Acid Base and Respiratory Disorders:

Getting the Most Information from Blood Gas Analysis

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Outline

Acid base and Respiratory physiology

- Normal homeostatic mechanisms

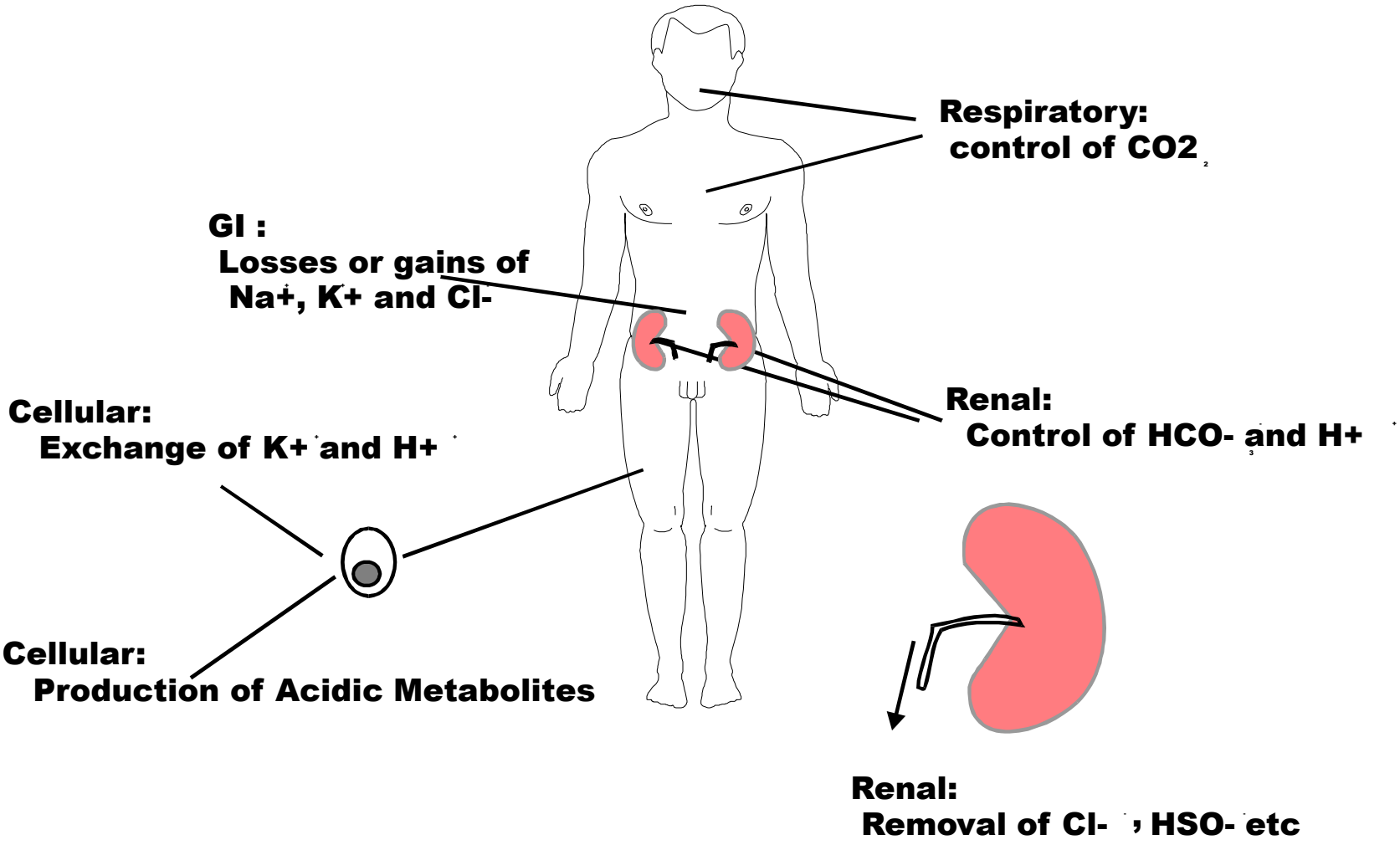
Acid base and Respiratory Pathologies

Compensation mechanisms

Cases

- Putting it all together

Acid - base Homeostatic Mechanisms



Buffering Systems

	pKA
• Haemoglobin	8.2
• Bicarbonate	6.1
• Phosphate	6.1
• Proteins	7
• Ammonia	9.2
• Misc organic acids	4 - 6

Henderson-Hasselbalch Equation

$$H^+ + HCO_3^- \rightleftharpoons H_2CO_3 \rightleftharpoons CO_2 + H_2O$$

$$pH = pK + \log\left[\frac{[HCO_3^-]}{pCO_2 \times \alpha}\right]$$

$[H^+]$ homeostasis requires a balance between

H^+ production and regeneration of HCO_3^-

Acid base Homeostasis

Respiration

Properties of Oxygen & Carbon dioxide

CO_2 Buffering > O_2

CO_2 Permiability >> O_2

- Pa CO_2 ~ PA CO_2

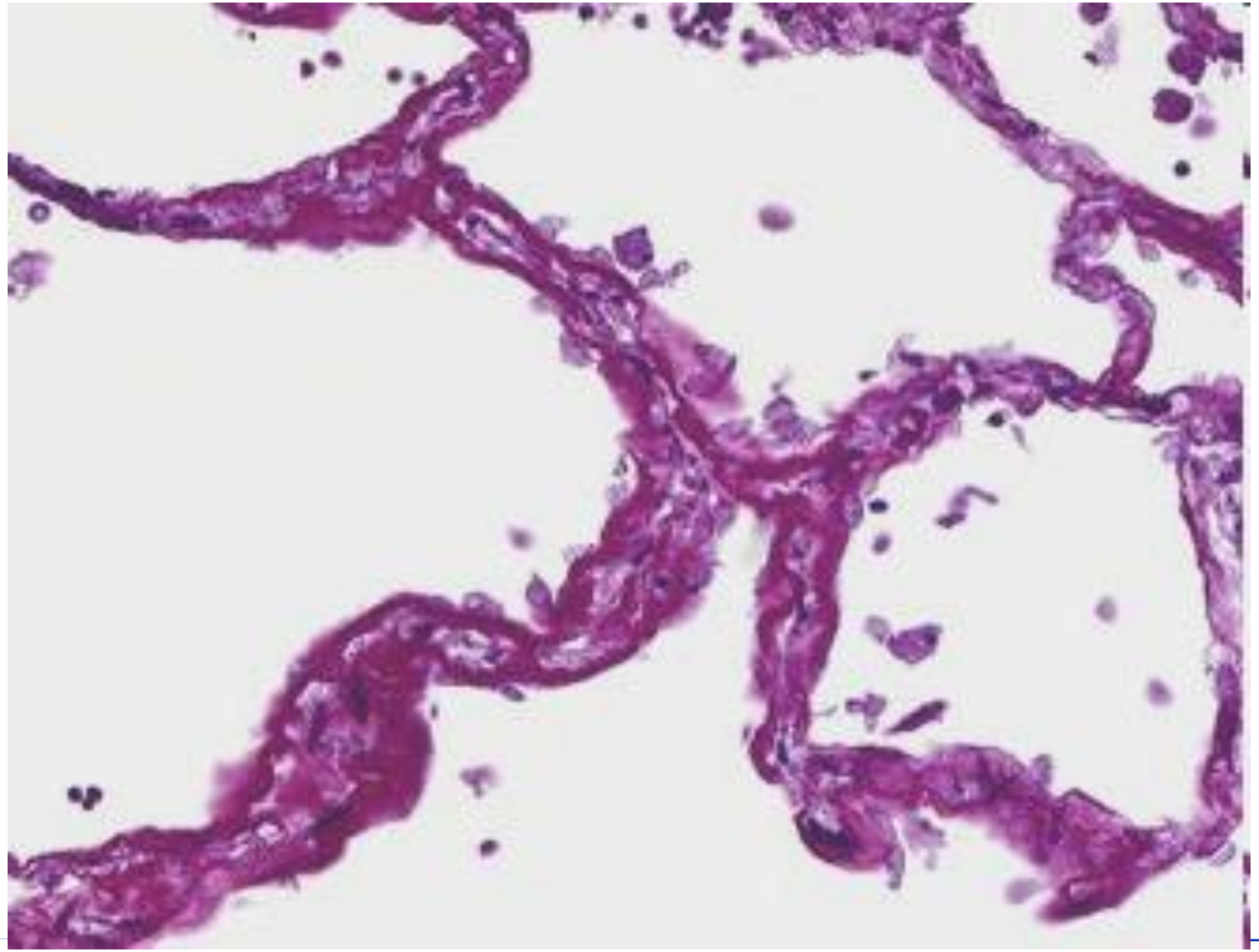
Arterial PO_2 = 90 mmHg PCO_2 = 40 mmHg

Venous PO_2 = 37 mmHg PCO_2 = 46 mmHg

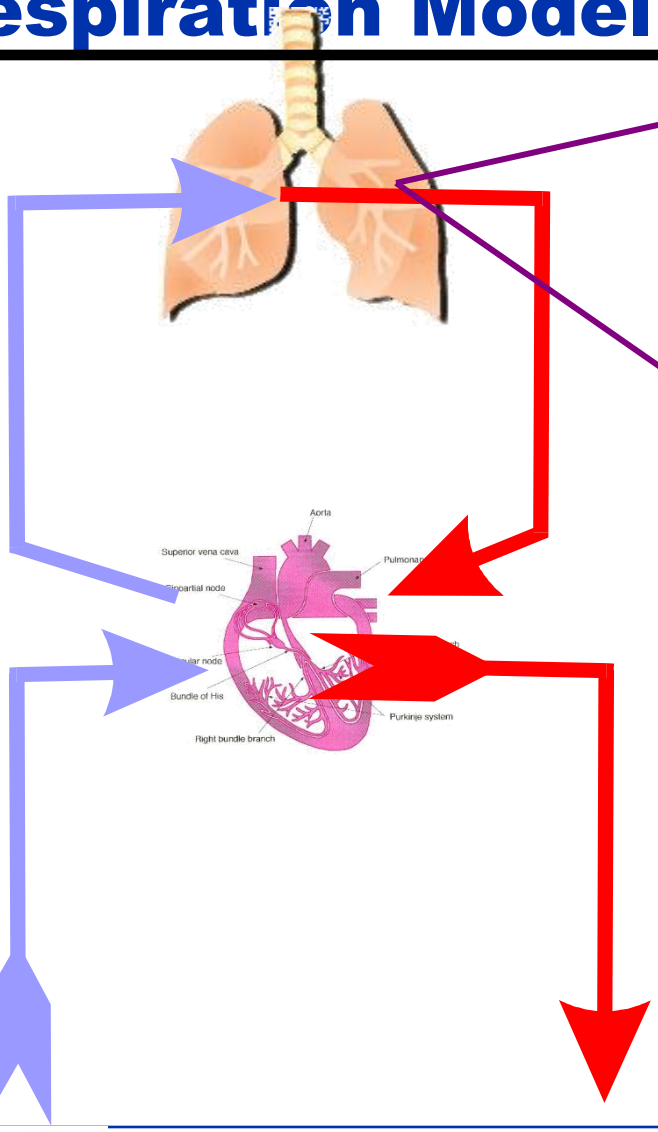
Arterial O_2 content = 20 %v/v CO_2 content = 49 %v/v

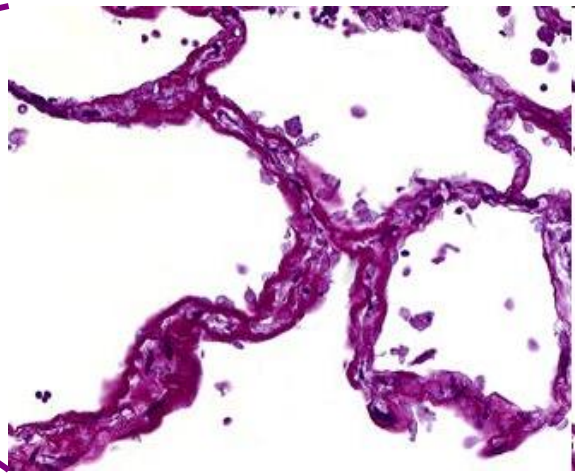
Venous O_2 content = 15 %v/v CO_2 content = 53 %v/v

Gas Exchange

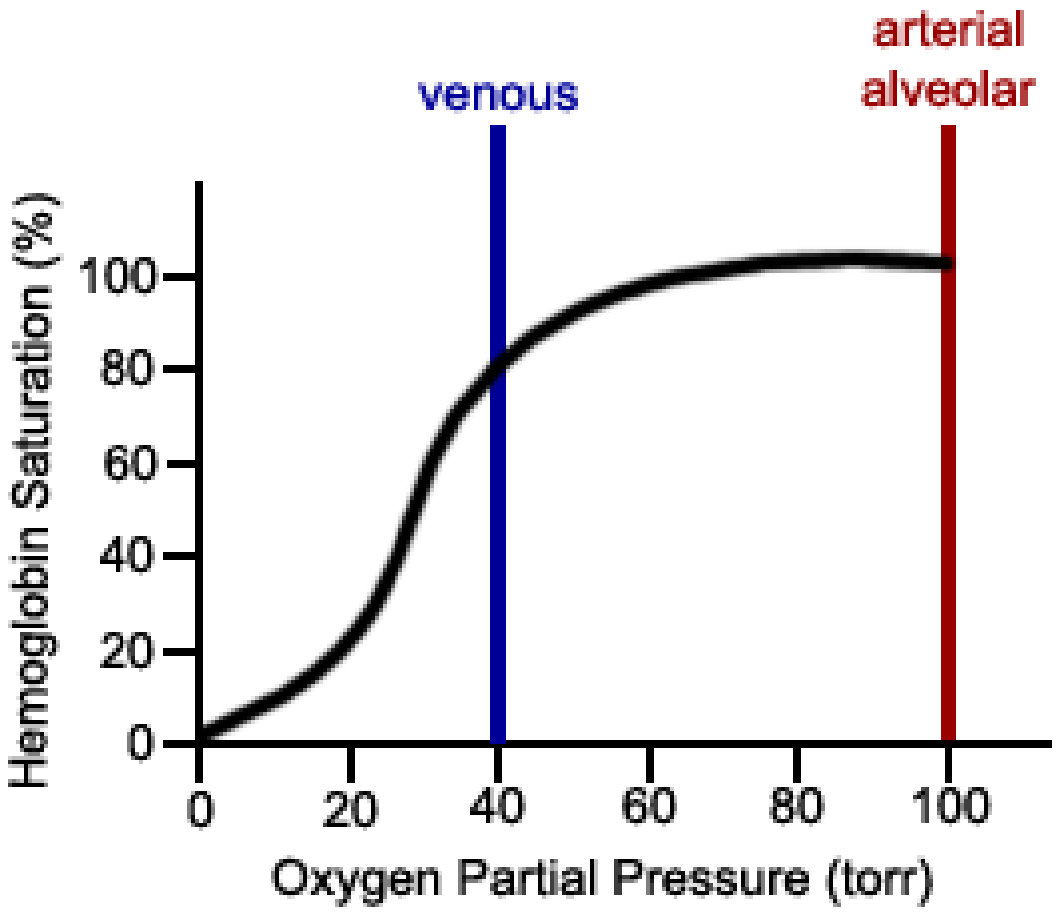


Respiration Model





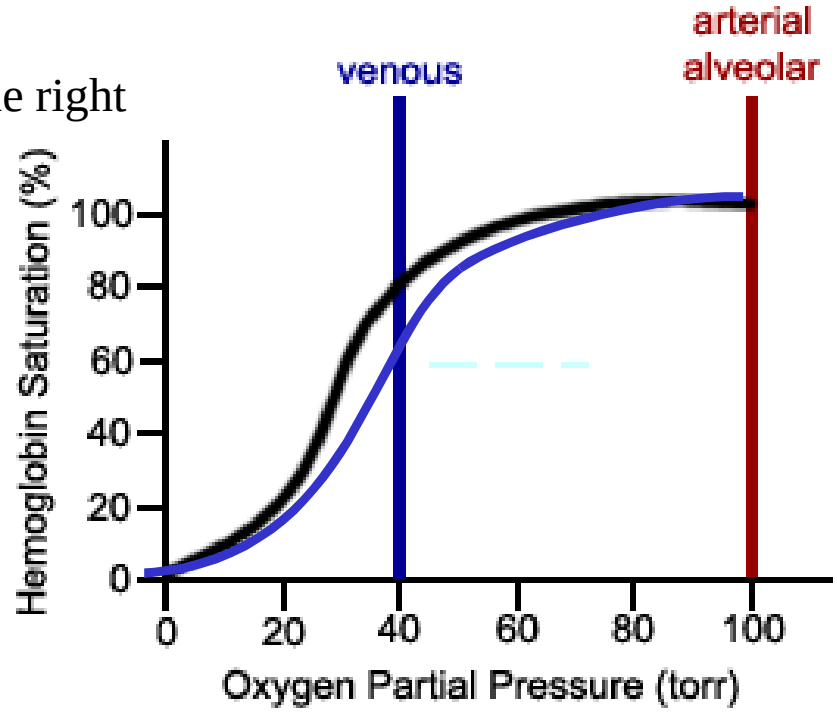
Hemoglobin Oxygen Dissociation Curve



O2 and CO2 Interdependence

⇧PCO2 shifts the O2 dissociation curve to the right

the Bohr effect.



- ⇧ temperature also shifts the curve to the right.

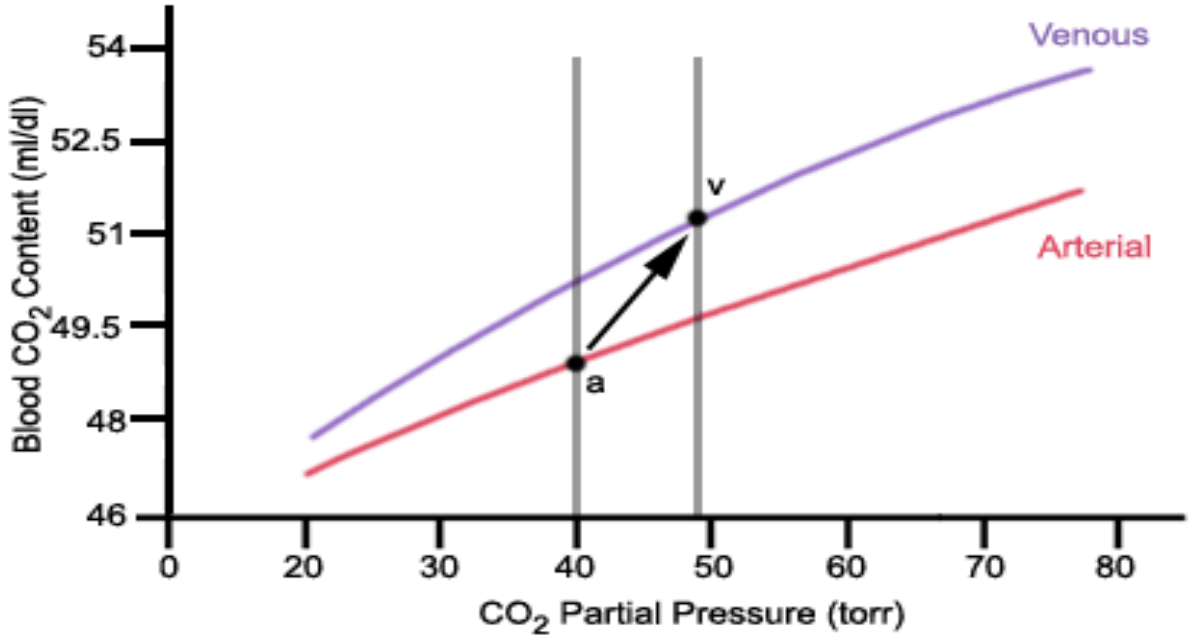
During exercise these effects increase the amount of O2 released to the tissues while having little effect on the arterial O2 content leaving the lungs.

CO_2 Transport by Hemoglobin

The Haldane Effect

-Oxygen binding to HgB decreases CO_2 affinity

→ Arterial HgB has less capacity for CO_2 than Venous HgB



Calculating Cardiac output:

The rate of O2 consumption is equal to the amount of O2 taken up by each unit volume of blood times the rate at which these units flow through the lungs, thus

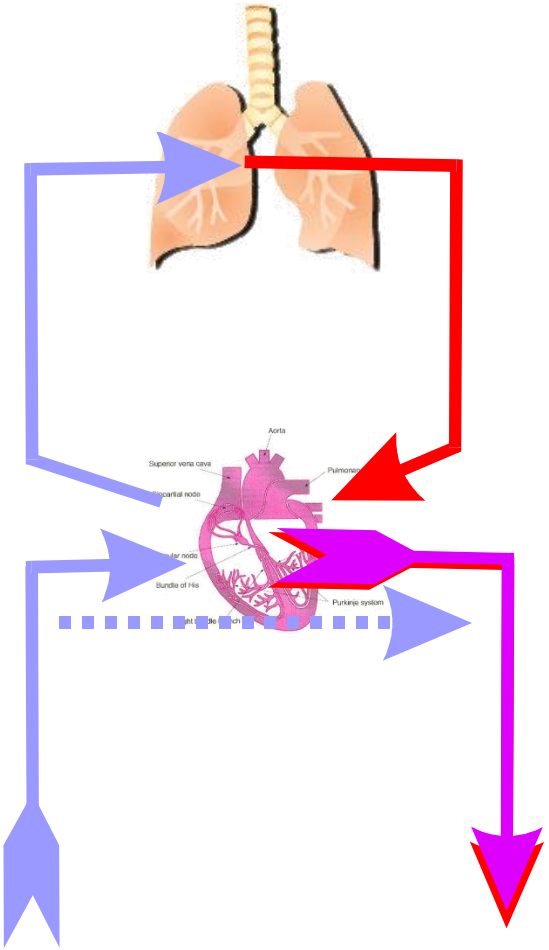
the Fick Equation $\dot{V}_{O2} = Qt \times (C_{aO2} - C_{vO2})$

- where CaO2 is the arterial O2 content (measured in litres of O2 at standard temperature and pressure per litre of blood), and
- CvO2 is the mixed venous blood oxygen content.

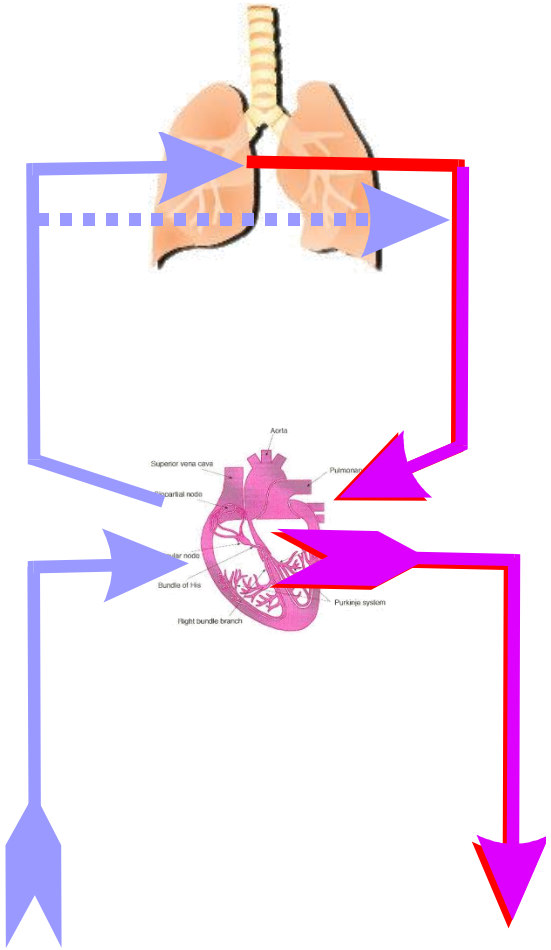
Calculating Cardiac output:

- Assumes: Cardiac Output = Pulmonary Perfusion rate
  - Qt = $V_{O2}/(Ca_{O2} - Cv_{O2})$ **Fick Equation rearranged**
- Measure Arterial and Venous Blood Gases and Hemoglobin
- O_2 Content = % Saturation X [Hgb]*1.34 + Dissolved O_2 (0.003 X PO2)
- V_{O2} = Ventillation rate X $\%O_2$

Respiration Anatomical Shunt

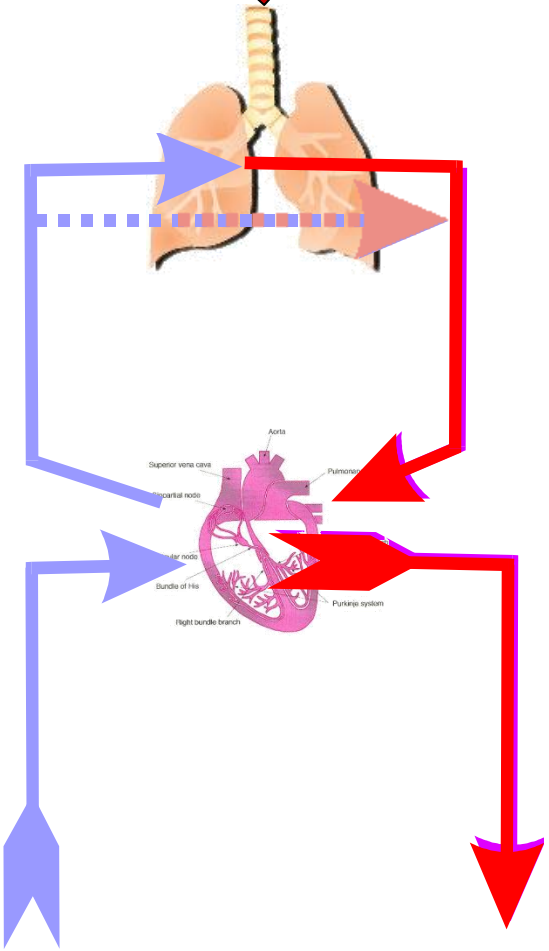


Respiration Physiological Shunt

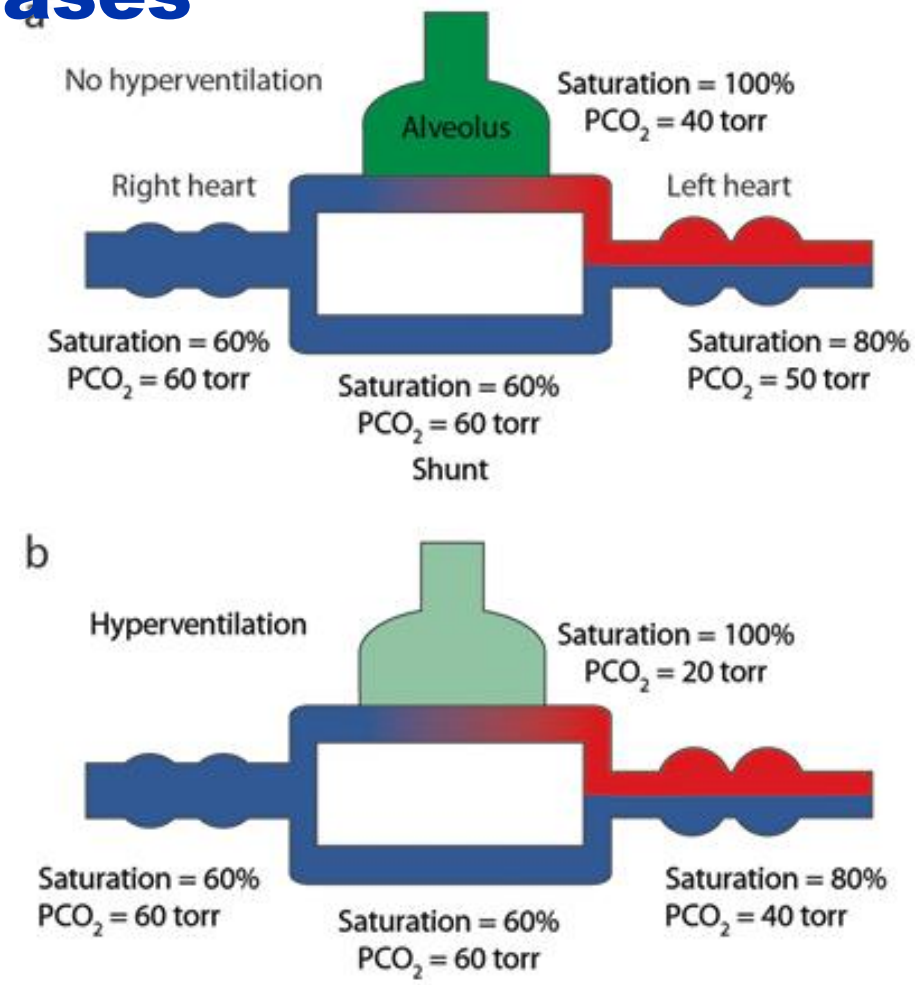


Respiration Physiological Shunt

100 % O2



Effect Of Venous Shunting on Arterial Blood Gases



REFERENCE VALUES FOR BLOOD GASES

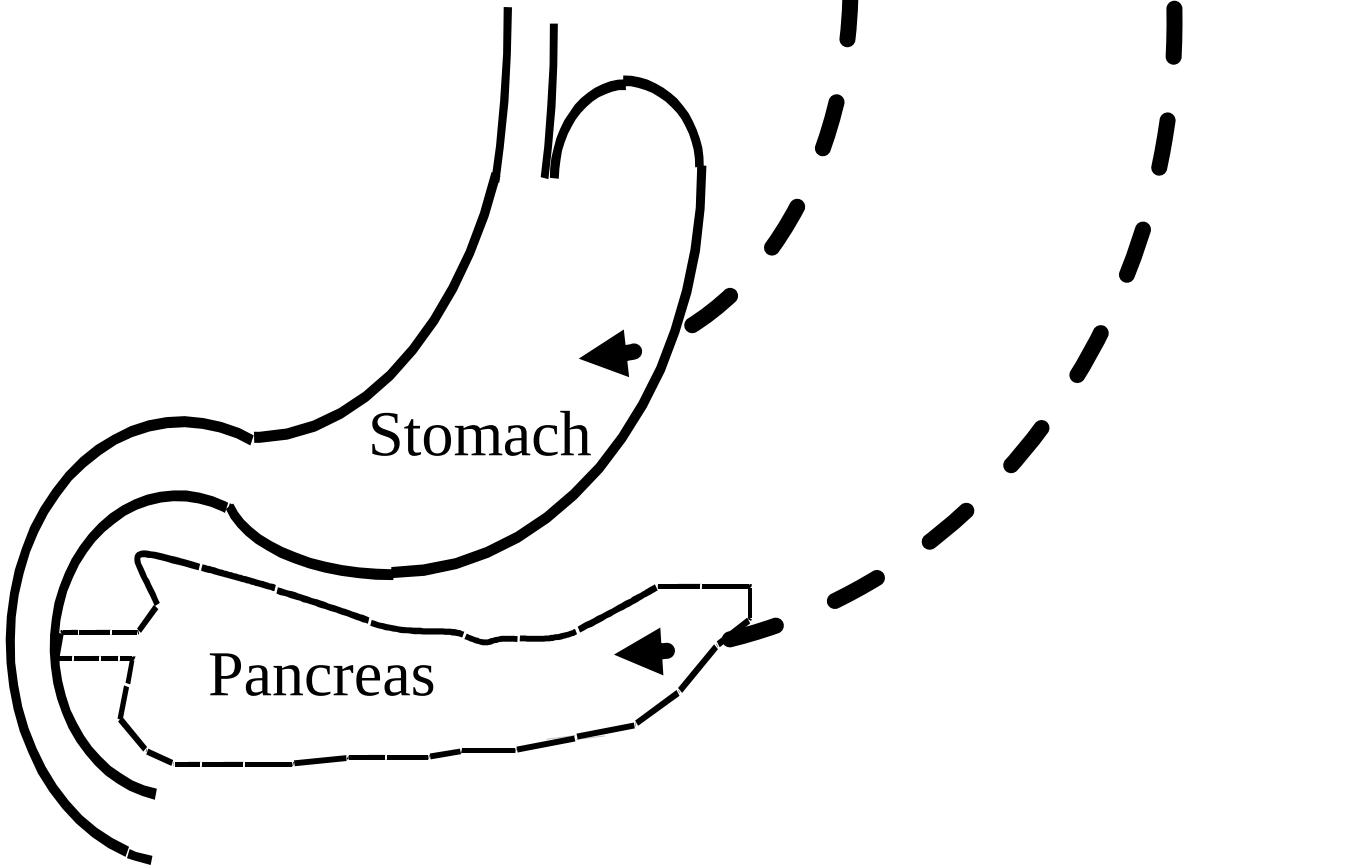
ANALYTE	ARTERIAL	VENOUS
p H	7.36 - 7.44	7.31 - 7.41
[H +]	44 - 36 nmol/L	49 - 39 nmol/L
p CO_2	38 - 42 mmHg	35 - 40 mmHg
p O_2	85 - 100 mmHg	35 - 40 mmHg

Acid base Homeostasis

Metabolic

Acid-Base in the G-I Tract

$$H_2O + CO_2 \longrightarrow H^+ + HCO_3^-$$



Protein Metabolism and H^+ Homeostasis

- amino-acids are catabolised to CO_2 ,H_2O ,NH_4^+ ,HCO_3^-

$$CO_2 + 2\ (NH_4^+) \rightarrow \text{Urea} + 2H^+$$

- Urea synthesis is energy dependent
- protein catabolism produces a slight excess of NH_4+

Miscellaneous sources of H^+

- Extra H^+ is derived from
  - sulphur containing a/a
  - dietary organic acids
  - organic acid metabolic products
- Excess NH_4^+ is excreted in urine

FIXED ACIDS

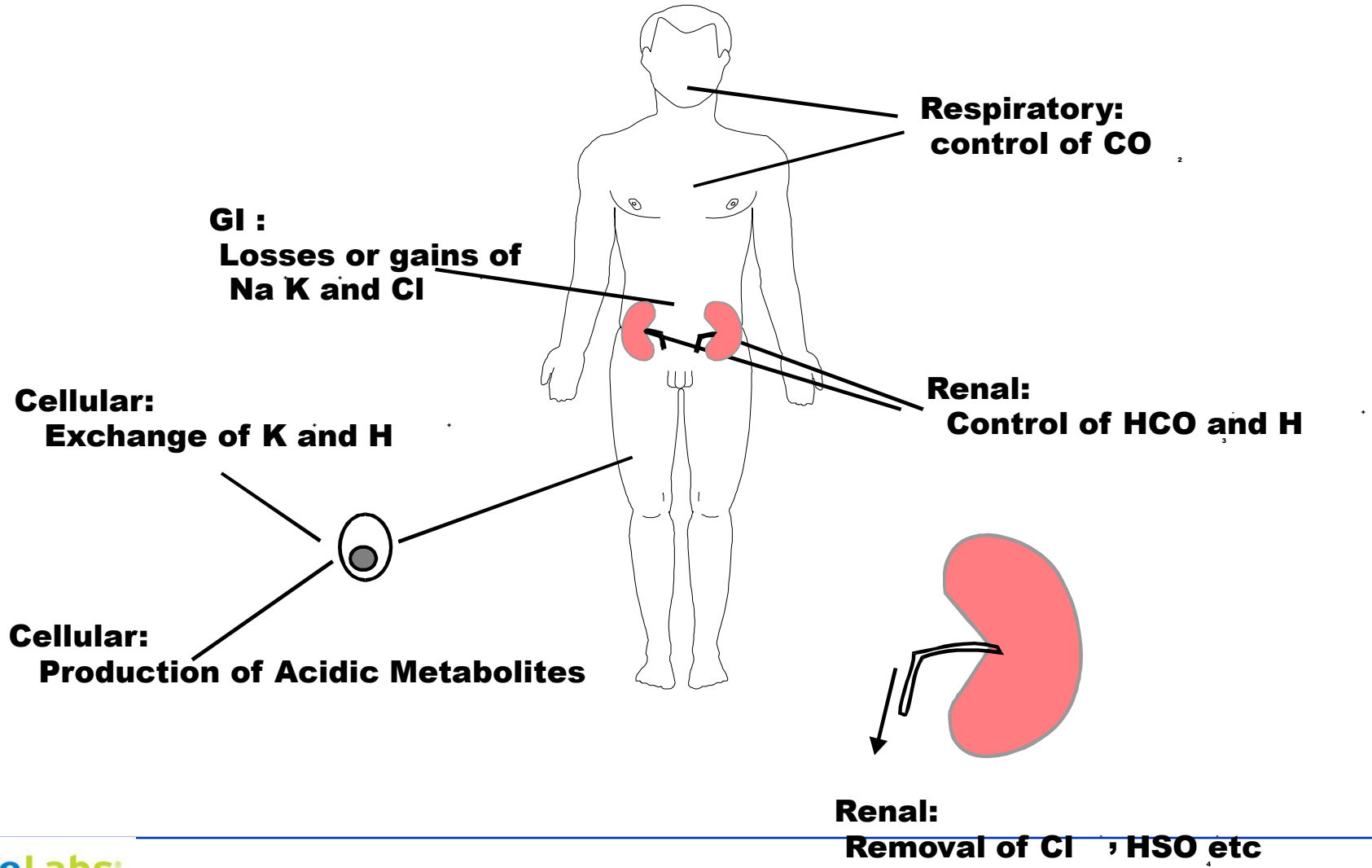
$$\text{Cysteine, methionine} \rightarrow \text{sulfate} + H+$$

$$\text{Phospholipids} \rightarrow \text{phosphate} + H+$$

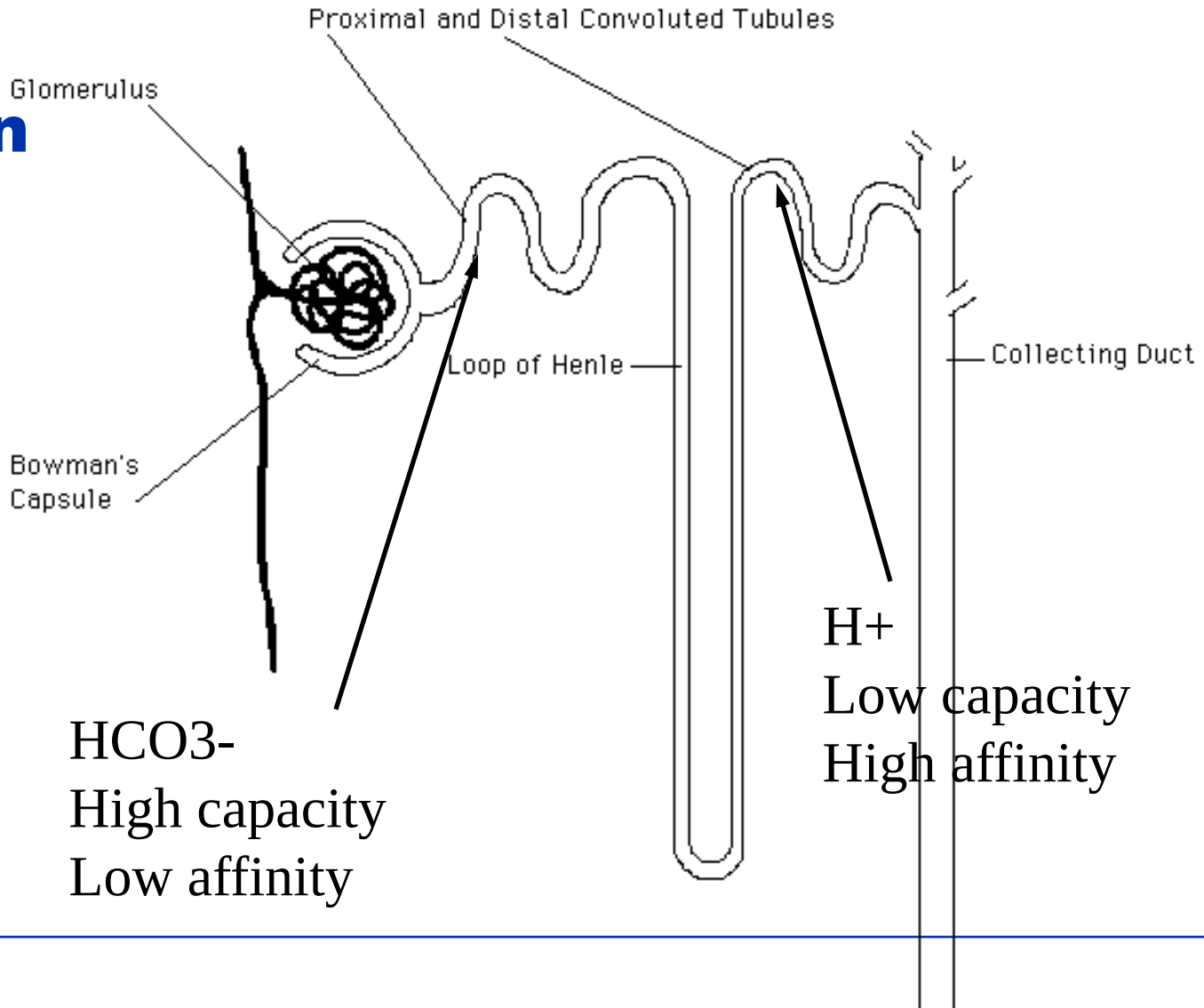
$$\text{Glucose} \xrightarrow{\text{anaerobic}} \text{lactate} + H+$$

ABOUT 50 mmoles
PRODUCED AND EXCRETED DAILY

Acid - Base Homeostatic Mechanisms



Nephron



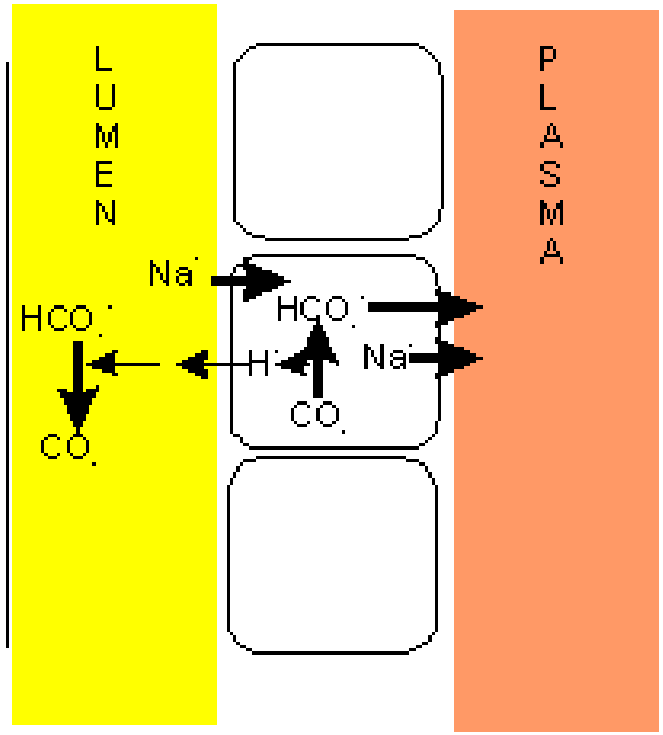
HCO3-
High capacity
Low affinity

H+
Low capacity
High affinity

Renal Control of Acid Base Balance

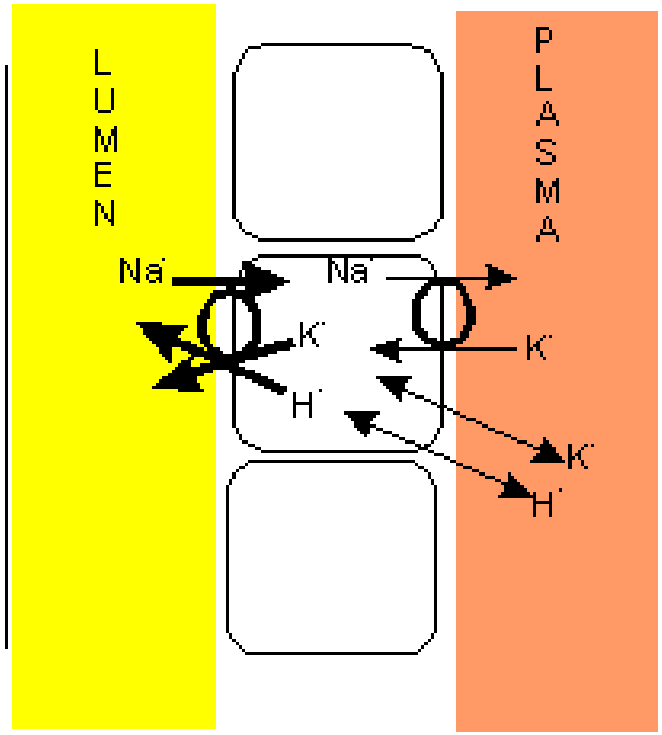
Proximal Tubule

Bicarbonate Reabsorption



Distal Tubule

Proton Excretion



Renal Ammoniagenesis

Increased NH_4^+ excretion in acidosis

glutamine → 2 oxo-glutarate + NH_4^+

glutaminase stimulated over hours/days

ascending loop of Henle

NH_4^+ absorbed and NH_3 excreted into collecting duct

H^+ secreted back into Loop of Henle and reclaims HCO_3^-

Acid-Base Pathology

Metabolic
- Acidosis ⇩ HCO_3^-
- Alkalosis ⇧ HCO_3^-

Respiratory
- Acidosis ⇧ CO_2
- Alkalosis ⇩ CO_2

Metabolic Acidosis

$H^+ + HCO_3^- \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$

- General Causes
  - Increased H^+ formation
  - Reduced renal H^+ excretion
  - Loss of bicarbonate

Metabolic Alkalosis

$H^+ + HCO_3^- \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$

- General Causes
  - Renal increased H+ excretion in Hypokalemia
  - Administration of HCO_3^-

Respiratory Acidosis

$H^+ + HCO_3^- \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$

CO_2 retention due to

- inadequate ventilation
- obstructive lung disease
- inadequate perfusion

Respiratory Alkalosis

$H^+ + HCO_3^- \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$

CO_2 reduction due to

-excessive ventilation

- CNS
  - Encephalopathy
  - Local Acidosis of Respiratory Center
- Pneumonia & other obstructive lung diseases
  - **Paradoxical?**

Metabolic acidosis - causes

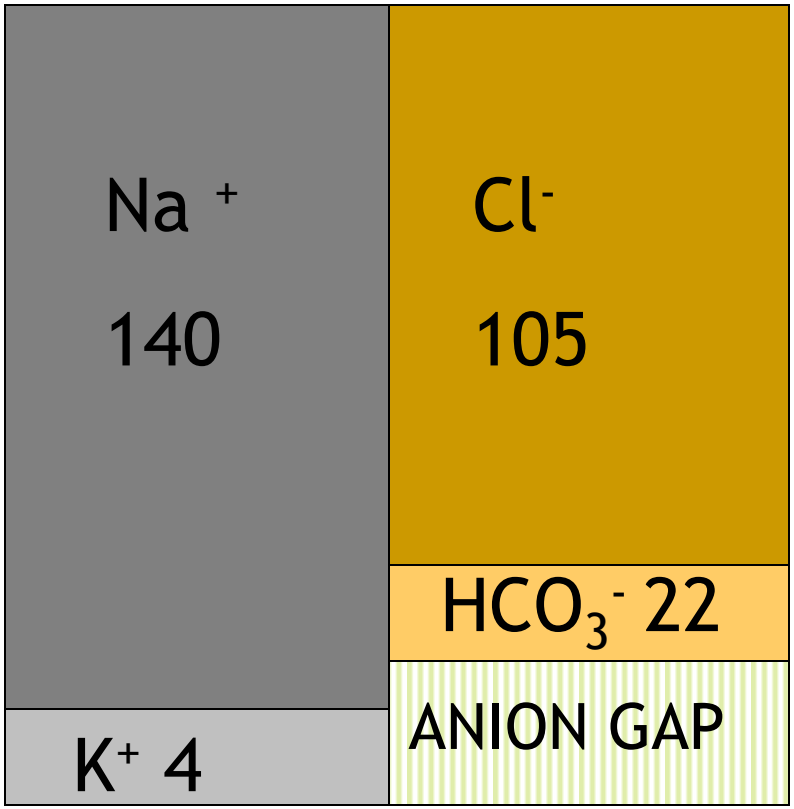
Increased H^+ formation

Acid ingestion

Reduced renal H^+ excretion

Loss of bicarbonate

ANION GAP



$$\text{ANION GAP} = [Na^+ + K^+] - [Cl^- + HCO_3^-] = 17$$

High Anion Gap Metabolic Acidosis

- Renal Failure
  ⇩⇩ GFR ⇨ ⇧ Hard Acids
- Ketoacidosis ⇧ Organic Acids
- Lactic Acidosis " "
- Toxins
  - Salicylate " "
  - Alcohols " "
  - Paraldehyde " "

Diabetic keto-acidosis

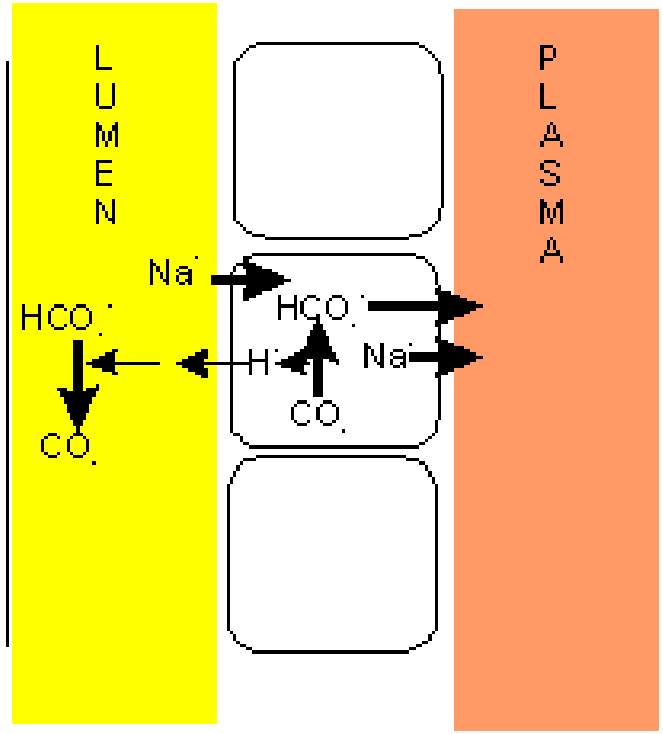
- Hyperglycemia, osmotic diuresis
- Hyperketonemia, increased FFA

→ lead to acidosis

Renal Control of Acid Base Balance

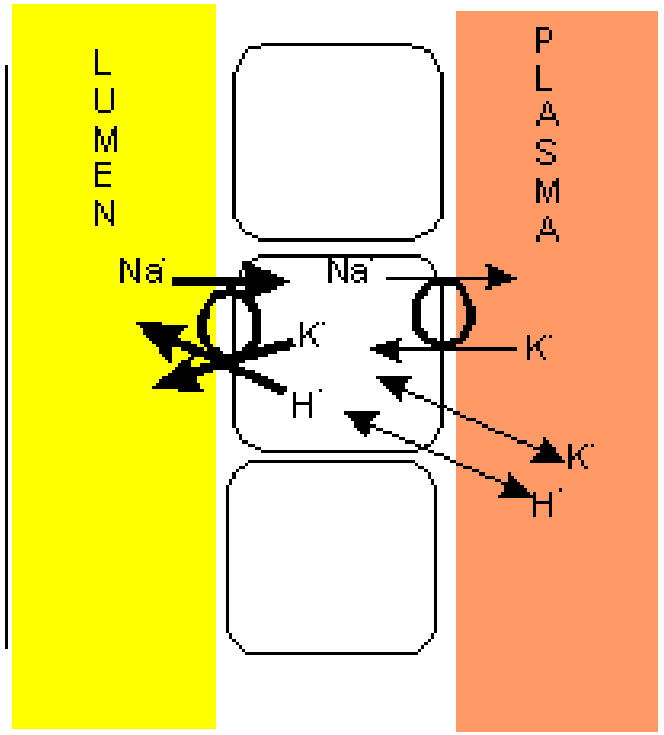
Proximal Tubule

Bicarbonate Reabsorption



Distal Tubule

Proton Excretion



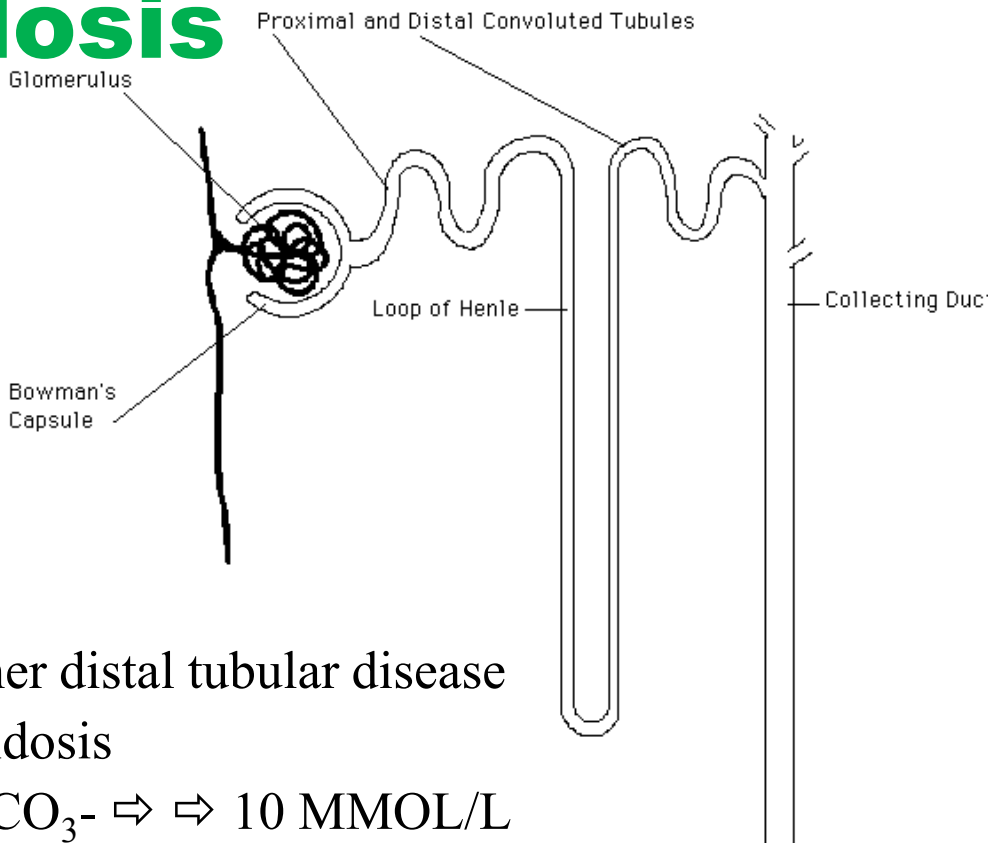
Normal Anion Gap Metabolic Acidosis

Normal Anion Gap (Hyperchloremic)

⇧ Chloride Load or Retention

- Ammonium Chloride ingestion ⇧ K+
- Obstructive Uropathy ⇧ K+
- Ureterosigmoidostomy ⇩ K+
- Obstructive Ileal Bladder ⇩ K+

Normal Anion Gap Metabolic Acidosis



- ⇧ Bicarbonate Loss
  - ⇩ Aldosterone
  - K+ sparing diuretics
  - interstitial nephritis or other distal tubular disease
  - proximal renal tubular acidosis
    - self limiting when HCO_3- ⇨ ⇨ 10 MMOL/L
  - distal renal tubular acidosis
    - UNLIMITED ⇨ ⇨ severe acidosis

Proximal RTA

Distal RTA

HCO3-
HCO3-
Proximal Tubule
Bicarbonate Reabsorption
LUMEN
PLASMA
Na+
HCO3-
H+
CO2
HCO3-
Na+
CO2
HCO3-
Distal Tubule
Proton Excretion
LUMEN
PLASMA
Na+
Na+
K+
K+
H+
K+
H+

Renal Failure

REDUCED NUMBER OF NEPHRONS

→ Increased volume load per nephron

Increased bicarbonate loss

Reduced NH_4^+ excretion

- NH_4^+ to liver for urea + H^+ synthesis
- reduced NH_4^+ derived from glutamine

Post Hypocapnic Acidosis

Hypocapnia (⇩CO2) → Alkalosis

Compensation is Metabolic Acidosis

- Loss of K+ in Distal Tubule

Post Hypocapnia (N – CO2)

- residual Acidosis from compensation

Causes of Metabolic Alkalosis

Chloride Depletion

- Gastric - vomiting
  - some severe diarrhoea

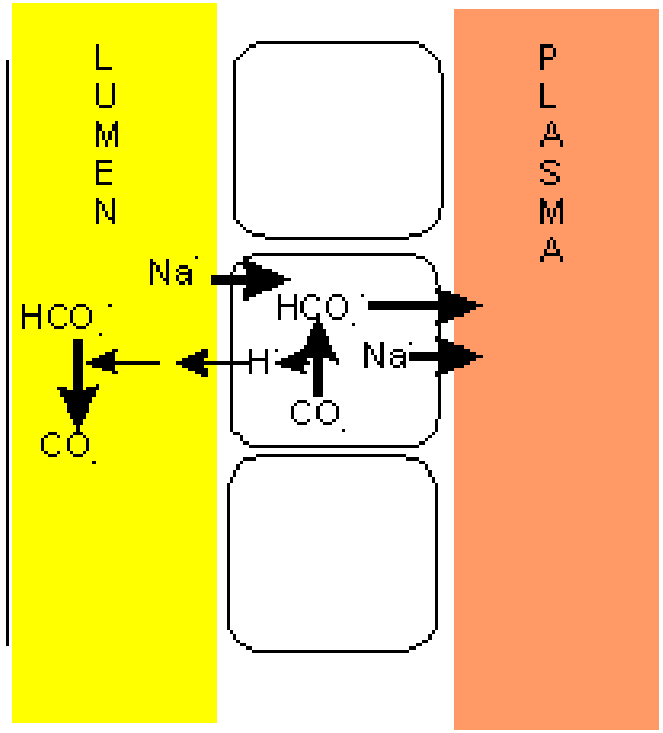
Potassium Loss

- Hyperaldosteronism
- Diuretics
- Bicarbonate administration

Renal Control of Acid Base Balance

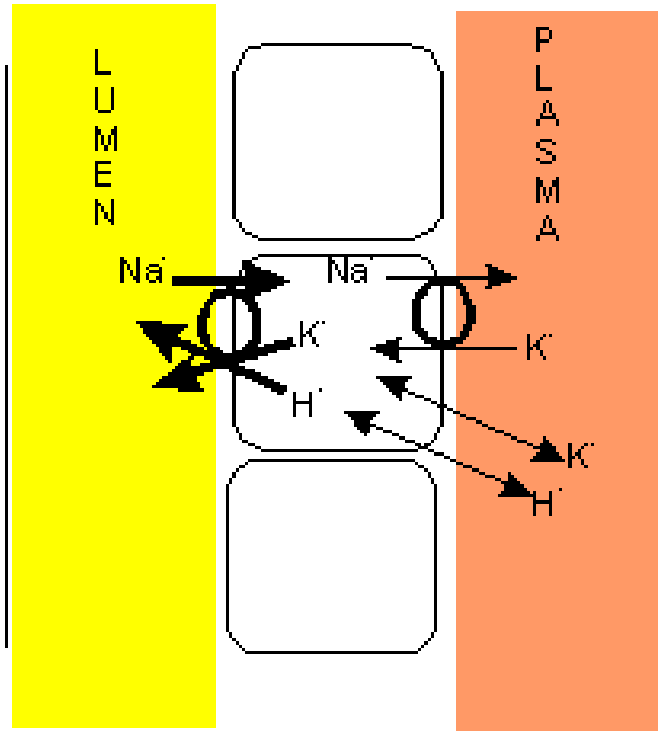
Proximal Tubule

Bicarbonate Reabsorption



Distal Tubule

Proton Excretion



Compensation

Objective pH → Normal

- Seldom achieve full compensation
- **Never** achieve over compensation
- Blood Gases identify
  - 1º Disorder
    - Acidosis or Alkalosis
    - Respiratory or Metabolic
  - Compensation
    - Appropriate
    - Inappropriate
  - Other disorder
    - 2º disturbance
      - or
    - **"Mixed acid-base disturbance"**

Compensation - Mechanisms

Respiration ⇧

→ ⇩ pCO_2 ⇩ pH

Renal Mechanisms

- Tubule

⇧ HCO_3^- excretion → ⇩ HCO_3^- ⇩ pH

⇧ H^+ excretion → ⇧ pH

NH_4^+ formation → ⇧ pH

Blood Gases

Measurement of:

- pH
- PCO2
- PO2

Calculation of [HCO3-]

Acid-Base Pathology

Metabolic

- Acidosis ⇩ HCO_3^-
- Alkalosis ⇧ HCO_3^-

Respiratory

- Acidosis ⇧ CO_2
- Alkalosis ⇩ CO_2

Respiratory Acidosis (Acute)

Compensation - **Metabolic Alkalosis**

Acute (10 minutes)

- $\mathbf{CO_2} + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + \mathbf{HCO_3^-}$
  ↘:Buffer
  $\mathbf{HCO_3^-}$ ⇧
- *Limit of compensation*

HCO_3^- → → 32 mmol/L

- If ***Measured*** $\mathbf{HCO_3^-} > 32$ ⇨ 1º Metabolic Alkalosis
- If ***Measured*** $\mathbf{HCO_3^-} < 23$ ⇨ 1º Metabolic Acidosis

Respiratory Alkalosis (Acute)

Compensation - Metabolic Acidosis

Acute (10 minutes)

- $\mathbf{CO_2} + H_2O \leftarrow H_2CO_3 \leftarrow H^+ + \mathbf{HCO_3^-}$

  ↖:Buffer $\mathbf{HCO_3^-}$ ⇩

- *Limit of compensation*

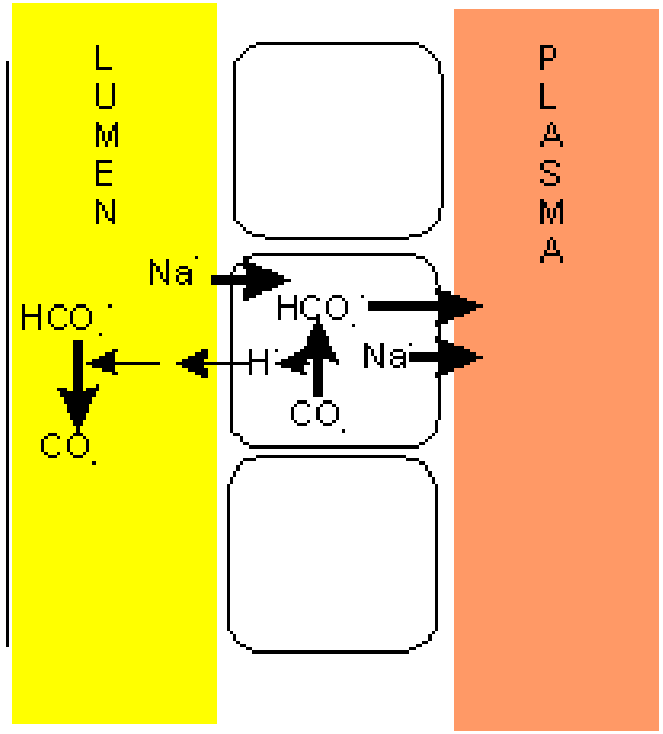
HCO_3^- → → 18 mmol/L

- If ***Measured*** $\boldsymbol{HCO_3^-}$ < 18 ⇨ 1º Metabolic Acidosis
- If ***Measured*** $\boldsymbol{HCO_3^-}$ > 23 ⇨ 1º Metabolic Alkalosis

Renal Control of Acid Base Balance

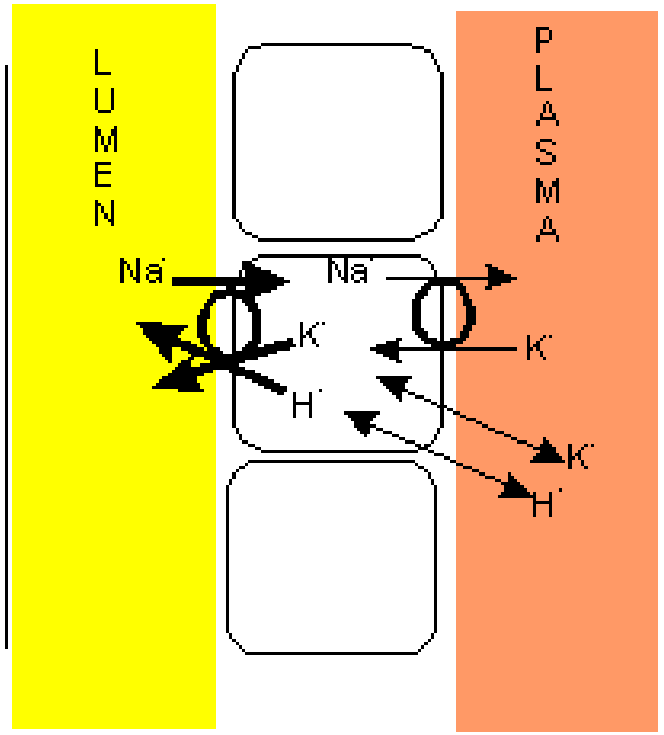
Proximal Tubule

Bicarbonate Reabsorption



Distal Tubule

Proton Excretion



Respiratory Acidosis (Chronic)

Compensation - **Metabolic Alkalosis**

Chronic (24- 96 hr)

- **Renal Reabsorbtion of Bicarbonate** **HCO_3^-** ⇧
- *Limit of compensation*

HCO_3^- → → 45 mmol/L

  - If ***Measured HCO_3^-*** > 45 ⇨ 1º Metabolic Alkalosis

- Normal Compensation
  - HCO_3^- = 0.43 X ***pCO2*** + 7.6 ±2

Respiratory Alkalosis: Chronic

Compensation - **Metabolic Acidosis**

Chronic (24- 96 hr <u>can fully compensate</u>)

- **Renal Loss of Bicarbonate** **HCO_3^- ⇩**
- *<u>Limit of compensation</u>*

  HCO_3^- → → 12 mmol/L

  - If ***Measured HCO_3^-*** < 12 ⇨ 1º Metabolic Acidosis
- Normal Compensation
  - HCO_3^- **=** 0.5 X ***pCO2*** + 5

Metabolic Acidosis

Compensation - **Respiratory Alkalosis**

- (H+ stimulates medulla oblongata)

Chronic (12 - 24 hr)

- ***pCO2*** ⇩

- *Limit of compensation*

pCO2 → → 10 mmHg

- If ***Measured*** ***pCO2*** < 10 ⇨ 1º Respiratory Alkalosis

- Normal Compensation

- pCO2 = 1.54 X HCO_3^- + 8.4 ±1.1

Metabolic Alkalosis

Compensation - **Respiratory Acidosis**

Chronic Irregular (12 - 24 hr)

- ***pCO2*** ⇧
- *Limit of compensation*

pCO2 → → 60 mmHg

  - If ***Measured pCO2*** > 60 ⇨ 1º Respiratory Acidosis

- Normal Compensation
  - pCO2 = 0.9 X HCO_3^- + 9

Normal Compensation Limits for Acid-base Disturbances				
Primary Disturbance		**Lower Limit**	**Upper Limit**	**Normal Compensation**
Respiratory Acidosis	Acute	HCO3 =23	HCO3 =32	
	Chronic 24-96 h		HCO3 =45	HCO3 = 0.43 x pCO2 +7.6 ±2
Respiratory Alkalosis	Acute	HCO3 =18	HCO3 =23	
	Chronic	HCO3 =14		HCO3 = 25 - (40- pCO2) x 0.5 ±1
Metabolic Acidosis	Chronic 12-24 h	pCO2 =10		pCO2 = 1.5 x HCO3 + 8.4 ±1
Metabolic Alkalosis	Chronic		pCO2 =60	pCO2 = 0.9 x HCO3 + 9

Acid base Case Study

45 year old asthmatic male presents to the emergency department in *status asthmaticus* (profound breathing difficulty) which has worsened over the past 12 hrs.

Plasma creatinine, potassium, sodium and chloride were normal.

Blood gases were as follows:

- pH 7.21 (7.35 – 7.45)
- PCO2 56 (34 – 45)mmHg
- PO2 75 (80 – 110)mmHg
- HCO3- 21 (20 – 30) mM

Acid base Case Study

A 61 year old female came to the emergency room with a history of a vomiting for the past 36 hours. In addition to her gastrointestinal problem she was quite tachypneic which raised the possibility that she also had aspiration pneumonia. On admission, her blood gas values were:

Test	Results	Reference range
pH	7.36	7.35 - 7.45
PCO_2	62	35 - 45
PO_2	55	80 - 110
HCO3	40	22 - 32

Acid base Case Study

14 Year old boy passed out in his bedroom. He was taken to the emergency room .

On Admission - he was difficult to arouse

Plasma creatinine, potassium, sodium and chloride were normal.

Blood gases were as follows:

- pH 7.40 (7.35 – 7.45)
- PCO2 20 (34 – 45)mmHg
- PO2 112 (80 – 110)mmHg
- HCO3- 14 (20 – 30) mM
- Anion Gap 22 (7 – 17) mM

Acid base Case Study

A newborn boy developed cyanosis in the labour delivery room. Arterial blood gas specimens were obtained and then the baby was started on 100 percent oxygen. The blood gas results were as follows:

On Room Air	Results	Reference range
pH	7.29	7.35 - 7.45
PCO_2	72	35 - 45
PO_2	35	55 - 80
HCO3	34	22 - 32

On 100% O_2		
pH	7.28	7.35 - 7.45
PCO_2	70	35 - 45
PO_2	33	55 - 80
HCO3	32	22 - 32

What do these results tell us concerning the cause of his cyanosis.

Acid - Basics

ie The take home message

- how pH homeostasis is maintained
- the common causes of acid base disturbances
- compensation mechanisms

- Use blood gas and electrolyte results to determine…
  - the primary pathology
    - acidosis or alkalosis
    - respiratory or metabolic
  - if there is appropriate compensation or a mixed acid base disorder