7, Cl 109, BUN 12, Glu 106, HCO_3 23,

pH 7.42, pCO_2 35, pO_2 138

Serum osmolality 319 mOsm/kg H_2O

Q: Acid base disorder present is:

A: No acid-base disorder is present

B: High Anion Gap Metabolic Acidosis

C: High Anion Gap Metabolic Acidosis and respiratory alkalosis

D: High Anion Gap Metabolic Acidosis and metabolic alkalosis

E: High Anion Gap Metabolic Acidosis, non gap acidosis and metabolic alkalosis

Board Answer 2

Q: Acid base disorder present is:

A: No acid-base disorder is present

1. Clinical stem (confusion ? intoxication)
2. pH: 7.42 can occur with mixed acid base disorders or no disorder
3. Pattern of HCO_3 and pCO_2 (not abnormal)
4. Is compensation appropriate? No compensation
5. Is Anion Gap (AG) present? AG= 3
6. Osmolar Gap

Calculated osmolarity = (2 x [Na+]) + glucose/18 + BUN/2.8 + ethanol/4.6

Calculated osmolarity = (2 x [135]) + 106/18 + 12/2.8 + 0/4.6 = 280

Osm Gap = 319-280 = 39 indicating

Methanol levels later returned at 30g/dl. Anion gap is absent as patient presented before methanol was metabolized to formaldehyde & formic acid (unmeasured anions)

Board Question 3

An 82 year old woman presented with profound weakness and areflexia. Her PO intake had been poor for a few days.

Lytes: Na^+ 146, K^+ 2.0, Cl^- 87, HCO_3 44, urine chloride 78 mmols/l.

pH 7.58, pCO_2 49, pO_2 - not given

Q: Acid base disorder present is:

A: No acid-base disorder is present

B: Respiratory alkalosis

C: High Anion Gap Metabolic Acidosis and respiratory alkalosis

D: Chloride responsive Metabolic alkalosis

E: Chloride resistant Metabolic alkalosis

Board Answer 3

Elderly woman with profound weakness and areflexia

Lytes: Na^+ 146, K^+ 2.0, Cl^- 87, HCO_3 44, urine chloride 78 mmols/l.

pH 7.58, pCO2 49, pO2 - not given

Q: Acid base disorder present is:

E: Chloride resistant Metabolic alkalosis

1. Clinical stem (not helpful)
2. pH: 7.58 alkalemia
3. Pattern of HCO_3 and pCO_2 (primary metabolic alkalosis)
4. Is compensation appropriate? Expected pCO2 = 0.7 [HCO3] + 20 = 51 yes
5. Is Anion Gap (AG) present? AG= 15 borderline
6. Hints in other investigations (urine chloride >20)

Severe metabolic alkalosis with life-threatening hypokalaemia.

The high urinary chloride suggests a cause in the chloride resistant group (excess steroids or current diuretic use).

Board Question 4

A 73 year old man presented with acute on chronic CHF. Patient had vomiting for 5 days. Patient stopped taking his medications. He was tachypneic and uncomfortable on oxygen.

Lytes: Na 128, K 5.2, Cl 78, HCO_3 20, urea 50, creatinine 6, gluc 108

pH 7.57, pCO_2 22, pO_2 145

Q: Acid base disorder present is:

A: No acid-base disorder is present

B: Respiratory Alkalosis

C: High Anion Gap Metabolic Acidosis with non gap metabolic acidosis and Respiratory Alkalosis

D: Metabolic Alkalosis

E: Primary Respiratory Alkalosis with high anion gap Metabolic Acidosis and Metabolic Alkalosis

Board Answer 4

Q: Acid base disorder present is:

E: Primary Respiratory Alkalosis with high anion gap metabolic acidosis and metabolic alkalosis

1. Clinical stem (CHF lactic acidosis, vomiting metabolic alkalosis, tachypnea Respiratory alkalosis, renal failure high anion gap metabolic acidosis)

2. pH: 7.57 alkalemia

3. Pattern of HCO_3 and pCO_2 (primary respiratory alkalosis)

4. Is compensation appropriate? Expected $HCO_3 = 24 - 5[(40\text{-Actual } pCO_2)/10]$ = **15**. Actual HCO_3 is 20 indicating metabolic alkalosis is present

5. Is Anion Gap (AG) present? AG= 30

6. Delta/Delta and Osmolar Gap

   Delta/Delta = (30-10)/(24-20) = 5 ∴ more HCO_3 than expected = metabolic alkalosis

7. Hints in other investigations (urine chloride >20)

References

- Gupta M, Wadhwa NK, Bukovsky R: Regional citrate anticoagulation for continuous venovenous hemodiafiltration using calcium-containing dialysate. Am J Kidney Dis 43: 67–73, 2004
- Sterns RH, Palmer BF. Nephrology Self-Assessment Program - Vol 5, No 1, January 2006
- 'Acid-base pHysiology' by Kerry Brandis -from http://www.AnaesthesiaMCQ.com
- Hoffman RS, Smilkstein MJ, Howland MA, Goldfrank LR. Osmol gaps revisited: normal values and limitations. J Toxicol Clin Toxicol. 1993;31(1):81-93.
- Seifter JL. N Engl J Med. 2014;371(19):1821-31.