(Renal Physiology 10 &11)

Acid-Base Balance 2 & 3

Buffer System & Acid Base Disorders

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Respiratory Regulation of Acid-Base Balance

- 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**.

Respiratory Regulation of Acid-Base Balance

- **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**.

Renal Regulation of Acid-Base

- **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 ***

Renal Regulation of Acid-Base

- Overall mechanism straightforward:

  - large [HCO_3^-] continuously filtered into tubules
  - large [H^+] secreted into tubules

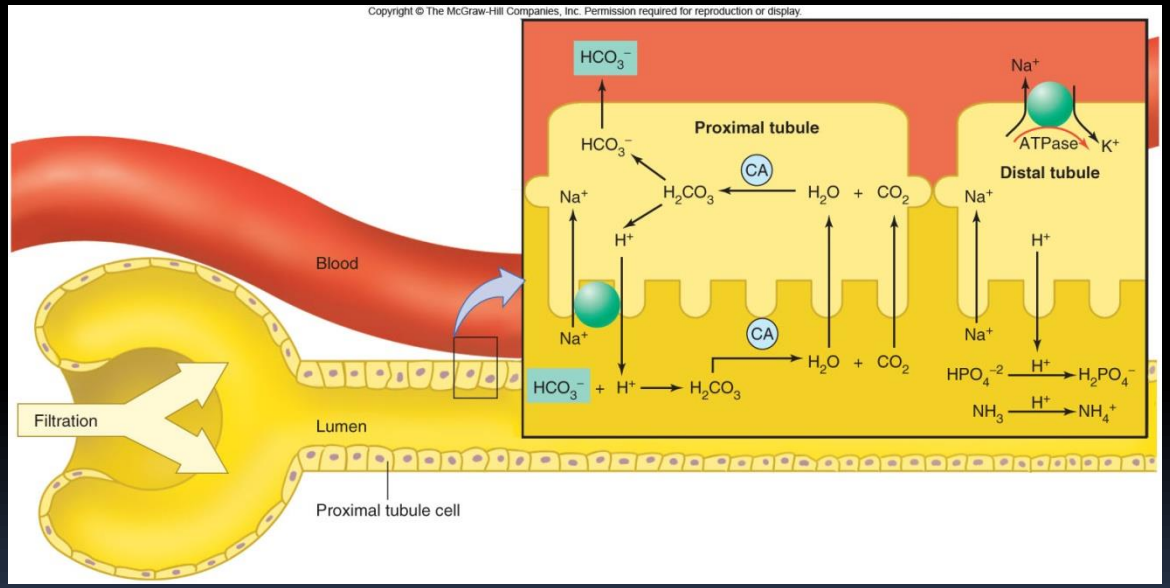
  $\Rightarrow$ if more H^+ secreted than HCO_3^- filtered
  = a net loss of ***acid*** $\Rightarrow$ ↑pH

  $\Rightarrow$ if more HCO_3^- filtered than H^+ secreted
  = a net loss of ***base*** $\Rightarrow$ ↓pH

H^+ / HCO_3^- Control by the Kidney

Renal H^+ Secretion

- H^+ enters filtrate by **FILTRATION** through glomeruli and **SECRETION** into tubules.
- Most H^+ secretion (80%) occurs across wall of PCT *via* Na^+/H^+ antiporter (& H^+ - ATPase in type A cells of DCT).
- This H^+ secretion enables HCO_3^- reabsorption.



- The primary factor regulating H^+ secretion is systemic acid-base balance

a) **ACIDOSIS** stimulates H^+ secretion

b) **ALKALOSIS** reduces H^+ secretion

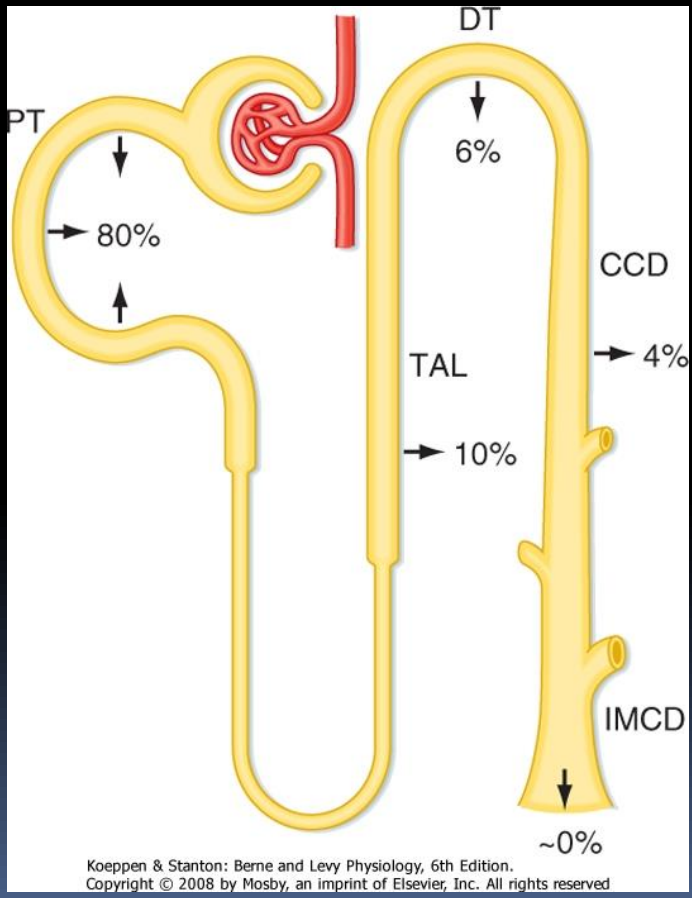
H^+ / HCO_3^- Control by the Kidney

Bicarbonate Handling

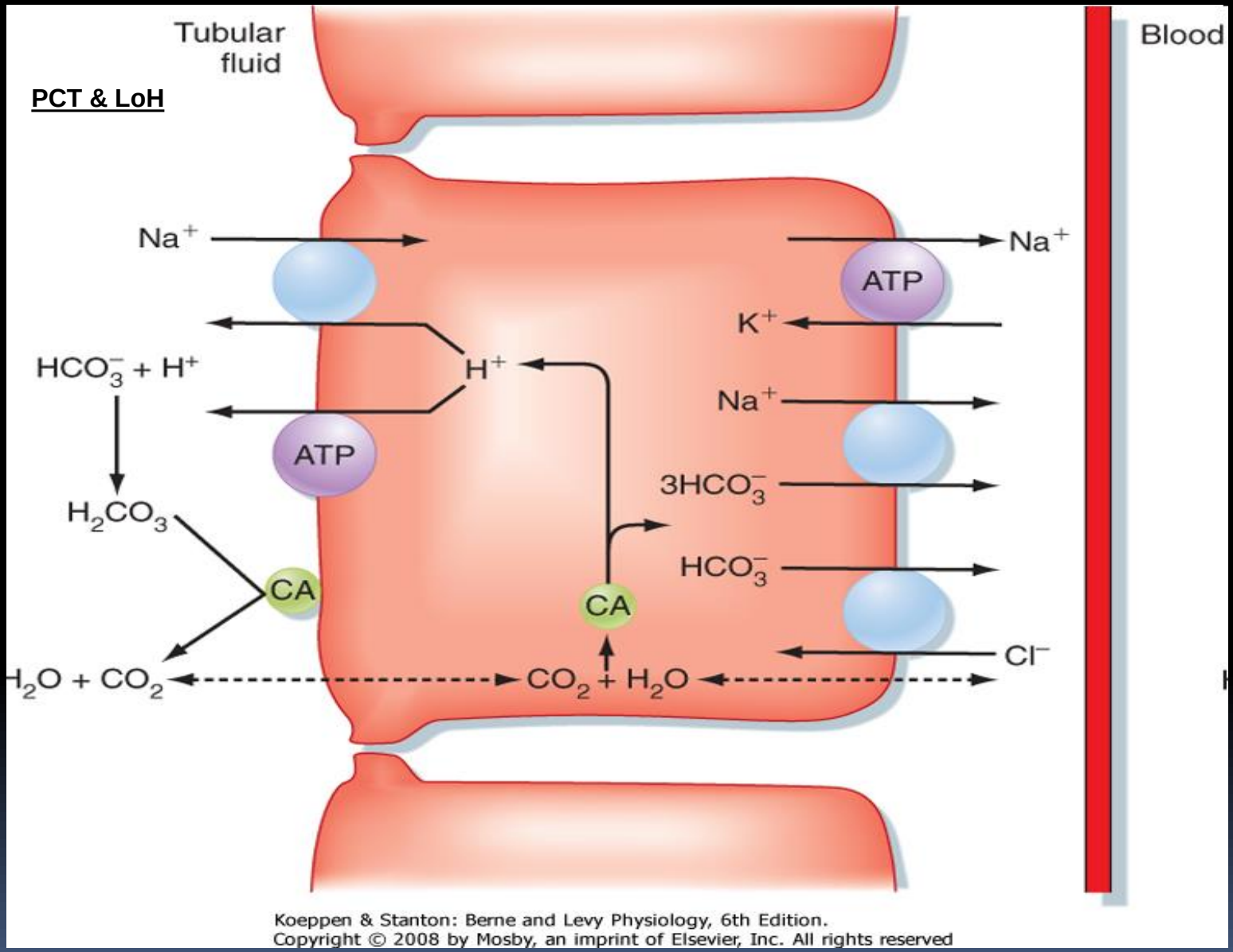
- HCO_3^- **FREELY FILTERABLE** at glomeruli (3 mM/min) and undergoes significant (> 99%) reabsorption in PCT, aLoH & cortical collecting ducts (CCDs).

- Mechanisms of HCO_3^- reabsorption at PCT (& aLoH) and CCD ***are similar but not identical***

- Renal HCO_3^- reabsorption is an **ACTIVE** process - **BUT** dependent on tubular secretion of H^+, **NO** ***apical*** transporter or pump for HCO_3^-.



PCT & LoH



Koeppen & Stanton: Berne and Levy Physiology, 6th Edition.

Disturbances of Acid-Base Balance

- Acid-base disturbances may be either RESPIRATORY or METABOLIC.

- pH problems due to a respiratory disorder result in **RESPIRATORY** acidosis or alkalosis.
  - pH problems arising from acids or bases of a non-CO_2 origin result in **METABOLIC** acidosis or alkalosis.

Respiratory Acidosis

- **Respiratory Acidosis**
  - Associated with **RESPIRATORY FAILURE** (*e.g.* COPDs like emphysema).
    - Inadequate alveolar ventilation
    - Impaired gas diffusion (*e.g.* pulmonary oedema)
  - **Characterised by ↑ Pco_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^-].

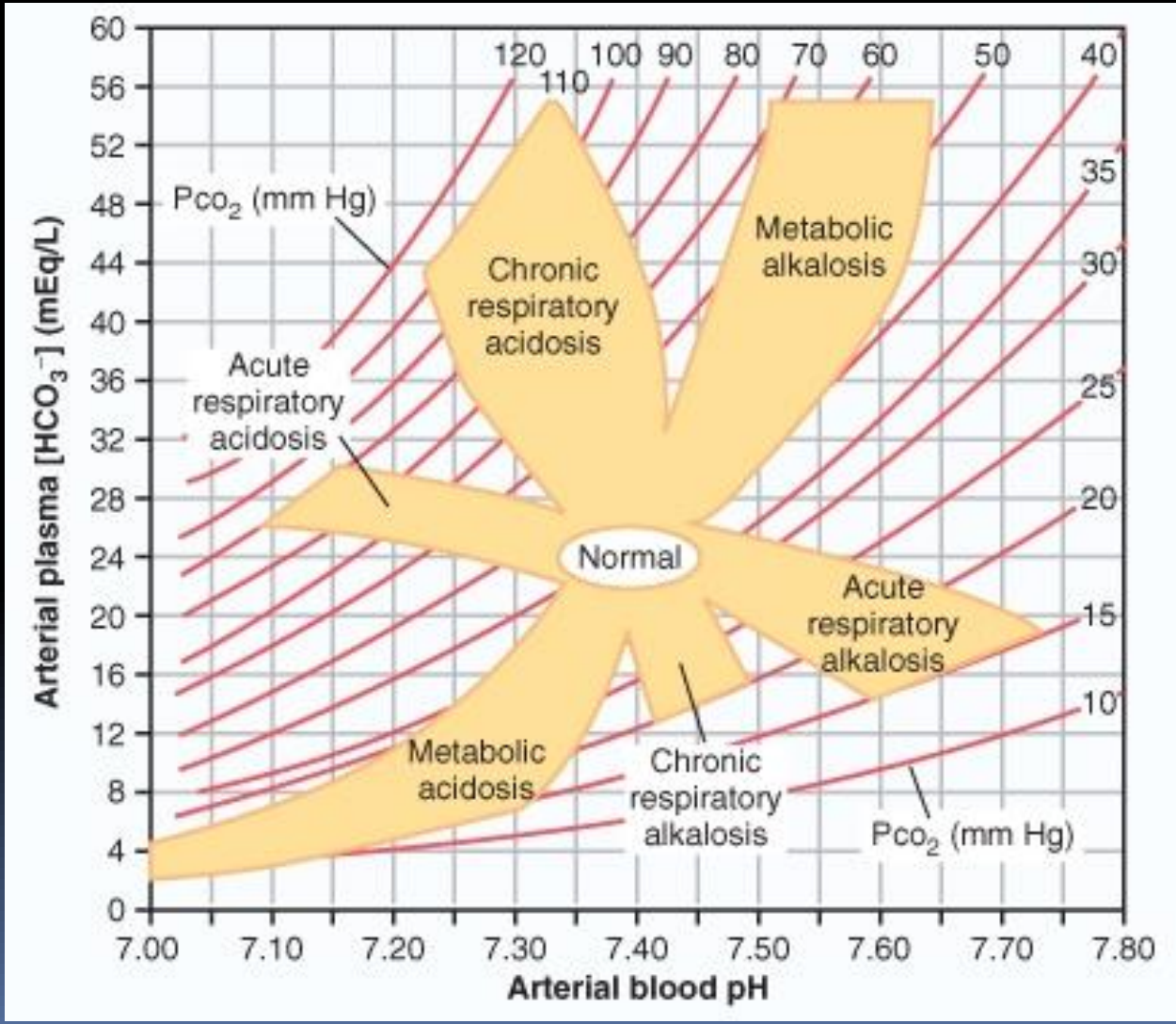
- **INCREASED** i) renal **SECRETION OF H^+** and ii) **ABSORPTION OF HCO_3^-** is **COMPENSATORY MECHANISM**

Davenport Diagram

Acid-base alterations

Respiratory Acidosis

↓ plasma pH, ↑ Pco_2, ↑ plasma [HCO_3^-]



Respiratory Alkalosis

- **Respiratory Alkalosis**
  - Reduced plasma Pco_2 (hypocapnia) and elevated pH
  - Caused by increased gas exchange mainly due to **HYPERVENTILATION**
    - Anxiety / fear
    - High altitude

- Characterised by ↓ Pco_2 and ↑ plasma pH.

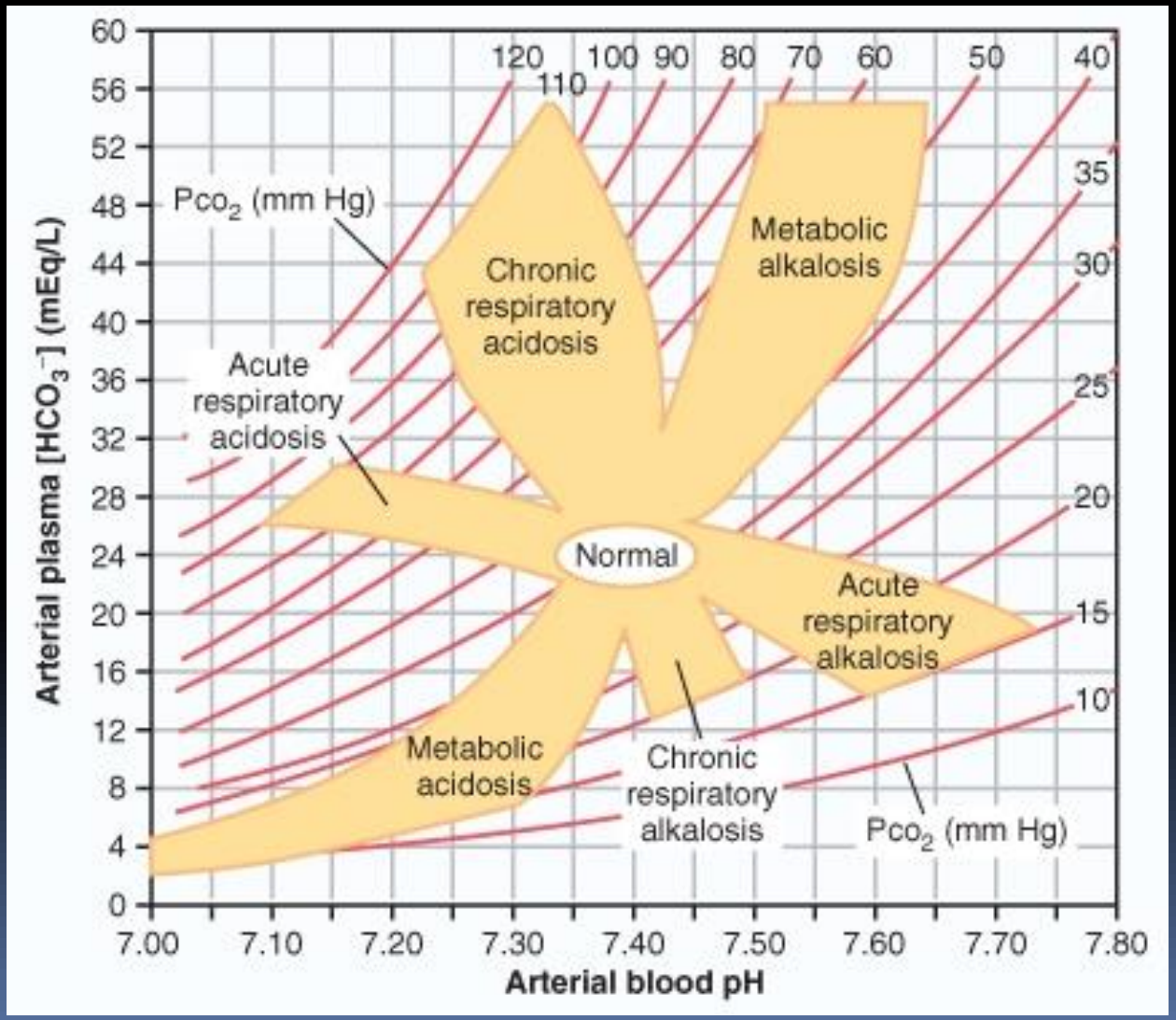
- Reduction in Pco_2 shifts buffering reaction to the left
  - **DECREASE** in ECF $[H^+]$ and plasma $[HCO_3^-]$
- **DECREASED** i) renal **SECRETION** of H^+ and ii) **ABSORPTION** of HCO_3^- is **COMPENSATORY MECHANISM.**

Davenport Diagram

Acid-base alterations

Respiratory Alkalosis

↑ plasma pH,↓ Pco_2,,
↓ plasma [HCO_3^-]



Metabolic Acidosis & Alkalosis

- Metabolic acidosis and alkalosis includes all situations other than those in which primary problem is respiratory.

- By definition, metabolic acidosis and alkalosis cannot be due to excess retention or loss of CO_2
  - does arterial Pco_2 remain unchanged in these cases?

NO!

- ↑ $[H^+]$ in acidosis will reflexly stimulate ventilation to lower Pco_2. Conversely, ventilation will be inhibited in alkalosis to restore $[H^+]$.

- Remember, plasma Pco_2 changes during metabolic acidosis / alkalosis are a *result* of, not *cause* of, compensatory reflex responses to non-respiratory abnormalities.

Metabolic Acidosis

- Caused by either i) **INCREASED** acid ***production*** or

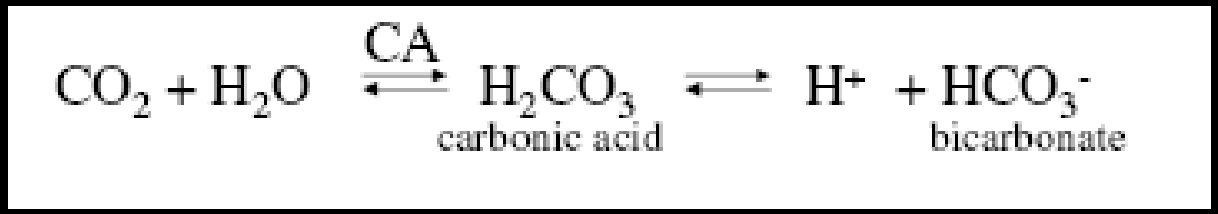
  ii) **IMPAIRED** acid ***excretion***.

Can occur in response to;

1) High protein diet - protein catabolism produces phosphoric acid and sulphuric acid.
2) High fat diet - fat catabolism produces fatty acids.
3) Heavy exercise – stimulates anaerobic metabolism, producing lactic acid.
4) Addition of fixed acids (*e.g.* diabetic ketoacidosis).
5) Severe diarrhoea – loss of bicarbonate from intestines.
6) Alterations in renal function (inability to excrete H^+).
7) Tissue hypoxia (produces lactic acid)
8) Ingested substances such as methanol, aspirin (acetylsalicylic acid), ethylene glycol.

Metabolic Acidosis

- First line of defence is shift of buffering reactions to the left to neutralise excess acid (for bicarbonate, cell* & bone buffers).

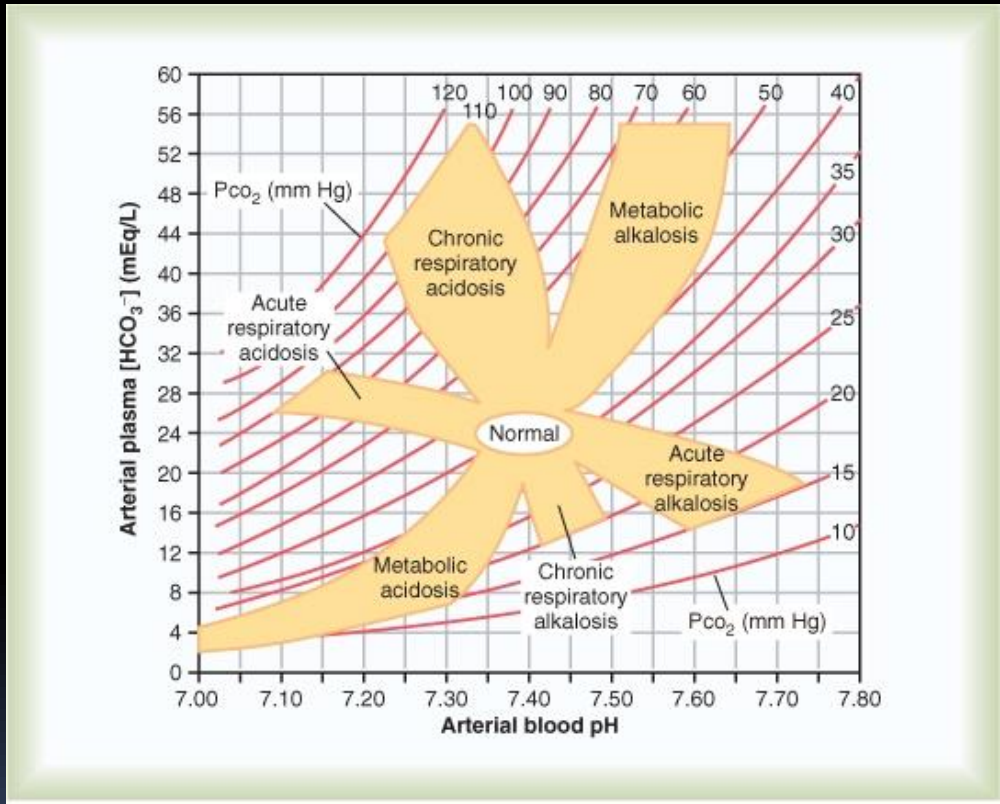


- Metabolic acidosis increases ventilation rate *via* chemoreceptor activation.
- Increased expiration of CO_2 reduces Pco_2 levels which increases pH of ECF (respiratory compensation).
- Acidosis **INCREASES** renal **SECRETION** of H^+ and **ABSORPTION** of HCO_3^- $\Rightarrow$ ECF $[HCO_3^-]$ increases.
- **Characterised by DECREASED $[HCO_3^-]$ (<25mM) and pH.**

Davenport Diagram
Acid-base alterations

Metabolic Acidosis

↓ plasma pH,
↓ plasma [HCO_3^-]
↓ Pco_2,



Metabolic Acidosis

* Uptake of excess H^+ by cells is accompanied, in part, by **LOSS** of ***intra***cellular K^+ (and Na^+) to ***extra***cellular fluid to maintain **ELECTRONEUTRALITY**.

- Thus, metabolic acidosis often associated with **INCREASED plasma [K^+]** relative to that expected from state of potassium balance.
- **HYPERKALEMIA** can develop even though body K^+ stores are diminished.
- Cation shift is **REVERSED** with correction of acidosis.

Metabolic Alkalosis

- Relatively rare phenomenon that can occur in response to;

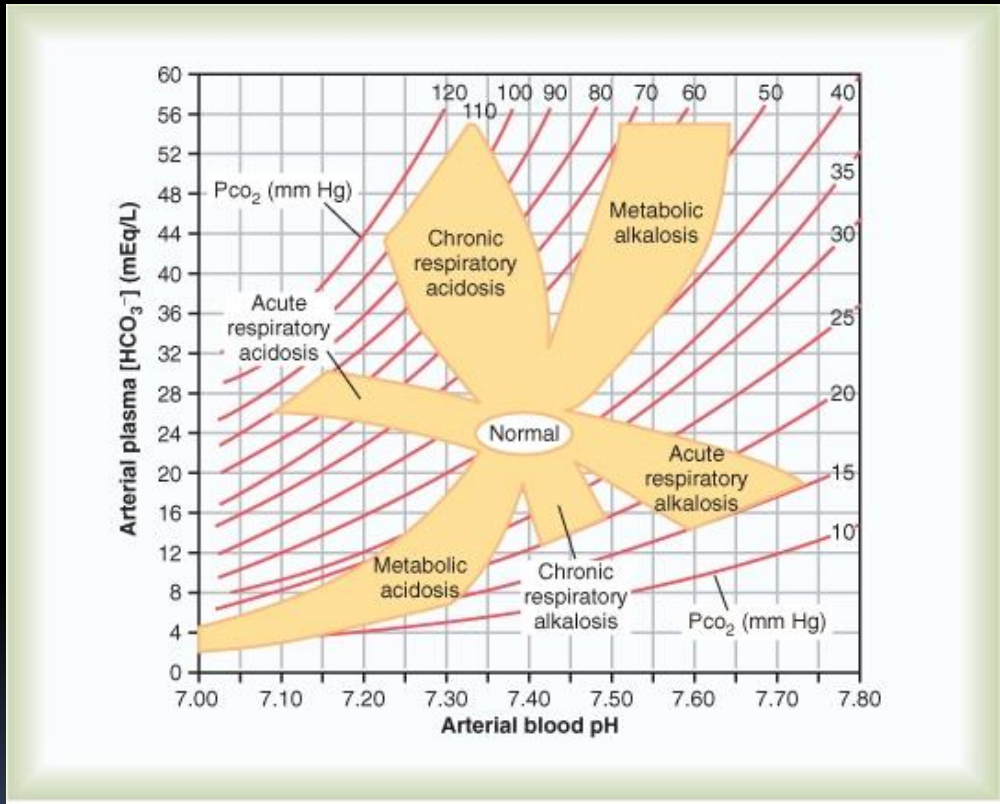
1) Excessive vomiting – loss of HCl from stomach ($\therefore$ retention of (duodenal) bicarbonate in circulation).
2) Alterations in renal function (↑ excretion of titratable acid *e.g.*, thiazide and loop diuretics ↑Na^+ reabsorption → ↑excretion of H^+).
3) Excessive ingestion of bicarbonate antacids paired with renal failure.
4) Volume contraction (*e.g via* diuretic therapy ↑ plasma [HCO_3^-]).
5) Excess aldosterone (stimulates collecting duct H^+-ATPases to excrete H^+) .

- Loss of acid ↑ dissociation of $H_2CO_3 \Rightarrow \uparrow HCO_3^-$.
- Increase in pH **REDUCES** ventilation rate, elevating Pco_2 levels.
- Reduction in renal absorption and ↑ excretion of HCO_3^- in the nephron.
- **Characterised by ELEVATED plasma [HCO_3^-] and pH.**

Davenport Diagram
Acid-base alterations

Metabolic Alkalosis

–plasma pH, ↑
↑ plasma [HCO_3^-] ,↑ Pco_2,



How to Analyze an ABG

1. PO_2 NL = 80 – 100 mmHg

2. pH NL = 7.35 – 7.45
   Acidotic <7.35
   Alkalotic >7.45

3. PCO_2 NL = 35 – 45 mmHg
   Acidotic >45
   Alkalotic <35

4. HCO_3 NL = 22 – 26 mmol/L
   Acidotic < 22
   Alkalotic > 26

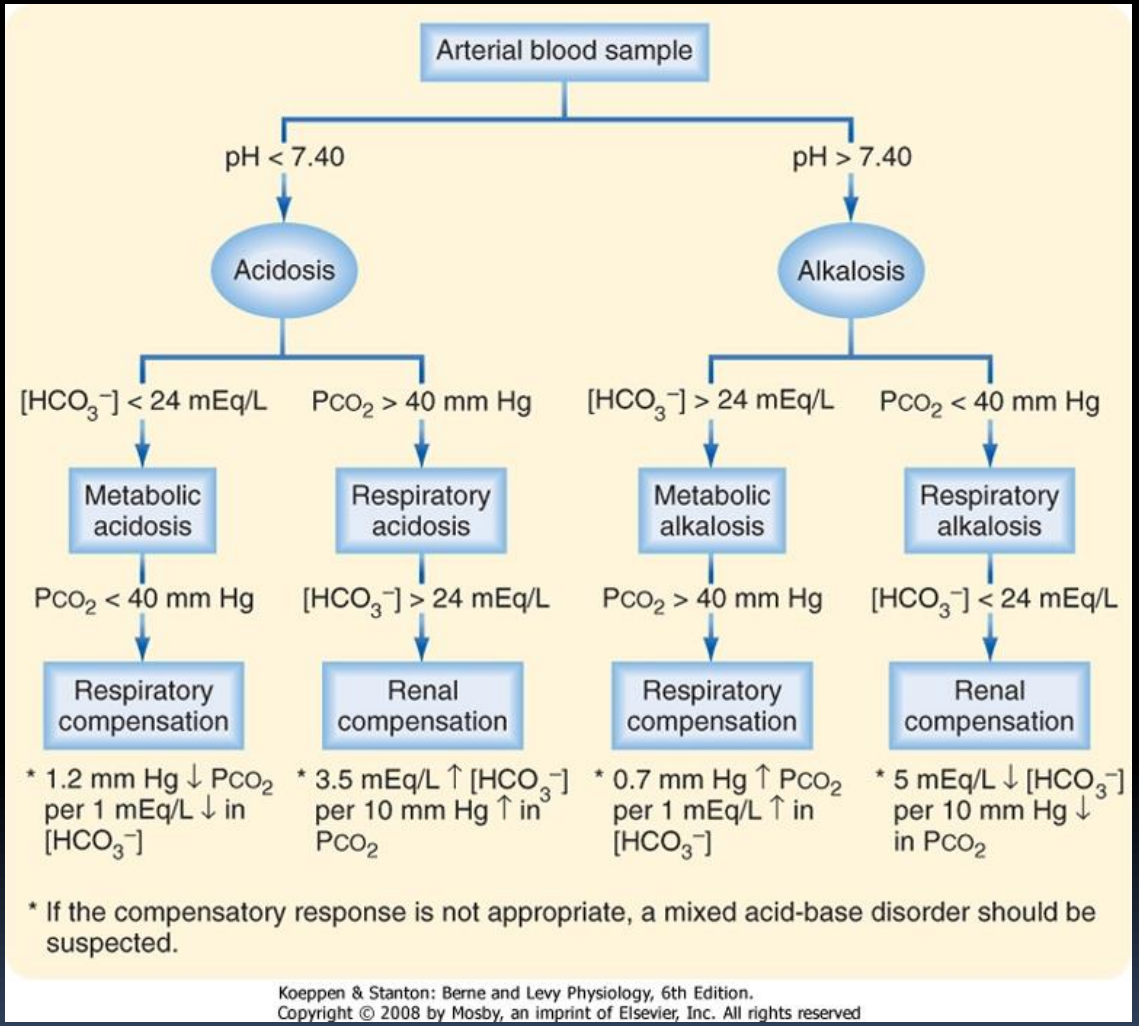
Analysis of Acid-Base Disorders

e.g. pH = 7.30
$[HCO_3^-]$ = 16mEq/L
PCO2 = 30 mm Hg

1) Evaluate pH - acid

2) Metabolic or respiratory source?
$[HCO_3^-]$ < 24mM = metabolic

3) Analysis of compensatory response.
↓ PCO_2 – respiratory compensation



- Mixed acid-base disorders can also occur (*e.g.* emphysema with diarrhea) in which an appropriate compensatory response has not occurred.

1) A 50 year-old man with history of type 2 diabetes was admitted to the emergency department with history of polyuria. On examination he had rapid and deep breathing. Blood analysis showed glucose level of 400 mg/dl.

- **The following is the arterial blood analysis report of this patient:**
- **pH = 7.1, PCO^2 = 40 mmHg and HCO^{3-} = 18 mmol/L**
- **(Normal reference ranges: PCO2 = 36.0-46.0 mmHg, HCO3- = 22.0-26.0 mmol/L)**

- **What is the acid base disturbance in this case?**

2) PH= 7.12, $PaCO_2$= 60mmHg, HCO_3^- = 24meq/L.

a) Compensated metabolic acidosis.
b) Uncompensated metabolic acidosis,
c) Compensated respiratory acidosis,
d) Uncompensated respiratory acidosis,

3) **PH= 7.51, $PaCO_2$= 40mmHg, HCO_3^- = 31meq/L.**

a) **Normal,**
b) **Compensated respiratory acidosis,**
c) **Uncompensated respiratory alkalosis.**
d) **Uncompensated metabolic alkalosis,**


Thanks