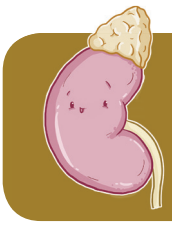

NOTES
ACID-BASE PHYSIOLOGY

ACID-BASE MAP & COMPENSATORY MECHANISMS

osms.it/acid-base_map_and_ compensatory_mechanisms

ACID-BASE MAP

- Main physiologic pH factors
  - HCO_3^-, CO_2
- Acid-base map
  - HCO_3^- concentration (x-axis)/CO_2 partial pressure (y-axis) diagram
- Henderson–Hasselbalch equation
  - $pH = 6.1 + \log([HCO_3^-]/0.03PCO_2)$
  - P_{CO2} is partial pressure of CO_2
- Diagonal lines
  - Drawn where each point on graph has same pH (isohydric lines)
- Drawing lines for pH = 7.35, pH = 7.45
  - Comprises area where all HCO_3^-, CO_2 combinations correspond to "normal" pH

pH out of normal range

- One of two ways
  - *Acidosis*: pH ↓ 7.35, enters top-left portion of map
  - *Alkalosis*: pH ↑ 7.45, enters bottom-right portion of map
- One of two reasons
  - *Respiratory*: P_{CO2} too ↑/↓
  - *Metabolic*: $[HCO_3^-]$ too ↑/↓

COMPENSATORY MECHANISMS

- Simple acid-base disorder
  - Single problem changing pH
- Mixed acid-base disorder
  - Multiple problems compounding/ cancelling out

Multiple compensatory mechanisms

- Respiratory acidosis
  - Kidneys retain more HCO_3^-
- Respiratory alkalosis
  - Kidneys excrete more HCO_3^-
- Metabolic acidosis
  - Lungs blow off CO_2 (deeper, more frequent breaths)
- Metabolic alkalosis
  - Lungs retain CO_2 (shallower, less frequent breaths)

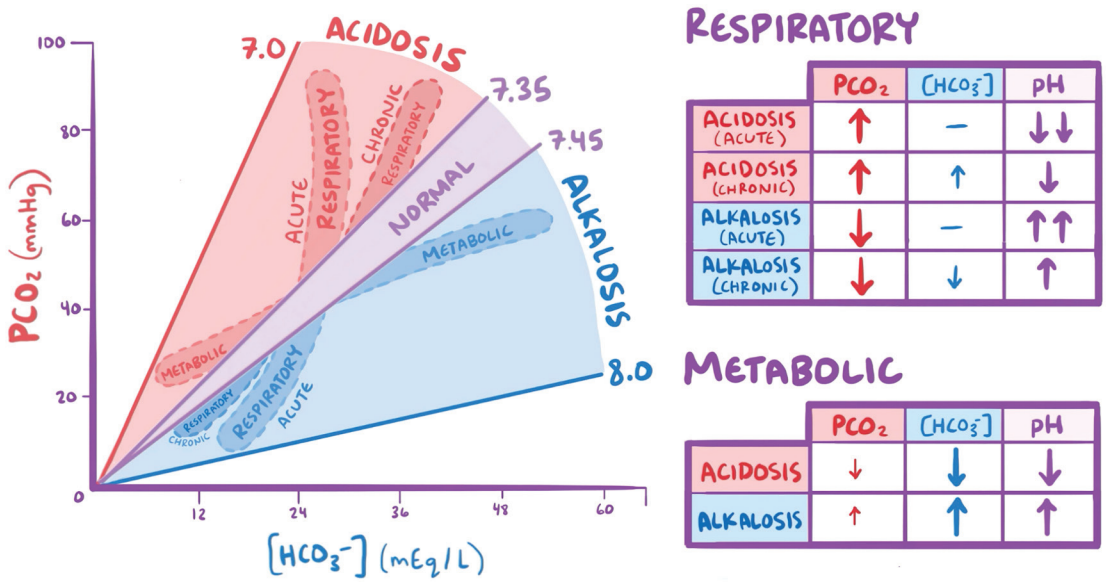

Figure 8.1 An acid-base map shows the relationship between pH, bicarbonate concentration, and partial pressure of carbon dioxide in respiratory and metabolic acidosis or alkalosis, and how these values are adjusted when there is renal or respiratory compensation. The accompanying tables depict the changes in PCO_2, $[HCO_3^-]$, and pH associated with respiratory/metabolic acidosis/alkalosis.

BUFFERING & HENDERSON-HASSELBALCH EQUATION

osms.it/buffering_&_henderson-hasselbalch_equation

BUFFERING

- *Buffers*: pH change-resisting solutions
- Can comprise
  - *Acidic buffer*: weak acid, conjugate base
  - *Basic buffer*: weak base, conjugate acid
- Weak acids, bases do not dissociate fully → equilibrium formation (e.g. $HA \rightleftarrows H^+ + A$ or $B + H_2O \rightleftarrows BH^+ + OH^-$)
  - *Le Chatelier's principle*: equilibriums move forward/backward, balance products/reactants' gain/loss

Resisting pH change

- Acidic, basic buffers resist all pH changes
- Strong base added to acidic buffer
  - OH^- ions react with H^+ ions → ↑ pH
  - H^+ ion loss shifts acid's equilibrium → more H^+ ions created, resists pH change
- Strong acid added to acidic buffer
  - H^+ ions would ↓ pH
  - Shifts acid equilibrium in opposite direction → conjugate base reacts with H^+ ions → resists pH change
- Strong acid added to basic buffer
  - H^+ ions would ↓ pH, also reacts with excess OH^- ions
  - OH^- loss ions shifts base's equilibrium → ↑ OH ion creation → resists pH change
- Strong base added to basic buffer
  - OH^- ions would react with H^+ ions to ↑ pH
  - Shifts base's equilibrium in opposite direction → conjugate acid reacting with OH^- ions → resists pH change

HENDERSON-HASSELBALCH EQUATION

- Henderson–Hasselbalch equation determines buffer's pH
  - $pH = pK + \log([A^-]/[HA])$
- This is derived
  - *Weak acid equilibrium*: equilibrium constant K → $K = [H^+][A^-]/[HA]$
  - Solving for H^+ → $[H^+] = K([HA]/[A^-])$
  - Negative log of both sides → $pH = pK + \log([A^-]/[HA])$
- Note
  - If $[A^-] = [HA]$, then $pH = pK$

PHYSIOLOGIC pH & BUFFERS

osms.it/physiologic-pH-and-buffers

PHYSIOLOGIC pH

- Measures balance between acids, bases in body
- *pH*: $-\log[H^+]$
  - *$[H^+]$*: hydrogen ion concentration
- *Ideal*: $[H^+] = 40 \times 10^{-9}$ Eq/L = 40 nEq/L → pH = 7.4 (slightly alkaline)
  - *Acidemia*: pH < 7.4
  - *Alkalemia*: pH > 7.4
- ↑ $[H^+]$ → ↓ pH (negative sign in equation)
- pH, $[H^+]$ has logarithmic (not linear) relationship

PHYSIOLOGIC BUFFERS

- Physiologic buffers occur naturally in body
  - Maintains stable pH between 7.35–7.45

Bicarbonate buffer system

- Extracellular, most important
- *Acidic buffer*: carbonic acid (H_2CO_3)
- *Conjugate base:* bicarbonate ion (HCO_3^-)
- Carbonic acid can be formed from H_2O, CO_2 (carbonic anhydrase catalyzes reaction)
- Equilibrium reaction
  - $H2O + CO_2 \rightleftarrows H_2CO_3 \rightleftarrows H^+ + HCO_3^-$
- Excess
  - CO_2 blown off by lungs
  - HCO_3^- eliminated by kidneys

Phosphate buffer system (extracellular)

- *Acidic buffer*: dihydrogen phosphate ($H_2PO_4^-$)
- *Conjugate base*: monohydrogen phosphate (HPO_4^{2-})
- Equilibrium reaction
  - $H_2PO_4^- \rightleftarrows H^+ + HPO_4^{2-}$

Protein buffer system (extracellular)

- Protein amino acids may have exposed carboxyl (-COOH), amine (NH_2) groups
- Results in separate acidic ($-COOH \rightleftarrows -COO^- + H^+$), basic ($-NH_2 + H^+ \rightleftarrows -NH_3^+$) buffers

Intracellular buffer systems

- *Hemoglobin*: buffer in red blood cells (selectively binds H^+ ions)
- Organic phosphates (e.g. ATP) can buffer similarly

PLASMA ANION GAP

osms.it/plasma-anion-gap

PLASMA ANION GAP

- Cations, anions coexist within plasma
  - To keep plasma electrically neutral sum of cation charges must equal sum of anion charges
- Not all cation, anion concentrations can be measured
  - Often gap ("plasma anion gap") between measured cation charges (mainly Na^+), smaller measured anion charges sum (mainly Cl^-, HCO_3^-)
- *Plasma anion gap range*: 3–11 mEq/L
  - High gap → high unmeasured anion number
  - Low gap → low unmeasured anion number
- Unmeasured anions include anion component of several organic acids, negatively charged plasma proteins (e.g. albumin)

DIAGNOSTIC TOOL

- Plasma anion gap serves as useful diagnostic tool

Metabolic acidosis

- Organic acids' H^+ ions convert HCO_3^- into H_2CO_3
  - Organic anions aren't measured → plasma anion gap ↑
  - Organic acids include lactic acid, ketoacids, oxalic acid, formic acid, hippuric acid
- Some cases (e.g. diarrhea/renal tubular acidosis)
  - Kidneys reabsorb more Cl– ions → plasma anion gap remains normal (hyperchloremic metabolic acidosis)

High gap may suggest

- Unmeasured anion buildup (e.g. hyperphosphatemia, hyperalbuminemia)
- Metabolic alkalosis (high pH triggers albumin to release H^+ ions → negative charge ↑ on unmeasured albumin molecules)

Low gap may suggest

- Unmeasured anion ↓ (e.g. hypoalbuminemia)
- Unmeasured cation ↑ (rarely)
  - E.g. hyperkalemia, hypercalcemia, hypermagnesemia

THE ROLE OF THE KIDNEY IN ACID-BASE BALANCE

osms.it/kidney_and_acid-base_balance

KIDNEYS' FUNCTION

- Kidneys maintain acid-base balance in two ways
  - *HCO_3^- reabsorption*: urine into blood
  - *H^+ secretion*: blood into urine
- Kidneys consist of nephrons
  - Each has glomerulus (capillaries clump)
- During filtration, plasma leaves glomerulus entering renal tubule (consists of proximal convoluted tubule, loop of Henle, distal convoluted tubule)

- Tubules lined with brush border cells (apical surface facing tubular lumen, basolateral surface facing peritubular capillaries)

HCO_3^- reabsorption

- Primarily in proximal convoluted tubule
  - Na+ ions exchanged for H^+ ions through apical surface → bind with HCO_3^- → form H_2CO_3
  - Carbonic anhydrase type 4 splits H_2CO_3 into H_2O, CO_2
  - H_2O, CO_2 diffuse across membrane
  - Carbonic anhydrase type 2 recombines them into H_2CO_3
  - H_2CO_3 dissolve into H^+,HCO_3^-
  - Sodium/chloride bicarbonate cotransporters on basolateral surface snatch up HCO_3^-, nearby sodium/chloride ion, moving both into blood

H^+ secretion

- Primarily in proximal convoluted tubule
  - *Sodium-hydrogen countertransport*: H^+ ions exchanged for Na^+ ions through apical surface
  - Another mechanism in distal convoluted tubule, collecting ducts involving alpha-intercalated cells
  - Chemical buffers (ammonia, phosphate) prevent urine pH from dropping too low in tubules (< 4.5)

METABOLIC ACIDOSIS

osms.it/metabolic-acidosis

METABOLIC ACIDOSIS

- HCO_3^- ion reduction → blood pH ↓ to < 7.35

TYPES

- Distinguished by high/normal anion gap
  - Measured cation concentration
  - E.g. Na^+ ions, minus measured anion concentration (e.g. Cl^-, HCO_3^- ions)

High anion gap

- H^+ ions from organic acids convert HCO_3^- to H_2CO_3
  - ↓ HCO_3^- ion concentration (measured in anion gap), ↑ organic anion concentration (not measured)
  - *Naturally-occurring organic acids*: e.g. lactic acid production (lactic acidosis), ketoacid production (diabetic ketoacidosis), excessive uric, sulfur-containing acid retention (chronic renal failure)
  - *Ingestible organic acids*: e.g. oxalic acid (antifreeze), formic acid (methanol), hippuric acid (toluene)

Normal anion gap

- HCO_3^- lost in various ways, Cl^- ↑ prevents anion gap change (hyperchloremic metabolic acidosis)
- Possible causes
  - Diarrhea, renal tubular acidosis

REGULATORY MECHANISMS

- Body has several regulatory mechanisms to reverse ↓ pH
  - H^+ ions moved from blood into cells, exchanged for K^+ ions (may cause hyperkalemia); if organic anions present, can enter cells with H^+ ions → K^+ ions are not released
  - Chemoreceptors fire more in low pH → ↑ respiratory rate, breath depth → ↑ ventilation, CO_2 movement out of body
  - H^+ ions excreted by kidneys → HCO_3^- reabsorbed (with normal renal function)

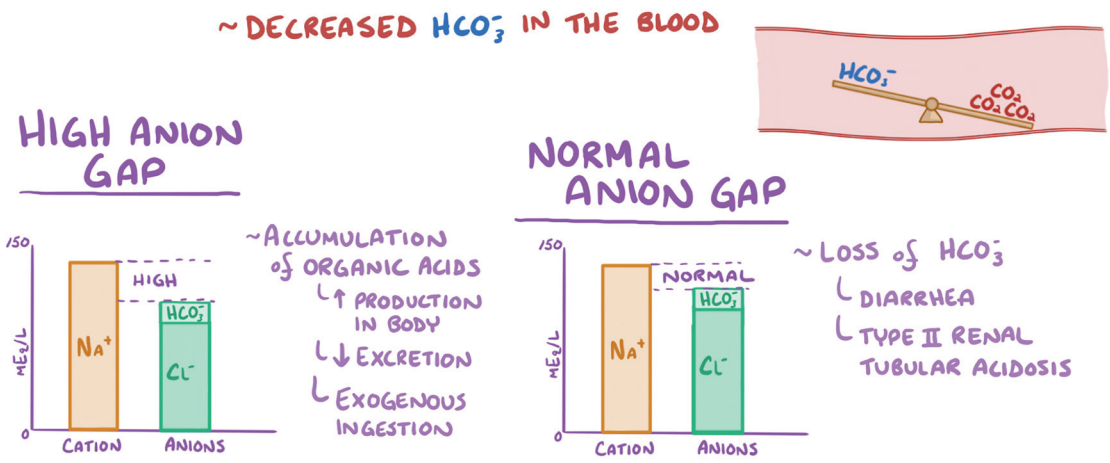

Figure 8.2 Illustration depicting the two kinds of metabolic acidosis: high anion gap (where H^+ from organic acids converts HCO_3^- to H_2CO_3), and normal anion gap (where a Cl^- increase maintains the normal anion gap).

METABOLIC ALKALOSIS

osms.it/metabolic-alkalosis

METABOLIC ALKALOSIS

- HCO_3^- ion gain → blood pH ↑ > 7.45

CAUSES

- Associated with direct HCO_3^- ion gain/ loss of H^+ ion loss (thus → HCO_3^- ion gain), usually both
- Hypokalemia
  - Metabolic alkalosis cause
  - May also be result of other root causes

Excessive H^+ ion loss causes

- Vomiting (gastric secretions acidic)
  - Also causes HCO_3^- ion buildup in pancreas (would normally neutralize gastric secretions)
- Abnormal renal function
  - E.g. adrenal tumors secrete aldosterone → distal convoluted tubule dumps H^+ ions, reabsorbs HCO_3^- ions

Excessive HCO_3^- ion gain causes

- ↑ kidney reabsorption
  - Volume contraction with loop/thiazide diuretics/severe dehydration cases (contraction alkalosis)
- Hypokalemia
  - Diarrhea/diuretic use, triggering renin-angiotensin-aldosterone mechanism → distal convoluted tubule dumps H^+ ions, reabsorbs HCO_3^- ions
- HCO_3^- ion ingestion
  - E.g. excessive antacid use ($NaHCO_3$)

REGULATORY MECHANISMS

- Body has regulatory mechanisms to reverse ↑ pH
  - K^+ ions move from blood into cells → exchanged for H^+ ions (may contribute to hypokalemia)
  - Chemoreceptors fire less in high pH → ↓ respiratory rate, breathing depth → ↓ ventilation, CO_2 retention
  - HCO_3^- ions excreted by kidneys → H^+ reabsorbed (normal renal function)

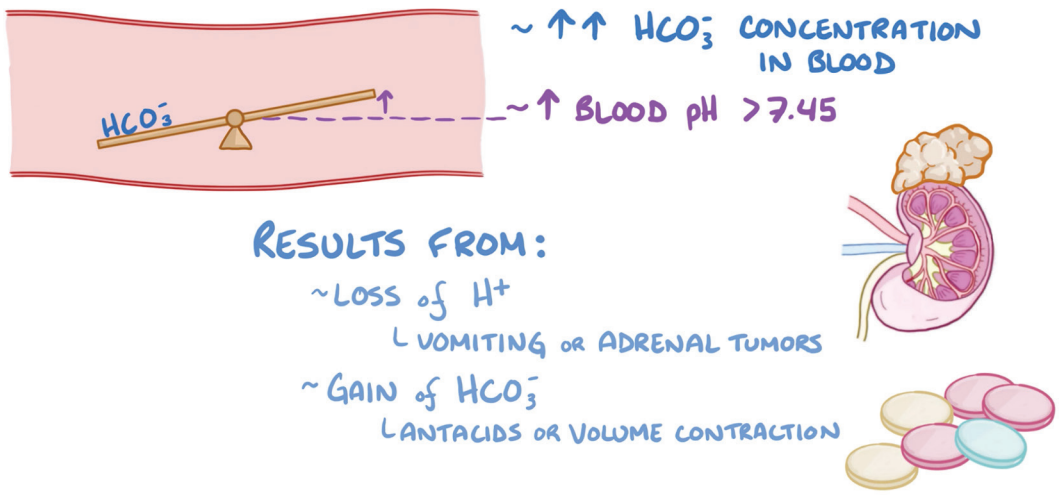

Figure 8.3 Illustration summarizing the definition and causes of metabolic alkalosis.

RESPIRATORY ACIDOSIS

osms.it/respiratory-acidosis

RESPIRATORY ACIDOSIS

- CO_2 gain → blood pH ↓ < 7.35

CAUSES

- Ventilation ↓ (frequency, breath depth) for variety of reasons → lungs blow off too little CO_2
  - Stroke/medication overdose/etc. → respiratory-center abnormality in brainstem
  - Obesity, trauma, neuromuscular disorders (myasthenia gravis), etc. → respiratory muscle-contraction failure
  - Airway obstruction
  - Alveoli damage (chronic obstructive pulmonary disease); alveoli fluid buildup (pneumonia); fluid buildup between alveoli, capillary walls (pulmonary edema) → impaired gas exchange between alveoli, capillary

REGULATORY MECHANISMS

- Body has several regulatory mechanisms to reverse pH ↓
  - Low pH → chemoreceptors fire more → attempted ↑ in respiratory rate, breathing depth → ↑ ventilation
  - H^+ ions bind to basic protein molecules (mainly exposed hemoglobin -NH_2 groups), although in small amounts
  - H^+ ions excreted by kidneys, HCO_3^- reabsorbed

RESPIRATORY ALKALOSIS

osms.it/respiratory-alkalosis

RESPIRATORY ALKALOSIS

- CO_2 loss → blood pH ↑ > 7.45

CAUSES

- Ventilation ↑ (frequency, breath depth) for variety of reasons → lungs blowing off too much CO_2
  - Respiratory-center abnormality in brainstem
  - Pneumonia, pulmonary embolism, etc. → low oxygen levels (hypoxia)
  - Anxiety, panic attacks, sepsis, salicylates overdose
  - Incorrectly-set ventilator → medical intervention

REGULATORY MECHANISMS

- Body has several regulatory mechanisms to reverse pH ↑
  - High pH → chemoreceptors fire less → attempted ↓ in respiratory rate, breathing depth → ↓ ventilation
  - H^+ ions released from acidic protein molecules (mainly exposed hemoglobin -COOH groups), although in small amounts
  - HCO_3^- ions excreted by kidneys, H^+ are reabsorbed