Lecture datafile
Pathophysiology
Medical faculty 3rd year
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GENERAL MEDICINE
DENTISTRY

Acid - base balance disturbances

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PHYSIOLOGICAL PRINCIPLES

Definitions and priciples

- **Acid** (HA) is defined as a compound that can release a proton (H^+)
- **Acidosis** (acidaemia) accumulation of acids in the extended ECV. The pH in the arterial blood is < 7.35
- **Base** (B^-) can bind H^+
- **Alkalosis** (alkalaemia) accumulation of bases in the extended ECV. The pH of the arterial blood is › 7.45
- **Buffer** is a mixture of compounds which have the ability to absorb small amounts of H^+ or OH^- with very little change of pH.

$pH = pK + \log c_s / c_A$

- Normally, the $[H^+]$ of arterial blood of humans is maintained by the **lungs, kidneys** and **liver** within the range of 40 ± 5 nM, corresponding to a pH of 7.35 - 7.45.
- **pH** = negative decadic logarithm of [H+] concentration of H+ ions : **$pH = -\log c(H+)$.**

- Physiologically 40 nmol/l of **H+** in the arterial blood: **pH = -log 40 x 10-9 mol/l = pH = 7,4**
- **pH = - log (40 x 10^{-9} mol/L) = 7.4**

A pH of 6.8 - 6.9 is not sustainable for long, and the patient is dying in a state of coma.

- **Source of acids** in the body is mainly **metabolism**, **source of bases** is predominantly **nutrient.**
- **Acids and bases** undergo either (1) **metabolic conversion** (e.g. lactate to glucose in gluconeogenesis, lactate to pyruvate and oxidation in cardiomyocytes), or (2) **excretion** from body.
- Human organism (healthy or not) every is overwhelmed with **acids.**
- **ATP production is coupled with H+ production.** Human body is evolutionary capable to **handle acid load**

Definition and principles

Arterial blood:

Direcly measured

1) **Arterial pHa = 7,4** (range **7,36 - 7,44**)
Incompatible: **6,8 > pHa > 7,8,**

alkalemia is > 7,44 ; acidemia < 7,36

2) **pCO2 = 4,8 – 5,9 kPa (35-45 mmHg), average is 5,3 kPa (40 mmHg)**

- pCO2 < 4,8 kPa is **hypocapnia**
- pCO2 > 5,9 kPa is **hypercapnia**

3) **pO2 = 9,9 – 13,3 kPa (80-100 mmHg)**

Calculated values:

4) **[HCO3-] = 22-26 mmol/l**

5) **BE = 0 ± 2,5 mmol/l**

Venous blood:

- **Venous pHv ~ 7,35**
- **Intracellular pHic** app **7,0** ([H+] = **100 nmol/l**); = varies considerably among cells; 2,5 x more H^+ than extracelular
- Gradient moves H^+ from inside of the cell into extracelullar space and the blood.

Definitions and principles

BE (base excess)

- Base excess is defined as **number of moles of strong acid** that is needed to add to one litre of fully oxygenated blood to achieve pH 7,4 when pCO2 is 5,3 kPa and temperature is 37°C. BE is optimal quantity for assessing metabolic component of acid-base balance. Normal values are 0 ± 2,5 mmol/l. **Negative value** indicates **excess of acids** (so the value is negative). Excess of acids is **metabolic acidosis. Positive value** indicates **excess of bases** (base excess), hence **metabolic alkalosis.**
- There is however one very similar quantity – base deficit (BD). It indicates deficit of bases in mmol/l.
- **Anion gap (AG)**
- **Anion gap** is a quantity which is almost equal to the **sum of concentrations of "unmeasurable" anions** (**albumin – plasma proteins, phosphates, sulphates, organic anions**). Unmeasurable is not accurate term, more precise is **commonly non-measured.**
- **AG is calculated as follows:**
- **AG = ([Na+] + [K+]) – ([Cl-] + [HCO3-])**
- Na+ (140) + K+ (5) = Cl- (105) + HCO3- (25) + AG (15)
- Normal AG: **14 ± 2 mmol/l**
- Anion gap is used for **assessing causes of the metabolic acidosis.** One of the causes is the **accumulation of the acids.** Concentrations of some of them are not commonly measured. When there is accumulation of commonly non-measured acids **unexpected rise in difference of measured cations and anions.** This increase in difference could be revealed by AG. Therefore when there is increased AG it indicates that commonly non-measured acids accumulated. They become part of AG. Thus greater AG indicates acidosis.

- increased AG is caused by:
- **1) Increase in concentration of ions that physiologically make the AG**
- **2) Presence of new anions**
- This method is unfortunately dependent on accuracy of the measurements. Little mistake in big numbers lead to greater mistake in the result. There are particular situations when we need to measure commonly non-measured acids (anions) concentrations. Then we measure:
- **1) Lactate in tissue hypoxia**
- **2) 3-hydroxybutyrate in diabetic ketoacidosis**
- **3) Phosphates and sulphates in renal failure**

External acids and alkali (in food)

ALKALI RESOURCES

- **Most fruits and vegetables, juices** = esp. bananas, watermelon, celery, kale, and onions (except peas); mushrooms; herbs / vinegars .
- sugar is neutral, brown sugar and honey are base
- tea, coffee, cocoa, mineral water, red /white wines
- margarine; olive, sunflower seed oils are neutral
- whey, the liquid left over after milk is base.
- Stout and draft beers; hazelnuts, which are base.
- **Exception of vegetables and fruits** = lemons, oranges, grapefruits, tomatoes and pineapples (acidic when eaten, but, metabolicaly turned into alkaline

ACID RESOURCES

- simple sugars (monosacharides = glucose, fructose) rapidly metabolized to pyruvic acid,
- simple fats (triacidglycerols) and proteins
- **grains / grain product**s = whole-meal, refined bread, asta, white and brown rice, amaranth, millet, oats, buckwheat, spelt, rye; pale beer
- **all animal flesh** = shellfish, sardines, prawns, trout, salmon ,goose, liver, rabbit, processed meats (canned, corned beef, lunch meat and salami. steak)
- **milk** (whole and reduced-fat milk), **kefir,** diary products (butter), ice cream , **cheese** (**cottage cheese,** processed cheese camembert, Eidam, parmeggiano, cedar; full-fat cheese is neutral,
- **eggs** especially **yolks; animal fat and oils**
- **most nuts, seeds;** beans and peas,
- **Exception of vegetables and fruits** = asparagus, cranberries, plums, prunes (all slightly acidic)

Acid Forming Foods


Hamburgers


Hot Dogs


Lunch Meat

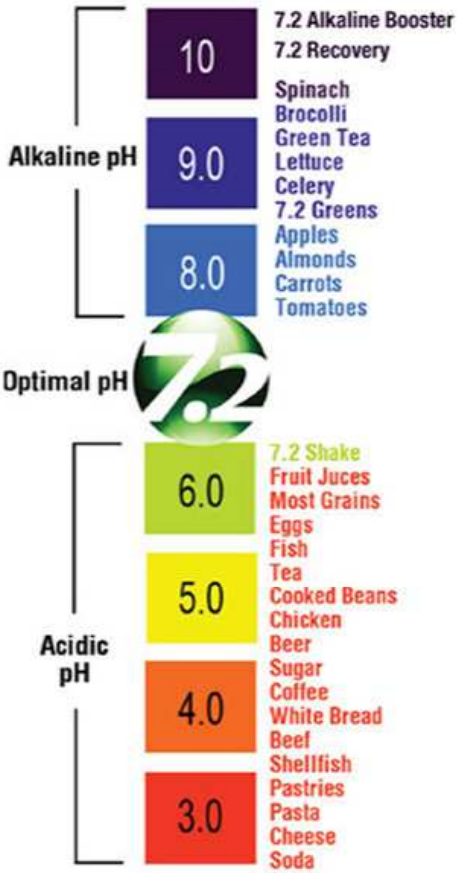

Candy


Cookies


Sugar


Alcohol


Soda



Alkaline Food Choices


Beets


Cauliflower


Celery


Kale


Apples


Avocados


Figs, dried


Lemon & Lime

Alkaline Foods

Alkaline—having the properties of an alkali, or containing alkali; having a pH greater than 7

 Avocado	 Amaranth a.k.a Callaloo	 Bell Peppers	 Kale - Curly, Russian and Dino	 Arugula	 Tomatoes-Cherry and Plum
 Okras	 Dandelion Greens	 Turnip Greens	 Lettuce (no iceberg)	 Watercress	 Tomatillos
 Green Onions	 Olives	 Zucchini	 Squash	 Yellow Squash	 Chayote - Mexican squash
 Mushrooms (no shitake)	 Cucumbers	 Cactus and Prickly Pears	 Burro Bananas	 Sour Sop	 Tamarind
 Papayas	 Cantaloupes	 Jelly Coconuts	 Plums	 Figs	 Peaches
 Mangoes	 Berries - Elderberries no cranberries	 Limes Seeded or Key Limes	 Oranges - Sayville or Sour	 Cherries	 Apples
 Pears	 Seeded Grapes	 Seeded Raisins	 Currants	Dates	Prunes

Acidifying

Meat & Meat Products

Fish

All Sugars

Dairy

Grains

Grain Products

Chocolate

Coffee & Tea

Fruit Juice & Soda

All Alcohol

ALKALINE FOODS

ACIDIC FOODS

RawForBeauty.com

Metabolic reaction producing H+

- **Three types** of metabol. reactions to impact the acid-base balance.

(1) proton-productive, (2) proton-consumptive, (3) proton-neutral.

1. Metabolic production of H^+ (proton-productive)

a) Anaerobic glycolysis: Glucose ⟶ pyruvate, lactate (2 CH3CHOHCOO-) + 2 **H^+**

b) Fast massive lipolysis - ketogenesis: Fatty acids ⟶ Ketone bodies + **H^+**

c) Lipolysis : Triacylglycerol TAG ⟶ 3 FA (fatty acids) + glycerol + 3 **H^+**

d) Ureagenesis: CO2 + 2 NH+4 ⟶ urea + H2O + 2 **H^+**

e) Proteolysis:Proteins ⟶ amino acids⟶ sulphate, urea + **H^+**

2. Metabolic consumption of H^+ (proton-consumptive)

a) Gluconeogenesis: 2 Lactate + 2 **H^+** ⟶ Glucose

b) Neutral and dicarboxylic amino acids oxidation

3. Proton-neutral reactions

a) Complete oxidation /Aerobic glycolysis: Kebs cycle provide H^+ for oxidative phosphorylation

Carbon cointainig compound ⟶ $CO_2 + H_2O \longrightarrow HCO_3^- + H^+$ $H^+ + O_2 \rightarrow H_2O$

b) Lipogenesis from glucose

Acids according to the route of elimination

(1) Volatile acids (acids that can be exhaled) = **carbonic acid** (H_2CO_3) is mainly exhaled by respiration or released into urine:

- human body produces **20 000 mmol CO_2** every day and the **same amount of H_2CO_3** ¬ $CO_2 + H_2O$

(2) Non-volatile acids (acids that can not be exaled); (a) **metabolised**, or (b) **excreted** by urine (main), stool, sweat):

- human body produces **30-80 mmol** of non- volatile acids (~ **1 mmol/kg of body** weight) every day.

(a) organic: products of metabolism and oxidized completely to CO2 and H2O.

(1) lactic acid, (2) fatty acids, (3) ketone bodies (acetoacetic acid, β-hydroxybutyric acid) produced by (incomplete oxidation of TAG, carbohydrates, proteins).

(b) inorganic: predominantly excreted in urine.

(a) **H_2SO_4** (sulphuric acid is produced by oxidation of -SH (sulfhydryl groups) – e.g. in amino acids that contain sulphur, i.e. cysteine, methionine),

(b) **H_3PO_4** (phosphoric acid produced by hydrolysis of phosphoproteins, phospholipids, nucleic acids).

Systems for maintenance of the acid-base balance

Chemical buffering systems

- **Buffers** are substances capable of **releasing** and **binding H+**. Each buffer keeps **its particular pH**. This pH could be calculated by means of the **Henderson-Hasselbalch equation: pH = pK + log [conjugated base]/[acid]**
- Buffers react **immediately** – acute regulation. Capacity of buffers is not indefinite ; act only in the **short-term** and **acute** changes in acid-base balance. Chemical buffering systems deal with pH deviations in common metabolism.

Localization	Buffer	Commentary
ISF	**Bicarbonate**	Buffers metabolic acids
	Phosphate	Low concentration – limited significance
	Proteins	Low concentration – limited significance
Blood	**Bicarbonate**	Buffers metabolic acids
	Haemoglobin	Buffers CO2 (carbonic acid production)
	Plasma proteins	Minor
	Phosphate	Low concentration – limited significance
ICF	**Proteins**	Significant buffer
	Phosphate	Significant buffer
Urine	**Phosphate**	Responsible for majority of the urine acidity
	Ammonium	Significant loss of ammonium nitrogen and protons

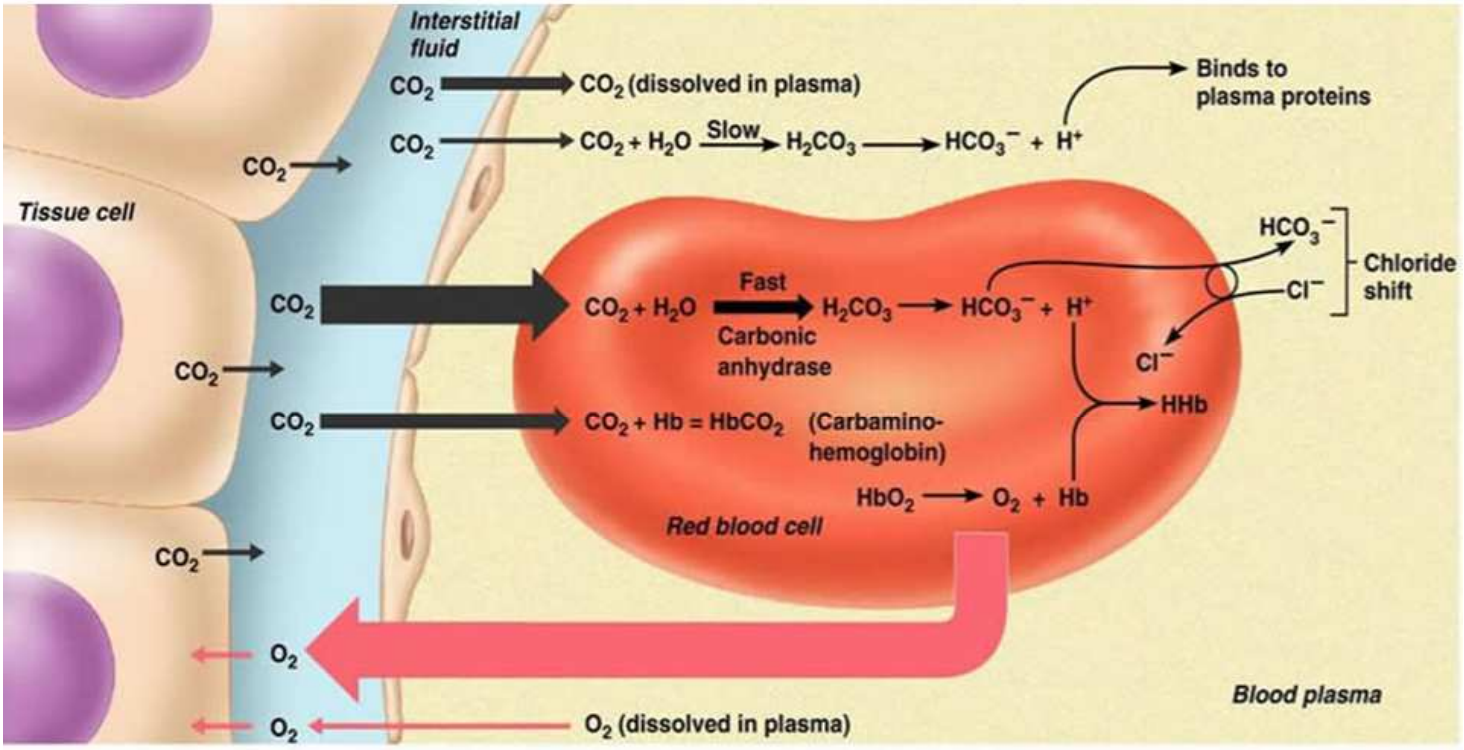
Chemical buffering systems

Buffer	Plasma	Erythrocytes	Together
HCO_3^- / CO_2	35 %	18 %	**53 %**
Hb / Hb-H^+	-	35 %	35 %
Plasma proteins	7 %	-	7 %
Inorganic phosphate	1 %	1 %	2 %
Organic phosphate	-	3 %	3 %
	43 %	**57 %**	**100 %**

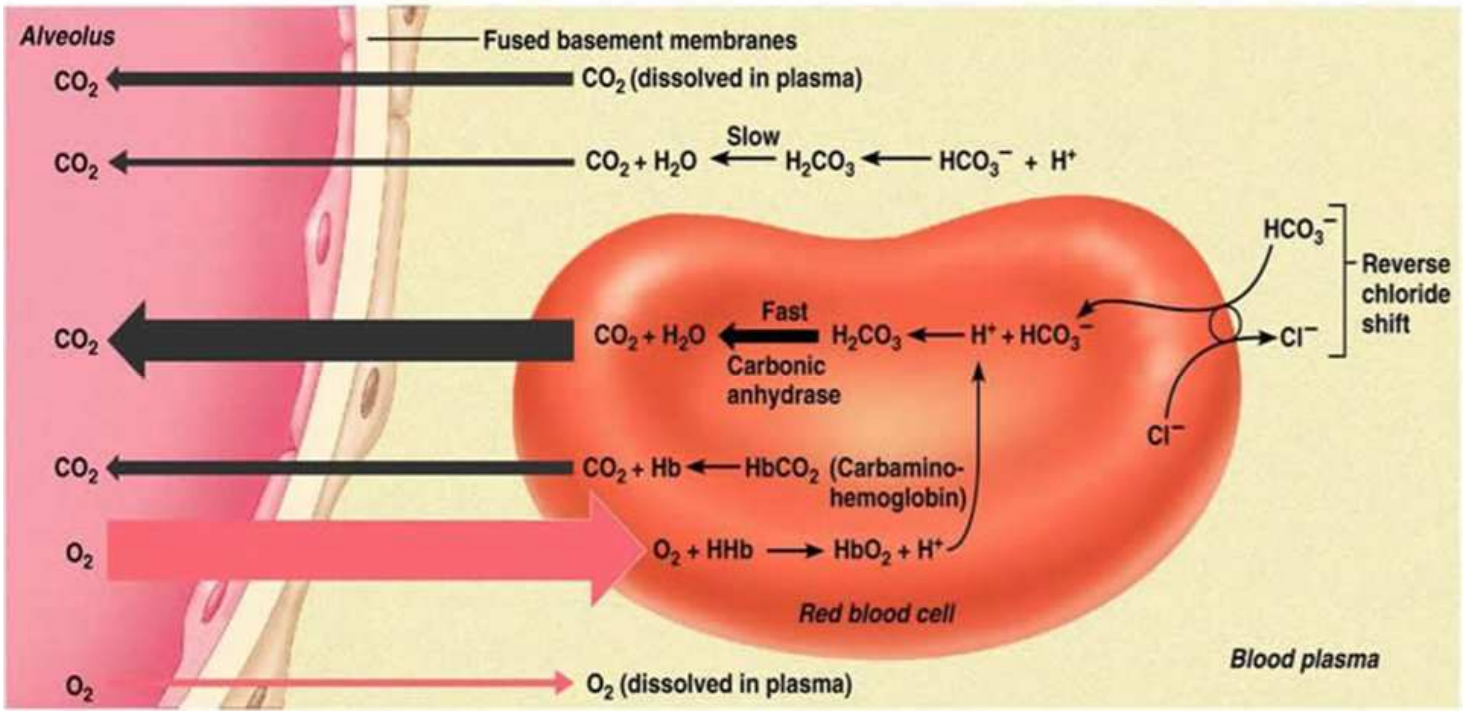
- **Bicarbonate buffer (HCO3-/CO2).** Bicarbonate buffer is the **most important buffer system in blood plasma** (generally in the extracellular fluid). This buffer consists of weak acid H2CO3 (pK1 = 6,1) and conjugated base HCO3- (bicarbonate).
- pH = pK + log ([HCO3-] / [H2CO3]); pH = 6,1 + log ([HCO3-] / pCO2 x α)
- pH = 6,1 + log (24 / 40 x 0,03), pH = 6,1 + 1,3, **pH = 7,4**

- **Protein buffers.** plasma proteins and intracellular) are the most **abundant** and the most **powerful buffer system in whole organism**. Some amino acids have acid or basic side chains (His, Lys, Arg, Glu, Asp).
- **Haemoglobin is the most important** = 35 % of buffering capacity of blood, remaining proteins provide only 7 %.

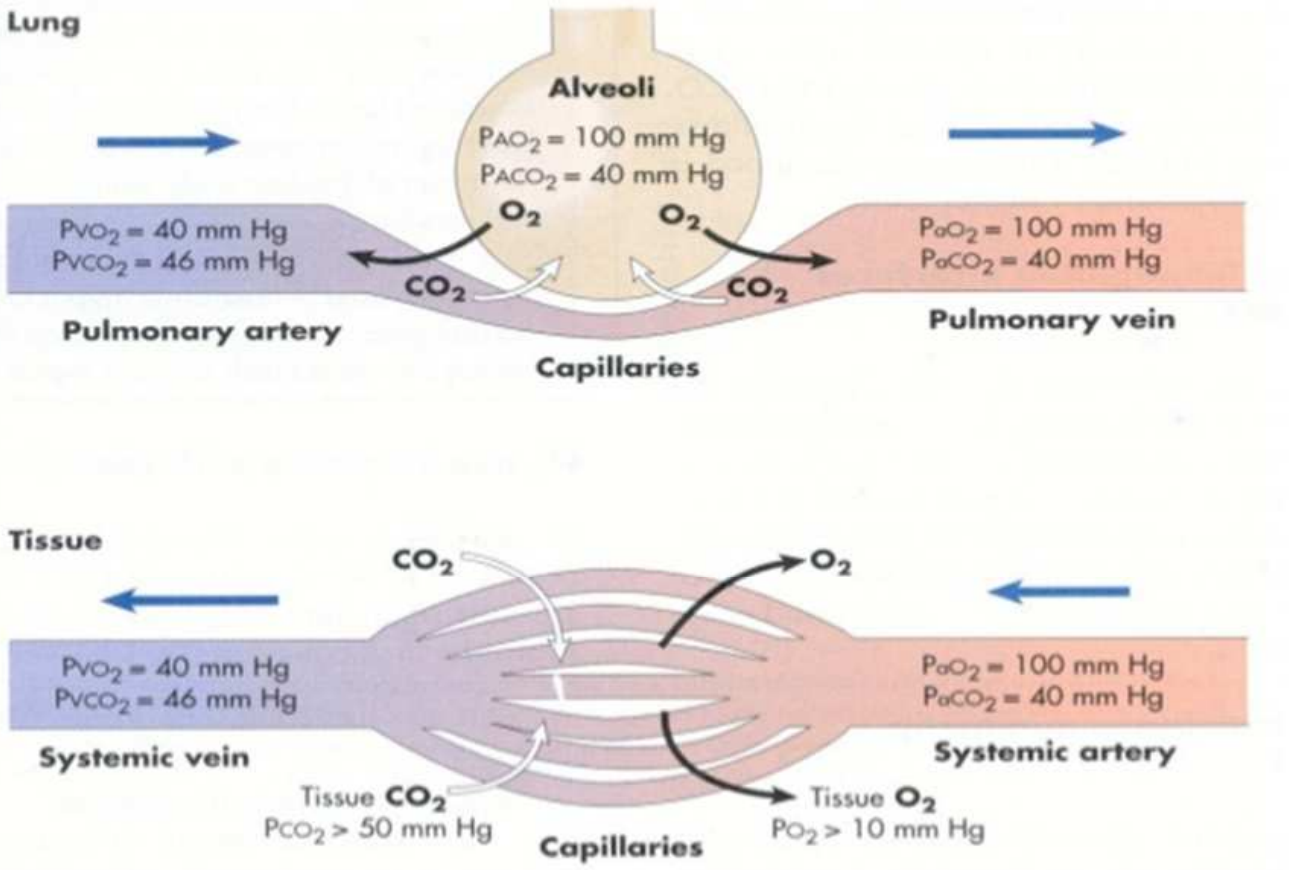
Transportation of CO2 from the tissue



Transportation of CO2 into lungs



CO2 transportation – summary data



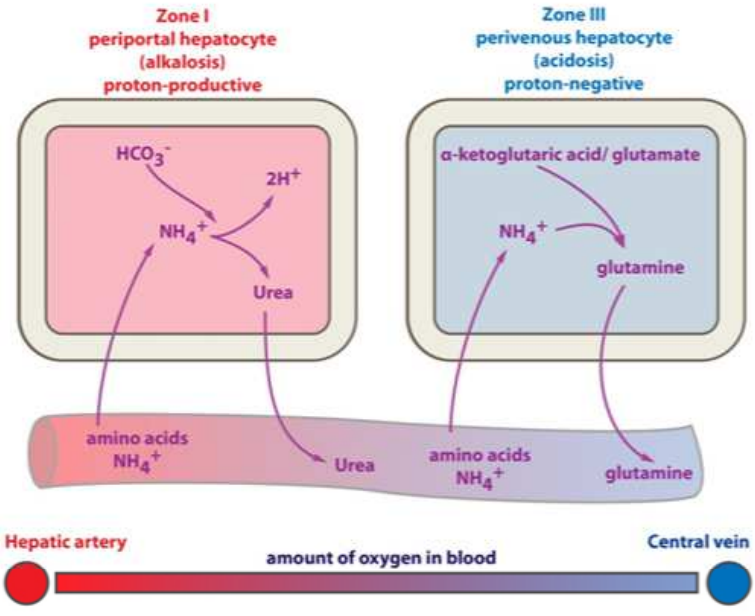
Liver

- the most important tissue where ammonium is detoxified in both (1) urea cycle, and (2) glutamine synthesis. Which one of these fates of ammonium is favoured closely depends on status of the acid-base balance:

a) NH4+ ⟶ **urea** + 2 H+ ⟶ acidification of the body

- CO2 + 2 NH4+ ⟶ CO(NH2)2 + 2 H+ + H2O
- H+ + HCO3- ⟶ H2O + CO2 (**consumption of bicarbonate-**)

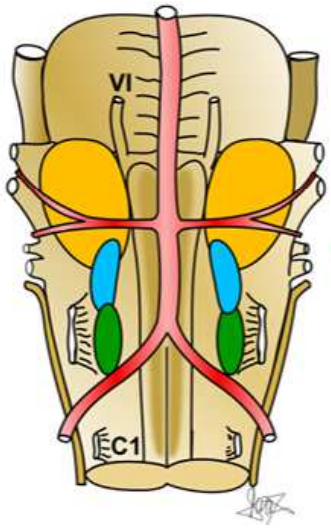
b) NH4+ ⟶ **glutamine synthesis** ⟶ H+ is not produced, glutamine is taken up by the kidneys. In the kidney is **H+ excreted as NH4+**



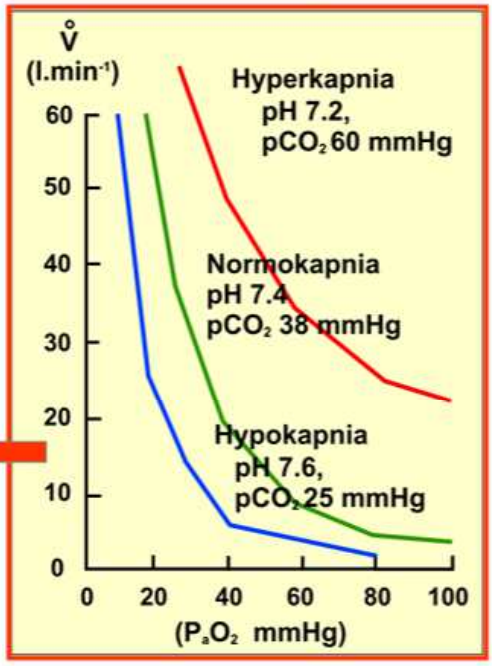
Breathing = central pH/CO_2 stimulation

*Respiration reacts in **1-3 minutes**. Respiratory system regulates **carbon dioxide**. Respiration is able to change pCO2 by its elimination or retention. Respiratory centre is in **brainstem**.*

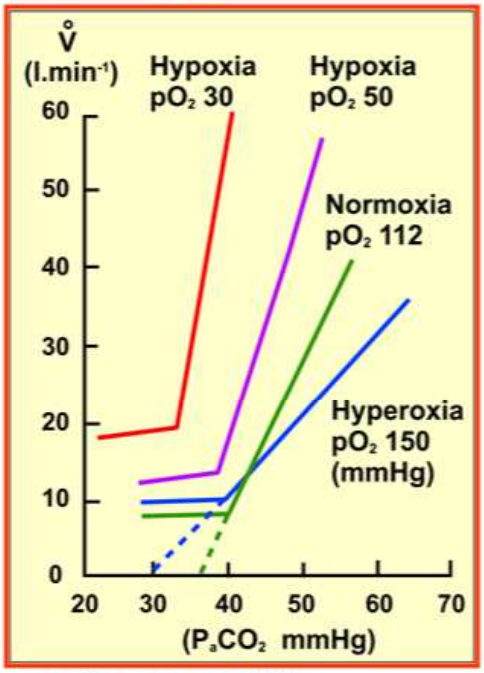
Central pH/CO_2 – sensitive structures in rostroventral medullary surface



CO_2 ➡ O_2



O_2 ➡ CO_2



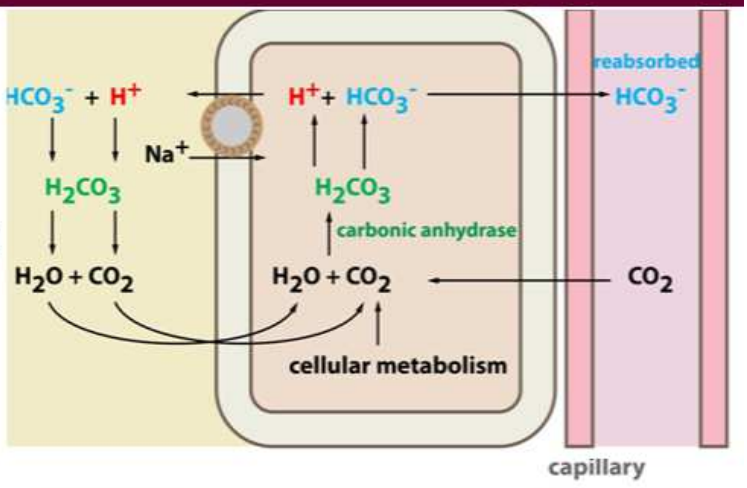
Millhorn a Eldridge (1986), Schlaefke (1987), Nattie (1998)

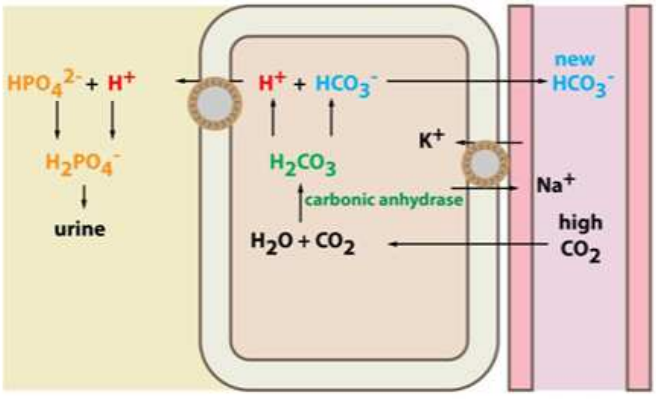
Kidney

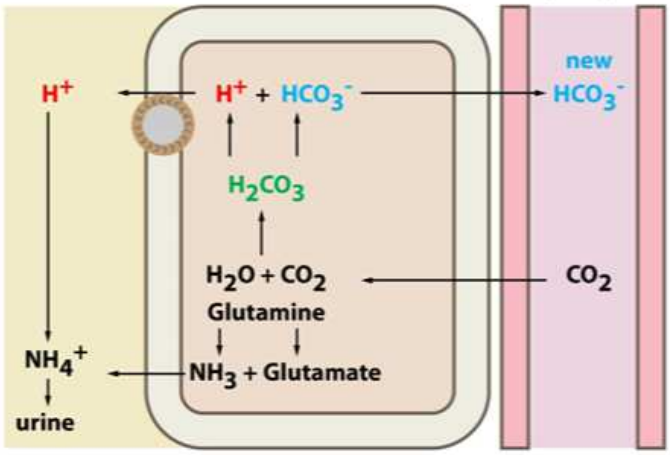
- Kidneys react in **hours-days**. Their role in acid-base balance is very complex.

1) Reabsorbing, excretion of HCO3-
2) Production of HCO3-
3) Excretion or H+

- **Bicarbonate reabsorption** takes place in proximal tubule cells
- **Bicarbonate production** takes place in **intercalated cells type A** of distal tubule and collecting duct.
- **Ammonium ion excretion**
- This process uses ammonium generated in **glutamine** metabolism in tubular cells.

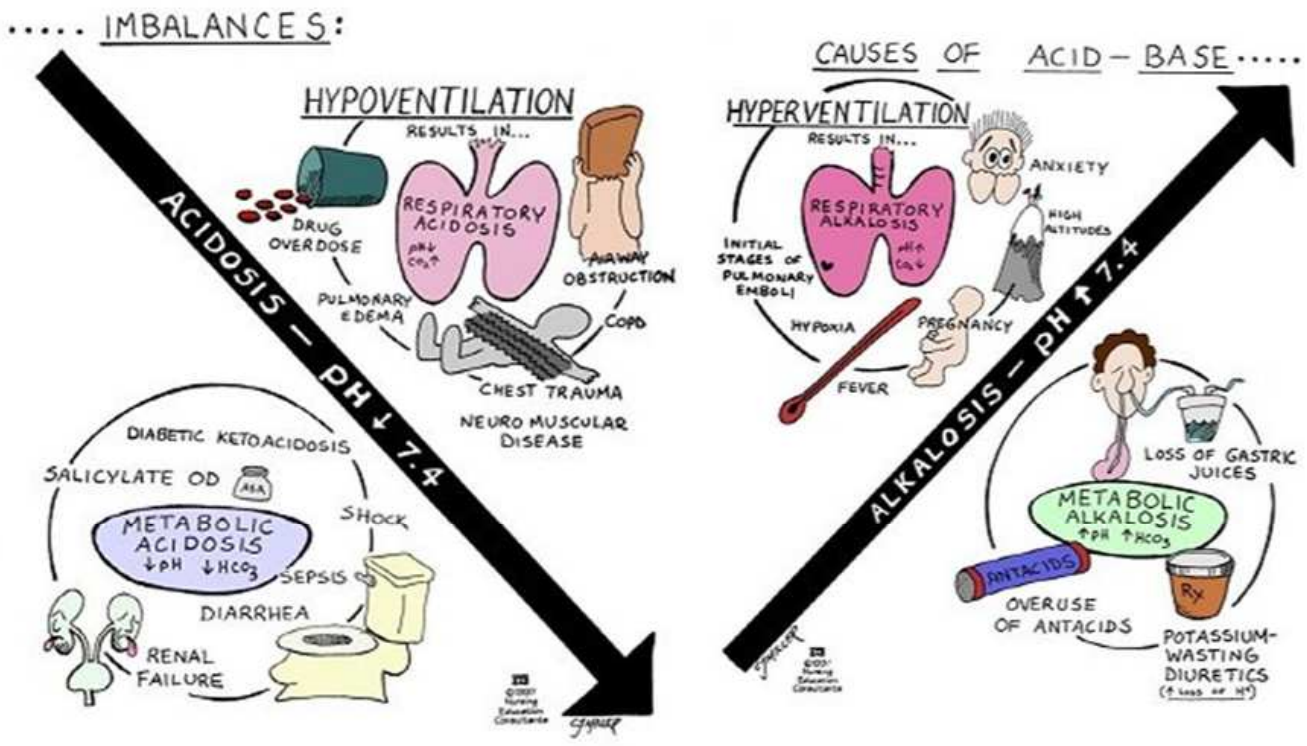






Main forms of acid –base balance disorders

Dysbalances



Main acid-base balance disorders

Form	Compensation	pH	P_aCO_2	HCO_3^-	Therapy
Respiratory acidosis Acute RAC Chronic RAC	Uncompensated	↓	↑	N	NA HCO3, KHCO3,
	Compensated	N ↓	↑	↑ ↑↑	THAM
Respiratory alkalosis Acute RAL Chronic RAL	Uncompensated	↑	↓	N	Rebreathing, bag wet
	Compensated	N ↑	↓	↓ ↓↓	towel, NH4Cl, Arginin hydrohloride
Metabolic acidosis	Uncompenated	↓	N	↓	Hyperventilation,
	Compensated	N↓	↓	↓	NAHCO3, THAM
Metabolic alkalosis	Uncompenated	↑	N	↑	Hypoventilation
	Compensated	N↑	↑	↑	

- **Four basic acid-base balance disturbances are distinguished:**

1) **Respiratory acidosis (RAC)**: decreased blood pH; its primary cause is **increased pCO2**

2) **Respiratory alkalosis (RAL)**: increased blood pH; its primary cause is **decreased pCO2**

3) **Metabolic acidosis (MAC)**: decreased blood pH; its primary cause is **decreased BE ([HCO3-])**

4) **Metabolic alkalosis (MAL)**: increased blood pH; its primary cause is **increased BE ([HCO3-])**

Respiratory induced dysbalances

Respiratory acidosis (RAC)

- Respiratory acidosis emerges when the lungs eliminate too few CO2 (it usually occurs in **hypoventilation**). Low CO2 elimination leads to increased pCO2 in the blood (**hypercapnia**). Increased pCO2 causes decreased pH.
- Causes leading to RAC can lead to ↓ pO2. Hypoxia results in aneronic production of lactate and **lactic acidosis: RAC + MAC.**

Respiratory alkalosis (RAL)

- The most coomon reason of RAL is **hyperventilation hypocapnia** (decreased pCO2).
- RAL is coomonly associated with **hypocalcemia,** musclular hyperexcitability, **tetany** and **spasms.** Serum albumin binds approximately 50 % of plasma calcium. In the same time it is H+ buffer . Under RAL ratio between **ionised** and **Alb-bound calcium chages in favor of** Ca2+ binding.
- HCO3- is slightly lowered as well in addition to CO2 . This is because pCO2 is lowered and thus – to keep equilibrium – part of bicarbonate is converted to CO2

Main acid-base balance disorders

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4) **Metabolic alkalosis (MAL)**: increased blood pH; its primary cause is **increased BE ([HCO3-])**

Respiratory acidosis - etiology

Acute RAC - Acute respiratory failure

1) **Central respiratory depression** (overdose bartiturates, opioids, diazepins, neurotoxins, analgestics, stroke), central sleep apnoea

2) **Breathing restrictions:** Parenchymal: lobar pneumonia,

- **Respir. muscle fatigue** : kurare, botulotoxin, organophosphates (biol. wapons)
- **Throrax defects:** pneumothorax, myorelaxants

3) **Air-away obstrucntions:** AIW collapse (OSA, obstructive sleep apnoea, alle

- rgic laryngospasm, asthmatic bronchospasm paroxysm, foreign body inhalation, intrabronchial tumour, intrapulmonary bleeding, alveolar edema etc.

Chronic RAC

1) **Insufficient ventilation of nervous regulation:** tumors of cerebral angle, intracranial hypertension, polyneurotis, ALS (motor neuron dis.), Duchene muscul. dystrophy, neuromusclular disorders (myasthenia, myotonias, myopathies)

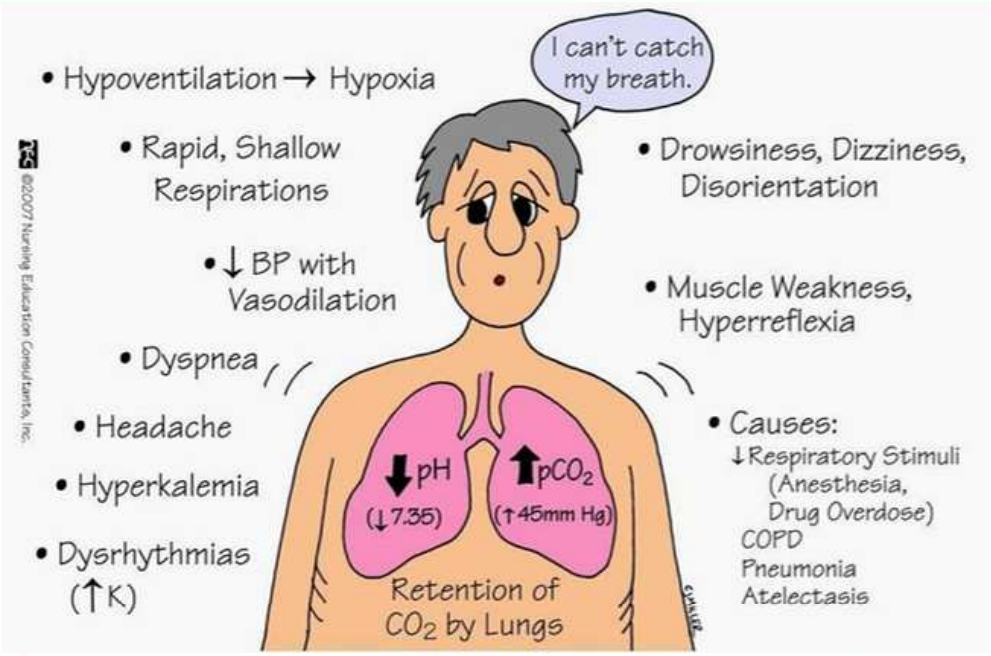
2) **Obstructive disorders:** cystic fibrosis, COPD (emphysema, chronic bronchitis)

3) **Breathing restriction:** pneumonia, spine deformities, tunerculosis, sarcoidosis,

- painful breathing (fractures, pleural strictures), pneumoconioses (occupational finrotic lung disordes, interstitial lung fibrosis, uremic pleuritis,

4) **Lung perfusion**: diffuse microembolisms, embolism collagenoses

Manifestations associated with respiratory acidosis



- Compensation:
- increased HCO3- **regeneration on account of increased acid realesed in kidney tubular cells** of the kidneys (**acidic urine is produced**)
- increased release of CO2 through kidney **and de-novo production of HCO3-**

- RAC is common conseq. of **global acute or chronic respiratory insufficiency; reasons** imply central depression, respiratory airways obstruction (obstructive dis.), or disease of lung distentibility, ribcage etc. **Dyspnoea, tachypnoe with hypopnoe, hypotension** may ensue
- **Hyperkalemia** often emerges and can lead to cardiac arrhythmias; acidosis favours neruromuscular hypoexcitability

Main acid-base balance disorders

		pH	P_aCO_2	HCO_3^-	Therapy
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Acute RAL = occurs rapidly; for every 10 mmHg drop of pCO_2 in arterial blood there is 2 mmol/L drop of HCO_3- due to *acute compensation*

Chronic RAL = long lasting; for every 10 mmHg drop of pCO_2 in arterial blood there is 5 mmol/L drop of HCO_3-

Respiratory alkalosis - Etiology

1) **Central respiratory stimulation - hyperventilation**

Non- structural causes

- **Psychological reaction** - panic disorder, emotions, fear, voluntary
- **Hypoxia, high humidity** or **high altitude** – low oxygen in air (hypoxia) leads to dyspnoea (catching for breaths) and compensatory tachypnoea and tachycardia
- **Pain** – labor, pregnancy, trauma, **Fever- hyperpyrexia (> 40 C), Gramm (-) sepsis**
- Cirrhosis, hepatic encephalopathy, **hypoxia die to high altitude**

Structural causes

- **CNS trauma** - phychogenic shock; in precomatose state - central neurogenic hyperventilation
- Cerebrovaskular accident (SAH – subarachnoid haemorrhage), brain tumors and metastasis

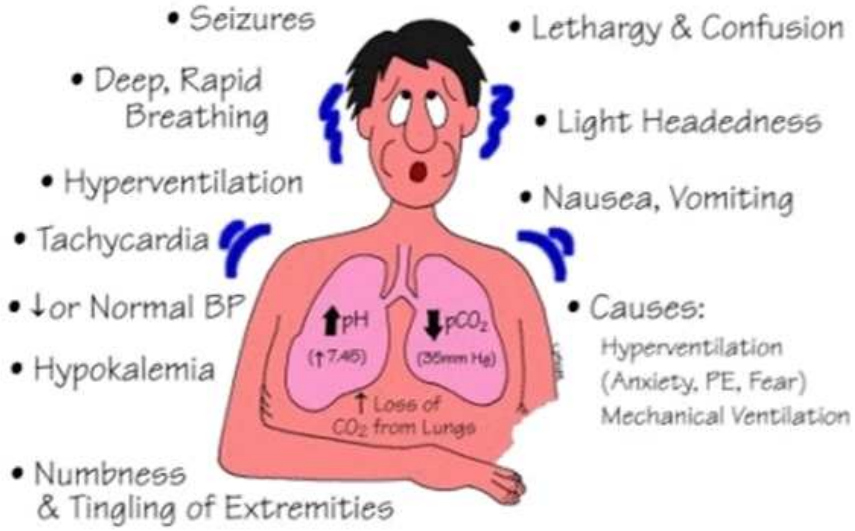
2) **Compensatory chronic hyponoeic tachypnoea due to hypoxia**

- **Pulmonary parenchymal disorders:** Pulmonary fibrosis, early pneumonia, asthma, pneumoconioses,
- **Pulmonary vascular disorders:** pulm. vascul remodelling, pulmonary hypertension, congestive heart failure
- Anemia, **iatrogenic overventilation of patient**

3) **Other reasons**

- **Exogenous poisoning:** Salicylate poisoning (Aspirin), Doxapram, Caffeine, progesterone, Adrenalin
- **Endogenous:** Hyperammonemia

Manifestations associated with respiratory alkalosis



- **Rebreathing** (breathing to bag) may be helpful
- Compensation is **decreased HCO3** provided by larger **excretion of HCO3-** by the kidneys.

- Alkalosis **increases nerve excitability, conductibility, decreases firing threshold of exitable tissue**; cramps, spasms, hypertonia, tetanic bursts develop in muscles, seisure in the brain, overexcitation, somatosensitive overexcitation – numbness, paraesthesias,
- Hyperventilation alkalosis leads to **cerebral vasoconstriction** leads light headness, fainting, nausea,, seizures; dconfusion, loss of conscoiousness normalizes ventilation
- Chronic RAL has comorbid **hypechloremia;** Bohr effect: **left shift in Hb –O2 dissociation curve**
- **Intracelular shifts of Na+, K+, and PO4-, reduced free Ca2+**

Metabolic acid base ballance disturbances

Metabolic acidosis

- **the most common acid-base balance disorder**
- **Accumulation of metabolic acids** (every acid in the body apart from carbonic acid)
- **Loss of bicarbonates** (bicarbonate are lost most commonly from the GIT; also from kidney)
- Normally bicarbonates is produced in pacreatic juice bicarbonate is reabsorbed in are resorbed in small intestine.
- **Loss of cations**, predominantly Na+ (compensated by decrease of HCO3)
- **Decreased pH** (increased H+) **pCO_2 is normal, negative BE** ([HCO3-]);
- Excessive production of acids leads to **high AG** (useful in dif. dg.of MAC). Elevated loss of bicarbonates has **normal AG**

Metabolic acidosis

- loss of H^+ from the body or a gain in HCO_3-. In its pure form, it manifests as **alkalemia** (pH >7.40).

Main acid-base balance disorders

		pH	P_aCO_2	HCO_3^-	Therapy
Respiratory acidosis	Uncompensated	↓	↑	**N**	NA HCO3, KHCO3,
Acute RAC Chronic RAC	Compensated	N ↓	↑	↑ ↑↑	THAM
Respiratory alkalosis	Uncompensated	↑	↓	**N**	Rebreathing, bag wet
Acute RAL Chronic RAL	Compensated	N ↑	↓	↓ ↓↓	towel, NH4Cl, Arginin hydrohloride
Metabolic acidosis	Uncompenated	↓	**N**	↓	Hyperventilation,
	Compensated	N↓	↓	↓	NAHCO3, THAM
Metabolic alkalosis	Uncompenated	↑	**N**	↑	Hypoventilation
	Compensated	N↑	↑	↑	

Metabolic acidosis

1) Lactic acidosis - anaerobic carbohydrate metab.

- **hypoxia - hypoxic or anemic;** tissues process glucose in **anaerobic glycolysis, pyruvate** is metabolized into **lactate.**
- shock or overdose of **biguanides** (metformin),

2) Ketoacidosis - overproduction of ketone bodies (acetoacetic acid and β-hydroxybutyric acid) excessive fatty acid catabolism in lack of glycolyis

- insulin deficiency in **diabetes mellitus I.type** (ketosis prone) ; **starvation** (afer 3-4 day)

3) Exogenous or drug induced

- **Alcohol intoxication** (e.g. ethanol, methanol, ethyleneglycol) are metabolised to strong organic acids (formic acid, oxalic acid).
- Overdose of **salicylates** (Aspirin poisoning), sotbitol, paralaldehyde intox.

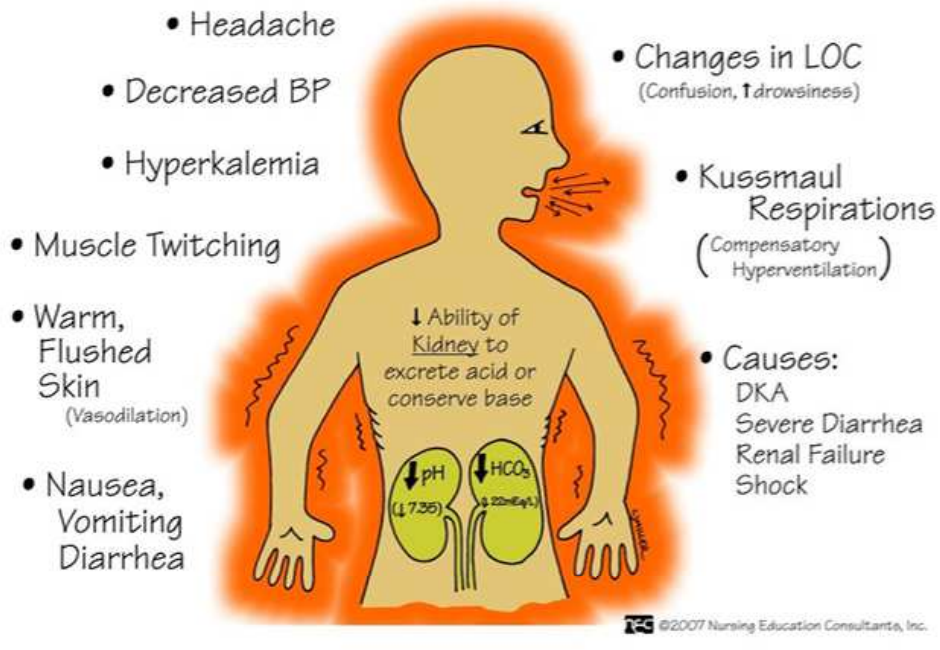
4) Renal acidosis

- Acute renal failure = **oliguria** – cummulation of acids (sulphates, phosphates, other anions)
- Chronic renal failure + tubulopathies = (no kidney recycle HCO_3- + no de-novo production of HCO_3-
- Renal tubular acidosis - loss of HCO_3- in the kidneys ; carbonic anhydrase inhibitors (acetazolamide)

5) Loss of HCO3- in GIT (pancreatic juice rich in HCO_3^- neutralizes acidic chyme from stomach)

- Heavy diarrhoea
- Intestinal malabsorption (short intestine syndrome; surgery)

Manifestations associated with metabolic acidosis



- Compensation:

1) buffers,
2) **hyperventilation** (pCO_2 , pH) **Kussmaul acidotic breathing** (deep slow breathing bycentral stimulation by high H+ concentration).
3) kidney
a) **increased excretion of H+**
b) **new bicarbonate production** (intercalated cells type A). This results in **acidic urine.**

- Signs and symptoms of MAC metabolic alkalosis result from the body's attempt to correct the acid-base imbalance, primarily through hypoventilation.
- Irritability, Picking at bedclothes (carphology), Twitching, Confusion, Nausea, Vomiting, Diarrhea
- Cardiovascular abnormalities (i.e. atrial tachycardia).

Main acid-base balance disorders

		pH	P_aCO_2	HCO_3^-	Therapy
Respiratory acidosis	Uncompensated	↓	↑	N	NA HCO3, KHCO3,
Acute RAC Chronic RAC	Compensated	N ↓	↑	↑ ↑↑	THAM
Respiratory alkalosis	Uncompensated	↑	↓	N	Rebreathing, bag wet
Acute RAL Chronic RAL	Compensated	N ↑	↓	↓ ↓↓	towel, NH4Cl, Arginin hydrohloride
Metabolic acidosis	Uncompenated	↓	N	↓	Hyperventilation,
	Compensated	N↓	↓	↓	NAHCO3, THAM
Metabolic alkalosis	Uncompenated	↑	N	↑	Hypoventilation
	Compensated	N↑	↑	↑	

Metabolic alkalosis

1) **Loss of hydrogen ions acids or anions (chlorides or proteins).** Loss of anions is often over compensated by replenishing of other anions, predominantly bicarbonates $HCO3^-$.

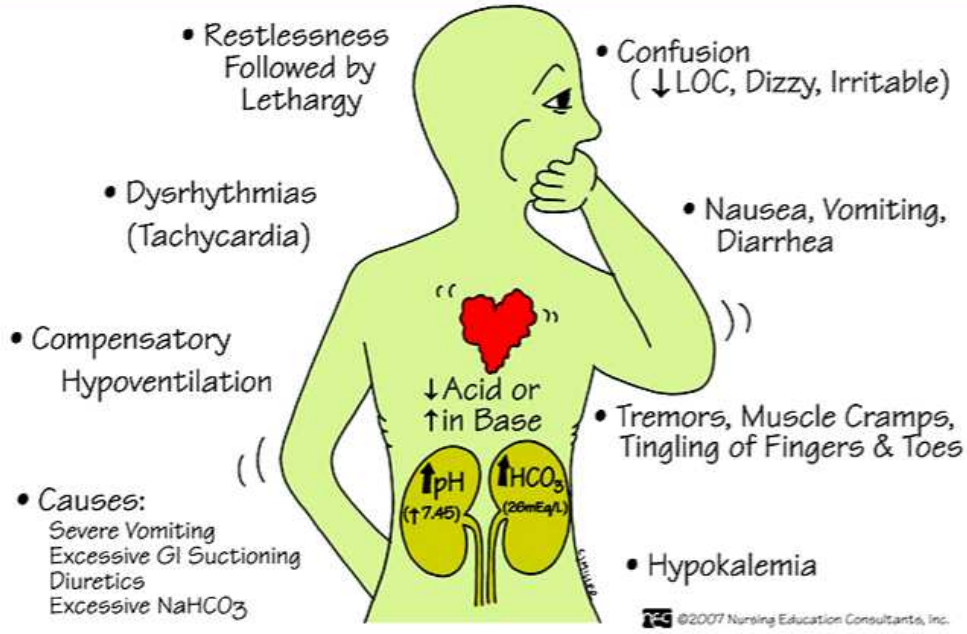
- Shift of hydrogen ions into the intracellular space
- **Vomiting** – loss of HCl in gastric juice (thus loss of H^+) leads metabolic state denoted as ***hypochloremic alkalosis***
- **Diuretics** - (e.g. furosemide) some may lead to loss of K^+ H^+ and Cl^-
- **Hyperaldosteronism.** High aldosterone increases retention of Na^+ C^{l-} and H_2O and urine loss of K^+ and H^+ - metabolic reaction known as ***hyperchloremic alkalosis***

2) **Bicarbonate overproduction**

- **Exogenous alkali intake** (e.g. iatrogenic - alkalising medication, bicarbonate infusion) **;**
- **Endogenous alkali load** (massive osteolysis)
- **Hypoproteinemia** – proteins are anions thus decreased protein concentration is compensated by increased bicarbonate concentration (i.e. bicarbonates replenish missing anions). Hypoproteinemia is caused by **liver failure**, **nephrotic syndrome** or **malnutrition.**

3) **Congenital alkalosis**

Manifestations associated with metabolic alkalosis



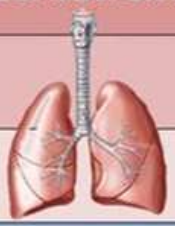
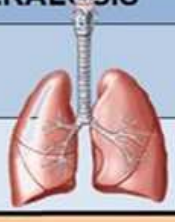
- Signs and symptoms of MAC metabolic alkalosis result from the body's attempt to correct the acid-base imbalance, primarily through **hypoventilation.**
- **Irritability,** Picking at bedclothes (carphology), **Twitching, Confusion, Nausea**, Vomiting, Diarrhea
- Cardiovascular abnormalities, **paliptations** (i.e. atrial tachycardia).

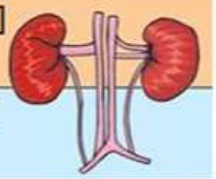
Mixed disturbances of acid-base balance

- Mixed disturbances of acid-base balance are **quite common.**
  (1) **combination of two** or **more basic disturbances of acid-base balance,**
  (2) **combination of more causes** that cause the same acid-base balance disturbance,
  (3) or both
- **hypoventilation** that leads not only to the **respiratory acidosis because less CO2 is exhaled** but also to the **metabolic acidosis because less O2 is delivered to the tissues.**

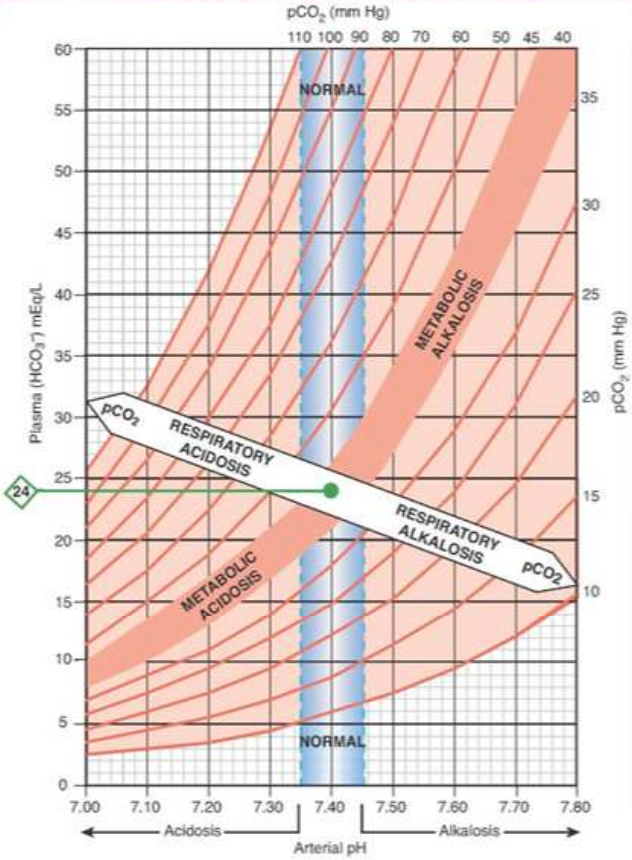
- **If all three values (pH, PaCO2, and HCO3-) are out of range it is classified as "combined acidosis/alkalosis"**
- Examples: pH = 7.49 , PaCO2 = 32 mmHg , HCO3- = 30 mmHg
  Combined alkalosis (pH = alkalotic range, PaCO2 = alkalotic range, HCO3- = alkalotic range)
- pH = 7.26, PaCO2 = 52 mmHg, HCO3- = 16 mmHg
  Metabolic acidosis (pH = acidotic range, PaCO2 = acidotic range, HCO3- = acidotic range)

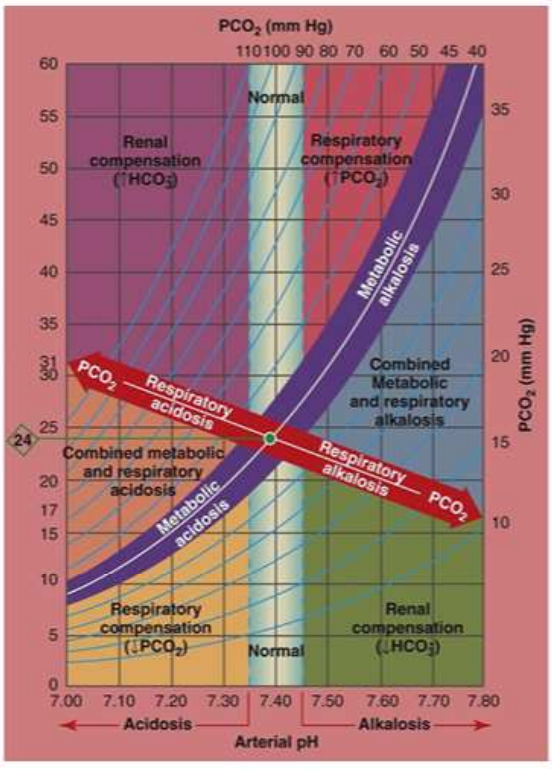
Compensatory responses in acid-base disturbances

Disturbance	Response	Expected Change
RESPIRATORY ACIDOSIS		
 **Acute**	↑ [HCO_3^-]	1 mmol/L/10mmHg increase in $PaCO_2$
Chronic	↑ [HCO_3^-]	4 mmol/L/10mmHg increase in $PaCO_2$
RESPIRATORY ALKALOSIS		
 **Acute**	↓ [HCO_3^-]	2 mmol/L/10mmHg decrease in $PaCO_2$
Chronic	↓ [HCO_3^-]	4 mmol/L/10mmHg decrease in $PaCO_2$
METABOLIC ACIDOSIS	↓ $PaCO_2$	1.2 x the decrease in [HCO_3^-]
METABOLIC ALKALOSIS	↑ $PaCO_2$	0.7 x the increase in [HCO_3^-]

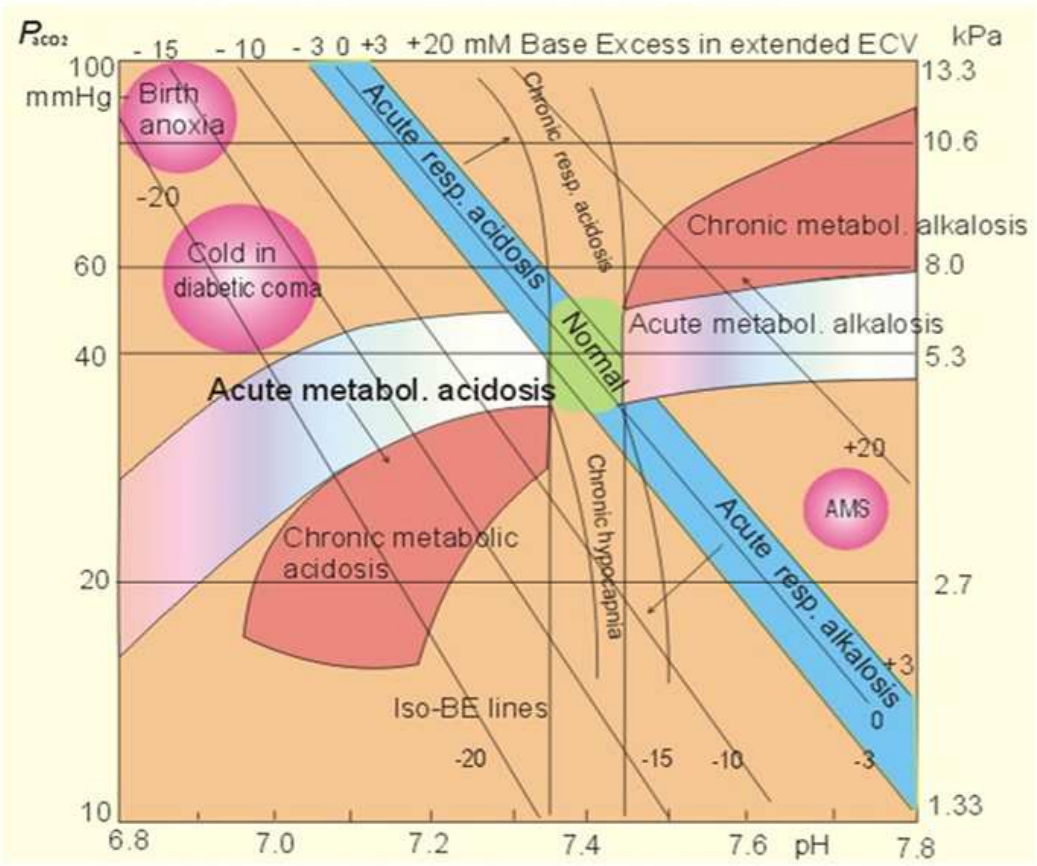


Nomogram – 9 variants of Van Slyke





Nomogram


P_{aCO_2}
- 15
- 10
- 3
0
+3
+20 mM Base Excess in extended ECV
kPa
100
mmHg
Birth anoxia
-20
Cold in diabetic coma
60
40
20
10
13.3
10.6
8.0
5.3
2.7
1.33
Acute resp. acidosis
Chronic resp. acidosis
Chronic metabol. alkalosis
Acute metabol. alkalosis
Normal
Acute metabol. acidosis
+20
AMS
Chronic metabolic acidosis
Chronic hypocapnia
Acute resp. alkalosis
+3
0
Iso-BE lines
-20
-15
-10
-3
6.8
7.0
7.2
7.4
7.6
pH
7.8