Acid-Base Disturbances - A plACIDly BASE-ic Approach for Clinical Pharmacists

Sample type	Arterial		
temp	37.0 °C		
Report Layout	a BGCOI		
Blood Gas Values			
↓ pH	7.323		[7.350 - 7.450]
↑ pCO_2	49.2	mmHg	[35.0 - 45.0]
pO_2	92.5	mmHg	[70.0 -]
Acid Base Status			
$cHCO_3$ (P)$_c$	24.8	mmol/L	[-]
cBase(B)$_c$	-0.9	mmol/L	[-]
Oximetry Values			
↓ ctHb	95	g/L	[120 - 160]
FO_2Hb	0.942		[0.940 - 1.000]
FCOHb	0.019		[0.000 - 0.050]
↓ FMetHb	-0.001		[0.000 - 0.015]
Oxygen Status			
ctO_{2c}	12.7	Vol%	[-]
Oximetry Values			
Hct_c	0.295		[-]

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Objectives

- Understand acid-base chemistry & physiology
- Systematic approach to acid-base interpretation
- Understand etiology of acid-base disturbances
- Identify drug-related acid-base disturbances
- Understand the principles of treatment

Workshop Outline

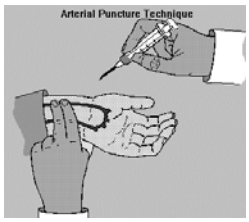
- Anatomy of an arterial blood gas (ABG)
- Acid-base chemistry & physiology
- Consequences of acid-base disturbances
- Stepwise approach → "Rules of Five"
- Acid-base disorders and their causes
- Acid-base disorders and their treatment
- Cases

Acid-Base Terminology

- Acid
- Base
- pH
- Buffer
- Henderson-Hasselbalch equation
- Acidemia
- Alkalemia
- Acidosis
- Alkalosis
- Anion gap
- Normal anion gap

Anatomy of an ABG

- Laboratory method
  - Co-oximetry
- Major components
  - pH
  - Pco_2
  - PaO_2
  - HCO_3^-
  - SaO_2



Anatomy of an ABG

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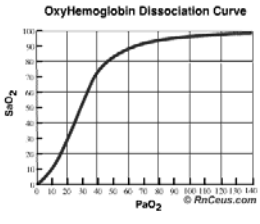
FCOHb	0.019		[0.000 - 0.050]
↓ FMetHb	-0.001		[0.000 - 0.015]
Oxygen Status			
ctO_{2c}	12.7	Vol%	[-]
Oximetry Values			
Hct_c	0.295		[-]

"Normal" Arterial Blood Gas (ABG)

- pH - 7.35 - 7.45
- P_{CO_2} - 40 mmHg
- PaO_2 - > 80 mmHg
- HCO_3^- - 24 mEq/L
- SaO2 - ≥ 0.94



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Consequences of Altered pH

Severe Acidemia (pH < 7.20)	Severe Alkalemia (pH > 7.60)
Obtundation/coma	↓ Cerebral blood flow
Impaired ♥ contractility	Tetany/seizures/delirium
Arteriolar dilatation	Arteriolar constriction
Venoconstriction	↓ ♥ blood flow
↓ BP	↓ Anginal threshold
Arrhythmias	Arrhythmias
Hyperventilation	Hypoventilation
Resp. muscle fatigue	↓ Ionized calcium
Insulin resistance	↓ Magnesium/phosphate
↑ K^+	↓ K^+

NEJM 1998;338:26-34.
NEJM 1998;338:107-111.

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Acid-Base Chemistry

Acid	Base
Donates protons (H^+)	Accepts protons (H^+)
HCl (Acid) → $H^+ + Cl^-$	NH_3 (Base) + $H^+ \rightarrow NH_4^+$

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Clinically Significant Acid-Base Pairs

Acid		Base
Carbonic acid (H_2CO_3)	⟷	Bicarbonate (HCO_3^-)
Monobasic PO_4 (H_2PO_4)	⟷	Dibasic PO_4 (HPO_4^-)
Ammonium (NH_4^+)	⟷	Ammonia (NH_3)
Lactic acid ($H_6C_3O_2$)	⟷	Lactate ($H_5C_3O_2^-$)

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"Potential of Hydrogen" (pH)

- pH devised to facilitate working with small $[H^+]$
  - $pH = -\log [H^+]$
- Lower the pH → more acidic
- Higher the pH → more alkaline

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Henderson-Hasselbalch Equation

$$pH = pKa + \log([base]/[acid])$$

- Henderson derived equation in 1908
- Hasselbalch later re-expressed Henderson's formula in logarithmic terms

J Chem Educ 2003;*80*:146.

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Buffering

"Ability of weak acid and its corresponding base to resist change in pH of a solution upon adding a strong acid or base"

- H_2CO_3/HCO_3^- is principal extracellular buffer

What are the sources of an acid-load?
What occurs when acid-load is introduced?

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Acid Production/Elimination in Humans

- Volatile acid (CO_2)
  - Majority of acid produced
  - Produced from CHO/lipid/protein metabolism
  - Average daily CO_2 production = 15,000 mmol
  - Eliminated via normal ventilation

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Acid Production/Elimination in Humans

- Fixed (non-volatile) acids
  - Digestion of dietary substances/tissue metabolism
  - Amino acids (cysteine & methionine)
  - Ingested sulfur
  - Protein/phospholipid metabolism → phosphates
  - Incomplete metabolism of neutral substances
    - Glucose → lactic acid & pyruvic acid
    - Fatty acids → acetoacetic acid & ß-hydroxybutyric acid
  - Eliminated by kidneys (0.8 mEq/kg/day)

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Buffering Applied

$$pH = pKa + \log([base]/[acid])$$

$$pH = 6.1 + \log([HCO_3^-]/[H_2CO_3])$$

$$pH = 6.1 + \log([HCO_3^-]/(P_{CO_2} \times 0.03))$$

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Buffering Applied

Example: in response to acid load, serum bicarbonate fell to 10 mEq/L, then predicted pH would be:

$[HCO_3^-] = 10$ mEq/L
$P_{CO_2} = 40$ mmHg
$pH = 6.1 + \log[10/(0.03 \times 40)]$
$pH = 6.1 + 0.92$
$pH = 7.02$

But, humans are so much more complex than that . . . . .

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The 3 Mechanisms of Acid-Base Homeostasis

1. Extracellular buffering
   - Immediately acts
   - The "first-responder"
2. Ventilatory regulation of CO_2 elimination
   - Fast onset (minutes)
   - Alveolar ventilation responds to P_{CO_2}
3. Renal regulation of H^+/HCO_3^- excretion
   - Slower onset (≥ 48 hr)
   - Kidney excretes excess $[H^+]$

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Acid-Base Homeostasis Applied

Example: in response to an acid load, serum bicarbonate fell to 10 mEq/L, however, normal respiratory response to an acid load is hyperventilation (↓P_{CO_2})

$[HCO_3^-]$ = 10 mEq/L
P_{CO_2} = 40 mmHg
pH = 6.1 + log[10/(0.03 x 40)]
pH = 6.1 + 0.92
pH = 7.02

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Being Human is a Beautiful Thing! Case Revisited

Buffering	Buffering + Physiology
$[HCO_3^-]$ = 10 mEq/L	$[HCO_3^-]$ = 10 mEq/L
P_{CO_2} = 40 mmHg	P_{CO_2} = 26 mmHg
pH = 6.1 + log[10/(0.03 x 40)]	pH = 6.1 + log[10/(0.03 x 26)]
pH = 6.1 + 0.92	pH = 6.1 + 1.1
pH = 7.02	pH = 7.2

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Approach to Acid-Base Disturbances

- **History**
  - **Prescription medications**
  - **OTC medications**
  - **Naturopathic products**
  - **Illicit drugs**
  - **Diagnostic agents**
- **Order ABG and serum chemistry/albumin**

Postgrad Med 2000;107:249-263. *SKG 2007*

Demystifying "Bicarbonate" Terminology

- **Arterial blood gas (ABG)**
  - **Determined by co-oximetry (hemoximetry)**
  - **HCO_3^- (calculated using H-H equation)**
- **Serum electrolytes**
  - **Total CO_2 (measured sum of HCO_3^-, H_2CO_3, P_{CO_2})**
  - **HCO_3^- should be 1-2 mEq/L less than total CO_2**

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Normal "ABG-Related" Values

- **pH: 7.35-7.45**
- **PCO_2: 40 mmHg**
- **Na^+ (cation): 135-145 mmol/L**
- **HCO_3^- (anion): 24 mmol/L**
- **Cl^- (anion): 95-107 mmol/L**
- **Anion gap: 7 ± 4 mmol/L**
- **Albumin: 40 g/L**

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Don't Break the Rules! Approach to ABG Interpretation

"Rules of Five"

Rule 1. Determine pH status
Rule 2. Determine primary process
Rule 3. Calculate serum anion gap
Rule 4. Check degree of compensation
Rule 5. Determine the delta anion gap

Consultant 1991;31:44-59. *SKG 2007*

Case Example

ID: 68 y/o male; wt: 75 kg; ethanol abuse

HPI: Found unresponsive on Downtown Eastside Vancouver; empty bottle of windshield washer antifreeze nearby; maintaining airway; unknown medical history

ABG: 7.20 / 26 / 98 / 10 / 0.96

Na: 139 mmol/L; **Cl^-:** 106 mmol/L; **CO_2:** 10 mmol/L;

Albumin: 20 g/L

Ethanol: Undetectable

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Rule 1 - Determine pH Status "-emia"

- "emia" - alterations in blood pH
  - pH < 7.35 → acidemia
  - pH > 7.45 → alkalemia

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Rule 1 - Determine pH Status "-emia" Case Revisited

ID: 68 y/o male; wt: 75 kg; ethanol abuse

ABG: (7.20) / 26 / 98 / 10 / 0.96

pH < 7.35, therefore it is an <u>ACIDEMIA</u>

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Rule 1 - Determine pH Status "-emia"

<u>Clinical Pearl</u>

NORMAL pH DOES NOT RULE OUT A SIGNIFICANT ACID-BASE DISTURBANCE!

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Rule 2 - Determine Primary Process "-osis"

"osis" - pathologic process that results in alterations in blood pH

- Primary process (es)
  - Metabolic Acidosis: HCO_3^- < 24 mmol/L
  - Respiratory Acidosis: PCO_2 > 40 mmHg
  - Metabolic Alkalosis: HCO_3^- > 24 mmol/L
  - Respiratory Alkalosis: PCO_2 < 40 mmHg

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Rule 2 - Determine Primary Process "-osis" Case Revisited

ID: 68 y/o male; wt: 75 kg; ethanol abuse

ABG: 7.20 / (26) 98 / (10) 0.96

Rule 1. pH < 7.35, therefore it is an ACIDEMIA

Rule 2. PCO_2 is <u>NOT</u> > 40, therefore primary process is <u>NOT</u> respiratory

HCO_3^- < 24, therefore primary process is <u>metabolic</u>

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Rule 2 - Determine Primary Process "osis" Case Revisited

Reminder

PCO_2 is an ACID that is regulated by the respiratory system; HCO_3^- is a BASE that is regulated by the kidneys!

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Rule 2 - Determine Primary Process "-osis"

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BOTH METABOLIC AND RESPIRATORY PROCESSES MAY SIMULTANEOUSLY BE THE PRIMARY ACID-BASE DISTURBANCE!

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Rule 3 - Calculate Serum Anion Gap

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Rule 3 - Serum Anion Gap

- Law of electrical neutrality
  - There are no sparks in our blood!
  - +VE = -VE
- Serum cations
  - Measured: Na^+
  - "Un-measured": Ca^{++}, K^+, Mg^{++}
- Serum anions
  - Measured: Cl^-, HCO_3^-
  - "Un-measured": phosphates, sulfates, organic anions, proteins (albumin)

Postgrad Med 2000;107:249-263.

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Rule 3 - Serum Anion Gap

Sources of unmeasured anions (+ve SAG)

- Consumption of HCO_3^- by organic acids (lactic acid, acetoacetic acid, ß-hydroxybutyric acid)
- Ingestion of toxins (methanol, ethylene glycol)
- Accumulation of organic anions, phosphates, sulfates in renal failure

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Rule 3 - Serum Anion Gap

$[Na^+] + [UCs] = ([Cl^-] + [HCO_3^-] + [UAs])$

$SAG = [Na^+] - [Cl^-] - [HCO_3^-]$

Normal SAG = 7 ± 4 mmol/L

SAG > 11 mmol/L can indicate metabolic acidosis

SAG > 20 mmol/L always indicates metabolic acidosis

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Rule 3 - Serum Anion Gap

- Corrected SAG
  - Albumin is negatively charged
  - For every 10 g/L below 40 g/L, ↑ SAG by 2.5
- Normal anion gap (hyperchloremic) metabolic acidosis
  - H^+ is accompanied by Cl^- therefore no ↑ SAG

Dis Mon 2004;50:117-162.
Postgrad Med 2000;107:249-263.

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Rule 3 - Calculate Serum Anion Gap Case Revisited

ID: 68 y/o male; wt: 75 kg; ethanol abuse

ABG: 7.20 / 26 / 98 / 10 / 0.96

Na: (139) mmol/L; **Cl^-:** (106) mmol/L; **CO_2** (10) mmol/L;

Albumin: (20) g/L

Rule 1. pH < 7.35, therefore it is an ACIDEMIA

Rule 2. Primary process is metabolic

Rule 3. Anion Gap: 139 - 106 - 10 = 23 mmol/L

Albumin correction: 2.5 x 2 = 5 mmol/L

Corrected Anion Gap: 23 + 5 = 28 mmol/L

This is an Anion Gap Metabolic Acidosis

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Rule 3 - Calculate Serum Anion Gap

Clinical Pearls

ALWAYS CALCULATE SAG!

ANION GAP > 11 mmol/L CAN INDICATE METABOLIC ACIDOSIS

ANION GAP > 20 mmol/L ALWAYS INDICATES A METABOLIC ACIDOSIS

FOR EVERY 10 G/L ALBUMIN IS LESS THAN 40 G/L, ADD 2.5 TO THE CALCULATED SAG

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Rule 4 - Check Degree of Compensation for Primary Disturbance

1. Extracellular buffering (see previous slide)
   - Immediately acts
   - The "first-responder"
2. Ventilatory regulation of CO_2 elimination
   - Fast onset
   - Alveolar ventilation responds to P_{CO_2}
3. Renal regulation of H^+/$HCO3^-$ excretion
   - Slower onset
   - Kidney excretes excess hydrogen ion

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Rule 4 - Acid-Base Compensation

Primary Disturbance	ABG Value Disturbed	Physiologic Response
Metabolic Acidosis	↓ HCO_3^-	Hyperventilation ↓ PCO_2
Metabolic Alkalosis	↑ HCO_3^-	Hypoventilation ↑ PCO_2
Respiratory Acidosis	↑ PCO_2	Buffering/↑ HCO_3^- resorption/ ↑ H^+ secretion ↑ HCO_3^-
Respiratory Alkalosis	↓ PCO_2	Buffering/↓ HCO_3^- resorption/ ↓ H^+ secretion ↓ HCO_3^-

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Rule 4 - Acid-Base Compensation

Primary Disturbance	ABG Value Disturbed	Expected Compensation
Metabolic Acidosis	↓ HCO_3^- 1 mmol/L	↓ PCO_2 1 mmHg
Metabolic Alkalosis	↑ HCO_3^- 1 mmol/L	↑ PCO_2 0.6 mmHg
Respiratory Acidosis	↑ PCO_2 10 mmHg ↑ PCO_2 10 mmHg	↑ HCO_3^- 1 mmol/L (A) ↑ HCO_3^- 4 mmol/L (C)
Respiratory Alkalosis	↓ PCO_2 10 mmHg ↓ PCO_2 10 mmHg	↓ HCO_3^- 2 mmol/L (A) ↓ HCO_3^- 5 mmol/L (C)

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Rule 4 - Check Compensation Case Revisited

ID: 68 y/o male; wt: 75 kg; ethanol abuse

ABG: 7.20 / (26) / 98 / (10) / 0.96

Na: 139 mmol/L; **Cl⁻:** 106 mmol/L; CO_2: 10 mmol/L; **Alb:** 20 g/L

Rule 1. pH < 7.35, therefore it is an ACIDEMIA

Rule 2. Primary process is metabolic

Rule 3. Anion Gap: Positive

Rule 4. Compensation for a metabolic acidosis → 1:1

- HCO_3^- is ↓ by 14, therefore PCO_2 should ↓ by 14
- PCO_2 should be 40-14 = 26 mmHg √

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Rule 4 - Check Compensation Altered Case Scenario

ID: 68 y/o male; wt: 75 kg; ethanol abuse

ABG: 7.10 / (33) / 98 / 10 / 0.96

Na: 139 mmol/L; **Cl⁻:** 106 mmol/L; CO_2: 10 mmol/L; **Alb:** 20 g/L

Rule 1. pH < 7.35, therefore it is an ACIDEMIA

Rule 2. Primary process is metabolic

Rule 3. Anion Gap: Positive

Rule 4. Compensation for a metabolic acidosis → 1:1

- HCO_3^- is ↓ by 14, therefore PCO_2 should ↓ by 14
- PCO_2 should be 40-14 = 26 mmHg
- PCO_2 is 33 mmHg (higher than predicted)
- Respiratory acidosis is secondary disturbance

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Rule 4 - Check Compensation

Clinical Pearls

ALLOWS DETERMINATION OF SECONDARY DISTURBANCES

MEMORIZE COMPENSATION RULES OR CARRY CHEAT-SHEET WITH COMPENSATION RULES

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Rule 5 - Determine Delta Anion Gap

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Rule 5 - Determine Delta Anion Gap

- **Only required if:**
  - Metabolic alkalemia or alkalosis not yet diagnosed
- **Relies on law of electroneutrality**
  - If an anion gap ↑, HCO_3^- must ↓ by same number
  - If HCO_3^- has dropped less than delta gap → metabolic alkalosis
  - If HCO_3^- has dropped more than delta gap → normal anion gap metabolic acidosis

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Rule 5 - Determine Delta Anion Gap Case Revisited

ID: 68 y/o male; wt: 75 kg; ethanol abuse

ABG: 7.20 / 26 / 98 / (10) / 0.96

Rule 1. pH < 7.35, therefore it is an ACIDEMIA

Rule 2. Primary process is metabolic

Rule 3. Anion Gap: Positive

Rule 4. Respiratory compensation appropriate

Rule 5. Determine delta anion gap

- Anion gap = 28; normal anion gap = 11
- Delta anion gap = 28 – 11 = 17 mmol/L
- HCO_3^- should ↓ by 17 mmol/L (24-17 = 7 mmol/L)
- HCO_3^- is 10 mmol/L "high" → metabolic alkalosis

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Rule 5 - Determine Delta Anion Gap

Clinical Pearl

THE DELTA ANION GAP IS MOST RELIABLE IN THE SETTING OF A POSITIVE ANION GAP METABOLIC ACIDOSIS

THE DELTA ANION GAP ALLOWS DIAGNOSIS OF METABOLIC ALKALOSIS EVEN IF THERE IS A POSITIVE ANION GAP METABOLIC ACIDOSIS

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"Rules of Five" at Work

ID: 68 y/o male; wt: 75 kg; ethanol abuse

HPI: Found unresponsive on Downtown Eastside Vancouver; empty bottle of windshield washer antifreeze nearby; maintaining airway; unknown medical history

ABG: 7.20/26/98/10/0.96

Na: 139 mmol/L; **Cl^-:** 106 mmol/L; **CO_2:** 10 mmol/L;

Albumin: 20 g/L

Ethanol: Undetectable

Acid-base disturbance: Primary anion gap metabolic acidosis with a secondary metabolic alkalosis

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Applying the "Rules of Five"

Clinical Pearl

COMMENTING ON AN ISOLATED SET OF ABGs WITHOUT BENEFIT OF ANY PERTINENT HISTORY CAN LEAD TO SERIOUS ERROR!

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Specific Acid-Base Disturbances

- Metabolic acidosis
  - Anion gap
  - Normal anion gap
- Metabolic alkalosis
  - NaCl-responsive
  - NaCl-resistant
- Respiratory acidosis
- Respiratory alkalosis

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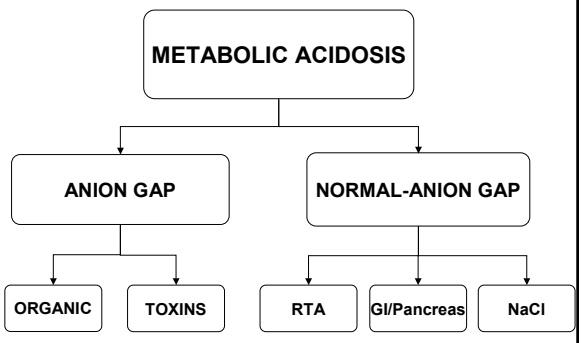

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Anion Gap Metabolic Acidosis - Pathophysiology

- ↓ pH due to primary ↓ HCO_3^-
- Causes of ↓ HCO_3^-
  - Endogenous acids
    - Buffering (consumes HCO_3^-) endogenous organic acids (lactic acid/ketoacids)
    - Progressive accumulation of endogenous acids (phosphates/sulfates) due to renal dysfunction
  - Exogenous acids
    - Buffering (consumes HCO_3^-) toxins (toxic alcohols)

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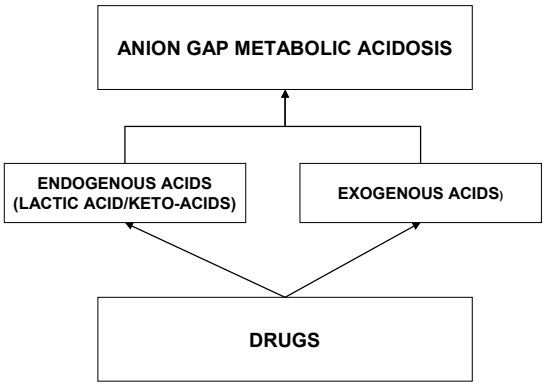

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Anion Gap Metabolic Acidosis – ↑ Endogenous Acids

- Lactic acidosis (↑ acid production)
  - ↓ tissue oxygenation (shock/anemia/CHF/asphyxia)
  - Deranged oxidative metabolism (DM/liver failure/seizures/genetic)
- Ketoacidosis (↑ acid production)
  - Diabetic
  - Alcoholic
  - Starvation
- Renal failure (acid accumulation)
  - Phosphates/sulfates/organic anions

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Anion Gap Metabolic Acidosis - Drug-Related Causes

- Medications at therapeutic doses
- Medications at toxic doses
- Toxins

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Anion Gap Metabolic Acidosis - Medications at Therapeutic Doses

- Atypical antipsychotics (DKA)
- ß$_2$-agonists (LA)
- Epinephrine (LA)
- HMG CoA reductase inhibitors (LA)
- Linezolid (LA)
- Metformin (LA)

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Anion Gap Metabolic Acidosis - Medications at Therapeutic Doses

- NRTIs (LA)
  - Stavudine, lamivudine, zidovudine, didanosine
- Sodium Nitroprusside (LA)
- Propofol (LA)
- Propylene glycol (LA)
  - Diazepam
  - Etomidate

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Anion Gap Metabolic Acidosis - Medications at Toxic Doses

- Acetaminophen (LA)
- Isoniazid (LA)
- Iron (LA)
- Paraldehyde (Metabolites/LA)
- Phosphate salts (Metabolites)
- Salicylates (Metabolites)

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Anion Gap Metabolic Acidosis - Toxins

- Carbon monoxide (LA)
- Cocaine (LA)
- Cyanide (LA)
- Ethanol (LA)
- Ethylene glycol (Mets)
- Formaldehyde (Mets)
- Hydrogen sulfide (LA)
- MDMA (LA)
- Methanol (Mets)
- Toluene (Hippuric Acid)

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Toxin Ingestion Suspected - Mind the Osmole Gap!

- Determine if:
  - +ve SAG metabolic acidosis AND
  - Suspected toxic alcohol ingestion

  Calculate plasma osmolality:

  (2 x [Na^+]) + [Glucose] + [Urea] + [Ethanol]

  Measure plasma osmolality

  Osmole gap (OG):

  OG = Measured Osmolality - Calculated Osmolality
- Normal OG $\rightarrow$ 10 - 20 mOsm/kg/H_2O

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Determine Osmole Gap Case Revisited

ID: 68 y/o male; wt: 75 kg; ethanol abuse; antifreeze

ABG: 7.20 / 26 / 98 / 10 / 0.96

Na: 139 mmol/L; **Gluc:** 10 mmol/L; **Urea:** 7 mmol/L; **ø EtOH**

Measured osmolality: 320 mOsm/kg/H_2O

Primary anion gap metabolic acidosis with secondary metabolic alkalosis

Calculated osmolality: (2 x 139) + 10 + 7 = 295 mOsm/kg/H_2O

Osmole gap: 320 - 295 = 25 mOsm/kg/ H_2O

Anion gap metabolic acidosis is likely due to toxic alcohol in antifreeze

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Anion Gap Metabolic Acidosis - Acronyms

Outdated Acronym	Modern Acronym
Methanol	Metformin/Methanol
Uremia	Uremia
DKA	DKA
Paraldehyde	Propofol
INH/Iron	INH/Iron
Lactic acidosis	Lactic acidosis/Linezolid
Ethylene glycol	Ethylene glycol
Salicylates/Starvation	Ingestions (cocaine/MDMA)
	NRTIs/Neuroleptics
	Glycol (Propylene)
	Salicylates/Starvation

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Normal Anion Gap Metabolic Acidosis - Pathophysiology

- $\downarrow$ pH due to primary $\downarrow$ HCO_3^-
- Causes of $\downarrow$ HCO_3^-
  - GI tract wastes HCO_3^-
  - Renal losses of HCO_3^-
  - Impaired renal acid excretion
  - Exogenous acid gain
  - Normal saline-induced (Cl^- induces acidosis)
- SAG remains normal because:
  - HCO_3^- losses are replaced by Cl^-

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Normal Anion Gap Metabolic Acidosis - Causes

- GI loss of HCO_3^-
  - Diarrhea (30 - 50 mEq/L)
  - Biliary drainage
  - Pancreatic fistula
  - Ureteral diversion into sigmoid colon
  - Isolated ileal loop

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Normal Anion Gap Metabolic Acidosis - Causes

- Renal loss of HCO_3^-
  - Proximal renal tubular acidosis (pRTA)
- Impaired renal acid excretion
  - Distal renal tubular acidosis (dRTA)

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Normal Anion Gap Metabolic Acidosis - RTA

- Type 1 (distal RTA)
  - ↓ net secretion of H^+ in collecting tubules
- Type 2 (proximal RTA)
  - Diminished HCO_3^- reabsorption
- Type 4 ("distal-like" RTA)
  - Aldosterone resistance or deficiency
  - Often associated with hyperkalemia

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Type 1 (distal) RTA

Signs

- Hypokalemia, hyperchloremic metabolic acidosis, inability to lower urine pH < 5.5

Drug-Related Causes

- Amphotericin B
- Foscarnet
- Lithium
- Methicillin
- Toluene
- Vitamin D intoxication

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Type 2 (proximal) RTA

Signs

- Hyperchloremic metabolic acidosis

Drug-Related Causes

- Acetazolamide
- Adefovir
- Aminoglycosides
- Cidofovir
- Didanosine
- Lamivudine
- Stavudine
- Tetracycline (outdated)
- Topiramate
- Valproic acid

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Type 4 ("distal-like") RTA

Signs

- Hyperkalemia, hyperchloremic metabolic acidosis

Drug-Related Causes

- ACE-inhibitors
- ARBs
- Heparin
- Spironolactone
- Trimethoprim/sulfamethoxazole

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Normal Anion Gap Metabolic Acidosis - Rule Out RTA

- Urinary Anion Gap (UAG)
  - Normal circumstances → urine is free of HCO_3^-
  - NH_4^+ is predominant UC in urine
  - NH_4^+ is accompanied by Cl^-
  - Measure spot urine electrolytes
  - UAG = $Na^+ + K^+ - Cl^-$
  - Normal UAG = -20 - 0 mEq/L
  - If non-renal source (diarrhea), normal response is dramatic ↑ NH_4^+ excretion in urine (UAG -20 → -50)
  - If RTA, UAG is positive (EXCEPTION: Type 2 RTA)

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Normal Anion Gap Metabolic Acidosis - Acronym

- Hyperalimentation
- Acetazolamide
- RTA
- Diarrhea
- Uretosigmoidostomy
- Pancreatic fistula

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Metabolic Acidosis - Clinical Presentation

- pH 7.20 - 7.35
  - Usually asymptomatic
- pH < 7.20
  - CNS: obtundation/coma
  - CVS: flushing/tachycardia/wide pulse pressure/reduced BP
  - RESP: Dyspnea/hyperventilation
  - GI: nausea/vomiting/loss of appetite
  - MET: insulin resistance/increased demands

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Metabolic Acidosis - Treatment

- Identify and remove cause(s)
- Effective treatment of underlying disease
  - Fosters conversion of organic acids to HCO_3^-
- Consider alkali therapy if pH < 7.20

NEJM 1998;338:26-34. SKG 2007

Metabolic Acidosis - Treatment

Goals of Alkali Therapy

- Prevent/reverse consequences of severe acidemia
- Return pH to ≥ 7.20 (↑ HCO_3^- to 8-10 mmol/L)

Pharmacotherapeutic Options

- IV Sodium bicarbonate

Dosing Sodium Bicarbonate

- Determine desired change in HCO_3^- (mmol/L)
- Determine sodium bicarbonate Vd (0.5 L/kg x Wt)
- Dose (mmol)= Desired change (mmol/L) x Vd (L)
- Ideally infuse over minutes - hours (avoid bolus)

NEJM 1998;338:26-34. SKG 2007

Metabolic Acidosis - Treatment

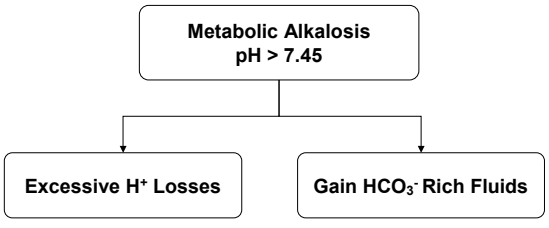
Monitoring

- Wait 30 minutes post-infusion to judge clinical effect
- Repeat ABGs (overshoot alkalemia)
- Serum chemistry (K^+ will ↓, Na^+ may ↑)
- Signs of extracellular volume overload

NEJM 1998;338:26-34. SKG 2007

Metabolic Alkalosis - Pathophysiology

- ↑ pH due to primary ↑ HCO_3^-
- Accounts for 50% of acid-base disorders



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Metabolic Alkalosis - Pathophysiology

- Gain HCO_3^-
  - Infusion of acetate, lactate, citrate
  - Milk-alkali syndrome (uncommon)
- Excessive H^+ losses
  - GI loss of H^+ via NG suctioning/vomiting
  - Renal loss of H^+ due to ↑ Na^+ delivery to CCD (loop/thiazide diuretics)
  - Renal loss of H^+ due to ↑ Na^+ delivery to CCD (intravascular volume contraction)

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Metabolic Alkalosis – Causes

- NaCl-responsive (urinary Cl^- < 20 mEq/L)
  - Vomiting or nasogastric suctioning
  - Chloride-rich diarrhea
  - Cystic fibrosis
  - Diuretic therapy (loop or thiazide diuretics)
  - Excessive bicarbonate therapy for acidosis
- NaCl-resistant (urinary Cl^- > 20 mEq/L)
  - Excess mineralocorticoid activity
  - Tubular abnormalities (Bartter/Gitleman/Liddle Syndrome)
  - Recent loop/thiazide diuretic use

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Metabolic Alkalosis - Clinical Presentation

- pH 7.45 - 7.60
  - Usually asymptomatic
- pH > 7.60
  - CNS: ↓ cerebral blood flow/ tetany/seizures/lethargy/delirium/stupor
  - CVS: arteriolar constriction/↓ coronary blood flow/↓ anginal threshold/PSVTs/VTs
  - RESP: Hypoventilation/hypoxemia
  - MET: stimulation organic acid production/hypokalemia/hypomagnesemia/ hypophosphatemia/↓ ionized calcium

NEJM 1998;338:107-111. *SKG 2007*

Metabolic Alkalosis - Treatment

- Identify and remove cause(s)
  - Vomiting treated with antiemetics
  - H_2-receptor antagonists/proton pump inhibitors
  - Reduce dose of loop/thiazide diuretics
  - Potentially add K^+-sparing diuretics (↓ distal acidification)
  - Discontinue lactate/citrate/acetate solutions
  - Reassess/discontinue mineralocorticoids
- Effective treatment of underlying disease

NEJM 1998;338:107-111. *SKG 2007*

Metabolic Alkalosis - Treatment

<u>Goals of Therapy</u>

- Moderation of the alkalemia
- Return pH to ≤ 7.55 (↓ HCO_3^- to < 40 mmol/L)

<u>Therapeutic Options – Cl^- Responsive</u>

- Volume contraction → NaCl ± KCl
- Volume or sodium intolerant → acetazolamide ± KCl
- Persistant alkalosis <u>OR</u> pH > 7.60 → HCl infusion

<u>Therapeutic Options – Cl^- Resistant</u>

- Remove/alter causes

NEJM 1998;338:107-111. *SKG 2007*

Respiratory Acidosis - Pathophysiology

- ↓ pH due to primary ↑ PCO_2
  - ↓ RR ± Tidal Volume
- Acute respiratory acidosis
- Chronic respiratory acidosis

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Respiratory Acidosis - Causes

- CNS: drugs (opioids, BZDs, TCAs), trauma, stroke, infection
- SPINE: trauma
- NERVE: trauma, MS, neuropathies
- NMJ: MG, paralytics, toxins (red tide/botulism)
- MUSCLE: CHO depletion, electrolyte depletion
- OBSTRUCTIVE: choking, asthma, COPD
- RESTRICTIVE: hemo/pneumothorax/empyema
- OTHER: TPN

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Respiratory Acidosis – Clinical Presentation

- CNS: abnormal behavior/seizures/stupor/coma
- CVS: refractory hypotension
- RESP: hypoventilation

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Respiratory Acidosis – Treatment

Goals of Therapy
- Provide adequate oxygenation
- Establish/maintain patent airway

Therapeutic Options
- Treatment depends on cause/chronicity
- Treat underlying cause (ie. bronchodilators → bronchospasm)

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Respiratory Alkalosis – Pathophysiology

- ↑ pH due to primary ↓ PCO_2
- CO_2 excretion exceeds metabolic production
- Hyperventilation - ↑ RR ± Tidal Volume
- Most common acid-base disorder

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Respiratory Alkalosis – Causes

- Central stimulation of respiration
  - Anxiety/pain/fever/CNS lesions/ TBI/pregnancy/progesterone/salicylates
- Peripheral stimulation of respiration
  - PE/CHF/altitude/asthma/pulmonary shunts/hypotension/pneumonia/sepsis/cirrhosis
- Voluntary hyperventilation

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Respiratory Alkalosis – Clinical Presentation

- CNS: syncope/seizures
- CVS: cardiac arrhythmias
- RESP: hyperventilation

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Respiratory Alkalosis – Treatment

Goals of Therapy

- Provide adequate oxygenation
- Establish/maintain patent airway

Therapeutic Options

- pH 7.45 - 7.50 → asymptomatic
- Identify/correct underlying cause
- Re-breathing devices

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Acid-Base Disorders – Role of the Pharmacist

- Identify patients at risk for acid-base disorders
  - Thorough medication history
- Identify acid-base disorders
  - "Rules of Five"
- Prevent acid-base disorders
  - Eliminate unnecessary potential culprits
  - Educate on proper use of potential culprits
- Treatment strategies for acid-base disorders

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www.vhpharmsci.com/Presentations/2007/GormanPPC2007.pdf

PRACTICE!
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PRACTICE!

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ACID-BASE DISTURBANCES – A pIACIDly BASE-ic APPROACH TO INTERPRETATION, DIAGNOSIS, AND TREATMENT FOR CLINICAL PHARMACISTS
Sean K. Gorman, PharmD 2007

CASE 1.
ID: 30 year-old female admitted to psychiatry with an "eating disorder".
Ht: 5'5" Wt: 37 kg

HPI: She stated that she had not induced vomiting for the last 3 weeks. Although she was cachectic, she denied other efforts to control her weight (denied laxative or diuretic abuse). She currently complains of lightheadedness when standing after lying in bed.

PMHx: Bulimia nervosa (self-induced vomiting)

MPTA: Nothing noted.

Allergies: NKDA

Physical Exam:

Vitals: Afebrile; BP 90/65 mmHg (lying); BP 80/62 (standing); HR 98 (lying); HR 112 (standing); RR 12/min
HEENT: Oral mucosa dry; temporal wasting
CVS: JVP (neck veins) flat; otherwise normal

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Laboratory:

ABG	Serum Electrolytes	Spot Urine Lytes	Urinalysis	Other Blood Work
pH 7.50	Na^+ 141 mEq/L		Dipstick Negative	Albumin 30 g/L
PCO_2 46 mmHg	K^+ 3.1 mEq/L			
HCO_3^- 34 mEq/L	Cl^- 98 mEq/L	Cl^- 8 mEq/L		
PO_2 92 mmHg	SCr: 88 µmol/L Urea 12 mmol/L			
SaO_2 0.98				

1. Using the Rules of Five, please determine this patient's acid-base disturbance.

Rule 1. pH > 7.45, alkalemia
Rule 2. HCO_3^- > 24 mEq/L, therefore metabolic alkalosis
Rule 3. Anion Gap = 141-98-34 = 9; correct for albumin of 30 g/L (add 2.5 to anion gap for every 10 g/L albumin is below 40 g/L); therefore, add 2.5 to anion gap = 9+2.5=11.5 ("normal")
Rule 4. Compensation for primary disturbance: rule for metabolic alkalosis is for each 1 mEq/L increase in HCO_3^- above 24 mEq/L, PCO_2 should increase 0.6 mmHg. HCO_3^- is up by 10, therefore PCO_2 should be up by 6 mmhg above normal (40). 40+6=46 mmHg √
Rule 5. Delta anion gap - not applicable because a metabolic alkalosis has already been diagnosed. Also, there is no positive anion gap, rendering the delta anion gap less reliable.
Acid-Base Disturbance: This is a metabolic alkalosis. An other way of stating this acid-base disturbance would be: This is a simple metabolic alkalosis.

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2. What are the potential causes of this patient's acid-base disturbance?

Metabolic alkalosis can be broken into 2 varieties: NaCl responsive, determined by a urine Cl- < 20 mEq/L; an d NaCl resistant, determined by urine Cl- > 20 mEq/L. Based on this person's urine Cl- of 8 mEq/L, it can be described as being NaCl responsive. Therefore, the causes of NaCl responsive metabolic alkalosis include vomiting, nasogastric suctioning, chloride-rich diarrhea, CF, diuretic therapy (chronic), and excessive exogenous bicarbonate therapy for treatment of acidosis. Given the history in this case, the most likely reason for the acid-base disturbance is vomiting. After a more detailed history, it was revealed that this indeed was the case.

3. Devise a brief treatment-plan for this patient's acid-base disturbance.

This appears to be NaCl responsive, therefore the primary treatment of choice is IV fluids. The fluid of choice is the crystalloid NaCl in this case. An example of a treatment strategy is as follows:
NaCl 500 ml IV X 2, then infuse a maintenance NaCl infusion at 150 ml/hr until intravascular volume status has been replenished. Monitor intravascular volume status, signs of fluid overload, repeat electrolytes in 12 hours.

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CASE 1a.
See the previous case, however, the labs were as follows:

ABG	Serum Electrolytes	Spot Urine Lytes	Urinalysis	Other Blood Work
pH 7.50	Na^+ 141 mEq/L		Dipstick Negative	Albumin 30 g/L
PCO_2 46 mmHg	K^+ 3.1 mEq/L			
HCO_3^- 34 mEq/L	Cl^- 98 mEq/L	**CT 48 mEq/L**		
PO_2 92 mmHg	SCr: 88 µmol/L Urea 12 mmol/L			
SaO_2 0.98				

1. What could be causing this acid-base disturbance?
Again, this is a metabolic alkalosis. However, this appears to be of the NaCl-resistant variety. One would want to rule out causes of NaCl-resistant metabolic alkalosis, including diseases associated with excess mineralocorticoid activity, exogenous mineralocorticoid use/abuse, renal tubular abnormalities such as Bartter/Gitelman/Liddle Syndromes, or recent (within hours) loop or thiazide diuretic use. Given the history of present illness, the most likely reason for this is recent loop diuretic abuse. Upon further history, this is confirmed by the patient.

CASE 2.
ID: 67 year-old male day 2 post-op aortic aneurysm repair.
Ht: 5'11" Wt: 90 kg

HPI: Had come into hospital for elective surgery to repair a AAA. The surgery was relatively uneventful 2 days ago, and he had been quickly extubated in the recovery room and has been resting comfortably on the cardiac surgery ward ever since. He was continued on all of his medications that he was on at home immediately post-op. However, in the last 12 hours, the RN has noted that he has not passed urine. Also, he is now tachycardic and appears to be hyperventilating. When assessed by the surgical resident, the patient is extremely confused.

PMHx: Type 2 Diabetes (no evidence of nephropathy – last SCr pre-admission = 85 µmol/L)
Hypertension

MPTA: Metformin 1000 mg po BID
Metoprolol 100 mg po BID
Amlodipine 10 mg po daily

Allergies: NKDA

Laboratory:

ABG	Serum Electrolytes	CBC	Other Blood Work
pH 6.91	Na^+ 144 mEq/L	Pending	Albumin 40 g/L
PCO_2 22 mmHg	K^+ 3.9 mEq/L		Glucose 2.1 mmol/L
HCO_3^- 6 mEq/L	Cl^- 112 mEq/L		Lactate 24 mmol/L
PO_2 130 mmHg	SCr: 287 µmol/L Urea: 19 mmol/L		
SaO_2 0.98			

1. Using the Rules of Five, identify the acid-base disturbance.

Rule 1. pH <7.35, acidemia
Rule 2. HCO_3^- < 24 mEq/L, therefore metabolic acidosis
Rule 3. Anion Gap = 144-112-6 = 26 (positive); no need to correct for albumin because it's normal.
Rule 4. Compensation for primary disturbance: rule for metabolic acidosis is for each 1 mEq/L decrease in HCO_3^- below 24 mEq/L, PCO_2 should decrease 1 mmHg. HCO_3^- is 18 mEq/L below 24, therefore PCO_2 should drop by 18 mmHg from normal (40-18=22 mmHg)√
Rule 5. Delta anion gap - Anion gap - high end of normal for anion gap = 26 - 11 = 15. Therefore, HCO_3^- should have dropped by at least 15 mEq/L from 24 mEq/L. It is currently 6 mEq/L, which is a drop of more than 15 mEq/L, therefore there is no secondary metabolic alkalosis.
Acid-Base Disturbance: This is a positive anion gap metabolic acidosis. Another way of stating this would be: A simple positive anion gap metabolic acidosis.

2. What are the potential causes of this acid-base disorder?
"MUDPILEINGS" - refer to handout for potential causes. In this person, you will notice that he has acute renal failure in the setting of metformin use. Also, his serum lactate is 24 mmol/L, which significantly higher than normal (< 4 mEq/L). Therefore, the most likely cause in this scenario is a metformin-induced lactic acidosis in the setting of acute renal failure.

CASE 3.
You are going about your daily routine seeing patients for identification of real or potential DRPs, when you come across the following blood work:

ABG	Serum Electrolytes	CBC	Spot Urine Lytes	Other Blood Work
pH 7.29	Na^+ 140 mEq/L	Pending	Na+ 48 mEq/L	Albumin 40 g/L
PCO_2 31 mmHg	K^+ 3.1 mEq/L		K+ 48 mEq/L	
HCO_3^- 15 mEq/L	Cl^- 117 mEq/L		Cl- 65 mEq/L	
PO_2 110 mmHg	SCr: 87 µmol/L Urea: 8 mmol/L			
SaO_2 0.97				

This is a 60 year old male who is status post-op day # 10 CABG. His primary medical problem as stated by the team is not cardiac, but rather, is a Candida albicans fungemia. He has received Amphotericin B deoxycholate 50 mg iv daily for 8 days.

1. Using the Rules of Five determine the acid-base disturbance.

Rule 1. pH <7.35, acidemia
Rule 2. HCO_3^- < 24 mEq/L, therefore metabolic acidosis
Rule 3. Anion Gap = 140-117-15 = 8 (normal); no need to correct for albumin because albumin is normal.
Rule 4. Compensation for primary disturbance: rule for metabolic acidosis is for each 1 mEq/L decrease in HCO_3^- below 24 mEq/L, PCO_2 should decrease 1 mmHg. HCO_3^- is 9 mEq/L below 24, therefore PCO_2 should drop by 9 mmHg from normal (40-9=31 mmHg)√
Rule 5. Delta anion gap - not reliable because there is not a positive anion gap.
Acid-Base Disturbance: This is a normal anion gap metabolic acidosis. Another way of stating this would be: A simple normal anion gap metabolic acidosis.

2. What could be causing this acid-base disturbance?
Normal anion gap metabolic acidosis can be caused by loss of bicarbonate via the GI tract or kidneys (proximal tubular problems), or because of impaired acid(NH4+)-secretion via the kidneys (distal tubular problems). A quick way to try to differentiate whether there is a kidney problem that's leading to the metabolic acidosis versus a GI tract reason, one should examine the Urine Anion Gap (UAG).

The UAG is calculated based on spot urine electrolyte concentration. Specifically, UAG = urine (Na^+) + (urine K^+) - (urine Cl^-). In normal individuals, the UAG should be between negative 20 to 0. However, in people with a metabolic acidosis, the normal response is the kidneys to excrete extra acid to attempt to maintain homeostasis. Therefore, the UAG should be negative 50 to negative 20. If there is a problem with acidification of the urine, as seen with distal renal tubular acidosis, the UAG will be more positive.

This person's UAG = 48+48-65= Positive 31. Therefore, there likely is a problem with the distal renal tubule's ability to excrete acid ($NH4^+$). Therefore, this could be a distal renal tubular acidosis (dRTA). A potential drug-related culprit could be Amphotericin B deoxycholate. The plan in this patient was to complete the course of antifungal therapy with fluconazole, which the Candida albicans should be fully susceptible to.

Remember, there is an acronym that can quickly get you in the right frame of mind with regards to causes of normal anion gap metabolic acidosis:

HARDUP (Refer to handout for details)

CASE 4.
ID: 28 year-old female
Ht: 5'4" Wt: 60 kg

HPI: 10-year history of type 1 diabetes who is moderately-well controlled on 24 units insulin glargine plus pre-meal doses of insulin lispro. Her family brings her to the ED where she complains of abdominal tenderness, nausea, and vomiting. She was well until 2 days ago when she awoke with nausea, vomiting, diarrhea and chills. Because she was unable to eat, she omitted her usual morning dose of insulin. Her GI symptoms progressed and she was brought to the ED because of lethargy. You notice a fruity odor to her breath.

PMHx: Type 1 DM X 10 years

MPTA: Insulin glargine 24 units
Insulin lispro pre-meal

Allergies: NKDA

Physical Exam:
Vitals: Temp 37 (axilla); BP 100/65 mmHg (lying); BP 80/45 mmHG (sitting); HR 110 (lying); HR 135 (sitting); RR 16/min
CVS: JVP (neck veins) flat
GI: Mild, diffuse tenderness over abdomen
Skin: Poor skin turgor

Laboratory:

ABG	Serum Electrolytes	CBC	Urinalysis	Other Blood Work
pH 7.04	Na^+ 146 mEq/L	Hgb 147	+ve glucose	Albumin 42 g/L
PCO_2 27 mmHg	K^+ 5.2 mEq/L	Hct 0.490	moderate ketones	Glucose 40 mmol/L
HCO_3^- 7 mEq/L	Cl^- 112 mEq/L	WBC 16		ß-hydroxybutyric acid 9 mmol/L (normal < 0.31 mmol/L)
PO_2 100 mmHg	SCr: 170 µmol/L	Platelets 300		
SaO_2 0.96				

1. Using the Rules of Five, please determine this patient's acid-base disturbance.

Rule 1. pH <7.35, acidemia
Rule 2. HCO_3^- < 24 mEq/L, therefore metabolic acidosis
Rule 3. Anion Gap = 146-112-7 = 27 (positive); no need to correct for albumin because albumin is normal.
Rule 4. Compensation for primary disturbance: rule for metabolic acidosis is for each 1 mEq/L decrease in HCO_3^- below 24 mEq/L, PCO_2 should decrease 1 mmHg. HCO_3^- is 17 mEq/L below 24, therefore PCO_2 should drop by 17 mmHg from normal (40-17=23 mmHg) However, PCO_2 is only down by 13 mmHg from normal (27 mmHg), therefore it is "high" for this primary disturbance. Therefore, there exists a secondary respiratory acidosis.
Rule 5. Delta anion gap = 27-11=16. Therefore, HCO_3^- should have dropped by at least 16 mEq/L from 24 mEq/L, which would be 8 mEq/L. Current HCO_3^- is 7 mEq/L, therefore this is no metabolic alkalosis.
Acid-Base Disturbance: This is a primary positive anion gap metabolic acidosis with a secondary respiratory acidosis.

2. What are the potential causes of this patient's acid-base disturbance?

With regards to the positive anion gap metabolic acidosis, this is a classic case of diabetic ketoacidosis. Urine is positive for glucose and ketones (not normal). Serum beta-hydroxybutyric acid is very high (9 mmol/L). This acid is the predominant keto-acid produced. Also, her history and blood sugar is suggestive of DKA. The respiratory acidosis is a consequence of respiratory muscle fatigue that would be expected if an otherwise healthy young diabetic were trying to "comensate" for the metabolic acidosis via increasing respiratory rate and/or tidal volume per breath over a period of time.

3. Very briefly devise a treatment-plan for this patient's acid-base disturbance.

Insulin 0.15 u/kg x1 IV, then start insulin infusion at 0.1 u/kg/hr and titrate according to blood sugars. Also, this patient will be administered copious amounts of IV NaCL. She may also require KCl prn. Sodium bicarbonate therapy is extremely controversial and currently reserved only for the most refractory/life-threatening acidemias associated with DKA.

CASE 4a.
See the above case. However, her labs are as follows:

ABG	Serum Electrolytes	CBC	Urinalysis	Other Blood Work
pH 7.09	Na^+ 146 mEq/L	Hgb 147	+ve glucose	Albumin 42 g/L
PCO_2 27 mmHg	K^+ 5.2 mEq/L	Hct 0.490	moderate ketones	Glucose 40 mmol/L
HCO_3^- 11 mEq/L	**Cl^- 106 mEq/L**	WBC 16		β-hydroxybutyric acid 9 mmol/L (normal < 0.31 mmol/L)
PO_2 100 mmHg	SCr: 170 µmol/L	Platelets 300		
SaO_2 0.96				

1. Calculate the delta anion gap. Is there a metabolic alkalosis present?
Anion gap = 29; delta anion gap = 29-11=18. Therefore, HCO3- should have dropped at least 18 mEq/L from 24 mEq/L which would be 6 mEq/L. However, current HCO3- is 11 mEq/L. Therefore, there must be a concomitant metabolic alkalosis present. The metabolic alkalosis is most likely due to vomiting.

CASE 5.
ID: 34 year-old male
Ht: 6' Wt: 90 kg
HPI: You have been asked to see a patient in order to optimize pharmacotherapeutic management of acute post-surgical pain. This man fractured his pelvis while water skiing (open book pelvic fracture). It was surgically repaired 48 hour ago. On your way to his room, "CODE-BLUE" is called to his room. You rush into the room and see the respiratory therapist placing a face mask with 100% oxygen on him. He is not rousable and his respirations look very slow and shallow. The code team is informed that the RT had sent an ABG 5 minutes prior to calling the CODE-BLUE.
PMHx: Nil
MPTA: Nil
Allergies: NKDA
Current Meds: Hydromorphone 2 mg po Q4H
Hydromorphone 0.4 mg IV Q30MIN prn
A quick survey of the patient reveals:
Vitals: Temp 37 (axilla); BP 110/60 mmHg; HR 70; RR 3/min
CVS: Pulses palpable
RESP: Very shallow, slow breaths
Skin: Cool peripheries

ABG	Serum Electrolytes	CBC	Other Blood Work
pH 7.21	Pending	Pending	Albumin 42 g/L
PCO_2 70 mmHg			
HCO_3^- 27 mEq/L			
PO_2 64 mmHg			
SaO_2 0.84			

CASE 5.
1. Using the Rules of Five, please determine this patient's acid-base disturbance.
Rule 1. pH <7.35, acidemia
Rule 2. PCO_2 > 40 mmHg, therefore respiratory acidosis
Rule 3. Anion Gap = not applicable. Serum electrolytes are pending.
Rule 4. Compensation for primary disturbance: rule for respiratory acidosis (acute) is for each 10 mmHg increase in PCO_2 above 40, HCO_3 should increase 1 mEq/L. PCO2 is 30 mmHG above normal, therefore HCO_3 should increase by 3 mEq/L from normal (24+3=27 mEq/L).√
Rule 5. Delta anion gap not applicable.
Acid-Base Disturbance: This is a primary respiratory acidosis. It could also be stated as: A simple respiratory acidosis.

2. What are the potential causes of this patient's acid-base disturbance?

The most likely cause of the respiratory acidosis is opioid toxicity. Opioids depress the respiratory centre in the brain, which in cases of toxicity, can result in apnea and hypoventilation, leading to a respiratory acidosis. Upon further history, the RN realized that a dosage error occurred with the hydormorphone.

3. What are some pharmacotherapeutic options?

Naloxone is the antidote of choice for presumed or confirmed opioid toxicity.

CASE 6.
ID: 52 year-old male
Ht: 5'11" Wt: 75 kg

HPI: Patient was involved in a skiing accident in Whistler 10 years ago. The injuries that he sustained included a spinal cord injury that left him paraplegic. His wife has noticed that he has become confused over the last 48 hours. He chronically has a silastic urinary catheter in place and she has noticed that his urine has become increasingly cloudy over the past 48 hours. Because he had become unresponsive, his wife called EHS and he was brought to the emergency department where you are now assessing him for drug-related problems.

PMHx: Recurrent urinary tract infections (E. coli susceptible to amoxicillin)
Chronic pain
Hypercholesterolemia
MPTA: Amoxicillin 500 mg po TID x 7 days (last filled 4 months ago)
Baclofen 10 mg po TID
Gabapentin 600 mg po TID
Acetaminophen 650 mg po QID prn
Diazepam 5 mg po TID prn
Allergies: NKDA
Physical Exam:
Vitals: Temp 39 (axilla); BP 85/45 mmHg; HR 125 (regular); RR 25/min
CVS: JVP (neck veins) flat; bounding peripheral pulses; warm to the touch; RN is now hanging norepinephrine
RESP: Clear; no signs of respiratory fatigue; receiving O_2 2 lpm via nasal prongs
GU: Cloudy urine; catheter in-situ; minimal urine output
Laboratory:

ABG	Serum Electrolytes	Urinalysis	Other Blood Work
pH 7.14	Na^+ 140 mEq/L	+ve WBCs +ve protein +ve nitrites	Albumin 40 g/L
PCO_2 24 mmHg	K^+ 3.7 mEq/L		Lactate - pending
HCO_3^- 8 mEq/L	Cl^- 105 mEq/L		
PO_2 90 mmHg	SCr: 100 µmol/L Urea 8 mmol/L		
SaO_2 0.96			

1. Using the Rules of Five, please determine this patient's acid-base disturbance.

Rule1. Acidemia
Rule 2. Metabolic acidosis
Rule 3. Anion gap = 140-105-8=27 (POSITIVE)
Rule 4. Compensation: 1:1 – PCO_2 should be down by 16 (24 mmHg) √, therefore no secondary disturbance
Rule 5. Delta Anion Gap = 27-11=16; therefore HCO_3 should be down at least 16 from normal (8) √

This is a primary positive anion gap metabolic acidosis.

2. What are the potential causes of this patient's acid-base disturbance?

MUDPILEINGS
Most likely cause is a lactic acidosis secondary to septic shock. Lactate is pending, however, it will most likely be elevated because of hypotension related to sepsis.

3. Devise a brief treatment-plan for this patient's acid-base disturbance.

Treat the underlying cause (Septic shock secondary to urinary tract infection):

Antibiotics
Fluids
Vasopressors +/- inotropes
? Corticosteroids
? screen for Activated Protein C
Consider $NaHCO_3$ to bring HCO_3 above 10 mEq/L; for dosing guidelines, refer to handout.