Week 4 lectures (Physiology 9,10 and 11)

Physiology 9

Acid – Base Balance

-Acid – Base Balance (**pH HOMEOSTASIS**)

-To avoid disturbances in [H^+], and to maintain its homeostasis, the amount generated / taken in MUST EQUAL the amount secreted.

-Most enzymes function optimally at pH ~ 7.4 (except gastric enzymes).

Bronsted-Lowry			
ACIDS		BASES	
Molecules containing hydrogen atoms that can (DONATE) H^+ into solution		ions or molecules that can ACCEPT H^+	
Strong	Weak	Strong	Weak
all their H^+ is dissociated completely in H_2O.	dissociate partially in H_2O and are efficient at preventing pH changes.	dissociate easily in H_2O and quickly bind H^+.	accept H^+ more slowly
			Proteins in body function as weak bases as some constituent AMINO ACIDS have net negative charge and attract H^+ (e.g. HAEMOGLOBIN).

- water is amphoteric compound:

*as a base, it accepts H^+ and forms a hydronium ion (H_3O^+).

*as an acid, it loses a proton, and forms a hydroxide ion (OH).

- The **pH** of a solution is a measure of the acidity of the solution. It is defined as:

$$\mathrm{pH} = -\log_{10}([\mathrm{H_3O^+}])$$

- **pH** does not measure the strength of an acid, but the acidity of a given solution (Conc. Of H+)

$$\mathrm{pH} = \log\frac{1}{[\mathrm{H^+}]} = -\log[\mathrm{H^+}]$$

Normal pH = -log [0.00000004] M = 7.4

- pH **INVERSELY** related to [H^+].

- Normal **BLOOD** pH range for adults = **7.35 – 7.45** maintained by:

chemical buffer systems, kidneys and lungs.

- DEATH likely if pH ↑7.8 or ↓6.8.

Sources of H^+ The body generally **PRODUCES** more acids than bases	
Cellular aerobic metabolism produces **15,000 mmol** CO_2/day.	**DIET** – incomplete metabolism of carbohydrates (lactate) lipids (ketones) and proteins (H_2SO_4, H_3PO_4)
$CO_2 + H_20 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$ (volatile acid)	**fixed (non-volatile) acids** ~50 -100 mEq per day
Normally all volatile acid **excreted by the lungs**	

How is $[H^+]$ Controlled? Three systems involved		
BUFFERS 1st defence	**LUNGS 2nd defence**	**KIDNEYS 3rd defence**
regulation of $[H^+]$	Excretion of CO_2 ($\downarrow H_2CO_3$) (removal of volatile acid)	Excretion of H^+ ($\uparrow HCO_3^-$) (fixed acids)
second – to – second (**fastest**)	in minutes - to - hours	Several hours to days. slowest, but most **POWERFUL**

- Relative concentrations of CO_2 and HCO_3 - in plasma / ECF determine pH (**HENDERSON-HASSELBALCH equation**), (show the relationship between pH, hydrogen ion conc. and the ratio of buffer membrane in a solution)

$$pH = pK + \log \frac{HCO_3^-}{(0.03 \times Pco_2)}$$

In health :

PK = 6.1

$[HCO_3^-]$ = 24 mmol/L

PCO_2 = 40 mm Hg

What happen to the pH using H-H ***IMPORTANT***	
In case if the HCO_3 in Plasma remains normal	**In case the Pco_2 remains normal**
If **Pco_2 increased**, the ratio of $[HCO_3]P/ 0.03\ Pco_2$ will decrease which lead to **acidosis**	**Increase bicarbonate** in plasma causes an increase in the ratio which leads to **alkalosis**
If **Pco_2 decrease**, the ratio will increase and pH will increase causing **alkalosis**	**Decrease** in bicarbonate in plasma causes a decrease in the ration which leads to **acidosis**

	pH	H^+	P_{CO_2}	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
Respiratory acidosis	↓	↑	↑↑	↑
Respiratory alkalosis	↑	↓	↓↓	↓
Metabolic acidosis	↓	↑	↓	↓↓
Metabolic alkalosis	↑	↓	↑	↑↑

The primary event is indicated by the double arrows (↑↑ or ↓↓). Note that respiratory acid-base disorders are initiated by an increase or decrease in P_{CO_2}, whereas metabolic disorders are initiated by an increase or decrease in HCO_3^-.

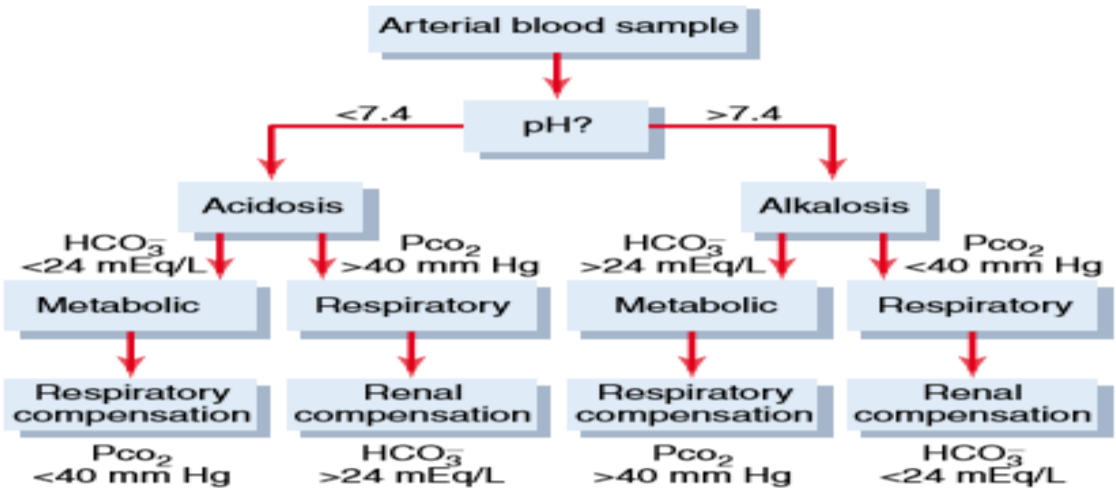


Figure 30-10 Analysis of simple acid-base disorders. If the compensatory responses are markedly different from those shown at the bottom of the figure, one should suspect a mixed acid-base disorder.

Physiology 10 (Buffering system)

BUFFERING SYSTEM: They do not eliminate H+from body, REVERSIBLY bind H+ until balance is reestablished.			
Bicarbonate buffer System	Phosphate Buffering System	Protein Buffers	Bone
Most important buffering system.	major intracellular buffer and important in renal tubular fluid	60 -70% of total chemical buffering of body fluids is located intracellularly	Probably involved in providing a degree of buffering (by ionic exchange) in most acid base disorders.
Works by acting as proton acceptor for carbonic acid	Main components are : HPO4 and H2PO4	Most important non bicarbonate buffering proteins are titratable groups on HAEMOGLOBIN	in Chronic metabolic acidosis

- Remember that all of these buffer systems work in tandem NOT in isolation.
- Buffers can only limit changes in pH, they cannot reverse them.
- Once arterial pH has deviated from normal value, can only be returned to normal by respiratory or renal compensation.

Renal regulation of Acid-Base Balance

Renal system
MOST EFFECTIVE regulator of pH but much **SLOWER** (*i.e.* max. activity after 5-6 days) than other processes.
Responsible for **ELIMINATING** the 80 -100 mEq of fixed **ACIDS** generated each day.
Normally, must also **PREVENT** renal **LOSS** of freely – filterable **HCO_3^-** in order to preserve this primary buffer system.
BOTH PROCESSES are dependent on both H^+ filtration / secretion into renal tubules and secretion / reabsorption of plasma $[HCO_3^-]$.
Kidneys also responsible for **COMPENSATORY CHANGES** in $[HCO_3^-]$ during respiratory acid-base disorders.

IF KIDNEYS FAIL, pH BALANCE WILL FAIL

- The kidneys complete or add up to the work of buffers and lungs, failure of the renal regulation will cause imbalances that disturb all other regulating systems.

Respiratory Regulation of Acid-Base Balance

Respiratory system
Pulmonary expiration of CO_2 normally **BALANCES** metabolic formation of CO_2.
Changes in alveolar ventilation can alter **plasma Pco_2** - ↑ ventilation, ↓Pco_2, ↑pH - ↓ ventilation, ↑ Pco_2, ↓ pH
Changes in $[H^+]$ also alters **ALVEOLAR VENTILATION.**
POWERFUL (1-2 x better than extracellular chemical buffers), but *cannot fully rectify* disturbances outside respiratory system, *i.e.* with fixed acids like lactic acid.
Acts relatively **RAPIDLY** to stop $[H^+]$ changing too much until renal buffering kicks in but **DOES NOT** eliminate H^+ (or HCO_3^-) from body.
Abnormalities of respiration can alter bodily $[H^+]$ resulting in; - **RESPIRATORY ACIDOSIS** Or - **RESPIRATORY ALKALOSIS.**

Physiology 11

Respiratory Acidosis

Associated with

- Respiratory failure (e.g. COPDs like emphysema).
- Inadequate alveolar ventilation
- Impaired gas diffusion (pulmonary edema)

- Characterized by ↑ P_{CO_2} *(hypercapnia)* and ↓ plasma pH.

Initial response is :

- Increased conversion of CO_2 to H^+ and HCO_3 **Increase** in ECF $[H^+]$ and plasma $[HCO_3^-]$.

- INCREASED
  - Renal **SECRETION** OF H^+
  - **ABSORPTION** OF HCO_3

  [COMPENSATORY MECHANISM]

Respiratory Acidosis
↓ plasma pH
↑ P_{CO_2}
↑ plasma $[HCO_3^-]$

Respiratory Alkalosis

- **Characterised by:**
  Reduced plasma P_{CO_2} *(hypocapnia)* and elevated pH
  ↓ P_{CO_2} & ↑ plasma pH

- **Causes:** (results from ↑ ventilation and ↓ P_{CO_2})
  increased gas exchange mainly due to
  HYPERVENTILATION *(Anxiety / fear/High altitude)*

Respiratory Alkalosis

↑ plasma pH
↓ P_{CO_2}
↓ plasma $[HCO_3^-]$

- **Reduction** in **P_{CO_2}** shifts buffering reaction to *the left*
  Decrease in ECF $[H^+]$ and plasma $[HCO_3^-]$

- COMPENSATORY MECHANISM :
  Decreased :
  *↓ Renal **Secretion** of H^+
  *↓ **Absorption** of HCO_3^- *(still an excess of HCO_3^- relative to H^+).*

Metabolic Acidosis

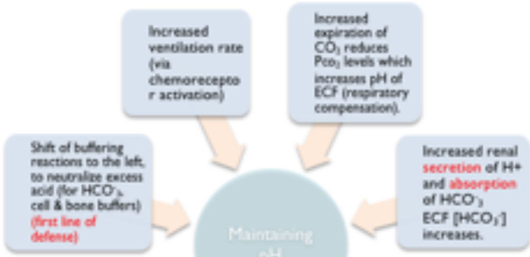
Characterized by :

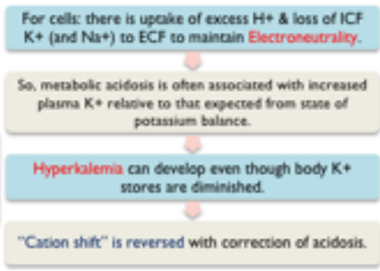
- Reduction in pH + ↑ in ECF H+ concentration
- DECREASED [HCO3-] (<25mM) and pH.

Metabolic acidosis is characterized by decreased HCO^-_3 (<25mM) and pH.

Caused by :

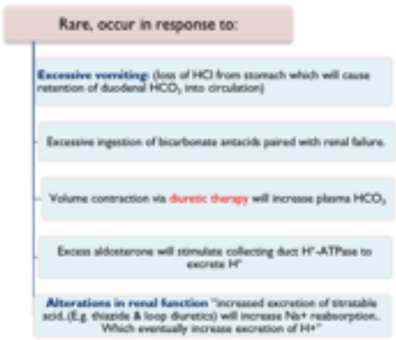
* Increased acid production
* Impaired acid excretion.





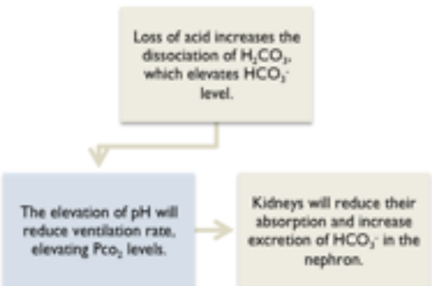
Metabolic Alkalosis

Characterized by elevated plasma HCO_3 & PH

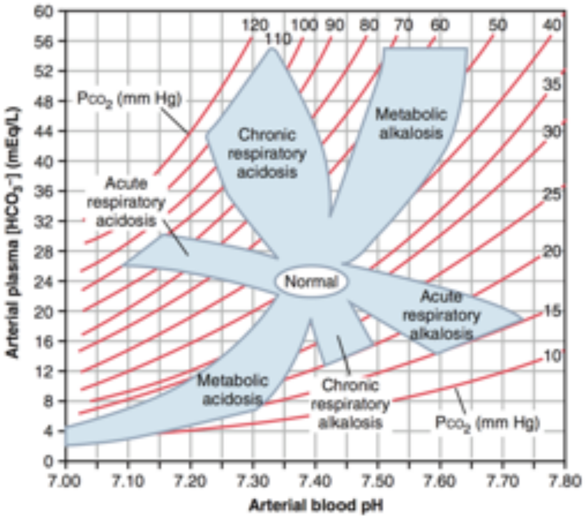


Major Causes of Metabolic Alkalosis

I. **Hydrogen loss**
   A. **Gastrointestinal loss**
      1. Removal of gastric secretions due to vomiting or nasogastric suction
      2. Antacids in advanced renal failure
   B. **Urinary loss**
      1. Loop or thiazide-type diuretics
      2. Primary mineralocorticoid excess (hyperaldosteronism)
      3. Posthypercapnic alkalosis
      4. Hypercalcemia and milk alkali syndrome
   C. **Movement of H^+ into the cells**
      1. Hypokalemia
II. **Administration of bicarbonate or an organic ion that can be metabolized to bicarbonate, such as citrate in blood transfusions**
III. **Contraction alkalosis**
   A. **Loop or thiazide-type diuretics in edematous patients**
   B. **Vomiting or nasogastric suction in achlorhydria**
   C. **Sweat losses in cystic fibrosis**



Davenport Diagram



In Metabolic Acidosis:

↓ plasma pH
↓ P_{CO_2}
↓ plasma $[HCO_3^-]$

In Metabolic Alkalosis:

↑ plasma pH
↑ plasma $[HCO_3^-]$
↑ P_{CO_2}

- pCo2 is low due to the respiratory compensation

- PCo2 is high due to respiratory compensation by accumulating it

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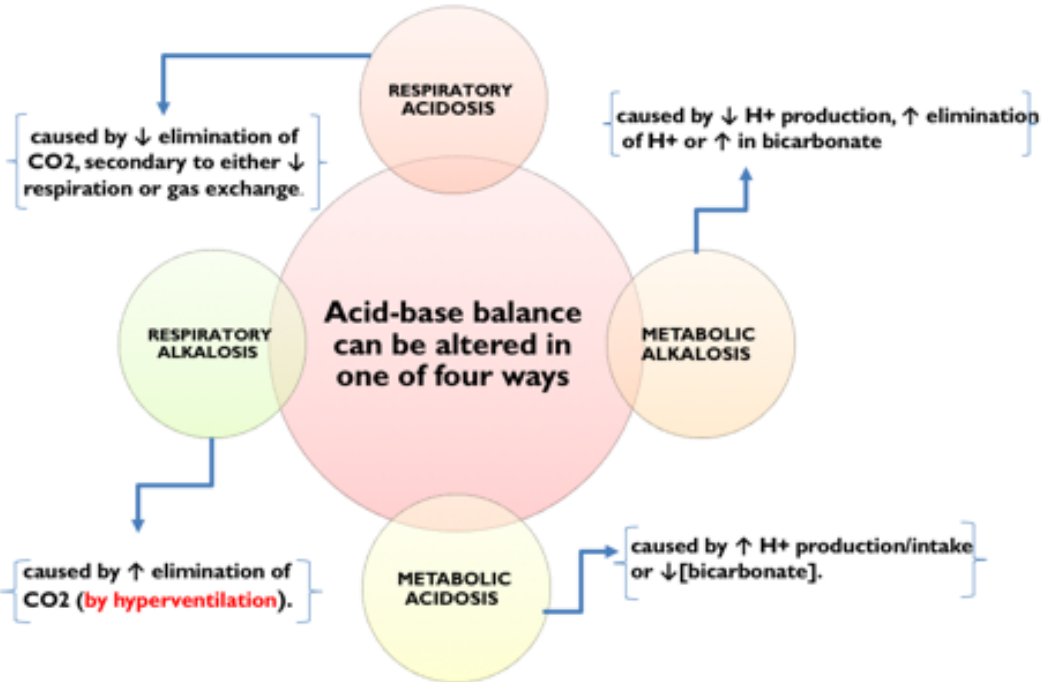
Acid-Base Imbalances *(Summary)*



Primary and compensatory changes in different acid-base disorders

Table 6.2 Primary and Compensatory Changes in Different Acid–Base Disorders

Disorder	Primary Change	Compensatory Response
Metabolic acidosis	Fall in plasma bicarbonate concentration	Reduction in PCO_2 averaging 1.2 mm Hg per 1-mEq/L reduction in plasma bicarbonate concentration
Metabolic alkalosis	Rise in plasma bicarbonate concentration	Elevation in PCO_2 averaging 0.6–0.7 mm Hg per 1-mEq/L rise in plasma bicarbonate concentration
Respiratory acidosis	Elevation in PCO_2	**Acute**: Rise in plasma bicarbonate concentration averaging 1 mEq/L per 10 mm Hg elevation in PCO_2 **Chronic**: Increase in plasma bicarbonate concentration averaging 3.5 mEq/L per 10 mm Hg rise in PCO_2
Respiratory alkalosis	Reduction in PCO_2	**Acute**: Fall in plasma bicarbonate concentration averaging 2 mEq/L per 10 mm Hg decline in PCO_2 **Chronic**: Fall in plasma bicarbonate concentration averaging 4 mEq/L per 10 mm Hg decline in PCO_2

Table 7-2 Summary of Acid-Base Disorders

Disorder	$CO_2 + H_2O$	↔	H^+	+	HCO_3^-	Respiratory Compensation	Renal Compensation or Correction
Metabolic Acidosis	↓		↑		**↓**	Hyperventilation	↑ HCO_3^- reabsorption (correction)
Metabolic Alkalosis	↑		↓		**↑**	Hypoventilation	↑ HCO_3^- excretion (correction)
Respiratory Acidosis	**↑**		↑		↑	None	↑ HCO_3^- reabsorption (compensation)
Respiratory Alkalosis	**↓**		↓		↓	None	↓ HCO_3^- reabsorption (compensation)

Bold arrows indicate initial disturbance.

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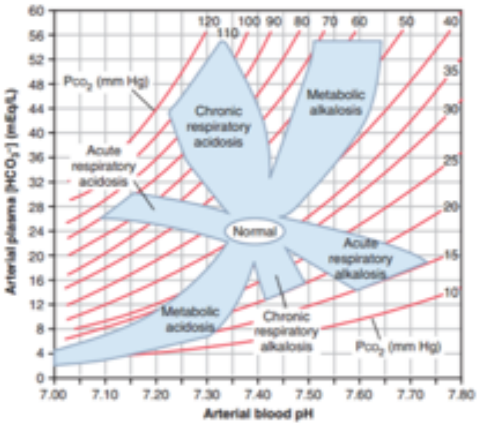
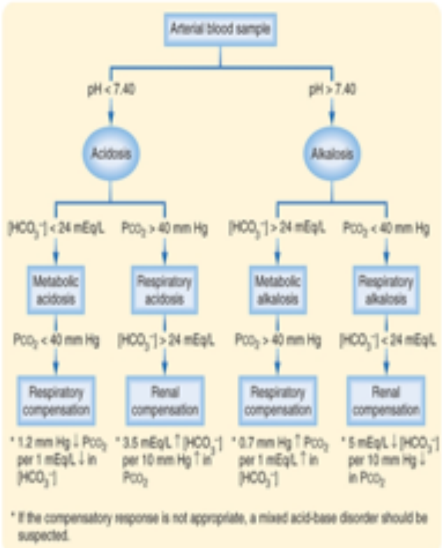
Analysis of Acid-Base Disorders

- Analysis aimed at identifying underlying cause of disorder such that appropriate therapy can be initiated.
- In addition to usual history taking and physical findings, sampling of arterial blood can yield valuable information.
- Analysis of blood sample data is straightforward if approached systematically either using the Davenport nomogram or flow diagram.





Acid-Base Disturbances

	pH	H^+	P_{CO_2}	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
Respiratory acidosis	↓	↑	↑↑	↑
Respiratory alkalosis	↑	↓	↓↓	↓
Metabolic acidosis	↓	↑	↓	↓↓
Metabolic alkalosis	↑	↓	↑	↑↑

How to Analyze an ABG

	PO2	pH	PCO2	HCO3
normal	80-100mmHg	7.35_7.45	35-45 mmHg	22-26 mmol/L
acidotic	-	<7.35	>45	< 22
alkalotic	-	>7.45	<35	> 26

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