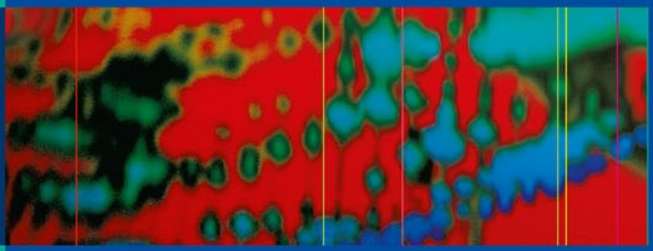
Ashfaq Hasan



Handbook of Blood Gas/Acid-Base Interpretation

Springer

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Ashfaq Hasan

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To my wife

Simplify, simplify!
– Henry David Thoreau

Preface

Blood gas analysis has become the "...single most helpful laboratory test in managing respiratory and metabolic disorders. (It is)... imperative to consider an ABG for virtually any symptom..., sign..., or scenario... that occurs in a clinical setting, whether it be the clinic, hospital, or ICU."[1]

For the uninitiated, the analysis of blood gas can be a daunting task. Hapless medical students, badly constrained for time, have struggled ineffectively with Hasselbach's modification of the Henderson equation; been torn between the Copenhagen and the Boston schools of thought; and lately, been confronted with the radically different strong-ion approach of Peter Stewart.

In the modern medical practice, the multi-tasking health provider's time has become precious—and his attention span short. It is therefore important to retain focus on those aspects of clinical medicine that truly matter. In the handling of those subjects rooted in clinical physiology (and therefore predictably difficult to understand), it makes perfect sense, in my opinion, to adopt an 'algorithmic' approach. A picture can say a thousand words; a well constructed algorithm can save at least a hundred—not to say, much precious time—and make for clarity of thinking. I have personally found this method

[1] Canham, EM, Beuther, DA, Interpreting Arterial Blood Gases, PCCU on line, Chest

relatively painless—and easy to assimilate. The book is set out in the form of flow charts in logical sequence, introducing and gradually building upon the underlying concepts.

The goal of this book is to enable medical students, residents, nurses and respiratory care practitioners to quickly grasp the principles underlying respiratory and acid-base physiology, and to apply the concepts effectively in clinical decision making. Each of these sections, barring a few exceptions, has been designed to fit into a single power point slide: this should facilitate teaching.

Over the years, many excellent books and articles have appeared on the subject. I have found the manuals by Lawrence Martin[2] and Kerry Brandis[3] thoroughly enjoyable as also the online tutorials of Alan Grogono[4] and Bhavani Shankar Kodali[5]: I have tried to incorporate into my own book, some of their energy and content.

No matter how small, a project such as this can never be accomplished without the support of well wishers and friends. I would like to acknowledge the unwavering support of my colleagues Dr TLN Swamy and Dr Syed Mahmood Ahmed; my assistants A Shoba and P Sudheer; and above all, my family who had to endure the painstaking writing of yet another manuscript.

Ashfaq Hasan

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[2] Martin, L. All you really need to know to interpret blood gases. 1999, Lippincott Williams and Wilkins.

[3] Kerry Brandis.Acid-Base Physiology; www.anaesthesiaMCQ.com

[4] Grogono, AW. www.acid-base.com

[5] Bhavani Shankar Kodali. 2007. Welcome to Capnography.com

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The Blood Gases

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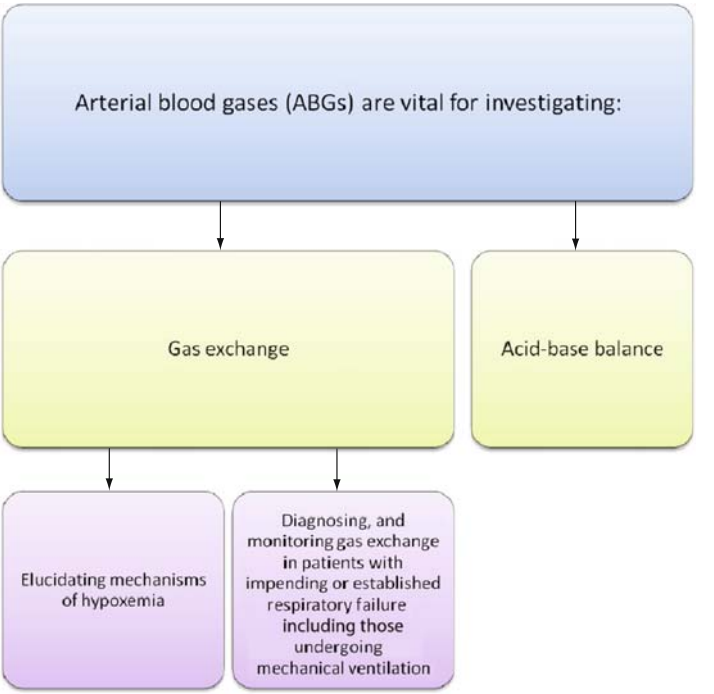
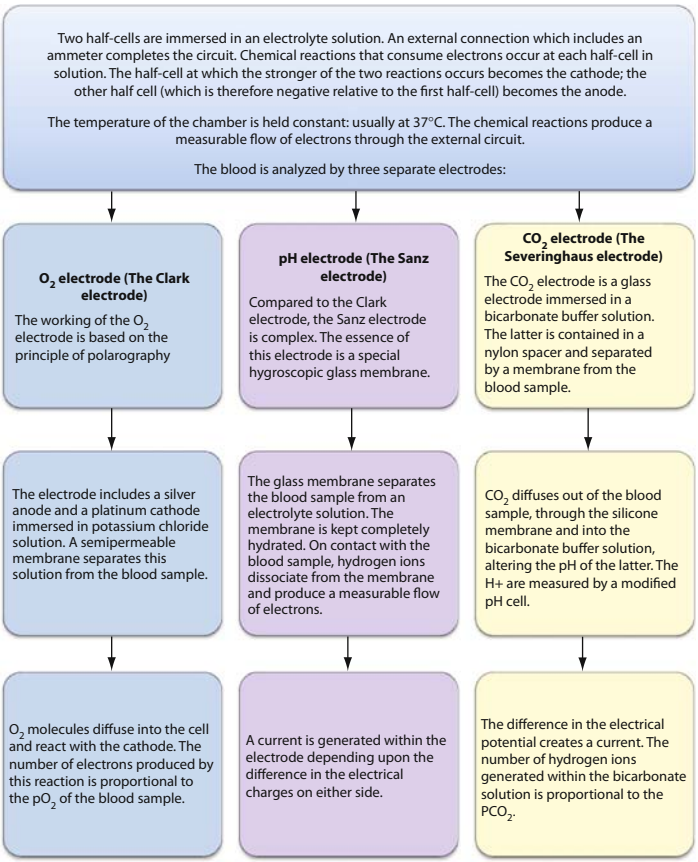
A. Hasan, *Handbook of Blood Gas/Acid–Base Interpretation*,
DOI 10.1007/978-1-84800-334-7_1,

1.1 The Utility of Blood Gases



1.2 Electrodes

The design of the electrodes in the blood gas analyser is based on the model of the electrochemical cell.



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Chapter 2
Gas Exchange

2

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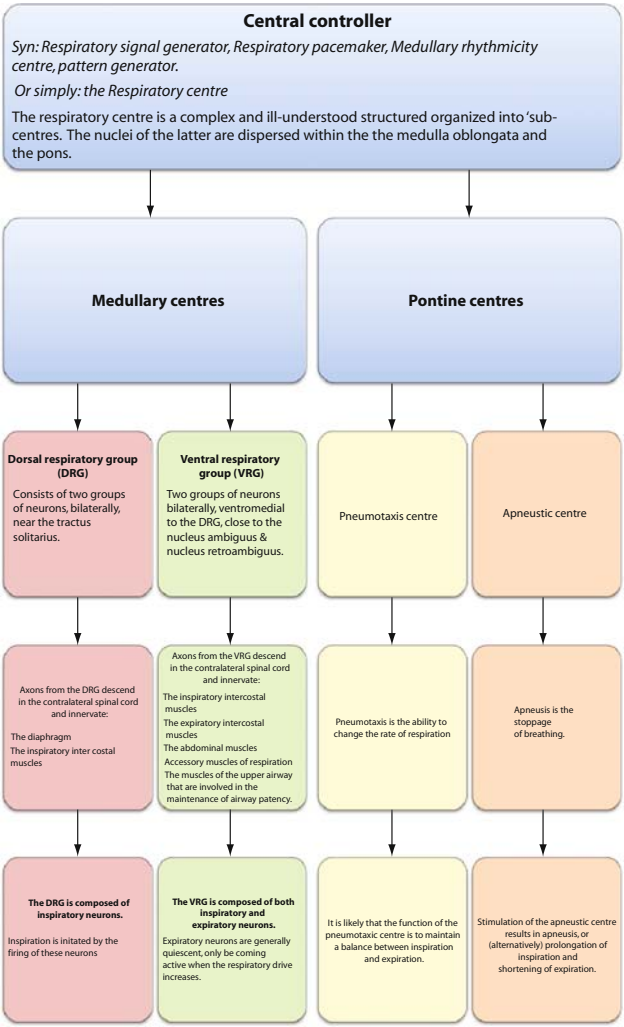
2.1 The Respiratory Center



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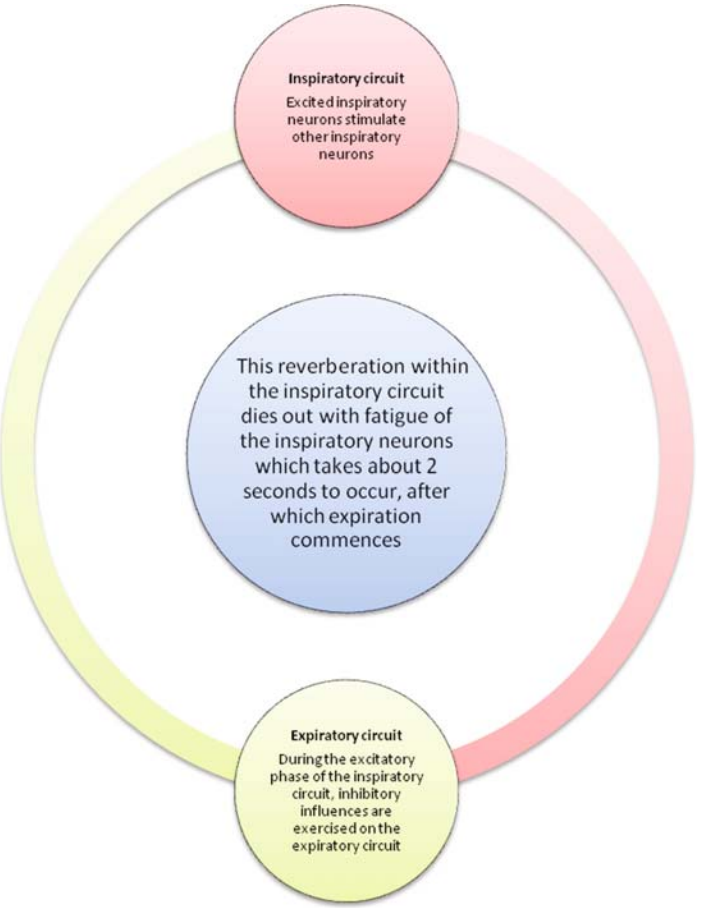
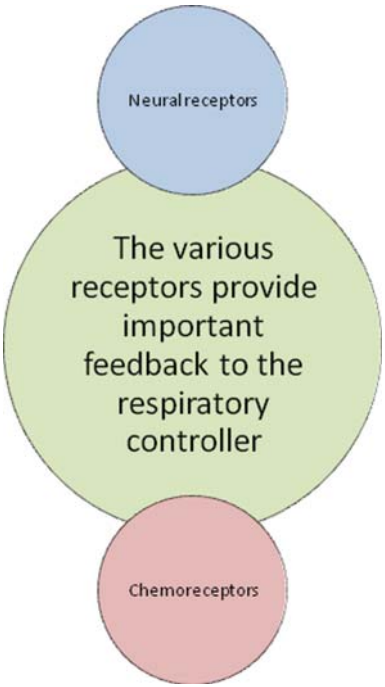
2.2 Rhythmicity of the Respiratory Center



This is the reason for the rhythmicity of the respiratory center.

2.3 Receptors

Neural and chemical receptors provide vital feedback to the respiratory center that enables the latter to regulate its output.



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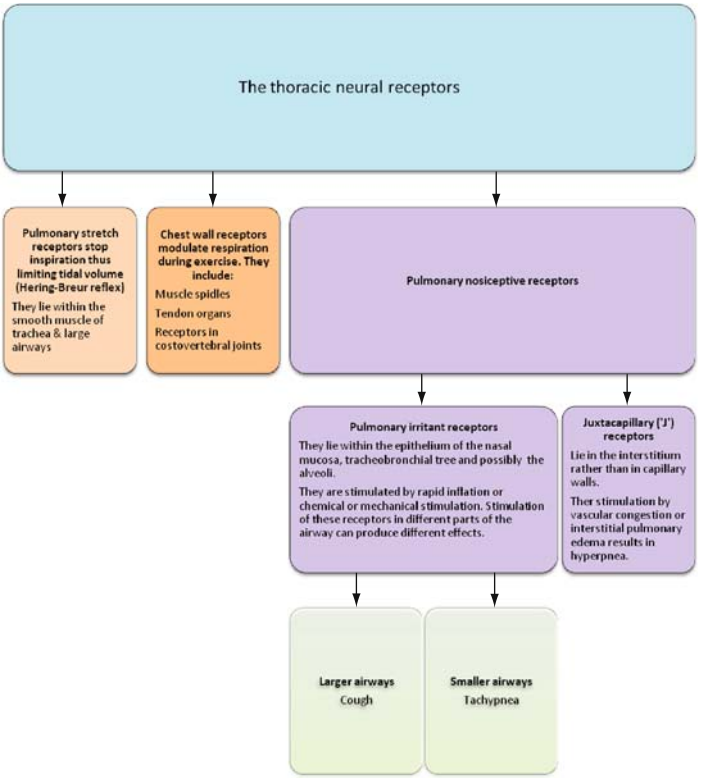
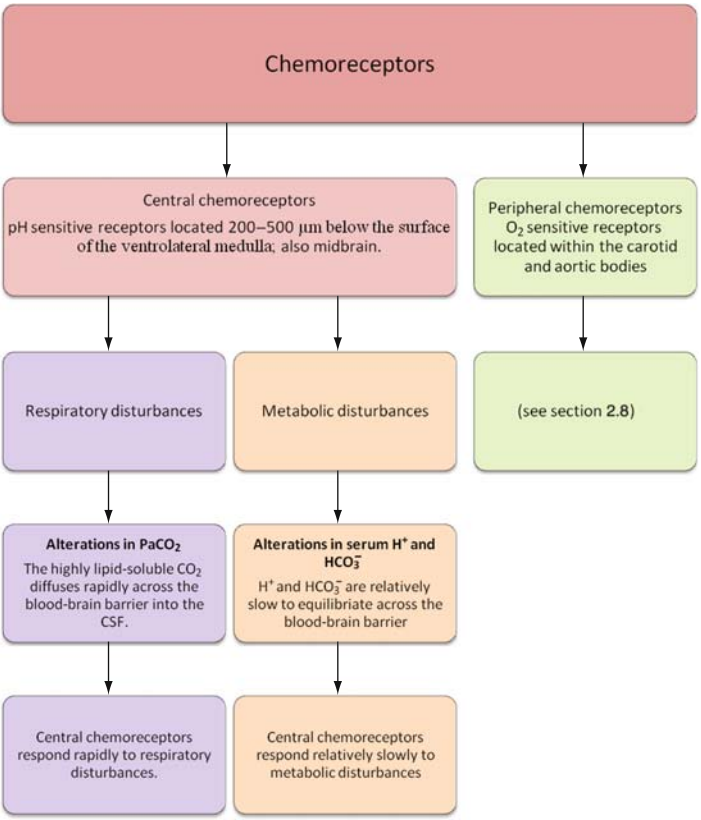
2.4 Neural Receptors



2.5 Chemoreceptors



Lambertsen, CJ. Chemical Control of Respiration At Rest, 14th ed, Mosby Company, St. Louis, 1980

Coleridge, HM, Coleridge, JCG. Reflexes evoked from tracheobronchial tree and lungs. In: Fishman, AP (Ed), Handbook of Physiology. The Respiratory System, American Physiological Society, Bethesda, MD, 1986

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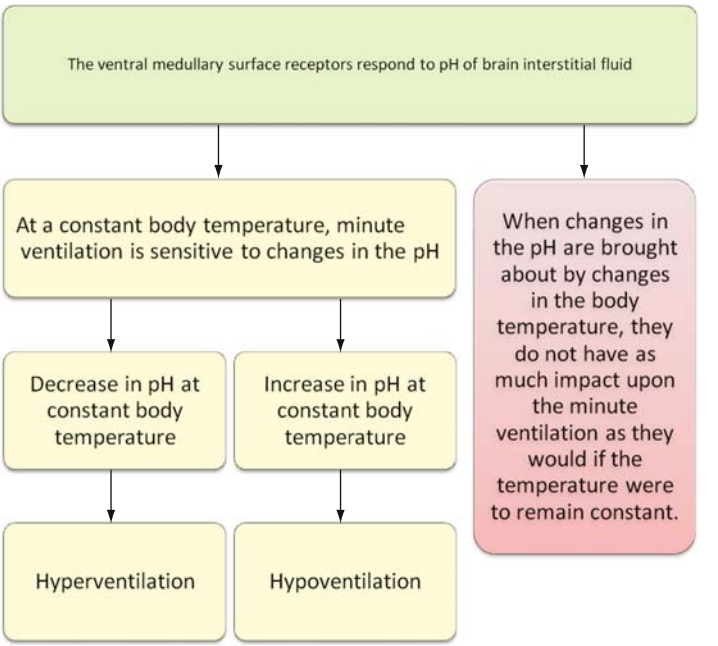
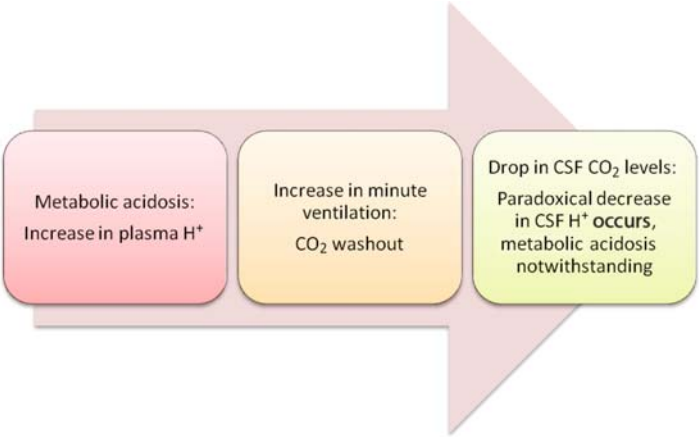
2.6 The Central Chemoreceptors: the Alpha-Stat Mechanism



Reeves, RB. An imidazole alphastat hypothesis for vertebrate acid base regulation: Tissue carbon dioxide content and body temperature in bullfrogs. Respir Physiol 1972; 14:219

Kazemi, H, Johnson, DC. Regulation of cerebrospinal fluid acid–base balance. Physiol Rev 1986; 66:953

2.7 Paradoxical CSF Response in Metabolic Acidosis



Bushinsky, DA, Coe, FL, Katzenberg, C, et al. Arterial PCO_2 in chronic metabolic acidosis. Kidney Int 1982; 22:311

Jennings, DB, Davidson, JSD. Acid–base and ventilatory adaptation in conscious dogs during chronic hypercapnia. Respir Physiol 1984; 58:377

Javaheri, S, Kazemi, H. Metabolic alkalosis and hypoventilation in humans. Am Rev Respir Dis 1987; 136:1011

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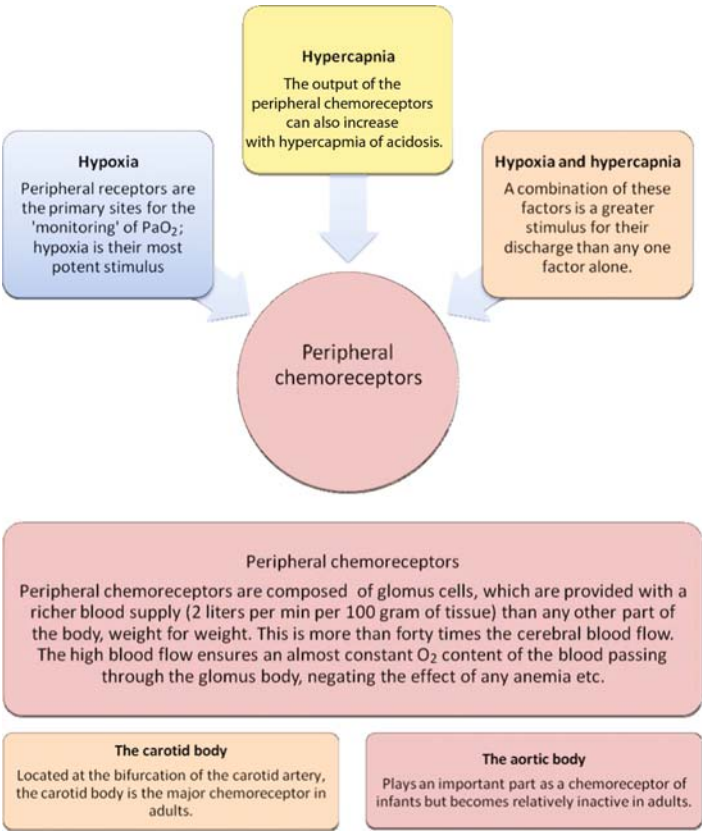
2.8 Peripheral Chemoreceptors

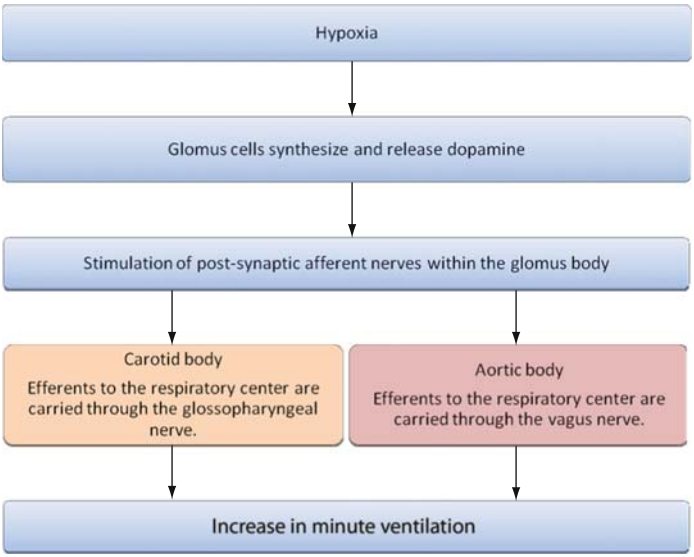


Lambertsen, CJ. Chemical Control of Respiration At Rest, 14th ed, Mosby Company, St. Louis, 1980

Burton, MD, Kazemi, H. Neurotransmitters in central respiratory control. Respir Physiol 2000; 122:111

2.9 Response to Hypoxia

Peripheral chemoreceptors in hypoxia



Coleridge, HM, Coleridge, JCG. Reflexes evoked from tracheobronchial tree and lungs. In: Fishman, AP (Ed), Handbook of Physiology. The Respiratory System, American Physiological Society, Bethesda, MD, 1986

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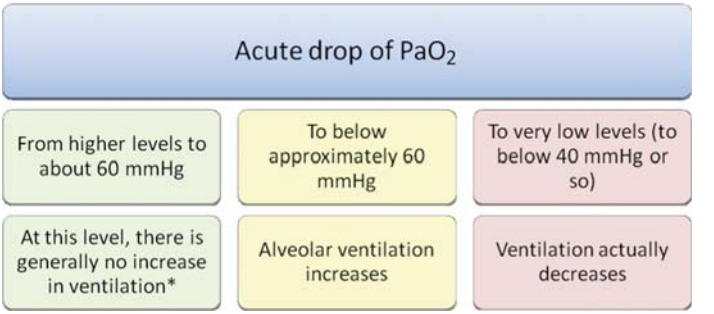
Response of the respiratory center to acute hypoxemia



* In contrast even a small rise in CO_2 above physiological levels results in an almost immediate increase in alveolar ventilation

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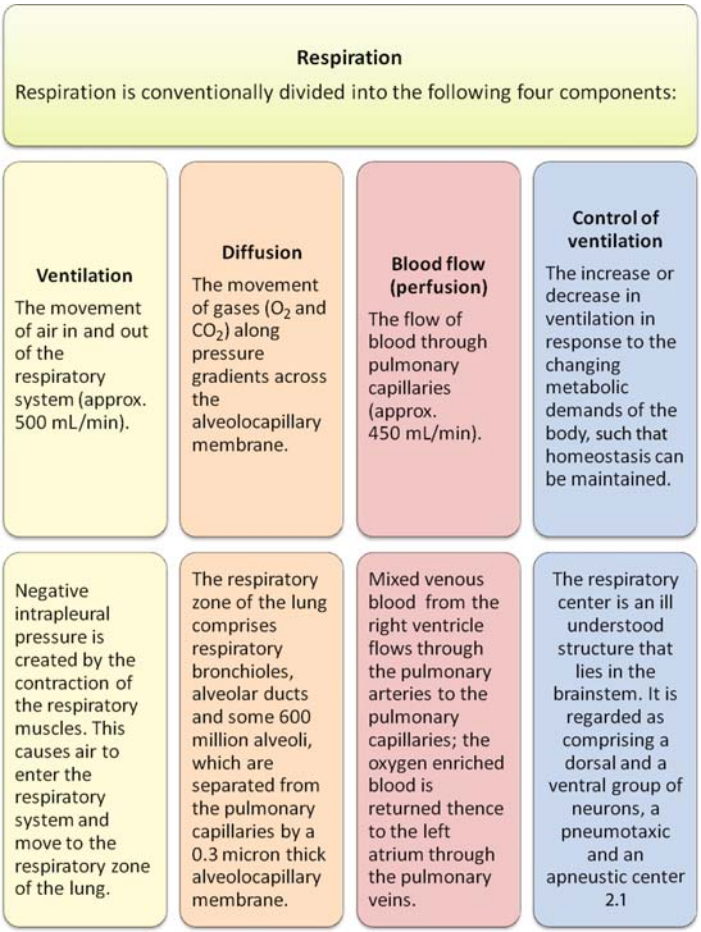
Igarashi, T, Nishimura, M, Kobayashi, S, et al. Dependency on the rate of change in PaO_2 of the ventilatory response to progressive hypoxia. Am J Respir Crit Care Med, 1995

2.10 Respiration

Respiration involves the sum of those complex processes that enable gas exchange between an organism and its environment.



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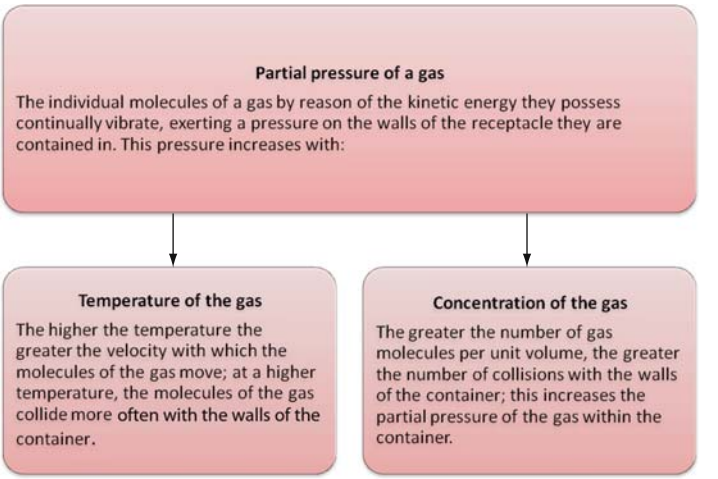
2.11 Partial Pressure of a Gas

The pressure exerted by a gas is a function of its concentration and the velocity with which its molecules move.



2.12 Partial Pressure of a Mixture of Gases

According to Dalton's law, the partial pressure of a gas in any gas mixture is the pressure the gas would exert if *it alone* occupied the entire volume occupied by the gas mixture.

Within a mixture of gases, the pressure exerted by each gas is independent of the pressure exerted by all others. A given gas within a mixture behaves as though it alone were present to the exclusion of all other gases.

Partial pressure

The pressure exerted by each gas is termed its partial pressure.

The total pressure exerted by a mixture of gases

The total pressure exerted by a mixture of gases is the sum of the individual partial pressures of the gases.

2

2.13 The Fractional Concentration (F_{gas}) of a Gas and its Partial Pressure

When the temperature of a gas mixture is held constant, the partial pressure of a gas is a reflection of the number of molecules of a gas (the concentration of the gas) in relation to all the molecules of the other gases present. This concentration is termed the fractional concentration of that gas.

Fractional concentration and partial pressure

The fractional concentration multiplied by the total pressure gives the partial pressure of a gas.

Partial pressure of major gases in room air:

Partial pressure of Oxygen

The molecules of O_2 comprise 21% of all the molecules in room air (FO_2=0.21).

At sea level, barometric pressure (PB) is 760 mmHg.

$PO_2 = FO_2 \times PB$

$PO_2 = 0.2l \times 760 = 159$ mmHg

Partial pressure of Nitrogen

The molecules of N_2 comprise 79% of all the molecules in room air (FN_2=0.79).

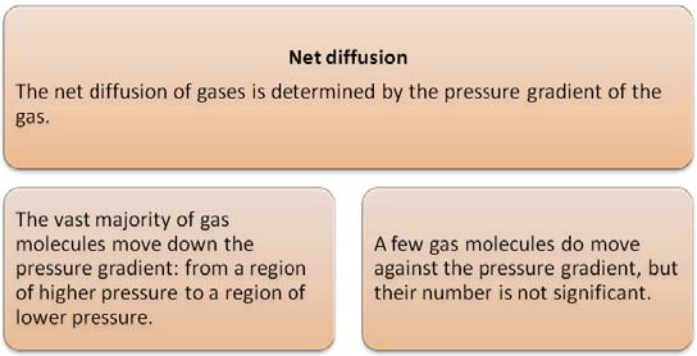
At sea level PB is 760 mmHg.

$PN_2 = FN_2 \times PB$

$PN_2 = 0.79 \times 760 = 600$ mmHg

2.14 Diffusion

Gases always diffuse down their respective partial pressure gradients.

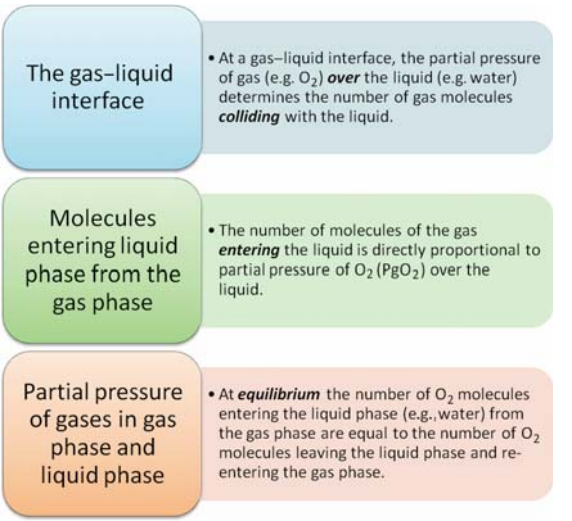


The partial pressures of gases determine their movement by passive diffusion. The rate of the movement of a given gas is proportional to its partial pressure gradient.

2

2.15 Henry's Law and the Solubility of a Gas in Liquid

Henry's Law states that the volume of a gas that will dissolve in a given volume of liquid is directly proportional to the partial pressure of the gas above it. In respect of water, the partial pressure of the O_2 dissolved in water (PwO_2) is directly proportional to the partial pressure of the O_2 in the gas phase (PgO_2).



2.16 Diffusion of O_2 and CO_2

The passage of gases between the alveolus and the blood are governed by the laws of simple diffusion.

Fick's Law

Fick's Law states that the quantity* of gas that can pass through a sheet of tissue is:

proportional to the area (A), the diffusion constant (D) and the difference in partial pressure (P_1-P_2);

and inversely proportional to the thickness of the tissue slice (T).

$V_{gas} = [(A/T) \times (P_1-P_2) \times D/T$

Graham's law

Graham's law states that the rate of diffusion of a gas is inversely proportional to the square root of its molecular weight.

The diffusion constant

The diffusion constant (D) is related to the solubility and the molecular weight of the gas:

$D \alpha Sol / \sqrt{MW}$

* Actually, the original Fick's law mentioned pressure, not quantity.

2

2.17 The Relative Solubilities of O_2 and CO_2 in Water

$$\text{Relative Rate } \frac{CO_2}{O_2} = \frac{\text{solubility } CO_2}{\sqrt{\text{MW } CO_2}} + \frac{\text{solubility } O_2}{\sqrt{\text{MW } O_2}}$$

$$= \frac{592}{\sqrt{44}} + \frac{0244}{\sqrt{32}}$$

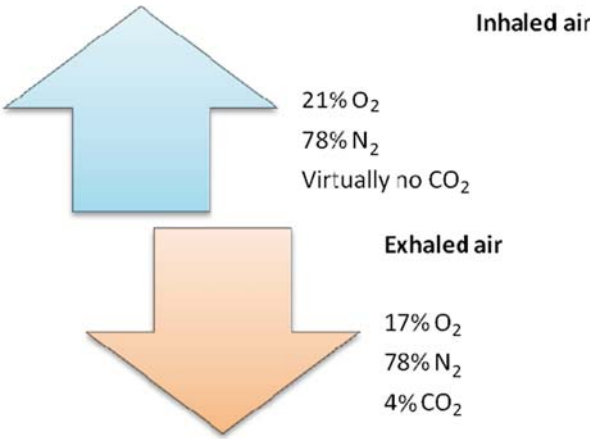
20.7/1

The alveolar-capillary barrier is only 0.2 to 0.5 microns thick. CO_2 diffuses with felicity across biological membranes. Thus, in parenchymal lung disease, even though hypoxemia may be present, CO_2 diffusion almost never presents a problem.

2.18 Inhaled Air

Inhaled air contains virtually no CO_2; in contrast, CO_2 comprises as much as 4% of exhaled air; the fractional concentration of N2 of the inhaled and exhaled air is the same.

O_2 and CO_2 are exchanged between the alveoli and the blood by diffusion; concentration gradients determine the passage of these gases across the alveolo-capillary membrane.



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2.19 The O_2 Cascade

At sea level, the partial pressure of O_2 is: 160 mmHg

760mmHg x 0.21 = 160 mm Hg

Oxygen is available for inspiration at sea level at a partial pressure of about 160 mm Hg

Within the respiratory tract the partial pressure of O_2 is about 150 mmHg

0.21 x (760-47) = 149 mmHg

As it enters the respiratory system, O_2 is humidified by the addition of water vapour (partial pressure 47 mmHg). Humidification serves to make the inspired air more breathable; it also results in the drop of the partial pressure of oxygen to about 150 mmHg.

In the alveoli the partial pressure of O_2 (PAO_2) is about 100 mmHg

149-(40/0.8) = 99 mmHg

40 is the normal value of $PaCO_2$ in mmHg.

CO_2 being easily diffusible across the alveolocapillary membrane, arterial CO_2 ($PaCO_2$) may be assumed to be the same as alveolar CO_2 ($PACO_2$).

0.8 is the respiratory quotient.

In the alveoli, oxygen diffuses into the alveolar capillaries and carbon dioxide is added to the alveolar air. The result of a complex interaction between three factors -- alveolar ventilation, CO_2 production (VCO_2) and the relative consumption of O_2 (VO_2)-- causes the partial pressure of O_2 in the alveolus to drop to 100 mmHg. This is the pressure of oxygen that equates with the pressure of oxygen in the pulmonary veins, and therefore, with the pressure of oxygen in the systemic arteries.

VCO_2 = 250ml Of CO_2 per minute

VO_2 = 300ml of O_2 per minute

In the systemic arteries the partial pressure of O_2 (PaO_2) is about 95 mmHg

A small amount of deoxygenated blood is added to the systemic arteries (because of a small physiological shunt that normally exists in the body). This is due to unoxygenated blood emptied by certain systemic arteries -- the bronchial and thesbesian veins-- back into the pulmonary veins and the left side of the heart. This 'shunt fraction' which represents about 2-5% of the cardiac output, causes the systemic arterial oxygen to fall fractionally from 100 mmHg, to about 95 mmHg or less.

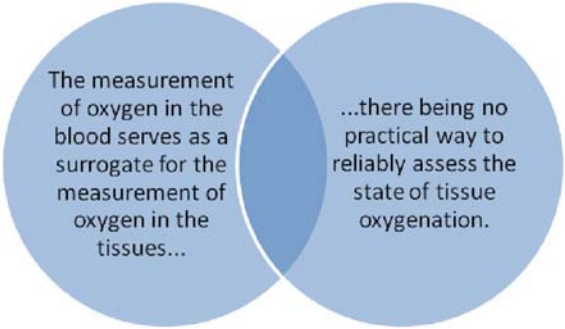
Thus, in spite of normal gas exchange, the PaO_2 may be 5-10 mmHg lower than the PAO_2.

In the mitochondrion the partial pressure of O_2 is unknown

Due to substantial diffusion barriers, the amount of oxygen made available to the oxygen-processing unit of the cell (the mitochondrion) is a relatively tiny amount. The mitochondrion appears to continue in its normal state of aerobic metabolism with minimal oxygen requirements. In hypoxia, a fall in the PaO_2 within mitochondria (to possibly less than 1 mmHg), is required to shift the energy producing pathways towards the much less efficient anaerobic metabolism.

Hasan, A. Understanding Mechanical Ventilation. Orient Longman, 2003

2.20 PaO_2


The measurement of oxygen in the blood serves as a surrogate for the measurement of oxygen in the tissues...
...there being no practical way to reliably assess the state of tissue oxygenation.

2

PaO_2 and Age

The normal level of PaO_2 declines with advancing age

PaO_2 in healthy young adults (at sea level)

Average PaO_2: 95 mm Hg
(range 85–100 mmHg)

In a healthy 60 year old (at sea level)

Average PaO_2: 83 mmHg

Predictive equation for the estimation of PaO_2 at (sea level) for a particular age

- $PaO_2 = 109 - 0.43 \times$ age in years

Sorbini, CA, Grassi, V, Solinas, E, et al. Arterial oxygen tension in relation to age in healthy subjects. Respiration 1968; 25:3–13

2.21 The Modified Alveolar Gas Equation

The value of PaO_2 (the partial pressure of O_2 in the arterial blood) cannot be interpreted in isolation. A PaO_2 which is low relative to the PAO_2 (the partial pressure of O_2 in alveolar air) implies a significant deficiency in the gas exchange mechanisms of the lung. The alveolar gas equation makes it possible to calculate the PAO_2. The difference between the PAO_2 (which is a calculated value) and the PaO_2 (which is measured in the laboratory) helps quantify the pulmonary pathology that is causing hypoxemia.

The partial pressure of the O_2 in the inspired air depends on the fraction of O_2 in the inspired air in relation to the barometric pressure at that altitude, and also upon the water vapour pressure (the upper airways completely saturate the inhaled air is with water).

$$PIO_2 = FIO_2\ (Pb - Pw)$$

Where,

PIO_2 = Inspired PO_2

Pb = Barometric pressure

Pw = Water vapour pressure, 47 mmHg at the normal body temperature

$$PAO_2 = PIO_2 - 1.2\ (PaCO_2)$$

Where,

PAO_2 = Partial pressure of O_2 in the alveolus

$PaCO_2$ = Partial pressure of CO_2 in the arterial blood. Because of the excellent diffusibility of CO_2 across biological membranes, the value of $PaCO_2$ is taken to be the same as the $PACO_2$ (the partial pressure of CO_2 in the alveolus).

Multiplying $PaCO_2$ by 1.2 is the same as dividing $PaCO_2$ by 0.8 (0.8 is the respiratory quotient)

Substituting the value of PIO_2 into the above equation,

$$PAO_2 = [FIO_2\ (Pb - Pw)] - [1.2 \times PaCO_2]$$

The above abbreviated form of the equation serves well for clinical use, in place of the alveolar air equation proper which is:

$$PAO_2 = PIO_2 - (PACO_2) \times [FIO_2 + \{(1 - FIO_2)/R]$$

Martin, L. Abbreviating the alveolar gas equation. An argument for simplicity. Respir Care 1986;31–40

2

2.22 The Determinants of the Alveolar Air Equation

The alveolar-arterial diffusion gradient (A-a DO_2) for oxygen is the difference between the partial pressure of O_2 in the alveolus (PAO_2) and the partial pressure of O_2 in the arterial blood (PaO_2).

$A\text{-}aDO_2 = PAO_2\text{-}PaO_2$

The determinants of PAO_2 are:

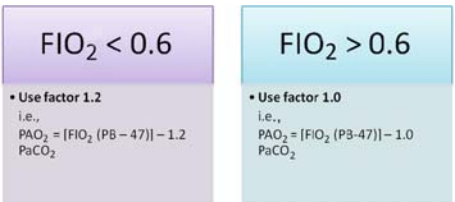
- **The fractional concentration of oxygen in the inhaled air (FIO_2)**
- **The partial pressure of CO_2 in the arterial blood ($PaCO_2$)**
- **Barometric pressure (PB)**
  PB is constant for a given altitude

The determinants of PaO_2 are:

- **Lung pathology**
  (see 2.27)
- **Mixed venous O_2 content**
  (see 00.00)

2.23 The Respiratory Quotient (RQ) in the Alveolar Air Equation

RQ, for all practical purposes, equals 0.8 mathematically.
$CO_2/0.8 = 1.2 \times CO_2$.
The quotient remains remarkably constant over a wide spectrum of clinical conditions, and therefore, in practice, the above formula usually suffices.
The factor 1.2 may change slightly depending upon the FIO_2 administered, in order to compensate for the N_2 that is washed out with higher fractions of O_2. At FIO_2's of 100% the factor approximates 1.0.



Cinel, D, Markwell, K, Lee, R, Szidon, P. Variability of the respiratory gas exchange Ratio during arterial puncture. Am Rev Respir Dis 1991;143:217

Martin, L. Abbreviating the alveolar gas equation. An argument for simplicity. Respir Care 1986;31–40

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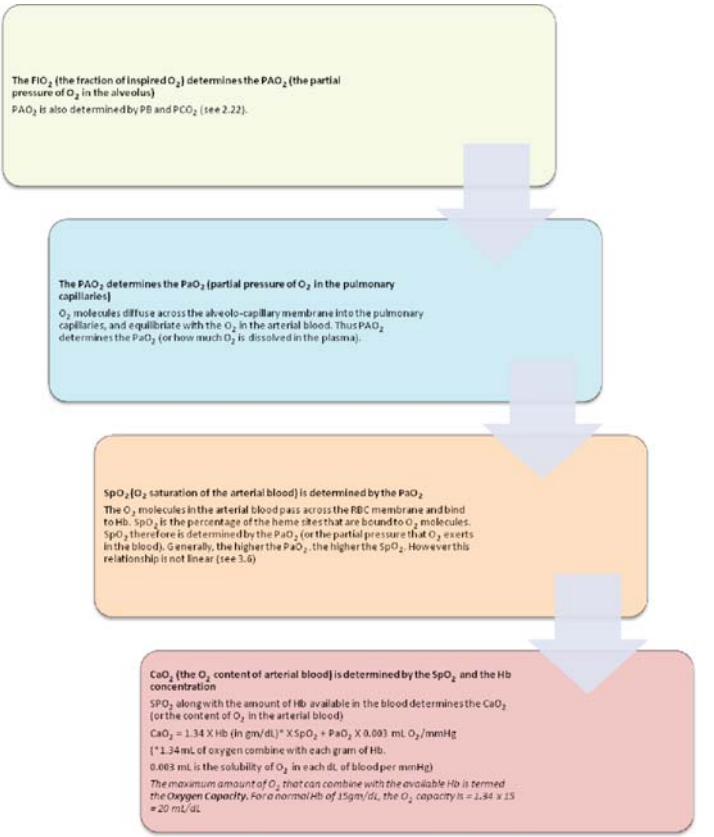
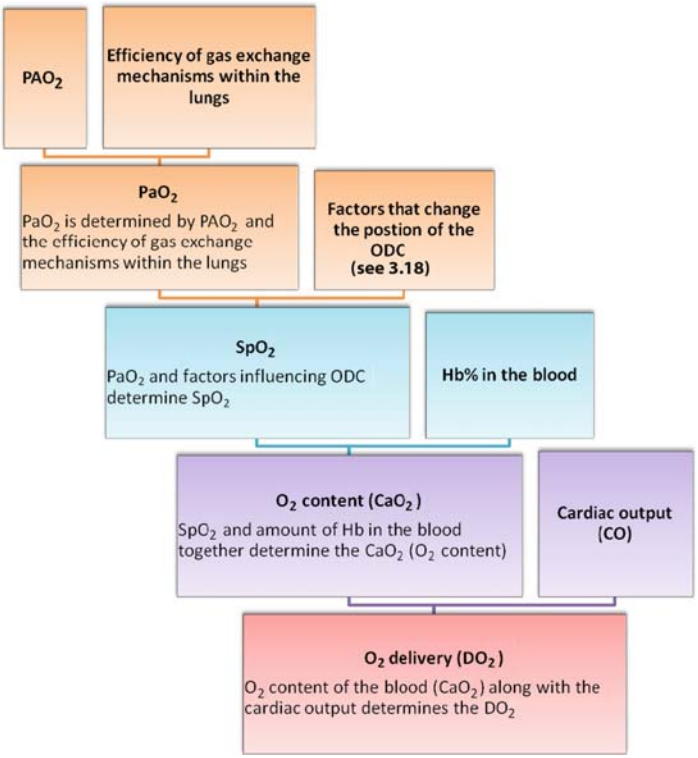
2.24 FIO_2, PAO_2, PaO_2 and CaO_2



Hasan, A. Understanding Mechanical Ventilation. Orient Longman, 2003

2.25 DO_2, CaO_2, SpO_2, PaO_2 and FIO_2

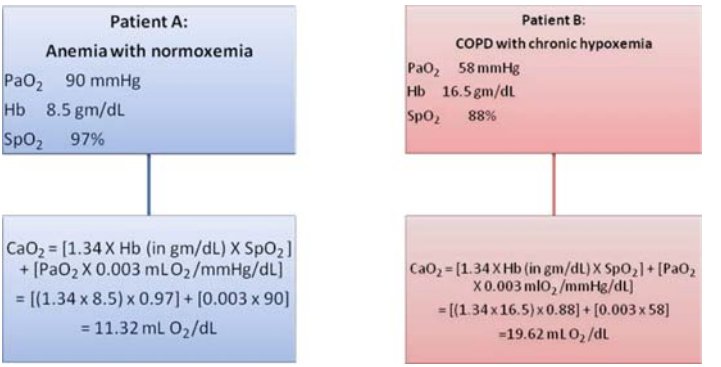


2

2.26 O_2 Content

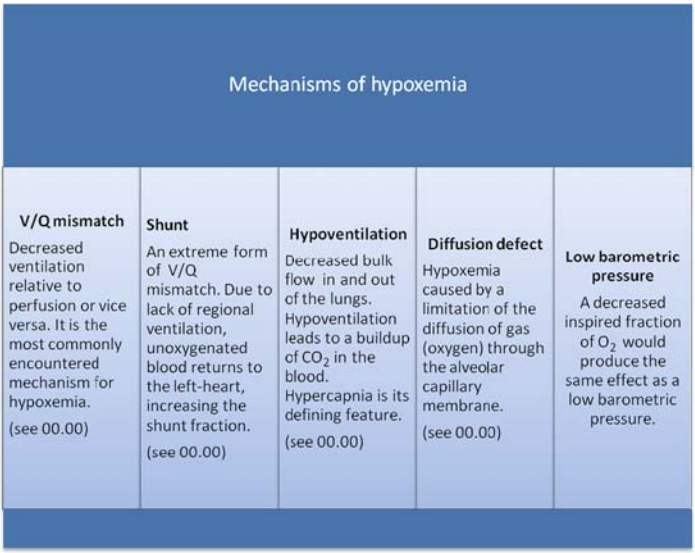
Recalling that the O_2 content of arterial blood, CaO_2

$$= [(1.34 \times \text{Hb in gm/dL}) \times SpO_2]$$
$$+ [PaO_2 \times 0.003 \text{ ml } O_2/\text{mmHg/dL}]$$



As it turns out, the PaO_2 (and therefore the dissolved O_2) contributes little to the CaO_2: one sixty seventh of that carried by the Hb, given that the Hb level is normal).
The principal determinants of CaO_2 are Hb and SpO_2: the latter, of course is determined by PaO_2. Thus, though the PaO_2 does not seemingly contribute much to the CaO_2, it can impact the CaO_2 after all, through its effect upon the SpO_2.

2.27 The Mechanisms of Hypoxemia



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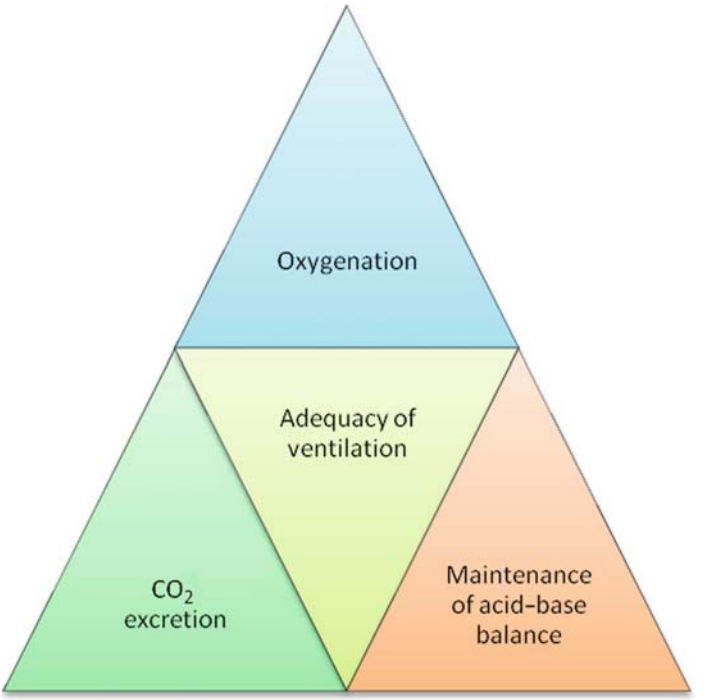
2.28 Processes Dependent on Ventilation

The adequacy of ventilation influences several key processes of the body.



2.29 Defining Hypercapnia

The value of CO_2 that defines hypercapnia is not universally agreed upon. However the following are generally accepted:

$PaCO_2$ of > 45 mmHg

In a previously normocapnic individual, a $PaCO_2$ of > 45 mmHg represents the threshold for acute hypercapnia .

A rise in $PaCO_2$ of > 5 mmHg above baseline

In a chronically hypercapnic person, a rise in $PaCO_2$ of > 5 mmHg above the baseline represents acute-on-chronic hypercapnic respiratory failure.

2

2.30 The Determinants of $PaCO_2$

$PaCO_2$

The level of $PaCO_2$ depends on the balance between CO_2 production and CO_2 elimination

CO_2 production

CO_2 production is dependent upon the rate of tissue metabolism

CO_2 elimination

CO_2 elimination is dependent upon the amount of alveolar ventilation

CO_2 elimination is much more important at determining $PaCO_2$ than is CO_2 production

CO_2 *production* almost never influences $PaCO_2$ in the presence of intact ventilatory mechanisms.

Hyperventilation or hypoventilation in response to increased or decreased CO_2 production respectively, promptly results in normalization of the $PaCO_2$.

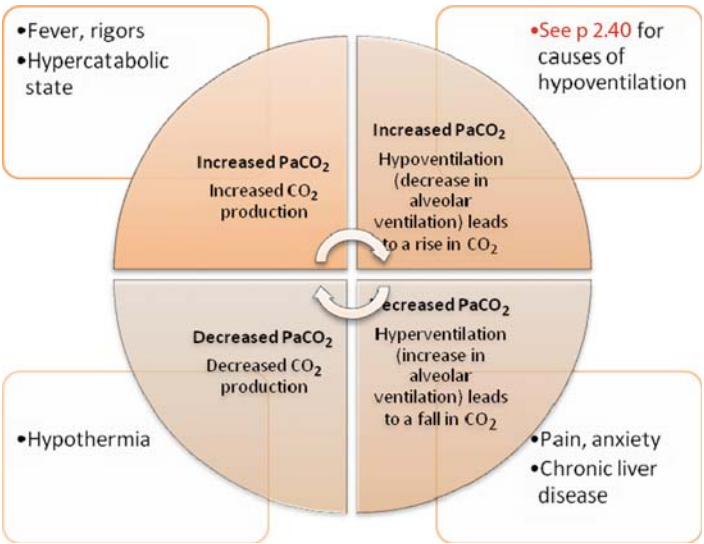
$PaCO_2$ rises when CO_2 *elimination* is low relative to CO_2 production.

Rise in $PaCO_2$ almost always implies inadequate removal of CO_2 from the circulation by the lungs, i.e., hypoventilation

$PaCO_2$ falls when CO_2 *elimination* is high relative to CO_2 production.

Fall in $PaCO_2$ almost always implies excessive washout of CO_2 from the circulation by the lungs, i.e., hyperventilation

2.31 CO_2 Production and Elimination



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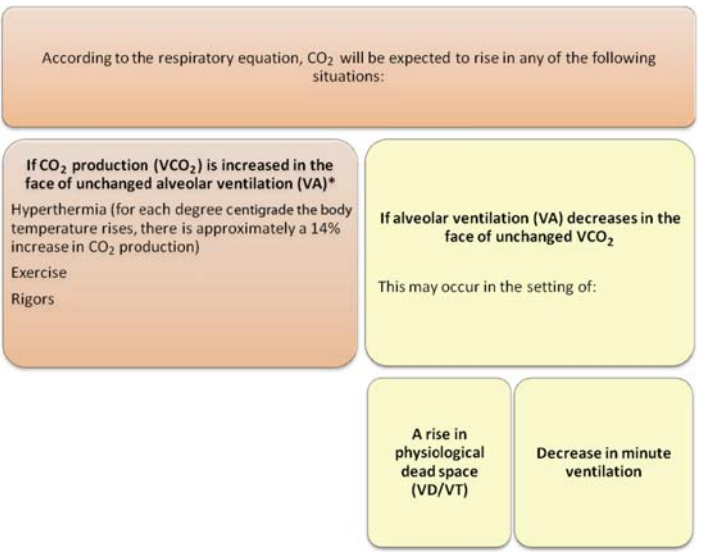
2.32 CO_2 Production and Elimination

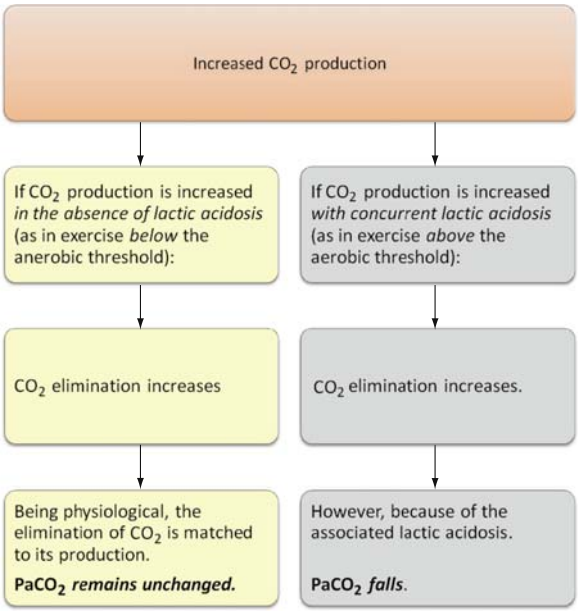
The relationship between CO_2 production and elimination can be summarized by the respiratory equation:
$PaCO_2 \alpha (VCO_2/VA)$
Where,
VCO_2 = CO_2 production
VA = alveolar ventilation
This relationship holds true provided there is no CO_2 in the inhaled gas.



* unchanged alveolar ventilation, as in the setting of a paralysed patient on controlled mechanical ventilation

2.33 Exercise and $PaCO_2$

During exercise there is an approximately linear increase in the respiratory rate, and a hyperbolic increase in tidal volume, and together these may produce a substantial increase in minute ventilation. Nonetheless, both $PaCO_2$ and PaO_2 are maintained within narrow limits.



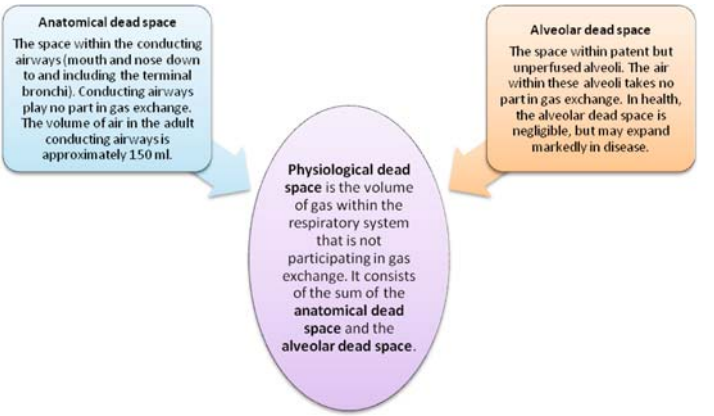
Wasserman, K, Whipp, BJ. Exercise physiology in health and disease. Am Rev Respir Dis 1975; 112:219

Hansen, JE, Sue, DY, Wasserman, K. Predicted values for clinical exercise testing. Am Rev Respir Dis 1984; 129(Suppl):S49

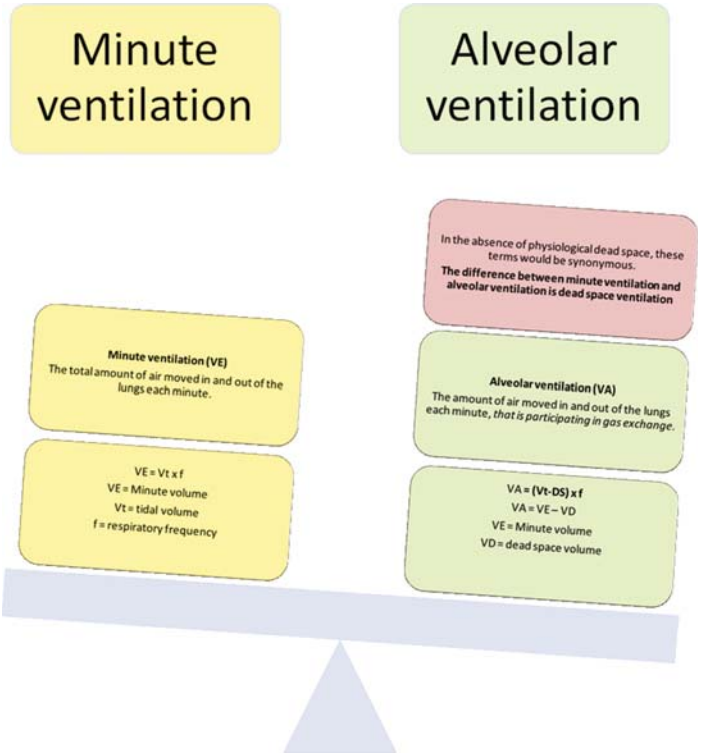
Casaburi, R, Daly, J, Hansen, JE, et al. Abrupt changes in mixed venous blood gas composition after the onset of exercise. J Appl Physiol 1989; 67:1106

2

2.34 Dead Space



2.35 Minute Ventilation and Alveolar Ventilation



2

2.36 The Determinants of $PaCO_2$

Alveolar ventilation is the most important determinant of $PaCO_2$.

The determinants of $PaCO_2$ can be predicted from the following equation:

$$VA = VE - VD$$

VA = alveolar ventilation
VE = minute ventilation. i.e., respiratory frequency x tidal volume
VD = deadspace ventilation. i.e., resp frequency x physiological dead space

Looking at the equation above it can be appreciated that low VA can only be possible if *VE is low* or *VD is high.*

Decreased VE

All the conditions causing a decrease in bulk flow into the lungs (see 2.40) are capable of producing hypoventilation.

Increased VD

In clinical practice, it is an increase in *alveolar* dead space that results in the expansion of the physiological dead space.

According to the $PaCO_2$ equation,

$$PaCO_2 \propto VCO_2 / VA$$

$PaCO_2$ = Partial pressure of CO_2 in the arterial blood
VCO_2 = CO_2 production in mL/min
VA = Alveolar ventilation in L/min

$PaCO_2$ is therefore the CO_2 production relative to the alveolar ventilation. Since CO_2 production is rarely a clinically important factor, the adequacy of alveolar ventilation is the most important determinant of $PaCO_2$.

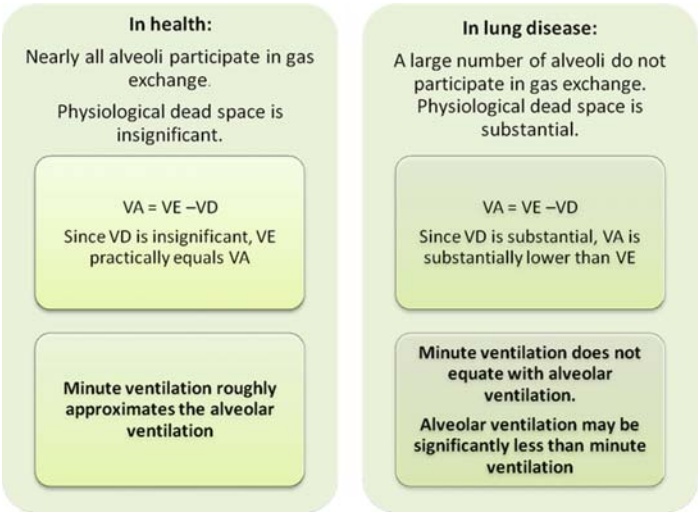
Increase in $PaCO_2$

Occurs when alveolar ventilation is low relative to CO_2 production.

Decrease in $PaCO_2$

Occurs when alveolar ventilation is high relative to CO_2 production.

2.37 Alveolar Ventilation in Health and Disease



Hasan, A. Understanding Mechanical Ventilation. Orient Longman, 2003

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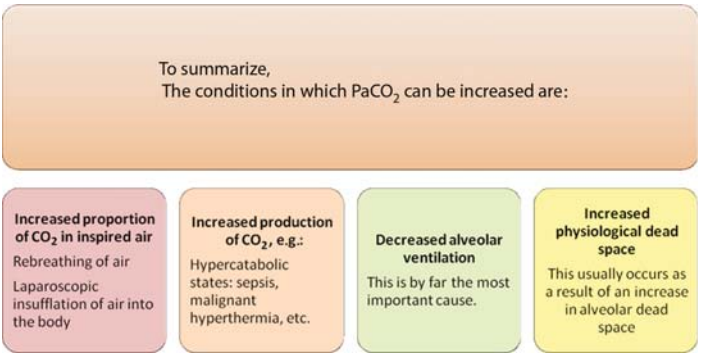
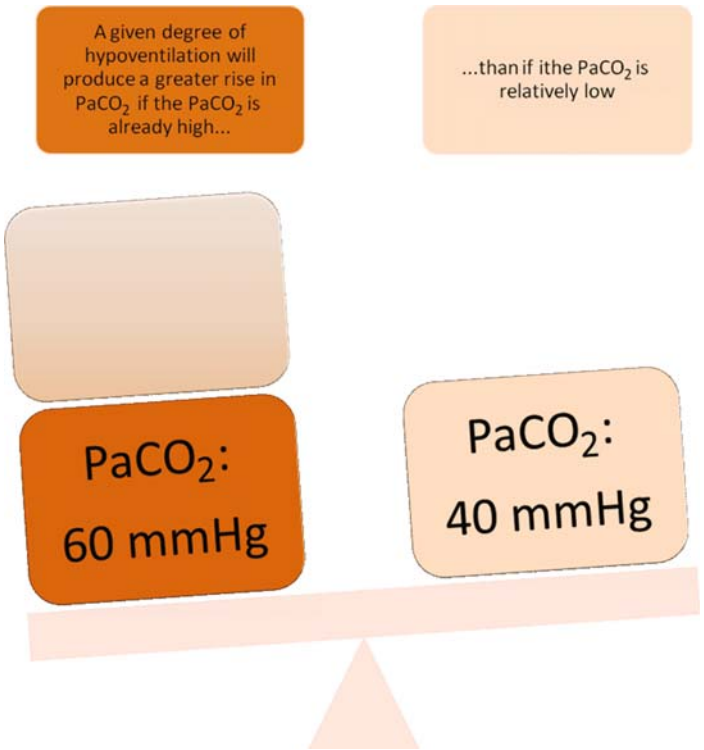
2.38 The Pathogenesis of Hypercarbia (Increased $PaCO_2$)



2.39 Hypoventilation and the Level of $PaCO_2$



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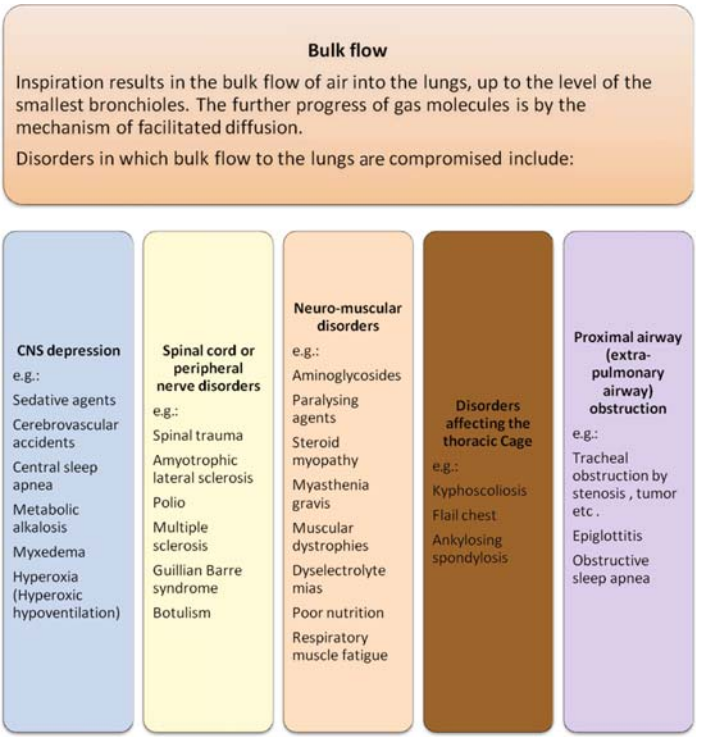
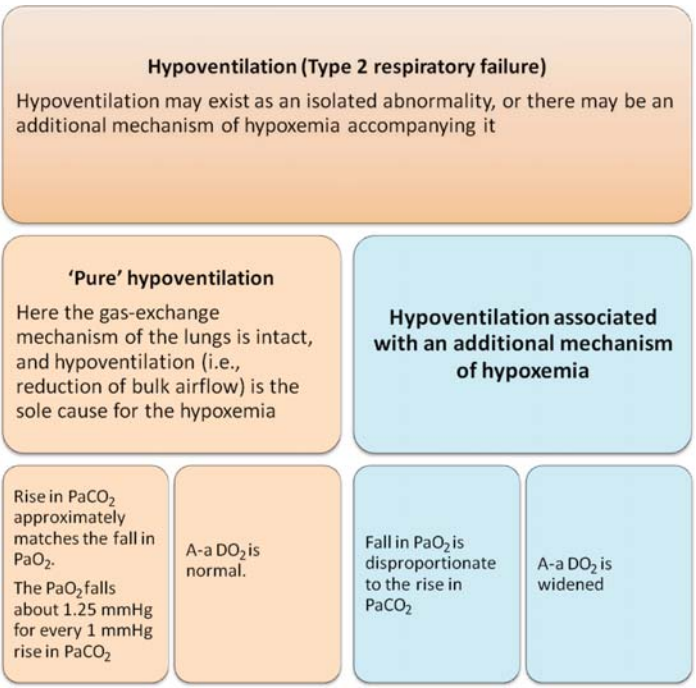
2.40 The Causes of Hypoventilation

Hypoventilation results from decreased bulk flow in and out of the lungs.



Severe intrapulmonary derangements such as tight airway obstruction in COPD and asthma are also capable of elevating the $PaCO_2$ by increasing physiological dead space.

2.41 Blood Gases in Hypoventilation



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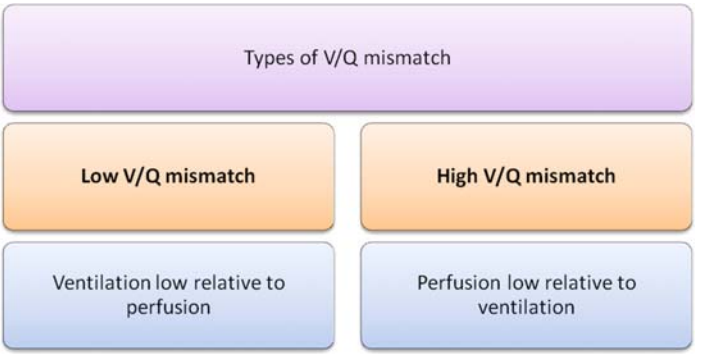
2.42 Types of V/Q Mismatch

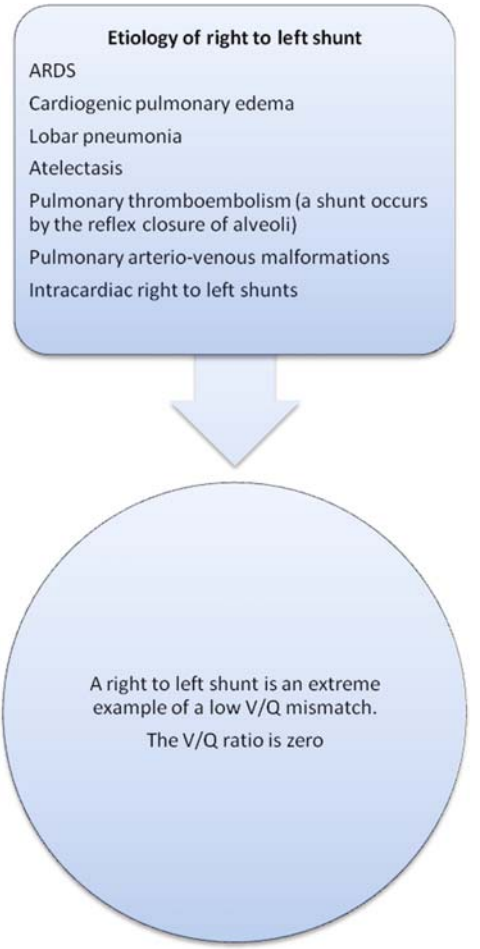


2.43 V/Q Mismatch – a Hypothetical Model

Forster II, RE, DuBois, AB, Briscoe, WA, Fisher, AB. The Lung: Physiological basis of pulmonary function tests. Year Book Medical Publishers, Inc., 1886

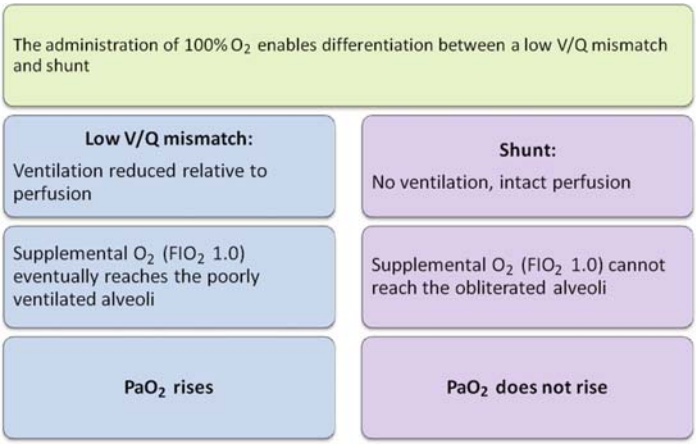
2

2.44 Etiology of Right to Left Shunts



2.45 The Difference Between V/Q Mismatch and Shunt

Low V/Q mismatch is the commonest mechanism of hypoxemia



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2.46 Quantification of Hypoxemia

Multiplying FIO_2 into 5, gives the approximate expected PaO_2 for that FIO_2 (provided that the lungs are normal).

- E.g., if the FIO_2 is 21% (as when a person is breathing room air) the expected $PaO_2 = 21 \times 5 = 105$ (approximately).
- Similarly breathing 50% O_2 (FIO_2 0.5) would result in a PaO_2 of roughly $50 \times 5 = 250$.
- If the measured PaO_2 is significantly below the expected PaO_2, there is a problem with the gas exchange.

The PaO_2:FIO_2 ratio

This (P:F ratio) makes it possible to compare the arterial oxygenation of patients breathing different FIO_2's.

- A normal person breathing room air would have a PaO_2 of approximately 100 mm Hg. The PaO_2/FIO_2 would be: 100/0.21 = 500.
- The normal range for the PaO_2/FIO_2 ratio is 300–500.
- In the appropriate setting a P:F ratio of less than 300 indicates acute lung injury (ALI) while a P:F ratio of less than 200 is diagnostic of ARDS.

The PaO_2/PAO_2 ratio

A better estimate of oxygenation than the P:F ratio.

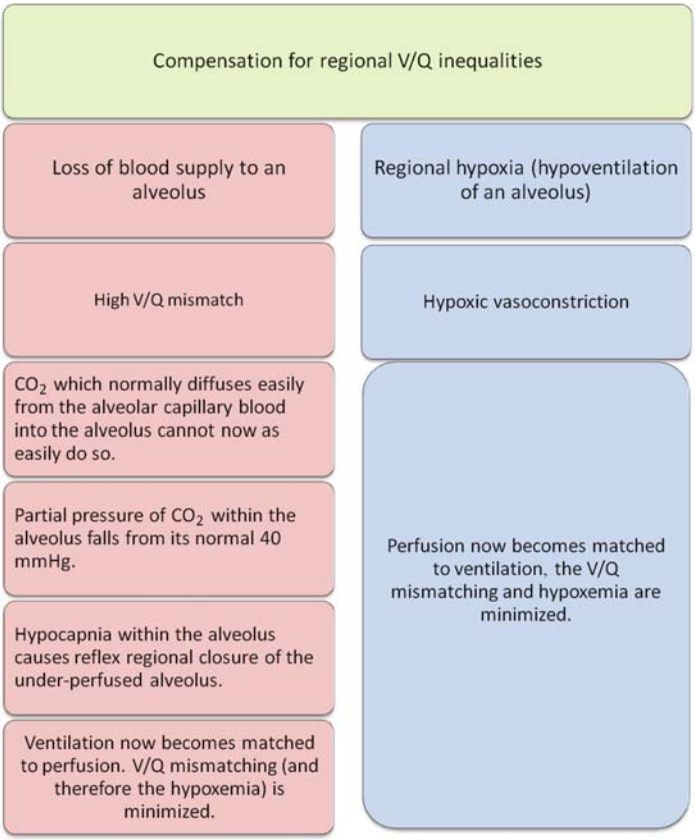
- The PaO_2 is obtained from the ABG
- The PAO_2 cannot be directly measured at the bedside and needs to be calculated from the modified alveolar air equation (see 2.21)
- PaO_2/PAO_2 ratio offers better accuracy over a broader range of FIO_2 than the PF ratio.

Bernard GR, Artigas A, Brigham KL, et al. The American European Consensus Conference on ARDS: definitions, mechanisms, relevant outcomes and clinical trial coordination. Am J Respir Crit Care Med 1994; 149:818–824

Peris, LV, Boix, JH, Salom, JV, et al. Clinical use of the arterial/alveolar oxygen tension ratio. Crit Care Med 1983; 11:888

Covelli, HD, Nessan, VJ, Tuttle, WK. Oxygen derived variables in acute respiratory failure. Crit Care Med 1983; 8:646

2.47 Compensation for Regional V/Q Inequalities



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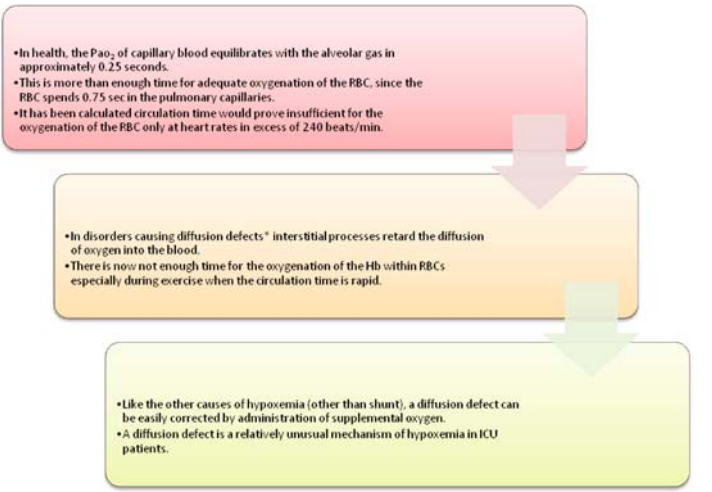
2.48 Defects of Diffusion



* Interstitial fibrosis is the classical cause, but even in this condition, it is a V/Q mismatch which is the primary mechanism for the hypoxemia

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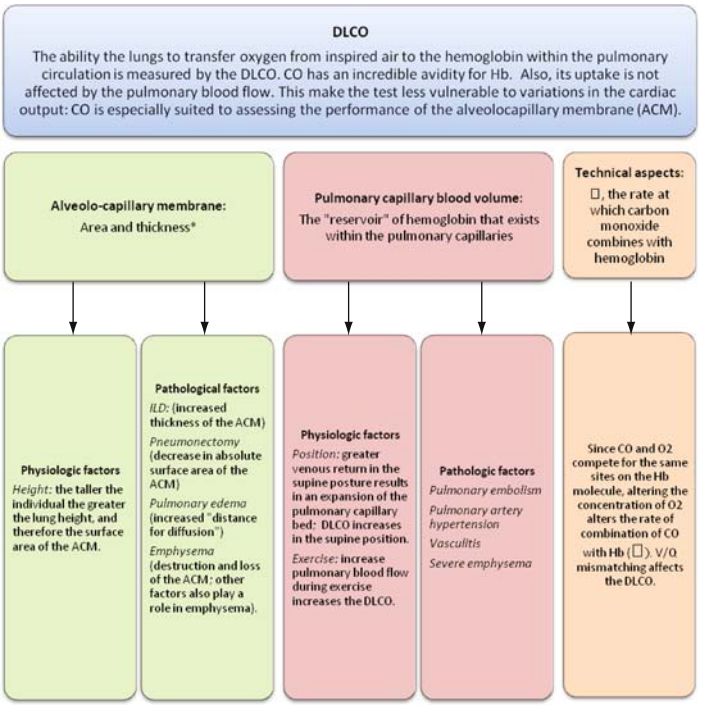
West, JB. Pulmonary Pathophysiology: The Essentials, 6th ed. Philadelphia, Lippincott Williams and Wilkins, 2003, 22–24

2.49 Factors that Determine Diffusion



* There is now evidence that the decreases in DLCO may be less dependent on a decreased surface area of the alveolocapillary membrane and more on the reduction of the red cell mass within the pulmonary cirrculation than earlier thought.

Enright PL, Diffusing capacity for carbon monoxide, 2008. www.UptoDate.com

2

2.50 Alveolo-Arterial Diffusion of Oxygen (A-aDO_2)

The alveolo-arterial diffusion of oxygen (A-a DO_2)

Represents the ease with which the administered oxygen diffuses into the blood, and therefore reflects the efficiency of the lungs in oxygenating the blood.

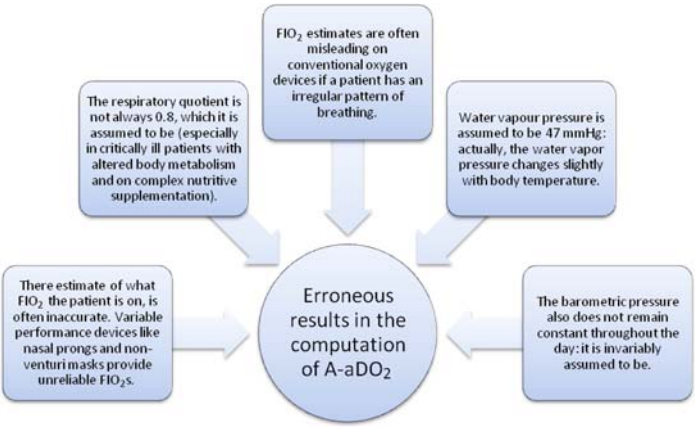
The A-a DO_2 is the difference between the alveolar O_2 tension (PAO_2) and the arterial oxygen tension (PaO_2).

- In order to compute the A-a DO_2 it is necessary to calculate the PAO_2 (from the modified alveolar gas equation):
  $PAO_2 = FIO_2 (Pb-Pw) - PaCO_2/R$ where,
- PaO_2 = alveolar oxygen tension
- FIO_2 = fraction of inspired oxygen
- Pb = atmospheric pressure in mmHg
- Pw = partial pressure of water (47 mmHg at body temperature)
- $PaCO_2$ = arterial CO_2 tension
- R = respiratory quotient

Mellemgaard, K. The alveolar-arterial oxygen difference: its size and components in normal man. Acta Physiol Scand 1966; 67:10

Kanber, GJ, King, FW, Eshchar, YR, Sharp, JT. The alveolar-arterial oxygen gradient in young and elderly men during air and oxygen breathing. Am Rev Respir Dis 1968; 97:376

2.51 Limitations of the A-aDO_2



Martin, L. All you really need to know to interpret blood gases. Lippincott Williams and Wilkins, 1999 p.53

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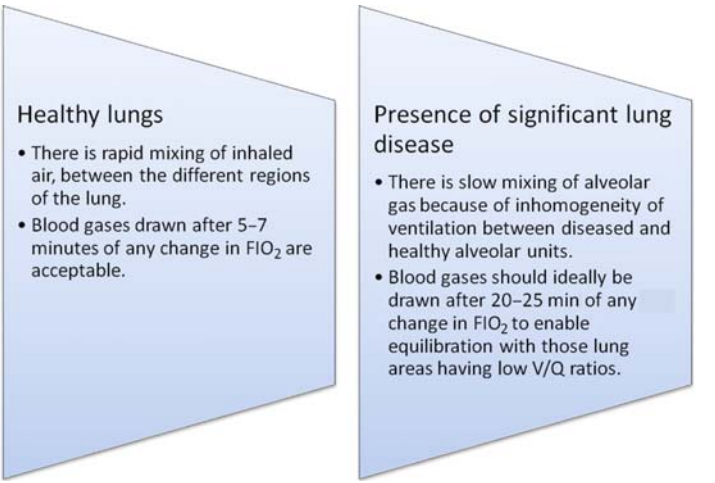
2.52 Timing the ABG

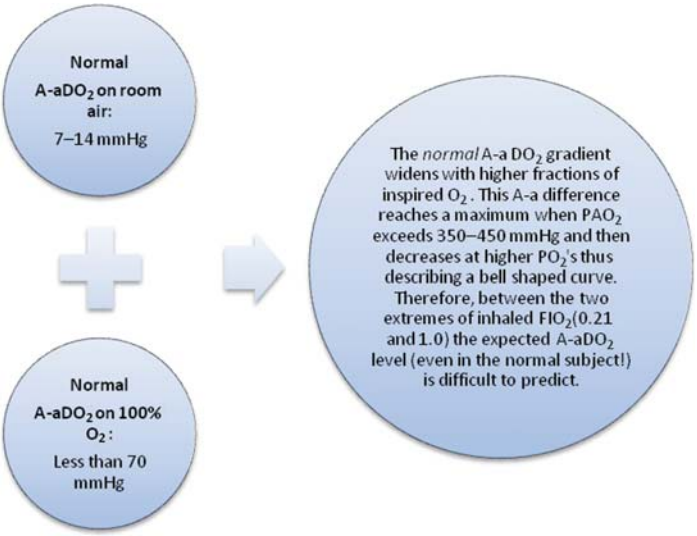


Cugell DW. How long should you wait [editorial]? Chest 1975; 67:253

2.53 A-aDO_2 on Intermediate Levels of FIO_2

The A-a DO_2 normally increases with age. The following formula predicts the A-aDO_2 for a given age:

$$A - a\,DO2 = 2.5 + (0.25 \times \text{Age in years})$$



Kanber, GJ, King, FW, Eshchar, YR, Sharp, JT. The alveolar-arterial oxygen gradient in young and elderly men during air and oxygen breathing. Am Rev Respir Dis 1968; 97:376

Gilbert, R, Keighley, JF. The arterial/alveolar oxygen tension ratio. An index of gas exchange applicable to varying inspired oxygen concentrations. Am Rev Respir Dis 1974; 109:142

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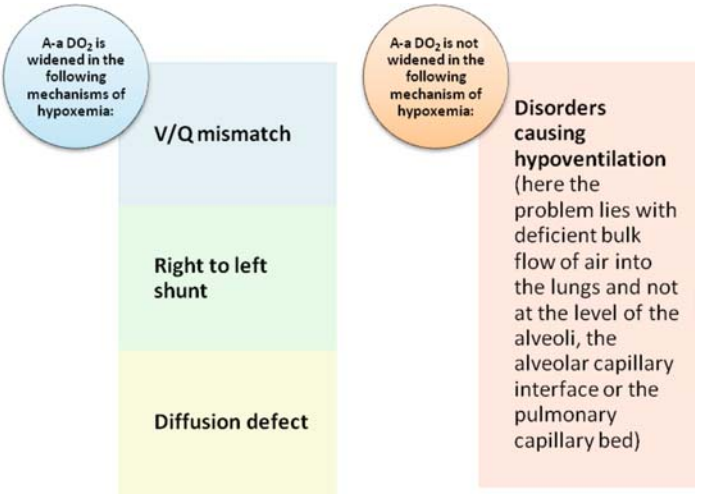
2.54 The Utility of A-aDO$_2$



Chapter 3
The Noninvasive Monitoring of Blood Gases

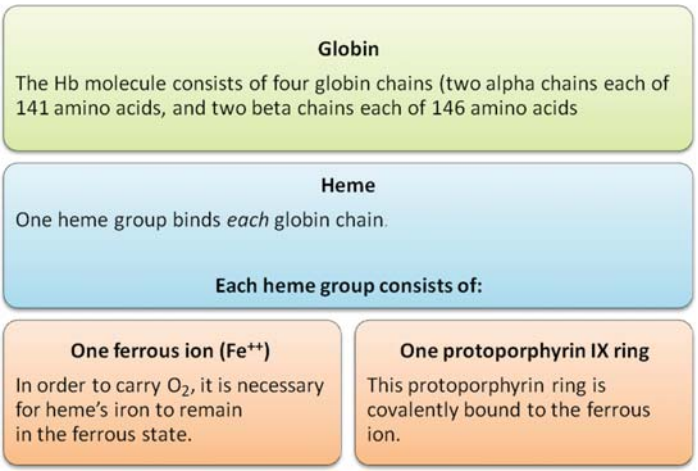
3

Contents

A. Hasan, *Handbook of Blood Gas/Acid–Base Interpretation*,
DOI 10.1007/978-1-84800-334-7_3,

3.1 The Structure of Hemoglobin

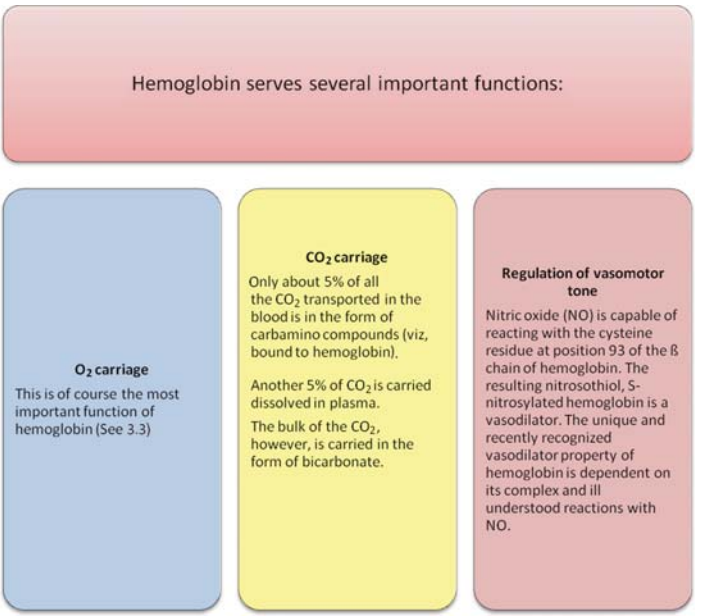
The special ability of hemoglobin to imbibe O_2 from the pulmonary capillaries and release it to the tissues derives from its unique quartenary structure.



Perutz, MF. Molecular anatomy, physiology, and pathology of hemoglobin. In: Stamatoyannopoulos, G, Nienhuis, AW, et al. (Eds). The Molecular Basis of Blood Disorders, WB Saunders, Philadelphia, 1987

Bunn, HF, Forget, BG. Hemoglobin: Molecular, Genetic and Clinical Aspects. WB Saunders, Philadelphia 1986

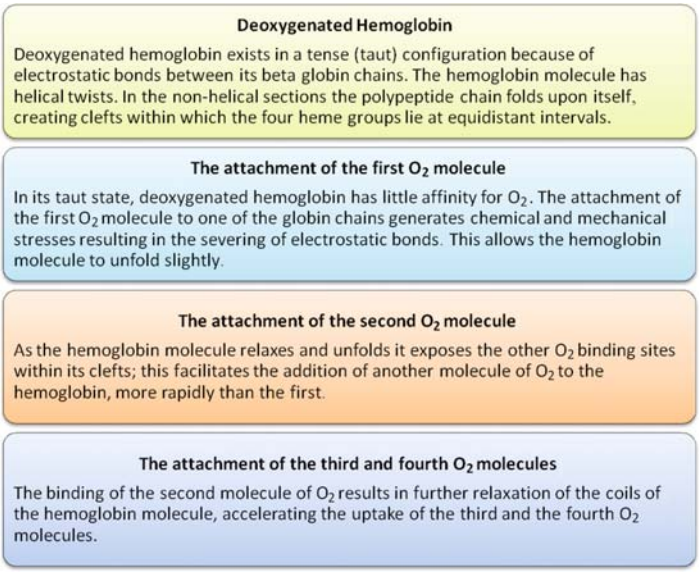
3.2 Functions of Hemoglobin



Stamler, JS, Jia, L, Eu JP, McMahon, TJ, Demchenko, IT, Bonaventura, J, Gernert, K, Piantadosi, CA. Blood flow regulation by S-nitrosohemoglobin in the physiological oxygen gradient. Science 1997; 276:2034–2037

McMahon, TJ, Moon, RE, Luschinger, BP, Carraway, MS, Stone, AE, Stolp, BW, Gow, AJ, Pawloski, JR, Watke, P, Singel, DJ, et al. Nitric oxide in the human respiratory cycle. Nat Med 2002; 8:711–717

3.3 Co-operativity

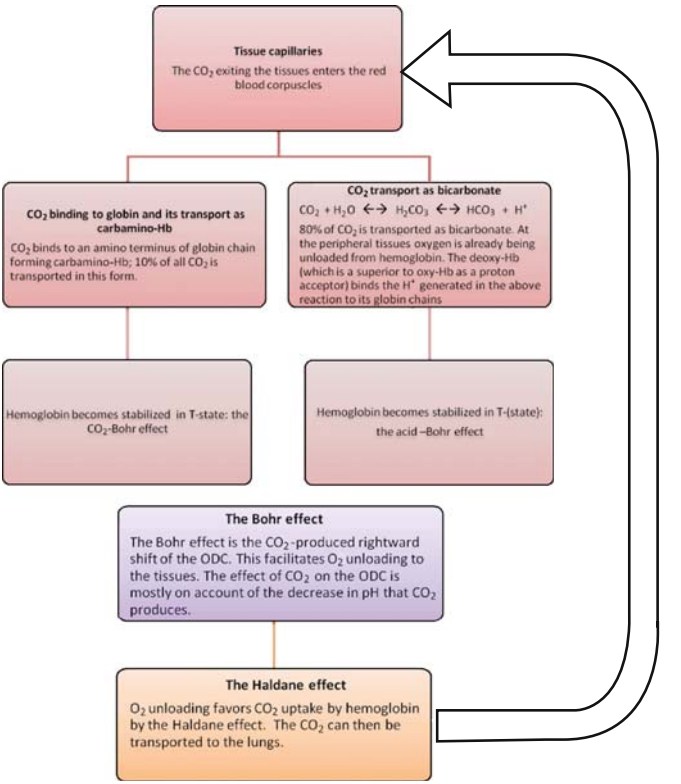


The co-operativity among its binding sites that results in the accelerated uptake of O_2 gives the oxy-hemoglobin dissociation curve its characteristic sigmoid shape.

Perutz, MF. Molecular anatomy, physiology, and pathology of hemoglobin. In: Stamatoyannopoulos, G, Nienhuis, AW, et al. (Eds). The Molecular Basis of Blood Disorders, WB Saunders, Philadelphia, 1987

Bunn, HF, Forget, BG. Hemoglobin: Molecular, Genetic and Clinical Aspects. WB Saunders, Philadelphia, 1986

3.4 The Bohr Effect and the Haldane Effect

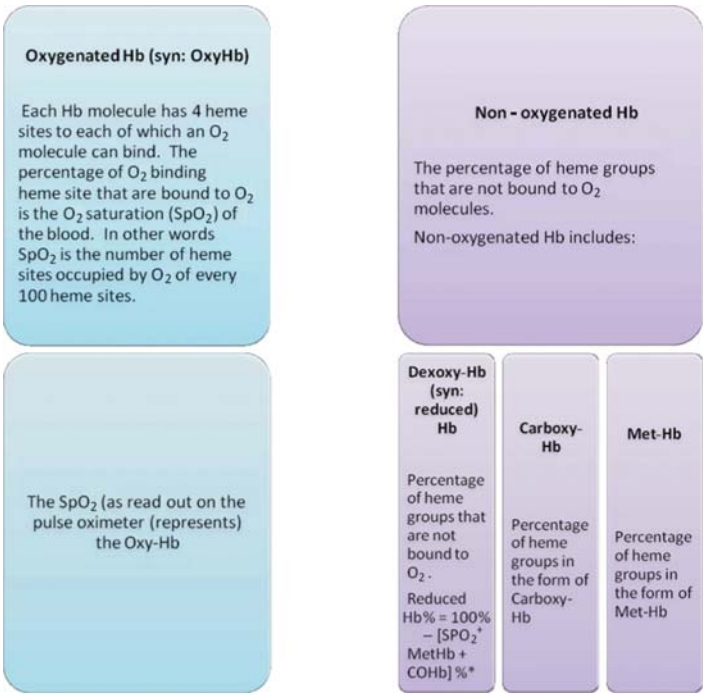


Bohr, C, Hasselbalch, K, Krogh, A. Ueber einen in biologischer Beziehung wichtigen Einfluss. den die Kohlen- sauerespannung des Blutes auf dessen Sauerstoffbinding ubt. Skand Arch Physiol 1904; 16:402

Busch, MR, Mace, JE, Ho, NT, Ho, C. Roles of the beta 146 histidyl residue in the molecular basis of the Bohr effect of hemoglobin: A proton nuclear magnetic resonance study. Biochemistry 1991; 30:1865

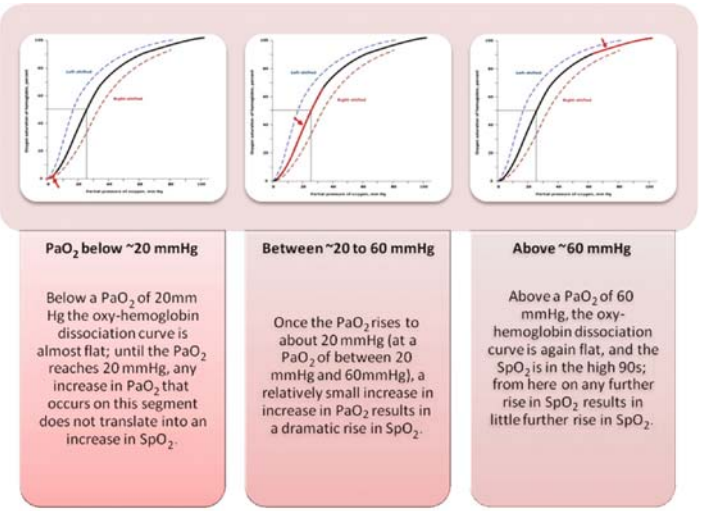
Klocke RA. Mechanism and kinetics of the Haldane effect in human erythrocytes. J Appl Physiol 1973; 35:673–681

3.5 Oxygenated and Non-oxygenated Hemoglobin

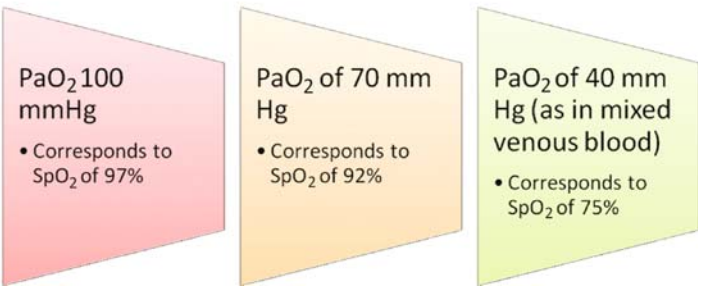


See Co-oximetry (3.22)

3.6 The Oxyhemoglobin Dissociation Curve



The following co-ordination points should be expected for an ODC that lies in its normal position:



Interpreting Arterial Blood Gases, *Canham EM, Beuther DA,* PCCU-on line, Chest.

3.7 Continuous Invasive O_2 Monitoring

Although direct measurement of arterial O_2 tension by arterial blood gas (ABG) sampling is a very accurate way of assessing oxygenation, it has its disadvantages.

Intermittent ABG sampling

- Inconvenience
- Pain
- Bleeding
- Infection
- Arterial thrombosis
- Gangrene of an extremity

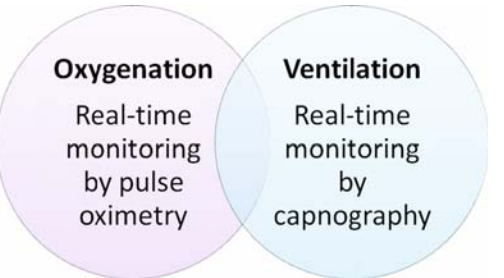
Continuous ABG sampling

- Obviates the need for frequent arterial punctures
- Generally used in unstable clinical situations
- However, continuous ABG sampling is *also associated with significant complications* as with intermittent sampling

Pierson, DJ. Pulse oximetry versus arterial blood gas specimens in long-term oxygen therapy. Lung 1990; 168 Suppl:782

Inman, KJ, Sibbald, WJ, Rutledge, FS. Does implementing pulse oximetry in a critical care unit result in substantial arterial blood gas savings? Chest 1993; 104: 543

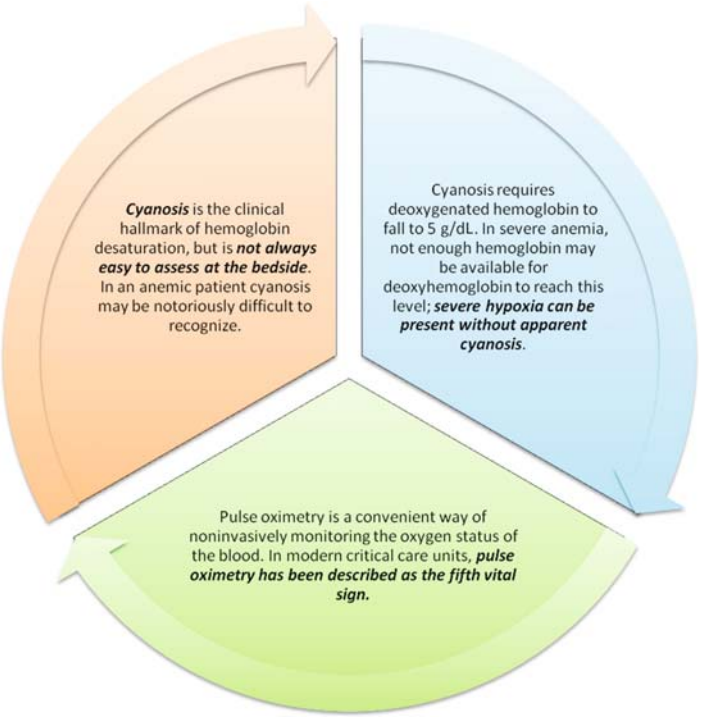
3.8 Noninvasive Monitoring of Blood Gases



Bongard, F, Sue, D. Pulse oximetry and capnography in intensive and transitional care units. West J Med 1992; 156:57

Greene, GE, Hassel, KT, Mahutte, CK. Comparison of arterial blood gas with continuous intraarterial and transcutaneous PO_2 sensor in adult critically ill parients. Crit Care Med 1987; 15:491

3.9 SpO_2 and Pulse Oximetry

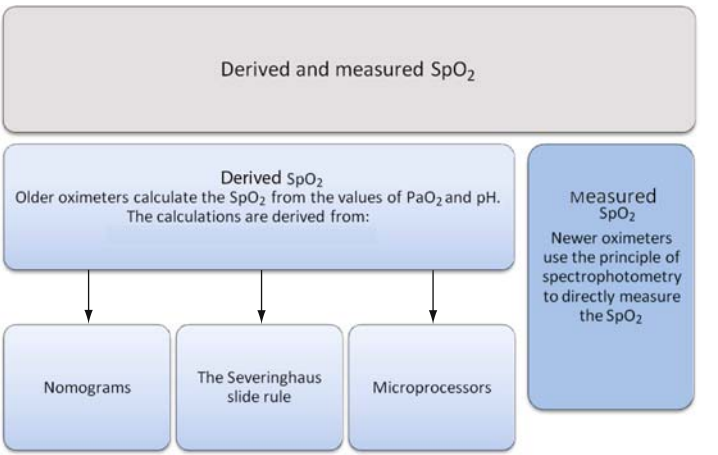


Comroe, JH Jr, Botelho, S. The unreliability of cyanosis in the recognition of arterial hpoxemia. Am J Med Sci 1947; 214:1

Martin, L, Khalil, H. How much reduced hemoglobin is necessary to generate central cyanosis? Chest 1990; 97:182

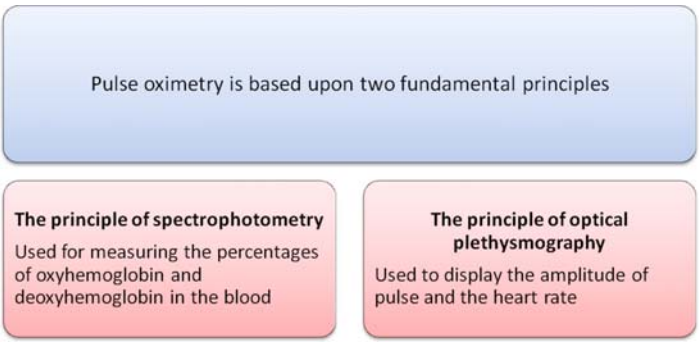
Neff, TA. Routine oximetry: A fifth vital sign? Chest 1988; 94:227

3.10 Derived and Measured SpO_2



Interpreting Arterial Blood Gases, *Canham EM, Beuther DA,* PCCU-on line, Chest.

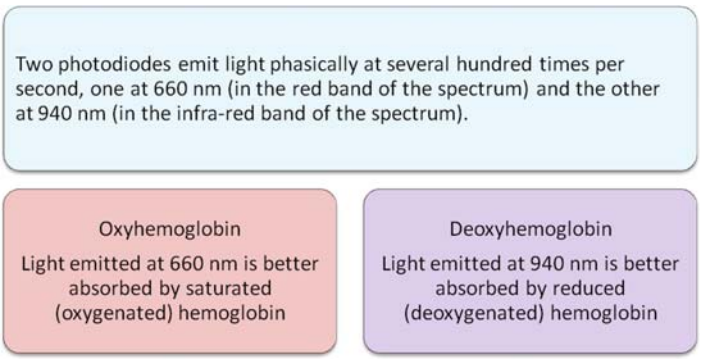
3.11 Principles of Pulse Oximetry



Hanning, CD, Alexander-Williams, JM. Pulse oximetry: A practical review. BMJ 1995

3.12 Spectrophotometry

The principle **of spectrophotometry** is based upon on the *Beer–Lambert law* which states that *the concentration of light-absorbing species within a sample is a logarithmic function of the amount of light absorbed by that sample*.
In respect of blood, the light-absorbing species are oxyhemoglobin and deoxyhemoglobin.



The phasic emission of light differentiates the light absorbance of the arterial blood from that of the light absorbance of venous blood and the surrounding tissue.

Mendelson, Y. Pulse oximetry: Theory and applications for noninvasive monitoring. Clin Chem 1992; 38:1601

3.13 Optical Plethysmography

The principle of optical plethysmography is made use of to display the amplitude of pulse and the heart rate. Each peak of the arterial waveform corresponds to one cardiac cycle. Occasionally a smaller secondary peak due to the venous pressure pulse can be distinguished. The phasic signal presented to the sensor calculates the pulse amplitude according to the relative absorbencies during systole and diastole.

Ventricular systole	Ventricular diastole
Phasic increase of blood volume in perfused organs.	Phasic decrease of blood volume in perfused organs.
Light has to travel a longer distance through the *distended* subcutaneous tissue (of the finger or ear lobe).	Light has to travel a shorter distance through the *contracted* subcutaneous tissue (of the finger or ear lobe).
Light transmission through the sampling site decreases.	Light transmission through the sampling site increases.

This difference is made use of to generate a waveform which is displayed on the monitor.

Mendelson, Y. Pulse oximetry: Theory and applications for noninvasive monitoring. Clin Chem 1992; 38:1601

3.14 Types of Pulse Oximeters in Contemporary Use

Two types of pulse oximeters are in contemporary use: transmission pulse oximeters and reflectance pulse oximeters. Transmission pulse oximeters are the more extensively used of the two

Transmission pulse oximeters

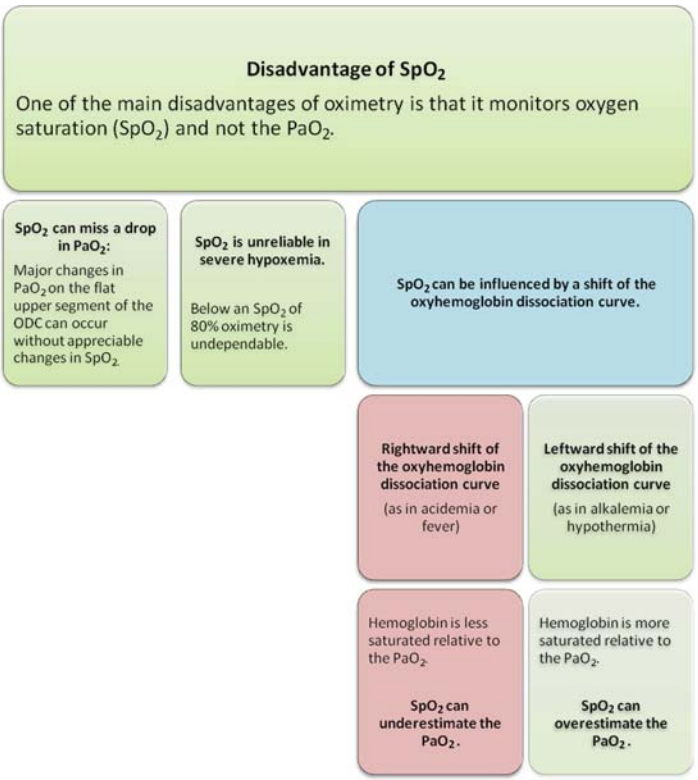
A pair of light emitting diodes (LEDs) emit light through interposed tissue (typically a finger, toe or an earlobe). The change in light frequency is read out by a photodetector placed on the *opposite side* of the interposed tissue.

Reflectance pulse oximeters

Photowaves from LEDs are bounced off an appropriate surface (e.g. the skull bone). The reflected beam of light passes back through the tissue, (e.g. the skin of the forehead), to reach a photodetector placed *adjacent* to the LEDs.

Tallon, RW. Oximetry: state-of-the-art. Nurs Manage 1996; 27:43

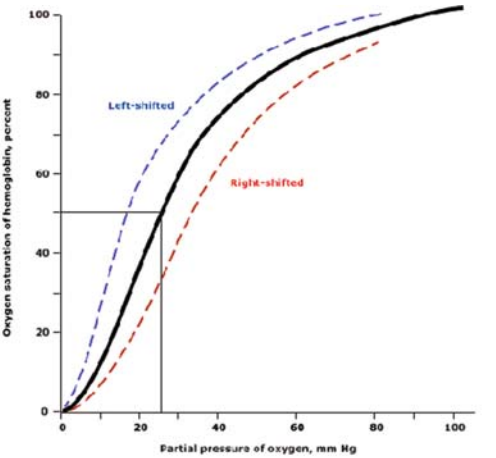
3.15 Pulse Oximetry and PaO_2



Stoneham, MD. Uses and limitations of pulse oximetry. Br J Hosp Med 1995; 54:35

Ralston, AC, Webb, RK, Runciman, WB. Potential errors in pulse oximetry. Anaesthesia 1991; 46:291

3.16 The P_{50}



P_{50}

The position of the oxy-Hb dissociation curve (ODC) can be assessed from the P_{50}, which is the PaO_2 at which the Hb is 50% saturated.

The normal P_{50} is 26.6 mm Hg

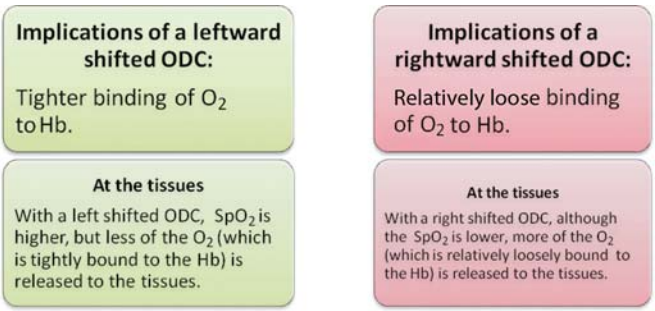
P_{50} < 26.6 mmHg

A lower than normal P_{50} means a leftward shifted ODC.

P_{50} > 26.6 mmHg

A higher than normal P_{50} means a rightward shifted ODC.

3.17 Implications of Shifts in the ODC



3.18 Conditions that Shift the ODC

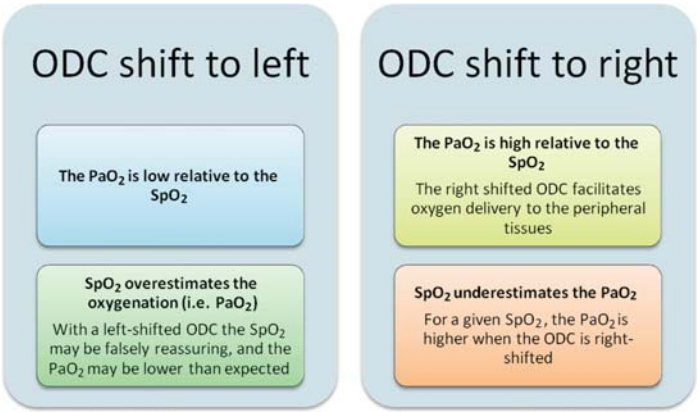
Leftward shift of the ODC occurs in the following conditions:

- Alkalemia
- Hypothermia
- Abnormal hemoglobins, e.g.:
  - *Carboxy-hemoglobin*
  - *Met-hemoglobin*
  - *Fetal hemoglobin*
  - *Myxedema*
- Low inorganic phosphates

Rightward shift of the ODC occurs in the following conditions:

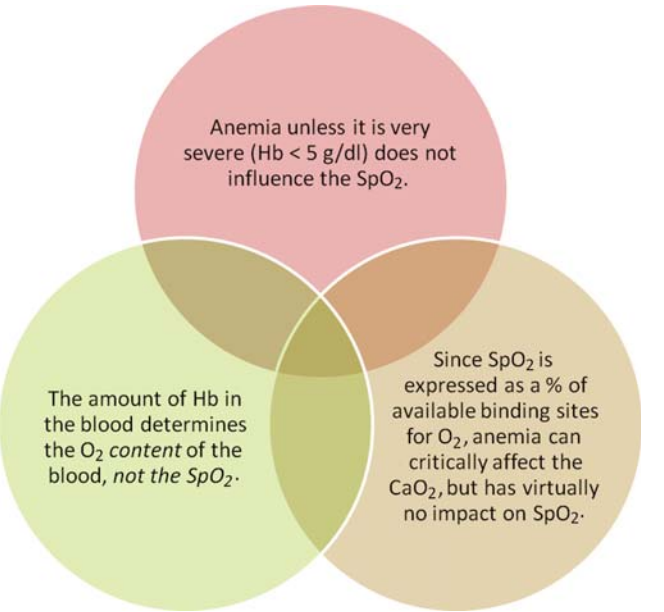
- Acidemia
- Fever
- Abnormal hemoglobins, e.g.:
  - *Hb Kansas*
- Thyrotoxicosis
- Raised inorganic phosphate
- Anemia
- Steroid therapy

3.19 The Position of the ODC



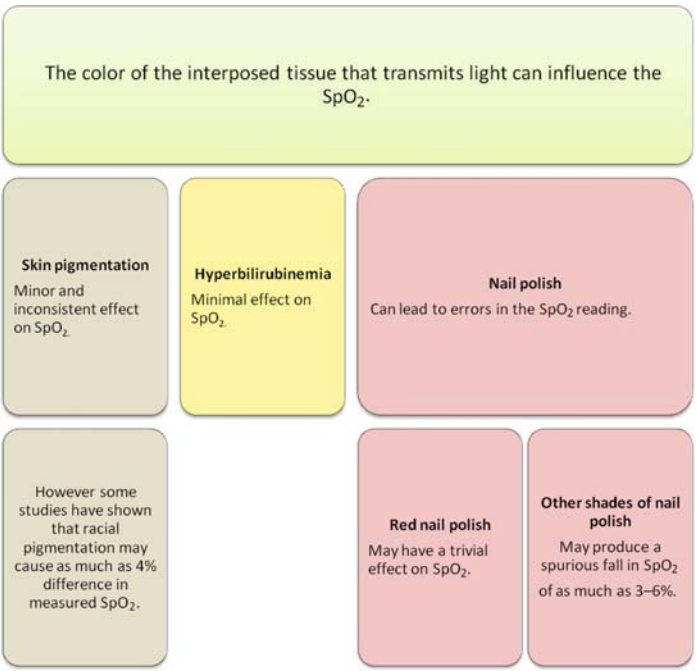
The SpO_2 therefore must be interpreted in the light of the position of the ODC.

3.20 SpO_2 and Anemia



Schnapp, LM, Cohen, NH. Pulse oximetry: Uses and abuses. Chest 1990; 98:1244

3.21 SpO_2 and Pigmentation



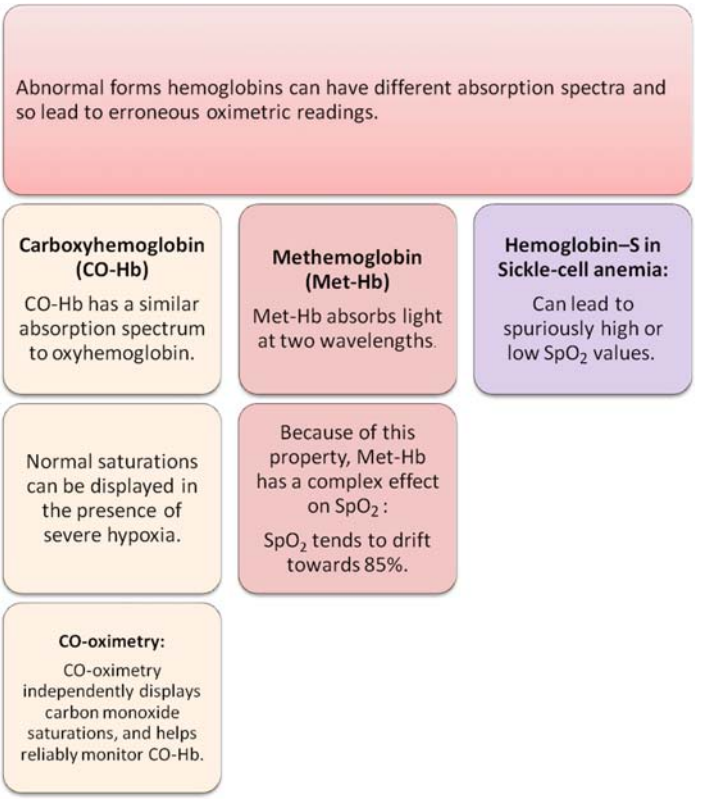
Ralston, AC, Webb, RK, Runciman, WB. Potential errors in pulse oximetry. III: Effects of interference, dyes, dyshaemoglobins and other pigments. Anaesthesia 1991; 46:291

Veyckemans, F, Baele, P, Guillaume, JE, et al. Hyperbilirubinemia does not interfere with hemoglobin saturation measured by pulse oximetry. Anesthesiology 1989; 70:118

Zeballos, RJ, Weisman, IM. Reliability of noninvasive oximetry in black subjects during exercise and hypoxia. Am Rev Resp Dis 1991; 144:1240

Brand, TM, Brand, ME, Jay, GD. Enamel nail polish does not interfere with pulse oximetry. J Clin Monit Comput 2002; 17:93

3.22 SpO_2 and Abnormal Forms of Hemoglobin



Eisenkraft, JI, Pulse oximeter desaturation due to methemoglobinemia. Anesthesiology 1988; 68:279

Ernst, A, Zibrak, JD. Carbon monoxide poisoning. New Engl J Med 1998; 339:1603–1608

Ortiz, FO, Aldrich, TK, Nagel, RL, Benjamin, LJ. Accuracy of pulse oximetry in sickle cell disease. Am J Respir Crit Care Med 1999; 159:447

3.23 Methemoglobinemia

Normal hemoglobin carries its iron as ferrous ions

Hb is capable of binding O_2 provided the ferrous iron remains in its reduced state. The special configuration of the hemoglobin chains appears to protect the ferrous ions from oxidation to the ferric state.

Pulmonary capillaries

In the pulmonary capillaries each ferrous ion binds an O_2 atom, in the process briefly donating an electron to the latter.

Tissue capillaries

At the tissue capillary level the O_2 atom cleaves away from the Hb molecule in the process reacquiring its electron. The reduction of the iron back to its ferrous form makes it free to bind and transport O_2 again.

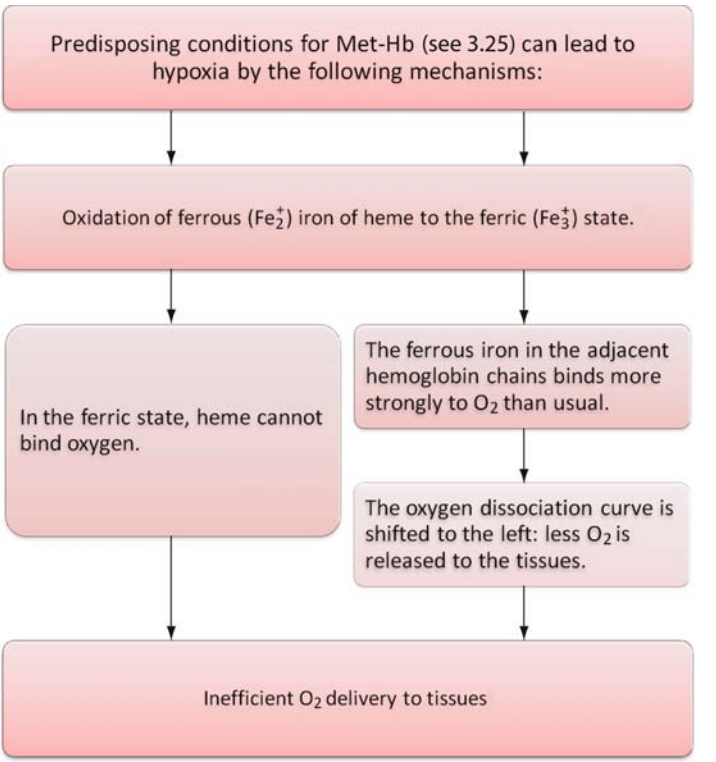
Met-Hb carries its iron as ferric ions

Met-Hb, as opposed to deoxy Hb carries its iron in the ferric form, in which state it is unable to bind O_2. The amount of Hb that exists as Met-Hb cannot participate in O_2 transport.

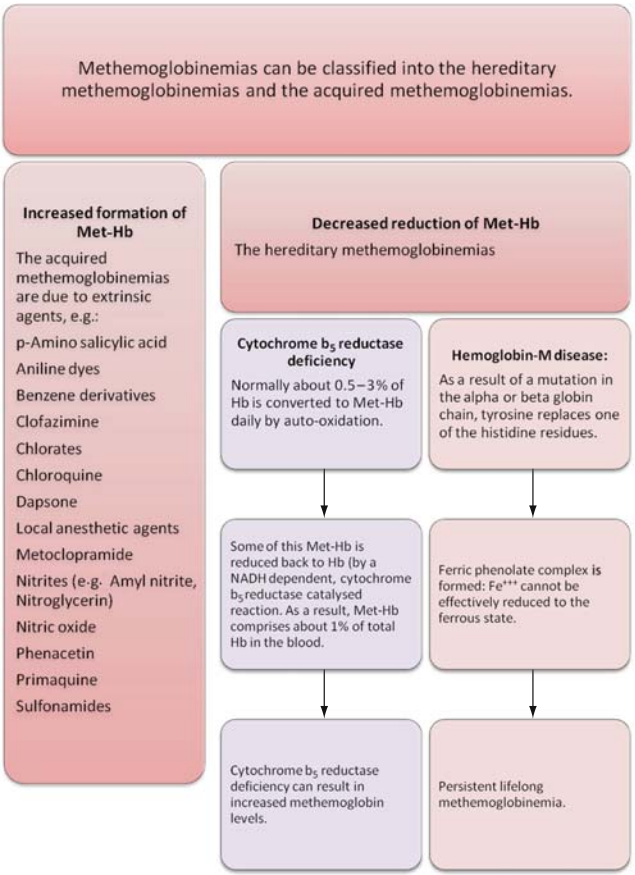
Wright, RO, Lewander, WJ, Woolf, AD. Methemoglobinemia: etiology, pharmacology, and clinical management. Ann Emerg Med 1999; 34:646–656

Curry S. Methemoglobinemia. Ann Emerg Med 1982; 11:214–221

3.24 Methemoglobinemia: Mechanisms of Hypoxia



3.25 Methemoglobinemias: Classification

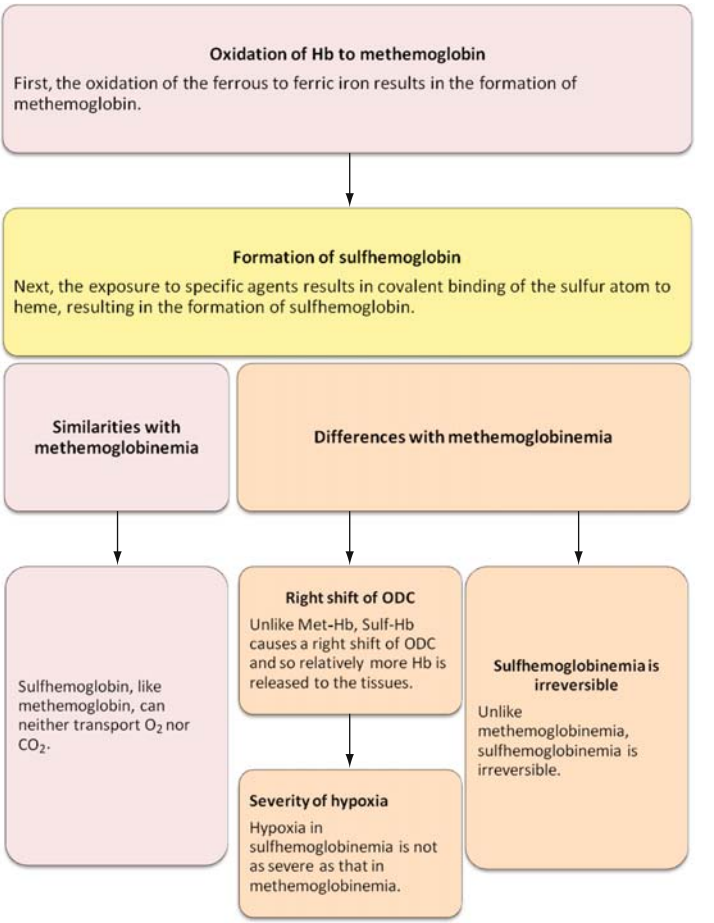


Curry, S. Methemoglobinemia. Ann Emerg Med 1982; 11:214–221

Jaffe, ER. Enzymopenic hereditary methemoglobinemia: a clinical/biochemical classification. Blood Cells 1986; 12:81–90

Prchal, JT. Diagnosis and treatment of methemoglobinemia, Uptodate.com

3.26 Sulfhemoglobinemia



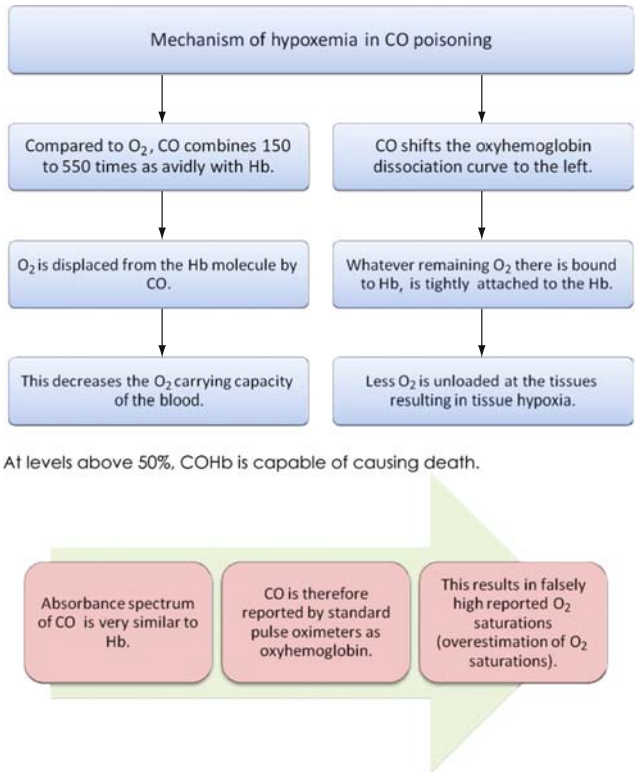
Oximeters that measure met-hb can erroneously read sulf-hb as met-hb

---

Park, CM, Nagel, RL. Sulfhemoglobinemia. N Engl J Med 1984; 310:1579–1584

3.27 Carboxyhemoglobin (COHb)

The incomplete combustion of hydrocarbons leads to the formation of CO, a colorless, odorless gas. Normally, the levels of COHb are < 3% (of total Hb) in the urban population; smokers have a COHb level of 5–10% (of total Hb) in their blood.



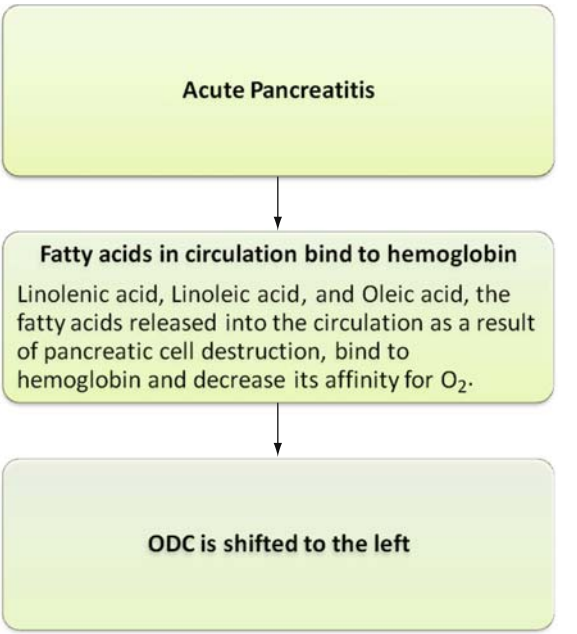
The clue to diagnosing CO poisoning is an elevated saturation gap (see 3.29). CO-oximetry relibly measures CO levels and can be used when CO poisoning is suspected.

Weaver, LK. Carbon monoxide poisoning. Crit Care Clin 1999; 15:297.

Caughey, WS. Carbon monoxide bonding in hemeproteins. Ann N Y Acad Sci 1970; 174:148.

3.28 Acute Pancreatitis

The ODC is left-shifted in 20–70% of acute pancreatitis



Greenberg, AG, Terlizzi, L, Peskin, G. Oxyhemoglobin affinity in acute pancreatitis. J Surg Res 22: 561–565, 1977

3.29 Saturation Gap

The O_2 analyses by the pulse oximeter and the ABG are based upon the premise that only 2 forms of Hb are possible: oxyhemoglobin and deoxyhemoglobin; and that no abnormal forms of hemoglobin are present.

SpO_2

The Hb saturation of O_2 as *measured* by pulse oximetry

SaO_2

The Hb saturation of O_2 as *calculated* by the ABG machine

The pulse oximeter measures light absorbance at 2 wavelengths (see 3.12). With significant levels of methemoglobin in the blood, the SpO_2 drifts towards 85% (see 3.22).

The ABG machine first measures the PaO_2 and then calculates the expected SaO_2 from this, based on the ODC. (In the absence of cardiopulmonary disease), even though hemoglobins may be present, the PaO_2 level is normal: therefore the SaO_2 is normal.

The saturation gap

When the difference in SaO_2 and SpO_2 is > 5%, a saturation gap is said to exist. A saturation gap is a clue to significant levels of Met-Hb and Sulf-Hb in the blood*.

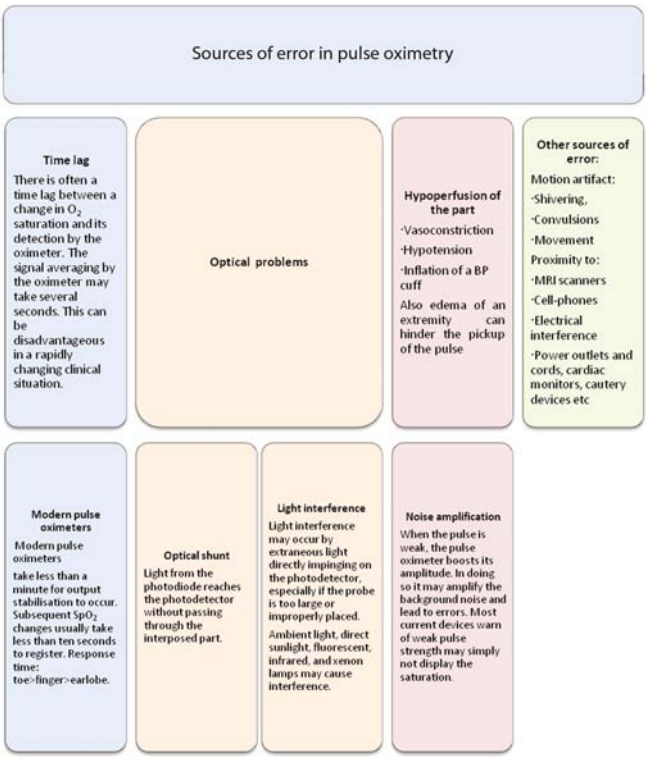
*Other substances associated with a saturation gap: carbon monoxide, cyanide, and hydrogen sulfide

Eisenkraft, JB. Pulse oximeter desaturation due to methaemoglobinemia. Anaesthesiology 1988; 68:279–282

Oesenberg, B. Pulse oximetry in methaemoglobinemia. *Anaesthesia* 1990;45:56

Mokhlesi, B, Leiken, JB, Murray, P, Corbridge, TC. Adult Toxicology in Critical Care, Part I: General Approach to the Intoxicated Patient. (Chest 2003; 123:577–592

3.30 Factors Interfering with the Measurement of SpO_2



Gehring, H, Hornberger, C, Matz, H, et al. The effects of motion artifact and low perfusion on the performance of a new generation of pulse oximeters in volunteers undergoing hypoxemia. Respir Care 2002; 47:48

Fluck, RR Jr, Schroeder, C, Frani, G, et al. Does ambient light affect the accuracy of pulse oximetry? Respir Care 2003; 48:677

Ralston, AC, Webb, RK, Runciman, WB. Potential errors in pulse oximetry. Anaesthesia 1991; 46:291

Van de, Louw A, Cracco, C, Cerf, C, et al. Accuracy of pulse oximetry in the intensive care unit. Intensive Care Med 2001; 27:1606

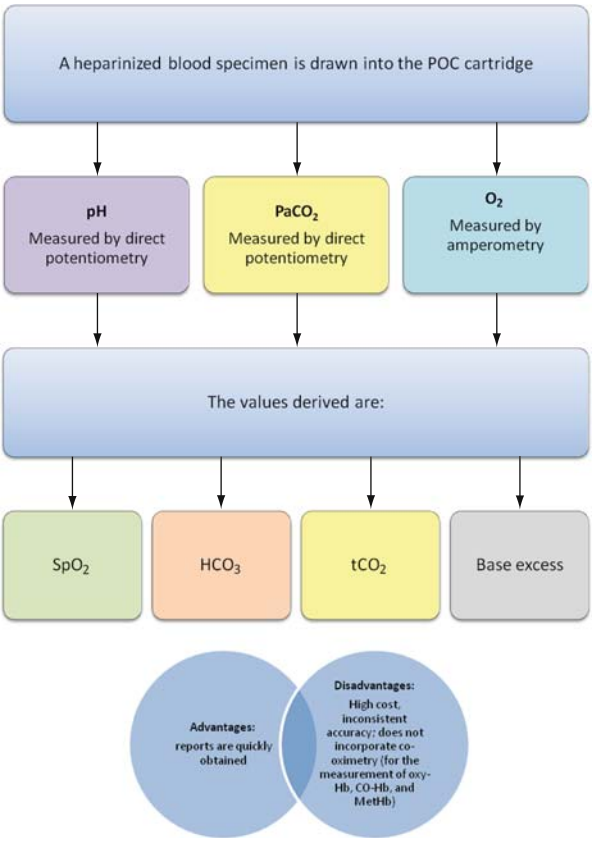
3.31 Low Signal Strength

Gehring, H, Hornberger, C, Matz, H, et al. The effects of motion artifact and low perfusion on the performance of a new generation of pulse oximeters in volunteers undergoing hypoxemia. Respir Care 2002; 47:48

Lee, WW, Mayberry, K, Crapo, R, Jensen, RL. The accuracy of pulse oximetry in the emergency department. Am J Emerg Med 2000; 18:427

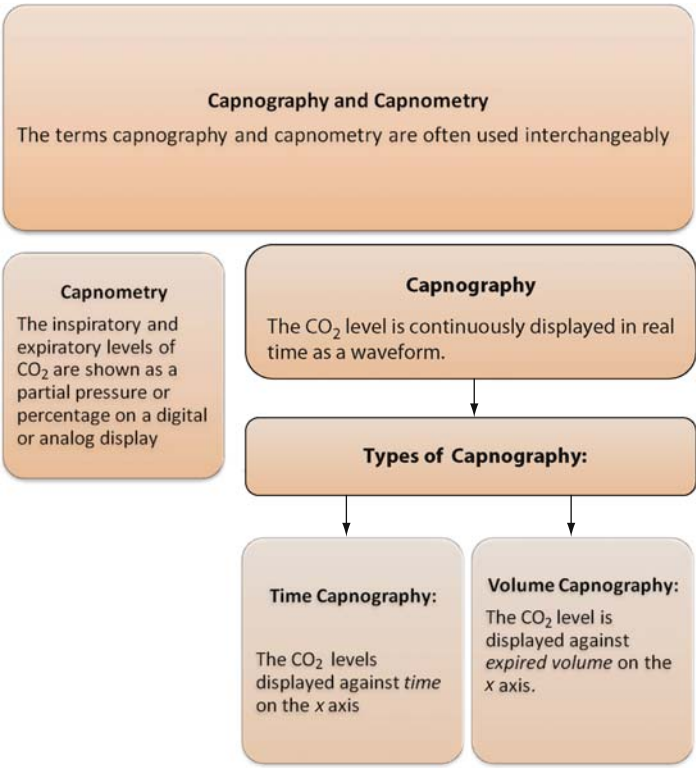
3.32 Point of Care (POC) Cartridges

Lately, handheld *Point of Care* (POC) cartridges are being used for the bedside measurement of the pH, $PaCO_2$, and PaO_2.



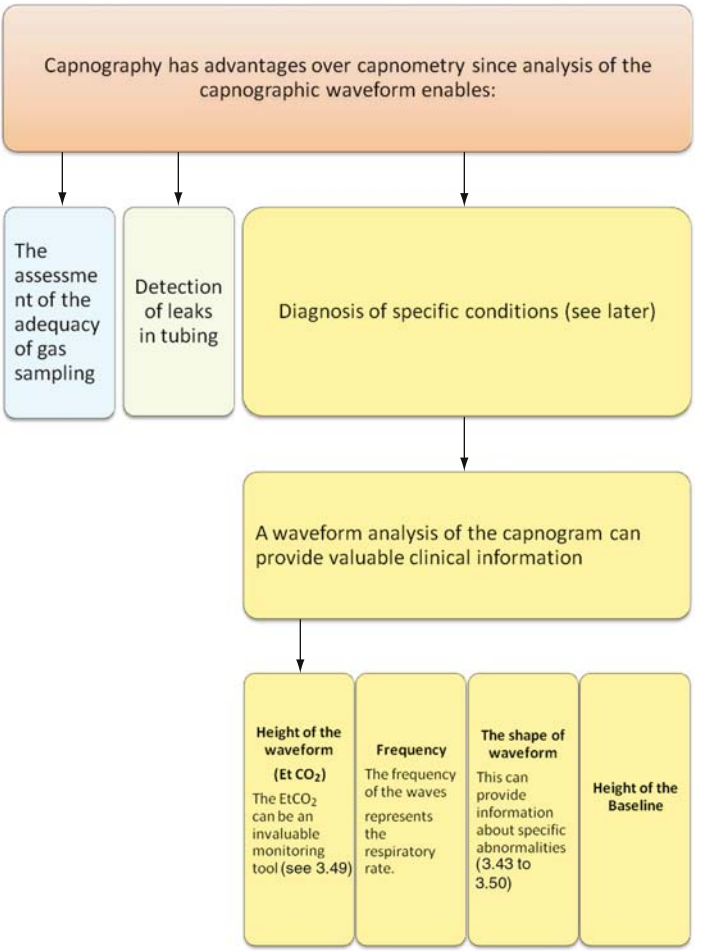
Canham, EM. Interpretation of arterial blood gases. In: Parsons, PE, Weiner-Kronish, JP, eds. Critical care secrets. 3rd ed. Philadelphia, Hanley and Belfus, Inc, 21–24, 2003

3.33 Capnography and Capnometry



3.34 Advantages of Capnography

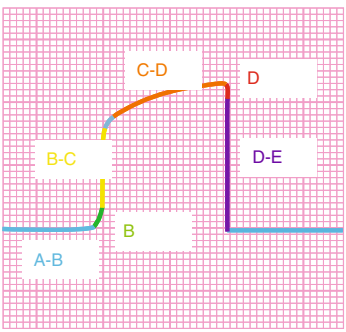
Capnometry is the non-invasive measurement of exhaled CO_2, which is displayed as an end expiratory (end-tidal) value. Capnography is the real time monitoring of the exhaled CO_2 over time: it is displayed as a waveform.



3.35 The Capnographic Waveform

The capnographic waveform can be divided into six distinct parts. The tracing begins with the analysis of the expired air.

A-B: dead-space exhalation	B: the onset of alveolar exhalation	B-C: the continuance of alveolar exhalation	C-D: the alveolar plateau	D: End-tidal CO_2 ($EtCO_2$)	D-E: inspiratory washout
The first part of exhalation contains air from the proximal airway (the conductive zone of the lung).	Alveolar air contains CO_2.	The CO_2 rises rapidly as alveolar gas mixed with dead-space gas arrives at the sensor.	Most of the gas received at the sensor is now alveolar gas.	The peak at the end of the plateau represents the averaging of alveolar CO_2 levels	The graph then falls rapidly to the baseline.
This air is devoid of CO_2, and so the CO_2 waveform is a flat line that lies close to the baseline.	As alveolar air begins to arrive at the sampling site, the capnograph shows a sudden upturn.	The capnograph shows a steep upslope.	The gradually upsloping plateau represents the constant emptying of viable alveoli.	The peak represents the end-tidal CO_2.	The nadir represents the negligible CO_2 concentrations (0.003% or 0.02 mm Hg) that reach the alveoli from the ambient air.



Stock, MC. Capnography for adults. Crit Care Clinics 1995; 11:219

3.36 Main-stream and Side-stream Capnometers

MAINSTREAM	SIDE STREAM
•The main unit incorporating a CO_2 sensor is itself directly attached to a T- adapter interposed between the ET and the patient-circuit.	•A relatively long sampling tube connected to the piece draws away the gas sample to a CO_2 sensor located in a central unit.
	•The sampling flow rate can be as high as 150 mL /min. This can result in substantial deformation of the waveform when low tidal volumes are used as in neonates and infants.
•There is no sampling tube. Sensor windows are prone to clogging by secretions, aerosols, or water droplets.	•Sampling tube prone to becoming obstructed as secretion can be sucked in by the rapid aspiration rate.
•Difficult to use in patients undergoing prone ventilation.	•Relatively easy to connect in prone position
•Unaffected by changes in water vapor pressure. The temperature within the mainstream sensors is maintained at around 39°C to prevent condensation.	•Affected by changes in water vapor pressure.
•No time lag.	•Time lag in display, owing to the relatively long distance of the sensor from the patient's airway.
•Cannot be used in the absence of an artificial airway.	•Can be used even in the absence of an artificial airway.
•Bulky – newer models less so	
•Can increase circuit dead-space and so elevate $PaCO_2$	
•Sterilization is difficult	•Easy to sterilize
	•Side stream capnometers using micro-stream technology have been developed. Using sampling flow rates of as low as 50 mL/min. The emitted wavelength is within a narrower IR band (4.2 – 4.35 hm) which more closely matches the absorption spectrum for CO_2.

Moon, RE, Camporesi, EM. Respiratory monitoring. In: RD Miller, ed. Miller's anesthesia. 6th ed. Philadelphia, PA: Elsevier/Churchill Livingstone, 2005

Kalenda, Z. Mastering infrared Capnography. The Netherlands, Kerckbosch-Ziest 1989

Carbon dioxide monitors. Health Devices 1986; 15:255–85

3.37 $PetCO_2$-a Surrogate for $PaCO_2$

CO_2 diffuses rapidly across all biological membranes including the alveolo-capillary membrane. Arterial CO_2 ($PaCO_2$) equilibrates rapidly with alveolar CO_2 ($PACO_2$), and is effectively identical with it.

$PetCO_2$ offers a non-invasive way of monitoring $PaCO_2$, especially given that:

In health:

1. The value of $PetCO_2$ is close to the value of $PACO_2$; and therefore to that of $PaCO_2$. PaCO2 and $PACO_2$ differ by such a small amount (generally < 5 mm) such as usually makes no clinical difference.
2. The trends in $PetCO_2$ closely match the trends in $PaCO_2$

In disease:

1. In disease, physiological dead-space is often increased because of patent but under-perfused alveoli. Due to the lack of an effective pulmonary circulation CO_2 cannot effectively diffuse into alveoli.

Under such circumstances, $PaCO_2$ can substantially exceed $PetCO_2$.

2. In spite of this, in the absence of major *changes* in dead-space ventilation, the $PetCO_2$ trends still match those of $PaCO_2$

CO_2 values cannot be used as an absolute surrogate for $PaCO_2$. However the $EtCO_2$ may be expected to *parallel* the changes in $PaCO_2$ (i.e., the [A-a] CO_2 gradient remains constant) provided that **the following are stable:**

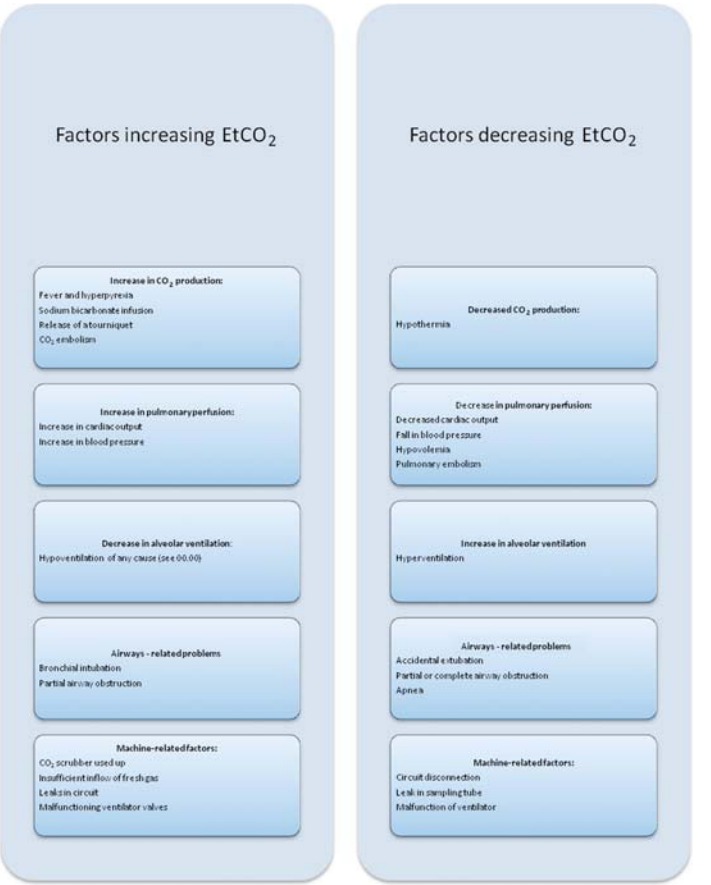
- Stable cardiac condition
- Stable pulmonary condition
- Stable body temperature

Nunn, JF, Hill, DW. Respiratory dead space and arterial to end-tidal CO_2 tension difference in anesthetized man. J Appl Physiol 1960; 15:383–9

Fletcher, R, Jonson, B. Deadspace and the single breath test for carbon dioxide during anaesthesia and artificial ventilation. Br J Anaeasth 1984; 56:109–119

Shankar, KB, Moseley, H, Kumar, Y, Vemula, V. Arterial to end-tidal carbon dioxide tension difference during cesarean section anaesthesia. Anaesthesia 1986; 41:698–702

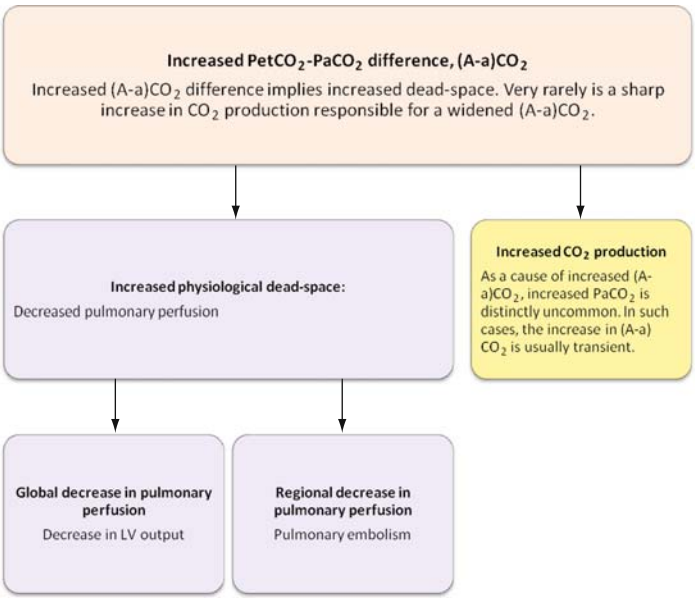
3.38 Factors Affecting $EtCO_2$



(Modified from: Bhavani Shankar. Factors influencing $PetCO_2$; March 2007: Welcome to capnography.com)

Bhavani, S. K, Moseley, H, Kumar, AY, Delph, Y. Capnometry and anaesthesia. Review article. Canadian J Anaesth 1992; 39:6:617–632

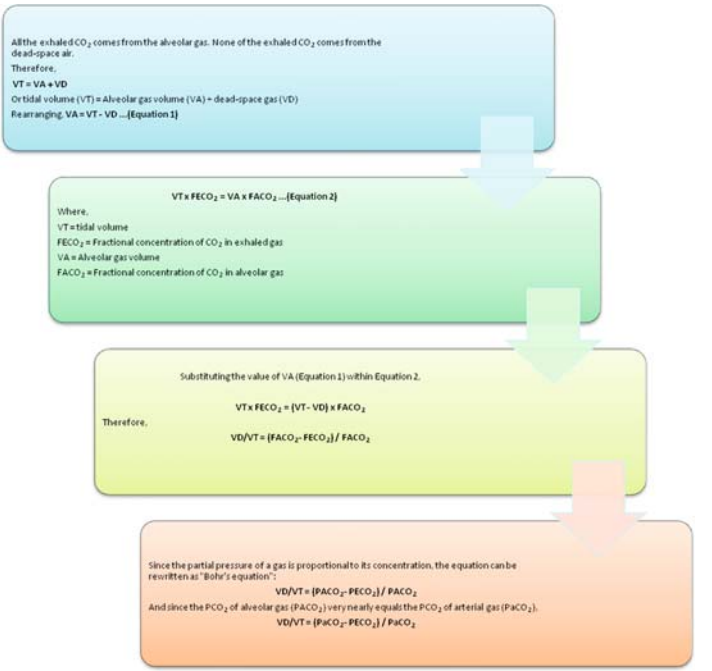
3.39 Causes of Increased $PaCO_2$-$PetCO_2$ Difference



Phan, CQ, Tremper, KK, Lee, SE, Barker, SJ. Noninvasive monitoring of carbon dioxide: A comparison of the partial pressure of transcutaneous and end-tidal carbon dioxide with the partial pressure of arterial carbon dioxide. J Clin Monit 1987; 3:149–54

3.40 Calculating Dead Space by Bohr's Equation

It is possible to estimate the dead space, utilizing Bohr's equation.

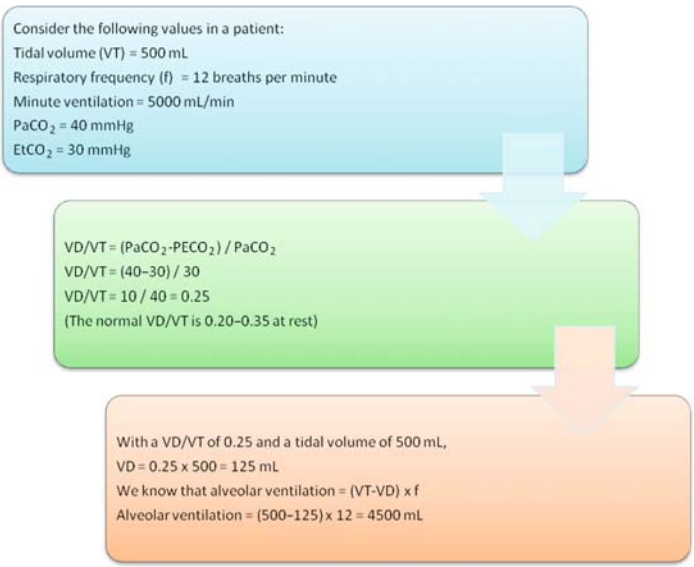


Thus by simultaneously measuring the end-expiratory CO_2($EtCO_2$) and the $PaCO_2$, the dead-space to tidal volume ratio can be calculated (see next page).

Bhavani, S K, Mosely, H, Kumar, AY, Delph, Y. Capnometry and anaesthesia. Canadian J Anaesth 1992; 39:6:617–632

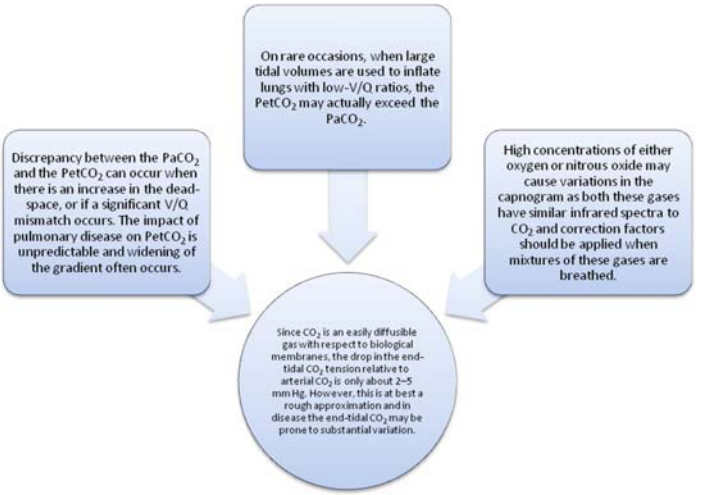
Criner, GJ, D'Alonzo, GE. Pulmonary Pathophysiology, Blackwell 1999

3.41 Application of Bohr's Equation



Criner, GJ, D'Alonzo, GE. Pulmonary Pathophysiology, Blackwell, 1999

3.42 Variations in $EtCO_2$

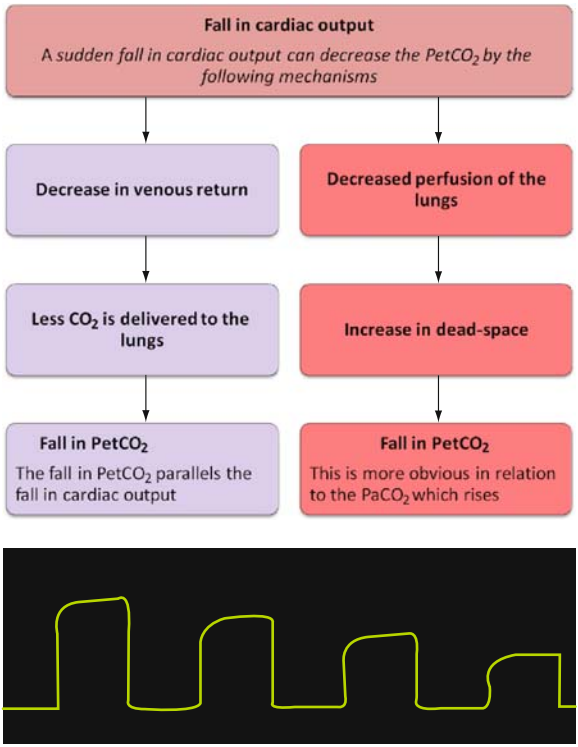


As is apparent in the discussion above, trends in arterial O_2 can be matched by the $PetCO_2$ when the lungs are healthy. But in cases of pulmonary disease, especially in a situation where there is unstable or evolving lung pathology, the end-tidal CO_2 may neither reflect nor parallel changes in $PaCO_2$, and this must be kept in mind.

Moorthy, SS, Losasso, AM, Wilcox, J. End-tidal PCo2 greater than $PaCO_2$. Chest 1984; 12:534

3.43 Capnography and Cardiac Output

When alveolar ventilation is constant, the $PetCO_2$ reflects pulmonary perfusion, which itself is dependent upon the cardiac output.



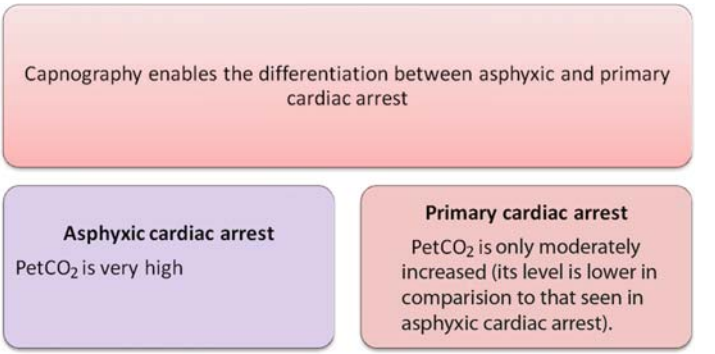
Real-time capnograph showing fall in cardiac output due to cardiac arrest

---

Isserles, S, Breen, PH. Can changes in end-tidal PCO_2 measure changes in cardiac output ? Anest h Anag\lg 1991; 73:808

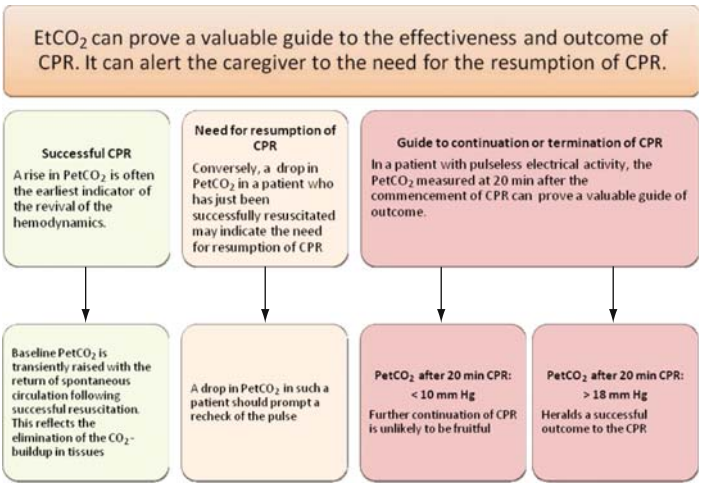
Shibutani, K, Shirasaki, S, Braaz, T, et al. Changes in cardiac output affect $PetCO_2$, CO_2 transport, and O_2 uptake during unsteady state in humans. J Clin Monit 1992; 8:175–176

3.44 Capnography-Clues to Cause of Cardiac Arrest



Grmec, S, Lah, K, Tusek-Bunc, K. Difference in end-tidal CO_2 between asphyxia cardiac arrest and ventricular fibrillation/pulseless ventricular tachycardia cardiac arrest in the prehospital setting. Crit Care 2003; 7:R139–R144

3.45 Capnography as a Guide to Successful CPR



No specific number can be used as a cut off value in distinguishing survivors from non-survivors, and it is believed that the chances for survival increase by 16% for every 1 mm Hg the $PetCO_2$rises (Acad. Em. Med, June 2001)

Falk, JL, Rackow, ED, Weil, MH, "End-tidal carbon dioxide concentration during cardiopulmonary resuscitation." N Engl J Med 1988; 318(10):607–611

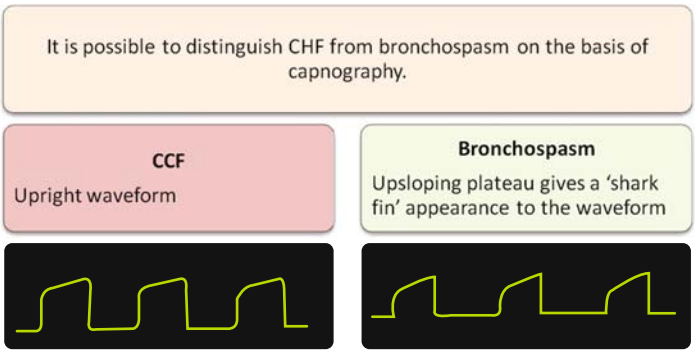
Grmec, S, Klemen, P. Does the end-tidal carbon dioxide ($ETCO_2$) concentration have prognostic value during out-of-hospital cardiac arrest? J Emerg Med 2001; 8:263–269

Callaham, M , Barton, C. Prediction of out come of cardiopulmonary resuscitation from end-tidal carbon dioxide concentration. Crit Care Med 1990; 18:358

Sanders, AB, Kern, KB, Otto, CW, et al. End-tidal carbon dioxide monitoring during cardiopulmonary resuscitation: a prognostic indicator for survival. JAMA 1989; 262:1347

Real-time capnograph showing the return of spontaneous circulation following successful CPR

3.46 Differentiating Congestive Heart Failure from Bronchospasm

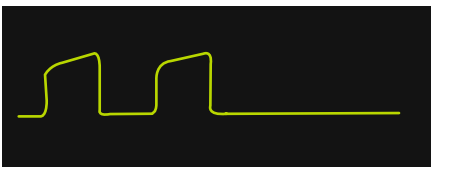


Bhavani Shankar Kodali. 2007. Welcome to Capnography.com

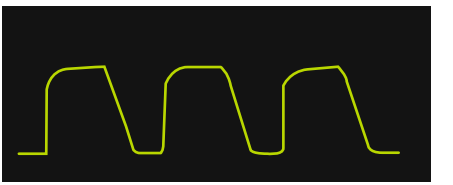
3.47 Capnography in Esophageal Intubation

Normal capnograph

Capnograph in esophageal intubation



Capnograph in self-extubation or disconnection



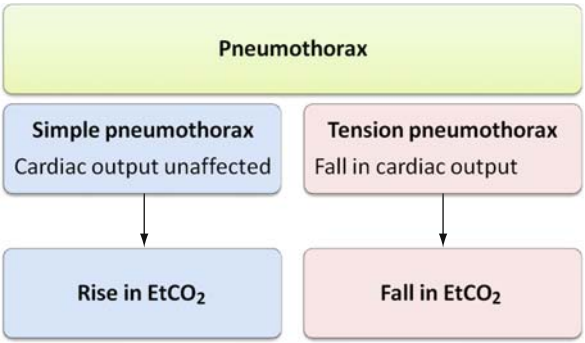
Ruptured ET cuff showing a gradual descent

Birmingham, PK, Cheney, FW, Ward, RJ. Esophageal intubation: a review of detection techniques. Anesth Analg 1986; 65:886–891

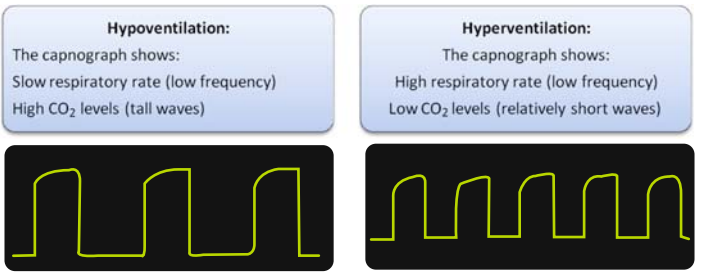
Linlo, K, Paloheimo, M, Tammisto, T. Capnography for detection of accidental oesophageal intubation. Acta Anaesthesiol Sand 1983; 27:199–202

'O' Flaherty, D, Adams, AP. The end-tidal carbon dioxide detector. Assessment of new method to distinguish oesophageal from tracheal intubation. Anaesthesia 1990; 45:653–655

3.48 Capnography in Pneumothorax



3.49 Capnography in Hypoventilation and Hyperventilation



3.50 Biphasic Capnograph

A biphasic pattern on the capnogram may be obtained under some circumstances.

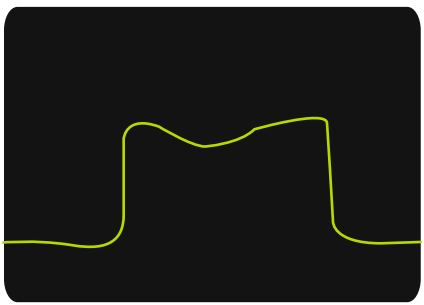
Severe kyphosioliosis

Air leaks in the sampling system

Lung volumes and lung mechanics may considerably differ on both sides

The phases of lung emptying can therefore be out of synchrony on the two sides.

The plateau of the capnogram shows a late hump.



Bhavani Shankar Kodali 2007.
Welcome to Capnography.com

Chapter 4
Acids and Bases

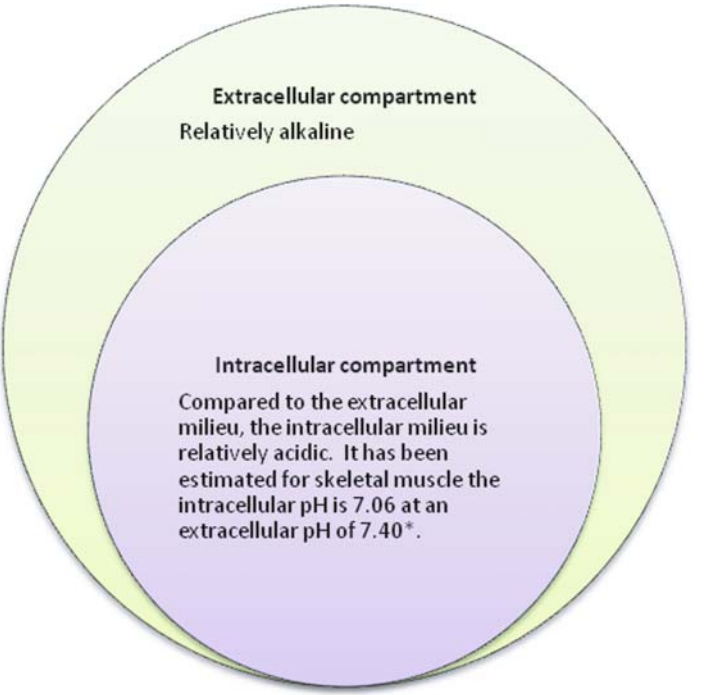
4

Contents

A. Hasan, *Handbook of Blood Gas/Acid–Base Interpretation*,
DOI 10.1007/978-1-84800-334-7_4,

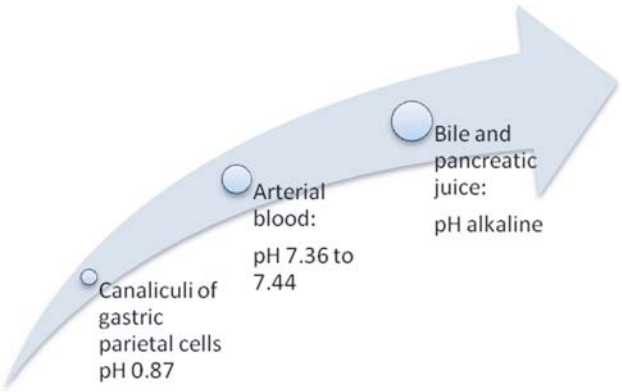
4.1 Intracellular and Extracellular pH

Most biological fluids are alkaline.



The pH range found in life: 6.8 to 7.8

This reflects a very large range of the hydrogen ion concentration: from 160 nanomoles/L (pH of 6.8) to just 16 nanomoles/L (pH 7.8).



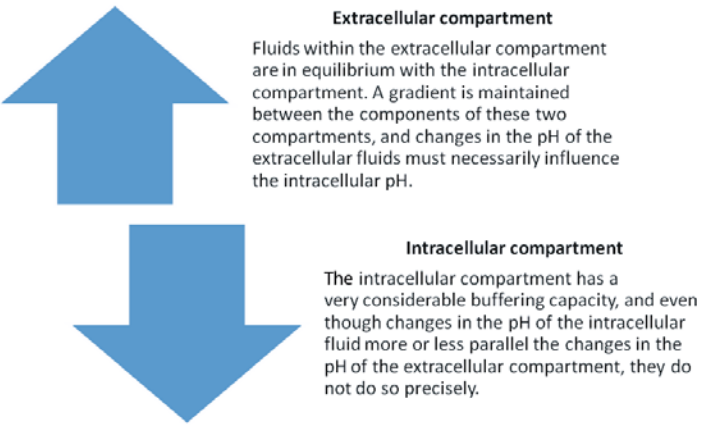
Concentrated hydrochloric acid has a pH of 1.1.

*Wray S. Smooth muscle intracellular pH: Measurement, regulation, and function. Am J Physiol 1988; 254:C213

Acid-base pHysiology. Kerry Brandis, www.anaesthesiaMCQ.com

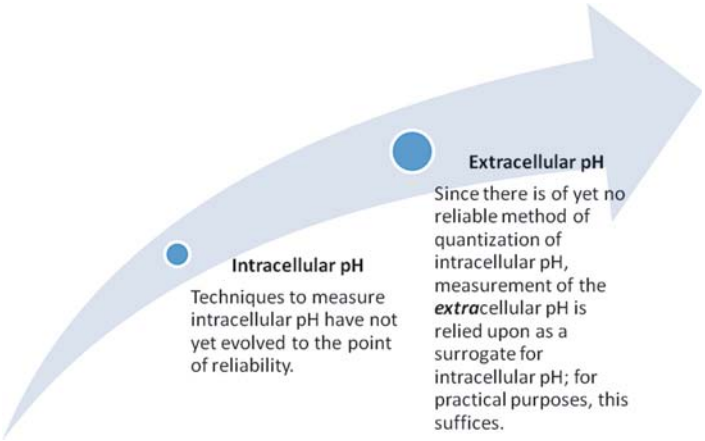
4.2 The Intracellular Environment

The intracellular microenvironment is complex, and so the pH is not uniform throughout the cell but varies between the different intracellular compartments. Since it is the cell that is the basic unit of any tissue, tissue function can best be assessed in relation to the activity of its cells.



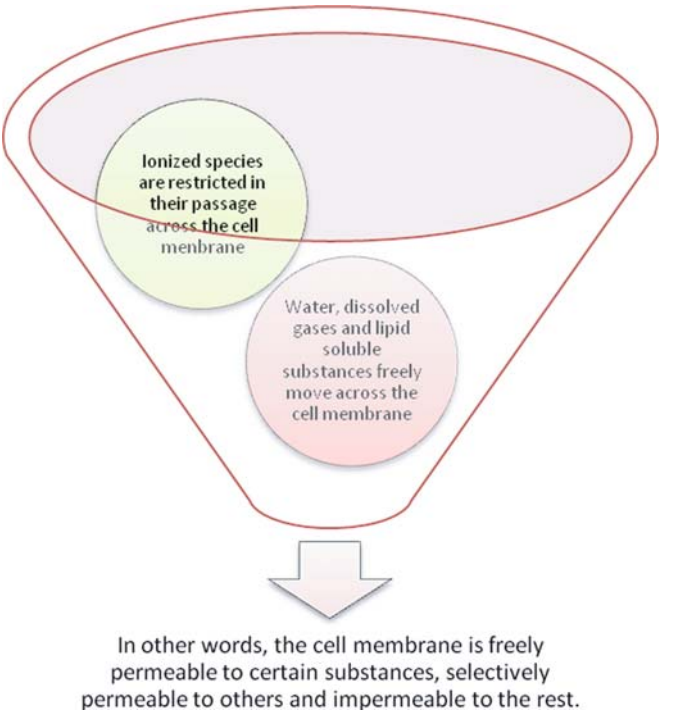
Ganapathy, V, Leibach, FH. Protons and regulation of biological functions. Kidney Int Suppl 1991; 33:S4

4.3 Surrogate Measurement of Intracellular pH



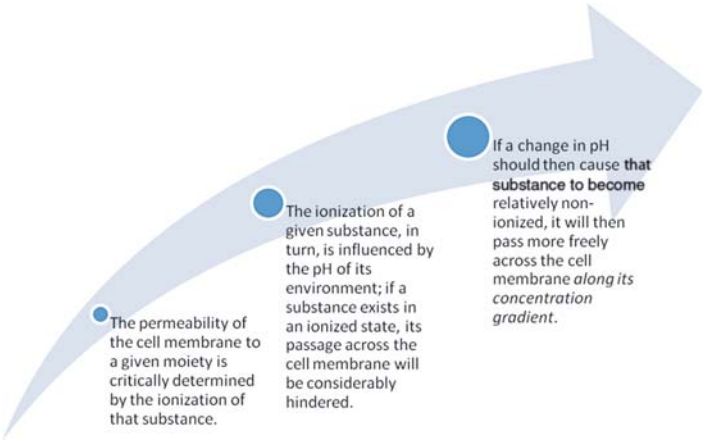
4.4 Preferential Permeability of the Cell Membrane

The intracellular microenvironment is protected by the cell membrane which is preferentially permeable to certain molecules only. The *selective* permeability of the cell membrane is one of the mechanisms that help maintain a concentration gradient between the intracellular and extracellular compartments. Other mechanisms exist also.



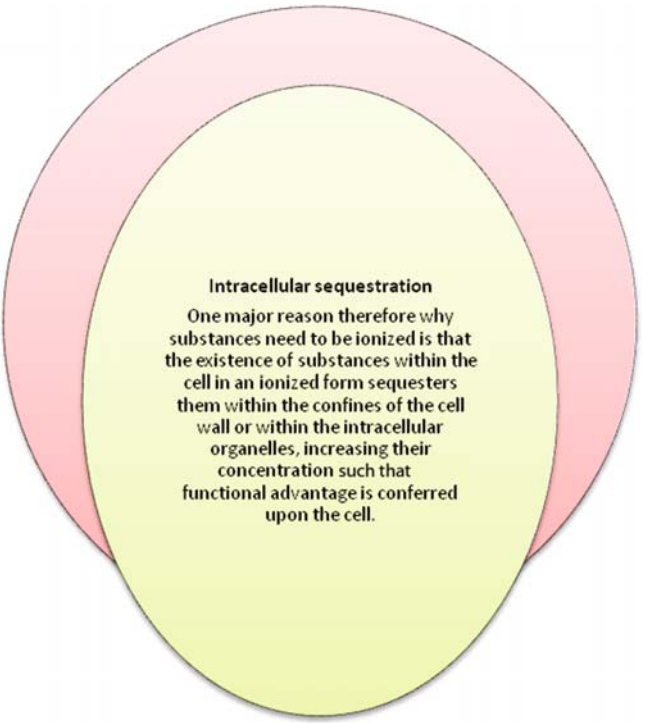
Davis, 1958

4.5 Ionization and Permeability



Davis, 1958

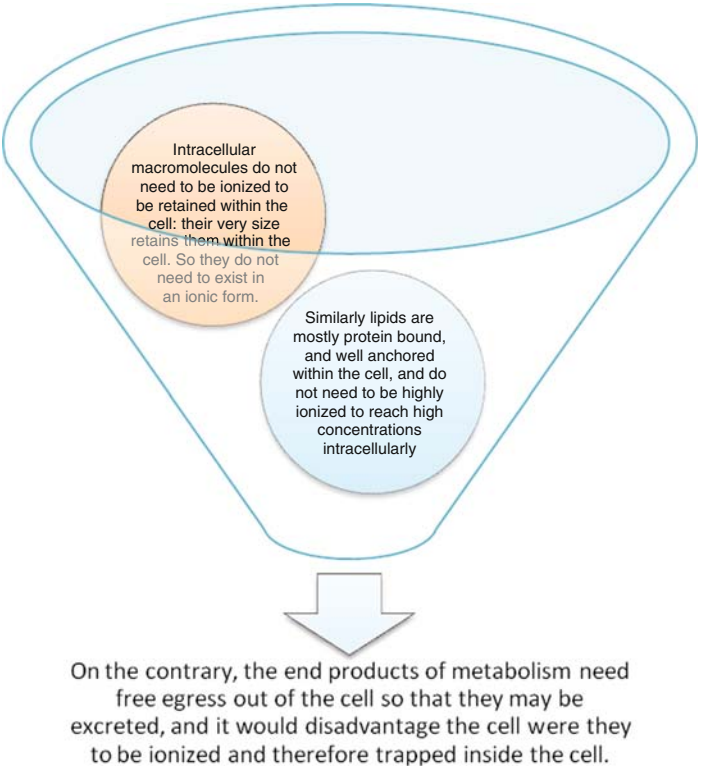
4.6 The reason why substances need to be ionised



In fact, at neutral pH (7.0, which is close to the pH of most cells), barring a few exceptions, all substances exist in highly ionized states. At neutral pH (again, barring these exceptions), all *low*-molecular-weight and water-soluble substances carry ionized groups (such as phosphate, ammonium, and carboxylate). Thus ionized, these low-molecular-weight and water-soluble moieties are prevented from diffusing into the extracellular fluid.

Davis, 1958

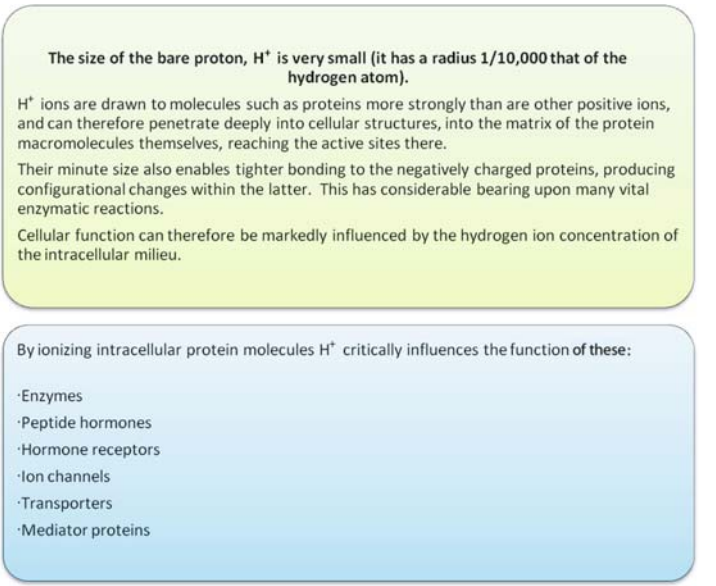
4.7 The Exceptions to the Rule



Davis, 1958

4.8 The Hydrogen Ion (H^+, Proton)

The hydrogen *ion* (proton) is a hydrogen *atom* that is bereft of its sole electron. Protons are for convenience represented as H^+. Strictly speaking, protons cannot exist as H^+ in body fluids but rather combine with water to form hydronium ions such as H_3O^+ and H_5O_2. It is for the sake of convenience that protons are represented as H^+ in chemical reactions.

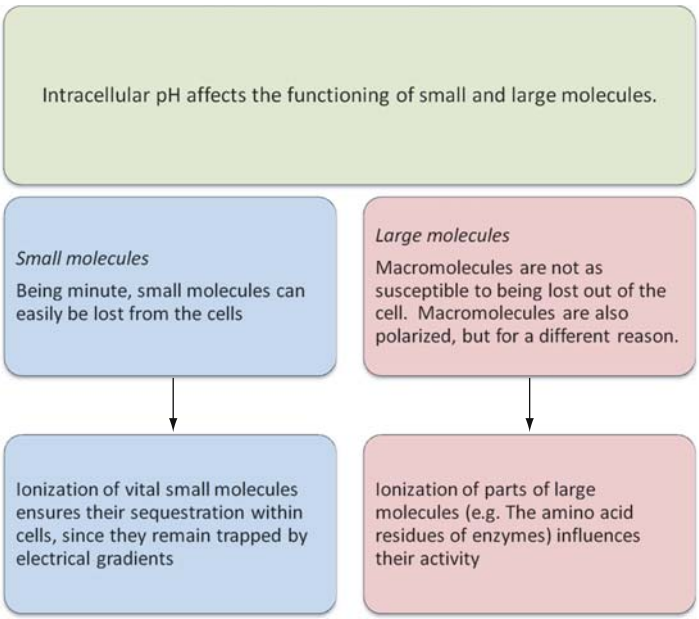


It is apparent therefore that the pH needs to be tightly regulated *in-vivo* to prevent molecular dysfunction.
The *extra*cellular space is but an extension of the intracellular space. The extracellular H^+ is in equilibrium with the intracellular H^+, and is sustained within a narrow range.

Ganapathy, V, Leibach, FH. Protons and regulation of biological functions. Kidney Int Suppl 1991; 33:S4

4.9 Intracellular pH

Intracellular pH determines the degree to which intracellular molecules are ionized.

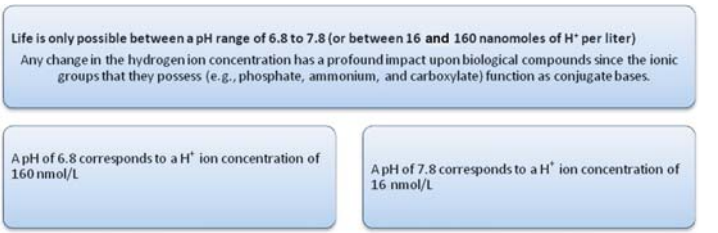


Thus, intracellular reactions are critically dependent upon pH; this is the reason that pH needs to be regulated within narrow limits.

Ganapathy, V, Leibach, FH. Protons and regulation of biological functions. Kidney Int Suppl 1991; 33:S4

4.10 pH and the H^+ Concentration

Protein molecules are components of ion channels and their transporters, and of peptide hormones and their receptors. The function of all these substances is exquisitely sensitive to changes in pH.



As is apparent, a narrow pH range does not mean a narrow range of hydrogen ion concentration: within the apparently narrow range of 6.8 – 7.8 the H^+ ion concentration can (vary) 100-fold.

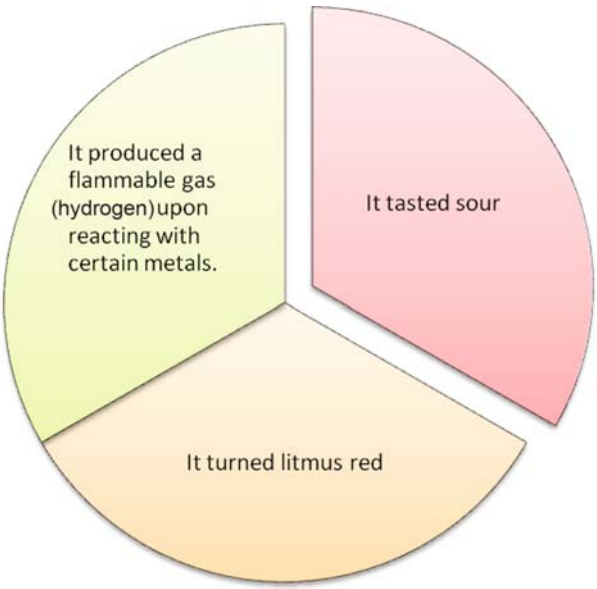
Equivalent values of pH and H^+

pH	$[H^+]$ (nanomoles/l)
6.8	158
6.9	125
7.0	100
7.1	79
7.2	63
7.3	50
7.4	40
7.5	31
7.6	25
7.7	20
7.8	15

Ganapathy, V, Leibach, FH. Protons and regulation of biological functions. Kidney Int Suppl 1991; 33:S4

4.11 The Earliest Concepts of Acids and Bases

(Latin *acidus* = sour):
The term acid derives from its Latin root *acidus,* meaning sour.
The hallmarks of an acid were considered to be:

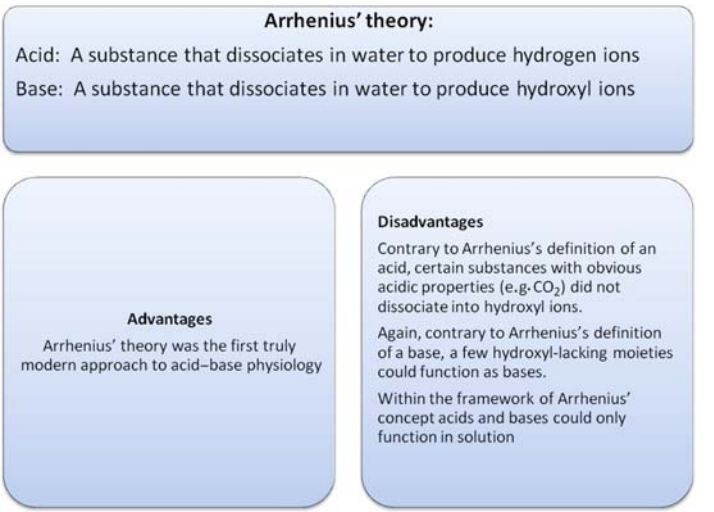


Relman, AS. What are 'acids' and 'bases' ? Am J Med 1954; 17:435

Rose, BD, Post, TW Clinical physiology of Acid-Base and Electrolyte Disorders,5th ed, McGraw-Hill, New York, 2001, pp. 328–347

4.12 Arrhenius' Theory

In 1887, Svante August Arrhenius redefined an acid. Although it was a vast improvement upon the existing definitions of acids and bases at that time, the theory of Arrhenius could only apply to aqueous solutions.



Relman, AS. What are "acids" and "bases" ? Am J Med 1954; 17:435

Severinghaus, JW, Astrup, P. History of blood gas analysis. Int Anesth Clin 1987; 25: 1–224

4.13 Bronsted–Lowry Acids

Improving upon Arrhenius' theory, Bronsted and Lowry in 1923 envisaged an acid as a proton donor and a base as a hydrogen ion acceptor, thus extending the scope of these beyond aqueous media

Bronsted–Lowry

According to the Bronsted–Lowry concept, upon losing a proton an acid becomes a conjugate base (so considered because it is capable of accepting a H^+ ion to form an acid).

Acid: a H^+ ion donor

Conjugate base: a H^+ ion acceptor (accepts H^+ fom the acid).

Advantages

The B–L theory overcomes the disadvantages of the Arrhenius' definition inasmuch as:

- To function as an acid, an entity does not necessarily require an aqueous solution.
- *The BL theory is now the universally applied clinical approach.*

Disadvantages

CO_2 has distinct acidic properties. Yet CO_2 does not fulfill the definition of a B–L acid: CO_2 contains no H^+ ions; obviously therefore, it cannot donate protons.

(This difficulty can be surmounted by viewing CO_2 as part of the carbonic acid system: see later).

Relman, AS. What are "acids" and "bases" ? Am J Med 1954; 17:435

Kerry Brandis. Acid–Base Physiology; www.anaesthesiaMCQ.com

4.14 Lewis' Approach

In that same year (1923), Lewis proposed his approach in which H^+ itself was defined an acid.

Acid: a potential acceptor of a pair of electrons (with the Lewis approach, H^+ itself became identified as an acid).

Base: a potential donor of a pair of electrons.

Advantages

Lewis' definition overcame the drawback of B–L theory: CO_2 could now be encompassed within the definition of an acid.

Disadvantages

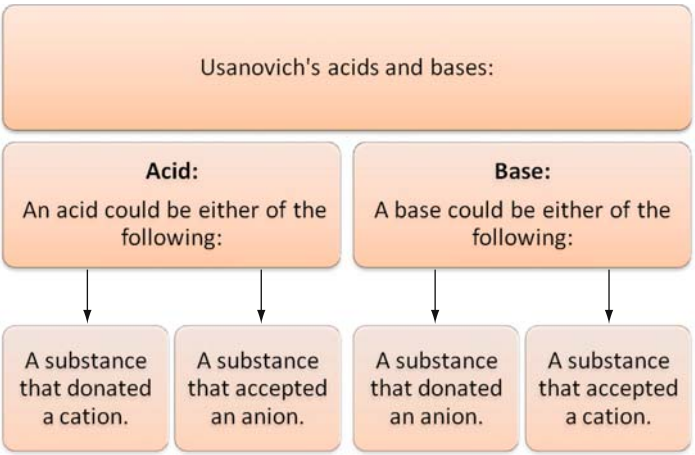
The electron concept is an uncomfortable one for clinicians!

Relman, AS. What are "acids" and "bases" ? Am J Med 1954; 17:435

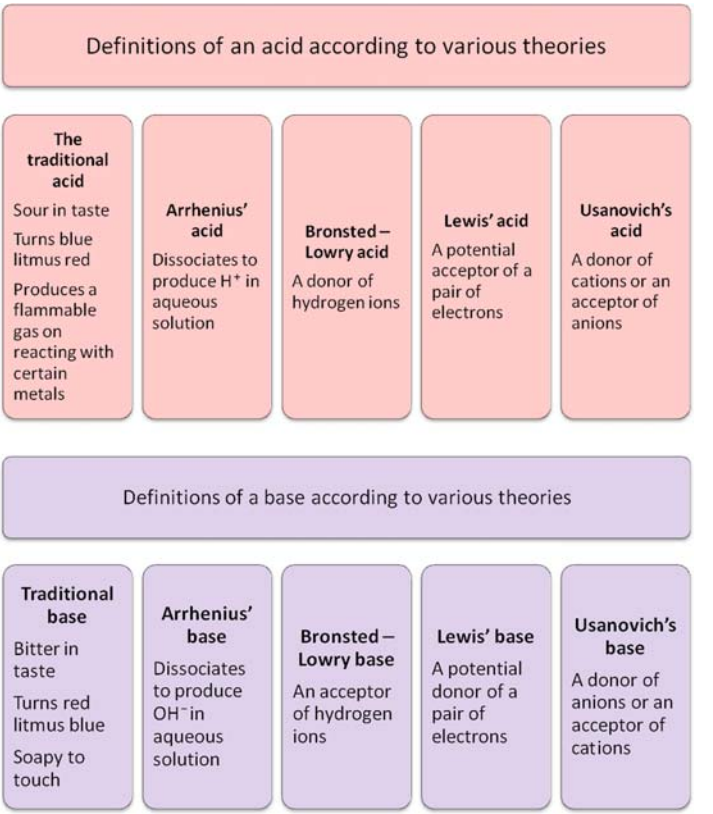
Kerry Brandis. Acid–Base Physiology; www.anaesthesiaMCQ.com

4.15 The Usanovich Theory

In 1939 Usanovich developed his unified theory



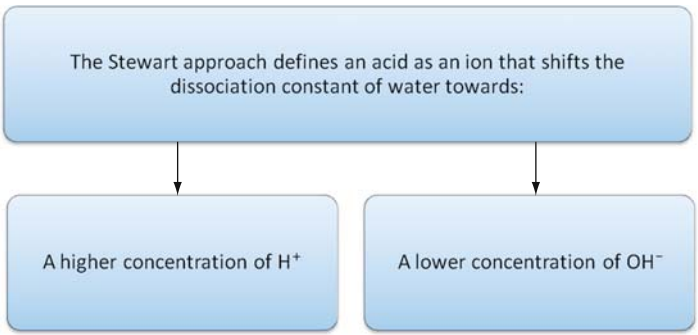
4.16 Summary of Definitions of Acids and Bases



4.17 Stewart's Physicochemical Approach

Peter Stewart's approach is founded upon basic physicochemical laws. Six simultaneous equations determine the relationship of H^+ ion to other variables.

The fundamental principle of this approach is that unlike in the B–L approach, the bicarbonate is not an individual variable: so the pH is not dependent upon the serum bicarbonate concentration.

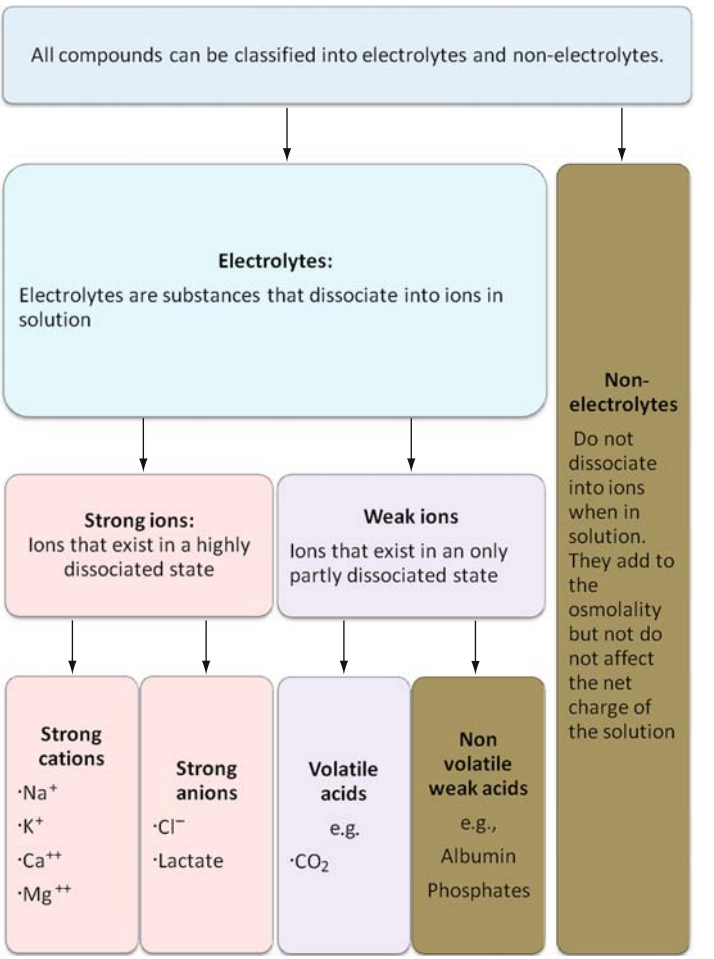


Stewart, PA. How to Understand Acid-Base. A Quantitative Acid-Base Primer for Biology and Medicine. Edward Arnold, ISBN 0-7131-4390-8, 1981

Stewart, PA. Can J Physiol Pharmacol 1983; 61: 1444, Modern quantitative acid-base chemistry

Gilfix BM, Bique M, Magder S. A physical chemical approach to the analysis of acid-base balance in the clinical setting. J Crit Care 1993; 8:187–197

4.18 Electrolytes, Non-electrolytes, and Ions

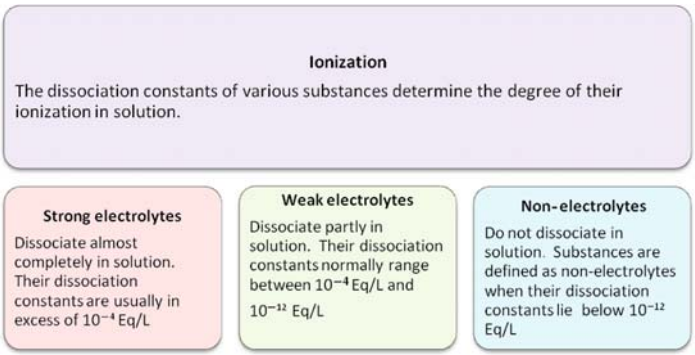


Stewart, PA. How to Understand Acid–Base. A Quantitative Acid–Base Primer for Biology and Medicine. Edward Arnold, ISBN 0-7131-4390-8, 1981

Stewart, PA. Can J Physiol Pharmacol 1983;61:1444, Modern quantitative acid–base chemistry

4.19 Strong Ions

Most strong anions are inorganic, but some such as lactate and sulfate are organic.

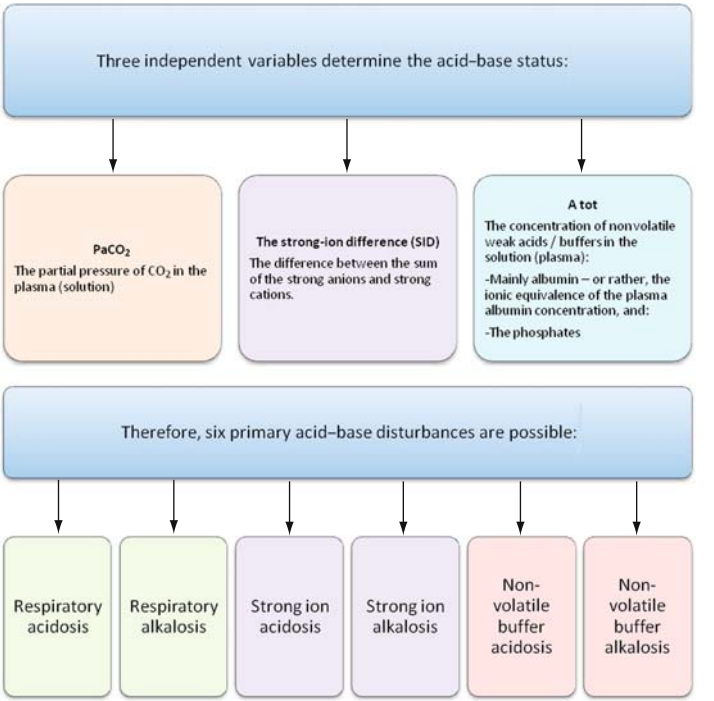


Stewart, PA. How to Understand Acid-Base. A Quantitative Acid–Base Primer for Biology and Medicine. Edward Arnold, ISBN 0-7131-4390-8, 1981

Stewart, PA. Can J Physiol Pharmacol 1983;61:1444, Modern quantitative acid-base chemistry

Brandis, K. Acid–Base Physiology; WWW.a naesthesiaMCQ.com

4.20 Stewart's Determinants of the Acid–Base Status



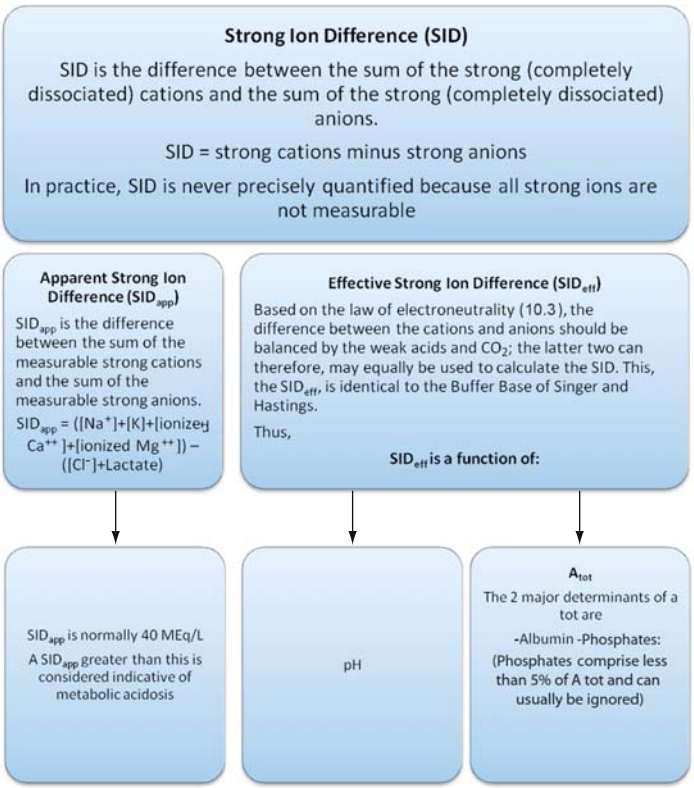
Note: pH is a *dependent* variable

Stewart, PA. How to Understand Acid-Base. A Quantitative Acid–Base Primer for Biology and Medicine. Edward Arnold, ISBN 0-7131-4390-8, 1981

Stewart, PA. Can J Physiol Pharmacol 1983; 61: 1444, Modern quantitative acid-base chemistry

Gilfix, BM, Bique, M, Magder, S. A physical chemical approach to the analysis of acid-base balance in the clinical setting. J Crit Care 1993; 8:187–197

4.21 Apparent and Effective SID



Normally, (in the absence of unmeasured ions).

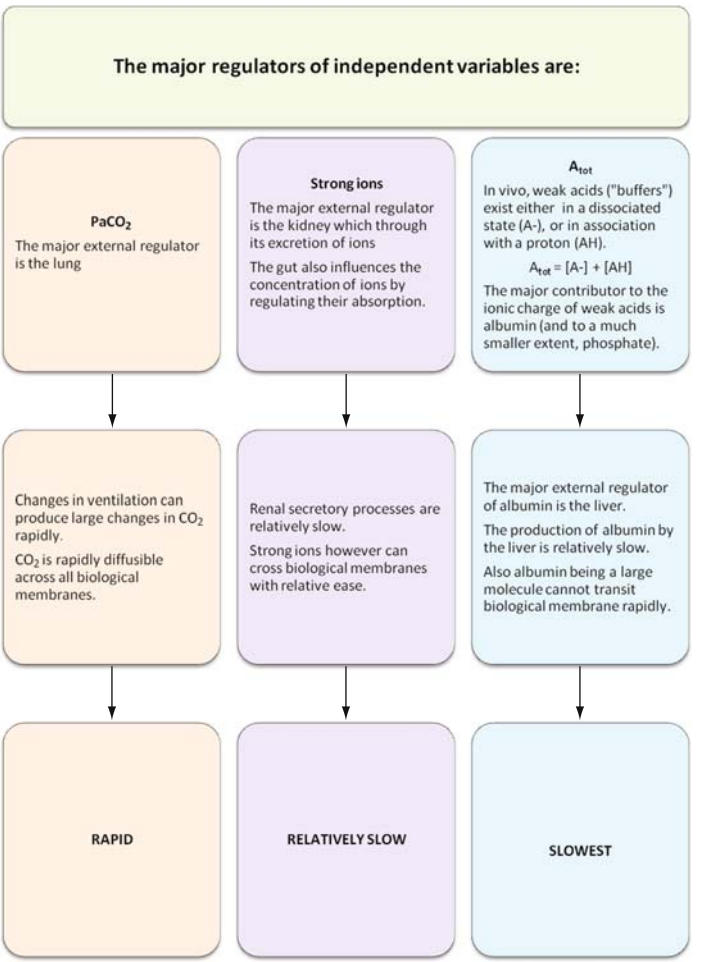
$$\mathbf{SIG = SIDapp = SIDeff}$$

and the difference between the two (namely the strong ion gap) should be zero. In practice the above situation is exceptional. The Strong Ion Gap is the difference between the two ways of measuring the Strong Ion Difference; it is thus a quantification of unmeasured anions (both strong and weak).

$$\mathbf{SIG{=}SIDapp{=}SIDeff}$$

Gilfix, BM, Bique, M, Magder, S. A physical chemical approach to the analysis of acid-base balance in the clinical setting. J Crit Care 1993; 8:187–197

4.22 Major Regulators of Independent Variables



4.23 Fourth Order Polynomial Equation

From the set of the six simultaneous equations, a 4th order polynomial equation is derived. Though complex and befuddling to clinicians, the equation can be quickly solved on computers.

Chapter 5
Buffer Systems

5

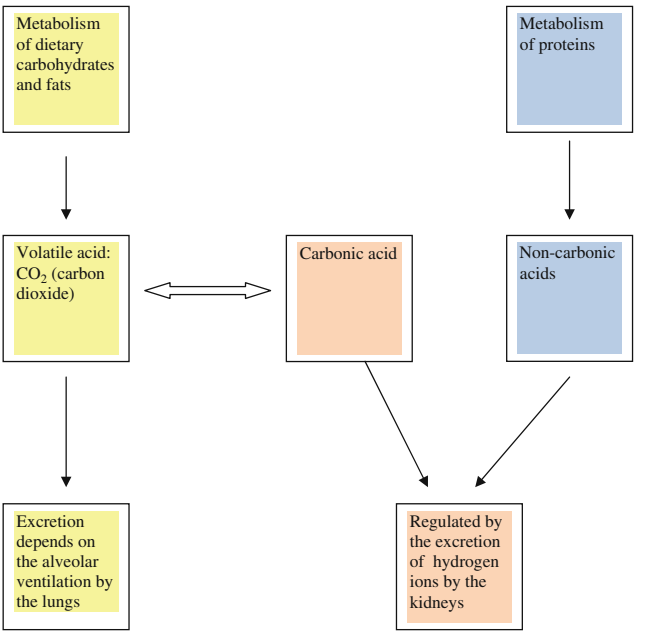
Contents

A. Hasan, *Handbook of Blood Gas/Acid–Base Interpretation*,
DOI 10.1007/978-1-84800-334-7_5,

5.1 The Generation of Acids

As a consequence of metabolic reactions in the body, considerable quantities of acid (and somewhat smaller quantities of base) are constantly being produced.

Acids are generated from the metabolism of sulfur containing amino acids (e.g. methionine and cystine) and cationic amino acids (arginine and lysine)



Halperin, ML, Jungas, RL. The metabolic production and renal disposal of hydrogen ions: An examination of the biochemical processes. Kidney Int 1983; 24:709

Kurtz, I, Maher, T, Hulter, HN. Effect of diet on plasma acid–base composition in normal humans. Kidney Int 1983; 24:670

5.2 Disposal of Volatile Acids

Basal CO_2 production

Under basal conditions about 12,000 mmol of CO_2 are produced per day.

CO_2 production: about 200 mL per minute

i.e. 200 x 60 x 24 mL = 288 liters per day

Since each gram-molecule of CO_2 takes up a volume of 22.4 liters at STP,

CO_2 production = 12 moles/day

With **usual** levels of activity CO_2 production ranges between 15,000 and 20,000 mmol/day

Changes in alveolar ventilation can rapidly alter intracellular pH.

Being highly lipid-soluble, CO_2 can easily diffuse across biological membranes.

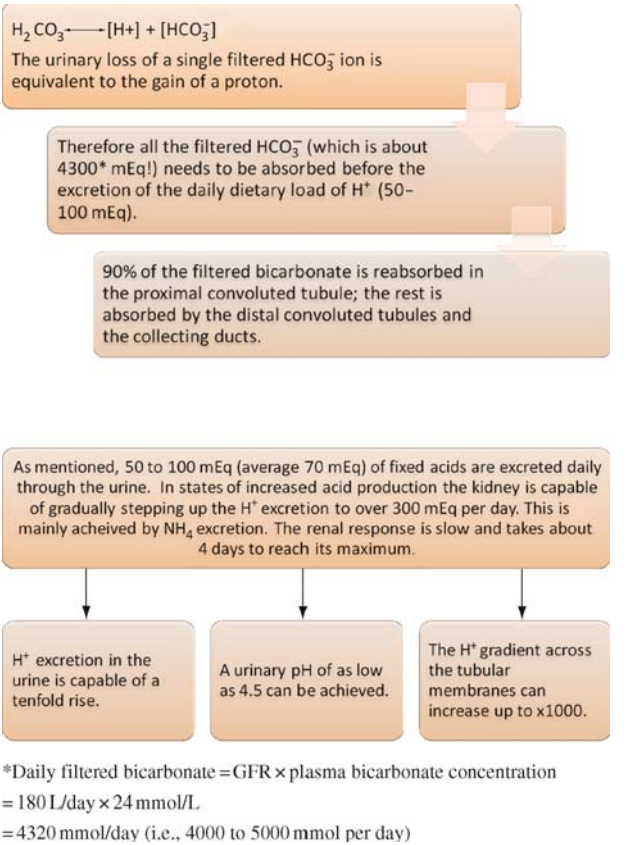
Large changes in alveolar ventilation can dramatically alter intracellular pH

CO_2 fluctuations can have an instantaneous and powerful effect on intracellular pH (and therefore on cellular metabolism) of all body tissues.

Grogono, AW. www.acid-base.com

5.3 Disposal of Fixed Acids

Although lungs quantitatively excrete more acid, there is no way to excrete fixed acids except through the kidney.



*Daily filtered bicarbonate = GFR × plasma bicarbonate concentration
= 180 L/day × 24 mmol/L
= 4320 mmol/day (i.e., 4000 to 5000 mmol per day)

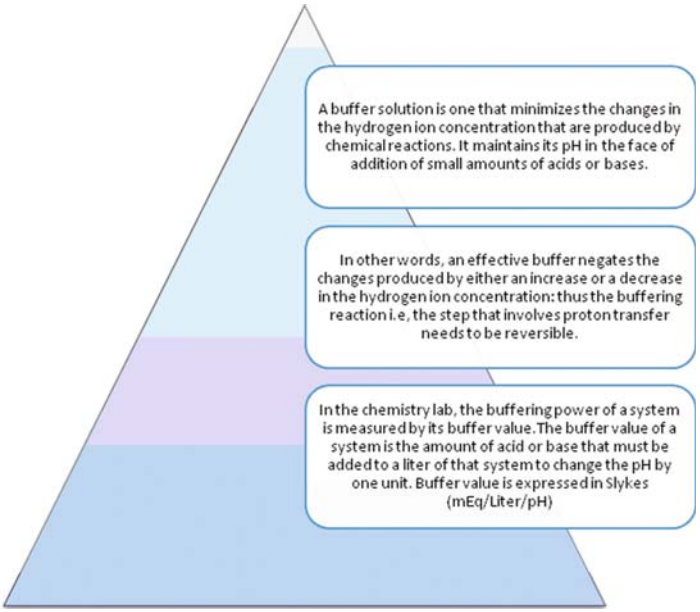
Malnic, G, Giebisch, G. Mechanism of renal hydrogen ion secretion. Kidney Int 1972; 1:280

Halperin, ML, Jungas, RL. The metabolic production and renal disposal of hydrogen ions: An examination of the biochemical processes. Kidney Int 1983; 24:709

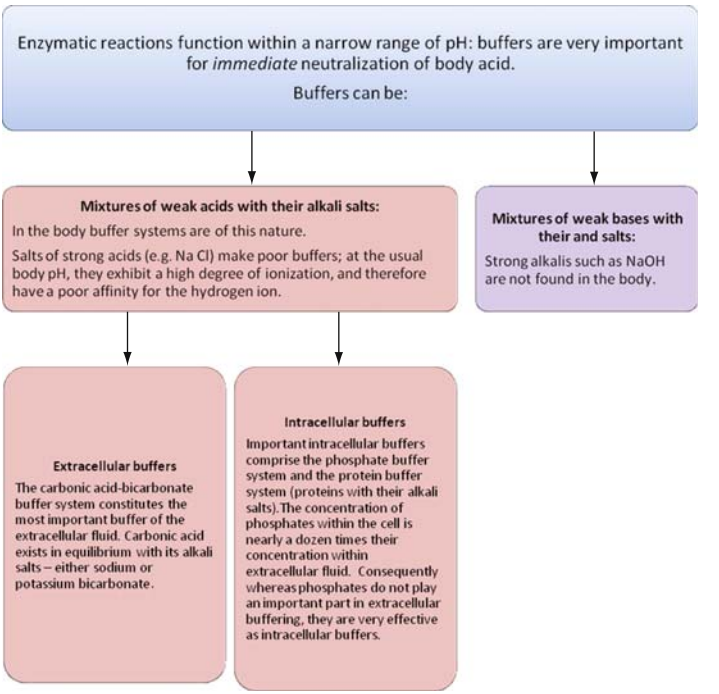
Grogono, AW. www.acid-base.com

5.4 Buffer Systems

Biologic fluids have in-built systems to defend their pH's against changes produced by chemical reactions. Since most enzymes operate effectively only within narrow ranges of the hydrogen ion concentration, changes in pH may adversely affect their functioning.



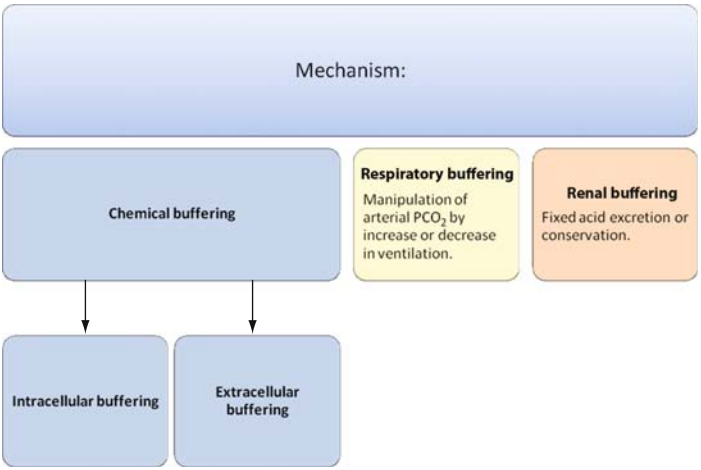
5.5 Buffers



5

Fernandez, PC, Cohen, RM, Feldman, GM. The concept of bicarbonate distribution space: The crucial role of body buffers. Kidney Int 1989; 36:747

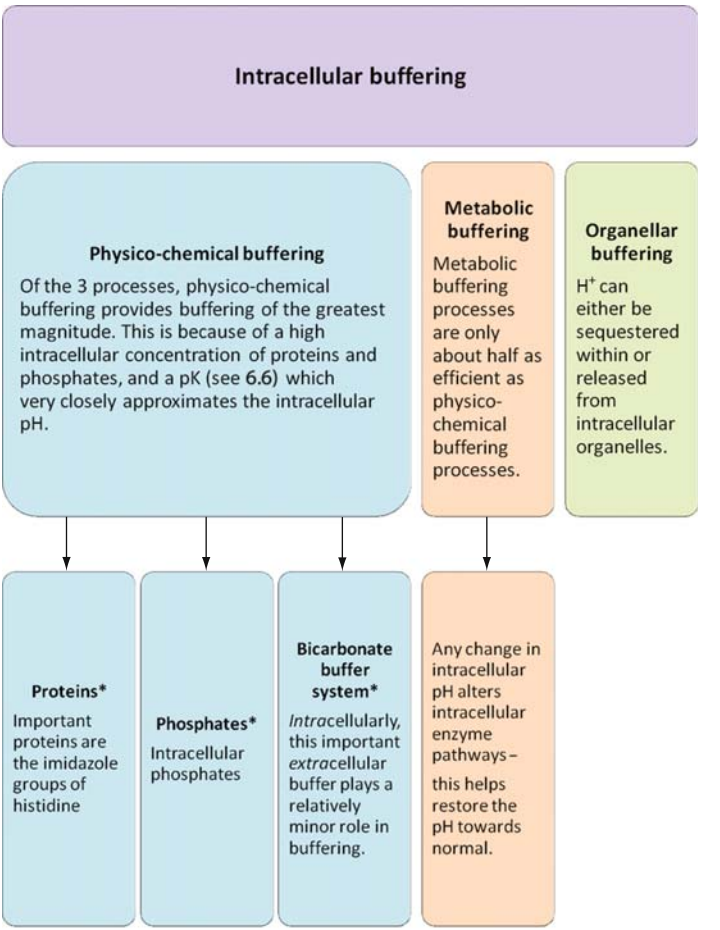
5.6 Mechanisms for the Homeostasis of Hydrogen Ions



Hamm, LL, Simon, EE. Roles and mechanisms of urinary buffer excretion. Am J Physiol 1987; 253:F595

Fernandez, PC, Cohen, RM, Feldman, GM. The concept of bicarbonate distribution space: The crucial role of body buffers. Kidney Int 1989; 36:747

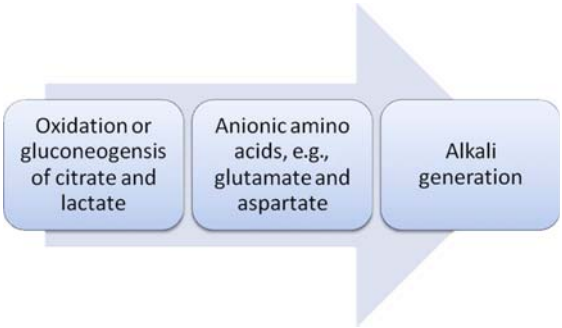
5.7 Intracellular Buffering



*Together, these 3 processes are responsible for virtually all the buffering that occurs in response to an acute acid load

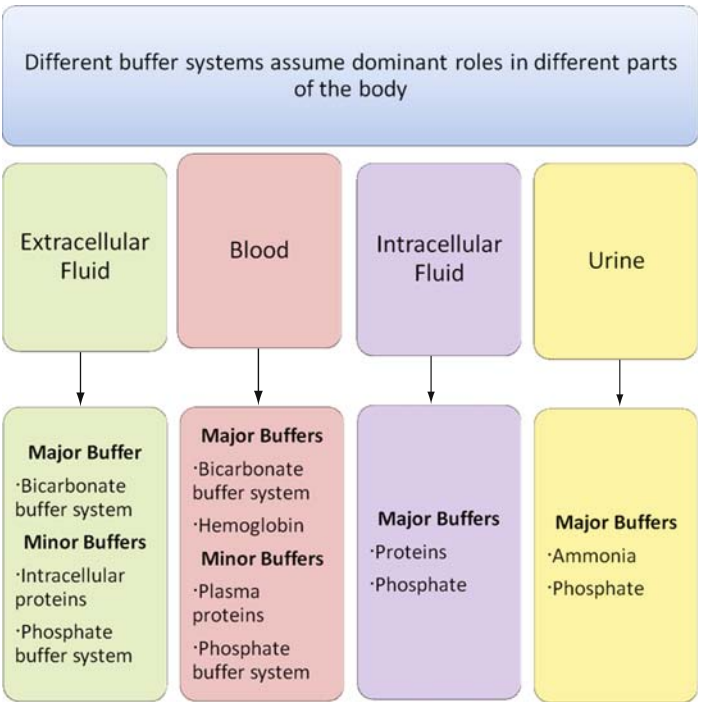
Madias, NE, Cohen, JJ. Acid–base chemistry and buffering. In: Acid/Base, Cohen, JJ, Kassirer, JP (Ed), Little, Brown, Boston, 1982

5.8 Alkali Generation



Madias, NE, Cohen, JJ. Acid–base chemistry and buffering. In: Acid / Base, Cohen, JJ, Kassirer, JP (Ed), Little, Brown, Boston, 1982

5.9 Buffer Systems of the Body

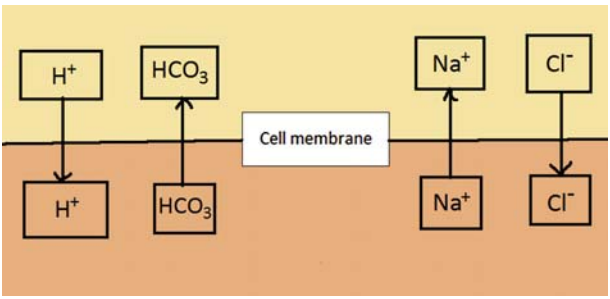


Brandis, K. Acid-Base Physiology. www.anaesthesiaMCQ.com

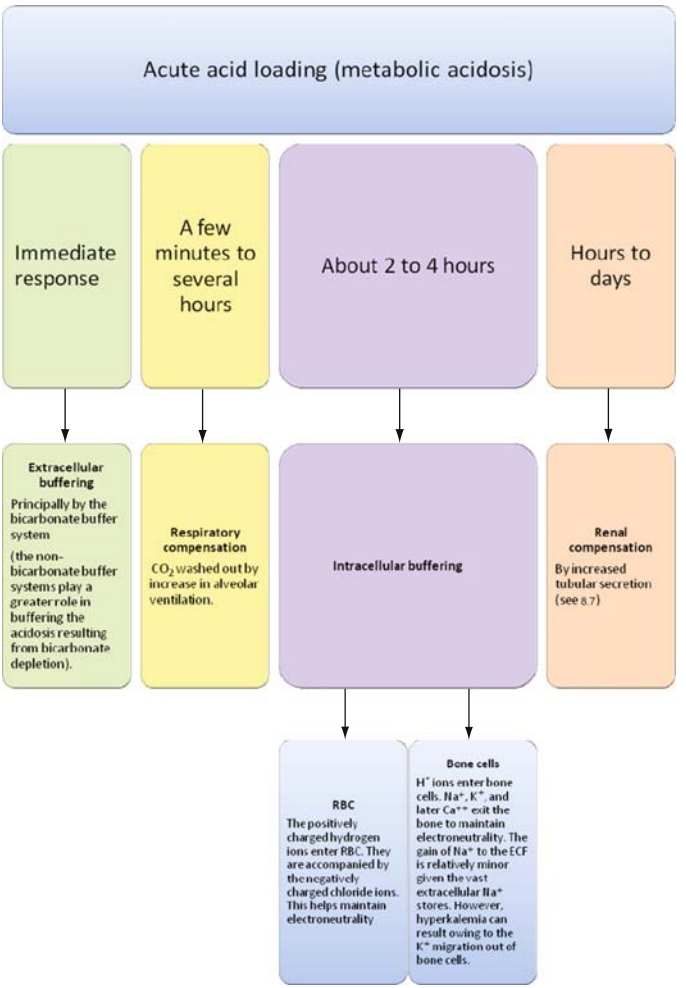
Madias, NE, Cohen, JJ. Acid-base chemistry and buffering. In: Acid / Base, Cohen, JJ, Kassirer, JP (Ed), Little, Brown, Boston, 1982

5.10 Transcellular Ion Shifts with Acute Acid Loading

The maintenance of pH in the face of acid loading is on account of ion fluxes across the cell membrane. The coupled exchange of ions (H^+ for HCO_3^- and Na^+ for Cl^-) is an electroneutral process; this means that the membrane potential remains unaltered.

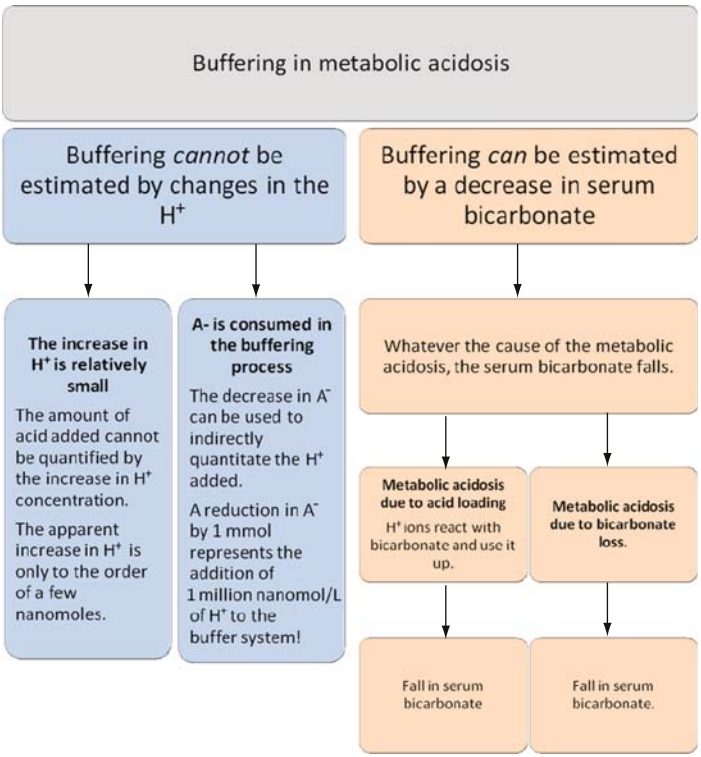


5.11 Time-frame of Compensatory Responses



Brandis, K. Acid-Base Physiology. www.anaesthesiaMCQ.com

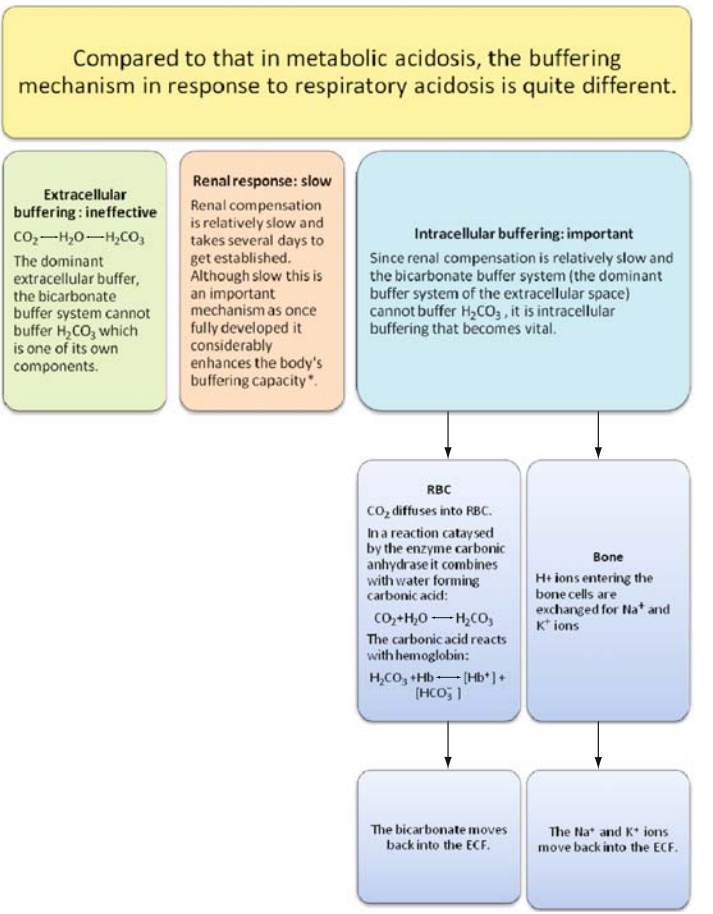
5.12 Quantifying Metabolic Buffering



Brandis, K. Acid-Base Physiology. www.anaesthesiaMCQ.com

Schwartz, WB, Orming, KJ, Porter, R. The internal distribution of hydrogen ions with varying degrees of metabolic acidosis. J Clin Invest 1957; 36:373

5.13 Buffering in Respiratory Acidosis

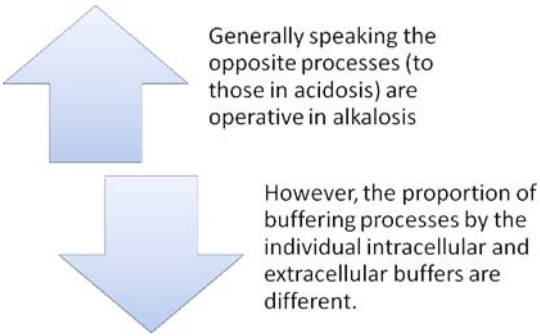


* Acutely the plasma HCO_3^- increases by 1 mmol/L for every 10 mmHg rise in PCO_2; later, once the renal response is established, it increases by about 3.5 mmol/L for a 10 mmHg increase in PCO_2.

Pitts, RF. Physiology of the Kidney and Body Fluids. Year Book, Chicago, 1974, Chapter 11.

Rose, B, Post, T. 2000, www.utd.com; Buffers-II

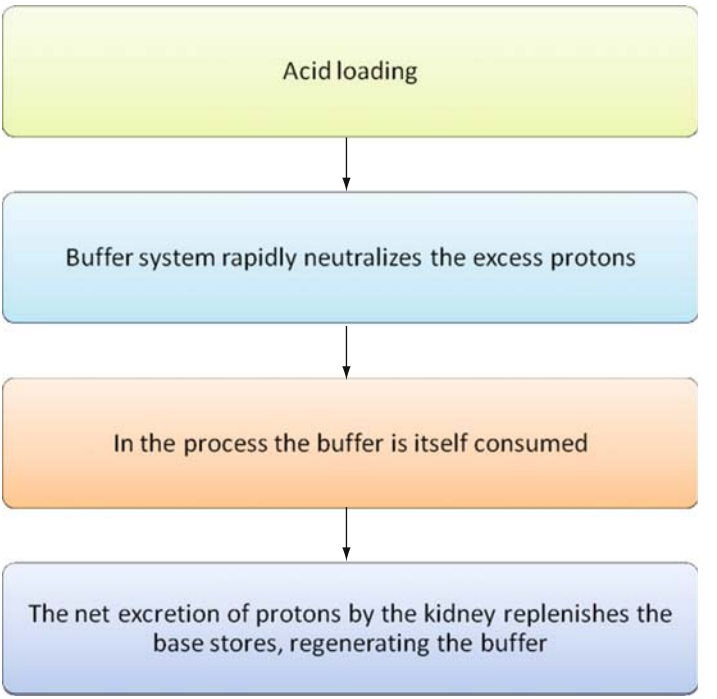
5.14 Buffering in Alkalosis



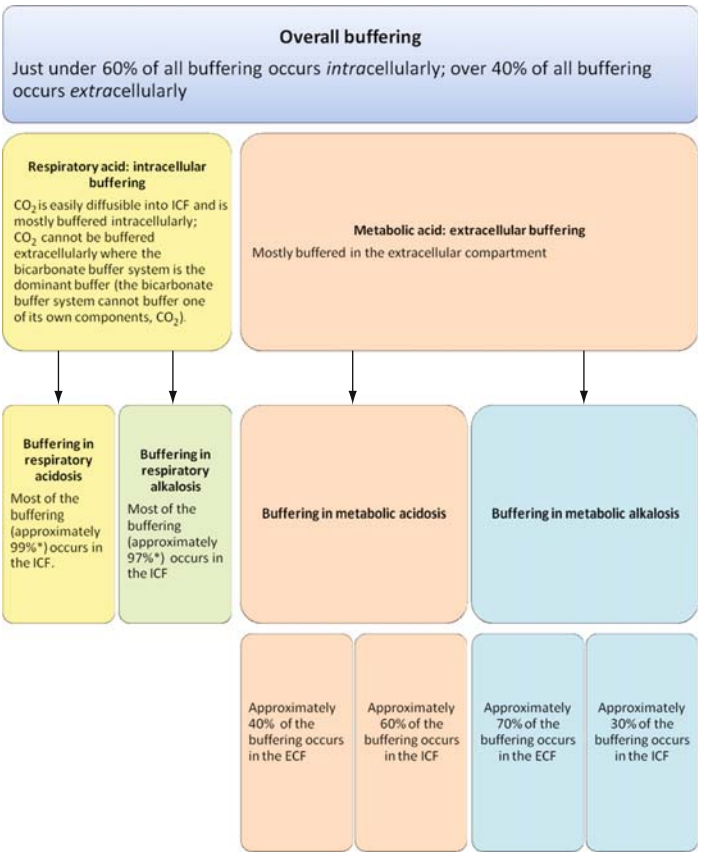
Pitts, RF. Physiology of the Kidney and Body Fluids. Year Book, Chicago, 1974, Chapter 11.

Rose, B, Post, T. 2000, www.utd.com; Buffers-II

5.15 Regeneration of the Buffer



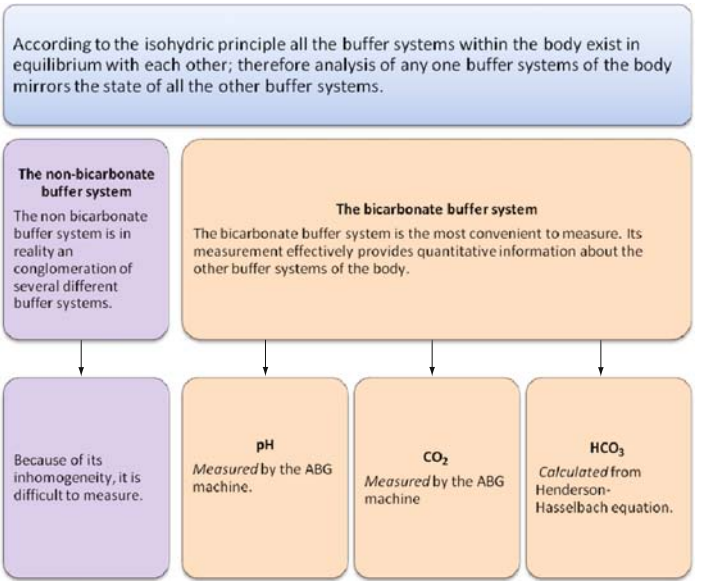
5.16 Site Buffering

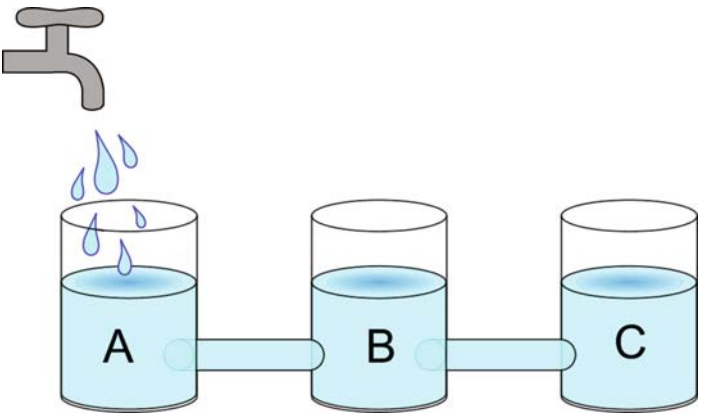


Madias, NE, Cohen, JJ. Acid–base chemistry and buffering. In: Acid / Base, Cohen, JJ, Kassirer, JP (Ed), Little, Brown, Boston, 1982

Brandis, K. Acid-Base Physiology. www.anaesthesiaMCQ.com

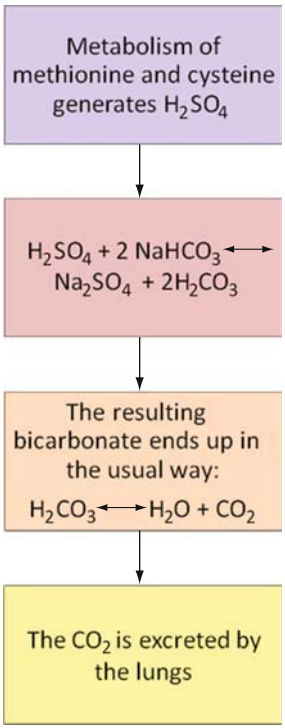
5.17 The Isohydric Principle





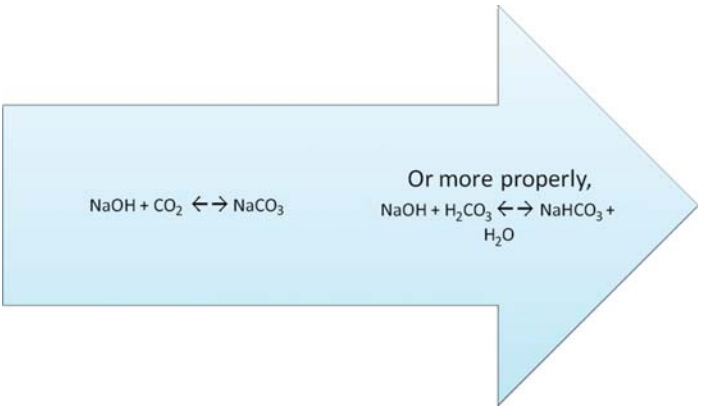
5.18 Isohydric Principle (cont'd)

Even when the acid that is added to the blood is a non-bicarbonic acid, it can be converted into the latter and then eliminated by the lungs as CO_2.



5.19 Base Buffering by the Bicarbonate Buffer System

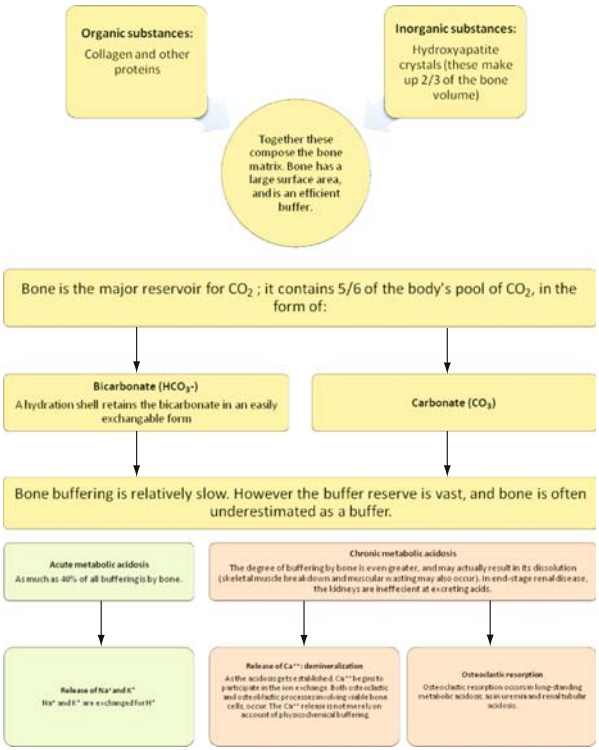
The bicarbonate buffer system is equally efficient at handling extraneous bases. In respect of added sodium hydroxide,



Pitts, RF. Physiology of the Kidney and Body Fluids. Year Book, Chicago, 1974, Chapter 11.

Rose, B, Post, T. 2000, www.utd.com; Buffers-II

5.20 Bone Buffering



Green, J, Kleeman, CR. Role of bone in regulation of systemic acid–base balance. Kidney Int 1991; 39:9

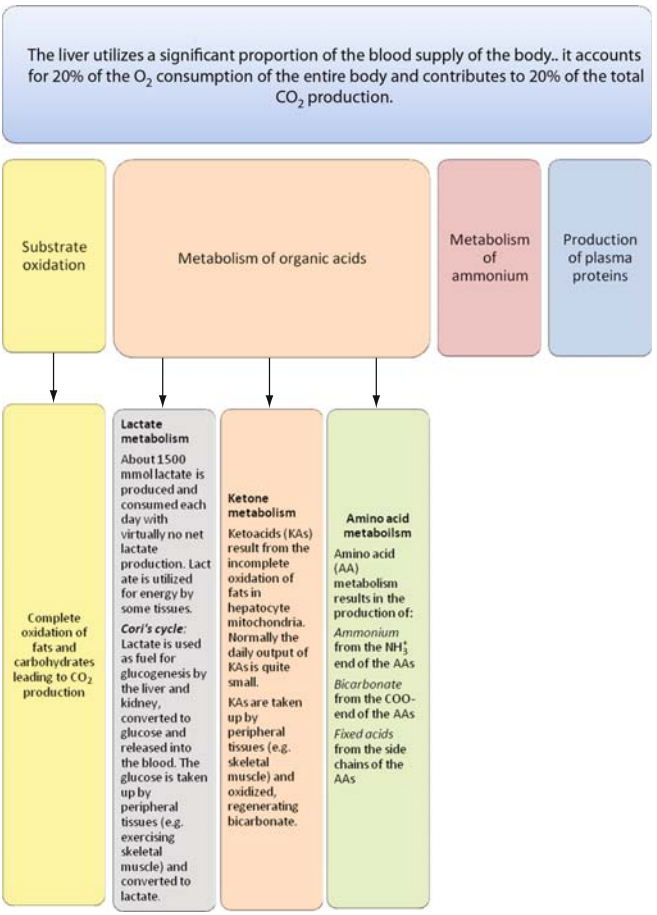
Chabala, JM, Levi-Setti, R, Bushinsky, DA. Alterations in surface ion composition of cultured bone during metabolic, but not respiratory, acidosis. Am J Physiol 1991; 261:F76

Krieger, NS, Sessler, NE, Bushinsky, DA. Acidosis inhibits osteoblastic and stimulates osteoclastic activity in vitro. Am J Physiol 1992; 262:F442

Burnell, JM. Changes in bone sodium and carbonate in metabolic acidosis and alkalosis in the dog. J Clin Invest 1971; 50:327

Lemann, J, Jr, Litzow, JR, Lennon, EJ. Studies on the mechanism by which chronic metabolic acidosis augments urinary calcium excretion in man. J Clin Invest 1967; 46:1318

5.21 Role of the Liver in Acid–Base Homeostasis



Brandis K. Acid–Base Physiology. www.anaesthesiaMCQ.com

Cohen, CD. Roles of the liver and kidney in acid—base regulation and its disorders. British J Anaes 67, (2) 154–164

Chapter 6
THE pH

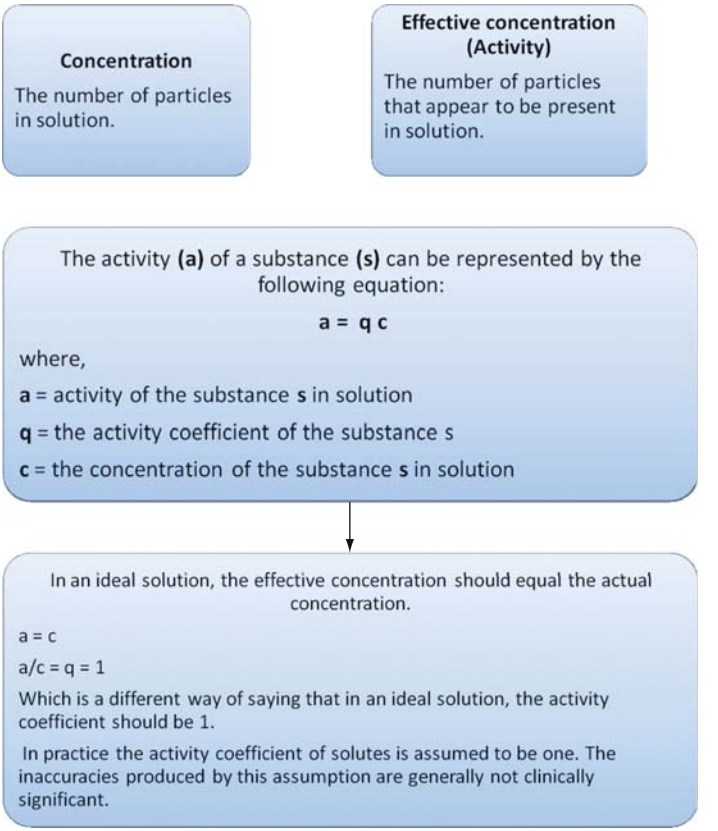
Contents

6

A. Hasan, *Handbook of Blood Gas/Acid–Base Interpretation*, DOI 10.1007/978-1-84800-334-7_6,

6.1 Hydrogen Ion Activity

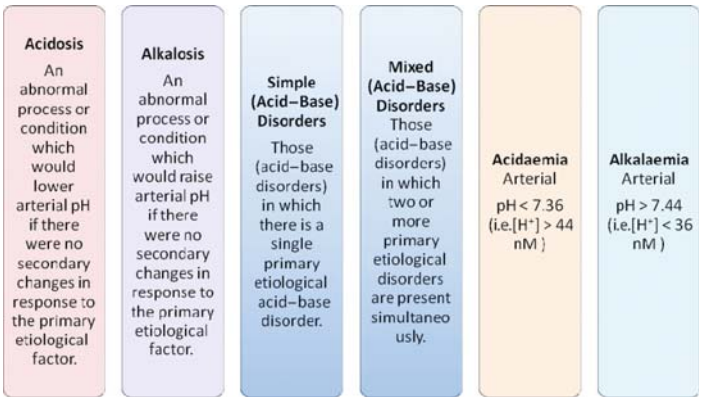
A distinction must be made between the actual concentration and the effective concentration of the hydrogen ion in solution.



Brandis K. Acid–Base Physiololy. www.anaesthesiaMCQ.com

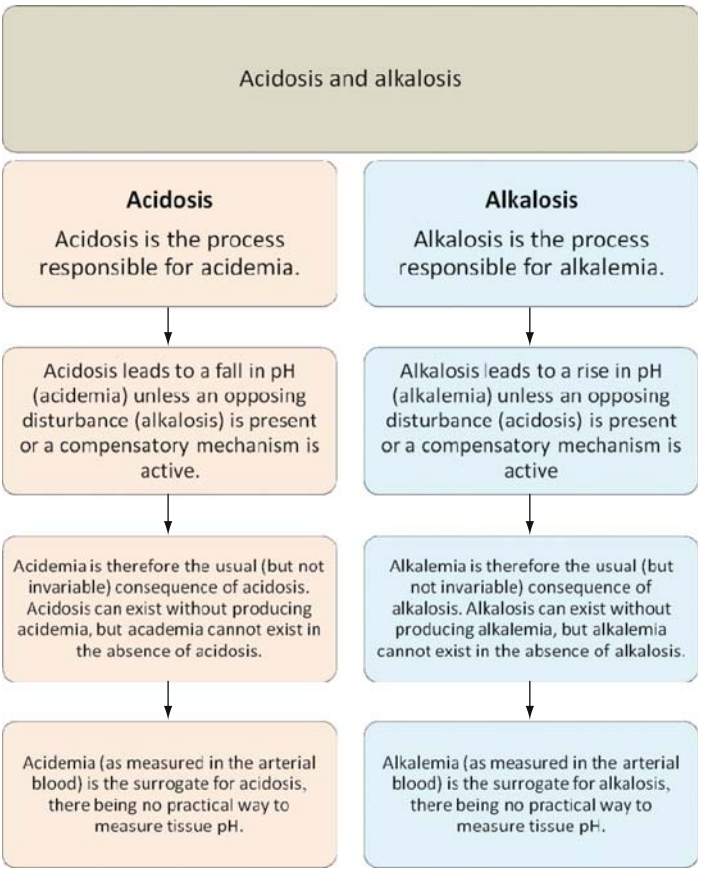
Cohen, JJ. Acid–base chemistry and buffering. In: Acid / Base, Cohen, JJ, Kassirer JP (Ed), Little, Brown, Boston, 1982

6.2 Definitions of Acid-Base Disorders



Statement on acid base terminology. Report of the ad hoc committee of the New York Academy of Sciences Conference. Nov. 23–24, 1964. Ann Intern Med 1965; 63:885

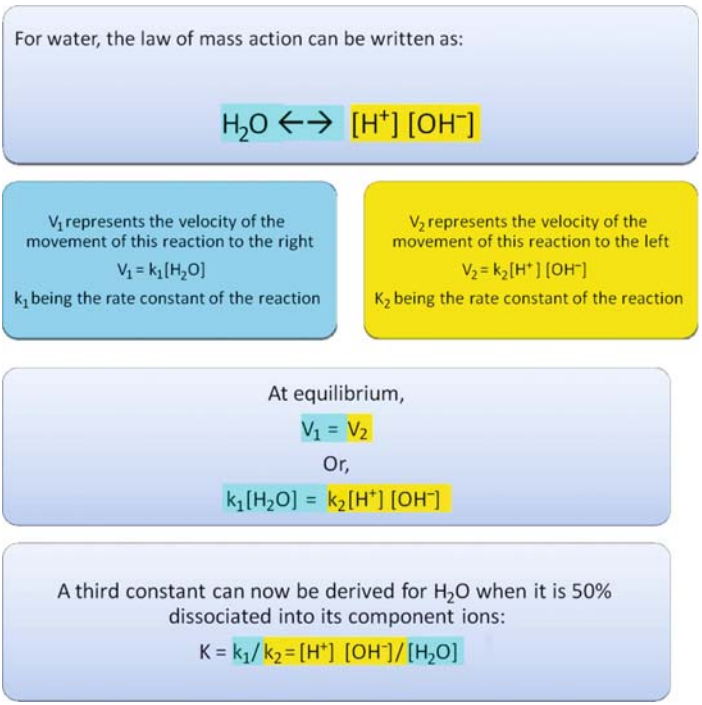
6.3 Acidosis and Alkalosis



Winters, RW. Terminology of acid–base disorders. Ann Intern Med 1965; 63:873

6.4 The Law of Mass Action

According to the law of mass action, the velocity of a reaction is proportional to the product of the concentration of its reactants.



Rose, BD, Post, TW. Clinical Physiology of Acid–Base and Electrolyte Disorders, 5th ed, McGraw-Hill, New York, 2001

Cohen, JJ, Kassirer, JP. Measurement of acid–base status. In: Acid / Base, Cohen, JJ, Kassirer, JP (Ed), Little, Brown, Boston, 1982

6.5 Dissociation Constants

In respect of an acid, the law of mass action may be written as:

$$HA \leftrightarrow [H^+]\,[A^-]$$

Or,

$$Ka = \frac{[H^+]\,[A^-]}{[HA]}$$

Where Ka is the dissociation constant for that acid.

Ka, the dissociation constant

Ka, the dissociation constant is different for each acid system. For all practical purposes, the ***value of Ka is always the same for a particular acid*** in a system (though it does change a little with temperature, the concentration of the solute and H^+).

The dissociation constant determines just how much of the acid dissociates in a system; it is a measure of the strength of an acid.

Stronger acids have larger dissociation constants

They tend to dissociate more completely in solution.

Weaker acids have smaller dissociation constants

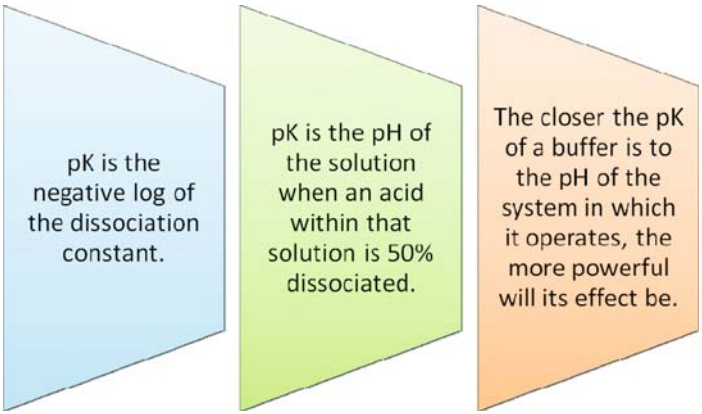
They tend to dissociate relatively less in solution.

The dissociation constant of an acid is represented by the letter kappa (k).

Kruse, JA, Hukku, P, Carlson, RW. Relationship between apparent dissociation constant of blood carbonic acid and disease severity. J Lab Clin Med 1989; 114:568

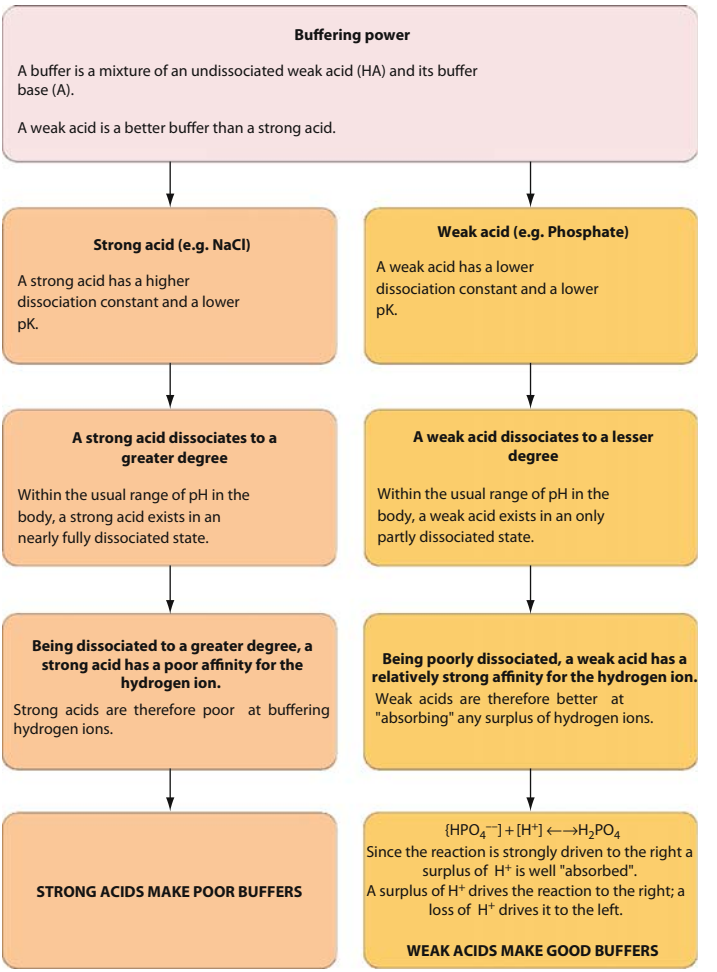
Gennari, FJ, Cohen, JJ, Kassirer, JP. Measurement of acid-base status. In: Acid / Base, Cohen, JJ, Kassirer, JP (Ed), Little, Brown, Boston, 1982

6.6 pK

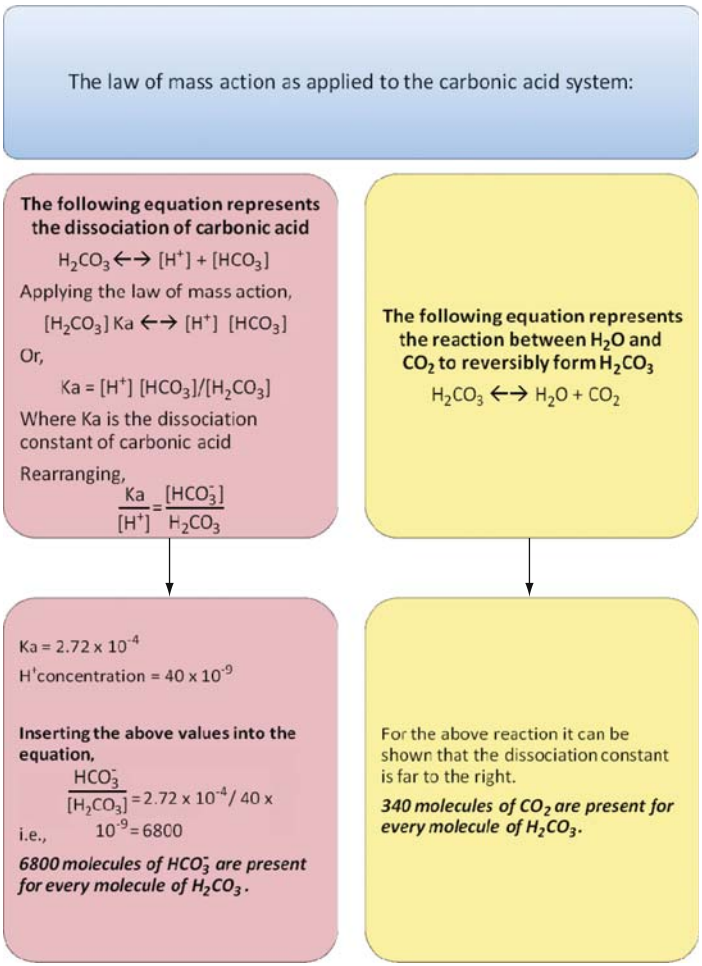


A buffer solution (see 5.4) is one that minimizes the changes in the hydrogen ion concentration that are produced by chemical reactions.

6.7 The Buffering Capacity of Acids

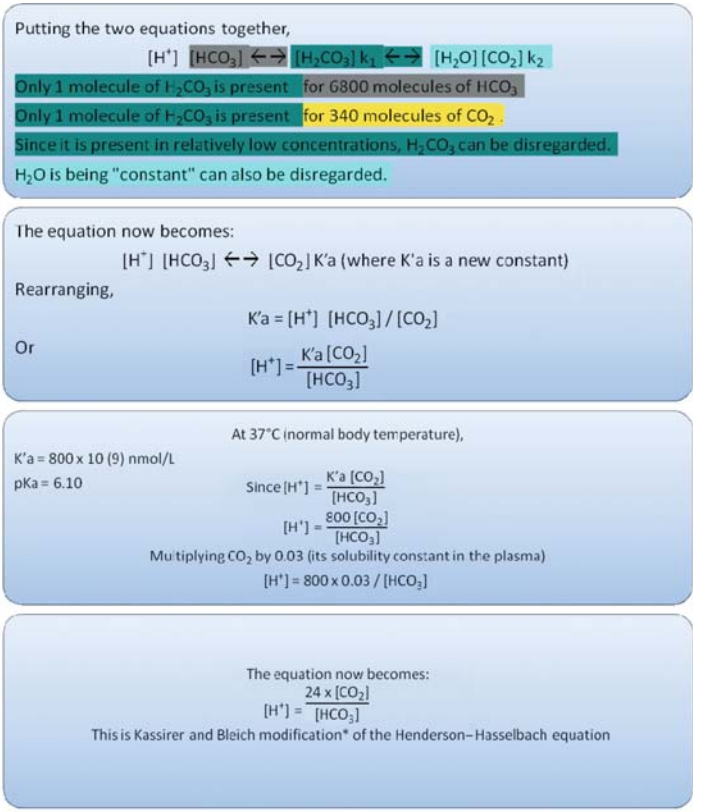


6.8 The Modified Henderson–Hasselbach Equation



Hills, AG. pH and the Henderson–Hasselbalch equation. Am J Med 1973; 55:131

*Narins RG, Emmet M. Simple and mixed acid–base disorders: a practical approach. Medicine (Baltimore) 59:161–187, 1980



*Narins RG, Emmet M. Simple and mixed acid-base disorders: a practical approach. Medicine (Baltimore) 59:161–187, 1980

Brandis, K. Acid–Base Physiology. www.anaesthesiaMCQ.com

Kassirer, JP, Bleich, HL. Rapid estimation of plasma CO_2 from pH and total CO_2 content. N Engl J Med 1965; 272:1067

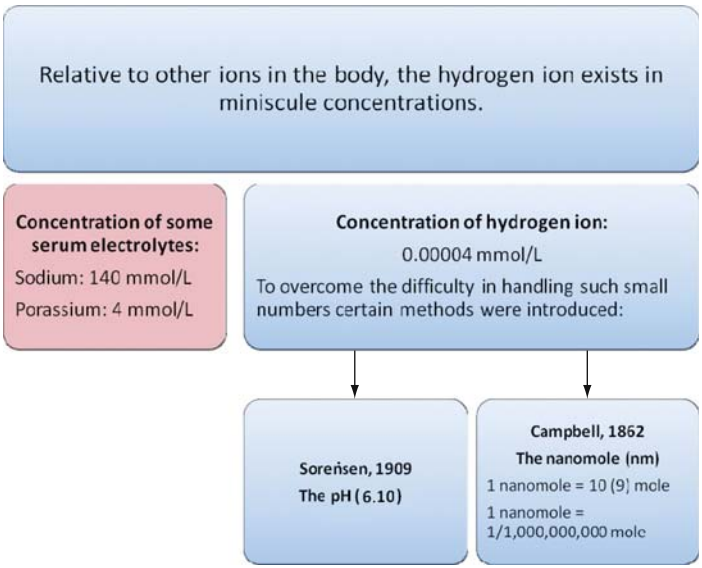
Kassirer, JP Serious Acid–Base Disorders. N Engl J Med 291, 773; 1974

Brandis, K. Acid–Base Physiology. www.anaesthesiaMCQ.com

Kassirer, JP, Bleich, HL. Rapid estimation of plasma CO_2 from pH and total CO_2 content. N Engl J Med 1965; 272:1067

Kassirer, JP Serious Acid–Base Disorders. N Engl J Med 291, 773; 1974

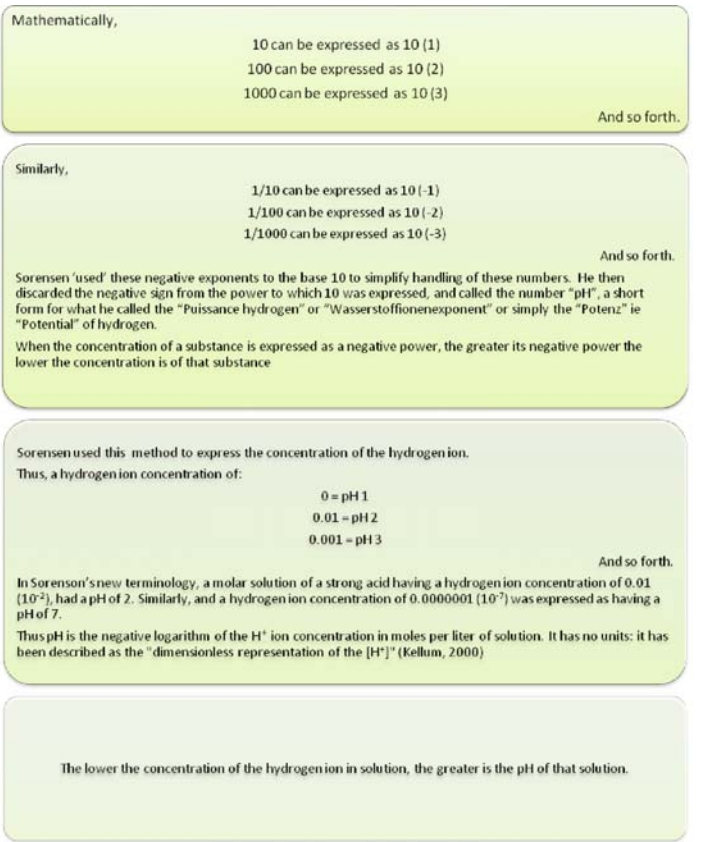
6.9 The Difficulty in Handling Small Numbers



Severinghaus, JW, Astrup, P. History of blood as analysis. Int Anestn Clin 1987; 25: 1–224

6.10 The Puissance Hydrogen

In 1909 a Danish biochemist published a landmark paper in French. Soren Peter Sorensen observed that enzymatic activity produced tiny but measurable changes in the H^+ concentration.

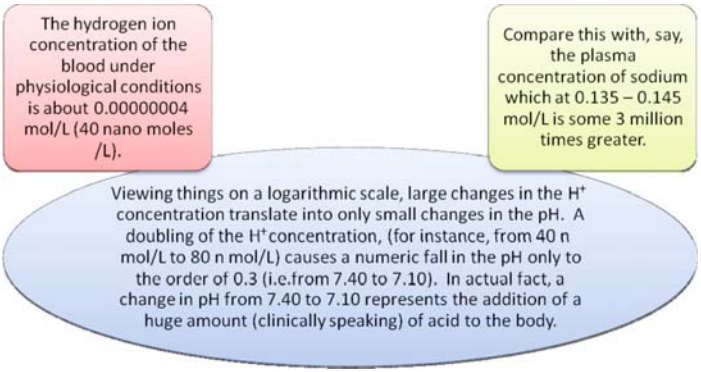


The lower the concentration of the hydrogen ion in solution, the greater is the pH of that solution.

Severinghaus, JW, Astrup, P. History of blood gas analysis. Int Anesth. Clin 1987; 25: 1–224

6.11 Why pH?

As mentioned above, the intent behind the use of the pH scale is to make the handling of very small numbers more convenient.



The pH range 6.8 to 7.8 (corresponding to a H^+ ion concentration of 160–16 n mol/L) is generally considered to be the range of pH within which life can exist.

6.12 Relationship between pH and the Hydrogen Ion Concentration

Analog scales have been developed to show the relationship between pH and H^+ ion concentration. A rule of the thumb proposed by Kassirer and Bleich enables approximate conversion from one to the other.

A pH of 7.40 corresponds to a H^+ ion concentration of 40 n Eq/L. Using Kassirer and Bleich's rule, change in pH by every 0.01 unit represents a change in H^+ ion concentration by 1 n Eq/L. Since pH and H^+ ion concentration are inversely related, a fall in pH from, for example, 7.40 to 7.38, represents a rise in the H^+ ion concentration from 40 to 42 n Eq/L.

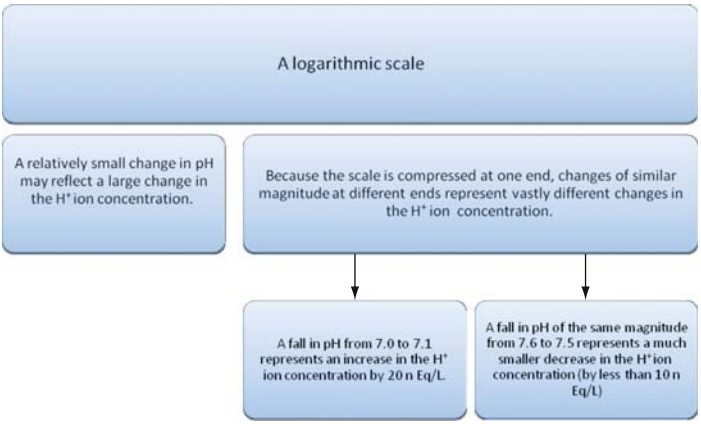
A similar calculation can also be used for checking if the data are reliable (see the first example in chapter 13)

Equivalent values of pH and H^+

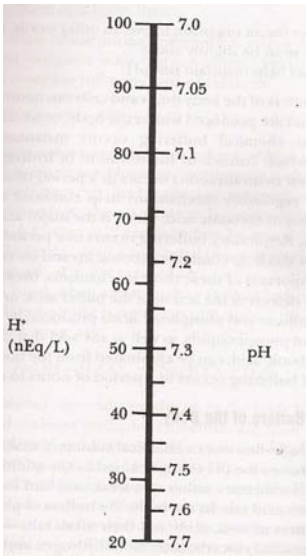
pH	$[H^+]$ (nanomoles/l)
6.8	158
6.9	125
7.0	100
7.1	79
7.2	63
7.3	50
7.4	40
7.5	31
7.6	25
7.7	20
7.8	15

Kassirer JP, Bleich HL. Rapid estimation of plasma CO_2 from pH and total CO_2 content. N Engl J Med 1965; 272:1067

6.13 Disadvantages of a Logarithmic Scale

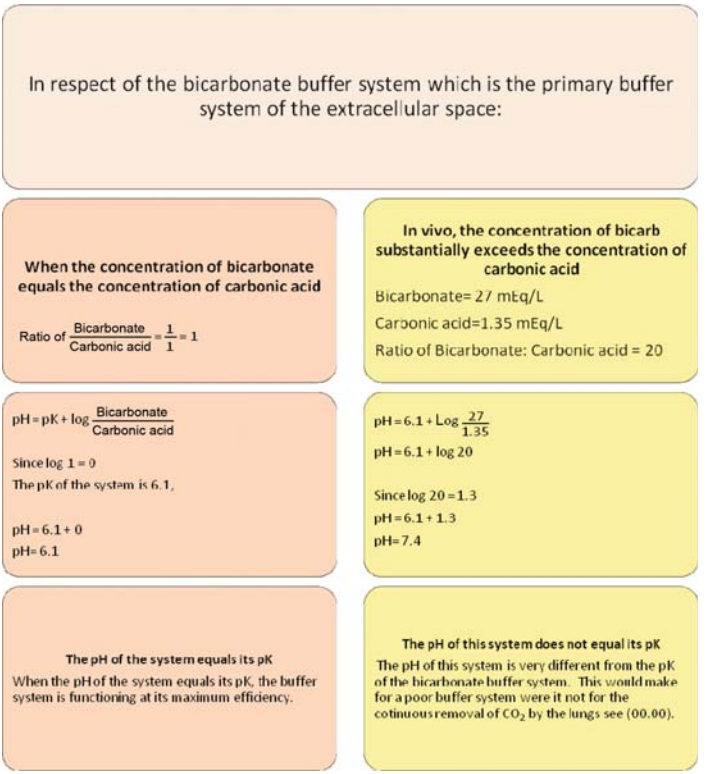


In other words, as the blood becomes increasingly acidic, much smaller changes of pH are produced by the addition of relatively large quantities of H^+ ions. Intuitively relying on pH to gauge the H^+ ion concentration therefore could result in gross inaccuracies.



6.14 The pH in relation to pK

The capacity of a buffer to defend changes in the pH depends not only on its concentration in the system but also on the relationship between the pK of the system to the prevailing pH.



6.15 Is the Carbonic Acid System an Ideal Buffer System?

Normal blood levels of HCO_3^- and CO_2

HCO_3 : 22–26(24) mEq/L

CO_2 : 40 mmHg

i.e.,

$0.03 \times 40 = 1.2$ mEq/L

(0.03 being the solubility coefficient of CO_2)

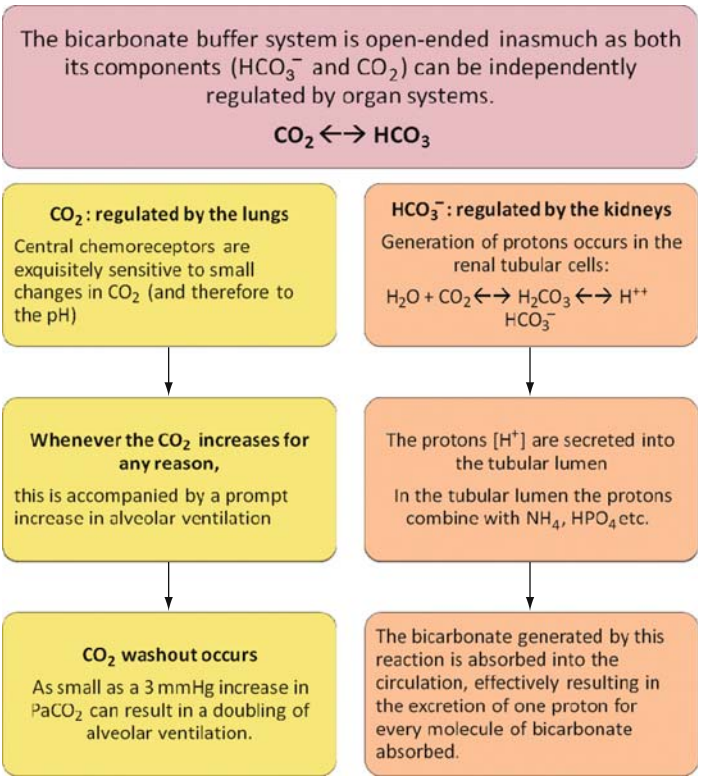
At the normal body pH of 7.4, the ratio of $HCO_3 : CO_2 = 24:1.2$

$= 20$

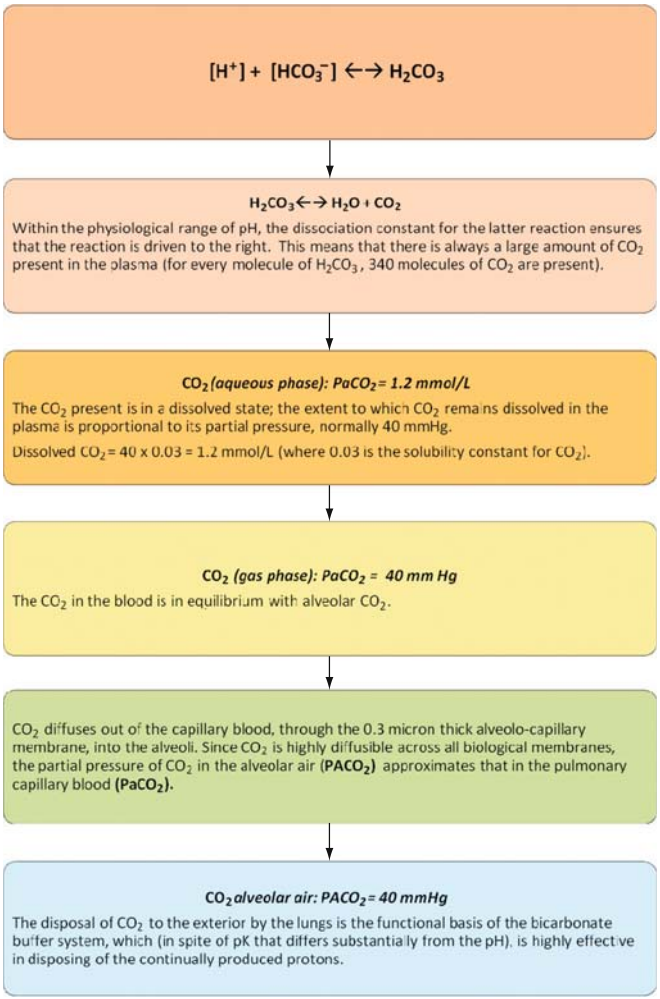
An ideal buffer system should have a ratio of 1:1.

A $HCO_3 : CO_2$ ratio of 20:1 would normally make for a poor buffer system if it were not possible to regulate HCO_3 or CO_2 concentrations. In fact both HCO_3 and CO_2 concentrations can be independently regulated: the former by the kidneys and latter by the lungs.

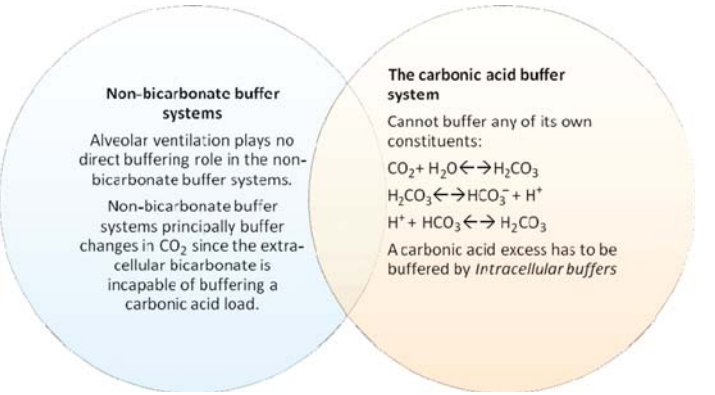
6.16 The Bicarbonate Buffer System is Open Ended



6.17 Importance of Alveolar Ventilation to the Bicarbonate Buffer System



6.18 Difference between the Bicarbonate and Non-bicarbonate Buffer Systems



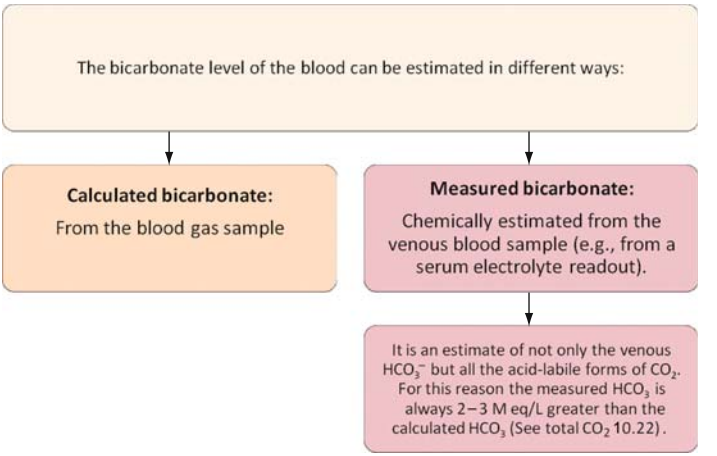
(see also isohydric principle 5.17)

6.19 Non-bicarbonate Buffers as a Measure of the pH

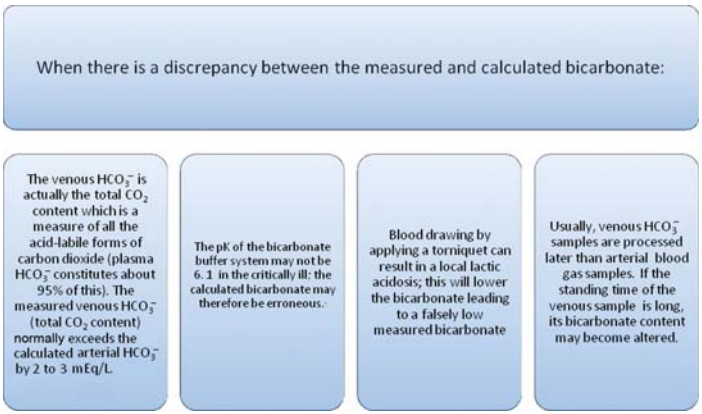
As mentioned, the non-bicarbonate systems principally buffer changes in carbon-dioxide. It is possible to arrive at the H^+ concentration or the pH of the blood by measuring the status of the non-bicarbonate buffer system. However, since the non-bicarbonate buffer system is in reality a conglomeration of several buffer systems, measurement is complex. It is far less complicated to rather measure the constituents of the bicarbonate buffer system in order to calculate the pH.

6.20 Measuring Bicarbonate

The measured HCO_3 is not the same as the calculated HCO_3^-.



6.21 When the Measured Bicarbonate is at Variance with the Calculated Bicarbonate



Chapter 7
Acidosis and Alkalosis

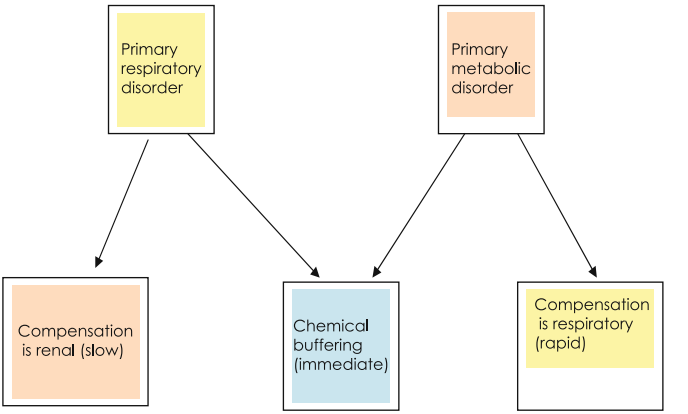
Contents

7

A. Hasan, *Handbook of Blood Gas/Acid–Base Interpretation*,
DOI 10.1007/978-1-84800-334-7_7,

7.1 Compensation

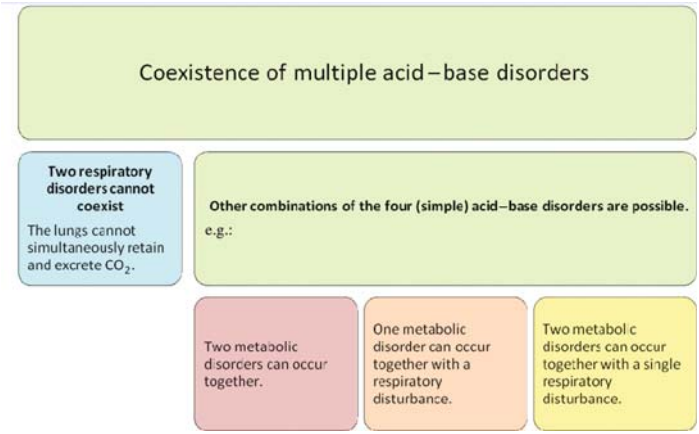
The body attempts to maintain its pH when confronted with acid–base disturbances. The compensatory processes are different for respiratory and renal disturbances.



Lennon, Ej, Lemann, J, Jr. pH- is it defensible? Ann Intern Med 1966; 65:1151

7.2 Coexistence of Acid–Base Disorders

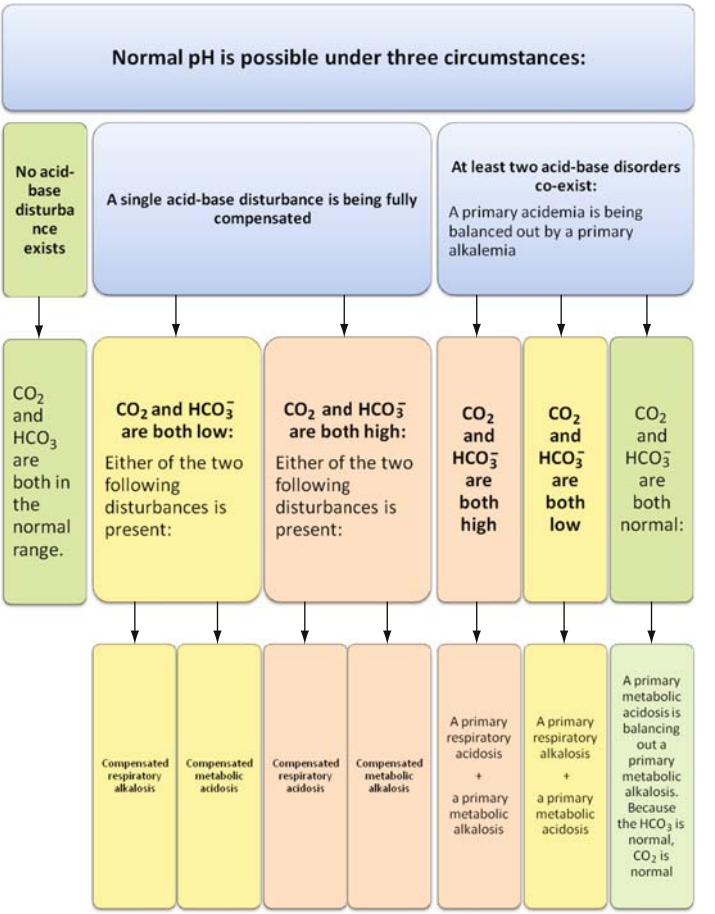
Frequently, two (sometimes three) acid–base disorders occur simultaneously.



Narins, RG, Emmet, M. Simple and mixed acid–base disorders: a practical approach. Medicine (Baltimore) 1980; 59:161

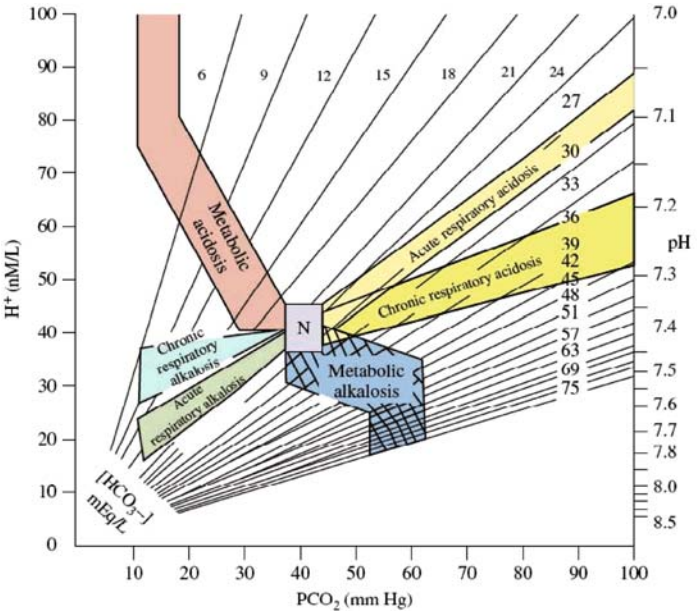
McCurdy, DK. Mixed metabolic and respiratory acid–base disturbances: diagnosis and treatment. Chest 1972; 63:355S

7.3 Conditions in which the pH can be normal



7.4 The Acid–Base Map

The acid–base map shows the relationship between pH (or H^+), $PaCO_2$ and HCO_3^-. Shown on the map are 95% confidence bands for the various acid–base disorders. When blood gas values are plotted on the map it becomes easy to rapidly diagnose single or mixed acid–base disturbances.



Goldberg, M, Green, SB, Moss, ML, et al. Computer based instruction and diagnosis of acid–base disorders: a systematic approach. JAMA 1973; 223: 269–275

7.5 Normal Values

Normal Arterial and Venous Values for pH, H^+ concentration, PCO_2, and HCO_3^- Concentration

	Arterial	Venous
pH	7.37–7.43	7.32–7.38
H^+, nanoeq/L	37–43	42–48
PCO_2, mmHg	36–44	42–50
HCO_3^-, meq/L	22–26	23–27

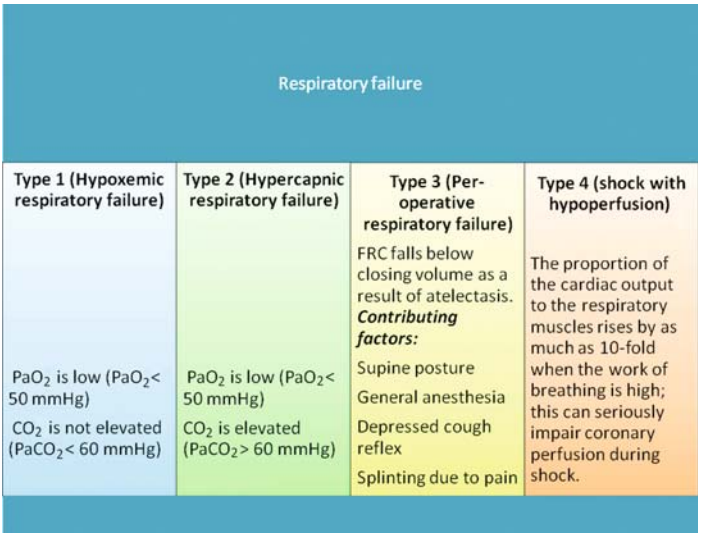
Chapter 8
Respiratory Acidosis

Contents

A. Hasan, *Handbook of Blood Gas/Acid–Base Interpretation*,
DOI 10.1007/978-1-84800-334-7_8,

8.1 Respiratory Failure

Although four types of respiratory failure have been described, it is usual to classify respiratory failure into Type-1 and Type-2: the latter is associated with hypoventilation and respiratory acidosis (see 8.2).



8.2 Respiratory Acidosis: Causes

In terms of CO_2 production and excretion, alveolar hypoventilation is the major mechanism for hypercarbia (See 2.29). Quite often however, increase in dead space is an important mechanism .

Causes of acute hypercapnia

Central depression of respiratory drive
Drugs
sedatives, opiates, anesthetic agents
CNS lesions
CNS trauma, strokes, encephalitis
Neuromuscular
Spinal cord lesions or trauma (at or above level of C_4)
High central neural blockade
Tetanus
Poliomyelitis
Amyotrophic lateral sclerosis
Myasthenia gravis
Organophosphate poisoning
Botulism
Muscular relaxants
Dyselectreolytemias
Chest wall
Flail chest
Diaphragmatic dysfunction: paralysis, splinting or rupture
Pleura
Pneumothorax
Rapid accumulation of a large pleural effusion
Lung parenchyma
Pulmonary edema, cardiogenic
ARDS
Pneumonia
Airways
Upper airway obstruction
Aspiration
Asthma or COPD
Other
Circulatory shock
Sepsis
Malignant hyperthermia
CO_2 insufflation into the body

Causes of chronic hypercapnia

Central depression of respiratory drive
Primary alveolar hypoventilation

Neuromuscular
Chronic neuromyopathies
Poliomyelitis
Dyselectreolytemias
Malnutrition

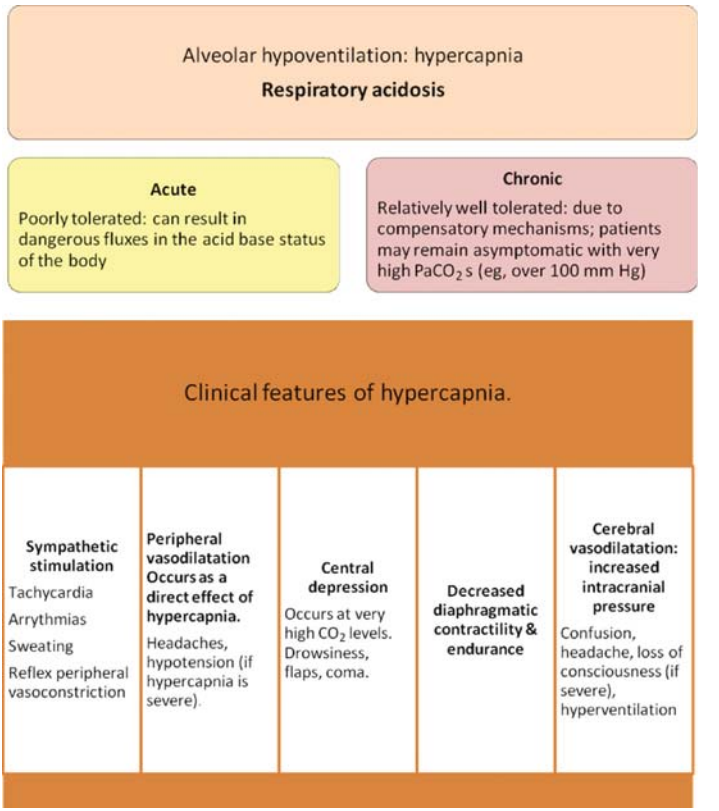
Chest wall
Kyphoscoliosis
Obesity
Thoracoplasty
Pleura
Chronic large effusions

Lung parenchyma
Long standing and severe ILD

Airways
Persistent asthma
Severe COPD
Bronchiectasis

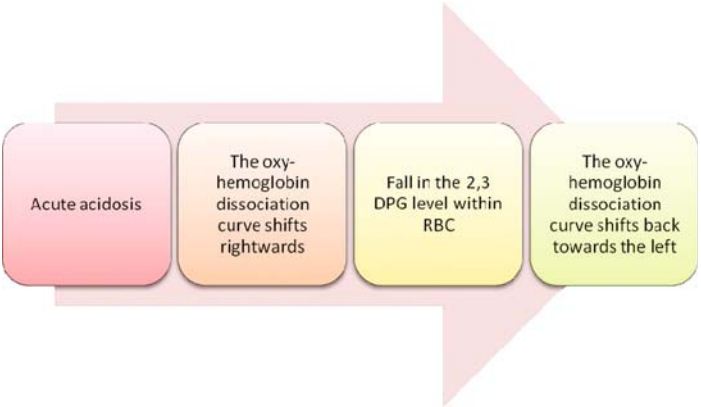
8.3 Acute Respiratory Acidosis: Clinical Effects

A rapid decrease in alveolar ventilation is poorly tolerated by the body.
Both acute hypercapnia and acute hypoxemia can be extremely damaging. On the other hand, surprising degrees of hypercapnia and hypoxemia can be tolerated by the body when chronic.



8.4 The ODC in Acute Respiratory Acidosis

Acute hypercapnia can transiently shift the oxy-hemoglobin dissociation curve to the right.

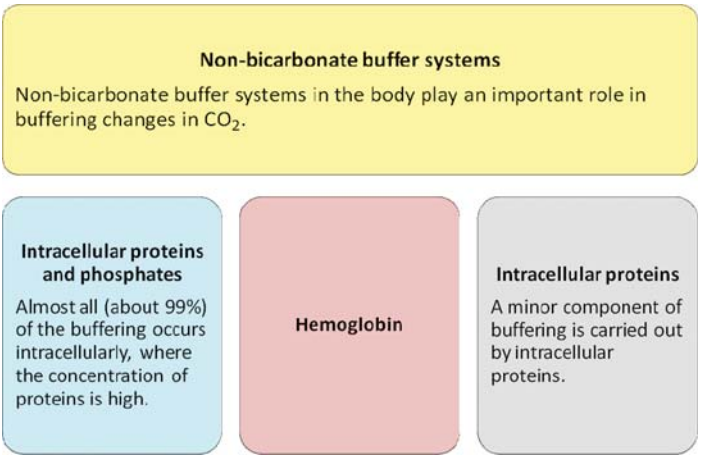


Bellingham, AJ, Detter, JC, Lenfant, C. Regulatory mechanisms of haemoglobin affinity in acidosis and alkalosis. J Clin Invest 1971; 50(3):700–706

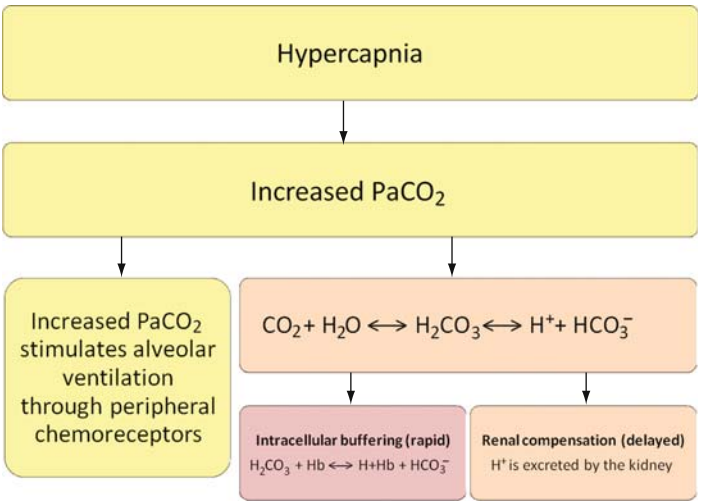
Brandis, K. Acid-Base Physiology. www.anaesthesiaMCQ.com

8.5 Buffers in Acute Respiratory Acidosis

The bicarbonate buffer system, quantitatively the most important buffer system in the body, cannot buffer changes produced by alterations in CO_2 levels: a buffer system cannot buffer its own components.

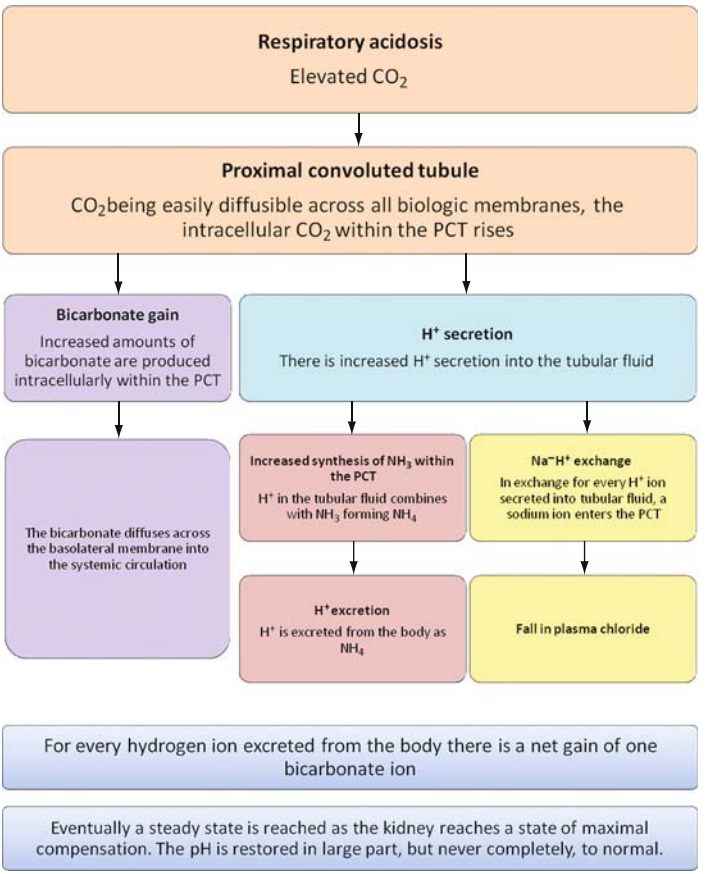


8.6 Respiratory Acidosis: Mechanisms for Compensation



Brackett, NC, Jr, Wingo, CF, Mureb, O, et al. Acid–base response to chronic hypercapnia in man. New Eng J Med 1969; 280:124–130

8.7 Renal Response to Acute Respiratory Acidosis



Brackett, NC, Jr, Wingo, CF, Mureb, O, et al. Acid–base response to chronic hypercapnia in man. New Eng J Med 1969; 280:124–130

8.8 Compensation for Acute Respiratory Acidosis

Acute respiratory acidosis (<24 hours)	Chronic respiratory acidosis (>24 hours)
• $\Delta\downarrow$*pH = 0.008 x $\Delta\uparrow PaCO_2$	• $\Delta\downarrow$pH = 0.003 x $\Delta\uparrow PaCO_2$
• $\Delta H+ = 0.8 \times \Delta PaCO_2$	• $\Delta H^+ = 0.3 \times \Delta PaCO_2$
• HCO_3 increases by up to 0.1 mEq/L for every mmHg rise in CO_2	• HCO_3 increases by up to 0.4 mEq/L for every mmHg rise in CO_2
• $H^+ = (0.8 \times PaCO_2) + 8$	• $H^+ = (0.3 \times PaCO_2) + 27$

Limits of compensation for respiratory acidosis

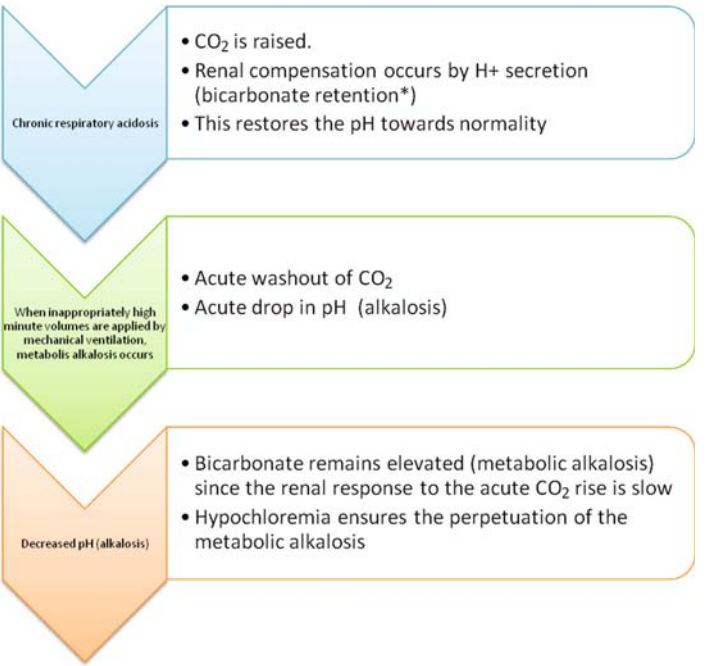
- The process of compensation is generally complete within 2 to 4 days
- The bicarbonate can increase to a maximum of 45 mmol/L; a bicarbonate level in excess of this may imply a coexistent primary metabolic alkalosis.

- *Δ = Change in; $\Delta\downarrow$ = Fall in; $\Delta\uparrow$ = Rise in

Smith, RM. In: Manual of Clinical Problems in Pulmonary Medicine. (Ed) Bordow, RA, Ries, AL, Morris, TA. Lippincott Williams and Wilkins. 6th ed, 2005

8.9 Post-Hypercapnic Metabolic Alkalosis

Although the immediate event is hyperventilation with CO_2 washout, the blood gas reflects metabolic alkalosis.

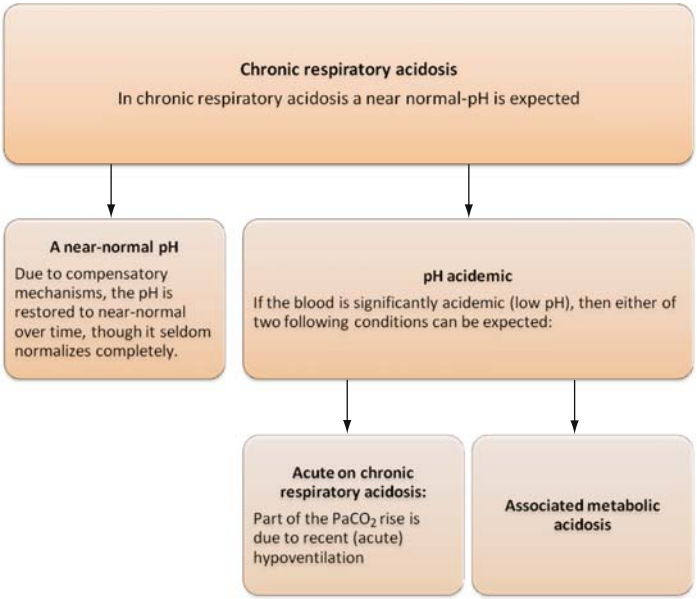


*The chronic elevation of bicarbonate results in chloride loss

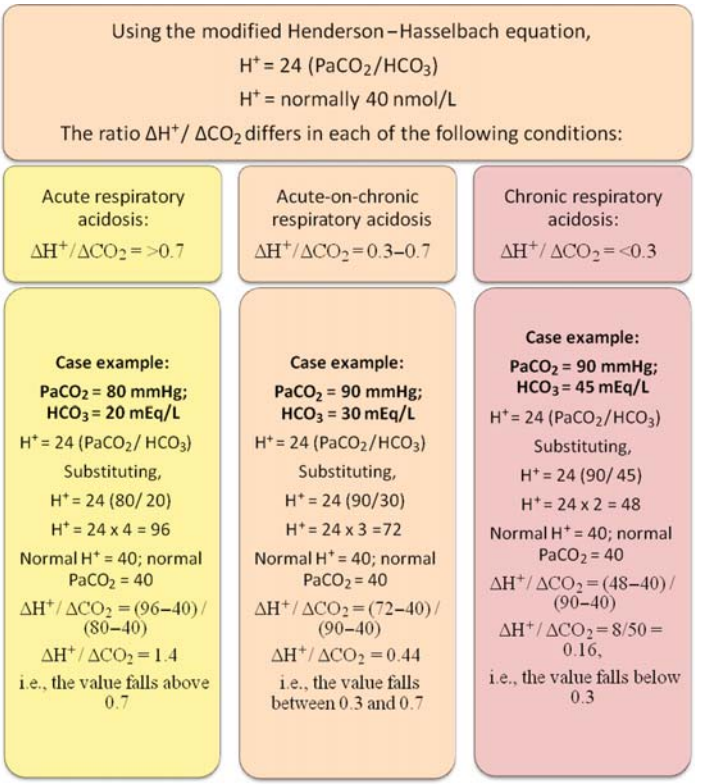
8

Schwartz, WB, Hays, RM, Polak, A, Haynie, G. Effects of chronic hypercapnia on electrolyte and acid–base equilibrium. II. Recovery with special reference to the influence of chloride intake. J Clin Invest 1961; 40:1238

8.10 Acute on Chronic Respiratory Acidosis



8.11 Respiratory Acidosis: Acute or Chronic?



Demer RR, Irwin RS. Management of hypercapnic respiratory failure: a systematic approach. R Resp Care Vol 24, p328: 1979

Chapter 9
Respiratory Alkalosis

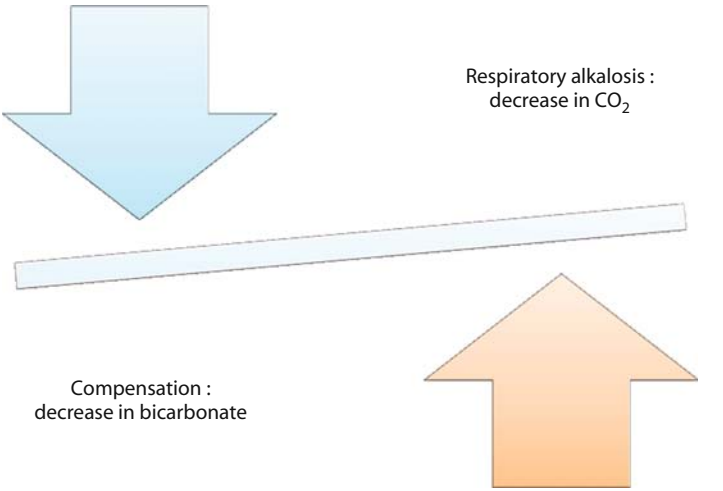
Contents

9

A. Hasan, *Handbook of Blood Gas/Acid–Base Interpretation*,
DOI 10.1007/978-1-84800-334-7_9,

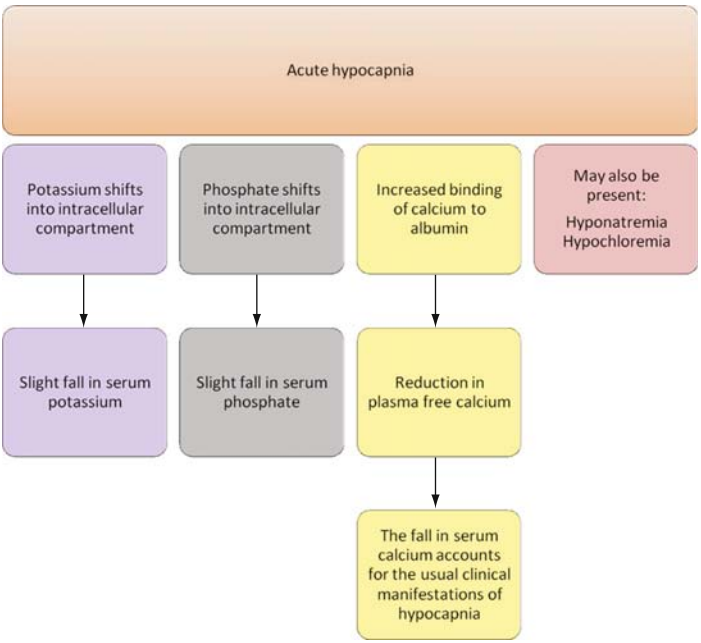
9.1 Respiratory Alkalosis

Unlike a metabolic alkalosis (where an additional mechanism is responsible for the maintenance of the acid–base disturbance), a respiratory alkalosis persists only as long as the inciting pathology is active.



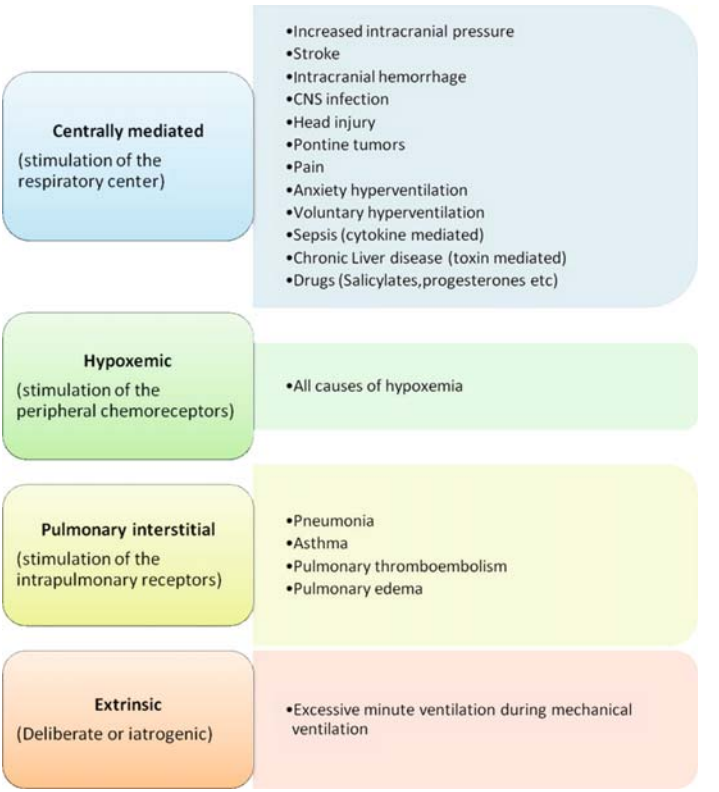
Rose, BD, Post, TW, Clinical Physiology of Acid–Base and Electrolyte Disorders, 5th ed, McGraw-Hill, New York, 2001, 615–619

9.2 Electrolyte Shifts in Acute Respiratory Alkalosis

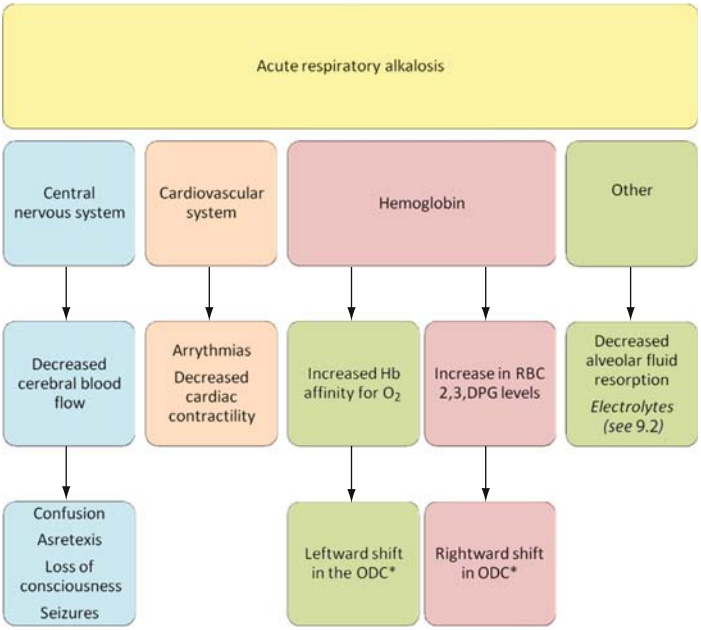


Wiseman, AC, Linas, S. Disorders of potassium and acid–base balance. Am J Kidney Dis 2005; 45(5): 941–9

9.3 Causes of Respiratory Alkalosis



9.4 Clinical Features of Acute Respiratory Alkalosis



*The overall effects are therefore unpredictable, but the position of the ODC may remain roughly unaltered

Kazmaier, S, Weyland, A, Buhre, W, et al. Effect of respiratory alkalosis and acidosis on myocardial blood flow and metabolism in patients with coronary artery disease. Anesthesiology 1998; 89(4):831–837

Kirsch, DB, Josefowicz, RF. Neurologic complications of respiratory disease. Neurol Clin 2002; 20(1): 247–64:

Myrianthefs, PM, Briva, A, Lecuona, E, et al. Hypocapnic but not metabolic alkalosis impairs alveolar fluid resorption. Am J Respir Crit Care Med 2005; 171(11): 1267–1271

9.5 Compensation for Respiratory Alkalosis

The magnitude of the fall in the serum bicarbonate as a compensatory process is different in acute and chronic respiratory alkalosis.

Acute respiratory alkalosis (<12 hours)

- $\Delta\uparrow pH = 0.01 \times \Delta\downarrow PaCO_2$*
- $\Delta\downarrow H^+ = 0.75 \times \Delta\downarrow PaCO_2$
- HCO_3^- falls by up to 0.2mEq/L for every mmHg fall in CO_2
- $H^+ = (0.75 \times PaCO_2) + 10$

Chronic respiratory alkalosis (>12 hours)

- $\Delta\uparrow pH = 0.003 \times \Delta\downarrow PaCO_2$
- $\Delta\downarrow H^+ = 0.3 \times \Delta\downarrow PaCO_2$
- HCO_3^- falls by up to 0.5mEq/L for every mmHg fall in CO_2
- $H^+ = (0.3 \times PaCO_2) + 28$

Limits of compensation for respiratory alkalosis

- The process of compensation is generally complete within 7 to 10 days
- The serum bicarbonate can fall to as low as 12 mmol/L; a lower bicarbonate level may imply a coexistent primary metabolic acidosis.

*This relationship holds good for a $PaCO_2$ between 40 to 80 mmHg.

Smith, RM. In: Manual of Clinical Problems in Pulmonary Medicine. Bordow, RA, Ries, AL, Morris, TA (eds.). Lippincott Williams and Wilkins. 6th ed, 2005

Arbus, GS, Hebert, LA, Levesque, PR, et al. Characterization and clinical application of "the significance band" for acute respiratory alkalosis. N Engl J Med 1969; 280:117

Krapf, R, Beeler, I, Hertner, D, Hulter, HN. Chronic respiratory alkalosis – The effect of sustained hyperventilation on renal regulation of acid-base equilibrium. N Engl J Med 1991; 324:1394

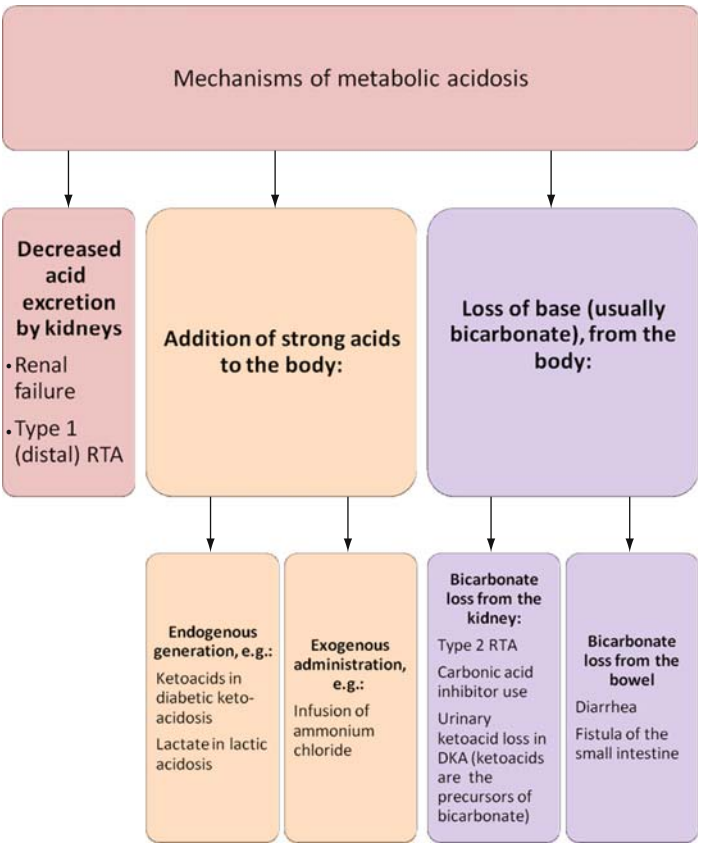
Gennari, FJ, Goldstein, MB, Schwartz, WB. The nature of the renal adaptation to chronic hypocapnia. J Clin Invest 1972; 51:1722

Chapter 10
Metabolic Acidosis

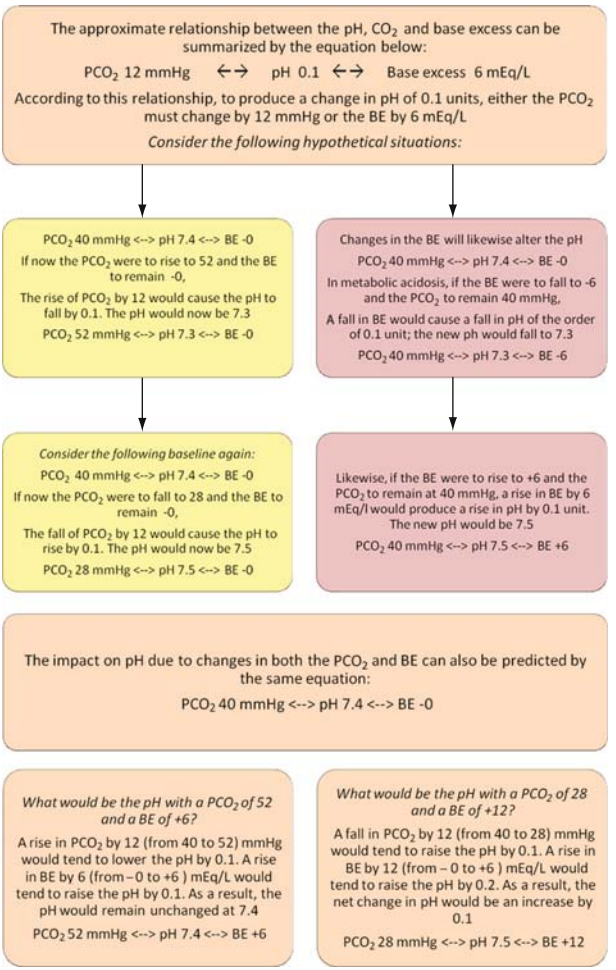
Contents

A. Hasan, *Handbook of Blood Gas/Acid–Base Interpretation*,
DOI 10.1007/978-1-84800-334-7_10,

10.1 The Pathogenesis of Metabolic Acidosis



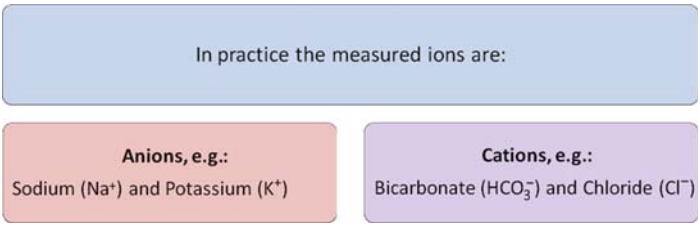
10.2 Relationships



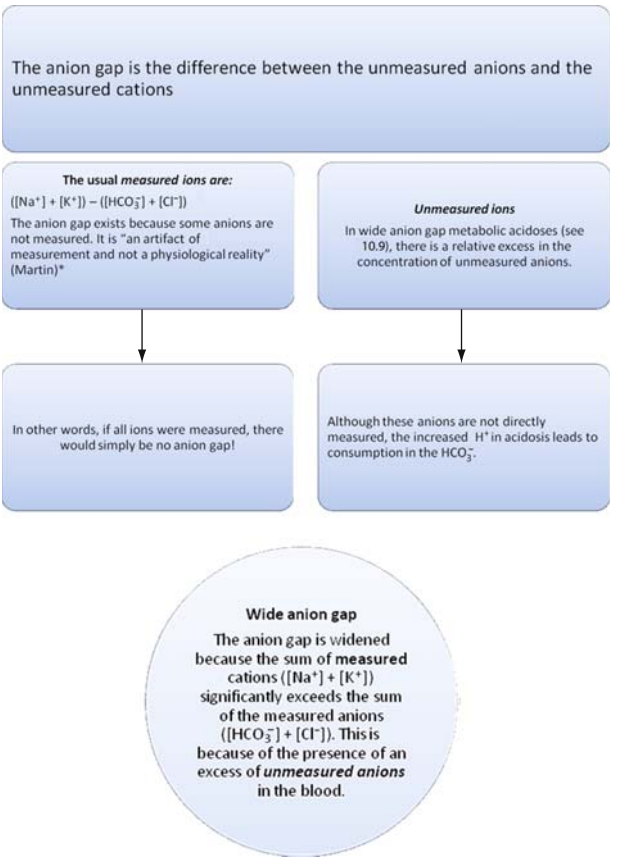
Grogono, AW. www.acid-base.com

10.3 The Law of Electroneutrality

The Law of Electroneutrality states that the sum of all the anions should equal the sum of all the cations.



10.4 The Anion Gap



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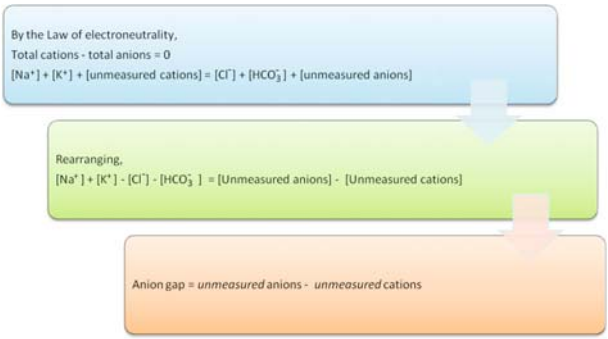
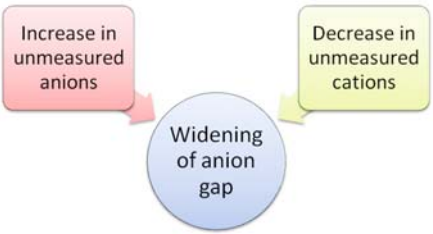
* Martin, L, All you Really Need to Know to Interpret Arterial Blood Gases. Lippincott, Williams and Wilkins, 1999

Rose, BD, Post, TW. Clinical Physiology of Acid–Base and Electrolyte Disorders, 5th ed, McGraw-Hill, New York, 2001, pp. 583–588

The anion gap widens when unmeasured anions are increased or unmeasured cations are decreased



By looking at the above equation it will be obvious that:



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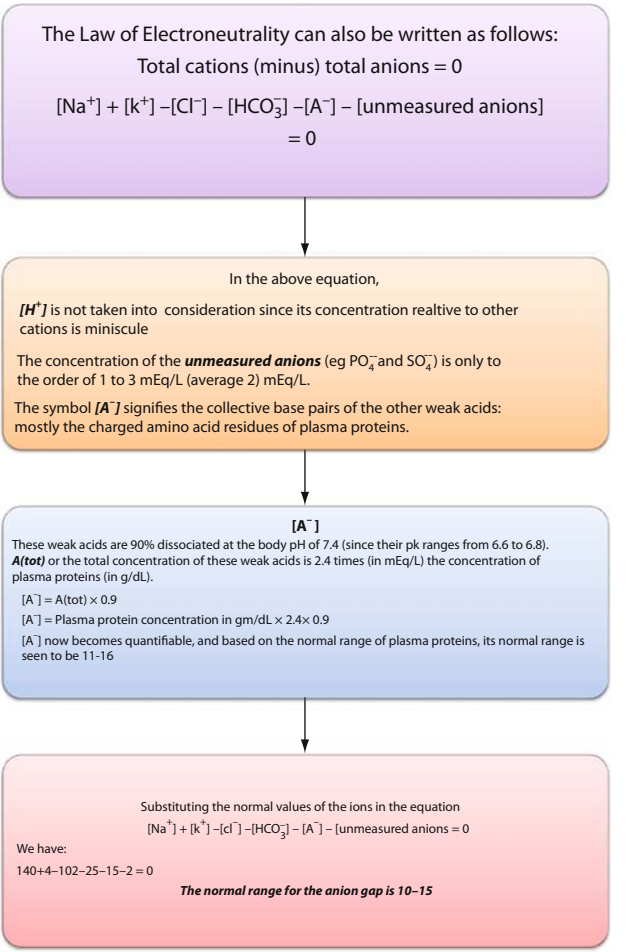
Gabow, PA. Disorders associated with an altered anion gap. Kidney Int 1985; 27:472

Rose, BD, Post, TW. Clinical Physiology of Acid–Base and Electrolyte Disorders, 5th ed, McGraw-Hill, New York, 2001, pp. 583–588

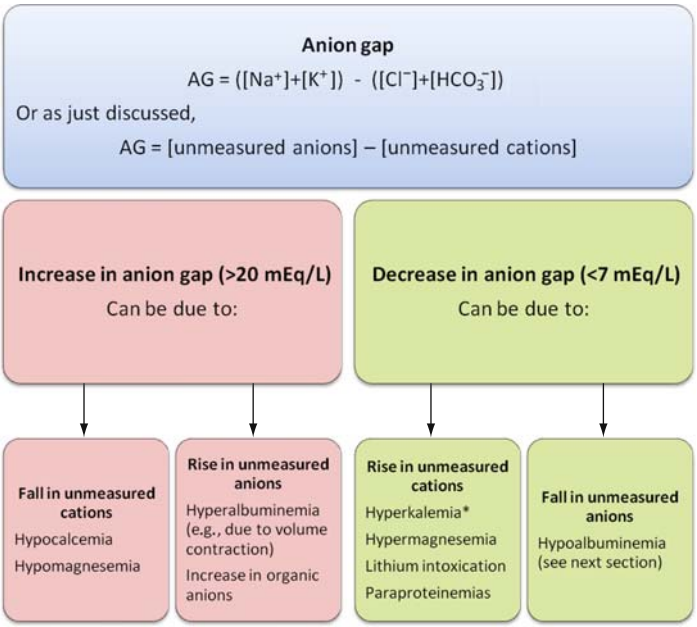
10.5 Derivation of the Anion Gap



Smith, RM. Evaluation of arterial blood gases and acid–base homeostasis. In: Manual of Clinical Problems in Pulmonary Medicine. Lippincott Williams and Wilkins, 2005

10.6 Electrolytes and the Anion Gap

Based on the Law of Electroneutrality:
$[Na^+] + [K^+] + [\text{unmeasured cations}] = [Cl^-] + [HCO_3^-] + [\text{unmeasured anions}]$, it can be predicted that certain electrolytes can widen or narrow the anion gap.



* If the usual formula–the one that doesn't incorporate K^{+-} is used, K^+ is in that sense an unmeasured cation

Gabow, PA. Disorders associated with an altered anion gap. Kidney Int 1985; 27:472

10.7 Calculation of the Anion Gap

Calculation of anion gap

For the calculation of anion gap either of the two following formulae can be used:

$(Na^+) - ([Cl^-] + [HCO_3^-])$

This is the generally used formula. K+ is excluded from the formula on the grounds that the value of K^+ is generally small enough to be disregarded.

Normal range: 12+/-4 mEq/L

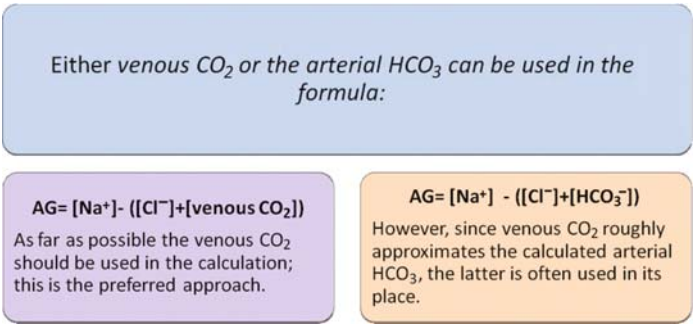
$([Na^+]+[K^+]) - ([Cl^-] + [HCO_3^-])$

This is the formula used when the value of K^+ is expected to vary significantly, as in renal patients.

Normal range: 16 +/- mEq/L

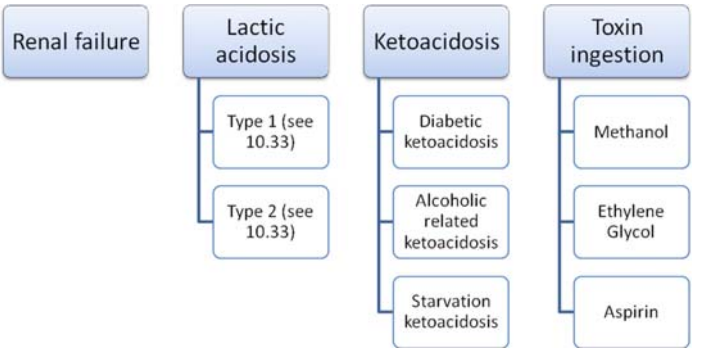
10.8 Laboratory Variation

Newer autoanalysers (which use ion-specific electrodes) report the normal serum Cl- at a higher value than did the "older" machines, (which measured electrodes with flame spectrophotometry); the normal range for the anion gap with the newer machines is lower, usually ranging between 3 and 11 mEq/L.

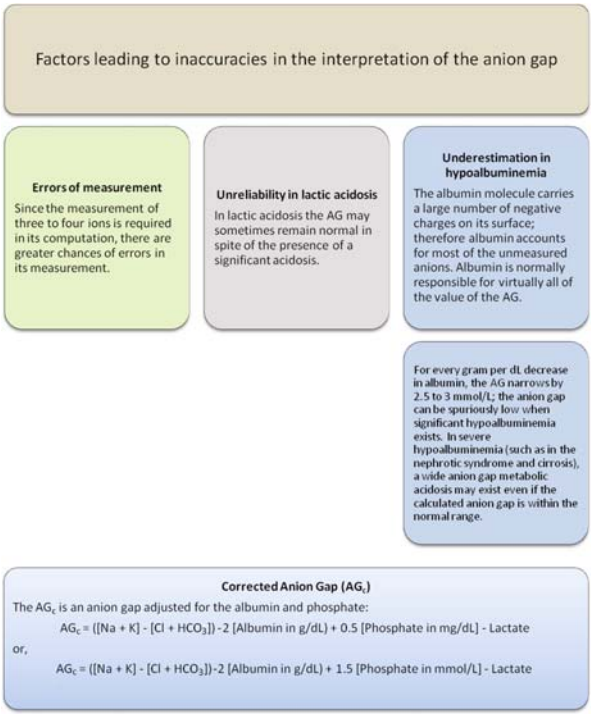


Martin, L. All you Really Need to Know to Interpret Arterial Blood Gases. Lippincott, Williams and Wilkins, 1999

10.9 Causes of a Wide Anion Gap



10.10 Limitations of the Anion Gap: The Corrected Anion Gap

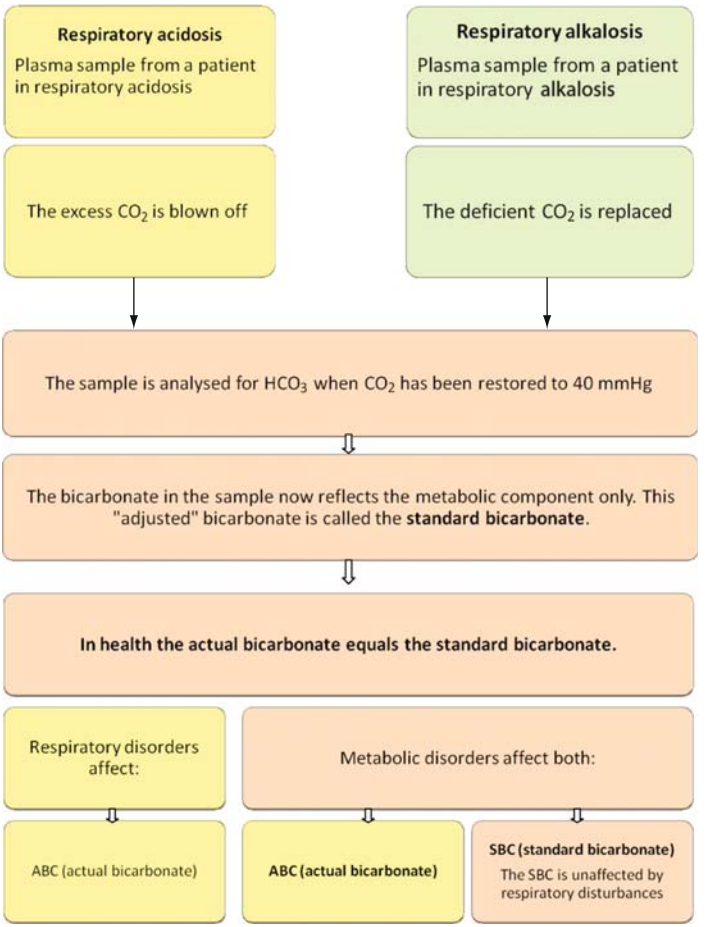


Gabow, PA. Disorders associated with an altered anion gap. Kidney Int 1985; 27:472

Kellum, JA, Kramer, DJ, Pinsky, MR. Closing the GAP: A simple method of improving the accuracy of the anion gap. Chest 1996; 110:18S

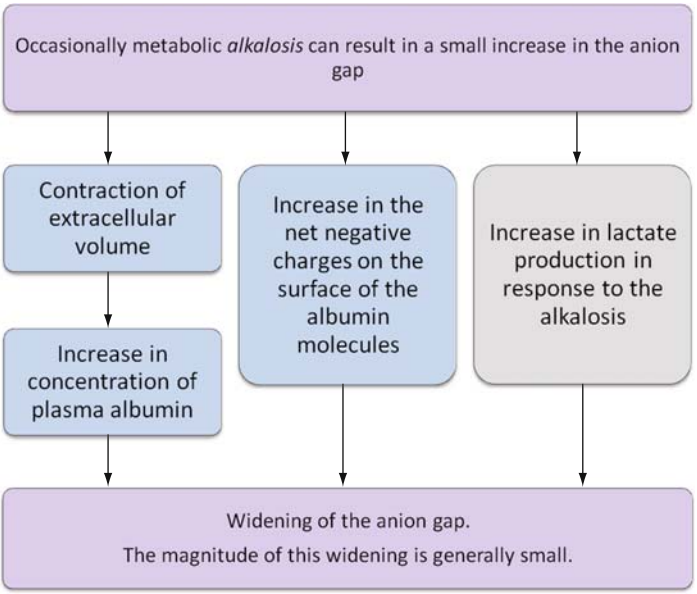
Kellum, JA. Disorders of acid–base balance. Crit Care Med 2007; 35 (11):2630–2636

10.11 Actual Bicarbonate and Standard bicarbonate



Standard bicarbonate is therefore more specific for metabolic disturbances.

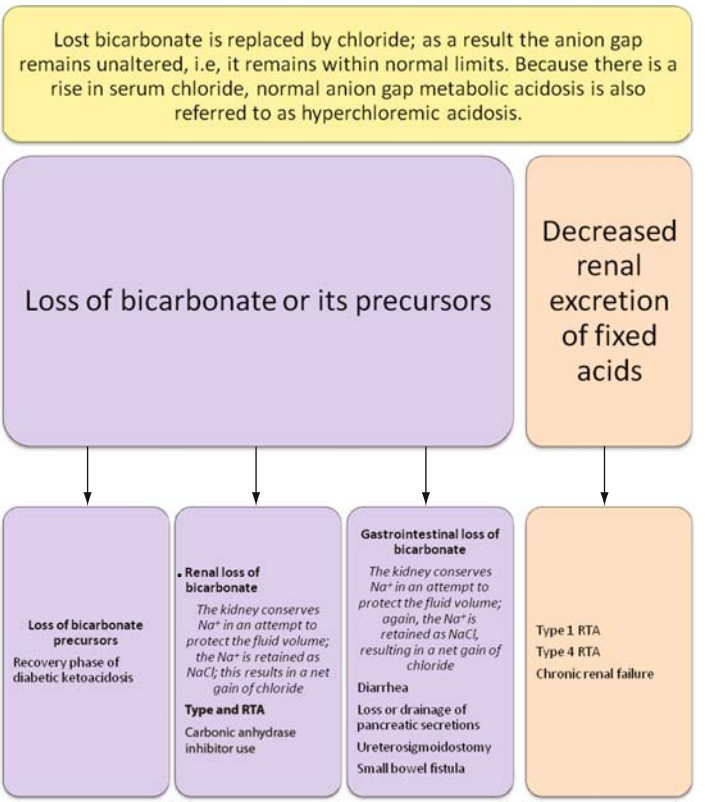
10.12 Wide Anion Gap in Metabolic alkalosis



Emmett, M. Anion-gap interpretation: The old and the new. Nat Clin Prac 2006; 2:4

Madias, NE, Ayus, JC, Adrogué, HJ. Increased anion gap in metabolic alkalosis: The role of plasma-protein equivalency. N Engl J Med 1979; 300:1421

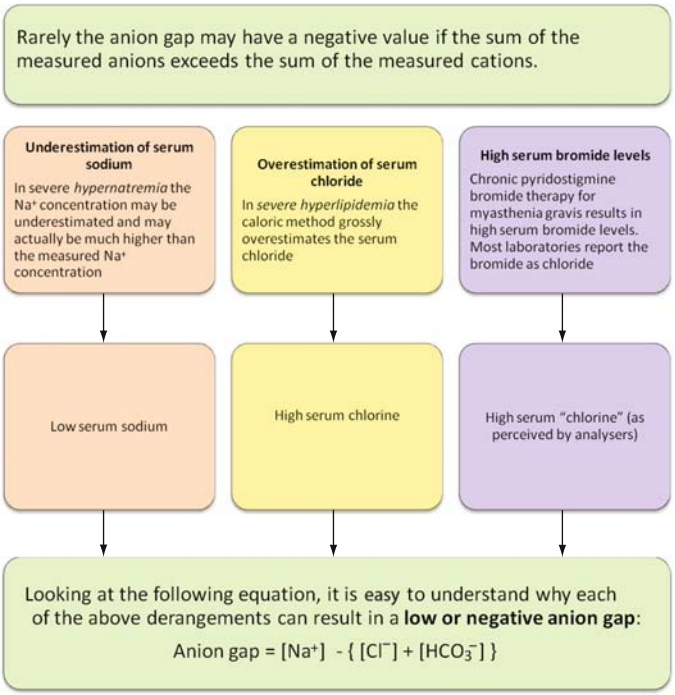
10.13 Normal Anion-Gap Metabolic Acidosis



Rose, BD, Post, TW. Clinical Physiology of Acid–Base and Electrolyte Disorders, 5th ed, McGraw-Hill, New York, 2001

Winter, SD, Pearson, JR, Gabow, PA, et al. The fall of the serum anion gap. Arch Intern Med 1990; 150:311

10.14 Negative Anion Gap

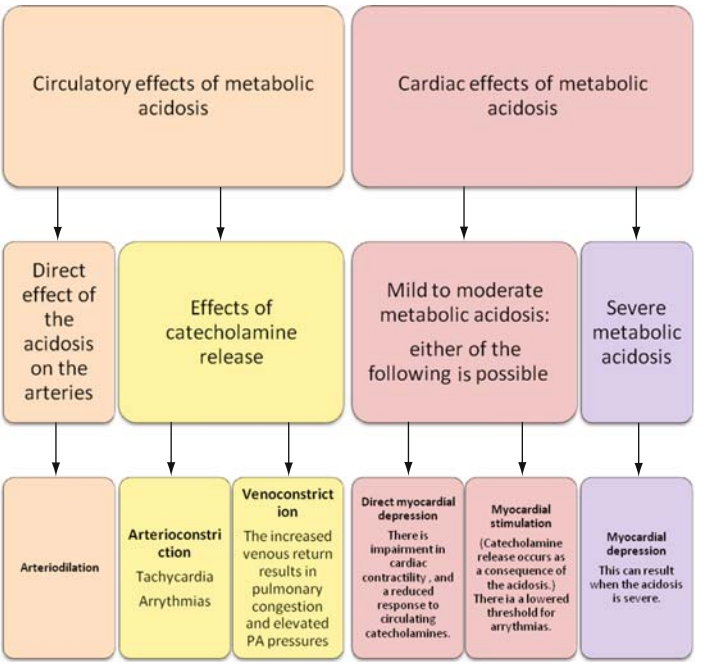


Kelleher, SP, Raciti, A, Arbeit, LA. Reduced or absent serum anion gap as a marker for severe lithium carbonate intoxication. Arch Intern Med 1986; 146:1839

Graber, ML, Quigg, RJ, Stempsey, WE, Weis, S. Spurious hyperchloremia and decreased anion gap in hyperlipidemia. Ann Intern Med 1983; 98:607

Faradji-Hazan, V, Oster, JR, Fedeman, DG, et al. Effect of pyridostigmine bromide on serum bicarbonate concentration and the anion gap. J Am Soc Nephrol 1991; 1:1123

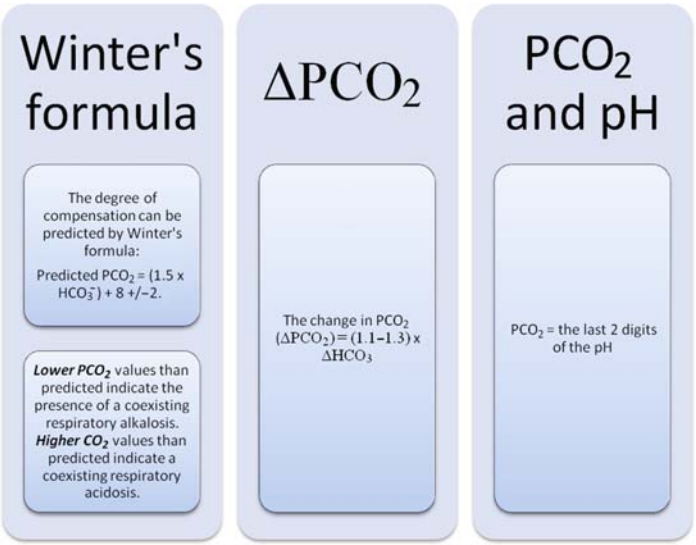
10.15 Cardiovascular Effects of Metabolic Acidosis



Orchard, CH, Kentish, JC. Effects of changes of pH on the contractile function of cardiac muscle. Am J Physiol 1990; 258:C967

Shapiro, JI. Functional and metabolic responses of isolated hearts to acidosis: Effect of sodium bicarbonate and Carbicarb. Am J Physiol 1990; 258:H1835

10.16 Compensation for Metabolic Acidosis

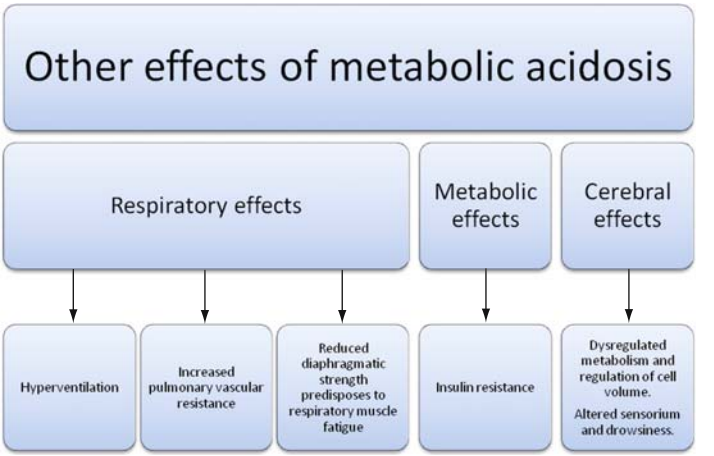


Smith RM. In: Bordow, RA, Ries, AL, Morris TA (Ed.) Manual of Clinical Problems in Pulmonary Medicine. Lippincott Williams and Wikins, 6th ed., 2005

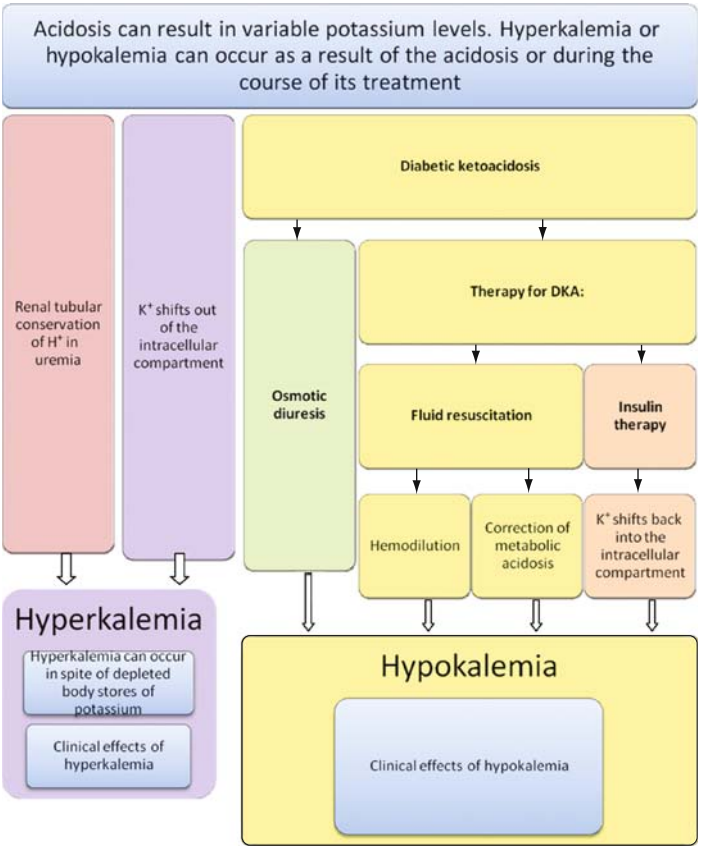
Albert, MS, Dell, RB, Winters, RW. Quantitative displacement of acid-base equilibrium in metabolic acidosis. Ann Intern Med 1967; 66:312–322

Schlichtig, R, Grogono, AW, Severinghaus, JW. Human $PaCo_2$ and standard base excess compensation for acid-base imbalance. Crit Care Med 1998; 28:1173–1179

10.17 Other consequences of Metabolic Acidosis



10.18 Potassium Shifts in Metabolic Acidosis

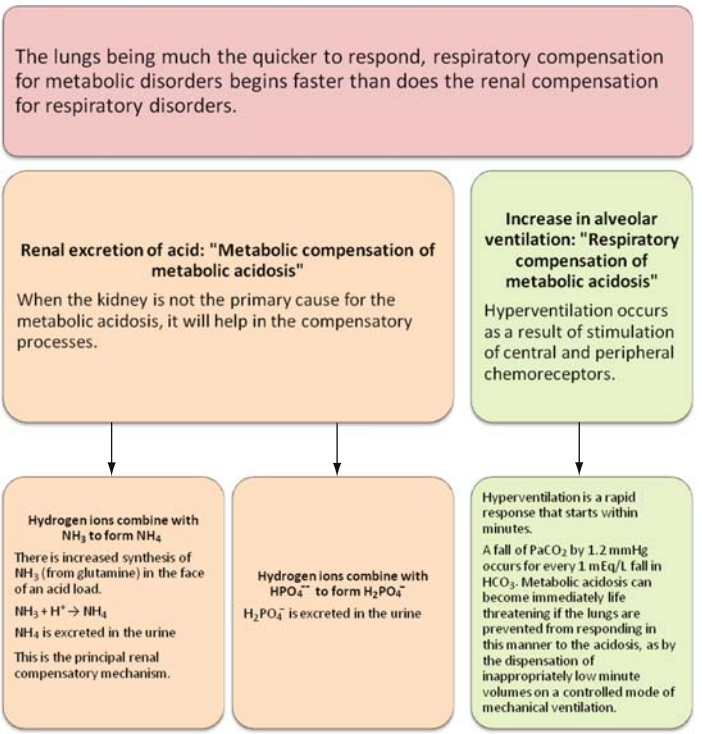


Wallia, R, Greenberg, AS, Piraino, B, et al. Serum electrolyte patterns in end-stage renal disease. Am J Kidney Dis 1986; 8:98

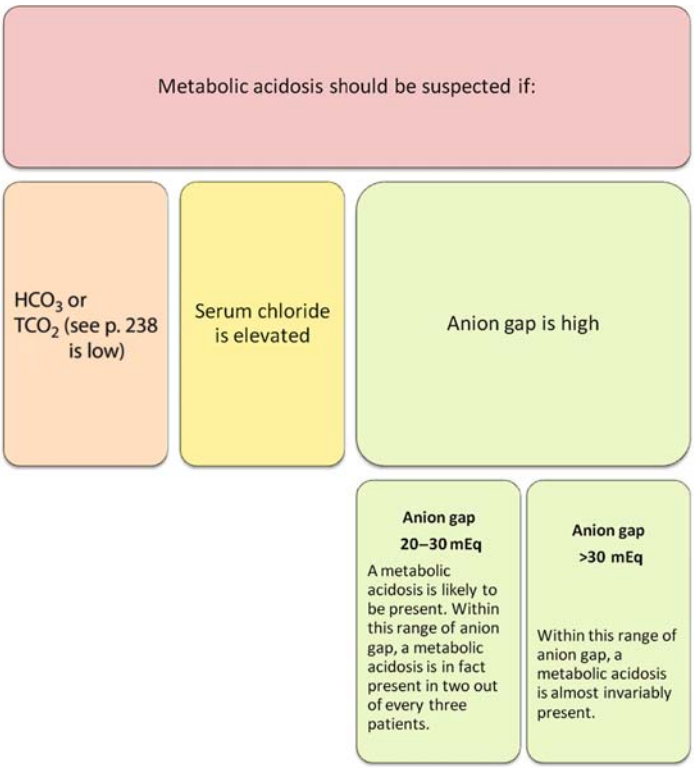
Wiederseiner, JM, Muser, J, Lutz, T, et al. Acute metabolic acidosis: Characterization and diagnosis of the disorder and the plasma potassium response. J Am Soc Nephrol 2004; 15:1589

10.19 Compensatory Response to Metabolic Acidosis

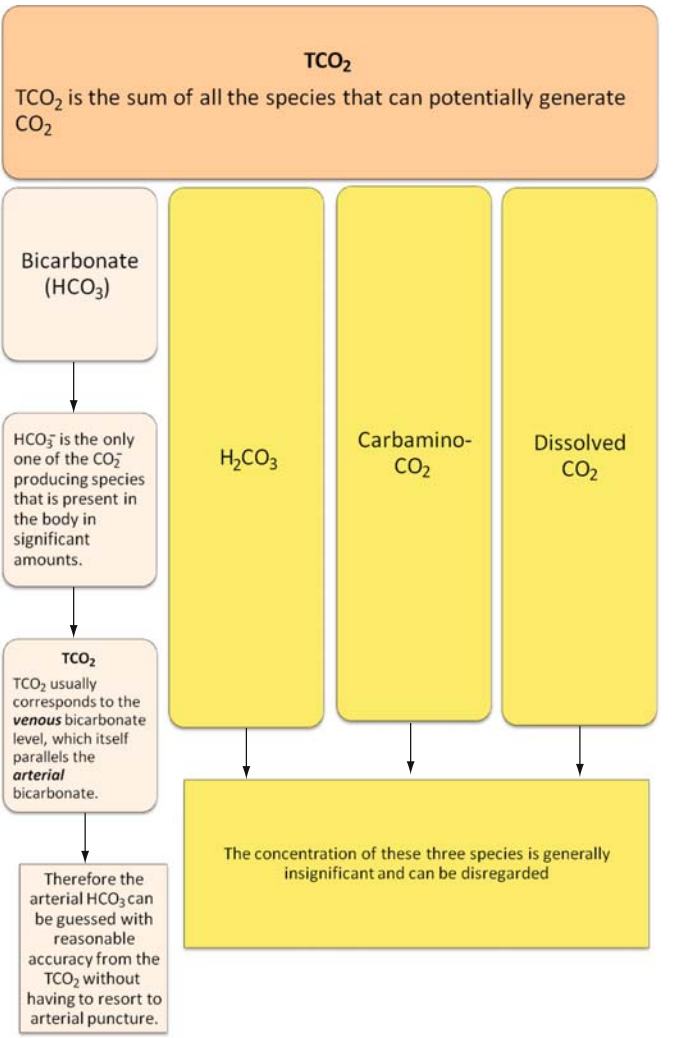
Rarely does a metabolic acidosis remain uncompensated (examples: presence of associated respiratory disease: a paralysed patient on ventilator who is being given inappropriately low minute volumes). In contrast to respiratory disorders which are well compensated by the kidney, compensation for metabolic disorders is rarely as perfect.



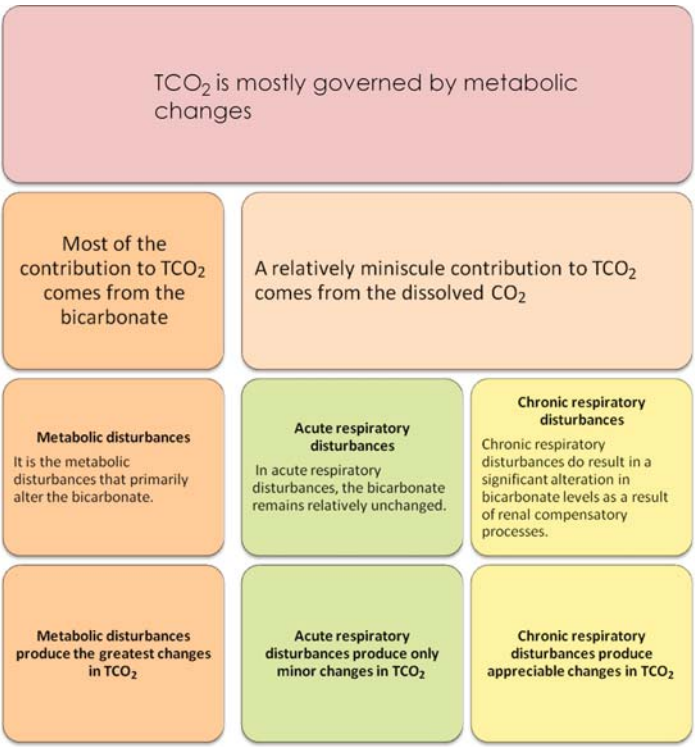
10.20 When to Suspect Metabolic Acidosis



10.21 Total CO_2 (TCO_2)



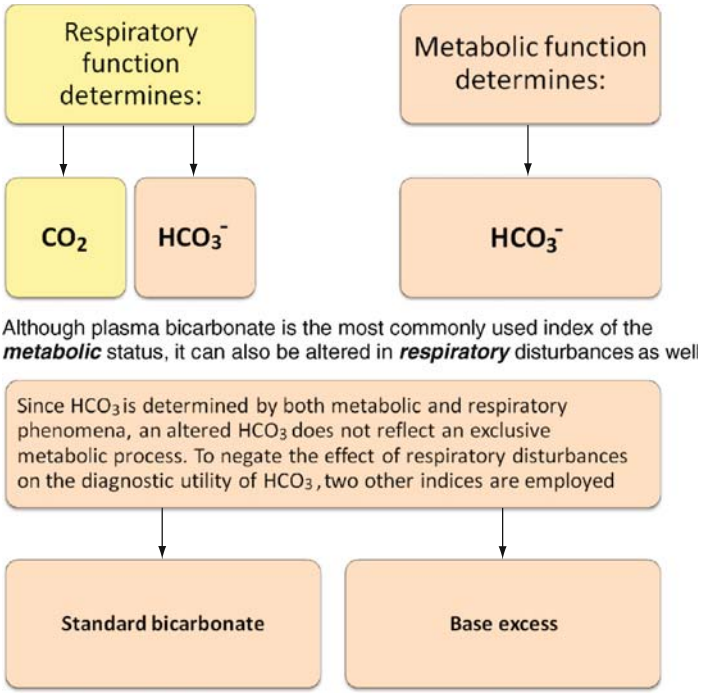
10.22 Clinical Utility of TCO_2



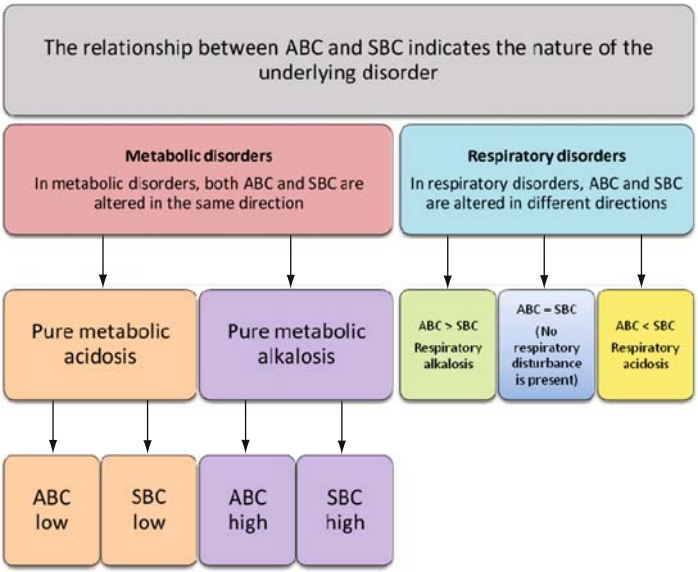
As mentioned earlier, at the usual body pH, the ratio of bicarbonate to carbonic acid is 20:1. This means that the TCO_2 is about 5% (or 2–3 mEq) higher than the serum bicarbonate. When the difference between the two is greater than this, a metabolic acidosis is usually present.

10.23 HCO_3 in Metabolic & Respiratory Disorders

An altered HCO_3 is not specific for metabolic derangements.

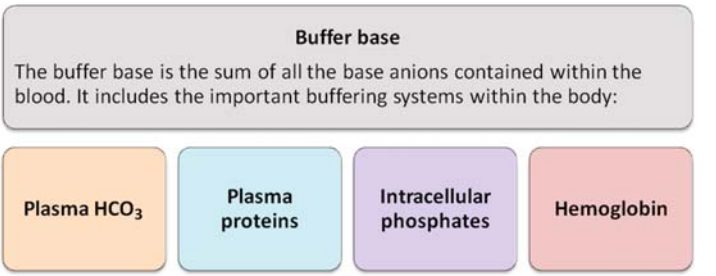


10.24 Relationship between ABC and SBC



10.25 Buffer Base

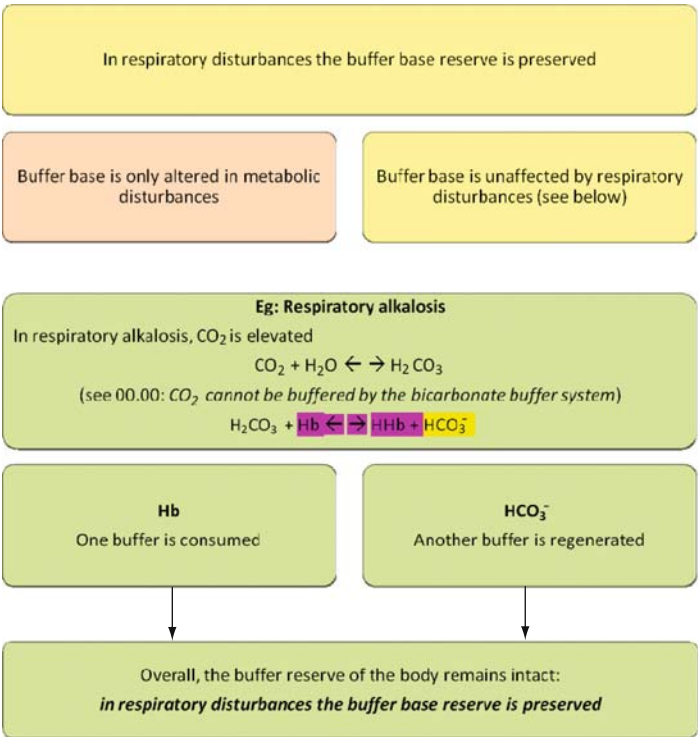
"Whole buffer base" (Singer and Hastings, 1948).



It may be that the buffer base mirrors electrolyte derangements the understanding of which may hold the key to this elusive concept.

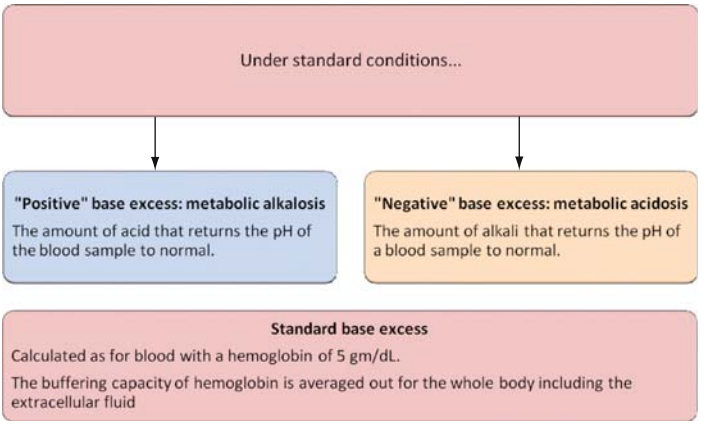
"Bluffer base". In: Acid–Base Balance: Common Ground? www.anaesthetist.com

10.26 Preservation of the Buffer Base in Respiratory Disturbances



10.27 Base Excess

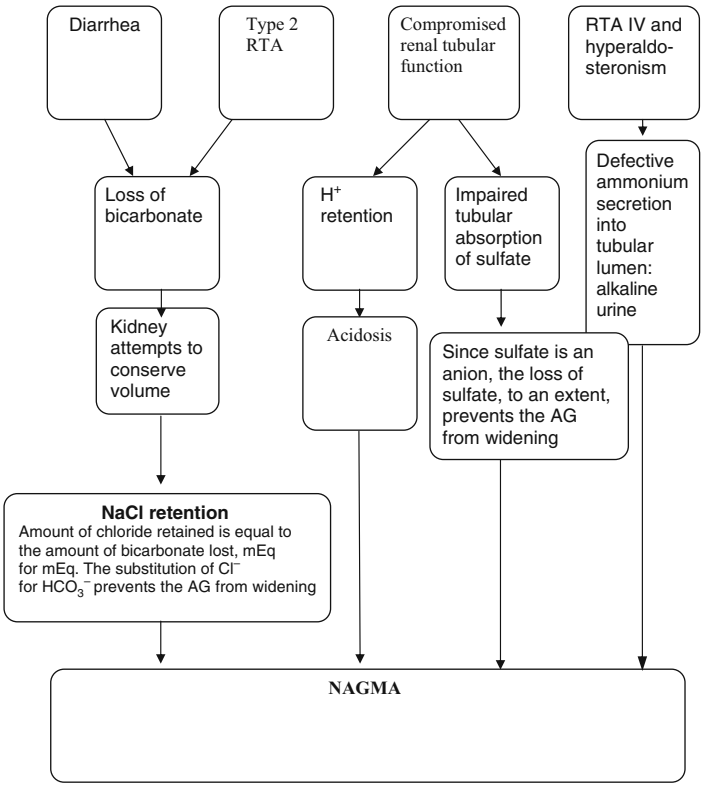
In 1958 Astrup and Siggard-Andersen described *Base Excess* as an improved indicator of *metabolic* acid–base disorders.



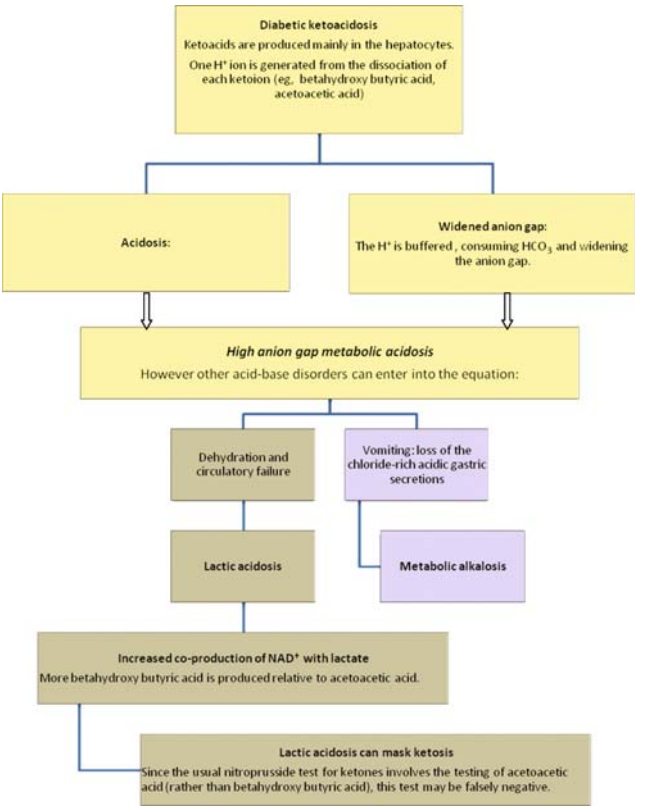
Schlichtig, R, Grogono, AW, Severinghaus, JW. Human $PaCO_2$ and standard base excess compensation for acid–base imbalance. Crit Care Med 1998; 26(7):1173–9

Barry, A. Utility of standard base excess in acid–base analysis (editorial). Crit Care Med 1998; 26(7):1146–1147

10.28 Mechanisms of Normal-Anion Gap Metabolic Acidosis



10.29 Wide Anion Gap Metabolic Acidosis in DKA

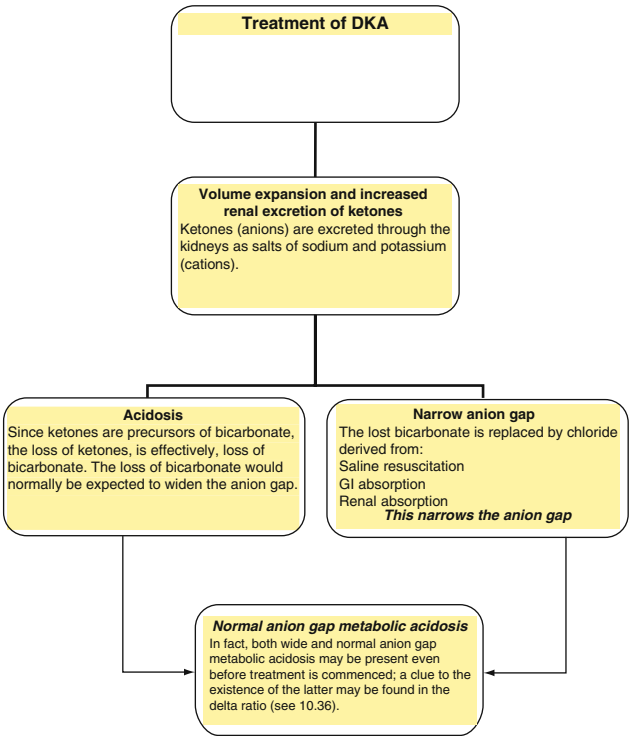


Adrogué, HJ, Wilson, H, Boyd, AE III, et al. Plasma acid-base patterns in diabetic ketoacidosis. N Engl J Med 1982; 307:1603

Rose, BD, Post, TW. Clinical Physiology of Acid-Base and Electrolyte Disorders, 5th ed, McGraw-Hill, New York, 2001, pp. 809–815

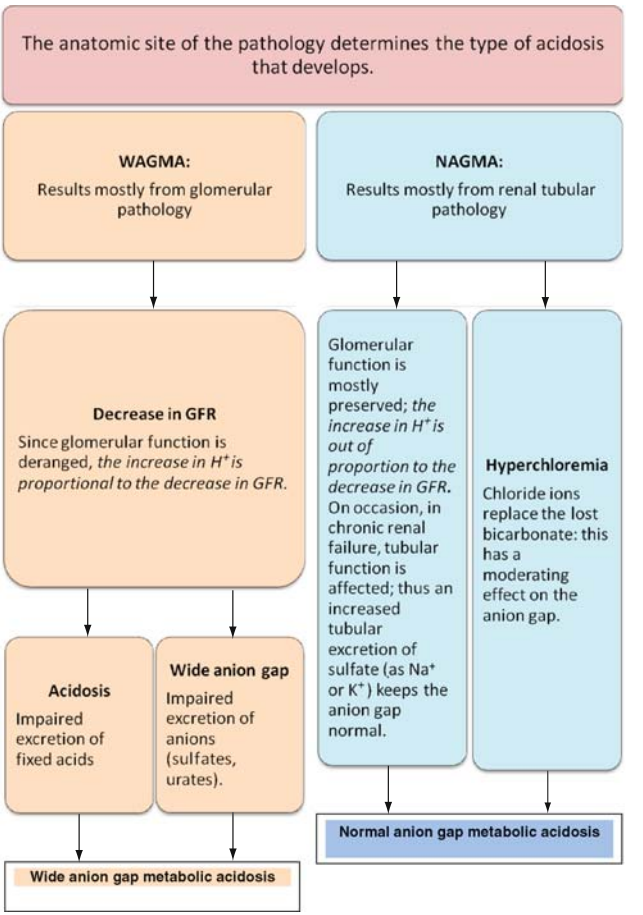
10.30 Normal Anion Gap Metabolic Acidosis During Treatment of DKA

Treatment of DKA can convert a high anion gap metabolic acidosis into a normal anion gap metabolic acidosis.



Oh, MS, Carroll, HJ, Goldstein, DA, Fein, IA. Hyperchloremic acidosis during the recovery phase of diabetic ketosis. Ann Intern Med 1978; 89:925

10.31 Renal Mechanisms of Acidosis

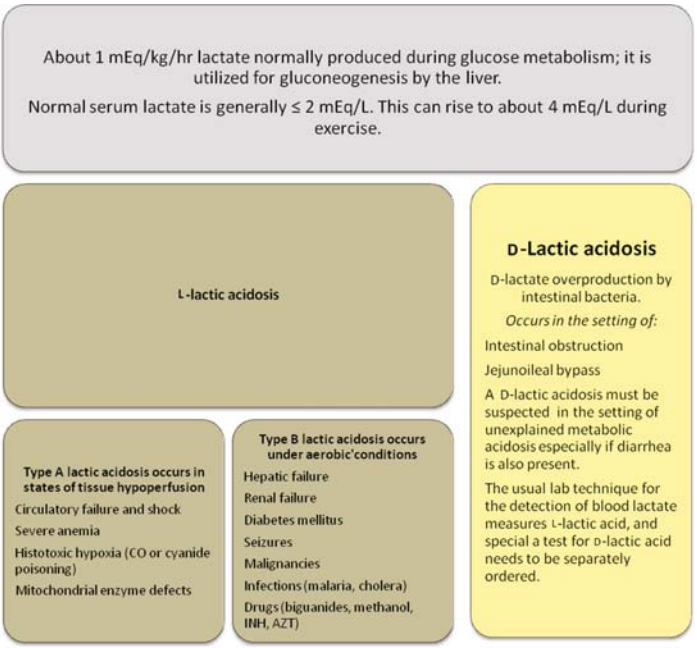


Wallia, R, Greenberg, AS, Piraino, B, et al. Serum electrolyte patterns in end-stage renal disease. Am J Kidney Dis 1986; 8:98

Rose, BD, Post, TW. Clinical Physiology of Acid–Base and Electrolyte Disorders, 5th ed, McGraw-Hill, New York, 2001, pp. 583–588

10.32 Lactic Acidosis

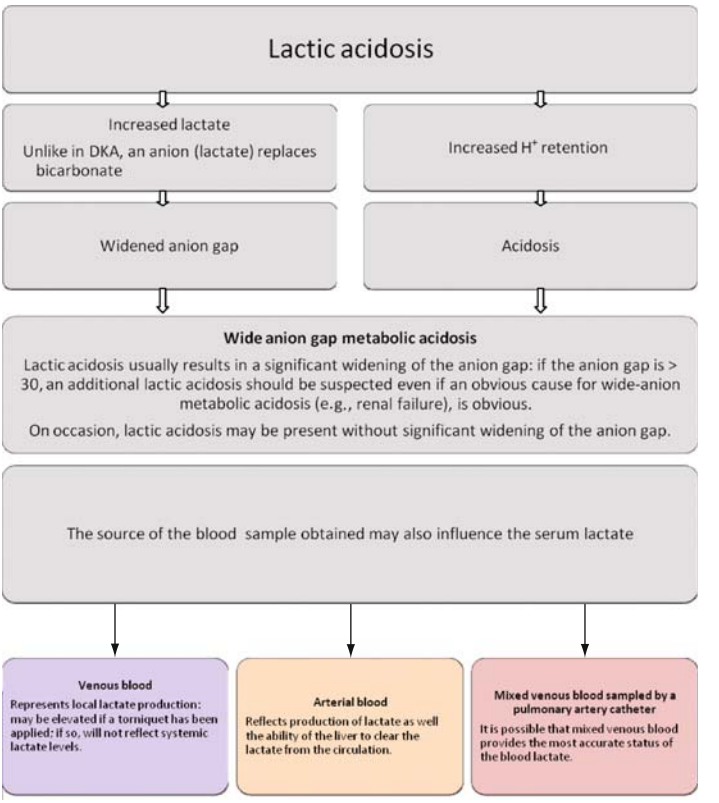
Lactic acidosis is probably the commonest cause of metabolic acidosis in the hospitalized patient: tissue hypoxia is the usual cause. To define the disorder, the serum lactate should be at least 5 mEq/L with associated metabolic acidosis.



Stolberg, L, Rolfe, R, Gitlin, N, et al. D-Lactic acidosis due to abnormal gut flora. N Engl J Med 1982; 306:1344

Uribarri, J, Oh, MS, Carroll, HJ. D-lactic acidosis. Medicine 1998; 77:73; Coronado, BE, Opal, SM, Yoburn, DC. Antibiotic-induced D-lactic acidosis. Ann Intern Med 1995; 122:839

10.33 The Diagnosis of Lactic Acidosis

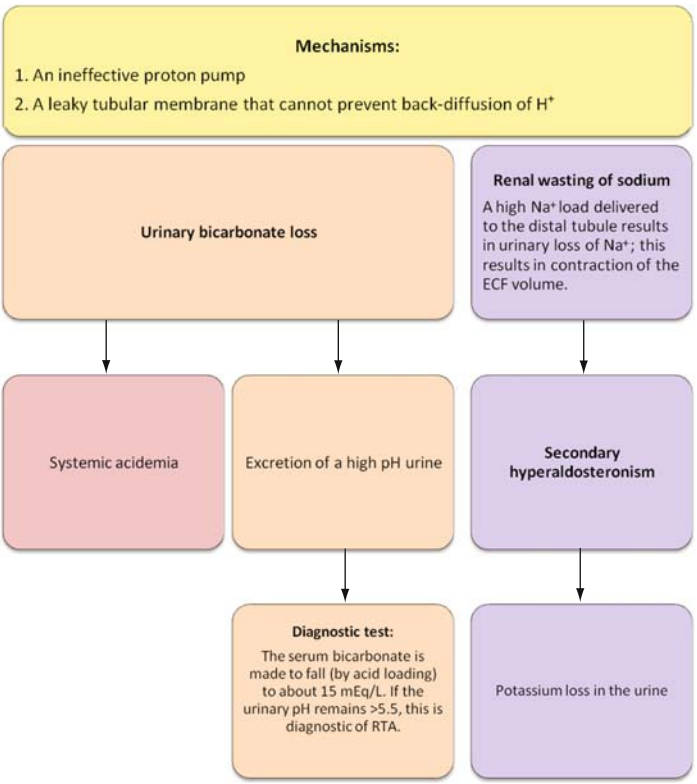


Weil, MH, Michaels, S, Rackow, EC. Comparison of blood lactate concentrations in central venous, pulmonary artery and arterial blood. Crit Care Med, 1987; 15:489–490

10.34 Distal RTA

Syn: Type I RTA, Classic RTA

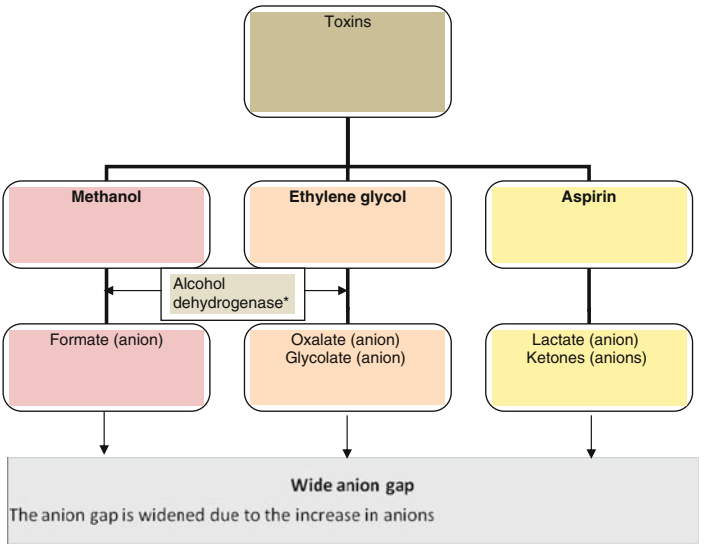
A urinary acidifying defect results in an alkaline urine remains (pH <5.5) in the face of severe acidemia. Distal RTA is generally more severe than proximal RTA.



Rodriguez Soriano, J. Renal tubular acidosis: the clinical entity. J Am Soc Nephrol 2002; 13:2160

Caruana, RJ, Buckalew, VM, Jr. The syndrome of distal (type 1) renal tubular acidosis. Medicine (Baltimore) 1988; 67:84

10.35 Toxin Ingestion



*The enzyme alcohol dehydrogenase helps in the catalysis of the reactions that lead to formation of the toxic metabolites. Co-ingested ethanol competes for the active sites on the enzyme alcohol dehydrogenase and so decreases the rate of formation of the methanol and ethylene glycol-induced toxic metabolites

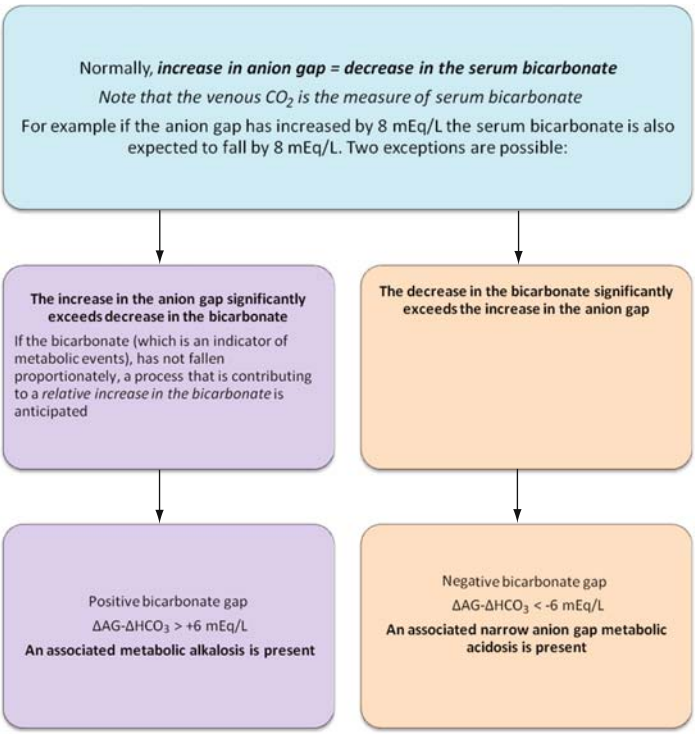
The first clue to the Methanol or Ethylene glycol poisoning is often the discovery of an osmolar gap (See Osmolar gap 10.41).

Post, TW, Rose, BD. Approach to the adult with metabolic acidosis. www.uptodate.com

10.36 Bicarbonate Gap (the Delta Ratio)

Syn: Delta gap, deviation from the 1:1 correlation

In wide anion gap metabolic acidosis, it is principally the decrease in the bicarbonate that accounts for the increase in the anion gap. If the decrease in the bicarbonate is less or more relative to the decrease in the anion gap, this implies the presence of an additional acid-base disorder. The difference between the increase in the anion gap (ΔAG) and the decrease in the bicarbonate (ΔHCO3) is termed the bicarbonate gap.

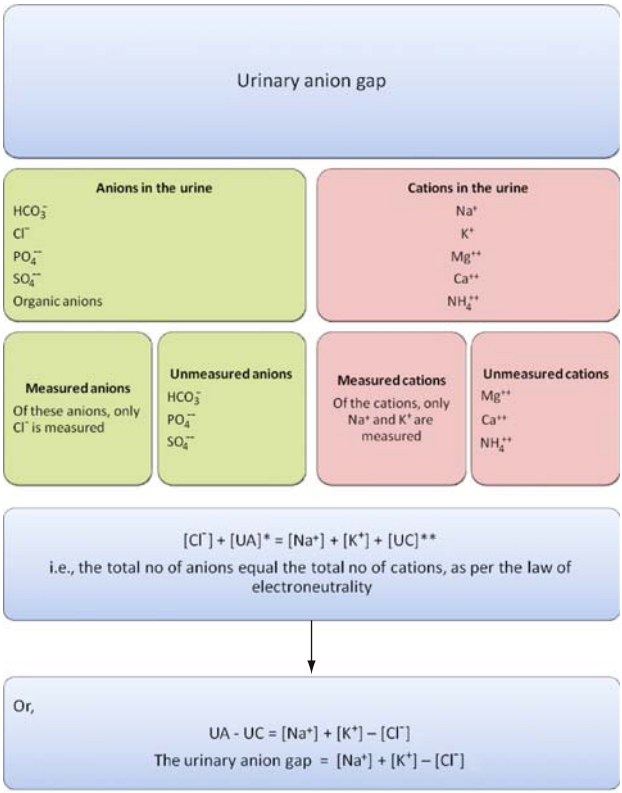


In a pure wide anion gap metabolic acidosis, the fall in the bicarbonate need not always exactly parallel the rise in the AG: although the bicarbonate is the principal extracellular buffer, it is not the only buffer; there are other buffer systems that are also participating in the buffering process.

Wren K. The delta (Δ)gap: an approach to mixed acid–base disorders. Ann Emerg Med 1990; 19:1310
Martin, L. All you Really Need to Know to Interpret Arterial Blood Gases. Lippincott, Williams and Wilkins, 1999

10.37 Urinary Anion Gap

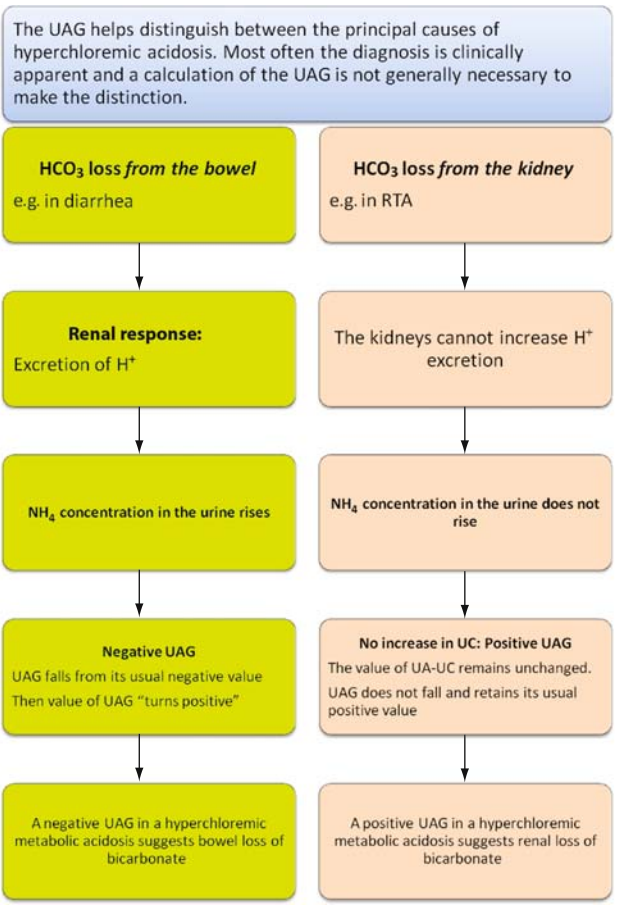
A useful tool in narrowing down the cause of a hyperchloremic acidosis is the urinary anion gap.



* Unmeasured Anions
**Unmeasured Cations

Battle, DC, Hizon, M, Cohen, E, Gutterman, C, Gupta, R. The use of the urinary anion gap in the diagnosis of hyperchloremic metabolic acidosis. New Eng J Med 1988; 318: 594–599

10.38 Utility of the Urinary Anion Gap



Battle, DC, Hizon, M, Cohen, E, Gutterman, C, Gupta, R. The use of the urinary anion gap in the diagnosis of hyperchloremic metabolic acidosis. New Eng J Med 1988; 18:594–599

10.39 Osmoles

Osmole:

The amount of substance that in an ideal solution, that would yield the number of particles (Avogadro's number) that would depress the freezing point of solvent by 1.86 K.

The usual circulating solutes in the body are:

Sodium (as chloride and bicarbonate salts)

Glucose

Urea

Under normal circumstances

(when no circulating solutes other than sodium bicarbonate and urea are present):

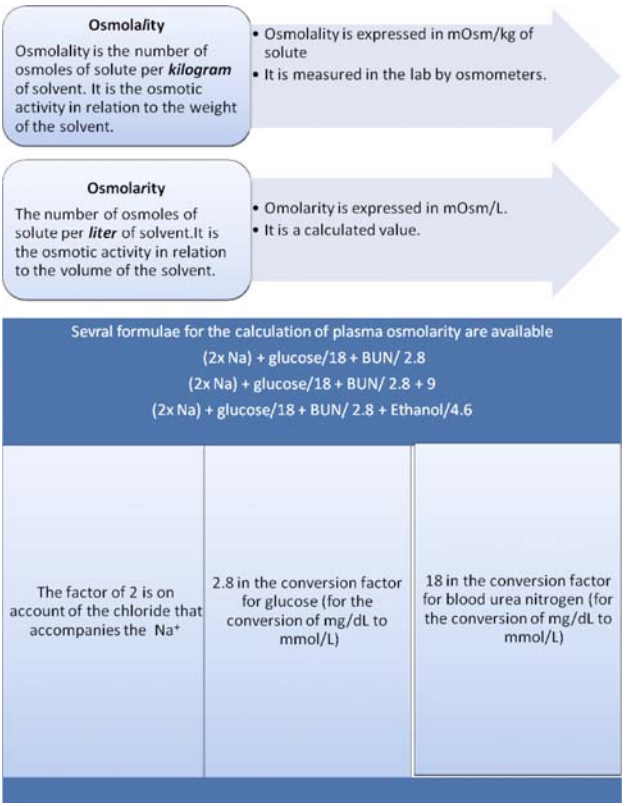
Using a formula that takes into account the concentration of the above solutes, *the calculated value of these solutes will equal their measured value.*

Under abnormal circumstances

(in the presence of other measurable solutes in the circulation):

The measured value of the solutes will exceed the calculated value, because the calculation does not take into account entities other than sodium, urea, and glucose

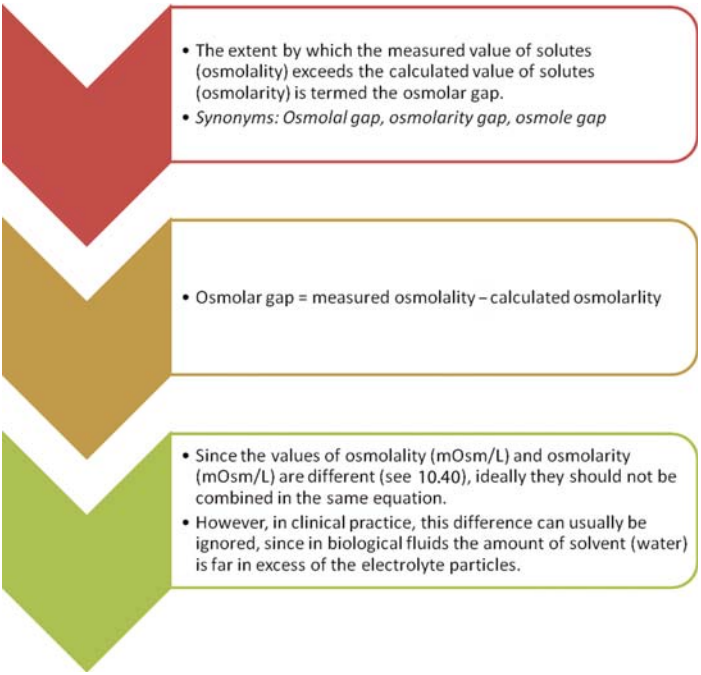
10.40 Osmolarity and Osmolality



Rose, BD. Clinical Physiology of Acid–Base and Electrolyte Disorders, 4th ed, McGraw-Hill, New York, 1994, 567–568

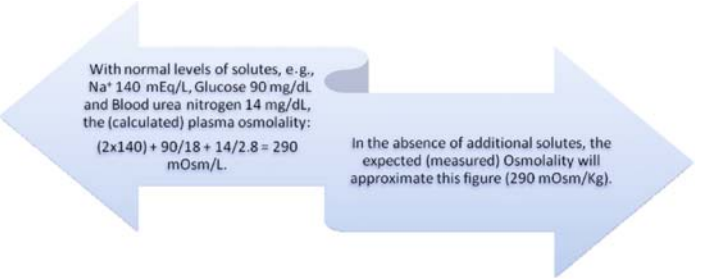
Warhol, RM, Eichenholz, A, Mulhausen, RO. Osmolality. Arch Intern Med 1965; 116:743

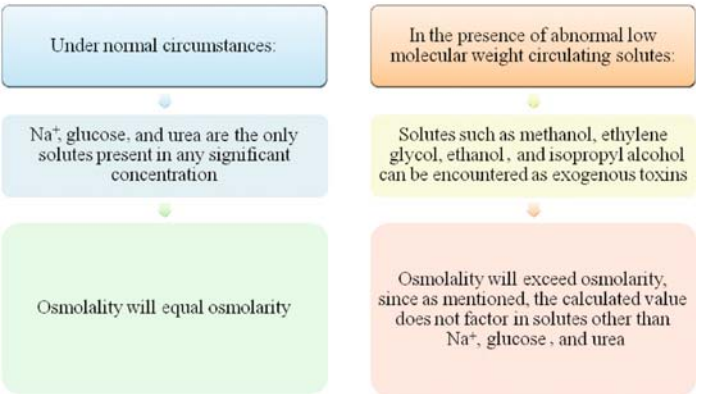
10.41 The Osmolar Gap



Gennari, FJ. Serum Osmolality. Uses and Limitations. N Engl J Med 1984; 301:102

10.42 Detection of Abnormal Solutes



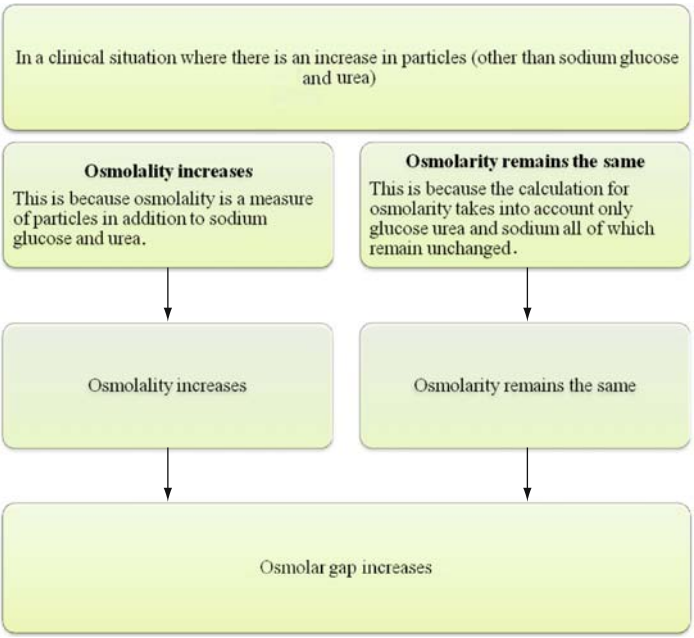


DiNubile, MJ. Serum osmolality (letter). N Engl J Med 1984; 310:1609

Walker, JA, Schwartzbard, A, Krauss, EA, et al. The missing gap: A pitfall in the diagnosis of alcohol intoxication by osmometry. Arch Intern Med 1986; 146:1843

Sweeney, TE, Beuchat, CA. Limitations of methods of osmometry: Measuring the osmolality of body fluids. Am J Physiol 1993; 264:R469

10.43 Factors influencing the Osmolar Gap



The main diagnostic value of osmolar gap lies in raising the possibility of poisoning by toxins as a cause of a wide-anion gap metabolic acidosis. It is important to remember that the osmolar gap is not infallible in its applications*.

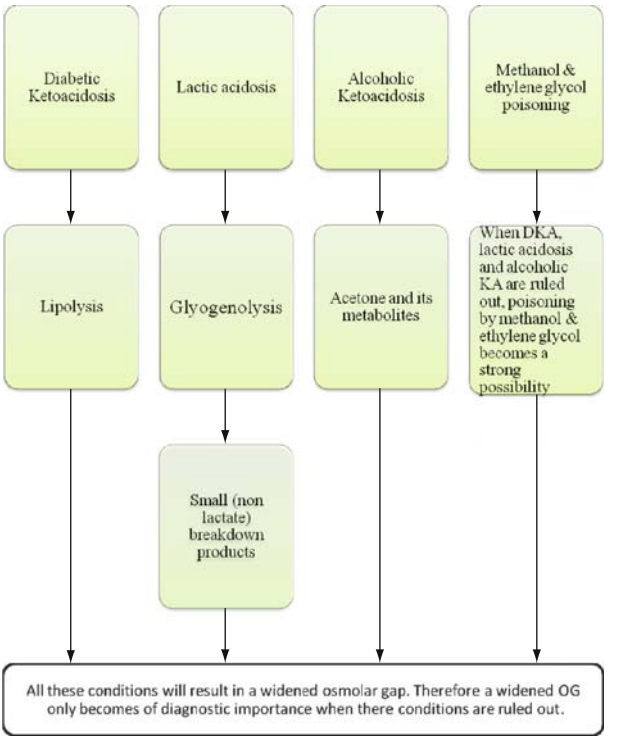
Walker, JA, Schwartzbard, A, Krauss, EA, et al. The missing gap: A pitfall in the diagnosis of alcohol intoxication by osmometry. Arch Intern Med 1986; 146:1843

*Sweeney, TE, Beuchat, CA. Limitations of methods of osmometry: Measuring the osmolality of body fluids. Am J Physiol 1993; 264:R469

Jacobsen D, et al. Anion and osmolal gaps in the diagnosis of methanol and ethylene glycol poisoning. Acta Med Scandinav 1982; 212:17

10.44 Conditions that can Create an Osmolar Gap

Although several conditions can widen the osmolar gap, the mechanism by which they do so remains uncertain. The probable mechanisms are given below:



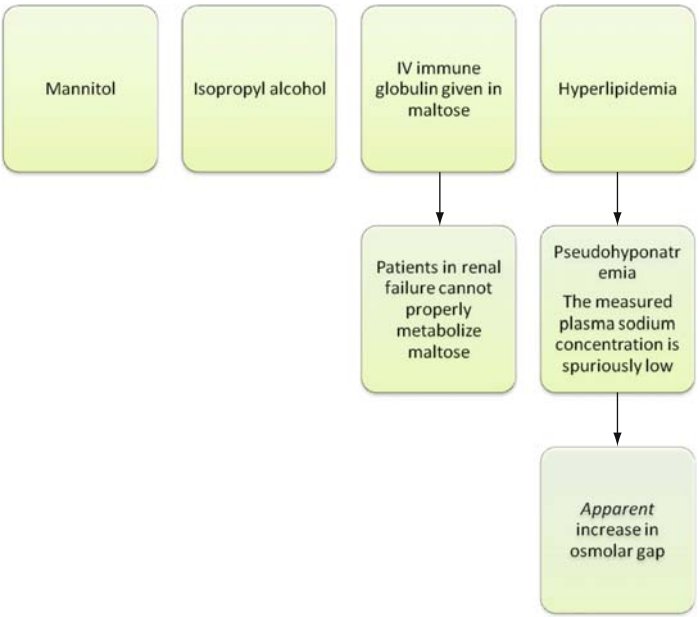
Sklar, AH, Linas, SL. The osmolal gap in renal failure. Ann Intern Med 1983; 98:481

Glasser, L, Sternglanz, PD, Combie, J, Robinson, A. Serum osmolality and its applicability to drug overdose. Am J Clin Pathol 1973; 60:695

Gabow, PA. Ethylene glycol intoxication. Am J Kidney Dis 1988; 11:277

Robinson, AG, Loeb, JN. Ethanol ingestion: Commonest cause of elevated plasma osmolality? N Engl J Med 1971; 284:1253

10.45 Less common Causes of a Widened Osmolar Gap



Aviram, A, Pfau, A, Czackes, JW, Ullman, TD. Hyperosmolality with hyponatremia caused by inappropriate administration of mannitol. Am J Med 1967; 42:648

Weinberg, LS. Pseudohyponatremia: A reappraisal. Am J Med 1989; 86:315

Chapter 11
Metabolic Alkalosis

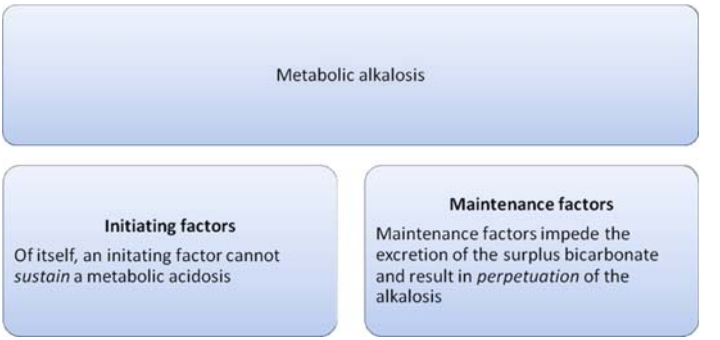
Contents

11

A. Hasan, *Handbook of Blood Gas/Acid–Base Interpretation*,
DOI 10.1007/978-1-84800-334-7_11,

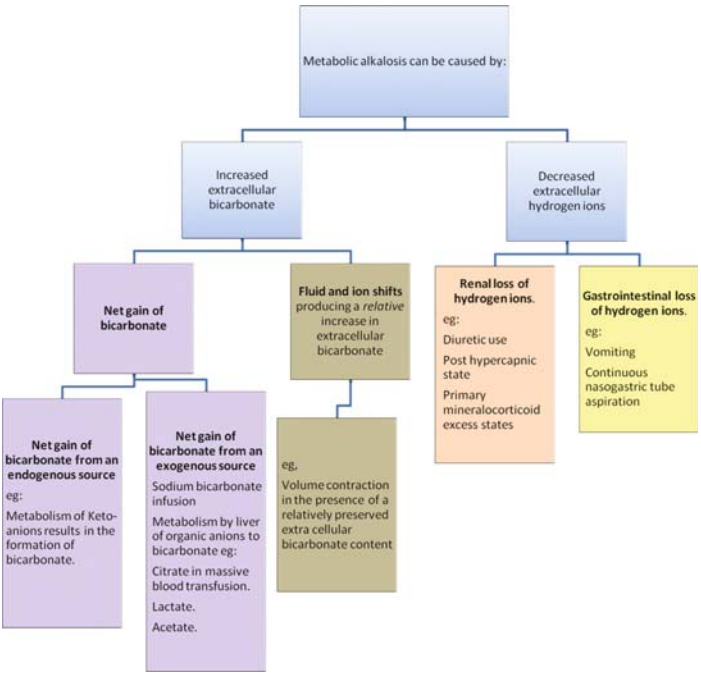
11.1 The Pathogenesis of Metabolic Alkalosis

The genesis of a metabolic alkalosis needs the presence of both initiating and maintenance factors.



Galla, JH. Metabolic alkalosis. J Am Soc Nephrol 2000; 11:369

11.2 Metabolic Alkalosis: Etiology



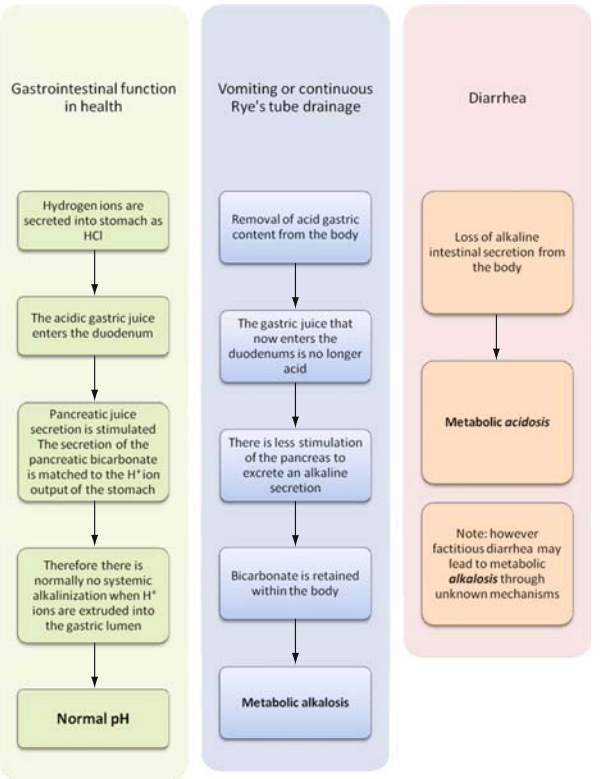
Galla, JH. Metabolic alkalosis. J Am Soc Nephrol 2000; 11:369

Palmer, BF, Alpern, RJ. Metabolic alkalosis. J Am Soc Nephrol 1997; 8:1462

Perez, GO, Oster, JR, Rogers, A. Acid–base disturbances in gastrointestinal disease. Dig Dis Sci 1987; 32:1033

Garella, S, Chang, BS, Kahn, SI. Dilution acidosis and contraction alkalosis: review of a concept. Kidney Int 1975; 8:279

11.3 Metabolic Alkalosis in Gastrointestinal Dysfunction

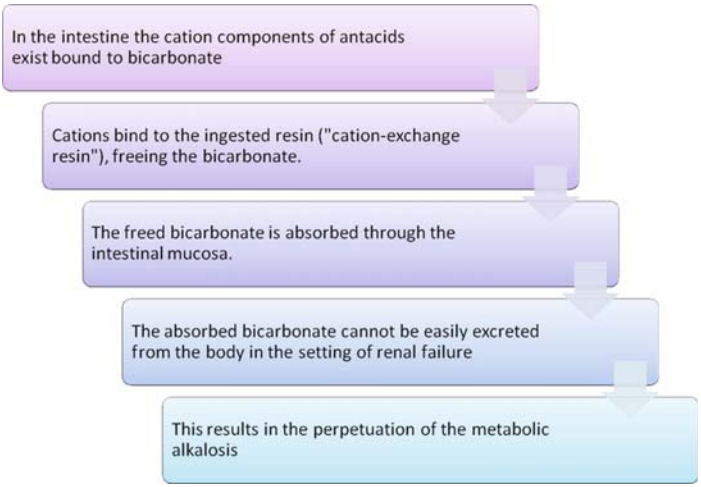


Kassirer, JP, Schwartz, WB. The response of normal man to selective depletion of hydrochloric acid. Factors in the genesis of persistent gastric alkalosis. Am J Med 1966; 40:10

Perez, GO, Oster, JR, Rogers, A. Acid-base disturbances in gastrointestinal disease. Dig Dis Sci 1987; 32:1033

11.4 Metabolic Alkalosis due to Cation Exchange Resins

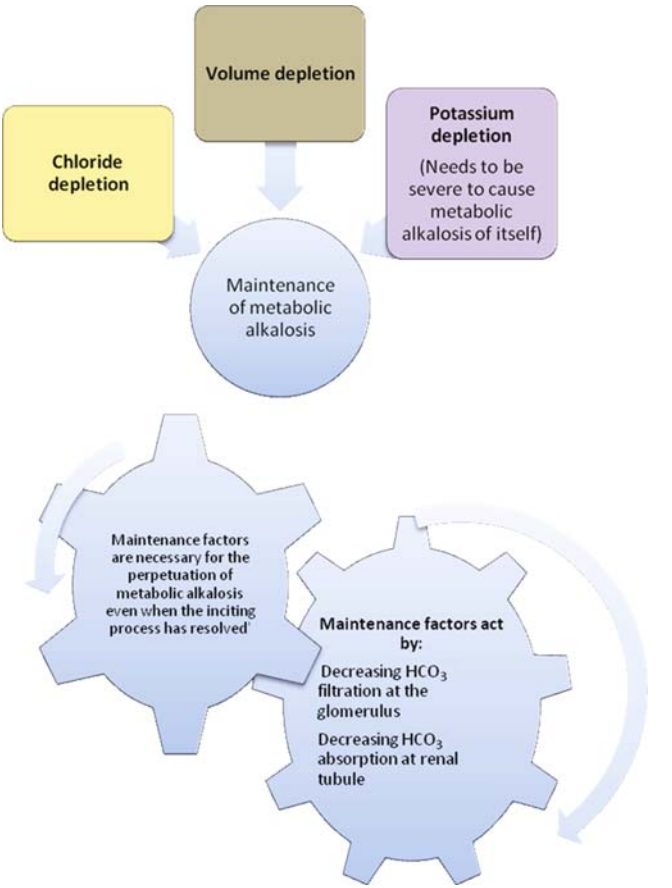
Cation exchange resins are used in the treatement of hyperkalemia.



Stemmer, CL, Oster, JR, Vaamonde, CA, et al. Effect of routine doses of antacid on renal acidification. Lancet 1986; 2:3

Madias, NE, Levey, AS. Metabolic alkalosis due to absorption of "non-absorbable" antacids. Am J Med 1983; 74:155

11.5 Metabolic Alkalosis: Maintenance Factors 1



11

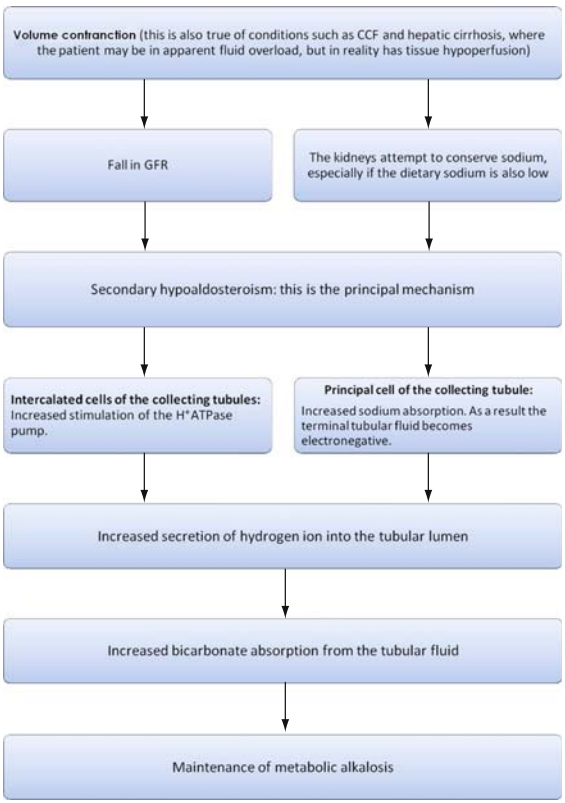
Sabatini, S, Kurtzman, NA. The maintenance of metabolic alkalosis: Factors which decrease bicarbonate excretion. Kidney Int 1984; 25:357

Berger, BE, Cogan, MG, Sebastian, A. Reduced glomerular filtration rate and enhanced bicarbonate reabsorption maintain metabolic alkalosis in humans. Kidney Int 1984; 26:205

11.6 Metabolic Alkalosis: Maintenance Factors 2

Bicarbonate absorption is increased by the following factors:

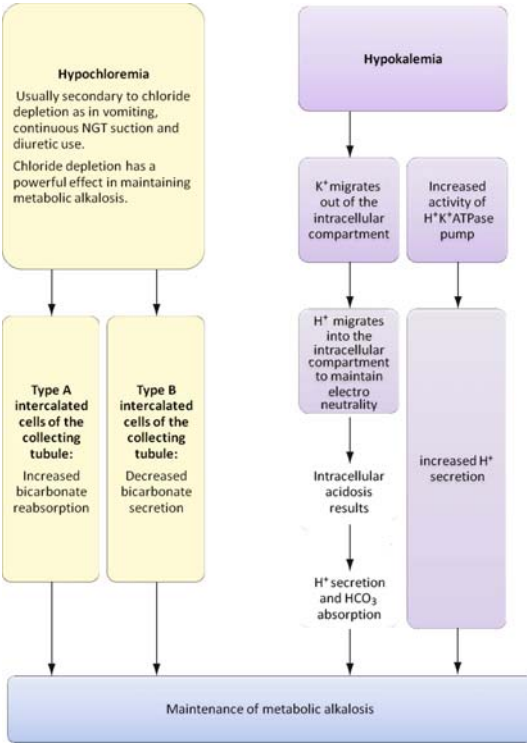
1. Volume contraction
2. Hypochloremia (this is the most common mechanism)
3. Hypokalemia
4. Low GFR



Sabatini, S, Kurtzman, NA. The maintenance of metabolic alkalosis: Factors which decrease bicarbonate excretion. Kidney Int 1984; 25:357

Berger, BE, Cogan, MG, Sebastian, A. Reduced glomerular filtration rate and enhanced bicarbonate reabsorption maintain metabolic alkalosis in humans. Kidney Int 1984; 26:205

11.7 Metabolic Alkalosis: Maintenance Factors 3

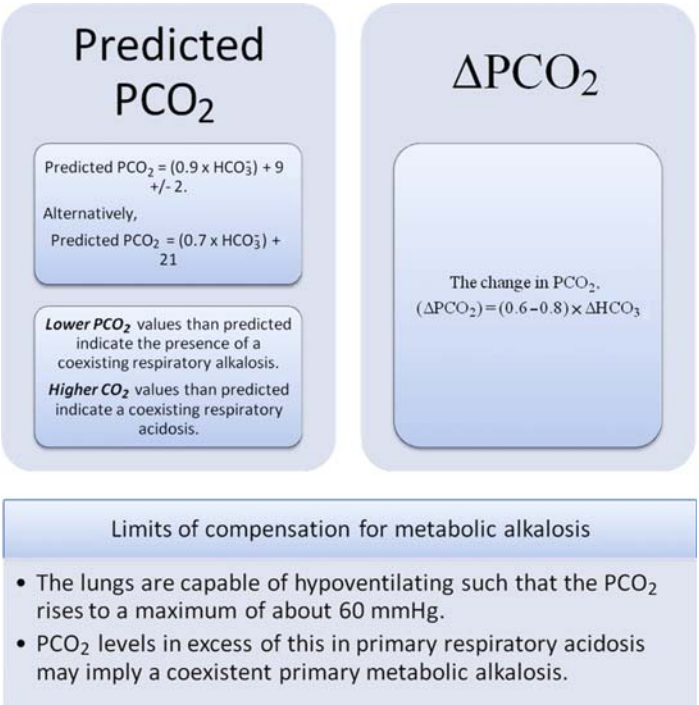


Galla, JH, Bonduris, DN, Luke, RG. Effects of chloride and extracellular fluid volume on bicarbonate reabsorption along the nephron in metabolic alkalosis in the rat. Reassessment of the classic hypothesis on the pathogenesis of metabolic alkalosis. J Clin Invest 1987; 80:41

Capasso, G, Jaeger, P, Giebisch, G, et al. Renal bicarbonate reabsorption in the rat. II. Distal tubule load dependence and effect of hypokalemia. J Clin Invest 1987; 80:409

Wingo, CS, Smulka, AJ. Function and structure of H-K-ATPase in the kidney. Am J Physiol 1995; 269:F1

11.8 Compensation for Metabolic Alkalosis

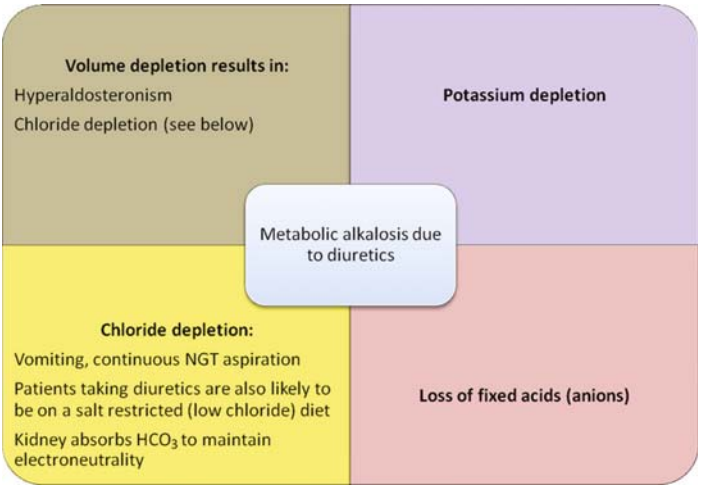


Smith RM. In: Bordow, RA, Ries, AL, Morris, TA. (Eds.) Manual of Clinical Problems in Pulmonary Medicine. Lippincott Williams and Wilkins, 6th ed, 2005

Miller, PD, Berns, AS. Acute metabolic alkalosis perpetuating hypercapnia: A role for acetazolamide in chronic obstructive pulmonary disease. JAMA 1977; 238:2400

11.9 Metabolic Alkalosis due to Diuretics

Diuretics can produce metabolic alkalosis through multiple mechanisms:



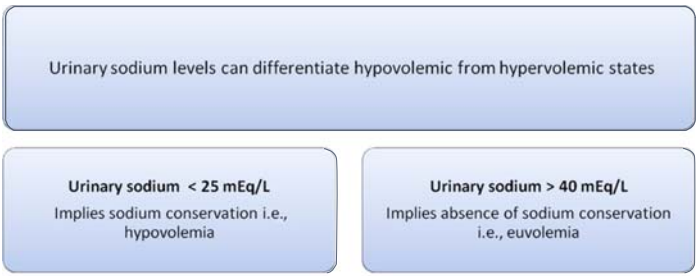
Garella, S, Chazan, JA, Cohen, JJ. Saline-resistant metabolic alkalosis or "chloride-wasting nephropathy". Ann Intern Med 1970; 73:31

Hropot, M, Fowler, N, Karlmark, B, Giebisch, G. Tubular action of diuretics: Distal effects on electrolyte transport and acidification. Kidney Int 1985; 28:477

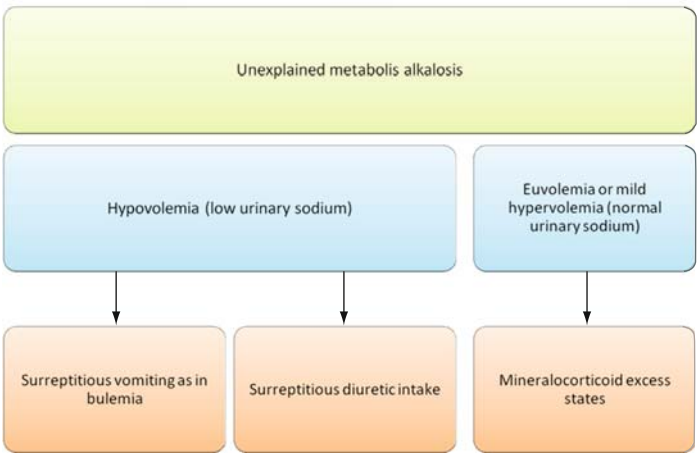
Cannon, PJ, Heinemann, HO, Albert, MS, et al. "Contraction" alkalosis after diuresis of edematous patients with ethacrynic acid. Ann Intern Med 1965; 62:979

11.10 Urinary Sodium

Most of the time, the etiology of metabolic alkalosis is self-evident from the history. In more obscure cases, the analysis of urinary electrolytes may provide a clue.



The urinary sodium may point to the broad etiology of the metabolic alkalosis

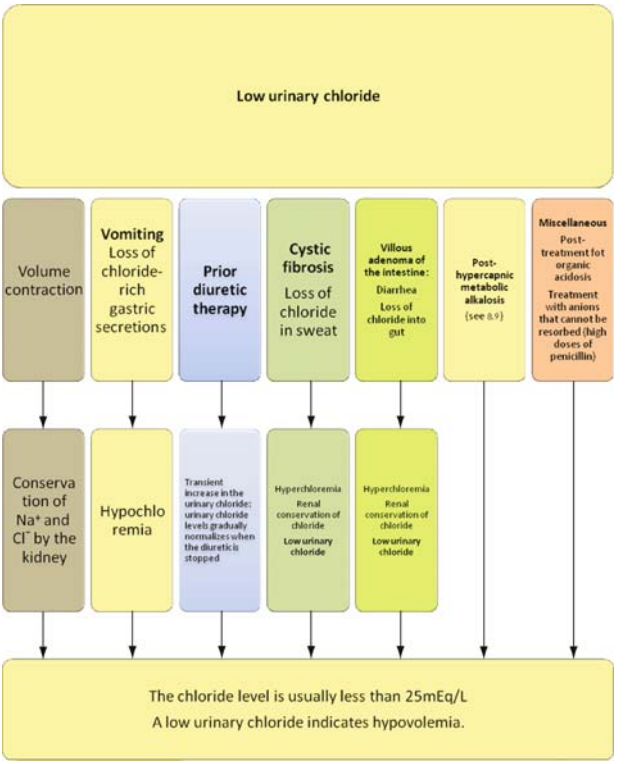


Rose, BD. Clinical Physiology of Acid–Base and Electrolyte Disorders, 4th ed, McGraw-Hill, New York, 1994, pp. 522–530

Sherman, RA, Eisinger, RP. The use (and misuse) of urinary sodium and chloride measurements. JAMA 1982; 247:3121

11.11 Urinary Chloride

Sometimes, for several reasons, urinary *sodium* may prove to be unreliable as an indicator of the subject's volume status especially when there is significant bicarbonaturia (pH > 7.0). Urinary *chloride* estimation may more accurately reflect the patient's volume status.

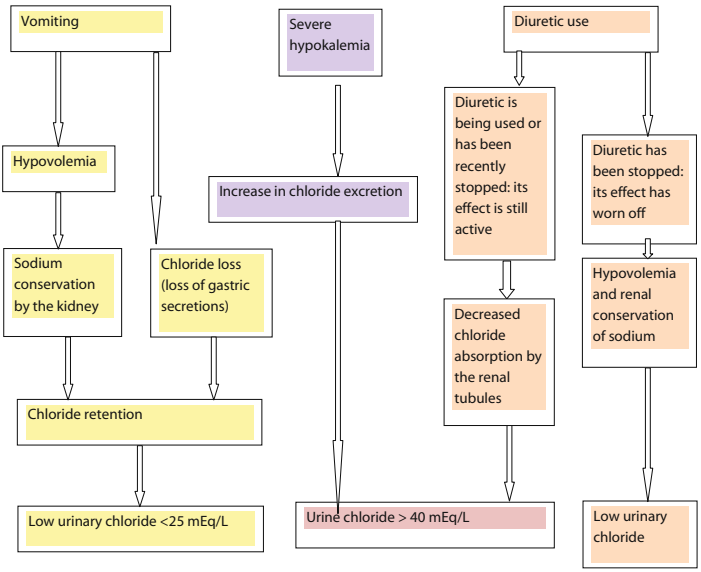


11

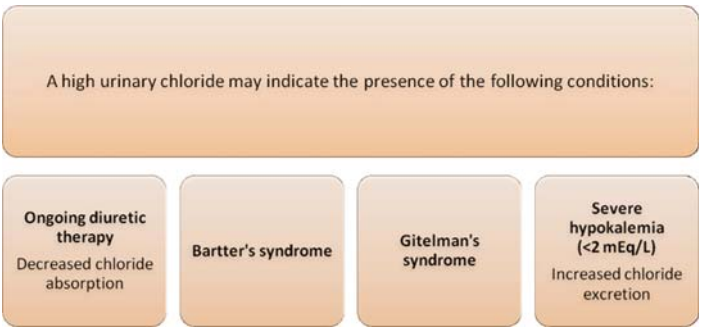
Sherman, RA, Eisinger, RP. The use (and misuse) of urinary sodium and chloride measurements. JAMA 1982; 247:3121

Garella, S, Chazan, JA, Cohen, JJ. Saline-resistant metabolic alkalosis or "chloride-wasting nephropathy". Ann Intern Med 1970; 73:31

11.12 The Diagnostic Utility of Urinary Chloride



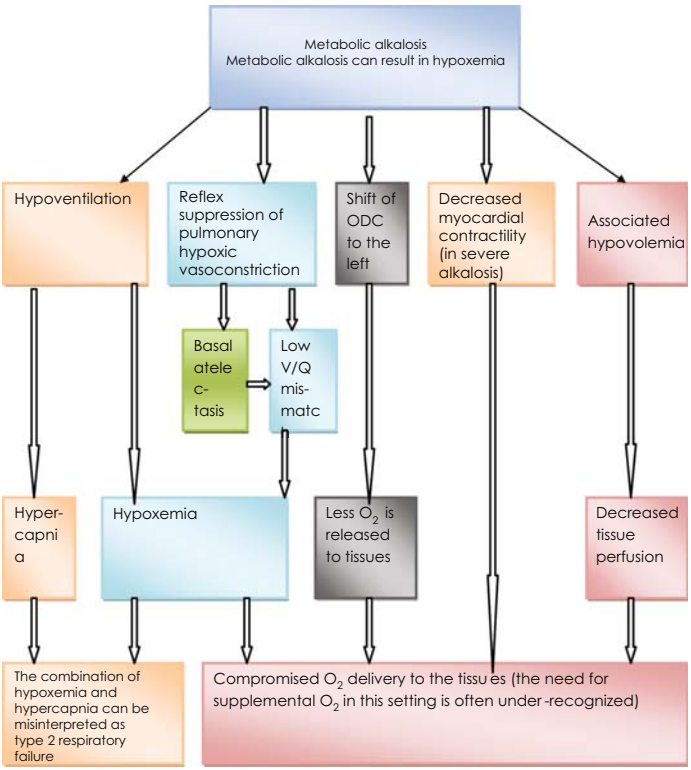
11.13 High Urinary Chloride



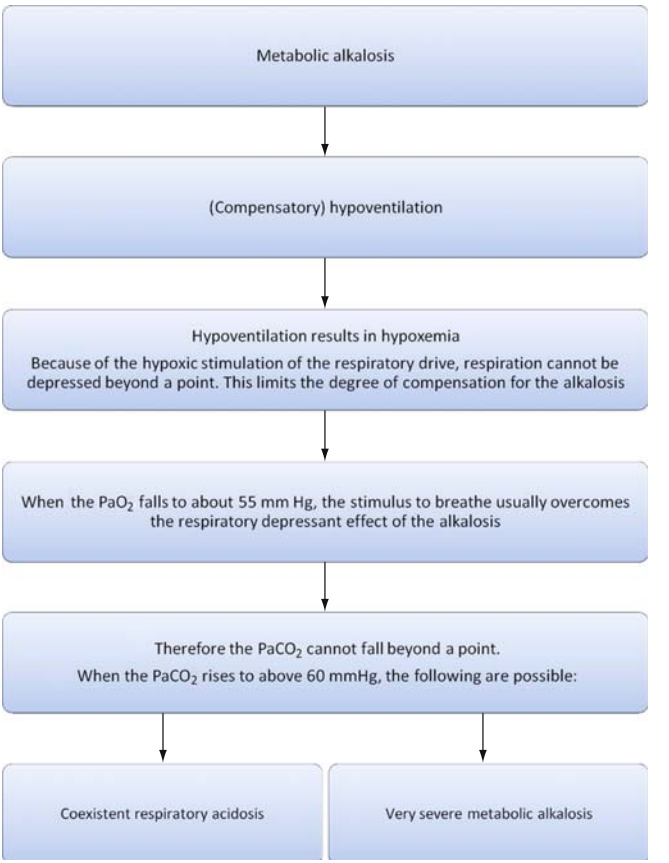
Rose, BD. Clinical Physiology of Acid–Base and Electrolyte Disorders, 4th ed, McGraw-Hill, New York, 1994, pp. 527–530

Sherman, RA, Eisinger, RP. The use (and misuse) of urinary sodium and chloride measurements. JAMA 1982; 247:3121

11.14 Metabolic Alkalosis and Hypoxemia



11.15 Metabolic Alkalosis and the Respiratory Drive



Javaheri, S. Compensatory hypoventilation in metabolic alkalosis. Chest 1982; 81:296

Javaheri, S, Kazemi, H. Metaboloc alkalosis and hypoventilation in humans. Am Rev Respir Dis 1987; 136:1011

Pierce, NF, Fedson, DS, Brigham, KL, et al. The ventilatory response to acute acid–base deficit in humans. Ann Intern Med 1970; 72:633

Chapter 12
The Analysis of Blood Gases & Factors Modifying the Accuracy of ABG Results

Contents

12

A. Hasan, *Handbook of Blood Gas/Acid-Base Interpretation*,
DOI 10.1007/978-1-84800-334-7_12,

12.1 Step One: History and Physical Examination

As in all other aspects of clinical medicine, the importance of the history and physical examination cannot be overemphasized; any interpretation of blood gases must be made in the appropriate clinical context. However for the purpose of brevity, clinical information has been truncated in the case histories; instead, an attempt at clinical correlation has been made at the end of each worked example.

Clinical conditions associated with specific acid–base disorders:

Vomiting	Metabolic alkalosis
Diarrhea	Metabolic alkalosis Metabolic acidosis (normal anion gap)
Severe diarrhea	Metabolic acidosis
Diuretic therapy	Metabolic alkalosis
Sepsis	Respiratory alkalosis Metabolic acidosis
Hypotension, low cardiac output states, severe anemia.	Metabolic (lactic) acidosis
Cirrhosis	Respiratory alkalosis
Renal failure	Metabolic acidosis
Diabetic ketoacidosis	Metabolic acidosis (wide anion gap) at presentation. A normal anion gap metabolic acidosis often develops during therapy.
Severe COPD; see also conditions listed under 'causes of hypoventilation' (00.00)	Respiratory acidosis

Morganroth, ML. An analytic approach to diagnosing acid–base disorders. J Crit Ill 1990; 5(2):138–150

Morganroth, ML. Six steps to acid–base analysis: clinical applications. J Crit Ill 1990; 5(5): 460–469

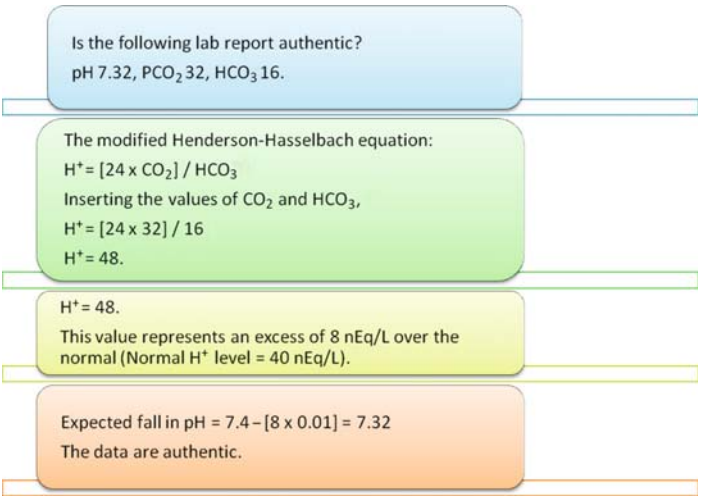
Narins, RG. Simple and mixed acid–base disorders: a practical approach. Medicine 1980; 59:161–187

(continued)

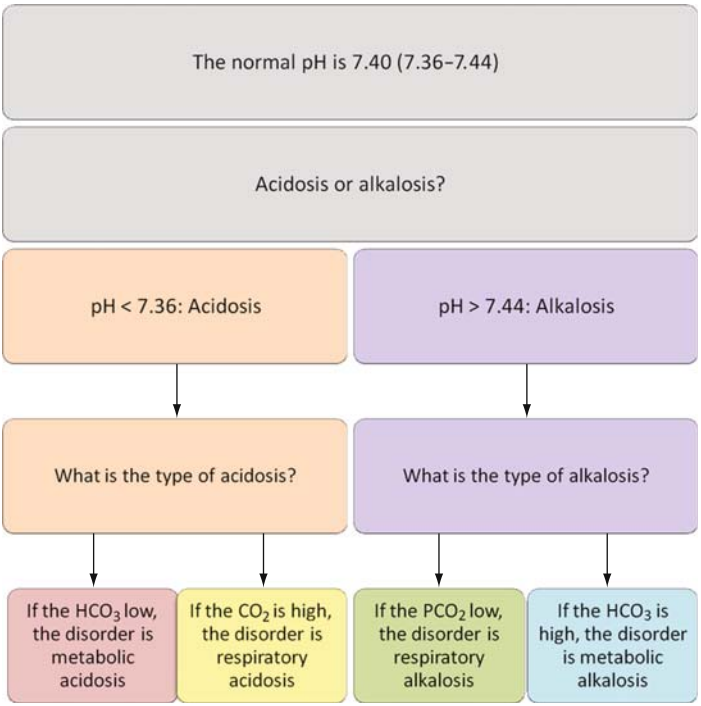
Pregnancy	Respiratory alkalosis
Hypoxemia	Respiratory alkalosis or acidosis depending on whether there is type 1 or type 2 respiratory failure respectively. Metabolic (lactic) acidosis if hypoxemia severe.
Pneumonia (reflex hyperventilation)	Respiratory alkalosis
ALI/ARDS (reflex hyperventilation)	Respiratory alkalosis
Asthma exacerbation	Respiratory alkalosis (respiratory acidosis when respiratory muscle fatigue occurs)
Pulmonary thromboembolism	Respiratory alkalosis
Seizures	Metabolic acidosis (lactic acidosis)
Cyanide, CO poisoning	Metabolic acidosis (lactic acidosis due to histotoxic hypoxia)
Biguanide, INH therapy	Metabolic acidosis (lactic acidosis)
Antibiotic therapy	Metabolic acidosis (D-lactic acidosis)
Renal tubular acidosis	Metabolic acidosis (normal anion gap)

12.2 Step Two: Authentication of Data

Kassirer and Bleich's rule and the Henderson–Hasselbach equation (see pH and H^+ equivalence) can be used to ascertain if the lab values obtained are reliable. A pH of 7.40 corresponds to a H^+ ion concentration of 40 nEq/L. Using Kassirer and Bleich's rule, change in pH by every 0.01 unit represents a change in H^+ ion concentration by 1 nEq/L.

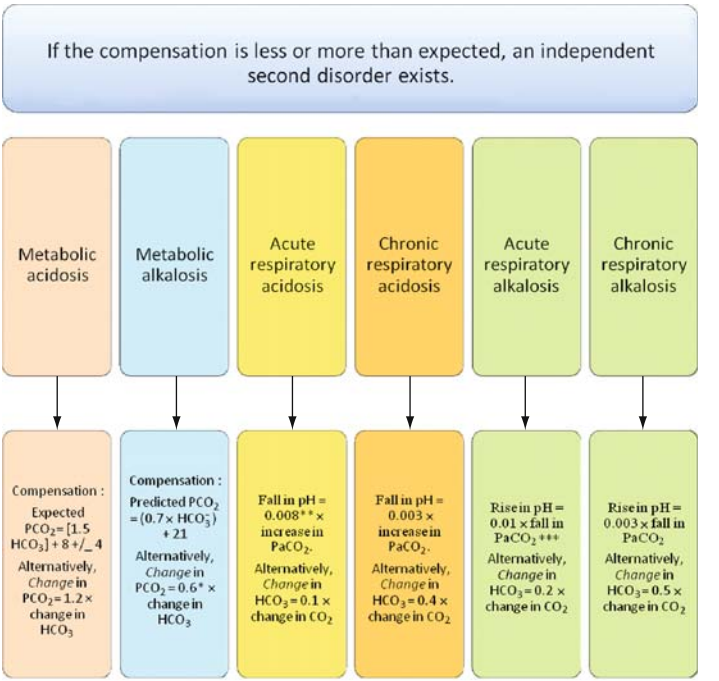


12.3 Step Three: Characterization of the Primary Acid–Base Disturbance



12.4 Step Four: Calculation of the Expected Compensation

The compensation for respiratory disorders is by renal processes and vice versa. It is worth re-emphasising that interpretation of acid–base disorders should always be made in the clinical context.

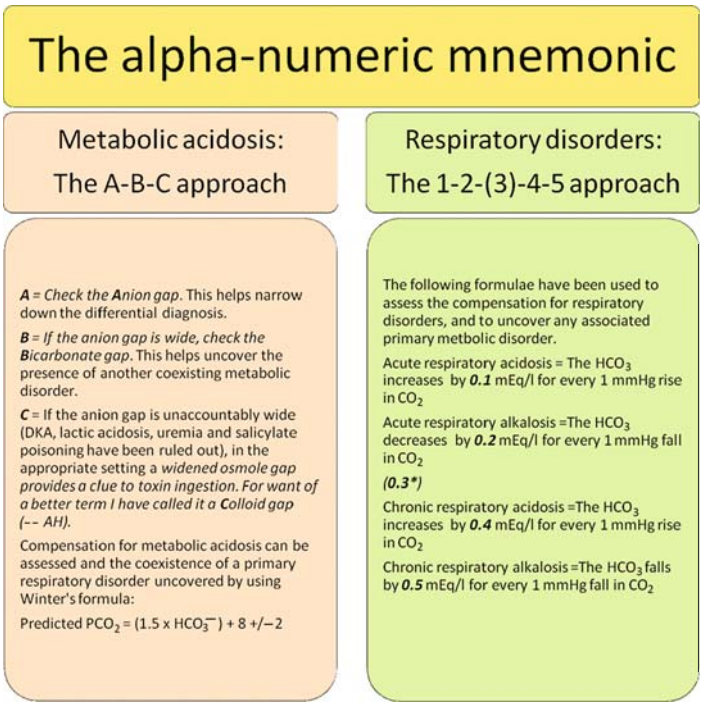


*0.6 to 0.8

**0.008 is virtually 0.01

***This relationship holds good for a $PaCO_2$ between 40 and 80 mmHg

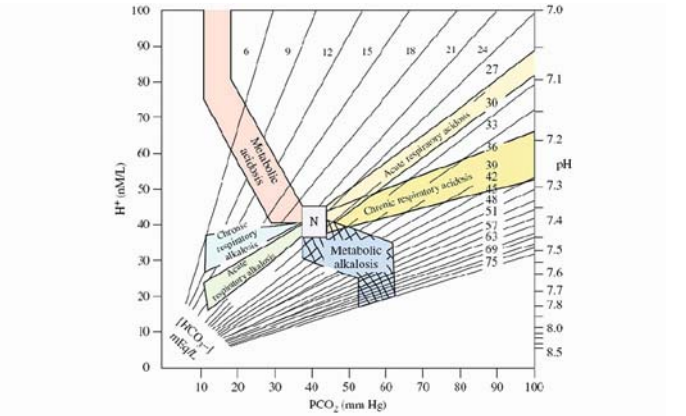
12.5 Step Four: The Alpha-Numeric Mnemonic



*The "0.3" in the mnemonic, for me, doesn't serve any obvious purpose—unless you can find one for it—(AH)!

12.6 Acid-Base Maps

Acid-base maps offer an alternative (and quick!) way of interpreting compensatory responses to simple acid-base disorders. They are also useful in confirming that the "compensatory" changes are physiologically possible. It is not possible to diagnose "triple disorders" (two metabolic disturbances with one of the respiratory disorders) by acid base mapping.



On the ordinate, the blood H± concentration (in nanomoles/L) is given on the left; the pH is given on the right. On the abscissa is represented the PCO_2 (in millimetres of mercury).
The diagonal lines running across the map are the isopleths for blood HCO_3 concentration (in mEq/L).

Within the box in the centre of the map falls the range of normal values. Six bands diverge from this box, each representing the 95% confidence limits for a simple acid-base disorder.

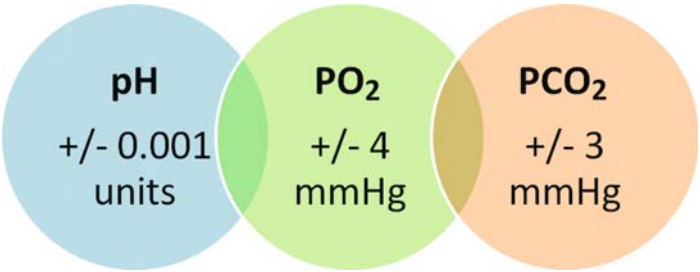
When a given patient's values fall upon any such band, a simple acid-base disorder corresponding to that band may be presumed: it is however not mandatory that a simple acid base disorder exists in such a patient.

When the values fall outside any of the bands a mixed acid-base disturbance is very likely.

Golberg, M, Green, SB, Moss, ML, et al. Computer-based instruction and diagnosis of acid-base disorders: a systemtic approach. JAMA

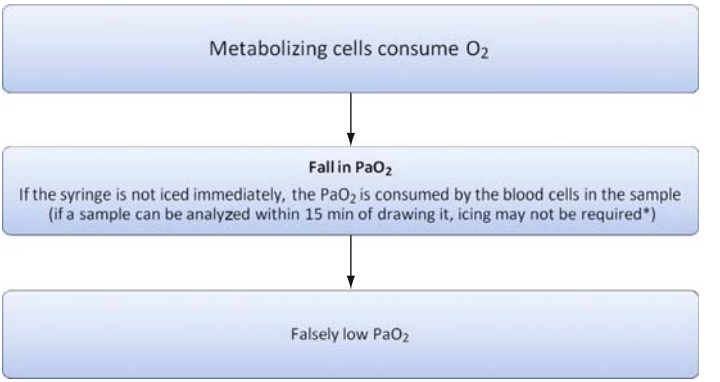
12.7 Accuracy of Blood Gas Values

With improvements in technology, the confidence limits for all values are very narrow.



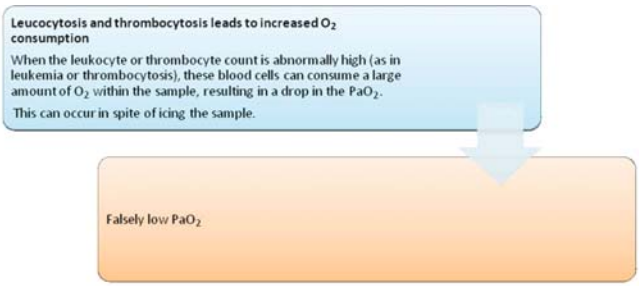
Glauser, FL, Morris, JF. Accuracy of routine arterial puncture for the determination of oxygen and carbon dioxide tensions. Am Rev Respir Dis 1972; 106:776

12.8 The Effect of Metabolizing Blood Cells within the ABG Sample

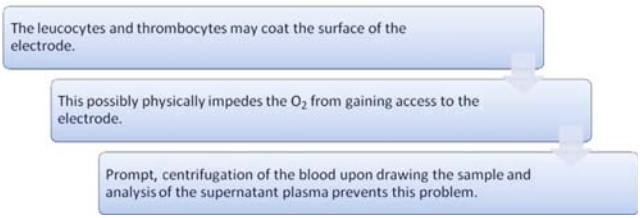


*Hansen JE. Arterial blood gases. In: Mahler, DA (ed). Pulmonary function testing. Clin Chest Med 1989; 5:227–237

12.9 Leucocyte Larceny



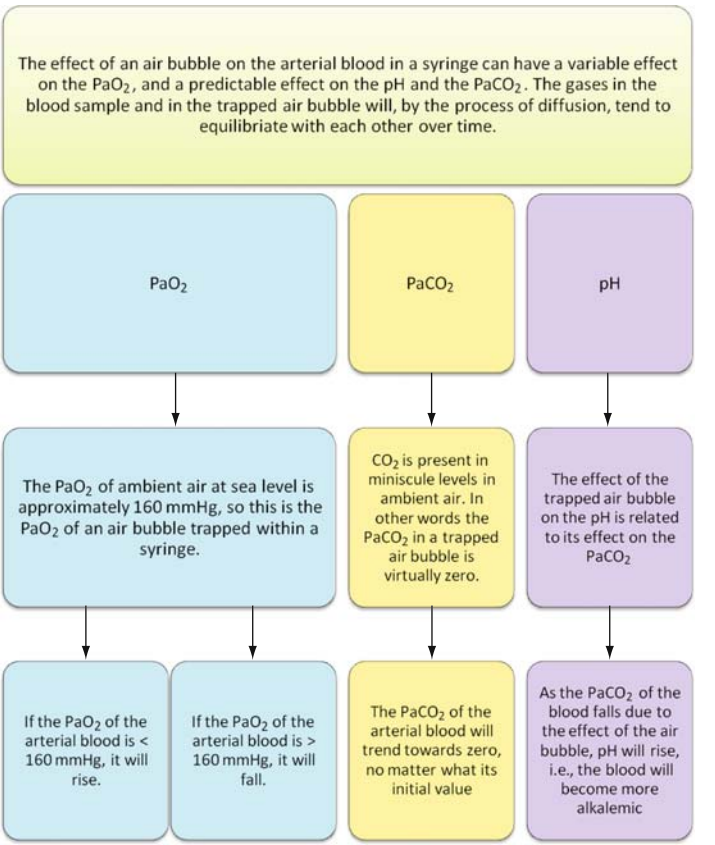
Because the pseudohypoxemia often persists despite prompt icing and analysis of the sample, another mechanism may be operative.



Hess, CE, Nichols, AS, Hunt, WB, et al. Pseudohypoxemia secondary to leukemia and thrombocytosis. N Engl J Med 1979; 301:361–363

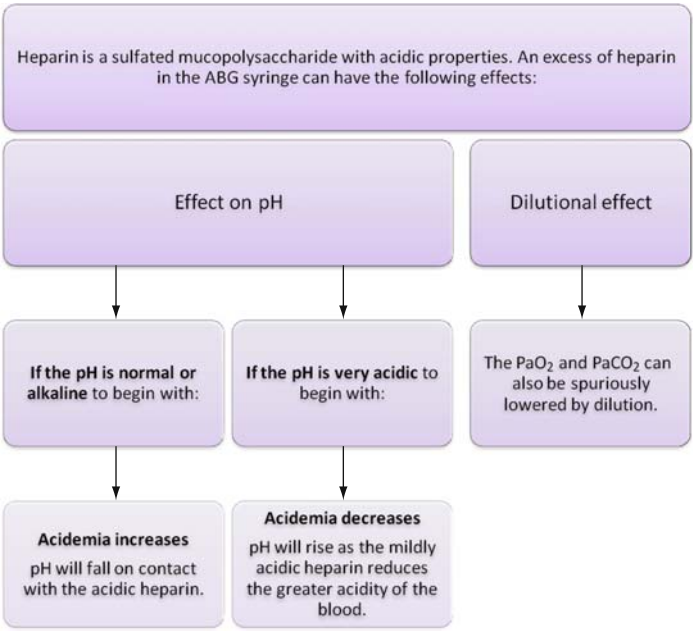
Charan, NB, Marks, M, Carvalho, P. Use of plasma for arterial blood gas analysis in leukemia. Chest 1994; 105:954–955

12.10 The Effect of an Air Bubble in the Syringe

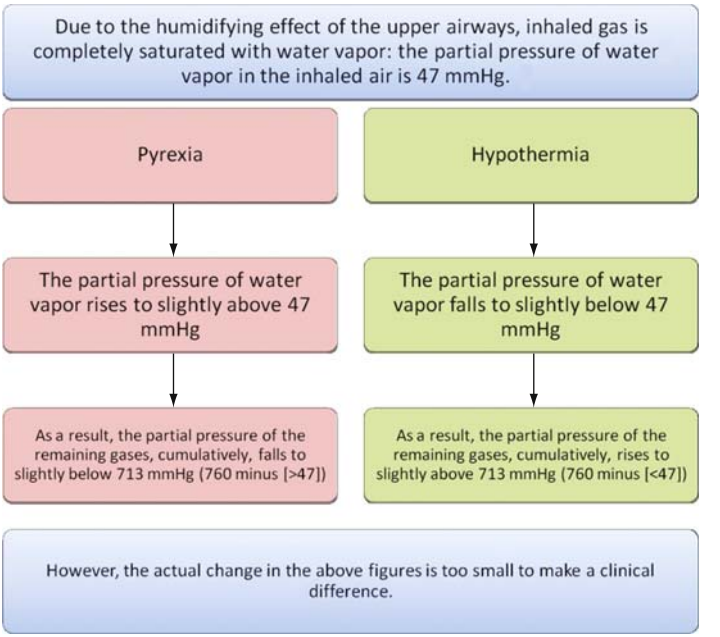


Mueller, RG, Lang, GE, Beam, JM. Bubbles in samples for blood gas determinations: A potential source of error. Am J Clin Pathol 1976; 65:242

12.11 Effect of Over-heparization of the Syringe



12.12 The Effect of Temperature on the Inhaled Gas Mixture

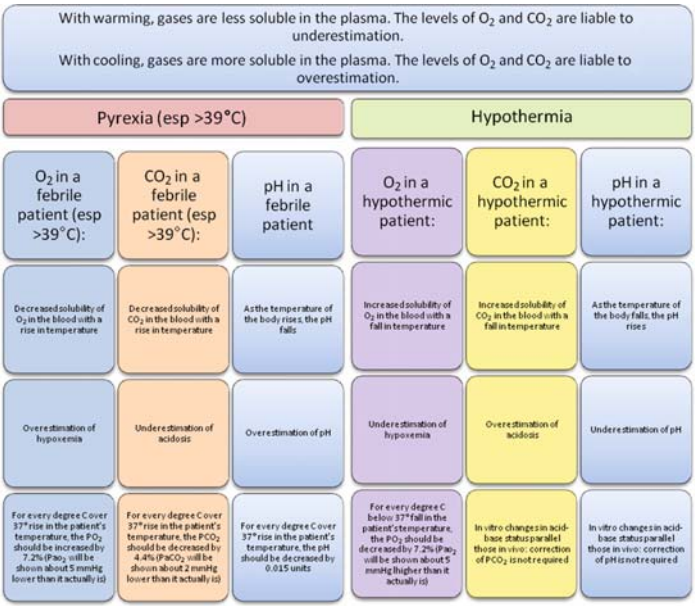


Shapiro, BA. Temperature correction of blood gas values. Respir Care Clin N Am 1995; 1:69

Bacher, A. Effects of body temperature on blood gases. Intensive Care Med 2005; 31:24

12.13 Effect of Temperature on Blood Gases

In clinical practice, the contribution of temperature to the measurement of blood gases is not considered important*. There is usually little change in the SpO_2 and CaO_2 with a change in temperature***



*Hansen, JE, Sue, DY. Should blood gas measurements be corrected for the patient's temperature? N Engl J Med 1980; 303:341

Rahn, H, Reeves, RB, Howell, BJ. Hydrogen ion regulation, temperature, and evolution. Am Rev Respir Dis 1975; 112:165–172

***Severinghaus, JW. Oxyhemoglobin dissociation curve correction for temperature and pH variation in human blood. J Appl Physiol 1958; 12:485–486

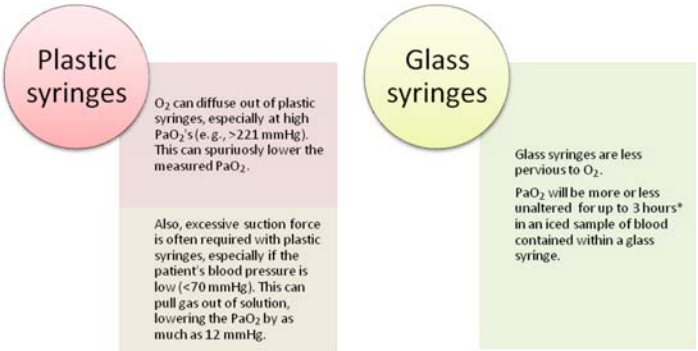
Shapiro, BA. Temperature correction of blood gas values. Respir Care Clin N Am 1995; 1:69

Bacher, A. Effects of body temperature on blood gases. Intensive Care Med 2005; 31:24

Curley, FJ, Irwin, RS. Disorders of temperature control: Part I. Hyperthermia. J Int Care Med 1986; 1:5

Curley, FJ, Irwin, RS. Disorders of temperature control: Part III. Hyporthermia. J Int Care Med 1986; 1:270

12.14 Plastic and Glass Syringes



Ansel, GM, Douce, FH. Effect of needle syringe material and needle size on the minimum plunger-displacement pressure of arterial blood gas syringes. Respir Care 1982; 27:127

Winkler, JB, Huntington, CG, Wells, DE, Befeler, B. Influence of syringe material on arterial blood gas determinations. Chest 1974; 66:518

*Canham, EM. Interpretation of arterial blood gases. In: Parsons, PE, Weiner-Kronish, JP, (Eds). Critical care secrets, 3rd ed, Philadelphia, Hanley and Belfus, Inc, 2003; 21–24

Chapter 13
Case Examples

Contents

A. Hasan, *Handbook of Blood Gas/Acid-Base Interpretation*,
DOI 10.1007/978-1-84800-334-7_13,

The first critical step in the evaluation of a blood gas sample is the bringing fourth of a detailed history. The importance of a reliable history cannot be overemphasized. From the history, a shortlist of the differential diagnoses is constructed, and the ABG sample is interpreted against this background.

However, in the examples to follow, the history has been deliberately abbreviated, and a clinical correiation has been attempted at the end of the analysis. In these examples, the algorithmic approach presented throughout this volume has been adhered to. Acid base maps (12.6) are presented on the facing page to enable familiarity with both methods.

Patient A: A 34 year old man with metabolic encephalopathy

A 34-year-old man presents to ER and is worked up for a possible metabolic encephalopathy.
His blood gases are as follows:

pH: 7.31, $PaCO_2$: 26mmHg, PaO_2: 94mmHg,
Na^+: 138mEq/L, k^+: 4.0 mEq/L, Cl^-: 103mEq/L,
HCO_3: 18mEq/L

The object of this example is the importance of verification of data. Regardless of the history, the ABG sample must be analyzed for internal consistency; if there is lack of internal consistency, the authenticity of the reported values becomes questionable.

We know that:

$[H^+] = 24 \times PaCO_2/HCO_3^-$

The equivalent values for $[H^+]$ and pH are as follows (see 00.00):

pH	$[H^+]$
7.6	25
7.5	32
7.4	40
7.3	50
7.2	63
7.1	79
7.0	100

$[H^+] = 24 \times 26/18$

$[H^+] = 34.7$

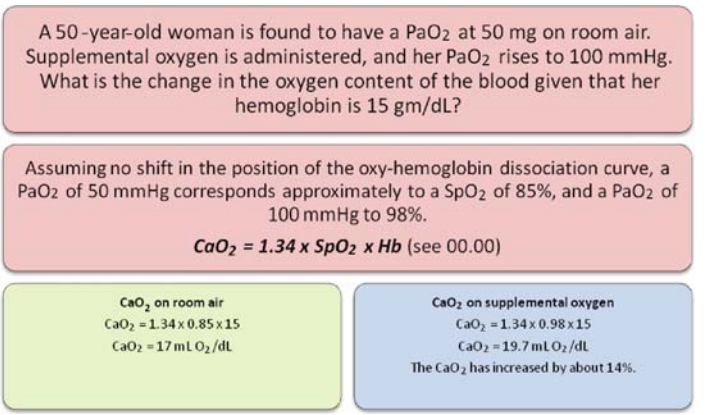
However the pH is about 7.3, and for that pH the H^+ should be 50. The data are inconsistent.

Patient B: A 40 year old breathless man

A 40-year-old breathless man is found to have a PaO_2 at 65 mg on room air. Supplemental oxygen is administered by nasal prongs, and a blood gas sample half an hour later reveals a PaO_2 of 100 mmHg. How much increase in the oxygen content of the blood has been produced by increasing the FIO_2?

Answer: virtually none. At a PaO_2 of 65 mm Hg, the SpO_2 approaches 100%. By increasing the FIO_2, the hemoglobin, fully saturated as it is, is not capable of being saturated any further. The CaO_2 therefore remains unaltered on this account. The increase in FIO_2 does result in a small increment in the dissolved O_2, but since the amount of dissolved O_2 is relatively tiny, the enhancement in the CaO_2 is negligible.

Patient C: A 50 year old woman with hypoxemia



The effect that a fall in Hb has on the CaO_2 can be profound. Looking at the equation:

$$CaO_2 = 1.34 \times SpO_2 \times Hb$$

It can be appreciated that a fall in the Hb produces a fall in CaO_2 of the same order of magnitude. For example if the Hb were to drop to half of its original value (to 7.5gm/dL from 15 gm/dL), the drop in CaO_2 would also be by 50%.

Patient D: A 20 year old breathless woman

A 20-year-old woman with no previous medical problems was brought to the hospital complaining of breathlessness. She had a PaO_2 of 118 mmHg and a $PaCO_2$ of 20 mmHg on room air.

A rule of the thumb is that on room air, the sum of the PaO_2 and the $PaCO_2$ should add up to about 140, which it does in this case (118 + 20 = 138). This makes an underlying mechanism of hypoxemia unlikely.

A more sensitive test for a defect in oxygenation is the A-aDO_2, which is of course the partial pressure of O_2 in the alveolus (PAO_2) minus the partial pressure of oxygen in the arterial blood (PaO_2).

$$A\text{-}aDO_2 = PAO_2 - PaO_2.$$

$$\boldsymbol{PAO_2 = FIO_2 (Pb\text{-}Pw) - PaCO_2/R}$$

Assuming a barometric pressure of 760 mmHg (sea level), and a respiratory quotient of 0.8:

$PAO2=[0.21(760-47)]-(20/0.8)$

$PAO_2=149-25$

$PAO_2=124$

$A\text{-}aDO_2 = PAO_2 - PaO_2 = 124-118$

$A\text{-}aDO_2 = 6$ (normal <14 on room air)

The A-aDO_2 is normal.

The patient gave a history of emotional turmoil. Subsequent evaluation did not turn up pulmonary thromboembolism or any other problem.

Patient E: A 35 year old smoker in the bronchoscopy suite

Diagnostic bronchoscopy for a non-resolving pneumonia has just been completed in a 35-year-old non-smoker, when his SpO_2 is seen to fall to 88% in spite of administration of 2 liters of oxygen per minute by nasal prongs. The patient had tolerated the bronchoscopy with a satisfactory SpO_2 on the same (liter-flow) of O_2. An ABG reveals a PaO2 of 110 mmHg

The PaO_2 seems slightly low for the FIO_2 being given. 2 litres per minute on nasal prongs are the equivalent of an FIO_2 of about 0.28. This would result in a PaO_2 of about 140 mmHg in a normal individual (28 x 5). In the clinical context, a mild V/Q mismatch post-bronchoscopy, and possibly the pneumonia itself, could account for a PaO_2 which is slightly lower than expected from the calculation.

A PaO_2 of 110 mmHg, however, certainly does not agree with a SpO_2 of 88%.

The clinical setting is compatible with local-anesthetic induced methemoglobinemia, and CO-oximetry should be used to confirm the diagnosis.

Patient F: A 30 year old man with acute coronary syndrome

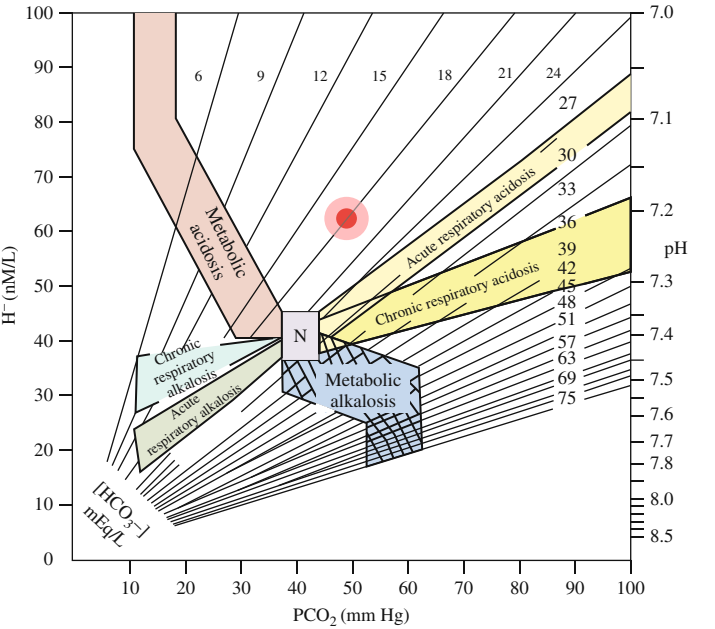
The SpO_2 of a 60-year-old man recovering in the ICU from an acute coronary syndrome, has fallen to 86% on supplemental oxygen. The chest X-ray shows possible mild interstitial pulmonary edema.

PH: 7.43, HCO_3: 24mEq/L, $PaCO_2$: 37mmHg, $PaO_2$126 mmHg on 35% oxygen by ventimask.

The PaO_2 seems slightly low for the FIO_2 being given, but can be accounted for by the recumbency and possible mild cardiogenic pulmonary edema. What is interesting is the disparity between the PaO_2 and SpO_2. The ABG shows no obvious acid–base disorder.

The clinical setting is that of an acute coronary artery syndrome, and it is safe to assume that the patient is on nitrates; the latter are commonly implicated in the genesis of methemoglobinemia.

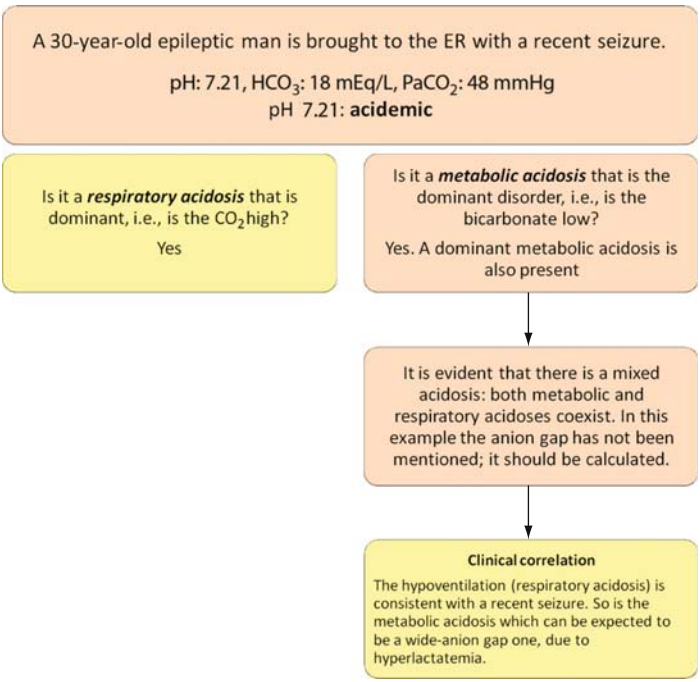
Methemoglobinemia was later confirmed on CO-oximetry.

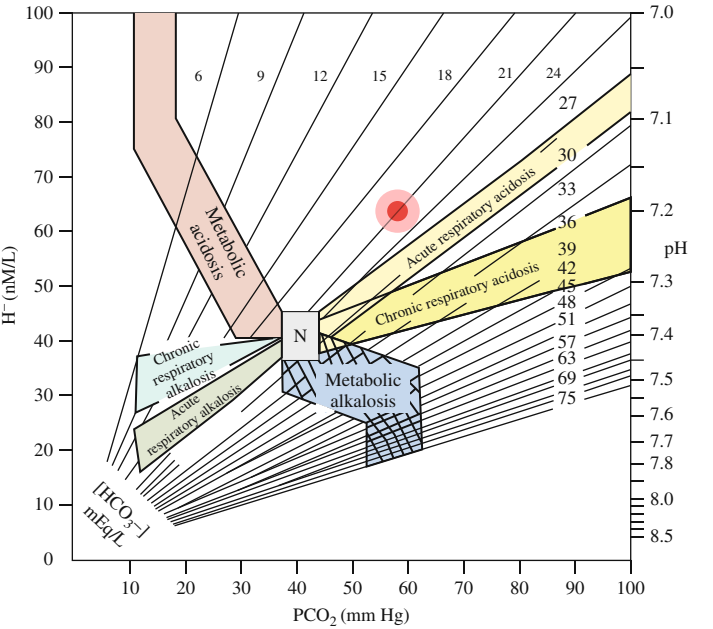


Patient G

This patients values fall on a point midway between the “95% confidence bands” of acute respiratory acidosis and metabolic acidosis. Both acute respiratory acidosis and metabolic acidosis are likely to be present.

Patient G: A 30-year-old man with an epileptic seizure

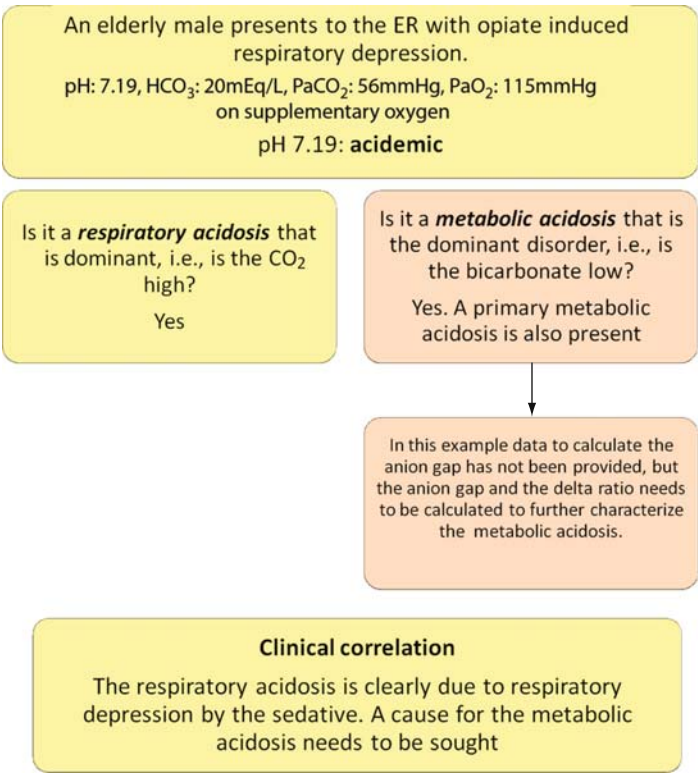


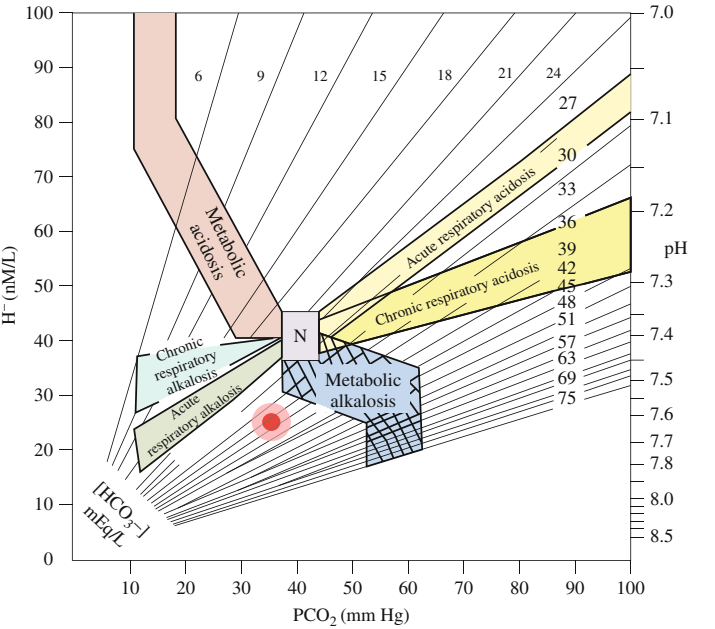


Patient H

As in the previous example, the patient's values fall on a point midway between the bands of acute respiratory acidosis and metabolic acidosis. Both acute respiratory acidosis and metabolic acidosis are therefore likely to be present.

Patient H: An elderly male with sedative overdose

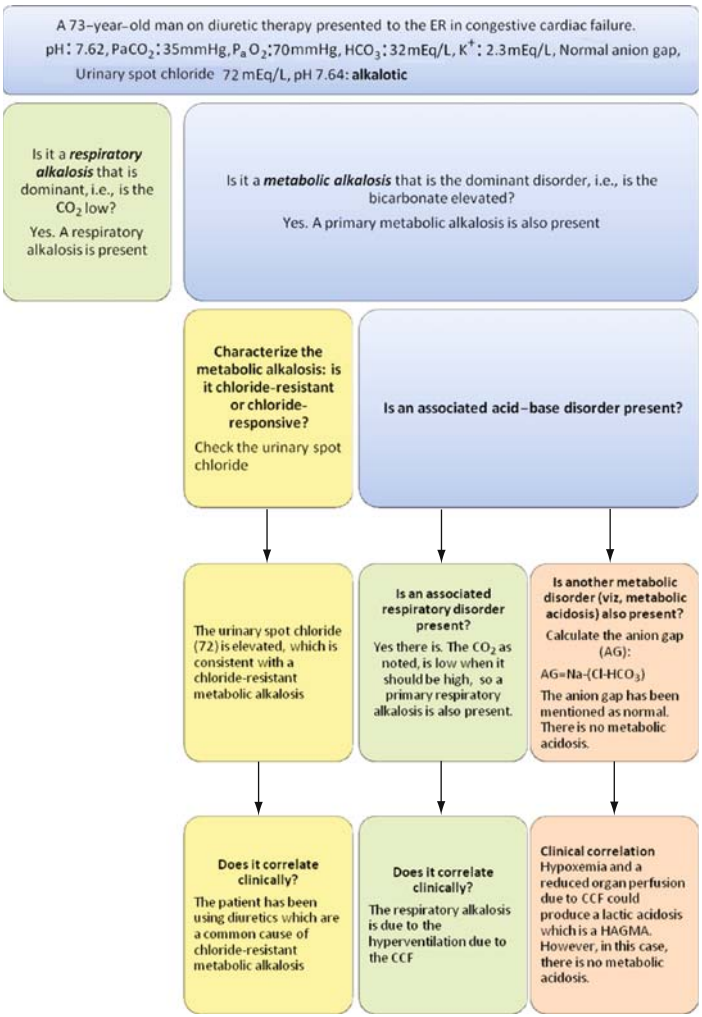


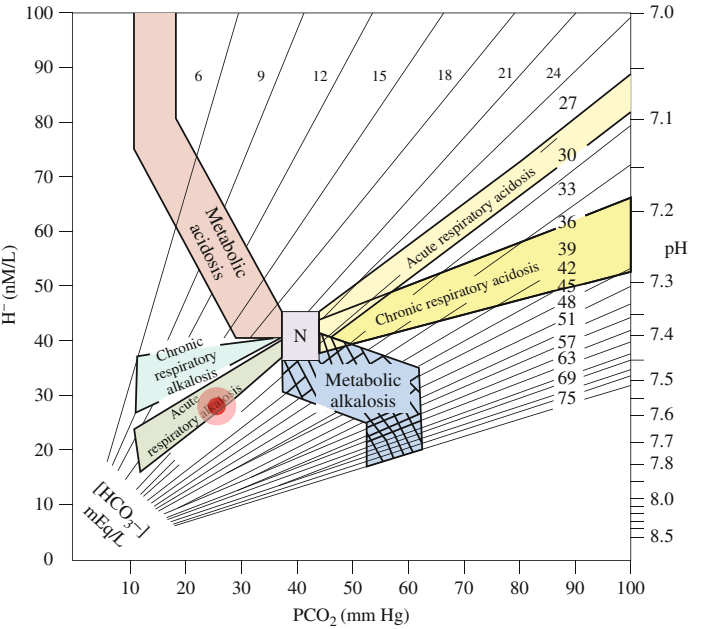


Patient I

This patients values fall on a point between the bands of acute respiratory alkalosis and metabolic alkalosis. Acute respiratory alkalosis and metabolic alkalosis are both likely to be present.

Patient I: A 73 year old man with congestive cardiac failure

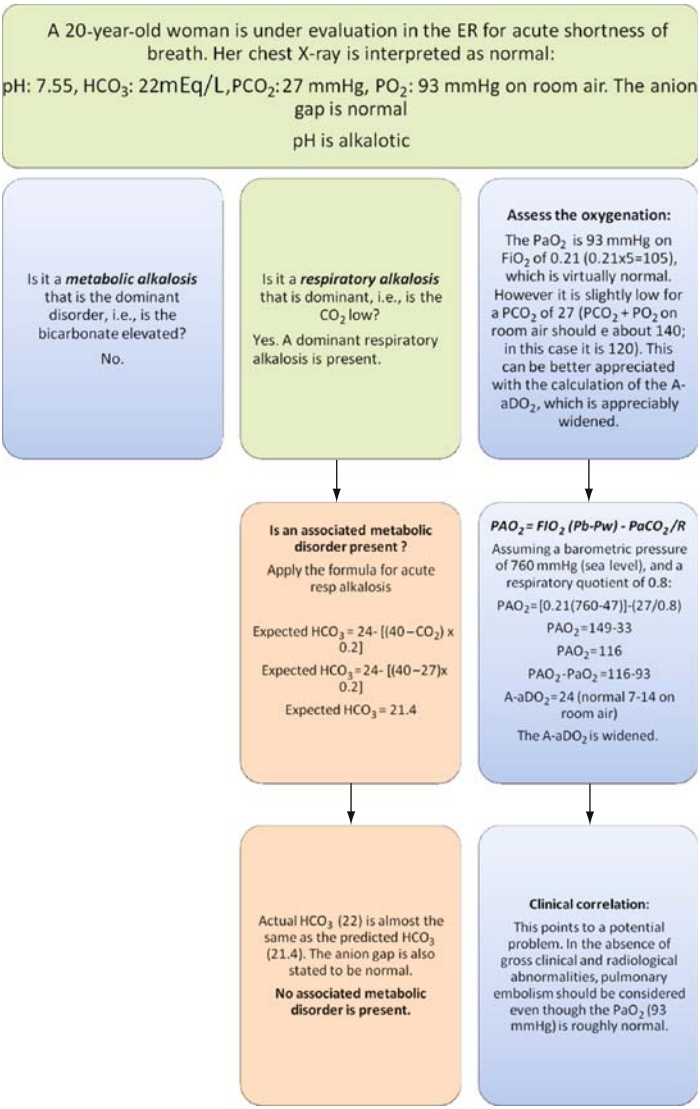


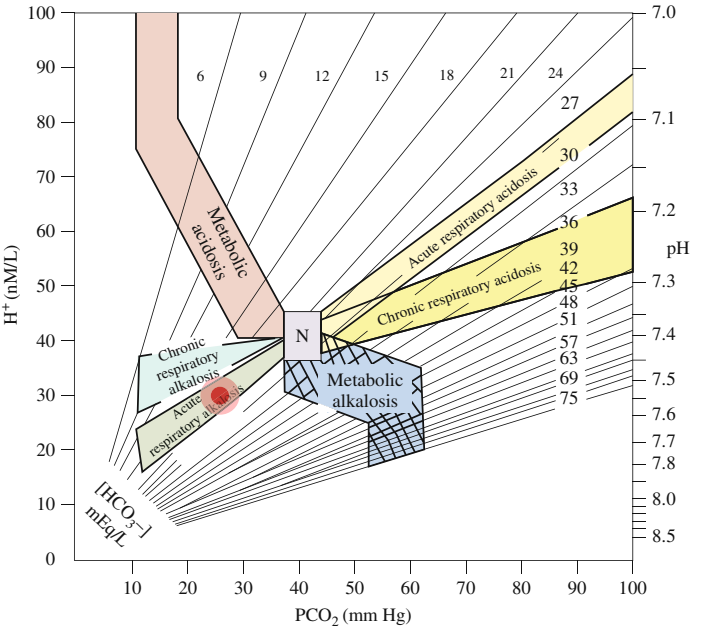


Patient J

The patient's values fall on the band of acute respiratory alkalosis. As mentioned in (00.00), when a patient's values fall on any of the "95% confidence bands", a simple acid-base disorder is likely to be present, in this case, acute respiratory alkalosis.

Patient J: A 20 year old woman with acuteshortness of breath

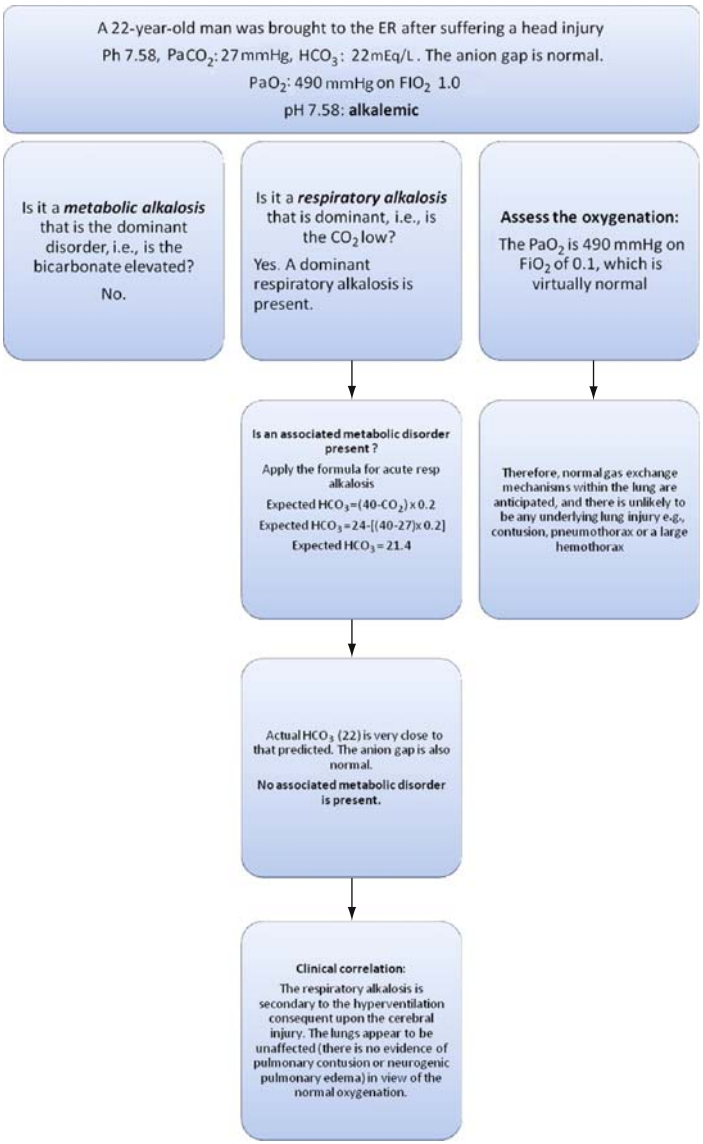


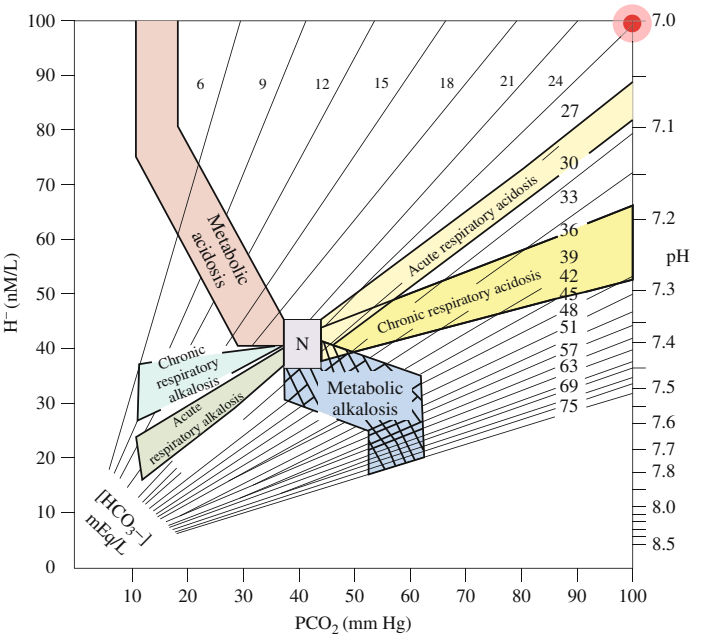


Patient K

As in the preceding example, this patient's values fall squarely on the band that represents acute respiratory alkalosis. A simple acid-base disorder, acute respiratory alkalosis, is present.

Patient K: A 22 year old man with a head injury

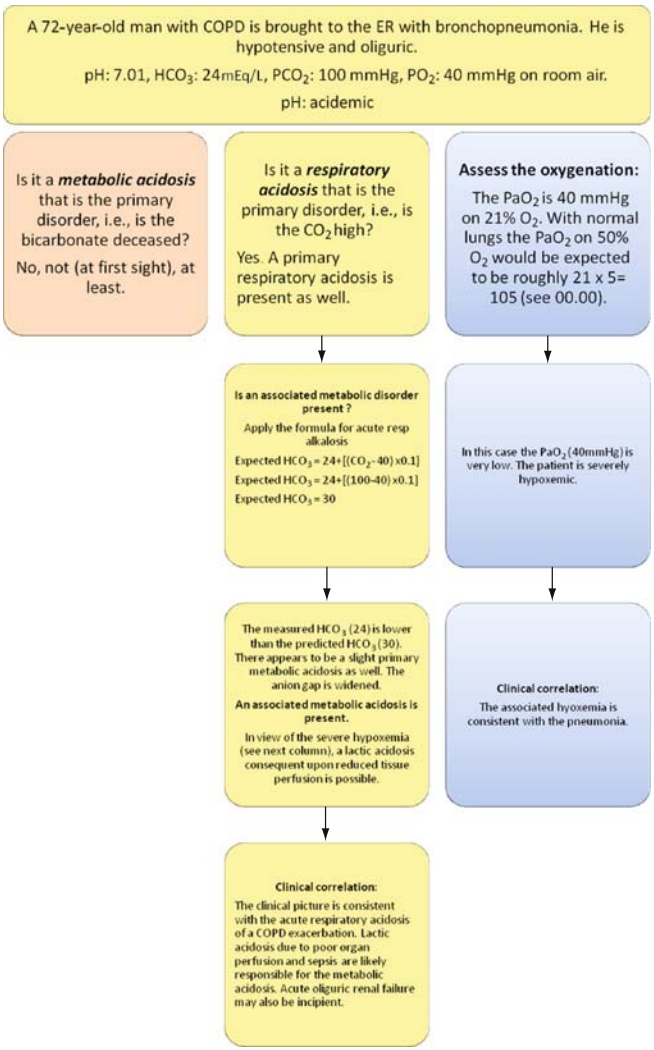


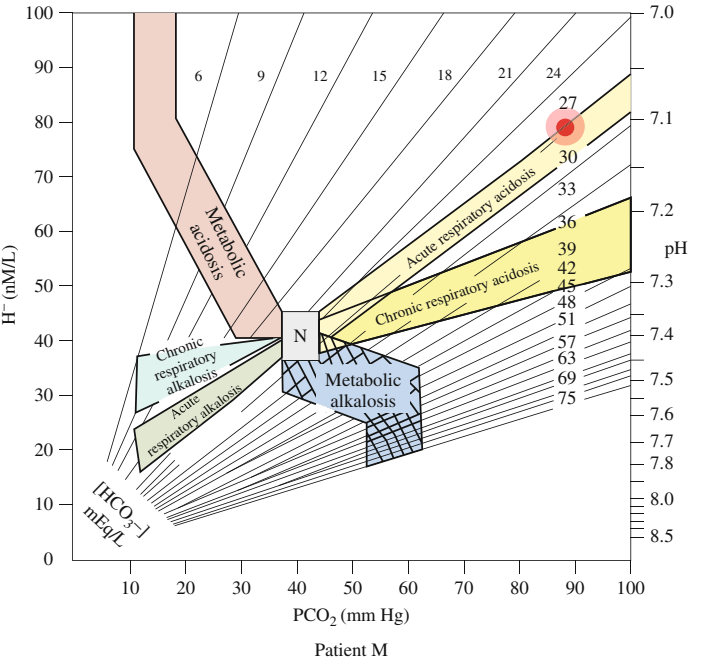


Patient L

This patients values have been graphed between the bands representing acute respiratory acidosis and metabolic acidosis, both of which can be shown to be present (see algorithm opposite).

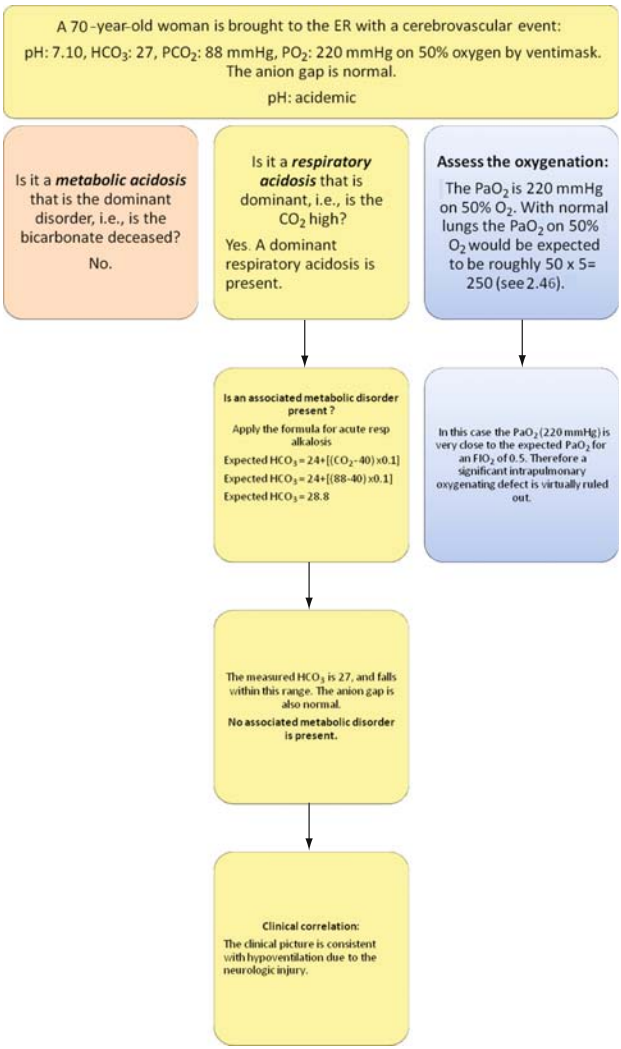
Patient L: A 72 year old man with bronchopneumonia

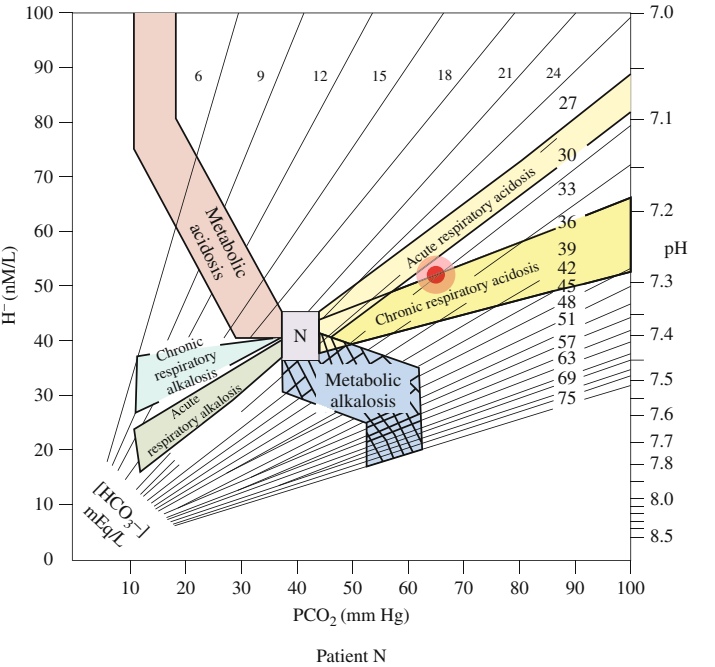




This patient's values fall on the band representing acute respiratory acidosis. No associate acid-base disorder appears to be present (see 00.00).

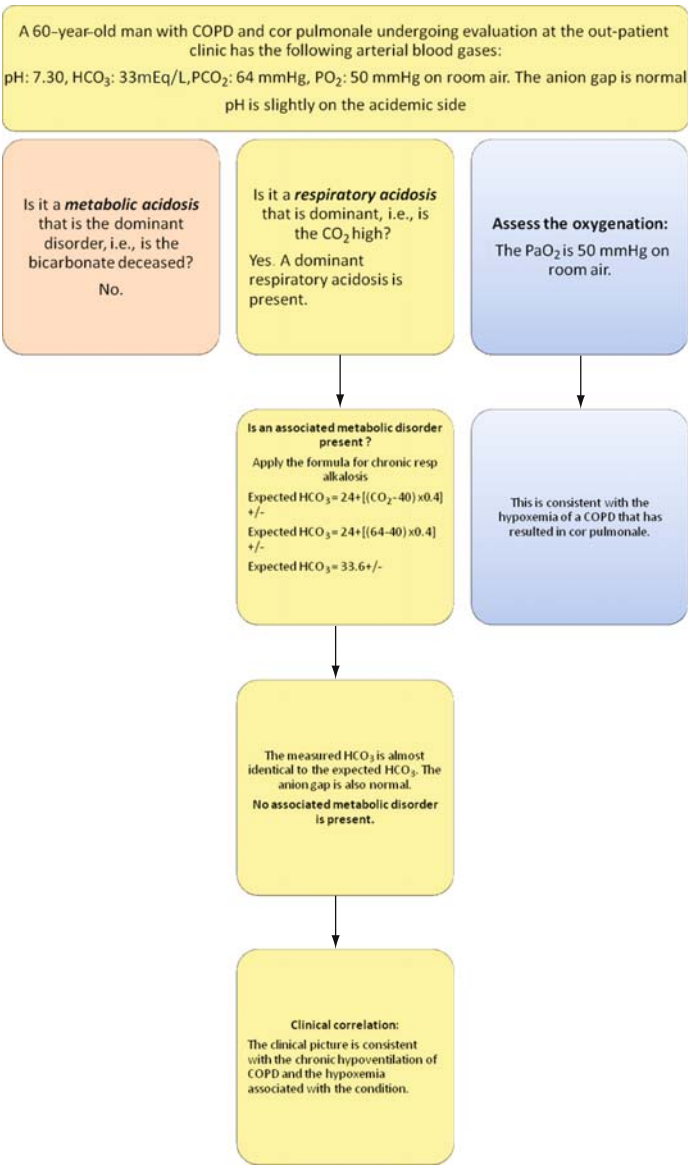
Patient M: A 70 year old woman with a stroke

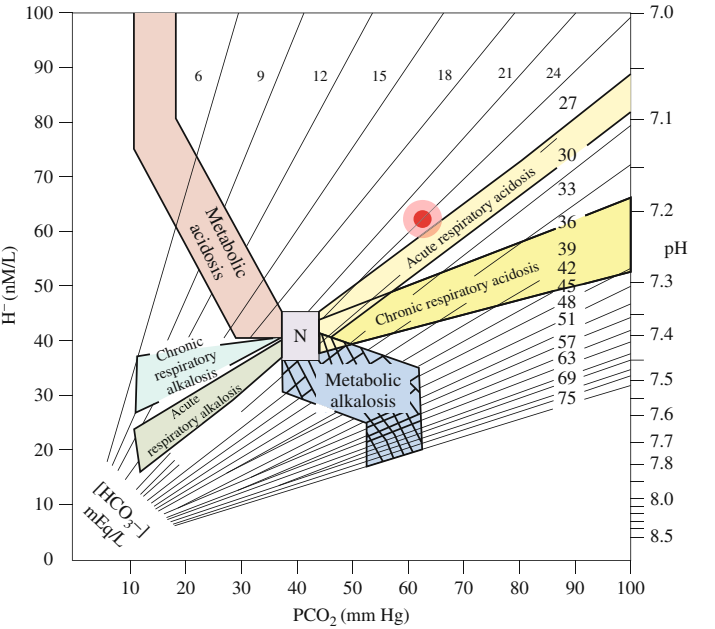




Chronic respiratory acidosis.

Patient N: A 60 year old male with stable COPD

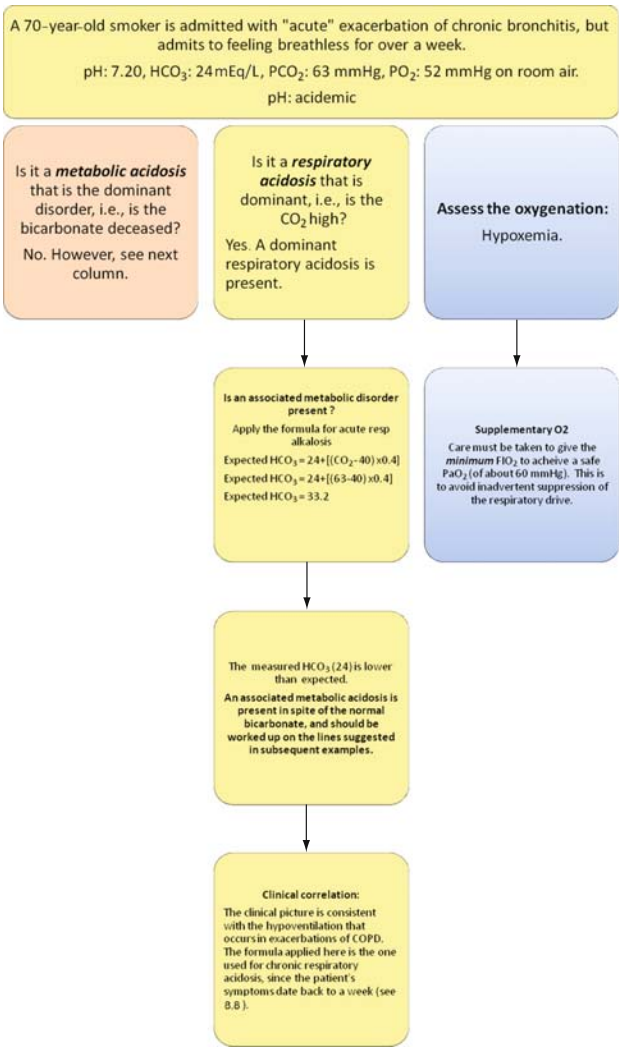


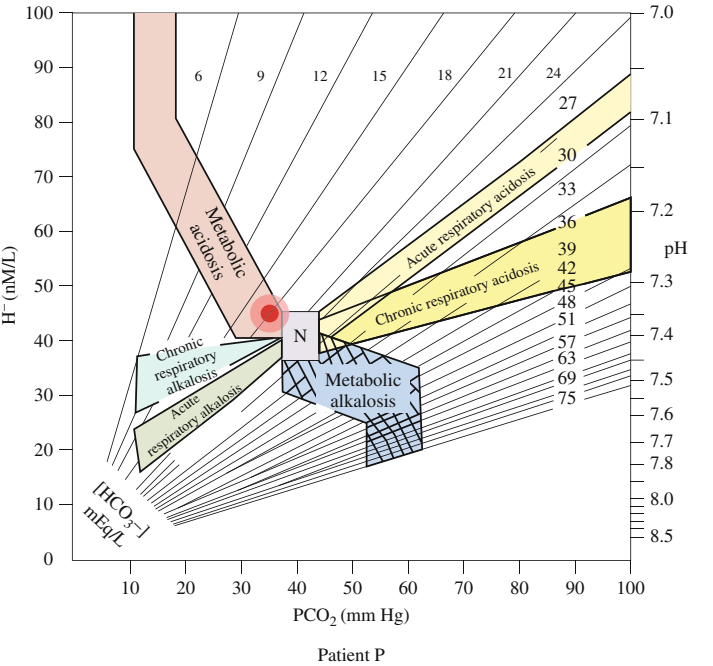


Patient O

The point plotted on this graph is close to the band for respiratory acidosis—in fact it lies between this band and the band of metabolic acidosis. As the algorithm on the opposite page suggests, both respiratory acidosis and metabolic acidosis are present.

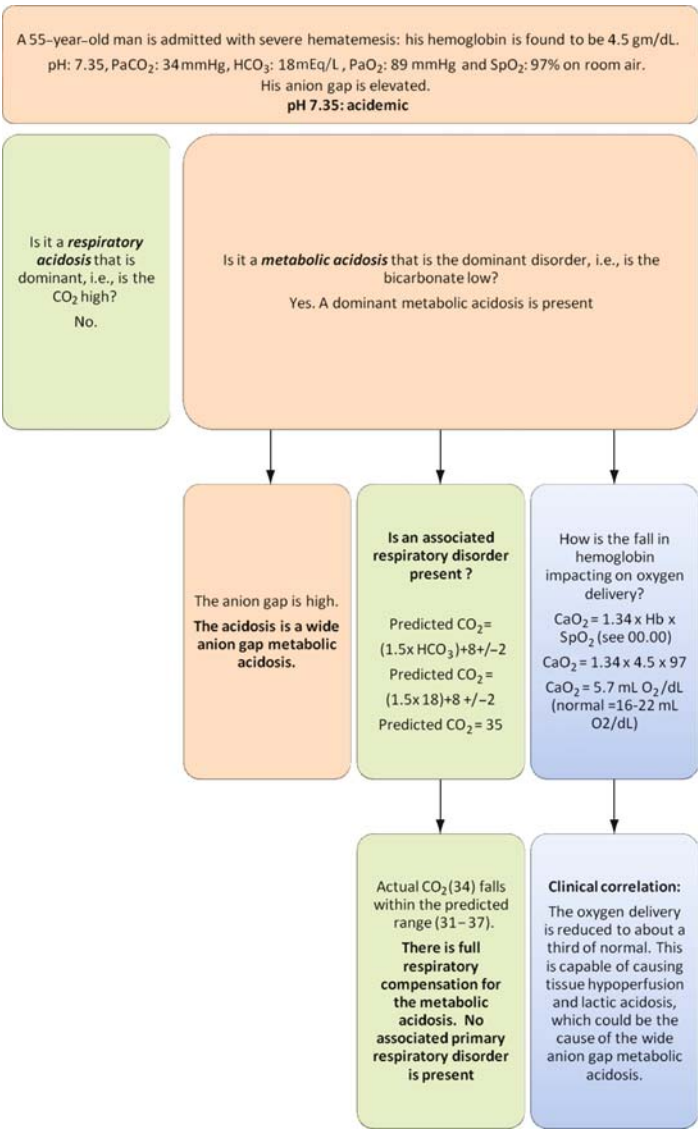
Patient O: A 70 year old smoker with AECB

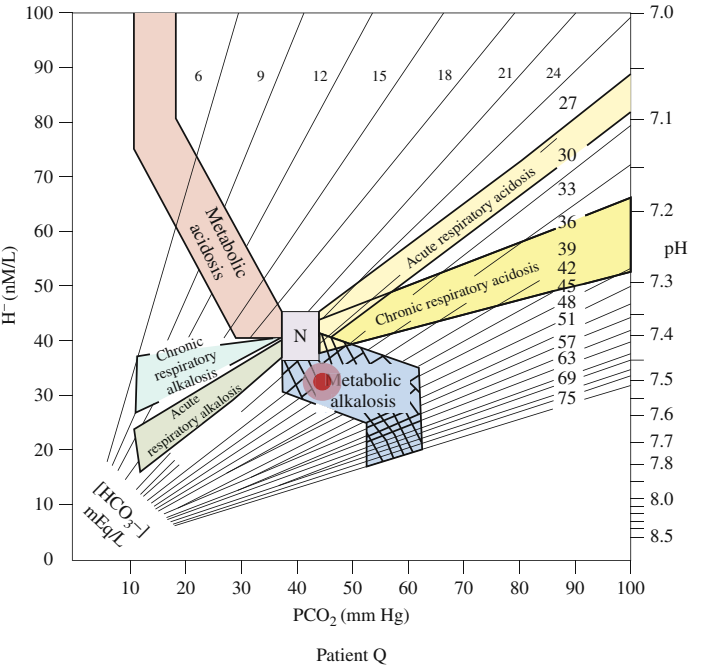




Metabolic acidosis.

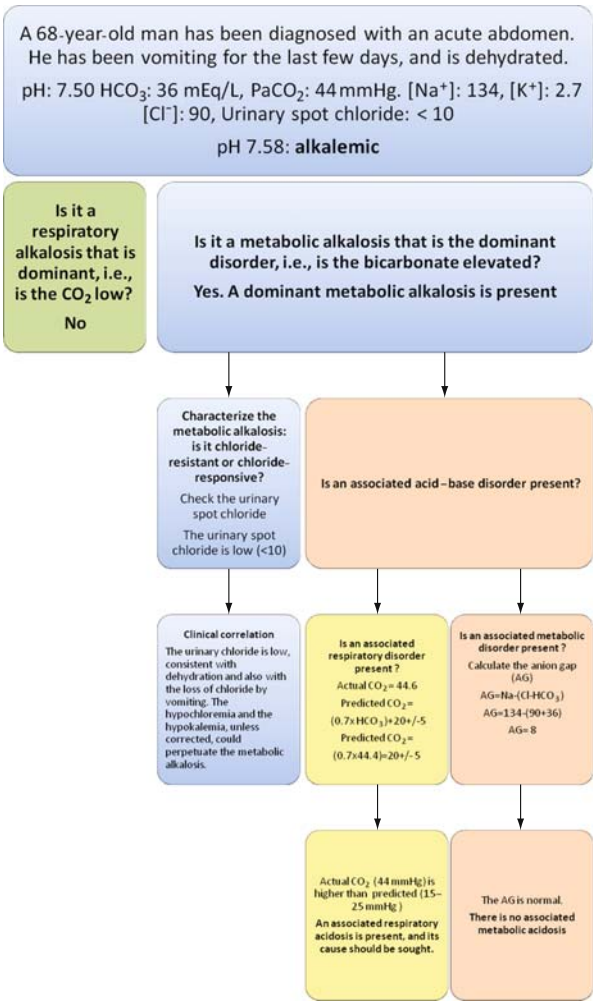
Patient P: A 55 year old man with hematemesis

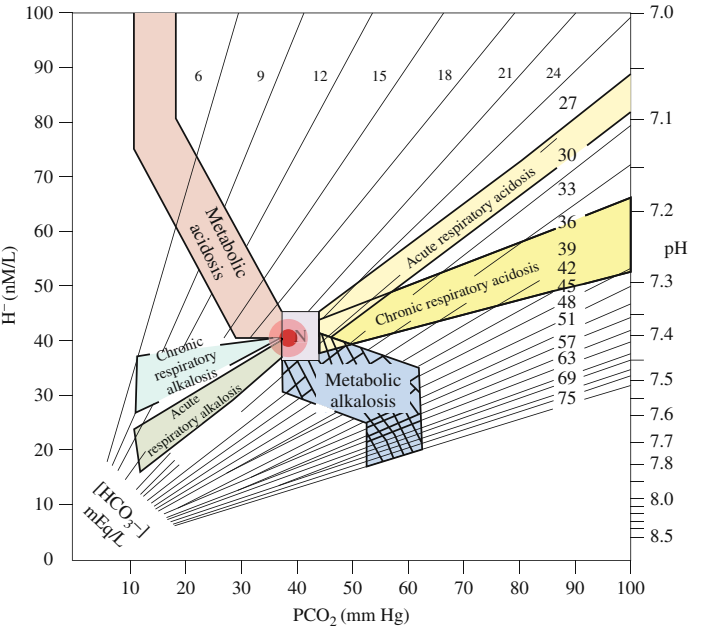




Metabolic alkalosis. Based on acid-base mapping alone, no other acid-base disturbance is expected to coexist. However the method is not infallible, and as the discussion on the facing page shows, an associated respiratory acidosis is in fact present.

Patient Q: A 68 year old man with an acute abdomen





Patient R

The point plotted falls in the zone of normality, as can occur when a metabolic acidosis is opposed by a metabolic alkalosis (see discussion on facing page).

Patient R: A young woman with gastroenteritis

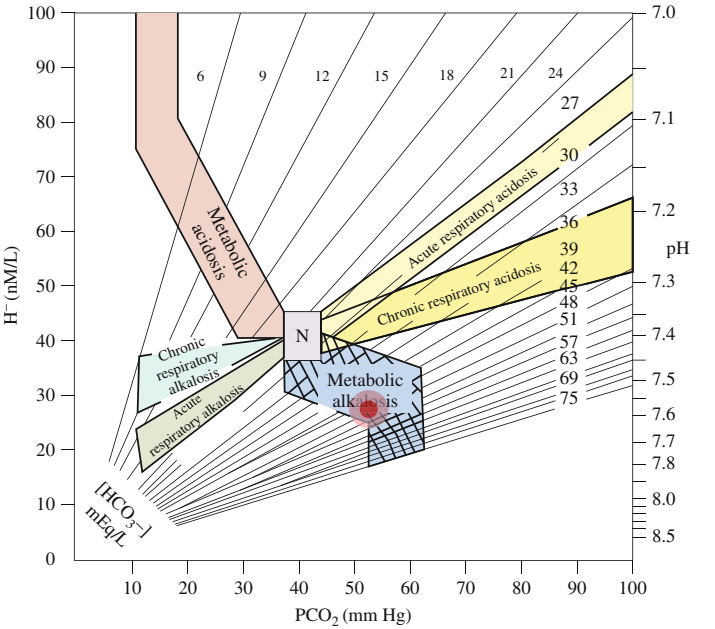
A young woman is admitted with dehydration due to gastroenteritis.
pH: 7.39, $PaCO_2$: 39mmHg, HCO_3: 21mEq/L, Na 145, K^+3.2, Cl^-94
pH: normal

However, note the anion gap which is clearly widened:
$AG=[Na^+]-([Cl^-]-[HCO_3])$
$AG= 145-(21+94)$
$AG= 30$

The anion gap is widened.
There is a wide anion gap metabolic acidosis.

Is an associated metabolic alkalosis present ?
Calculate the delta ratio (10.37)
Delta ratio=ΔAG-ΔHCO3
=(30−12)−(24−21)
=18−3
=15 (normal +6 to−6)
There is a coexistent metabolic alkalosis

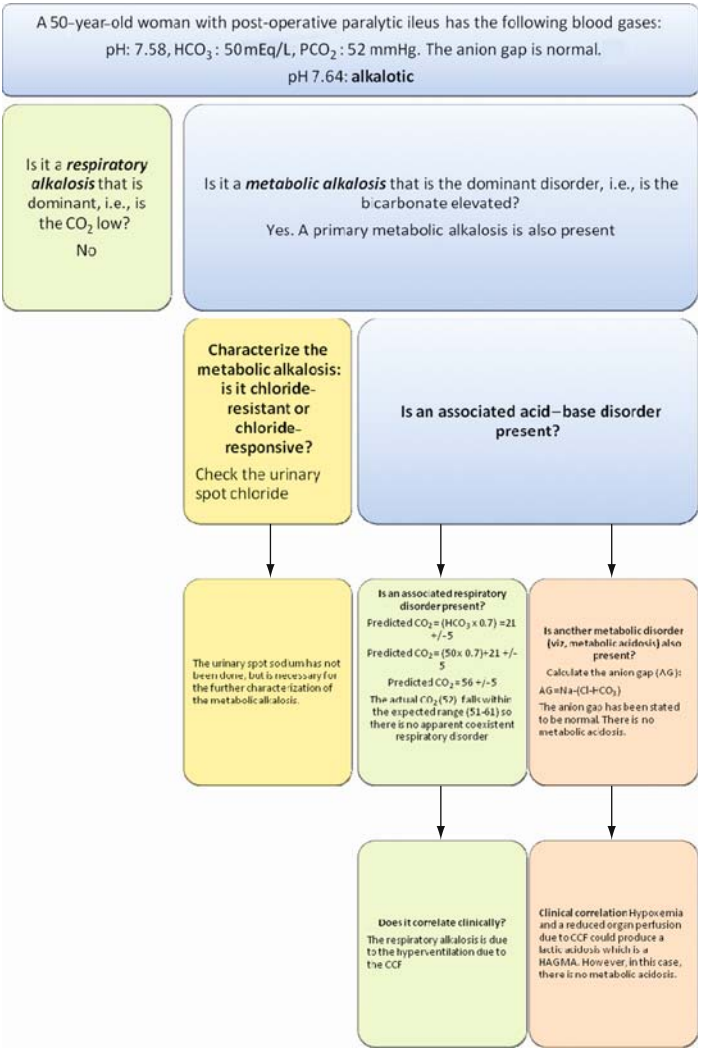
Clinical correlation:
The metabolic acidosis is presumably on account of the hypoperfusion and a possible pre-renal component. The metabolic alkalosis can be accounted for by the dehydration and volume contraction.

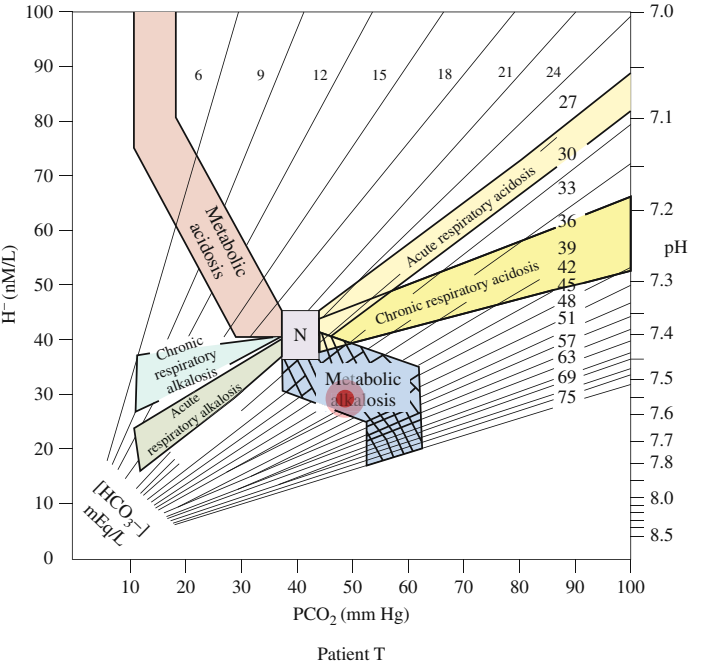


Patient S

One of the limitation of the acid-base mapping is that it is not possible to diagnose a "triple disorder" by this method. Although the above patient's values fall well within the band of metabolic alkalosis, there are two additional coexistent acid-base disturbances, as the algorithm on the opposite page reveals.

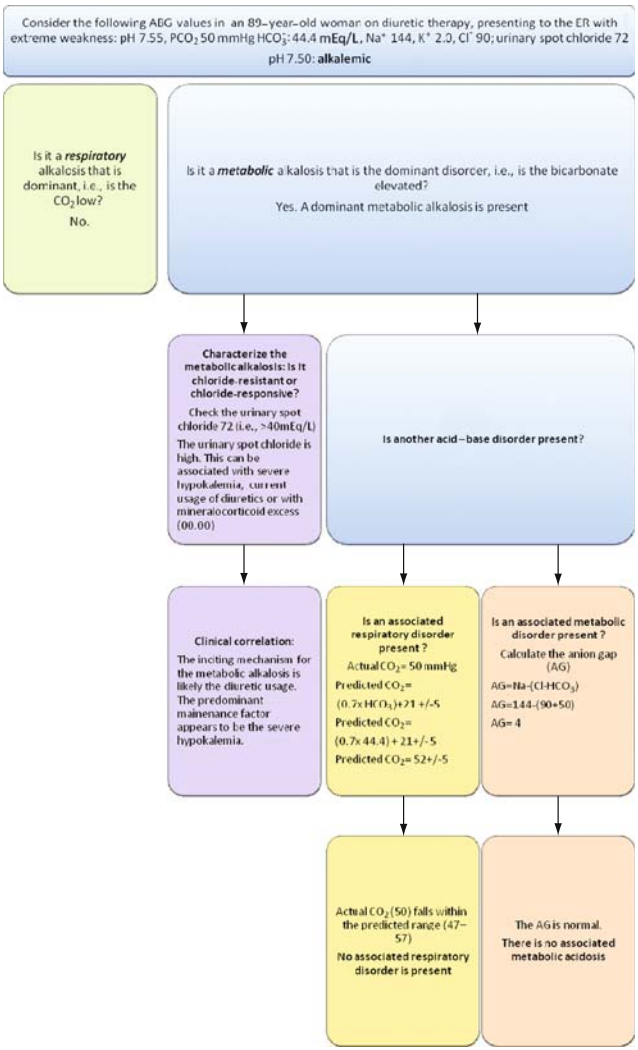
Patient S: A 50 year old woman with paralytic ileus

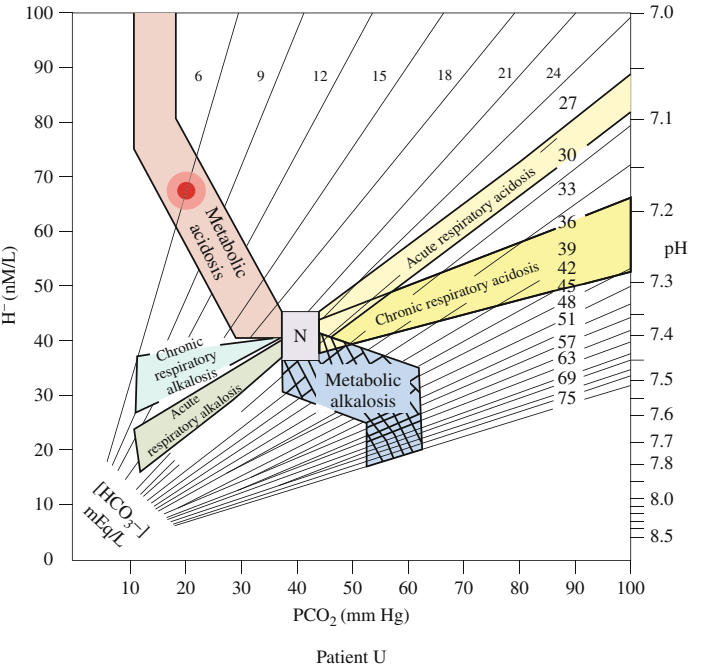




Metabolic alkalosis.

Patient T: An 89 year old woman on diuretic therapy

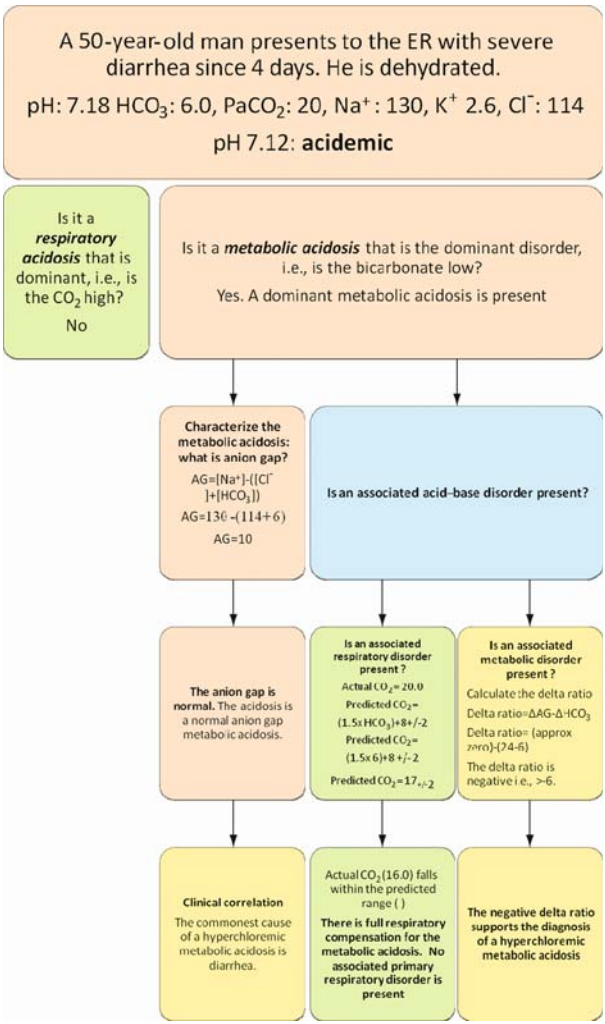


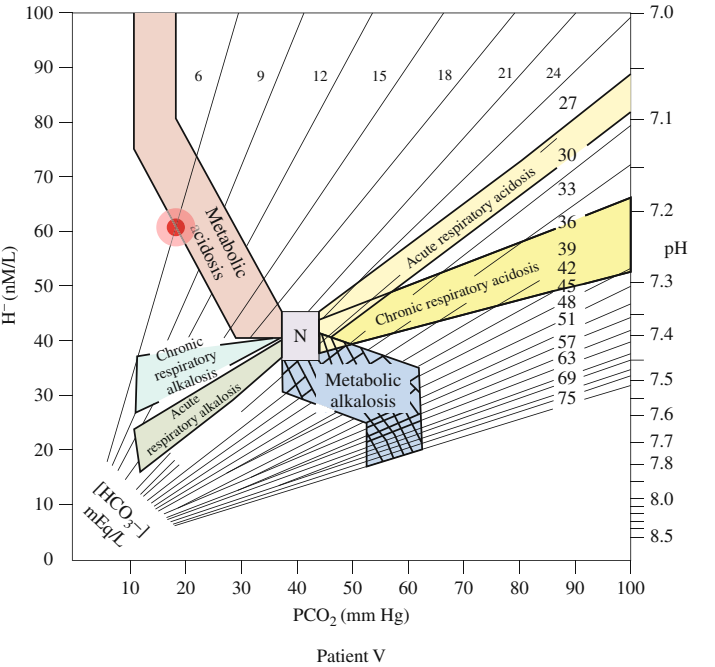


Patient U

Metabolic acidosis.

Patient U: A 50 year old man with severe diarrhea

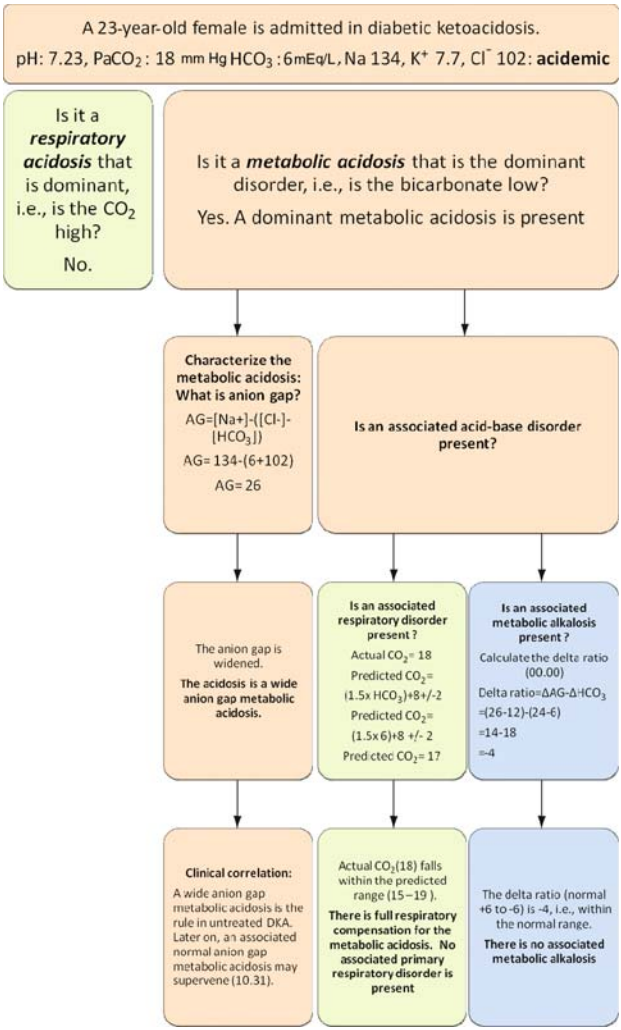


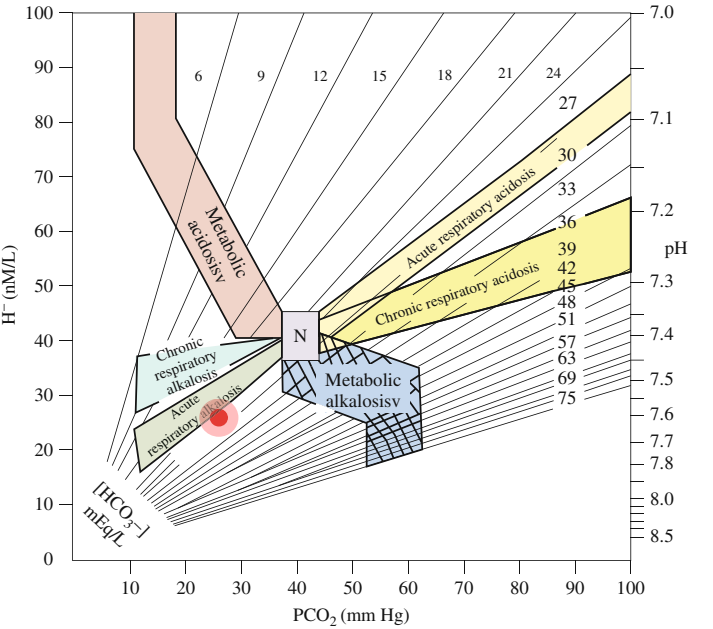


Patient V

Metabolic acidosis.

Patient V: A 23 year old female with diabetic ketoacidosis

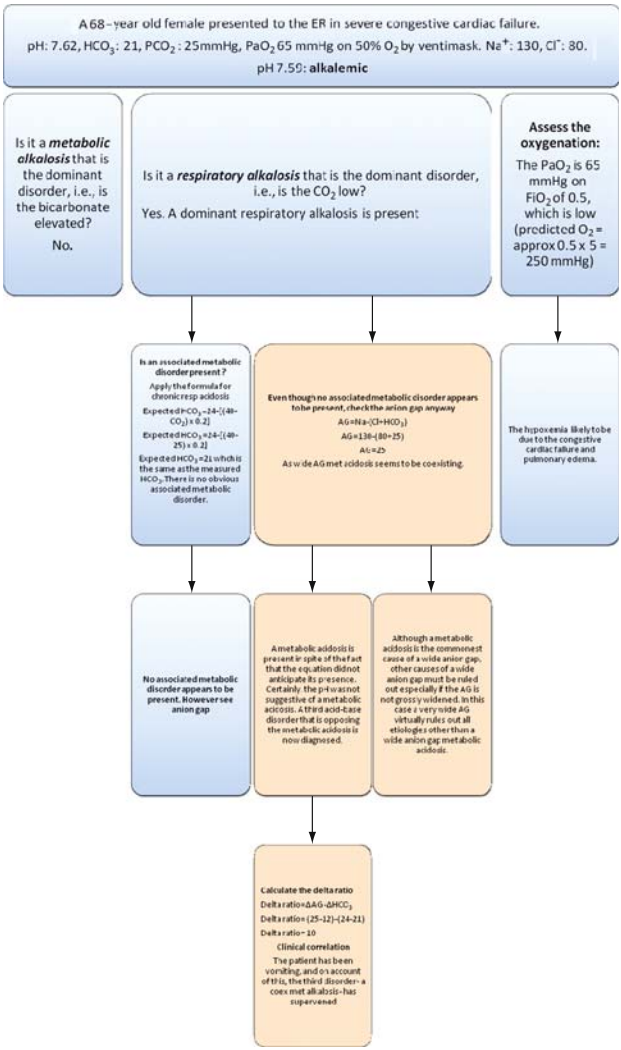


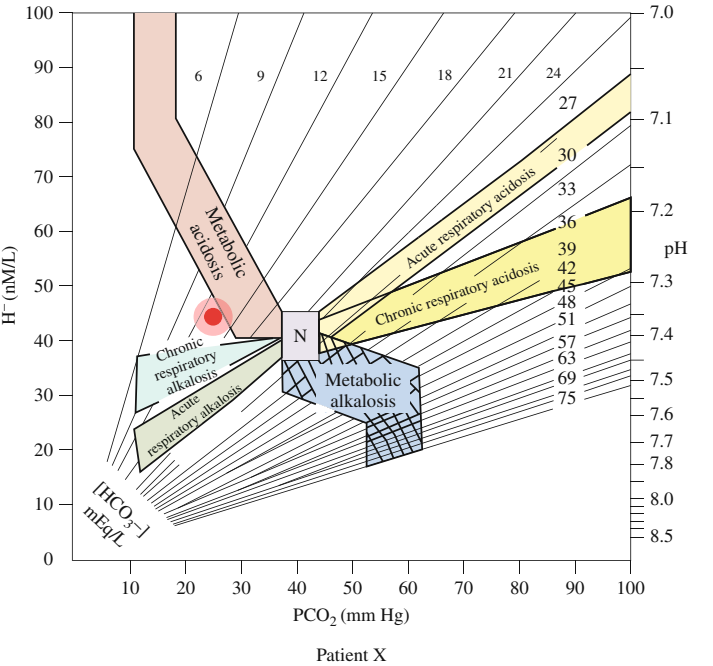


Patient W

To all appearances, an acute respiratory alkalosis with a probable metabolic alkalosis is present. As in the case of patient S, this patient's acid-base mapping has failed to reveal a triple disorder (see discussion opposite).

Patient W: A 68 year old woman in congestive heart failure

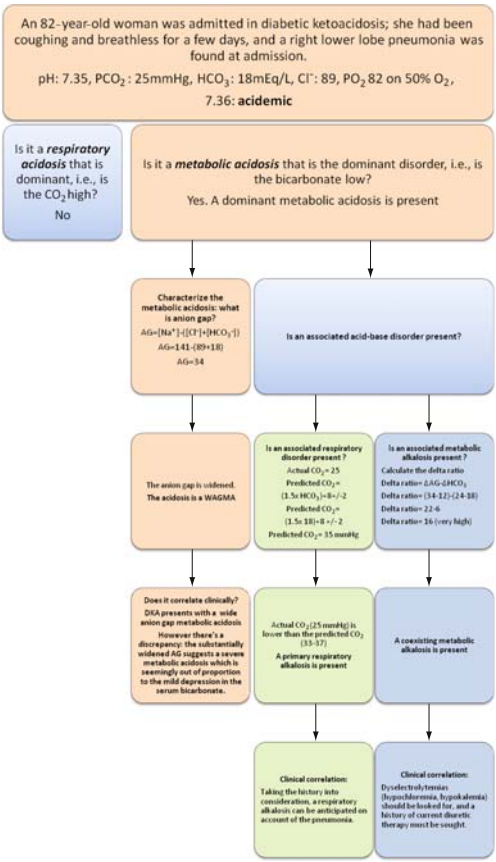


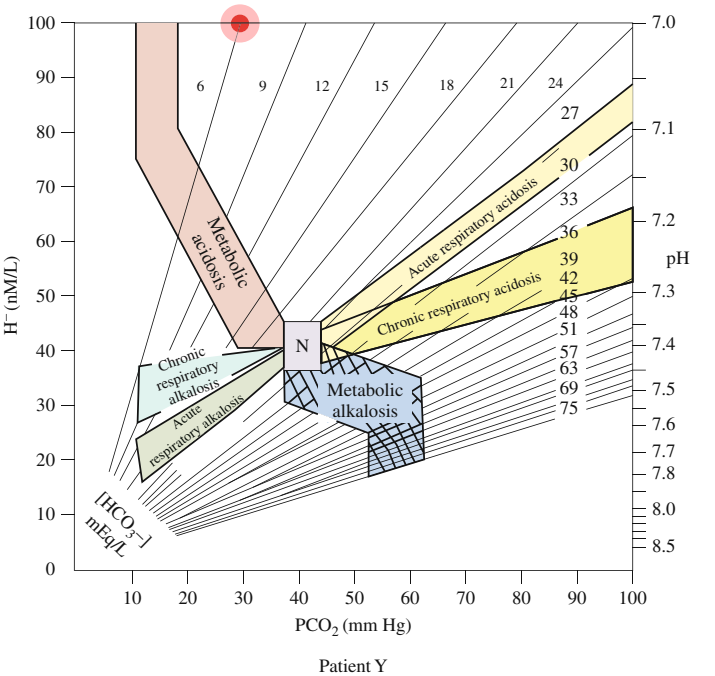


Patient X

Impression: metabolic acidosis with chronic respiratory alkalosis. In fact, a triple disorder is present (see discussion opposite).

Patient X: An 82 year old diabetic woman with pneumonia

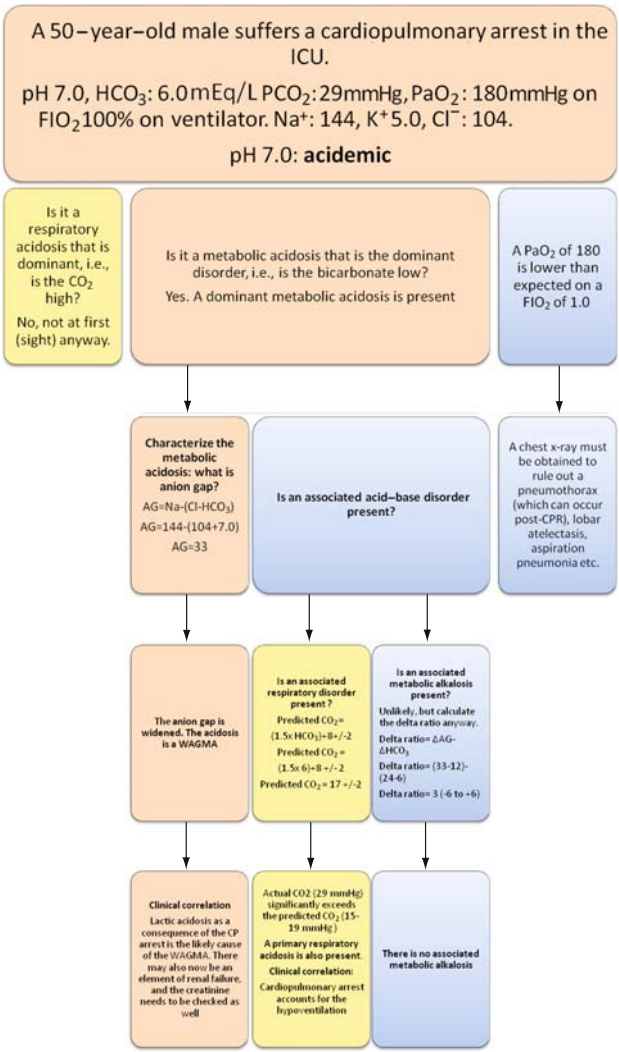


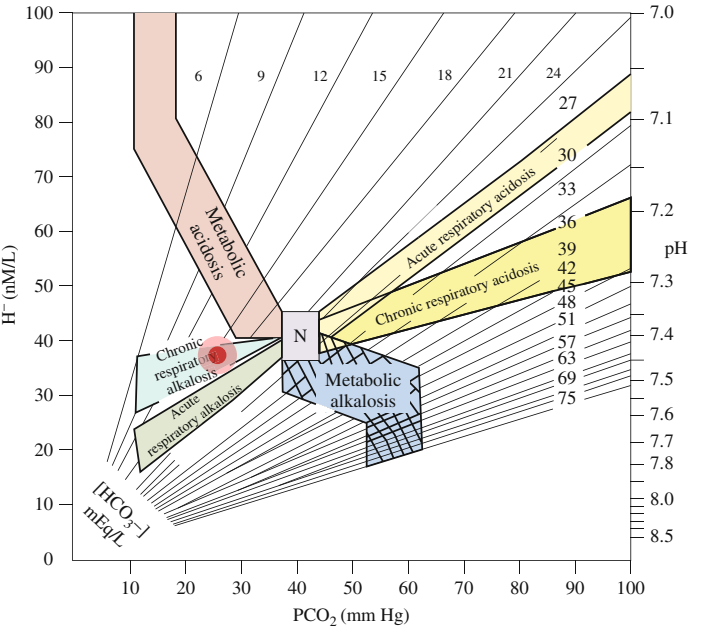


Patient Y

Severe metabolic acidosis with acute respiratory alkalosis.

Patient Y: Cardiopulmonary arrest in a 50 year old male

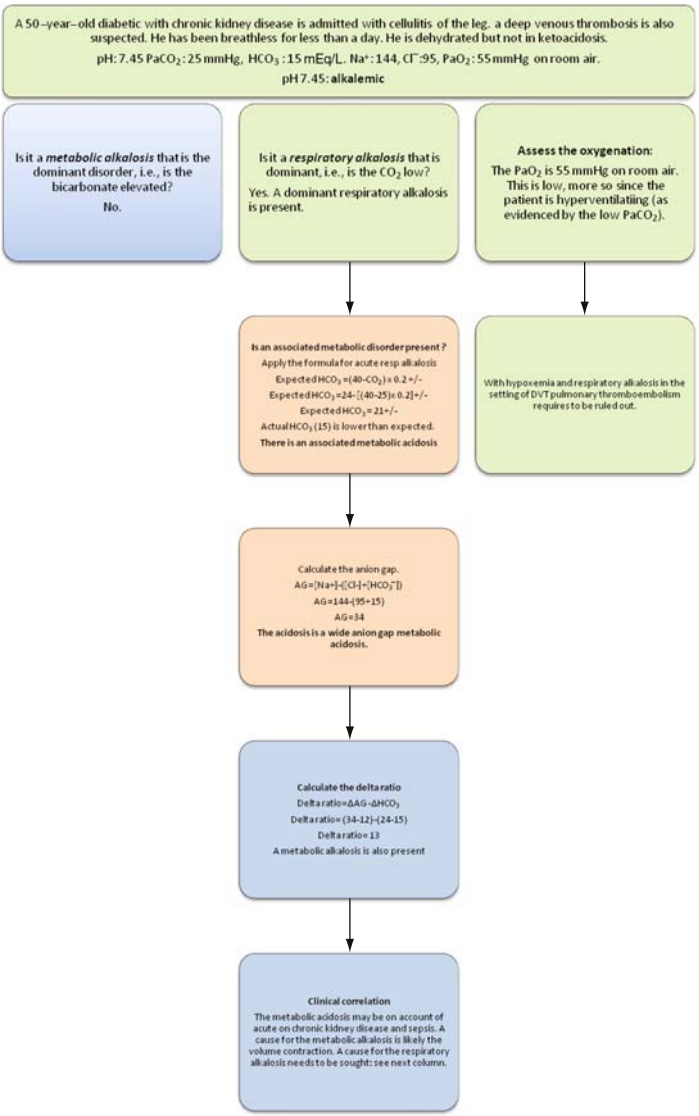




Patient Z

This patient's acid-base map conveys the impression of chronic respiratory alkalosis. In actual fact, a triple disorder is present (see discussion opposite).

Patient Z: A 50 year old diabetic with suspected pulmonary thromboembolism



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