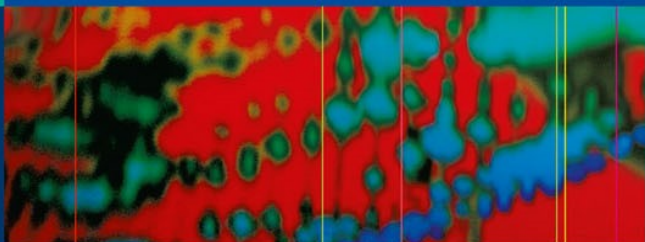


Ashfaq Hasan



Handbook of Blood Gas/Acid-Base Interpretation

 Springer

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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 Martin² and Kerry Brandis³ thoroughly enjoyable as also the online tutorials of Alan Grogono⁴ and Bhavani Shankar Kodali⁵: 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

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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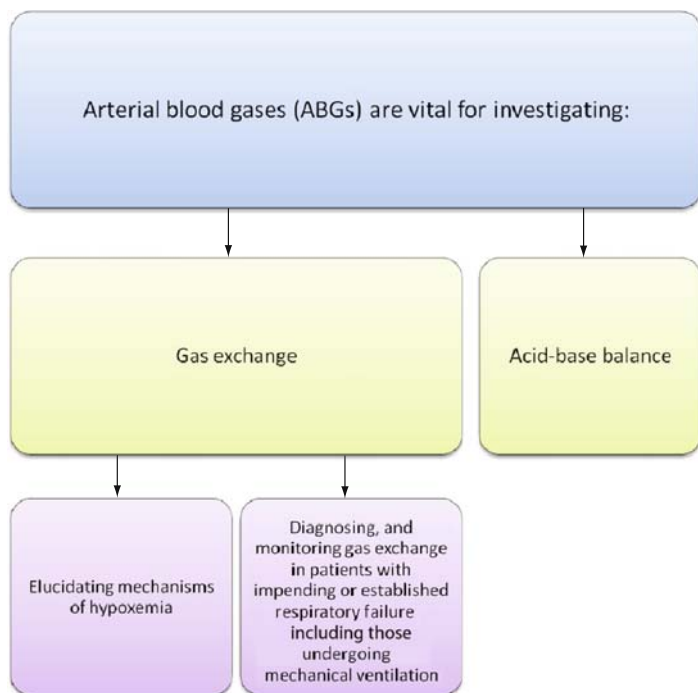
Chapter 1

The Blood Gases

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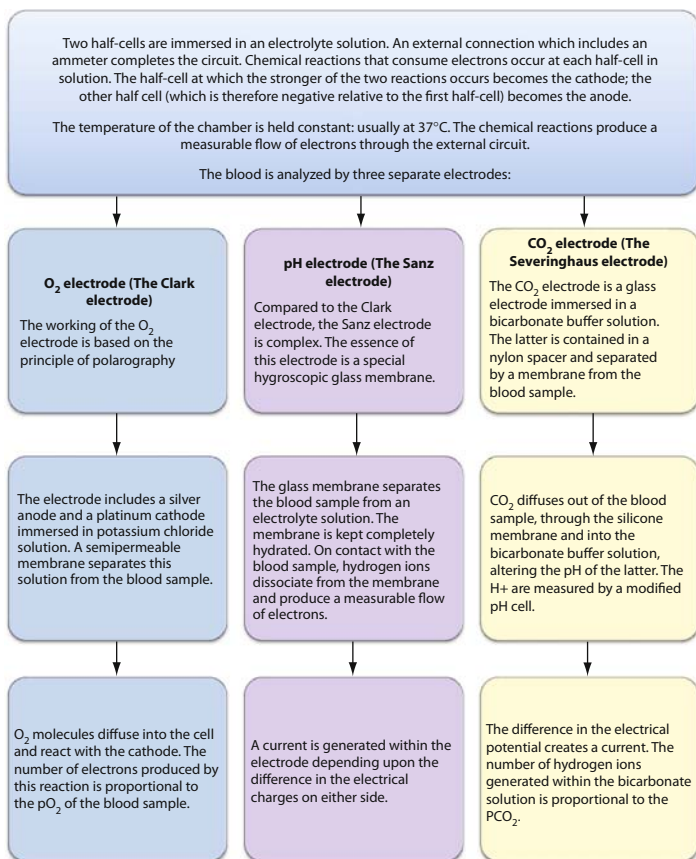
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1.1 The Utility of Blood Gases



1.2 Electrodes

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



Hansen, JE. Arterial blood gases. In: Mahler DA, ed. Pulmonary Function Testing. Clin Chest Med 1989; 5:227–237

Madama, VC. In: Pulmonary Function Testing and Cardiopulmonary Stress Testing, 2nd ed., Delmar, 1998

Chapter 2

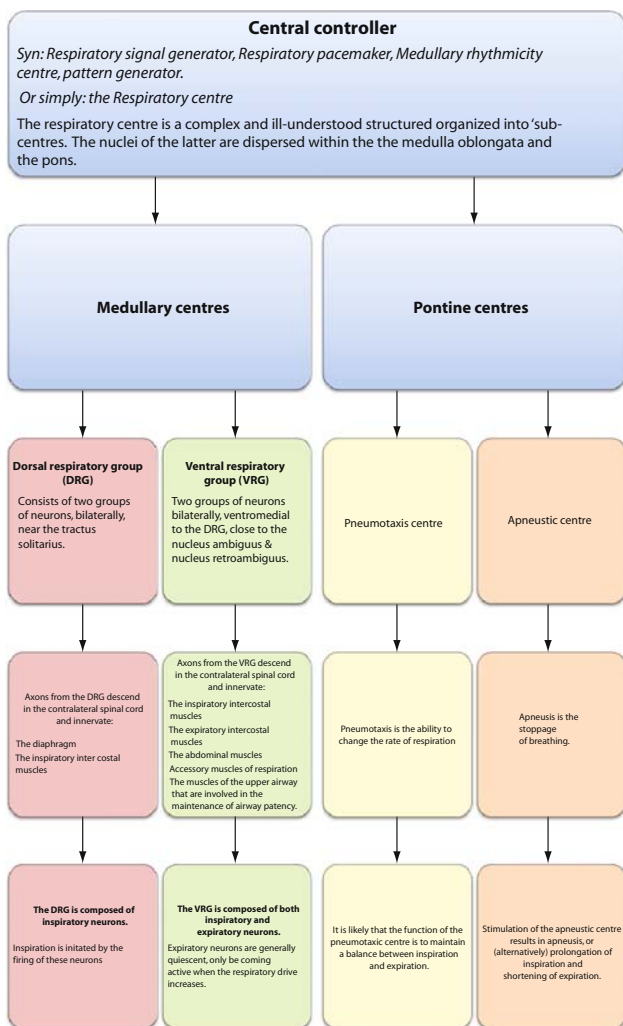
Gas Exchange

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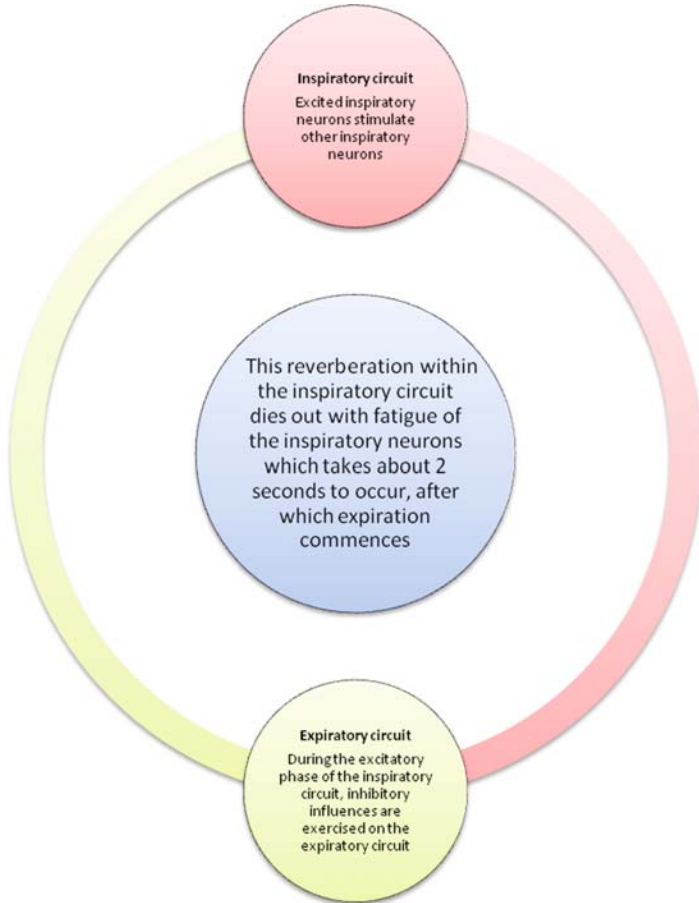
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2.1 The Respiratory Center



2

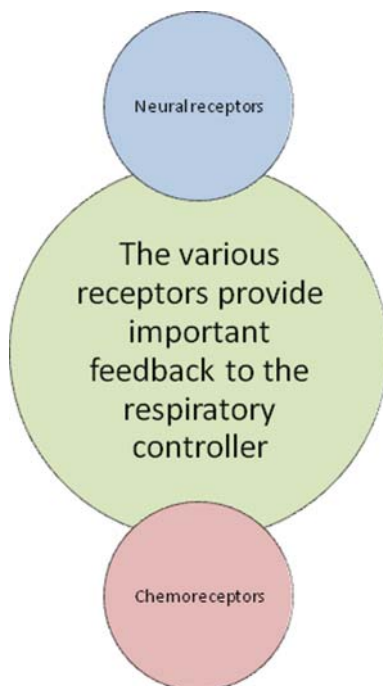
2.2 Rhythmicity of the Respiratory Center



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

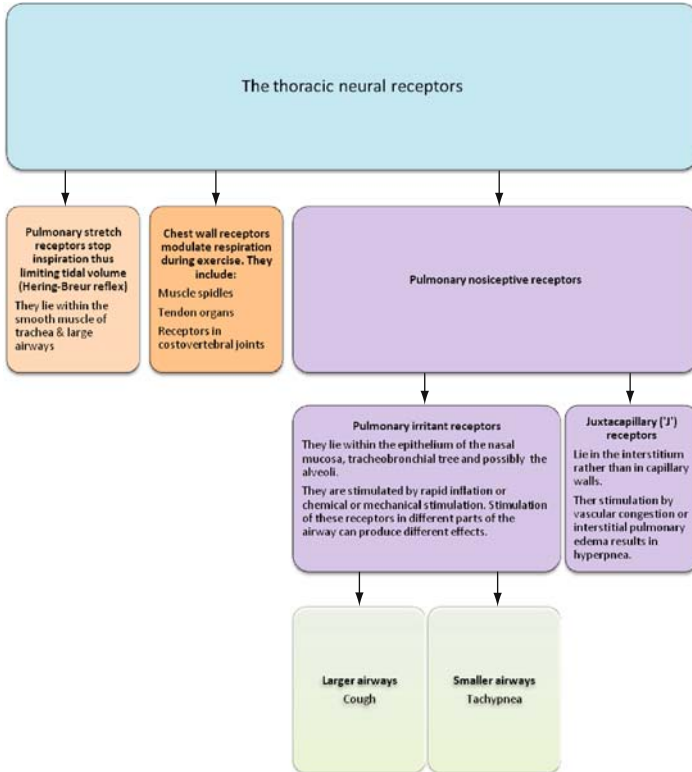
2.3 Receptors

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

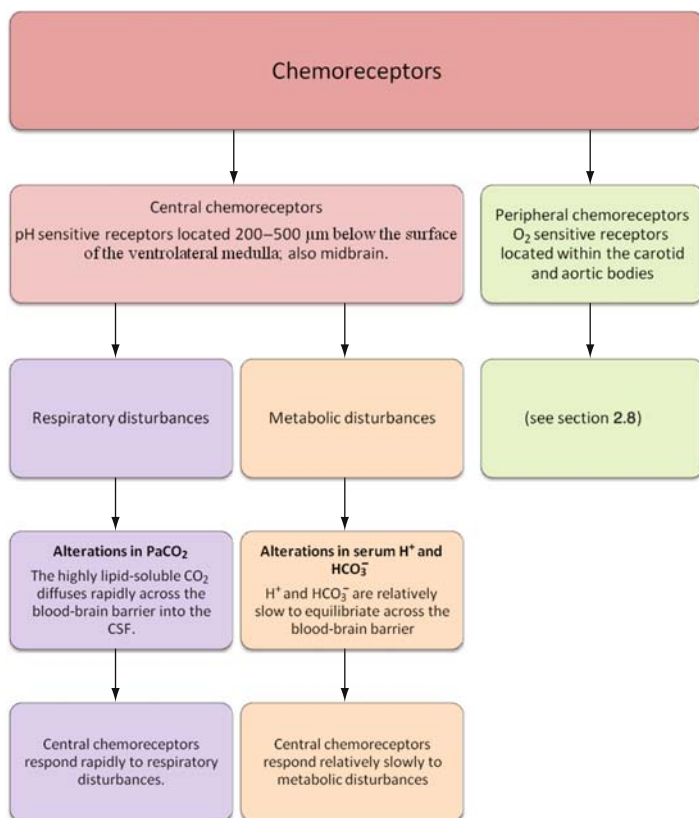


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2.4 Neural Receptors



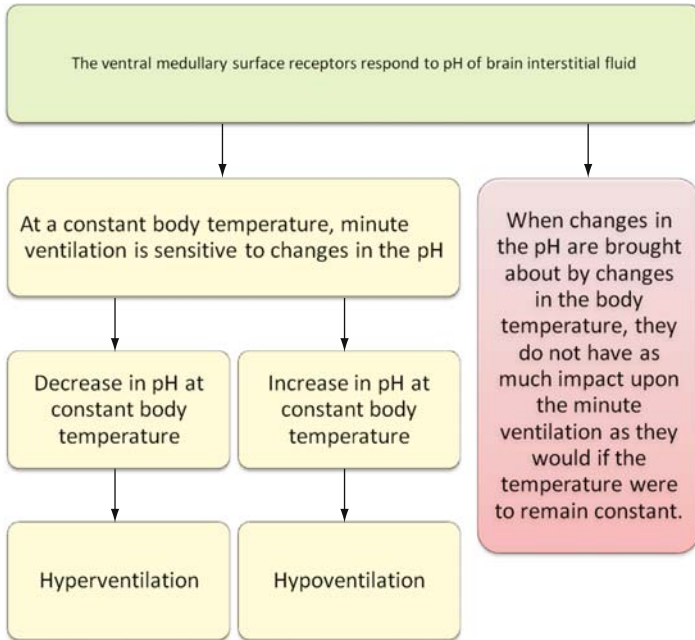
2.5 Chemoreceptors



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

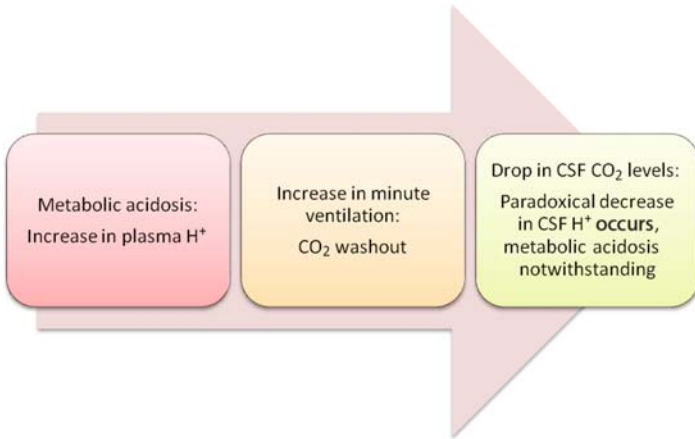
2.6 The Central Chemoreceptors: the Alpha-Stat Mechanism



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



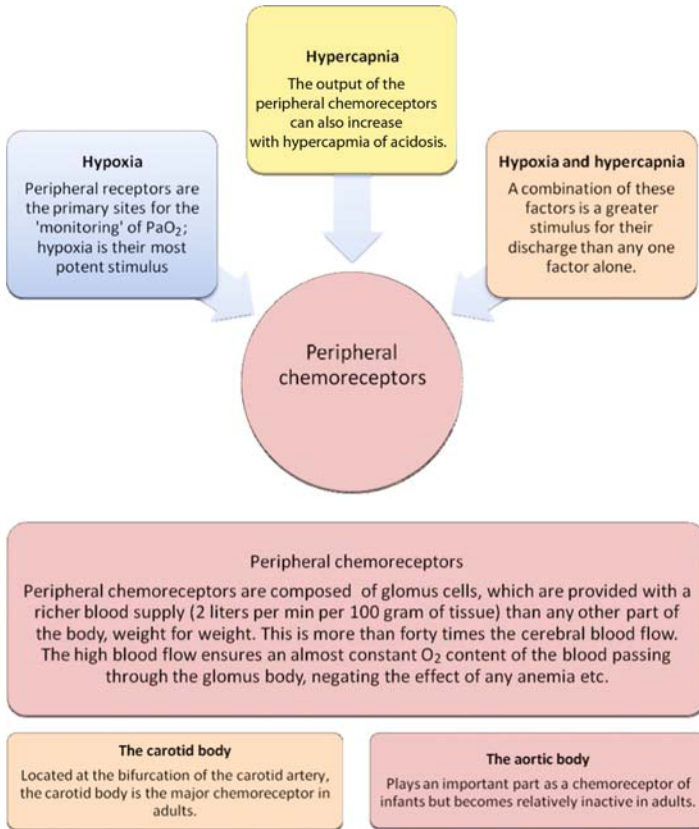
Bushinsky, DA, Coe, FL, Katzenberg, C, et al. Arterial PCO_2 in chronic metabolic acidosis. *Kidney Int* 1982; 22:311

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

2

2.8 Peripheral Chemoreceptors

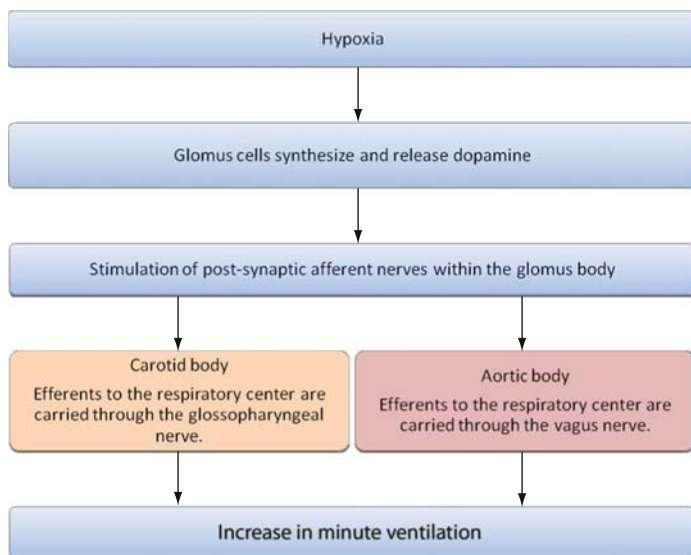


Lambertsen, CJ. Chemical Control of Respiration At Rest, 14th ed, Mosby Company, St. Louis, 1980

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

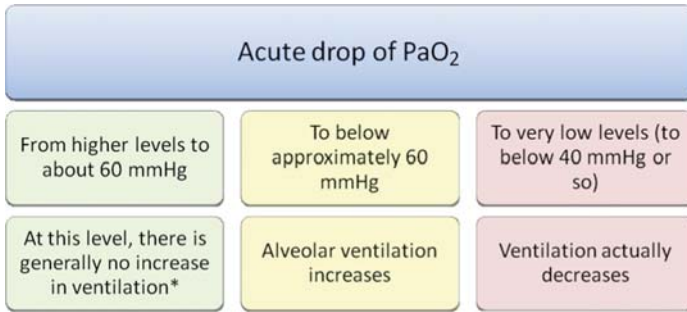
2.9 Response to Hypoxia

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

2 *Response of the respiratory center to acute hypoxemia*

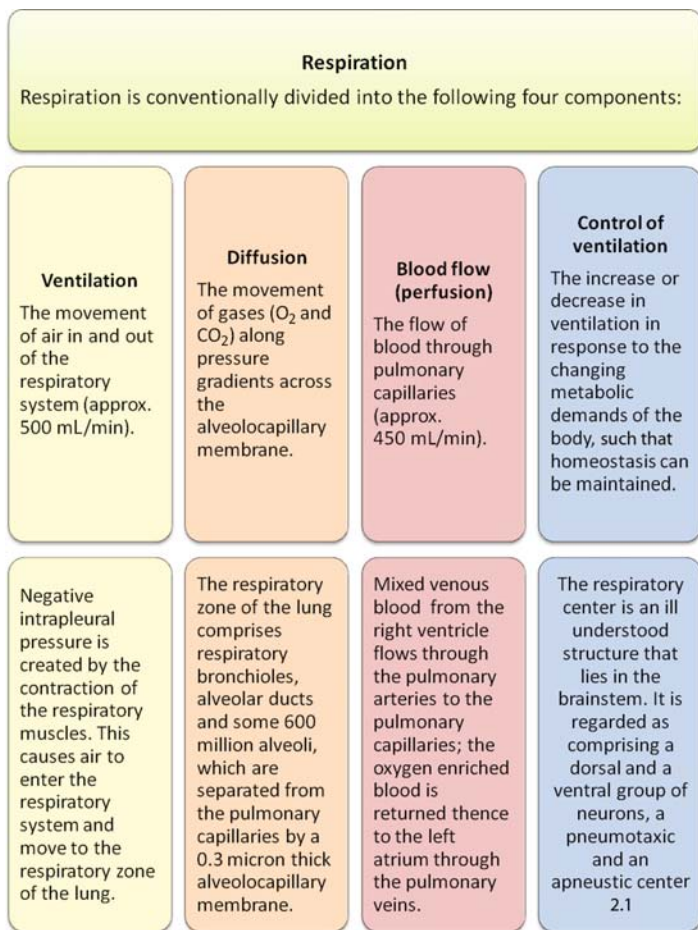


* In contrast even a small rise in CO₂ above physiological levels results in an almost immediate increase in alveolar ventilation

Igarashi, T, Nishimura, M, Kobayashi, S, et al. Dependency on the rate of change in PaO₂ of the ventilatory response to progressive hypoxia. Am J Respir Crit Care Med, 1995

2.10 Respiration

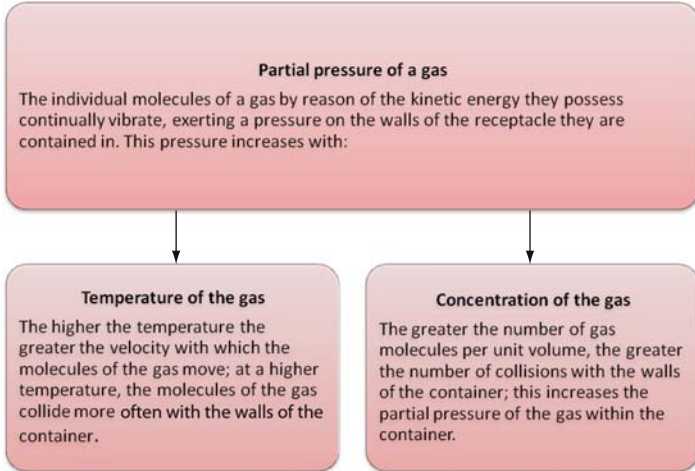
Respiration involves the sum of those complex processes that enable gas exchange between an organism and its environment.



2

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 ($F_{O_2}=0.21$).

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

$$P_{O_2} = F_{O_2} \times PB$$

$$P_{O_2} = 0.21 \times 760 = 159 \text{ mmHg}$$

Partial pressure of Nitrogen

The molecules of N_2 comprise 79% of all the molecules in room air ($F_{N_2}=0.79$).

At sea level PB is 760 mmHg.

$$P_{N_2} = F_{N_2} \times PB$$

$$P_{N_2} = 0.79 \times 760 = 600 \text{ mmHg}$$

2.14 Diffusion

Gases always diffuse down their respective partial pressure gradients.

Net diffusion

The net diffusion of gases is determined by the pressure gradient of the gas.

The vast majority of gas molecules move down the pressure gradient: from a region of higher pressure to a region of lower pressure.

A few gas molecules do move against the pressure gradient, but their number is not significant.

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 (P_{wO_2}) is directly proportional to the partial pressure of the O_2 in the gas phase (P_{gO_2}).

The gas-liquid interface

- At a gas-liquid interface, the partial pressure of gas (e.g. O_2) **over** the liquid (e.g. water) determines the number of gas molecules **colliding** with the liquid.

Molecules entering liquid phase from the gas phase

- The number of molecules of the gas **entering** the liquid is directly proportional to partial pressure of O_2 (P_{gO_2}) over the liquid.

Partial pressure of gases in gas phase and liquid phase

- At **equilibrium** the number of O_2 molecules entering the liquid phase (e.g., water) from the gas phase are equal to the number of O_2 molecules leaving the liquid phase and re-entering the gas phase.

2.16 Diffusion of O₂ and CO₂

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 (P₁-P₂);

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

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

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:

$$D \propto \text{Sol} / \sqrt{\text{MW}}$$

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

2

2.17 The Relative Solubilities of O₂ and CO₂ in Water

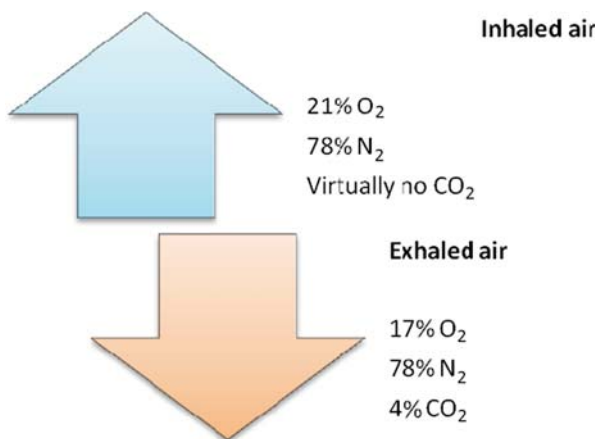
$$\begin{aligned} \text{Relative Rate } \frac{\text{CO}_2}{\text{O}_2} &= \frac{\text{solubility CO}_2}{\sqrt{\text{MW CO}_2}} + \frac{\text{solubility O}_2}{\sqrt{\text{MW O}_2}} \\ &= \frac{592}{\sqrt{44}} + \frac{0244}{\sqrt{32}} \\ &= 20.7/1 \end{aligned}$$

The alveolar-capillary barrier is only 0.2 to 0.5 microns thick. CO₂ diffuses with facility across biological membranes. Thus, in parenchymal lung disease, even though hypoxemia may be present, CO₂ 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 N_2 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.



2.19 The O₂ Cascade

At sea level, the partial pressure of O₂ is: 160 mmHg

$$760\text{mmHg} \times 0.21 = 160\text{ mmHg}$$

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

Within the respiratory tract the partial pressure of O₂ is about 150 mmHg

$$0.21 \times (760 - 47) = 149\text{ mmHg}$$

As it enters the respiratory system, O₂ 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 O₂ (PAO₂) is about 100 mmHg

$$149 - (40/0.8) = 99\text{ mmHg}$$

40 is the normal value of PaCO₂ in mmHg.

CO₂ being easily diffusible across the alveolocapillary membrane, arterial CO₂ (PaCO₂) may be assumed to be the same as alveolar CO₂ (PACO₂).

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, CO₂ production (VCO₂) and the relative consumption of O₂ (VO₂) – causes the partial pressure of O₂ 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.

$$VCO_2 = 250\text{ml of CO}_2 \text{ per minute}$$

$$VO_2 = 300\text{ml of O}_2 \text{ per minute}$$

In the systemic arteries the partial pressure of O₂ (PaO₂) is about 95 mmHg

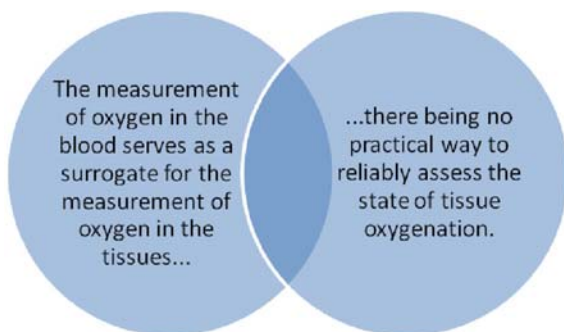
A small amount of deoxygenated blood is added to the systemic arteries (because of a small physiological shunt that normally exists in the body). This is due to unoxygenated blood emptied by certain systemic arteries – the bronchial and thebesian veins – back into the pulmonary veins and the left side 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 PaO₂ may be 5-10 mmHg lower than the PAO₂.

In the mitochondrion the partial pressure of O₂ 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 PaO₂ within mitochondria (to possibly less than 1 mmHg), is required to shift the energy producing pathways towards the much less efficient anaerobic metabolism.

2.20 PaO₂



2

PaO₂ and Age

The normal level of PaO₂ declines with advancing age

PaO₂ in healthy young adults (at sea level)

Average PaO₂: 95 mm Hg
(range 85–100 mmHg)

In a healthy 60 year old (at sea level)

Average PaO₂: 83 mmHg

Predictive equation for the estimation of PaO₂ at (sea level) for a particular age

$$\bullet \text{ PaO}_2 = 109 - 0.43 \times \text{age in years}$$

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).

$$\text{PIO}_2 = \text{FIO}_2 (\text{Pb} - \text{Pw})$$

Where,

PIO_2 = Inspired PO_2

Pb = Barometric pressure

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

$$\text{PAO}_2 = \text{PIO}_2 - 1.2 (\text{PaCO}_2)$$

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,

$$\text{PAO}_2 = [\text{FIO}_2 (\text{Pb} - \text{Pw})] - [1.2 \times \text{PaCO}_2]$$

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

$$\text{PAO}_2 = \text{PIO}_2 - (\text{PACO}_2) \times [\text{FIO}_2 + \{(1 - \text{FIO}_2)/\text{R}\}]$$

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 DO₂) for oxygen is the difference between the partial pressure of O₂ in the alveolus (PAO₂) and the partial pressure of O₂ in the arterial blood (PaO₂).

$$A-aDO_2 = PAO_2 - PaO_2$$

The determinants of PAO₂ are:

The determinants of PaO₂ are:

The fractional concentration of oxygen in the inhaled air (FIO₂)

The partial pressure of CO₂ in the arterial blood (PaCO₂)

Barometric pressure (PB)
PB is constant for a given altitude

Lung pathology
(see 2.27)

Mixed venous O₂ content
(see 00.00)

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

RQ, for all practical purposes, equals 0.8 mathematically.

$$\text{CO}_2/0.8 = 1.2 \times \text{CO}_2.$$

The quotient remains remarkably constant over a wide spectrum of clinical conditions, and therefore, in practice, the above formula usually suffices.

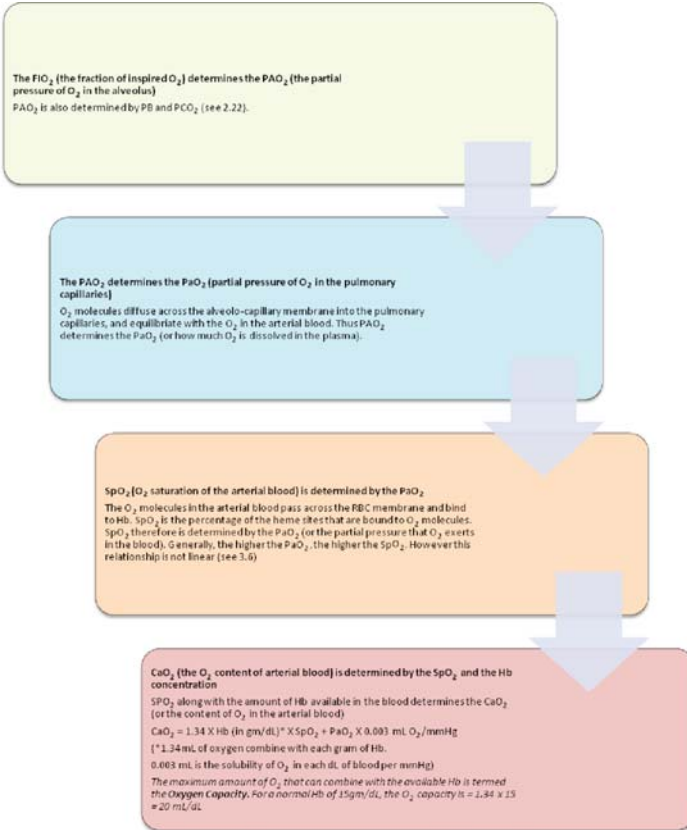
The factor 1.2 may change slightly depending upon the FIO_2 administered, in order to compensate for the N_2 that is washed out with higher fractions of O_2 . At FIO_2 's of 100% the factor approximates 1.0.

$\text{FIO}_2 < 0.6$	$\text{FIO}_2 > 0.6$
<ul style="list-style-type: none"> • Use factor 1.2 i.e., $\text{PAO}_2 = [\text{FIO}_2 (\text{PB} - 47)] - 1.2$ PaCO_2 	<ul style="list-style-type: none"> • Use factor 1.0 i.e., $\text{PAO}_2 = [\text{FIO}_2 (\text{PB} - 47)] - 1.0$ PaCO_2

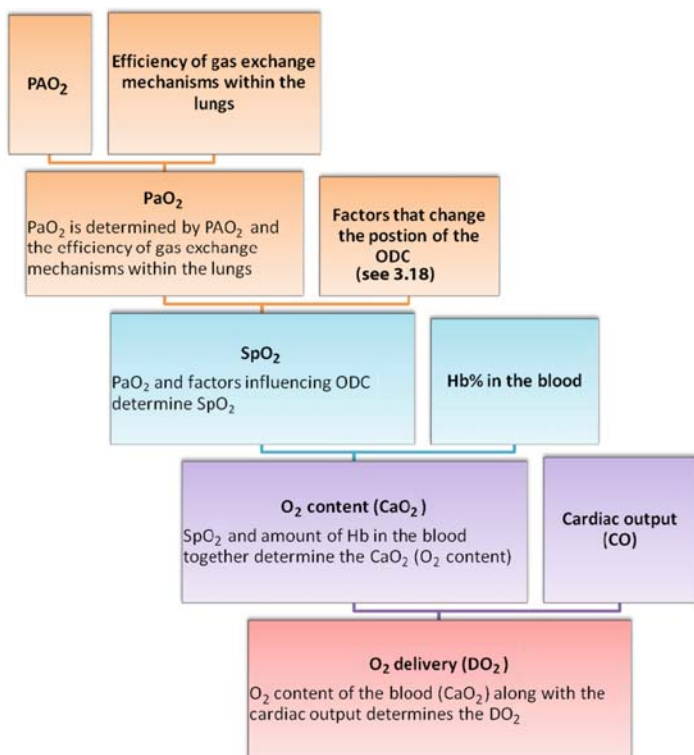
Cinel, D, Markwell, K, Lee, R, Szidon, P. Variability of the respiratory gas exchange Ratio during arterial puncture. *Am Rev Respir Dis* 1991;143:217

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

2

2.24 FIO₂, PAO₂, PaO₂ and CaO₂

2.25 DO_2 , CaO_2 , SpO_2 , PaO_2 and FIO_2



2

2.26 O₂ Content

Recalling that the O₂ content of arterial blood, CaO₂

$$= [(1.34 \times \text{Hb in gm/dL}) \times \text{SpO}_2] \\ + [\text{PaO}_2 \times 0.003 \text{ ml O}_2/\text{mmHg/dL}]$$

Patient A:
Anemia with normoxemia
 PaO₂ 90 mmHg
 Hb 8.5 gm/dL
 SpO₂ 97%

CaO₂ = [1.34 X Hb (in gm/dL) X SpO₂]
 + [PaO₂ X 0.003 mL O₂/mmHg/dL]
 = [(1.34 x 8.5) x 0.97] + [0.003 x 90]
 = 11.32 mL O₂/dL

Patient B:
COPD with chronic hypoxemia
 PaO₂ 58 mmHg
 Hb 16.5 gm/dL
 SpO₂ 88%

CaO₂ = [1.34 X Hb (in gm/dL) X SpO₂] + [PaO₂
 X 0.003 mL O₂/mmHg/dL]
 = [(1.34 x 16.5) x 0.88] + [0.003 x 58]
 = 19.62 mL O₂/dL

As it turns out, the PaO₂ (and therefore the dissolved O₂) contributes little to the CaO₂: one sixty seventh of that carried by the Hb, given that the Hb level is normal).

The principal determinants of CaO₂ are Hb and SpO₂: the latter, of course is determined by PaO₂. Thus, though the PaO₂ does not seemingly contribute much to the CaO₂, it can impact the CaO₂ after all, through its effect upon the SpO₂.

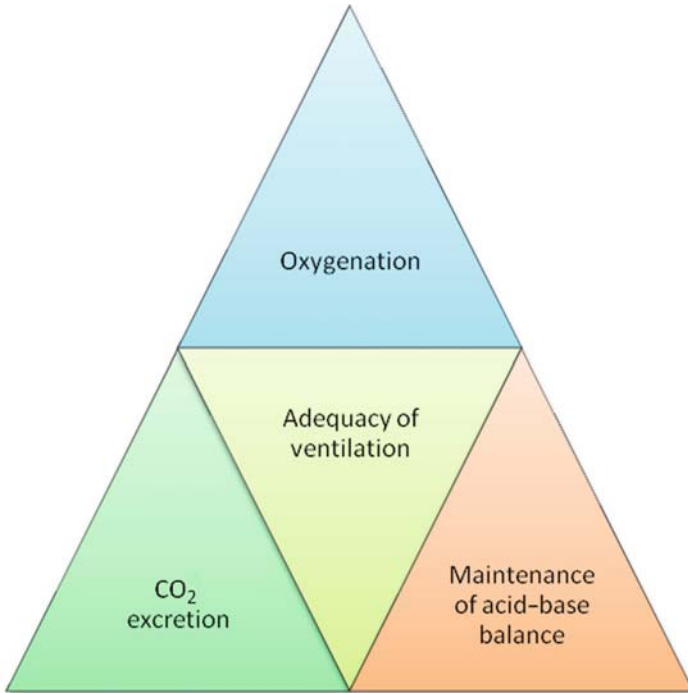
2.27 The Mechanisms of Hypoxemia

Mechanisms of hypoxemia				
<p>V/Q mismatch</p> <p>Decreased ventilation relative to perfusion or vice versa. It is the most commonly encountered mechanism for hypoxemia. (see 00.00)</p>	<p>Shunt</p> <p>An extreme form of V/Q mismatch. Due to lack of regional ventilation, unoxygenated blood returns to the left-heart, increasing the shunt fraction. (see 00.00)</p>	<p>Hypoventilation</p> <p>Decreased bulk flow in and out of the lungs. Hypoventilation leads to a buildup of CO₂ in the blood. Hypercapnia is its defining feature. (see 00.00)</p>	<p>Diffusion defect</p> <p>Hypoxemia caused by a limitation of the diffusion of gas (oxygen) through the alveolar capillary membrane. (see 00.00)</p>	<p>Low barometric pressure</p> <p>A decreased inspired fraction of O₂ would produce the same effect as a low barometric pressure.</p>

2

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:

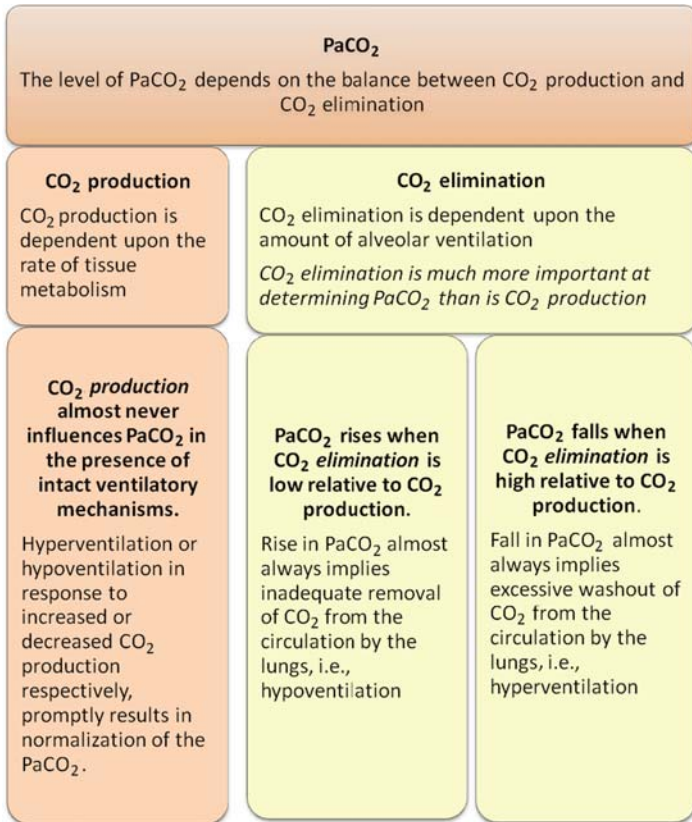
PaCO_2 of > 45 mmHg

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

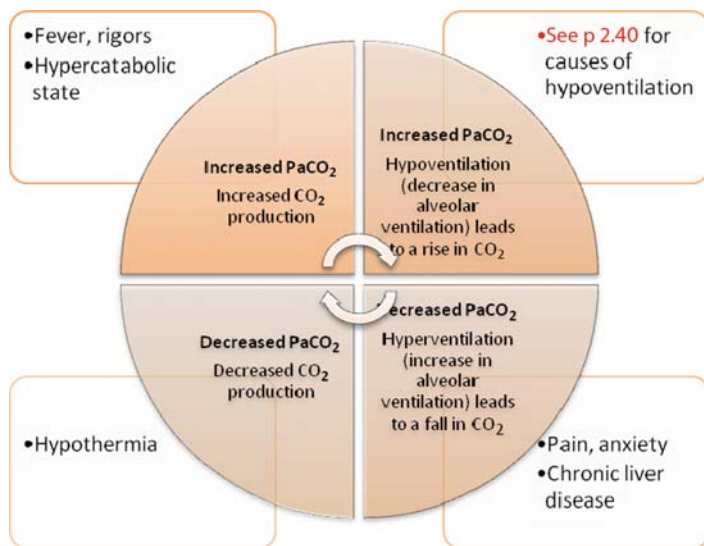
A rise in PaCO_2 of > 5 mmHg above baseline

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

2.30 The Determinants of PaCO₂



2.31 CO₂ Production and Elimination



2

2.32 CO₂ Production and Elimination

The relationship between CO₂ production and elimination can be summarized by the respiratory equation:

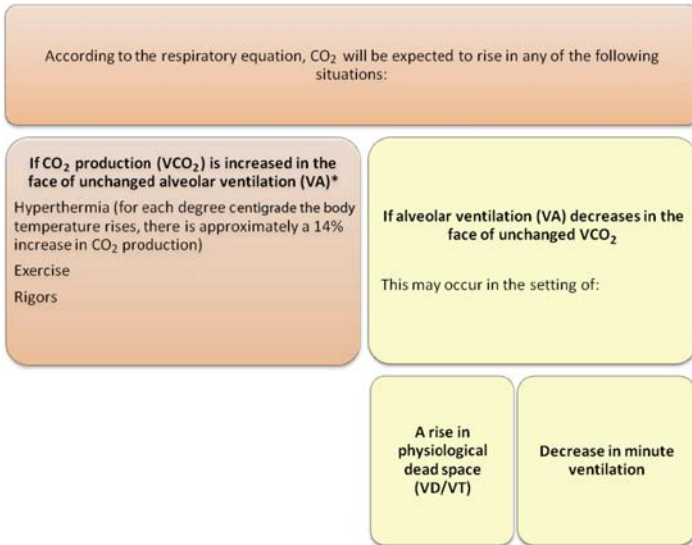
$$PaCO_2 \propto (VCO_2 / VA)$$

Where,

VCO₂ = CO₂ production

VA = alveolar ventilation

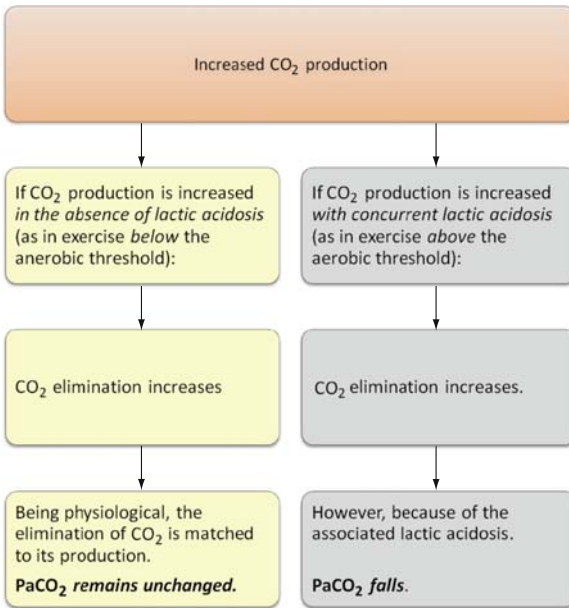
This relationship holds true provided there is no CO₂ in the inhaled gas.



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

2.33 Exercise and PaCO₂

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 PaCO₂ and PaO₂ are maintained within narrow limits.



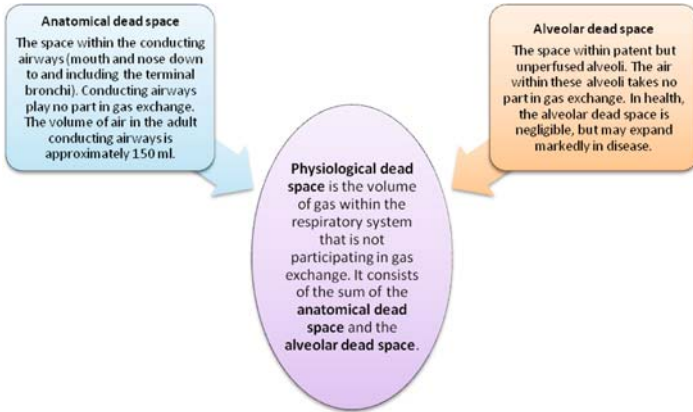
Wasserman, K, Whipp, BJ. Exercise physiology in health and disease. Am Rev Respir Dis 1975; 112:219

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

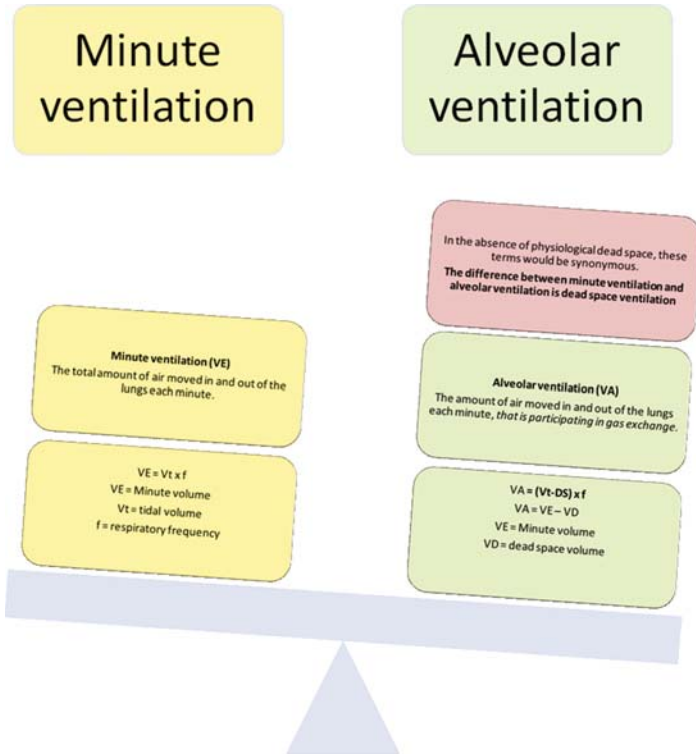
Casaburi, R, Daly, J, Hansen, JE, et al. Abrupt changes in mixed venous blood gas composition after the onset of exercise. J Appl Physiol 1989; 67:1106

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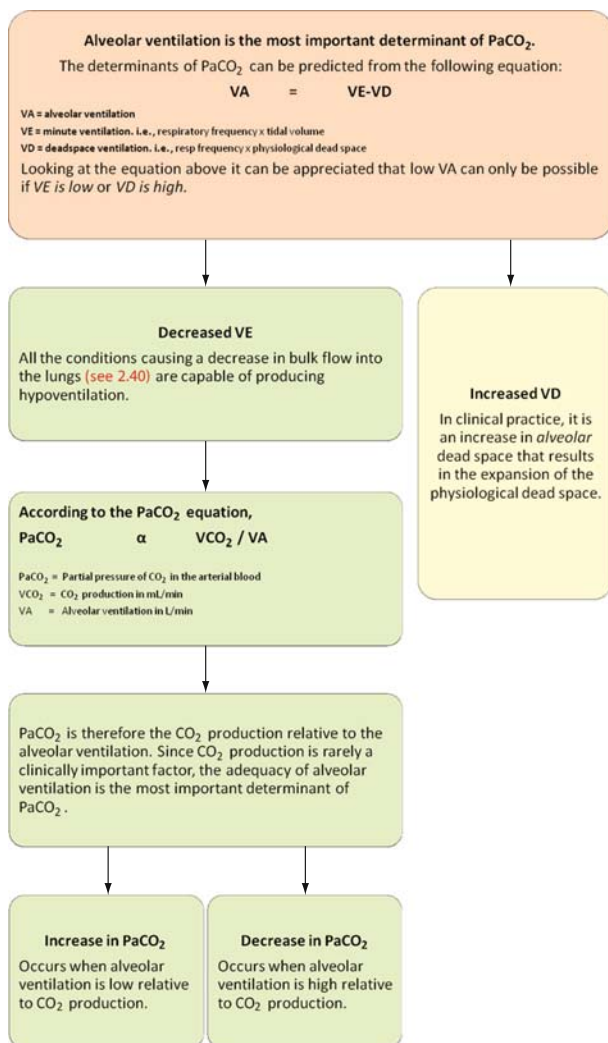
2.34 Dead Space



2.35 Minute Ventilation and Alveolar Ventilation



2.36 The Determinants of PaCO₂



2.37 Alveolar Ventilation in Health and Disease

In health:	In lung disease:
Nearly all alveoli participate in gas exchange. Physiological dead space is insignificant.	A large number of alveoli do not participate in gas exchange. Physiological dead space is substantial.
$VA = VE - VD$ Since VD is insignificant, VE practically equals VA	$VA = VE - VD$ Since VD is substantial, VA is substantially lower than VE
Minute ventilation roughly approximates the alveolar ventilation	Minute ventilation does not equate with alveolar ventilation. Alveolar ventilation may be significantly less than minute ventilation

2

2.38 The Pathogenesis of Hypercarbia (Increased PaCO₂)

To summarize,
The conditions in which PaCO₂ can be increased are:

Increased proportion of CO₂ in inspired air

Rebreathing of air
Laparoscopic insufflation of air into the body

Increased production of CO₂, e.g.:

Hypercatabolic states: sepsis, malignant hyperthermia, etc.

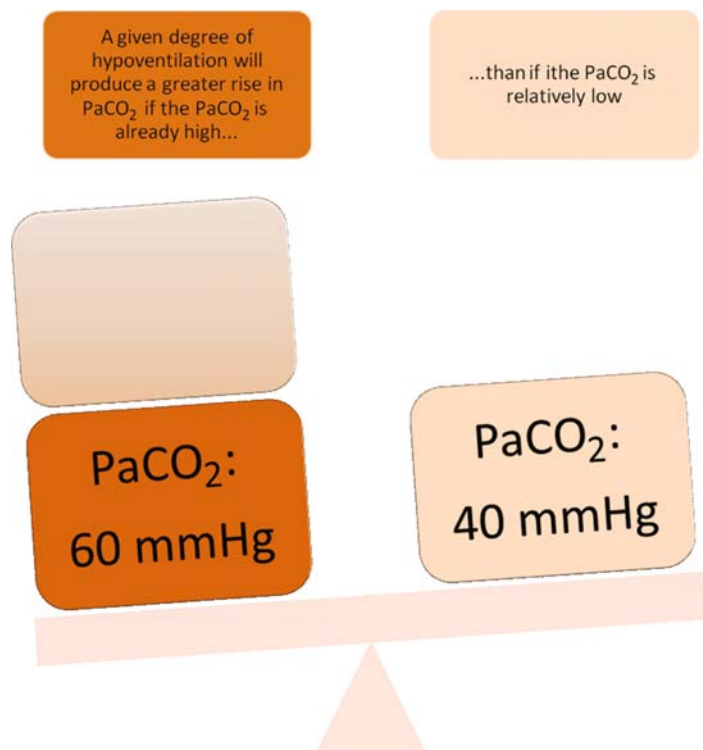
Decreased alveolar ventilation

This is by far the most important cause.

Increased physiological dead space

This usually occurs as a result of an increase in alveolar dead space

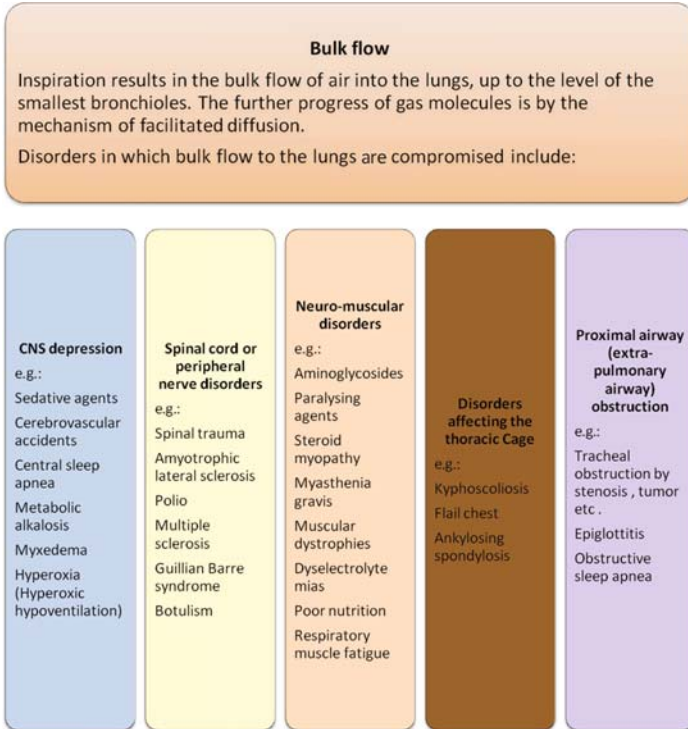
2.39 Hypoventilation and the Level of PaCO₂



2

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

Hypoventilation (Type 2 respiratory failure)

Hypoventilation may exist as an isolated abnormality, or there may be an additional mechanism of hypoxemia accompanying it

'Pure' hypoventilation

Here the gas-exchange mechanism of the lungs is intact, and hypoventilation (i.e., reduction of bulk airflow) is the sole cause for the hypoxemia

Hypoventilation associated with an additional mechanism of hypoxemia

Rise in PaCO_2 approximately matches the fall in PaO_2 .

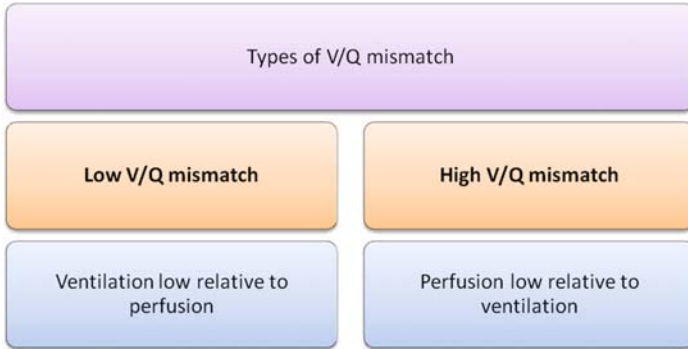
The PaO_2 falls about 1.25 mmHg for every 1 mmHg rise in PaCO_2

A-a DO_2 is normal.

Fall in PaO_2 is disproportionate to the rise in PaCO_2

A-a DO_2 is widened

2

2.42 Types of V/Q Mismatch

2.43 V/Q Mismatch – a Hypothetical Model

Assume the normal minute ventilation : $2v$.
Assume the normal perfusion : $2q$

Right lung accounts for half of the total ventilation and half of the total perfusion
Ventilation to the right lung = v
Perfusion to the right lung = q

Left lung account for half of the total ventilation half of the total perfusion.
Ventilation to the left lung = v
Perfusion to the left lung = q

Assume that the ventilation of the right lung is artificially reduced to zero. Assume that the perfusion of the right lung is doubled
Ventilation = 0
Perfusion = $2q$

Assume that the ventilation of the left lung is doubled. Assume that the perfusion of the left lung is reduced to zero.
Ventilation = $2v$
Perfusion = 0

Therefore, the total minute ventilation to *both* lungs:
= $2v$ (which is normal).
And the total perfusion to *both* lungs:
= $2q$ (this is normal too).

Yet *there is complete mismatching of ventilation to perfusion*: none of the air ventilating lungs comes into contact with the blood perfusing it, and life is not possible on account of hypoxemia.

Right lung:
Ventilation = 0
Perfusion = $2q$

Left lung:
Ventilation = $2v$
Perfusion = zero

V/Q ratio = $0/2q$ = zero

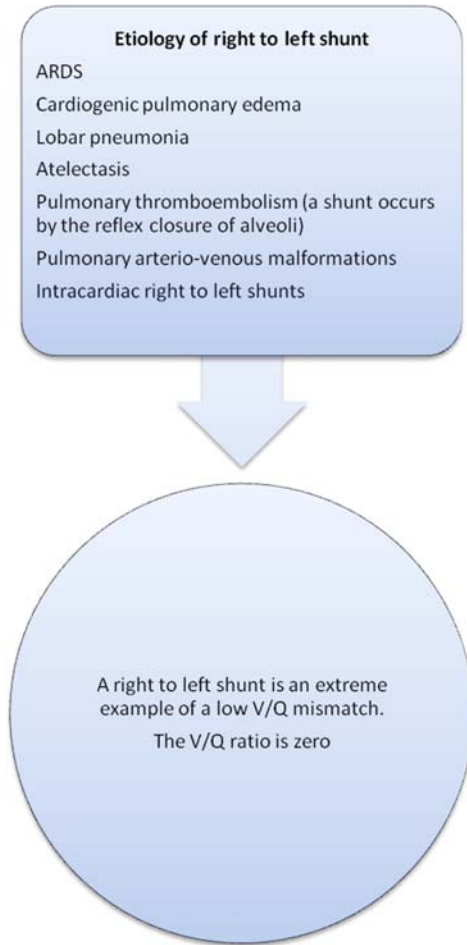
V/Q ratio = $2v/0$ = infinity

This is an example of an extreme low V/Q mismatch, i.e., the right to left shunt.

This is an example of an extreme high V/Q mismatch, i.e. dead space ventilation.

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

The administration of 100% O₂ enables differentiation between a low V/Q mismatch and shunt

Low V/Q mismatch:

Ventilation reduced relative to perfusion

Supplemental O₂ (FIO₂ 1.0) eventually reaches the poorly ventilated alveoli

PaO₂ rises

Shunt:

No ventilation, intact perfusion

Supplemental O₂ (FIO₂ 1.0) cannot reach the obliterated alveoli

PaO₂ does not rise

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.

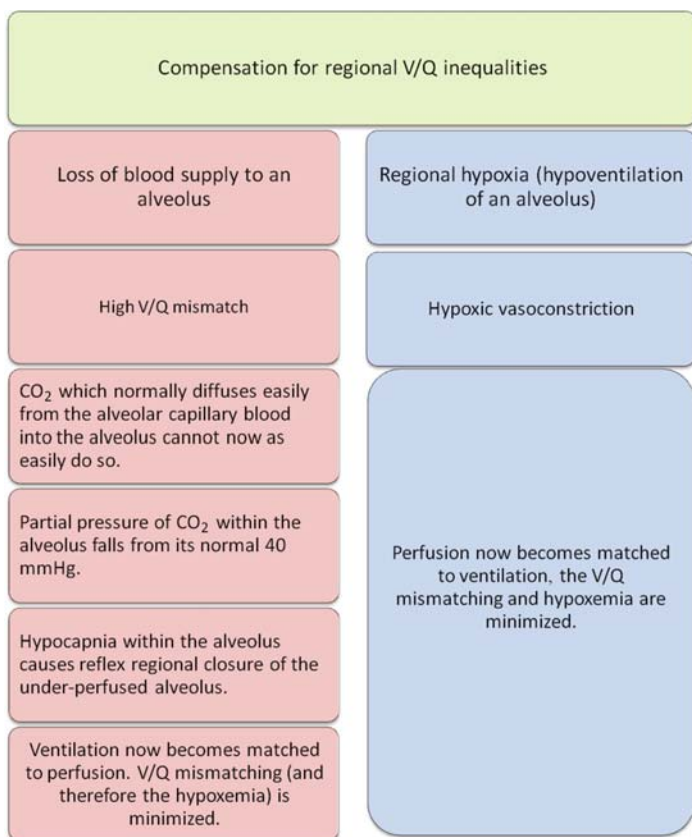
- The PaO_2 is obtained from the ABG
- The PAO_2 cannot be directly measured at the bedside and needs to be calculated from the modified alveolar air equation (see 2.21)
- PaO_2/PAO_2 ratio offers better accuracy over a broader range of FIO_2 than the PF ratio.

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

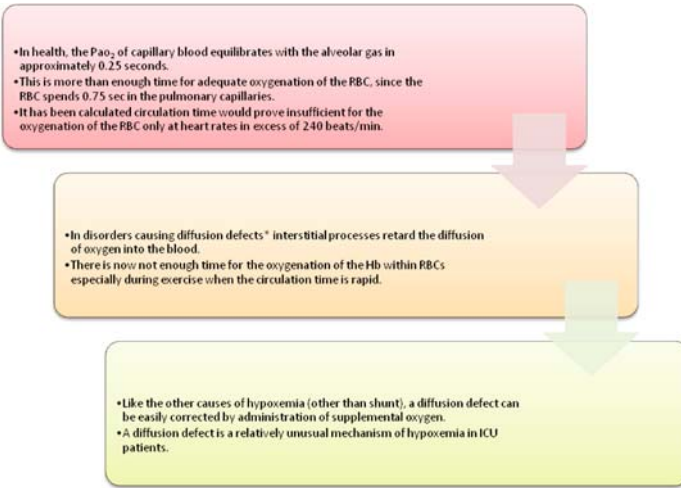
Covelli, HD, Nesson, VJ, Tuttle, WK. Oxygen derived variables in acute respiratory failure. *Crit Care Med* 1983; 8:646

2.47 Compensation for Regional V/Q Inequalities



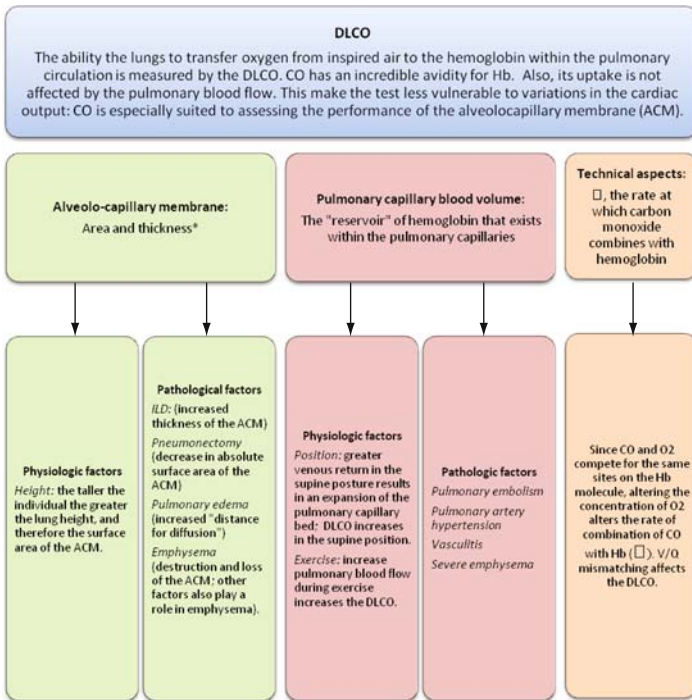
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2.48 Defects of Diffusion



* 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

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 circulation than earlier thought.

2.50 Alveolo-Arterial Diffusion of Oxygen (A-aDO₂)

The alveolo-arterial diffusion of oxygen (A-a DO₂)

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 DO₂ is the difference between the alveolar O₂ tension (PAO₂) and the arterial oxygen tension (PaO₂).

• In order to compute the A-a DO₂ it is necessary to calculate the PAO₂ (from the modified alveolar gas equation):

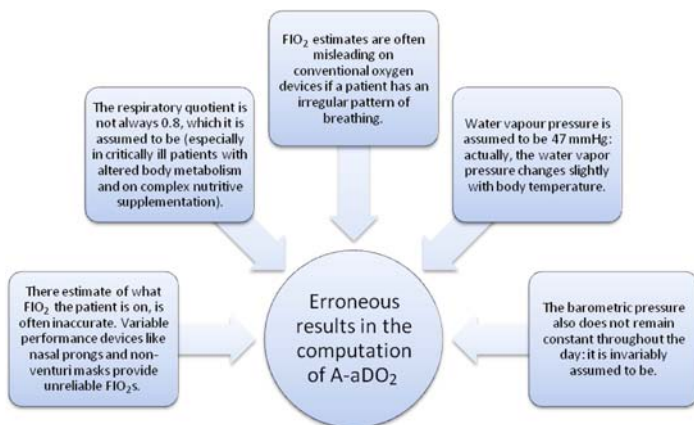
$$PAO_2 = FIO_2 (Pb - Pw) - PaCO_2 / R \quad \text{where,}$$

- PaO₂ = alveolar oxygen tension
- FIO₂ = fraction of inspired oxygen
- Pb = atmospheric pressure in mmHg
- Pw = partial pressure of water (47 mmHg at body temperature)
- PaCO₂ = arterial CO₂ tension
- R = respiratory quotient

Mellemaard, 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-aDO₂



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

2

2.52 Timing the ABG**Healthy lungs**

- There is rapid mixing of inhaled air, between the different regions of the lung.
- Blood gases drawn after 5–7 minutes of any change in FIO_2 are acceptable.

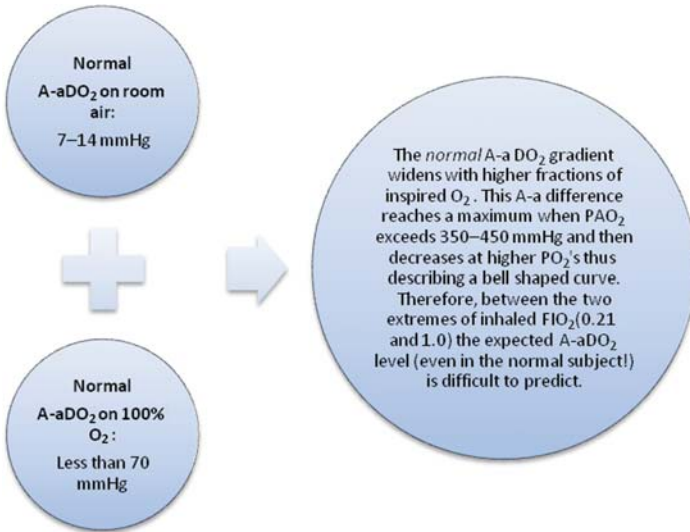
Presence of significant lung disease

- There is slow mixing of alveolar gas because of inhomogeneity of ventilation between diseased and healthy alveolar units.
- Blood gases should ideally be drawn after 20–25 min of any change in FIO_2 to enable equilibration with those lung areas having low V/Q ratios.

2.53 A-aDO₂ on Intermediate Levels of FIO₂

The A-a DO₂ normally increases with age. The following formula predicts the A-aDO₂ for a given age:

$$A - a \text{ DO}_2 = 2.5 + (0.25 \times \text{Age in years})$$

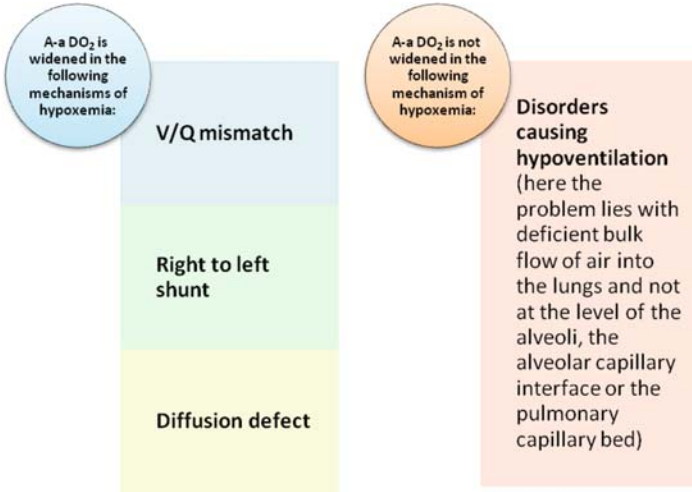


Kanber, GJ, King, FW, Eshchar, YR, Sharp, JT. The alveolar-arterial oxygen gradient in young and elderly men during air and oxygen breathing. *Am Rev Respir Dis* 1968; 97:376

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-aDO₂



Chapter 3

The Noninvasive Monitoring of Blood Gases

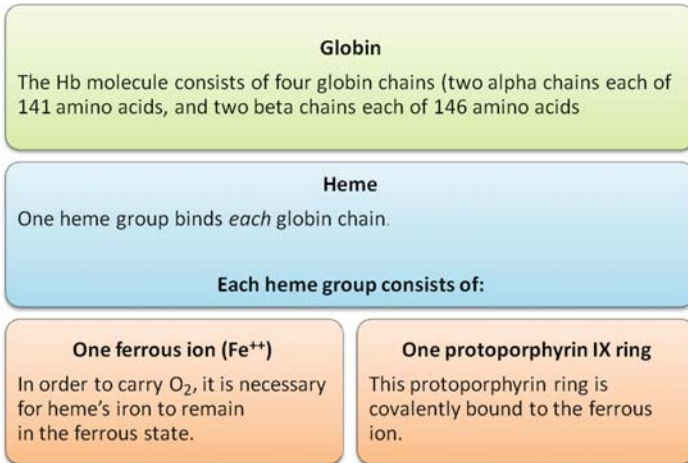
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3.1 The Structure of Hemoglobin

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

3

Hemoglobin serves several important functions:

O₂ carriage

This is of course the most important function of hemoglobin (See 3.3)

CO₂ carriage

Only about 5% of all the CO₂ transported in the blood is in the form of carbamino compounds (viz, bound to hemoglobin).

Another 5% of CO₂ is carried dissolved in plasma.

The bulk of the CO₂, however, is carried in the form of bicarbonate.

Regulation of vasomotor tone

Nitric oxide (NO) is capable of reacting with the cysteine residue at position 93 of the β chain of hemoglobin. The resulting nitrosothiol, S-nitrosylated hemoglobin is a vasodilator. The unique and recently recognized vasodilator property of hemoglobin is dependent on its complex and ill understood reactions with NO.

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

Deoxygenated Hemoglobin

Deoxygenated hemoglobin exists in a tense (taut) configuration because of electrostatic bonds between its beta globin chains. The hemoglobin molecule has helical twists. In the non-helical sections the polypeptide chain folds upon itself, creating clefts within which the four heme groups lie at equidistant intervals.

The attachment of the first O₂ molecule

In its taut state, deoxygenated hemoglobin has little affinity for O₂. The attachment of the first O₂ molecule to one of the globin chains generates chemical and mechanical stresses resulting in the severing of electrostatic bonds. This allows the hemoglobin molecule to unfold slightly.

The attachment of the second O₂ molecule

As the hemoglobin molecule relaxes and unfolds it exposes the other O₂ binding sites within its clefts; this facilitates the addition of another molecule of O₂ to the hemoglobin, more rapidly than the first.

The attachment of the third and fourth O₂ molecules

The binding of the second molecule of O₂ results in further relaxation of the coils of the hemoglobin molecule, accelerating the uptake of the third and the fourth O₂ molecules.

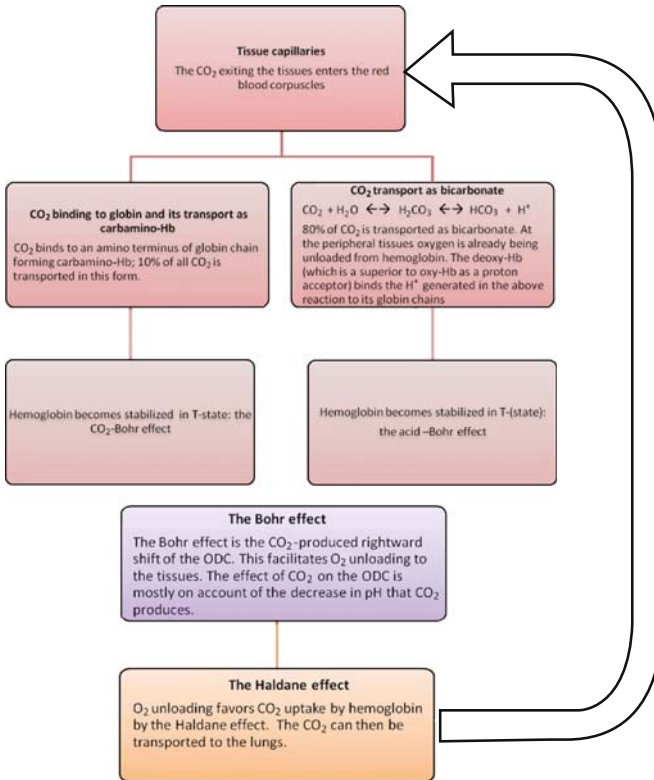
The co-operativity among its binding sites that results in the accelerated uptake of O₂ gives the oxy-hemoglobin dissociation curve its characteristic sigmoid shape.

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

3



Bohr, C, Hasselbalch, K, Krogh, A. Ueber einen in biologischer Beziehung wichtigen Einfluss, den die Kohlen- sauerespannung des Blutes auf dessen Sauerstoffbindung 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

3

Oxygenated Hb (syn: OxyHb)

Each Hb molecule has 4 heme sites to each of which an O₂ molecule can bind. The percentage of O₂ binding heme site that are bound to O₂ is the O₂ saturation (SpO₂) of the blood. In other words SpO₂ is the number of heme sites occupied by O₂ of every 100 heme sites.

The SpO₂ (as read out on the pulse oximeter (represents) the Oxy-Hb

Non - oxygenated Hb

The percentage of heme groups that are not bound to O₂ molecules.

Non-oxygenated Hb includes:

Dexoxy-Hb (syn: reduced) Hb

Percentage of heme groups that are not bound to O₂.

Reduced Hb% = 100% - [SpO₂ + MetHb + COHb] %*

Carboxy-Hb

Percentage of heme groups in the form of Carboxy-Hb

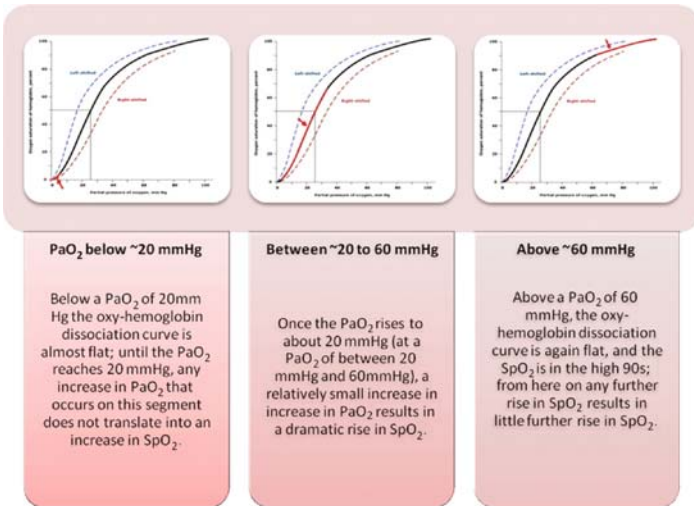
Met-Hb

Percentage of heme groups in the form of Met-Hb

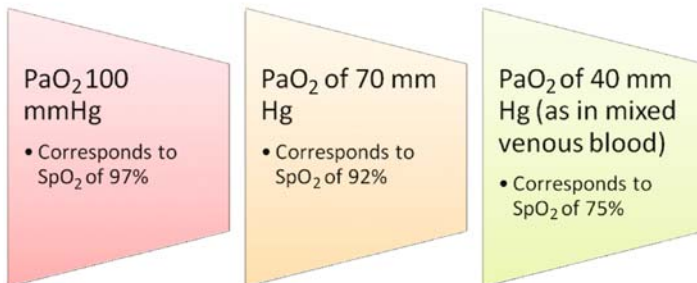
See Co-oximetry (3.22)

3.6 The Oxyhemoglobin Dissociation Curve

3



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-online, Chest.

3.7 Continuous Invasive O₂ Monitoring

Although direct measurement of arterial O₂ 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

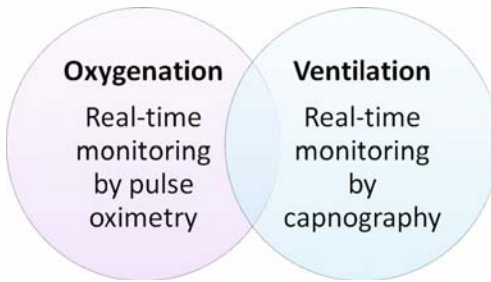
- Obviates the need for frequent arterial punctures
- Generally used in unstable clinical situations
- However, continuous ABG sampling is *also associated with significant complications* as with intermittent sampling

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

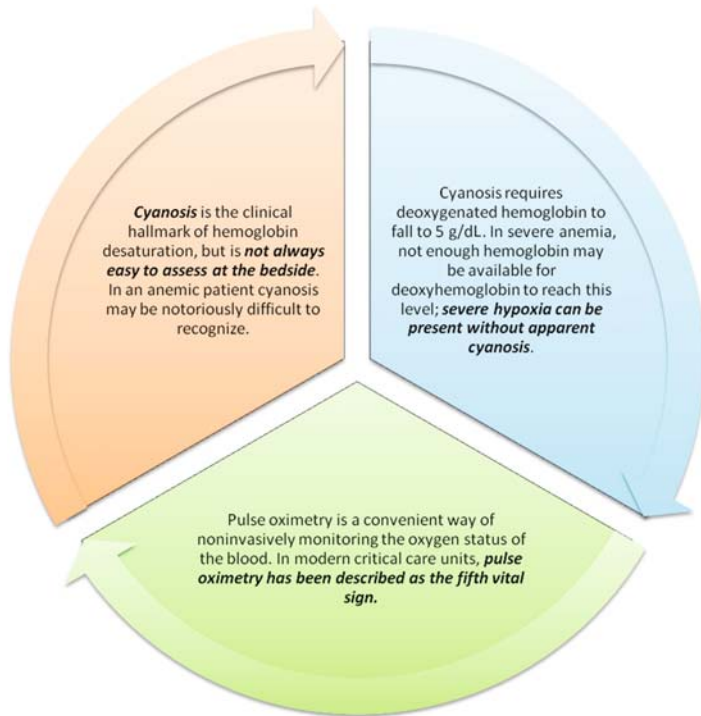
3



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 PO₂ sensor in adult critically ill patients. *Crit Care Med* 1987; 15:491

3.9 SpO₂ and Pulse Oximetry



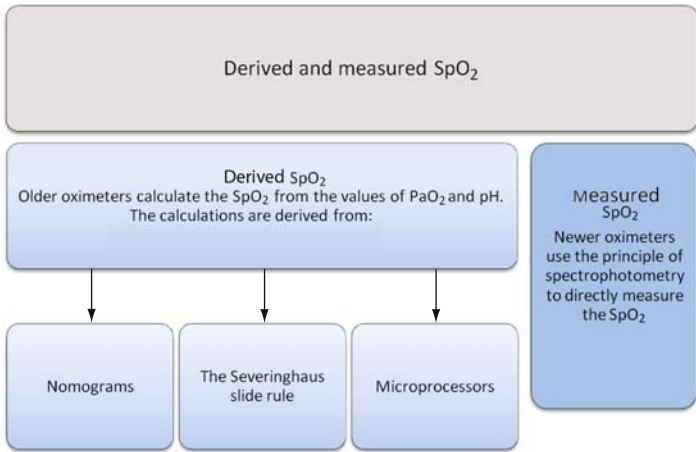
Comroe, JH Jr, Botelho, S. The unreliability of cyanosis in the recognition of arterial hypoxemia. *Am J Med Sci* 1947; 214:1

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 SpO₂

3



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

3.11 Principles of Pulse Oximetry

Pulse oximetry is based upon two fundamental principles

The principle of spectrophotometry

Used for measuring the percentages of oxyhemoglobin and deoxyhemoglobin in the blood

The principle of optical plethysmography

Used to display the amplitude of pulse and the heart rate

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.

Two photodiodes emit light phasically at several hundred times per second, one at 660 nm (in the red band of the spectrum) and the other at 940 nm (in the infra-red band of the spectrum).

Oxyhemoglobin

Light emitted at 660 nm is better absorbed by saturated (oxygenated) hemoglobin

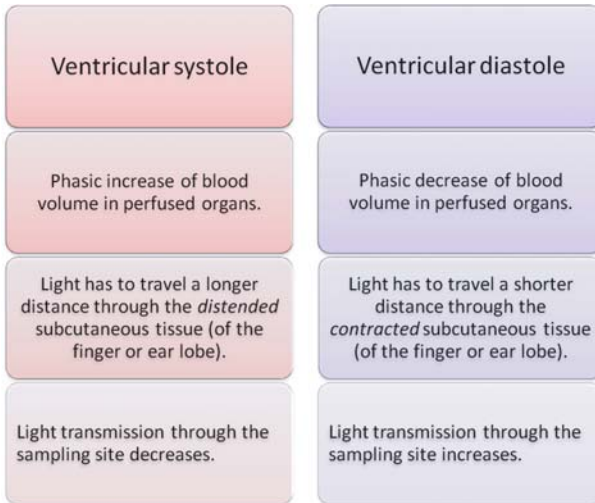
Deoxyhemoglobin

Light emitted at 940 nm is better absorbed by reduced (deoxygenated) hemoglobin

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.

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.



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

3

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

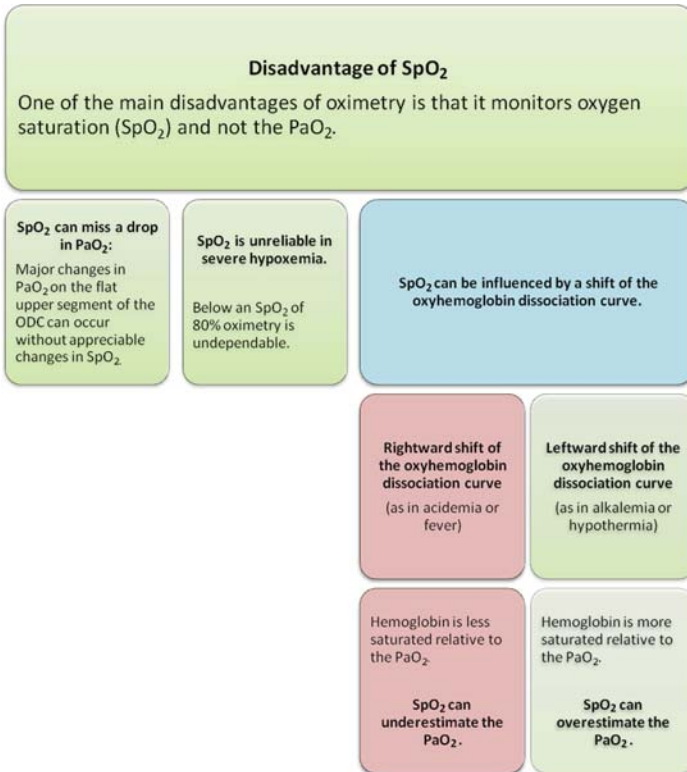
Transmission pulse oximeters

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.

3.15 Pulse Oximetry and PaO₂

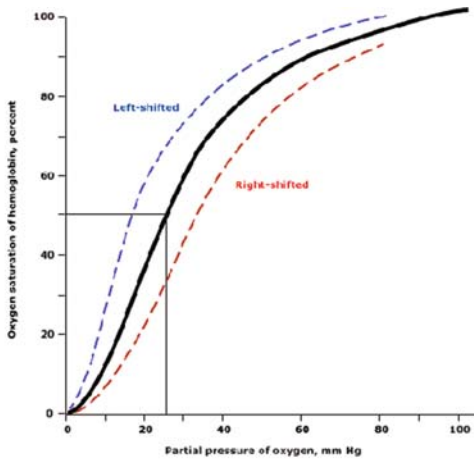


Stoneham, MD. Uses and limitations of pulse oximetry. *Br J Hosp Med* 1995; 54:35

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

3.16 The P_{50}

3



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

Implications of a leftward shifted ODC:

Tighter binding of O_2 to Hb.

At the tissues

With a left shifted ODC, SpO_2 is higher, but less of the O_2 (which is tightly bound to the Hb) is released to the tissues.

Implications of a rightward shifted ODC:

Relatively loose binding of O_2 to Hb.

At the tissues

With a right shifted ODC, although the SpO_2 is lower, more of the O_2 (which is relatively loosely bound to the Hb) is released to the tissues.

3.18 Conditions that Shift the ODC

3

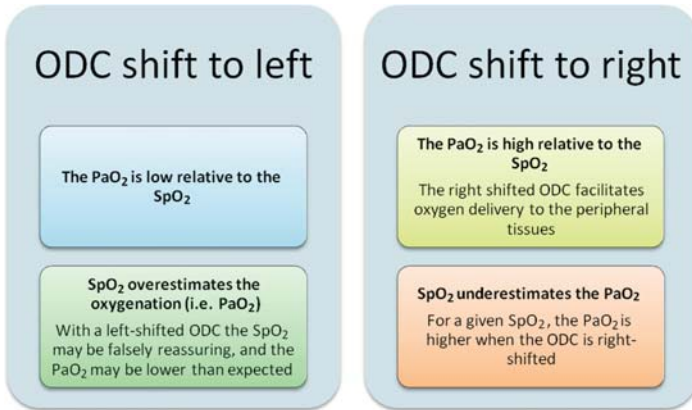
Leftward shift of the ODC occurs in the following conditions:

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

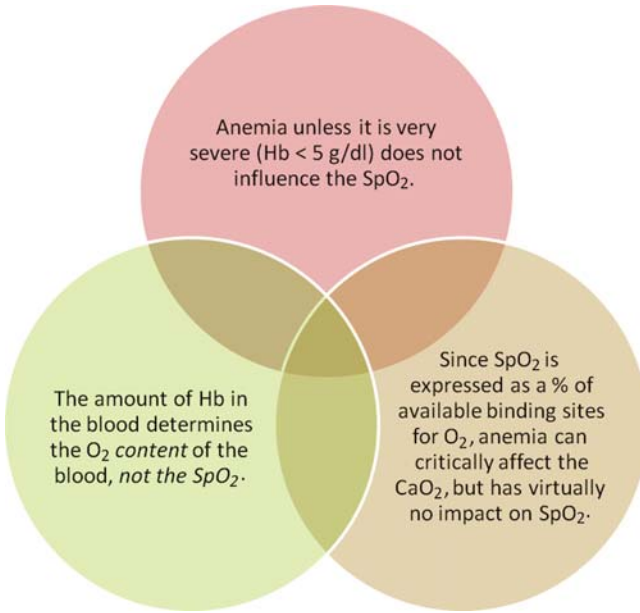


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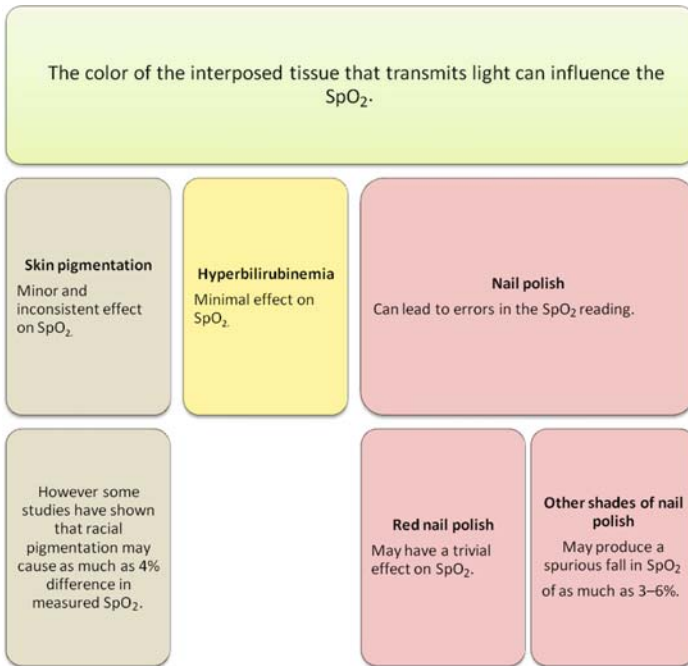
The SpO_2 therefore must be interpreted in the light of the position of the ODC.

3.20 SpO₂ and Anemia

3



3.21 SpO₂ 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 Res 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 SpO₂ and Abnormal Forms of Hemoglobin

3

Abnormal forms hemoglobins can have different absorption spectra and so lead to erroneous oximetric readings.

Carboxyhemoglobin (CO-Hb)

CO-Hb has a similar absorption spectrum to oxyhemoglobin.

Methemoglobin (Met-Hb)

Met-Hb absorbs light at two wavelengths.

Hemoglobin-S in Sickle-cell anemia:

Can lead to spuriously high or low SpO₂ values.

Normal saturations can be displayed in the presence of severe hypoxia.

Because of this property, Met-Hb has a complex effect on SpO₂:
SpO₂ tends to drift towards 85%.

CO-oximetry:

CO-oximetry independently displays carbon monoxide saturations, and helps reliably monitor CO-Hb.

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

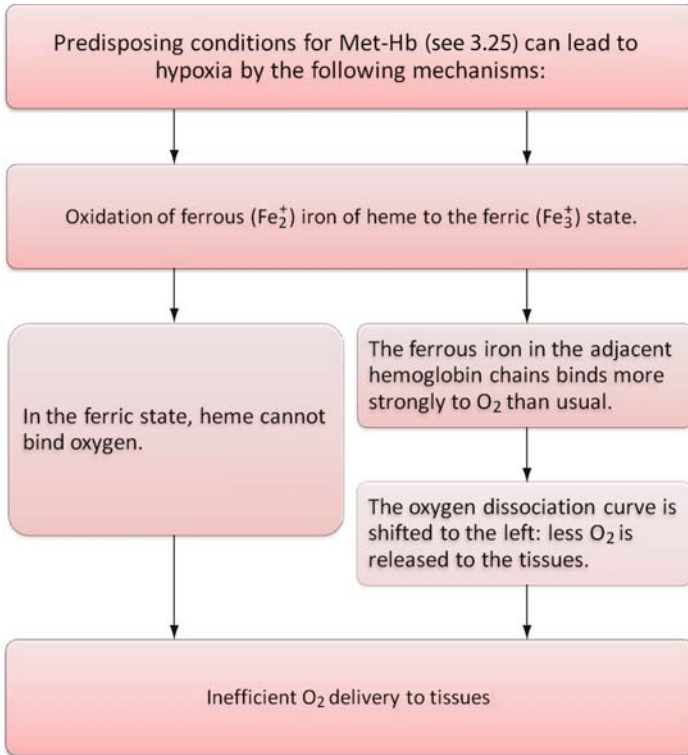
Met-Hb, as opposed to deoxy Hb carries its iron in the ferric form, in which state it is unable to bind O_2 . The amount of Hb that exists as Met-Hb cannot participate in O_2 transport.

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

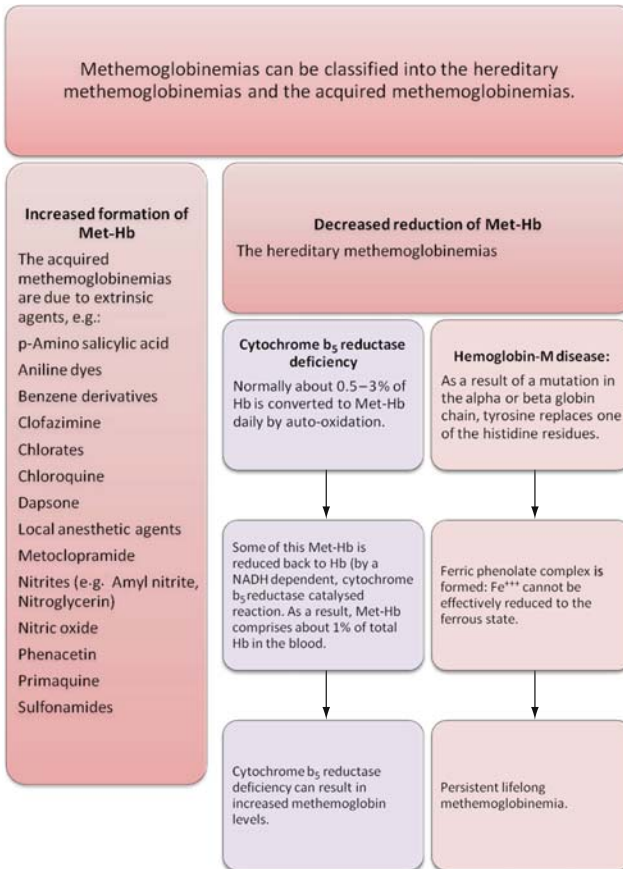
Curry S. Methemoglobinemia. *Ann Emerg Med* 1982; 11:214–221

3.24 Methemoglobinemia: Mechanisms of Hypoxia

3



3.25 Methemoglobinemias: Classification



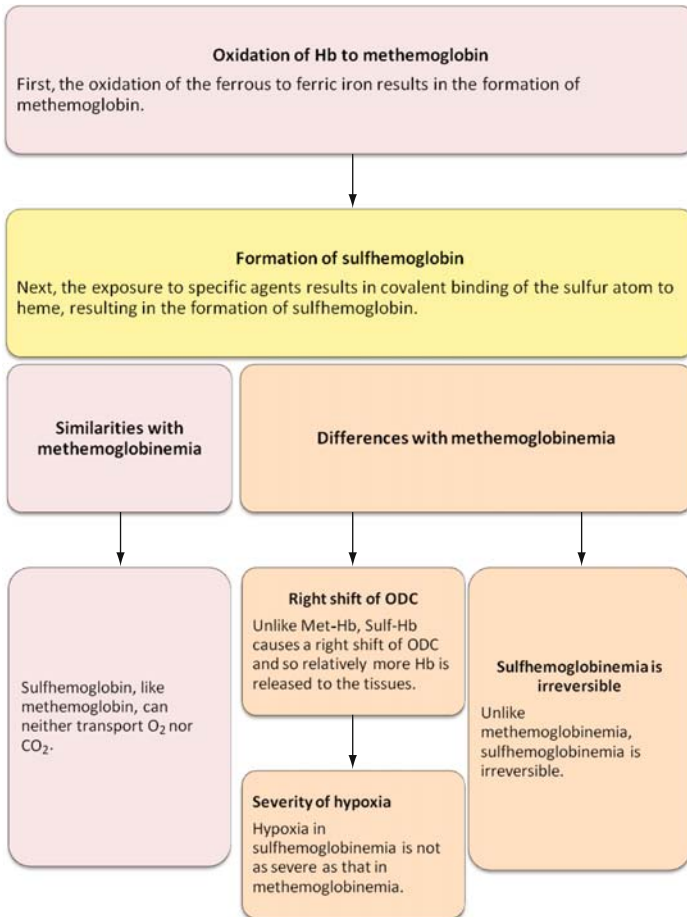
Curry, S. Methemoglobinemia. *Ann Emerg Med* 1982; 11:214–221

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

3

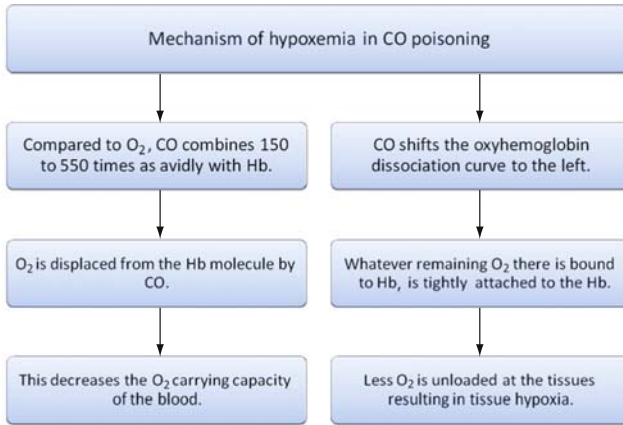


Oximeters that measure met-hb can erroneously read sulf-hb as met-hb

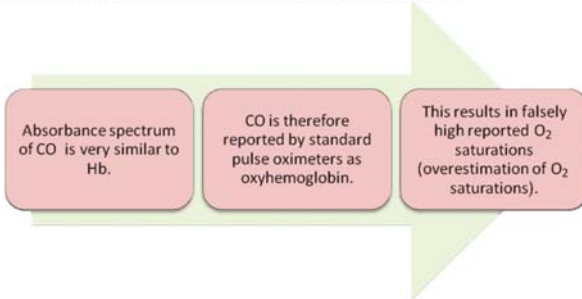
Park, CM, Nagel, RL. Sulfhemoglobinemia. N Engl J Med 1984; 310:1579–1584

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.



At levels above 50%, COHb is capable of causing death.



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

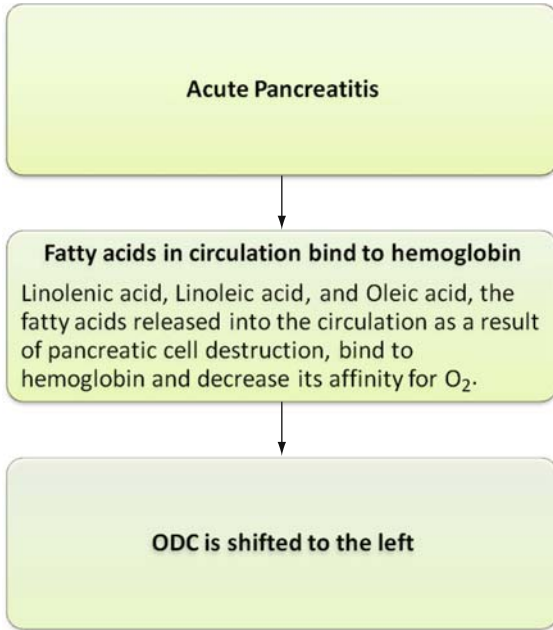
Weaver, LK. Carbon monoxide poisoning. *Crit Care Clin* 1999; 15:297.

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

3.28 Acute Pancreatitis

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

3



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

3.29 Saturation Gap

3

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

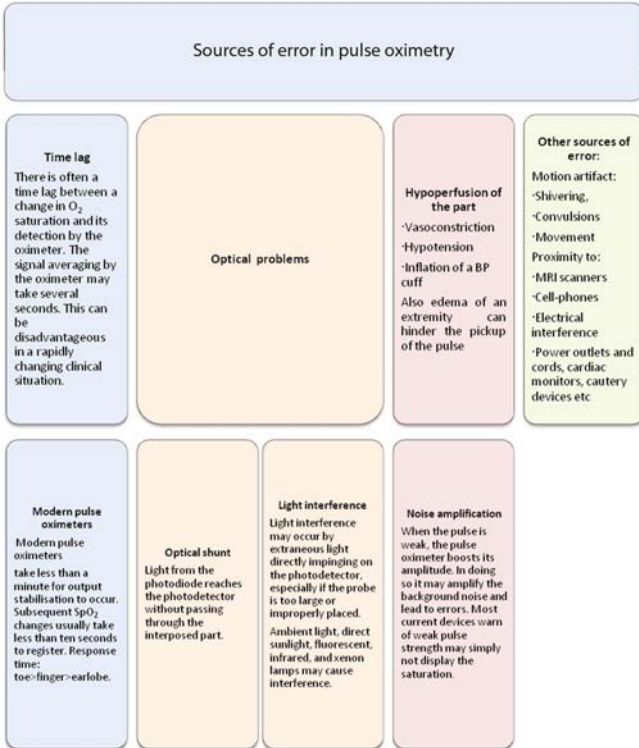
Eisenkraft, JB. Pulse oximeter desaturation due to methaemoglobinemia. *Anaesthesiology* 1988; 68:279–282

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 SpO₂

3



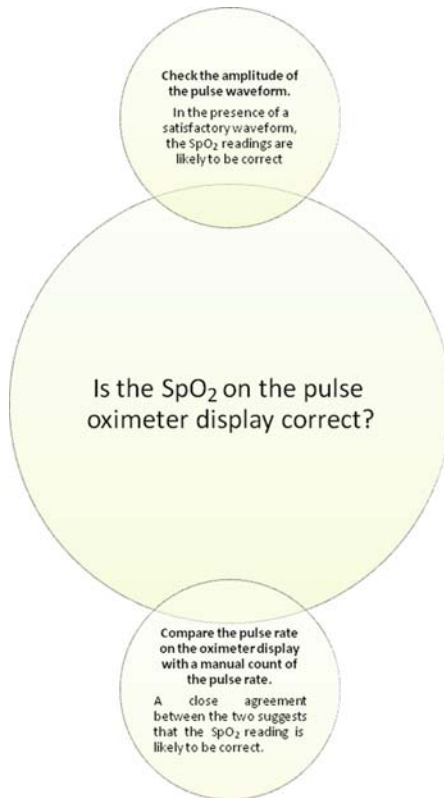
Gehring, H, Hornberger, C, Matz, H, et al. The effects of motion artifact and low perfusion on the performance of a new generation of pulse oximeters in volunteers undergoing hypoxemia. *Respir Care* 2002; 47:48

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

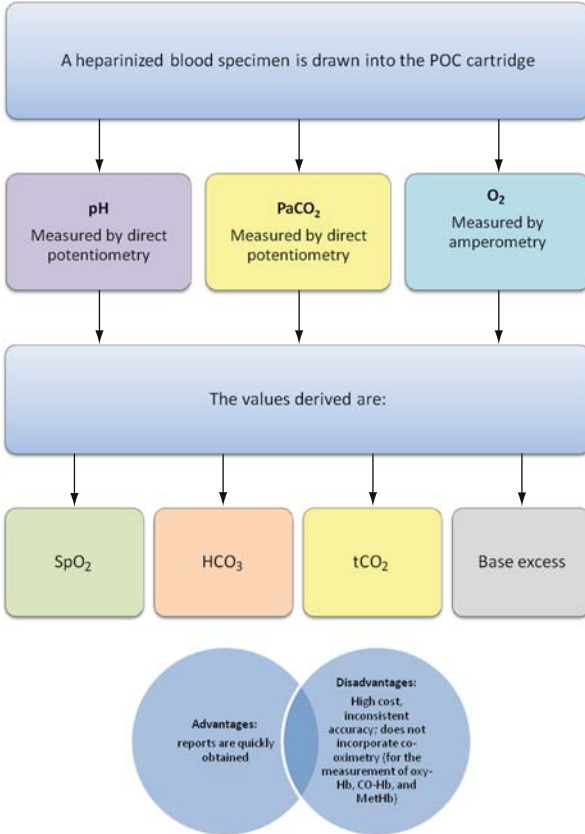


Gehring, H, Hornberger, C, Matz, H, et al. The effects of motion artifact and low perfusion on the performance of a new generation of pulse oximeters in volunteers undergoing hypoxemia. *Respir Care* 2002; 47:48

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

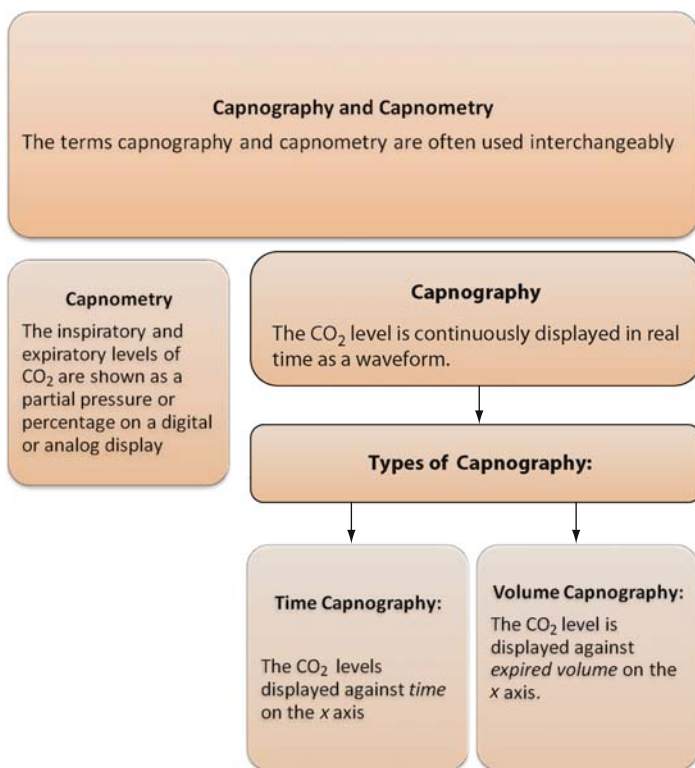
3.32 Point of Care (POC) Cartridges

Lately, handheld *Point of Care* (POC) cartridges are being used for the bedside measurement of the pH, PaCO₂, and PaO₂.



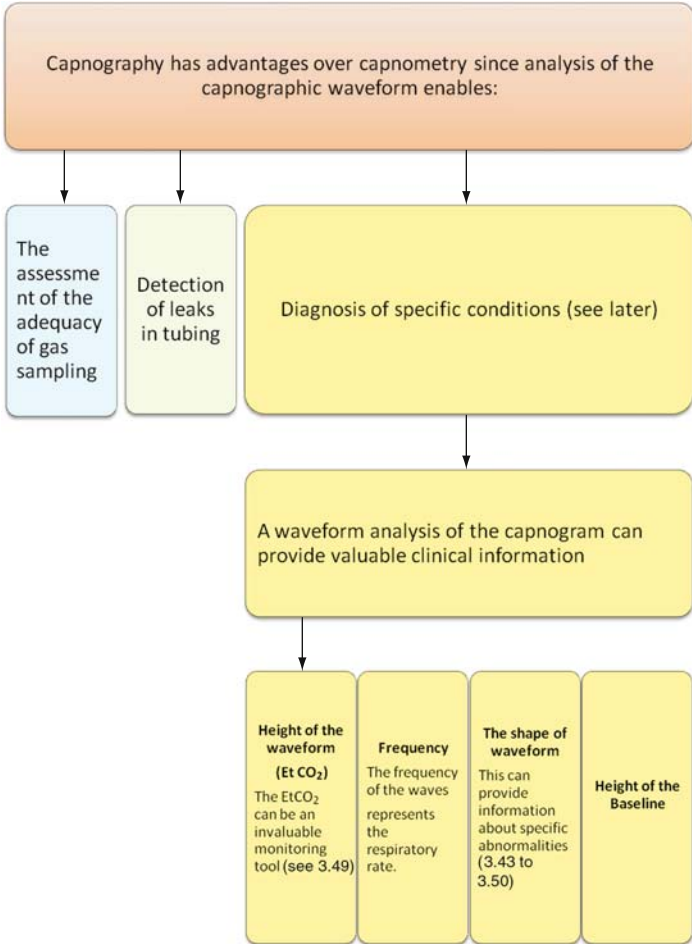
Canham, EM. Interpretation of arterial blood gases. In: Parsons, PE, Weiner-Kronish, JP, eds. *Critical care secrets*. 3rd ed. Philadelphia, Hanley and Belfus, Inc, 21–24, 2003

3.33 Capnography and Capnometry

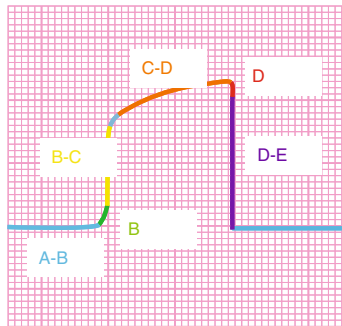
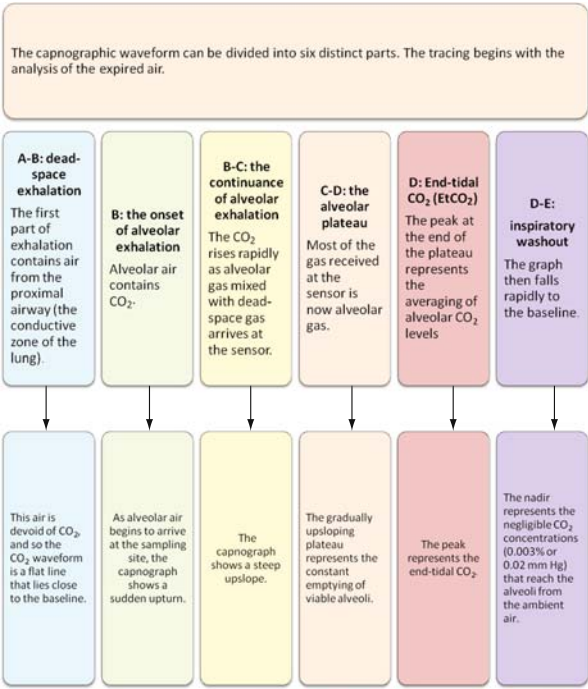


3.34 Advantages of Capnography

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



3.36 Main-stream and Side-stream Capnometers

3

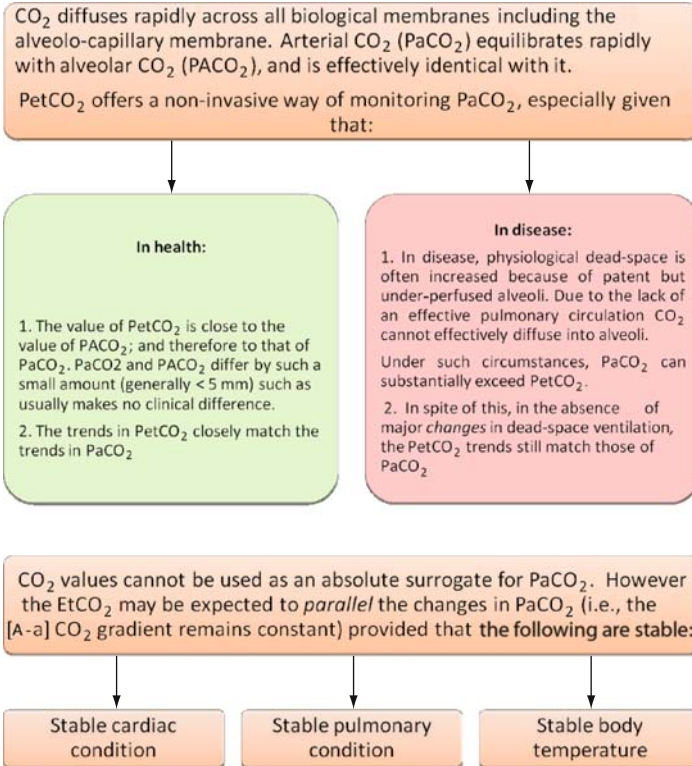
MAINSTREAM	SIDESTREAM
<ul style="list-style-type: none"> •The main unit incorporating a CO₂ sensor is itself directly attached to a T- adapter interposed between the ET and the patient-circuit. •There is no sampling tube. Sensor windows are prone to clogging by secretions, aerosols, or water droplets. •Difficult to use in patients undergoing prone ventilation. •Unaffected by changes in water vapor pressure. The temperature within the mainstream sensors is maintained at around 39°C to prevent condensation. •No time lag. •Cannot be used in the absence of an artificial airway. •Bulky – newer models less so •Can increase circuit dead-space and so elevate PaCO₂ •Sterilization is difficult 	<ul style="list-style-type: none"> •A relatively long sampling tube connected to the piece draws away the gas sample to a CO₂ 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. •Sampling tube prone to becoming obstructed as secretion can be sucked in by the rapid aspiration rate. •Relatively easy to connect in prone position •Affected by changes in water vapor pressure. •Time lag in display, owing to the relatively long distance of the sensor from the patient's airway. •Can be used even in the absence of an artificial airway. •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 μm) which more closely matches the absorption spectrum for CO₂.

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 PetCO₂-a Surrogate for PaCO₂



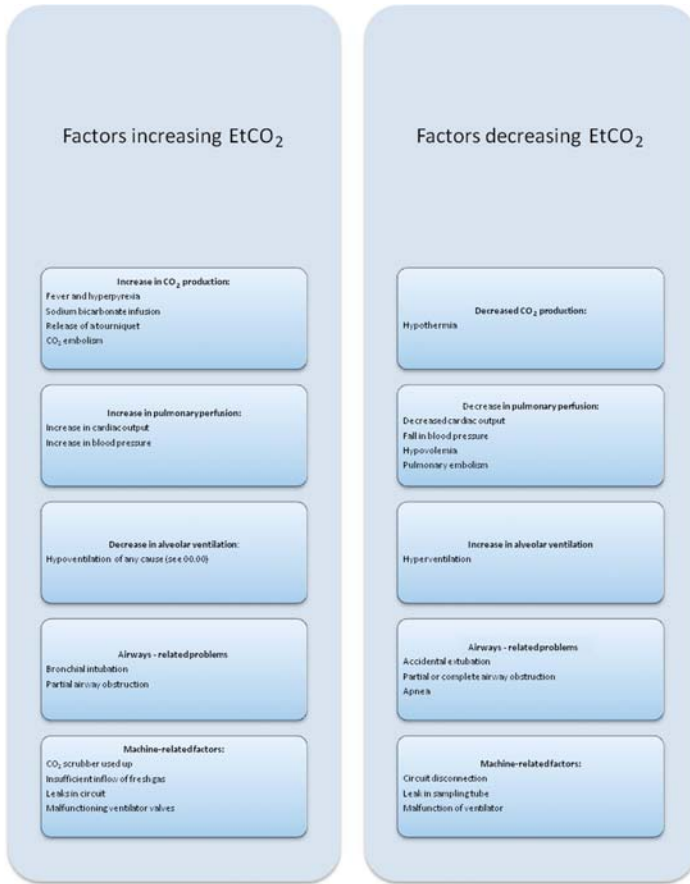
Nunn, JF, Hill, DW. Respiratory dead space and arterial to end-tidal CO₂ tension difference in anesthetized man. *J Appl Physiol* 1960; 15:383–9

Fletcher, R, Jonson, B. Dead-space and the single breath test for carbon dioxide during anaesthesia and artificial ventilation. *Br J Anaesth* 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 EtCO₂

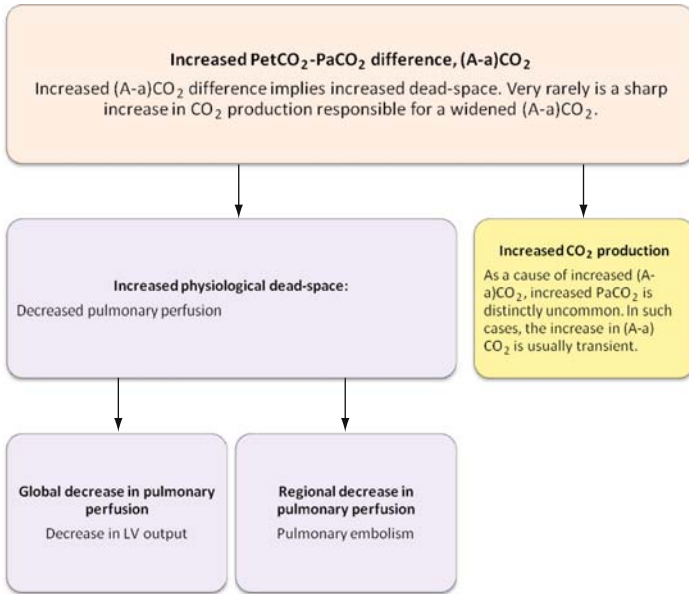
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(Modified from: Bhavani Shankar. Factors influencing PetCO₂; March 2007; Welcome to capnography.com)

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 PaCO₂-PetCO₂ Difference



3

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.

3

All the exhaled CO_2 comes from the alveolar gas. None of the exhaled CO_2 comes from the dead-space air.

Therefore,

$$V_T = V_A + V_D$$

Or tidal volume (V_T) = Alveolar gas volume (V_A) + dead-space gas (V_D)

Rearranging $V_A = V_T - V_D$... [Equation 1]

$$V_T \times F_{\text{ECO}_2} = V_A \times F_{\text{ACO}_2} \dots \text{[Equation 2]}$$

Where,

V_T = tidal volume

F_{ECO_2} = Fractional concentration of CO_2 in exhaled gas

V_A = Alveolar gas volume

F_{ACO_2} = Fractional concentration of CO_2 in alveolar gas

Substituting the value of V_A (Equation 1) within Equation 2,

$$V_T \times F_{\text{ECO}_2} = [V_T - V_D] \times F_{\text{ACO}_2}$$

Therefore,

$$V_D / V_T = [F_{\text{ACO}_2} - F_{\text{ECO}_2}] / F_{\text{ACO}_2}$$

Since the partial pressure of a gas is proportional to its concentration, the equation can be rewritten as "Bohr's equation":

$$V_D / V_T = [P_{\text{ACO}_2} - P_{\text{ECO}_2}] / P_{\text{ACO}_2}$$

And since the P_{CO_2} of alveolar gas (P_{ACO_2}) very nearly equals the P_{CO_2} of arterial gas (P_{aCO_2}),

$$V_D / V_T = [P_{\text{aCO}_2} - P_{\text{ECO}_2}] / P_{\text{aCO}_2}$$

Thus by simultaneously measuring the end-expiratory CO_2 (P_{ECO_2}) and the P_{aCO_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

Consider the following values in a patient:

Tidal volume (VT) = 500 mL

Respiratory frequency (f) = 12 breaths per minute

Minute ventilation = 5000 mL/min

PaCO₂ = 40 mmHg

EtCO₂ = 30 mmHg

$$VD/VT = (PaCO_2 - PECO_2) / PaCO_2$$

$$VD/VT = (40 - 30) / 40$$

$$VD/VT = 10 / 40 = 0.25$$

(The normal VD/VT is 0.20–0.35 at rest)

With a VD/VT of 0.25 and a tidal volume of 500 mL,

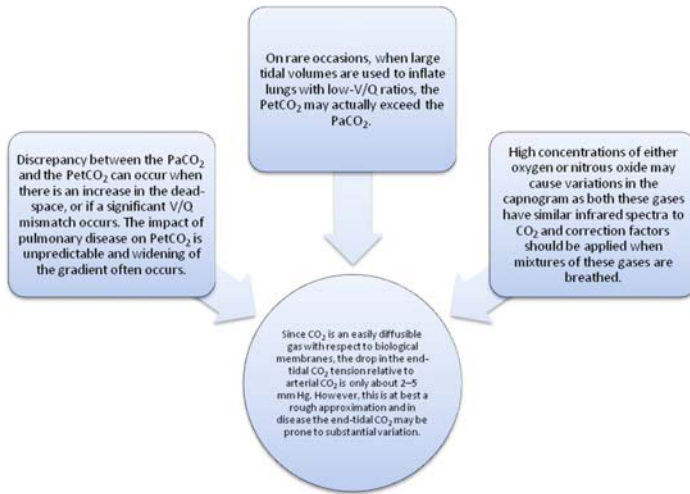
$$VD = 0.25 \times 500 = 125 \text{ mL}$$

We know that alveolar ventilation = (VT - VD) x f

$$\text{Alveolar ventilation} = (500 - 125) \times 12 = 4500 \text{ mL}$$

3.42 Variations in EtCO₂

3

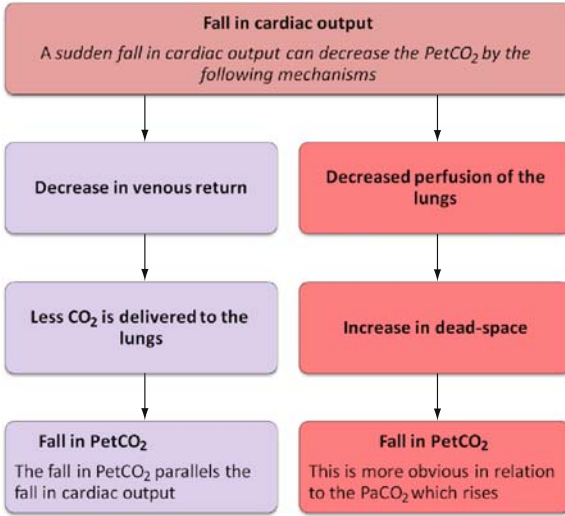


As is apparent in the discussion above, trends in arterial O₂ can be matched by the PetCO₂ when the lungs are healthy. But in cases of pulmonary disease, especially in a situation where there is unstable or evolving lung pathology, the end-tidal CO₂ may neither reflect nor parallel changes in PaCO₂, and this must be kept in mind.

Moorthy, SS, Losasso, AM, Wilcox, J. End-tidal PCo₂ greater than PaCO₂. Chest 1984; 12:534

3.43 Capnography and Cardiac Output

When alveolar ventilation is constant, the $P_{et}CO_2$ 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? *Anesth Analg* 1991; 73:808

Shibutani, K, Shirasaki, S, Braaz, T, et al. Changes in cardiac output affect $P_{et}CO_2$, 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

3

Capnography enables the differentiation between asphyxic and primary cardiac arrest

Asphyxic cardiac arrest

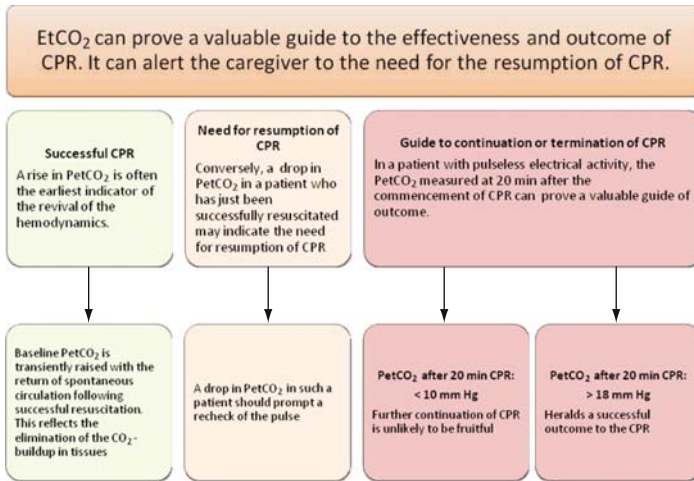
PetCO₂ is very high

Primary cardiac arrest

PetCO₂ is only moderately increased (its level is lower in comparison to that seen in asphyxic cardiac arrest).

Grmec, S, Lah, K, Tusek-Bunc, K. Difference in end-tidal CO₂ 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 PetCO₂ 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 (ETCO₂) 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

3



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

3.46 Differentiating Congestive Heart Failure from Bronchospasm

It is possible to distinguish CHF from bronchospasm on the basis of capnography.

CCF
Upright waveform

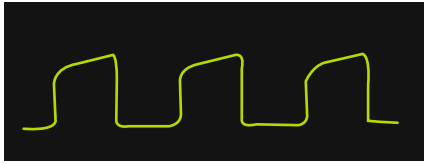


Bronchospasm
Upsloping plateau gives a 'shark fin' appearance to the waveform



3.47 Capnography in Esophageal Intubation

3



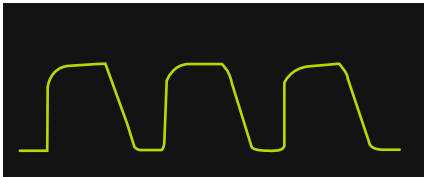
Normal capnograph



Capnograph in esophageal intubation



Capnograph in self-extubation or disconnection



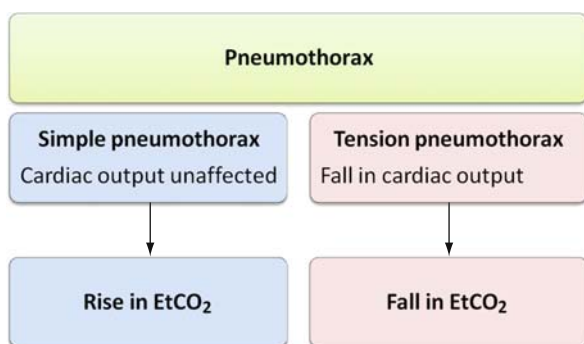
Ruptured ET cuff showing a gradual descent

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 Scand* 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

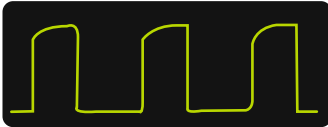


3.49 Capnography in Hypoventilation and Hyperventilation

3

Hypoventilation:

The capnograph shows:
Slow respiratory rate (low frequency)
High CO₂ levels (tall waves)

**Hyperventilation:**

The capnograph shows:
High respiratory rate (low frequency)
Low CO₂ levels (relatively short waves)



3.50 Biphasic Capnograph

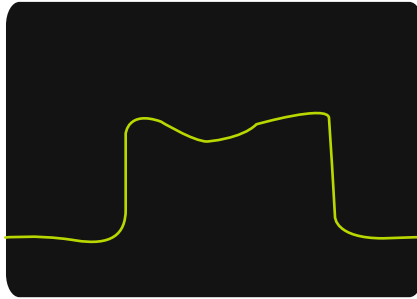
A biphasic pattern on the capnogram may be obtained under some circumstances.

Severe kyphoscoliosis

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.



Chapter 4

Acids and Bases

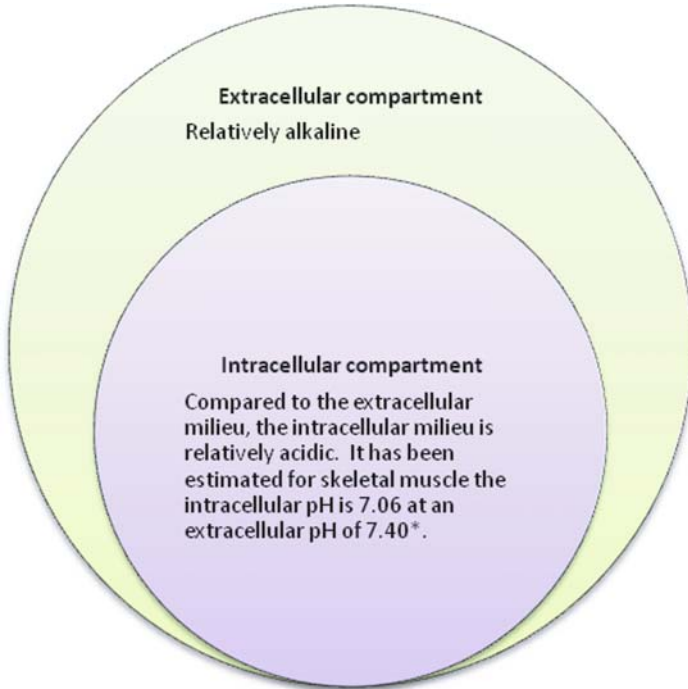
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4.1 Intracellular and Extracellular pH

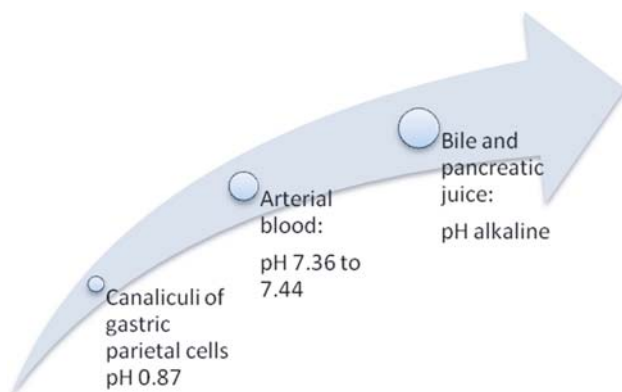
Most biological fluids are alkaline.

4



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).



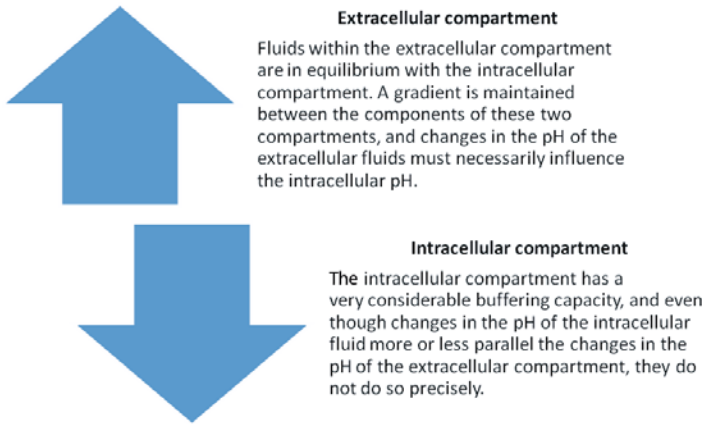
Concentrated hydrochloric acid has a pH of 1.1.

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

4.2 The Intracellular Environment

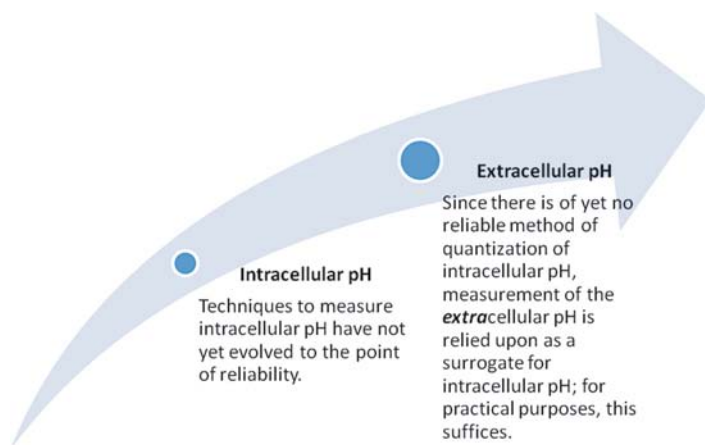
The intracellular microenvironment is complex, and so the pH is not uniform throughout the cell but varies between the different intracellular compartments. Since it is the cell that is the basic unit of any tissue, tissue function can best be assessed in relation to the activity of its cells.

4



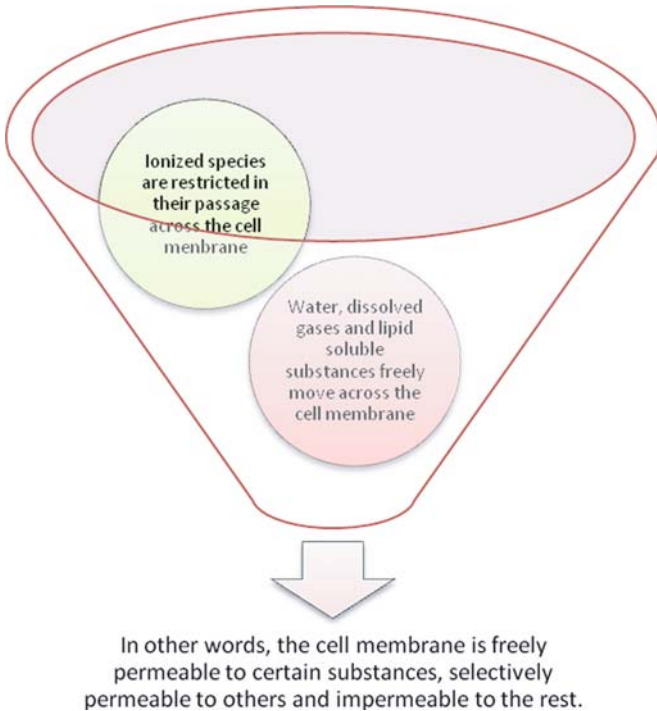
Ganapathy, V, Leibach, FH. Protons and regulation of biological functions. *Kidney Int Suppl* 1991; 33:S4

4.3 Surrogate Measurement of Intracellular pH

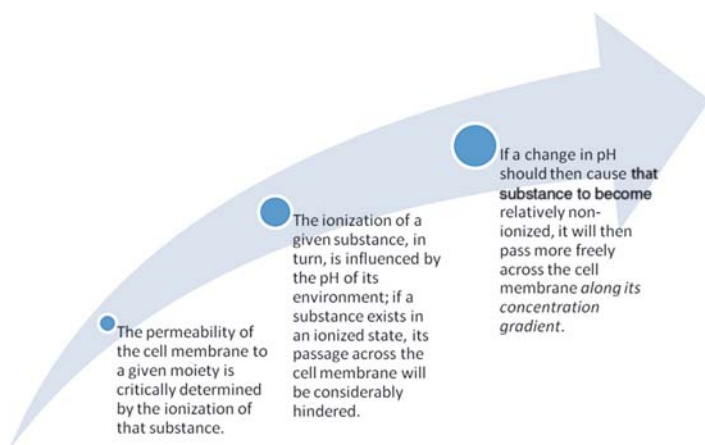


4.4 Preferential Permeability of the Cell Membrane

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.

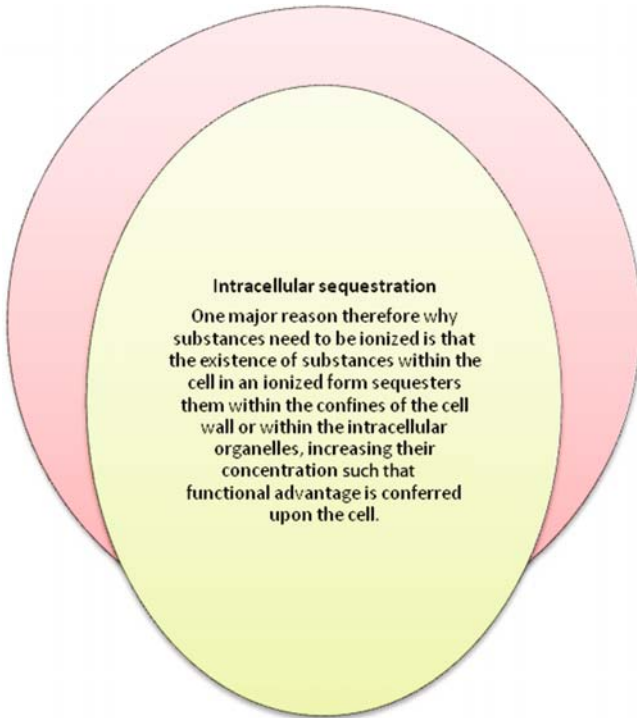


4.5 Ionization and Permeability



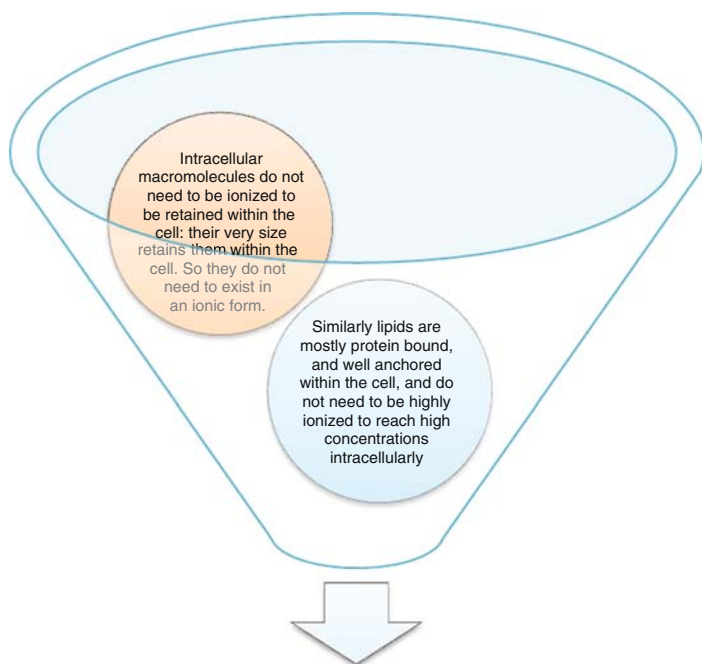
4.6 The reason why substances need to be ionised

4



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.

4.7 The Exceptions to the Rule



4

On the contrary, the end products of metabolism need free egress out of the cell so that they may be excreted, and it would disadvantage the cell were they to be ionized and therefore trapped inside the cell.

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.

The size of the bare proton, H^+ is very small (it has a radius 1/10,000 that of the hydrogen atom).

H^+ ions are drawn to molecules such as proteins more strongly than are other positive ions, and can therefore penetrate deeply into cellular structures, into the matrix of the protein macromolecules themselves, reaching the active sites there.

Their minute size also enables tighter bonding to the negatively charged proteins, producing configurational changes within the latter. This has considerable bearing upon many vital enzymatic reactions.

Cellular function can therefore be markedly influenced by the hydrogen ion concentration of the intracellular milieu.

By ionizing intracellular protein molecules H^+ critically influences the function of these:

- Enzymes
- Peptide hormones
- Hormone receptors
- Ion channels
- Transporters
- Mediator proteins

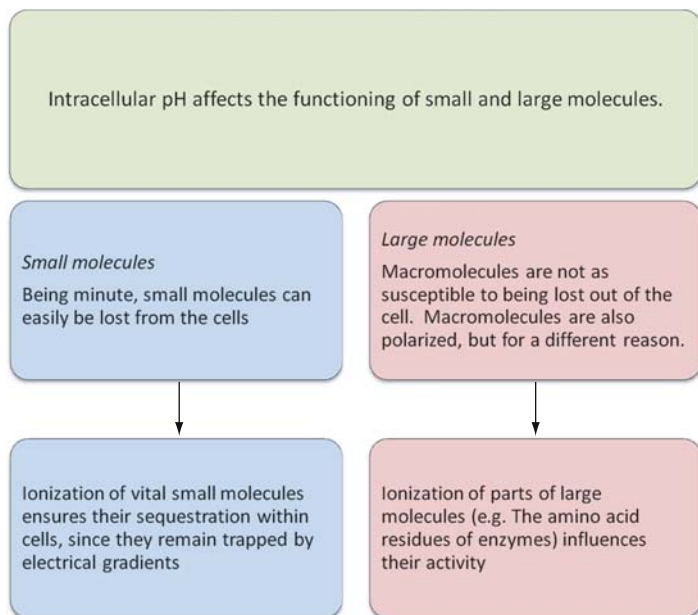
It is apparent therefore that the pH needs to be tightly regulated *in-vivo* to prevent molecular dysfunction.

The *extracellular* 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.

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.

4

Life is only possible between a pH range of 6.8 to 7.8 (or between 16 and 160 nanomoles of H⁺ per liter)
Any change in the hydrogen ion concentration has a profound impact upon biological compounds since the ionic groups that they possess (e.g., phosphate, ammonium, and carboxylate) function as conjugate bases.

A pH of 6.8 corresponds to a H⁺ ion concentration of 160 nmol/L

A pH of 7.8 corresponds to a H⁺ ion concentration of 16 nmol/L

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

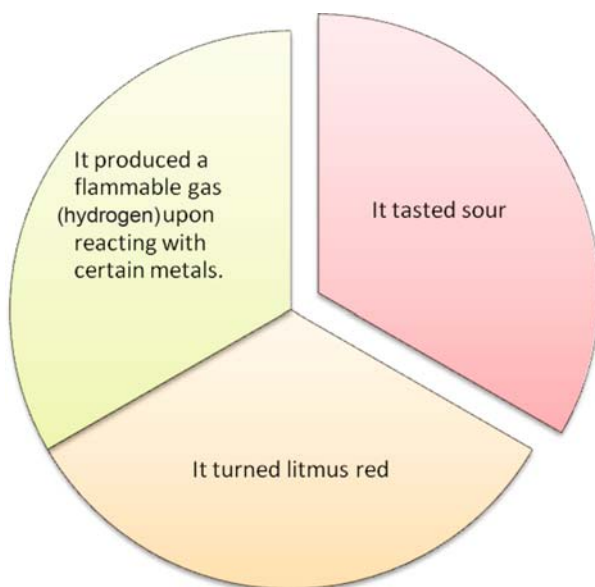
Ganapathy, V, Leibach, FH. Protons and regulation of biological functions. *Kidney Int Suppl* 1991; 33:S4

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.

4

Arrhenius' theory:

Acid: A substance that dissociates in water to produce hydrogen ions

Base: A substance that dissociates in water to produce hydroxyl ions

Advantages

Arrhenius' theory was the first truly modern approach to acid–base physiology

Disadvantages

Contrary to Arrhenius's definition of an acid, certain substances with obvious acidic properties (e.g. CO_2) did not dissociate into hydroxyl ions.

Again, contrary to Arrhenius's definition of a base, a few hydroxyl-lacking moieties could function as bases.

Within the framework of Arrhenius' concept acids and bases could only function in solution

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^+ from 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.

4

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

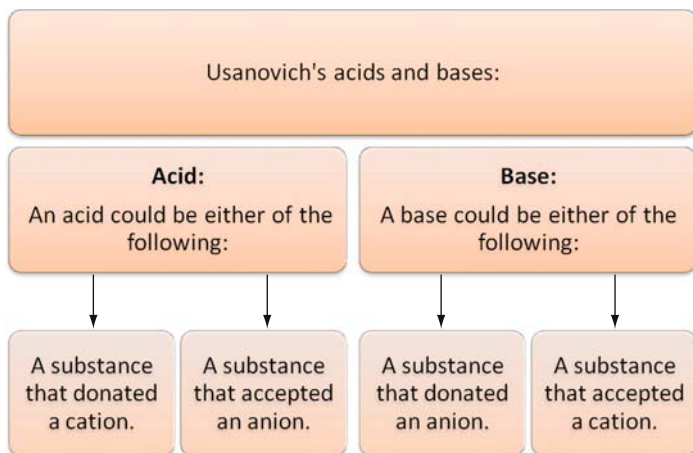
Lewis' definition overcame the drawback of B-L theory: CO_2 could now be encompassed within the definition of an acid.

Disadvantages

The electron concept is an uncomfortable one for clinicians!

4.15 The Usanovich Theory

In 1939 Usanovich developed his unified theory



4.16 Summary of Definitions of Acids and Bases

Definitions of an acid according to various theories

The traditional acid Sour in taste Turns blue litmus red Produces a flammable gas on reacting with certain metals	Arrhenius' acid Dissociates to produce H^+ in aqueous solution	Bronsted – Lowry acid A donor of hydrogen ions	Lewis' acid A potential acceptor of a pair of electrons	Usanovich's acid A donor of cations or an acceptor of anions

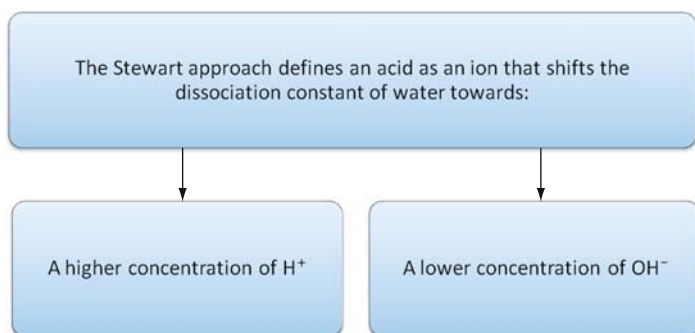
Definitions of a base according to various theories

Traditional base Bitter in taste Turns red litmus blue Soapy to touch	Arrhenius' base Dissociates to produce OH^- in aqueous solution	Bronsted – Lowry base An acceptor of hydrogen ions	Lewis' base A potential donor of a pair of electrons	Usanovich's base A donor of anions or an acceptor of cations

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.

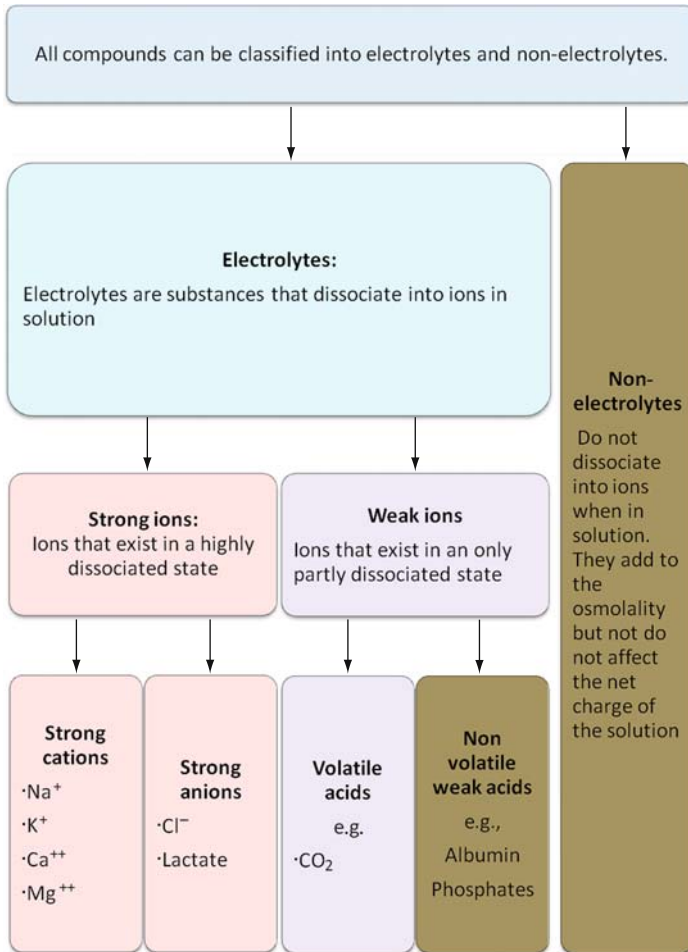


Stewart, PA. How to Understand Acid-Base. A Quantitative Acid-Base Primer for Biology and Medicine. Edward Arnold, ISBN 0-7131-4390-8, 1981

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

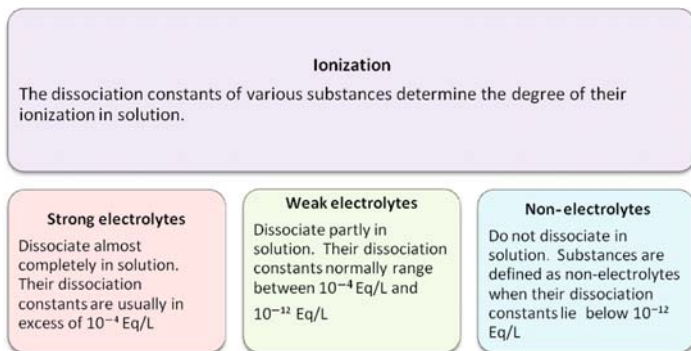


Stewart, PA. How to Understand Acid–Base. A Quantitative Acid–Base Primer for Biology and Medicine. Edward Arnold, ISBN 0-7131-4390-8, 1981

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.



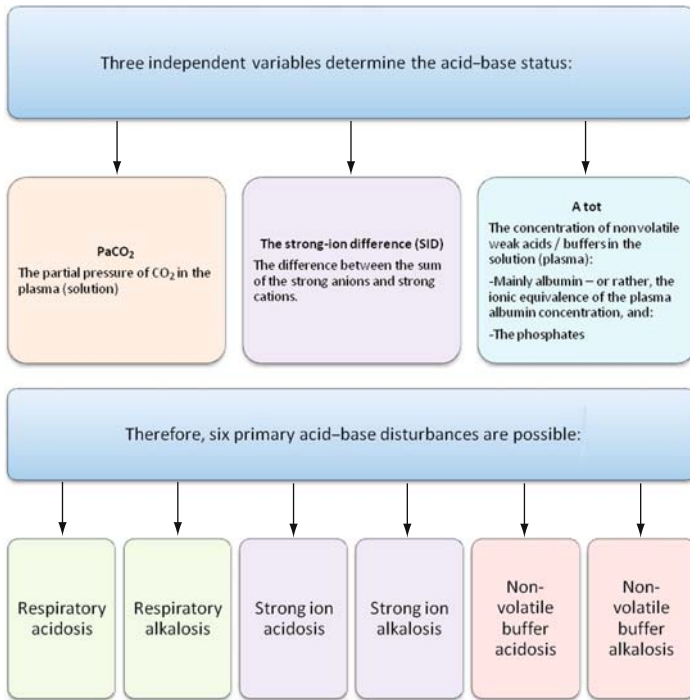
Stewart, PA. How to Understand Acid-Base. A Quantitative Acid-Base Primer for Biology and Medicine. Edward Arnold, ISBN 0-7131-4390-8, 1981

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

4



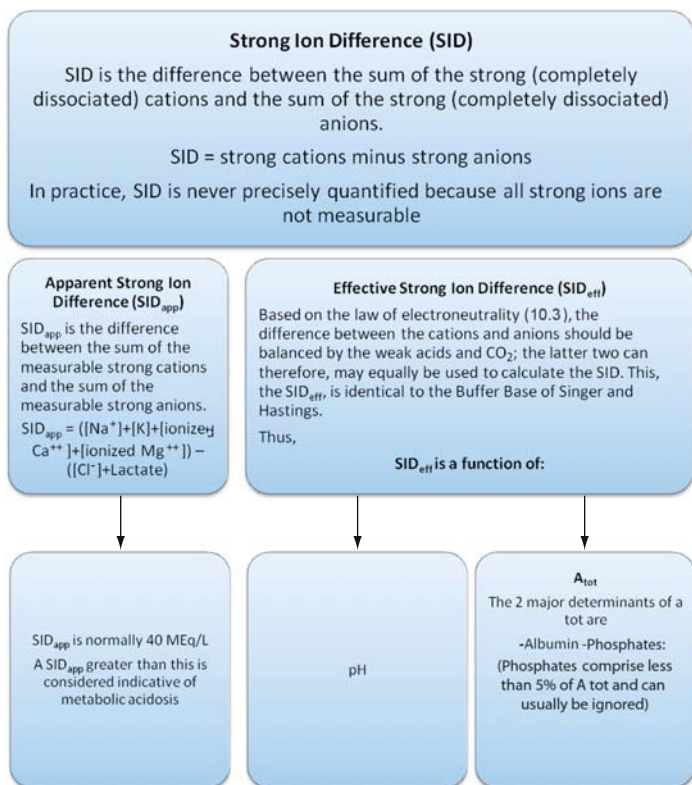
Note: pH is a *dependent* variable

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).

$$SIG = SID_{app} = SID_{eff}$$

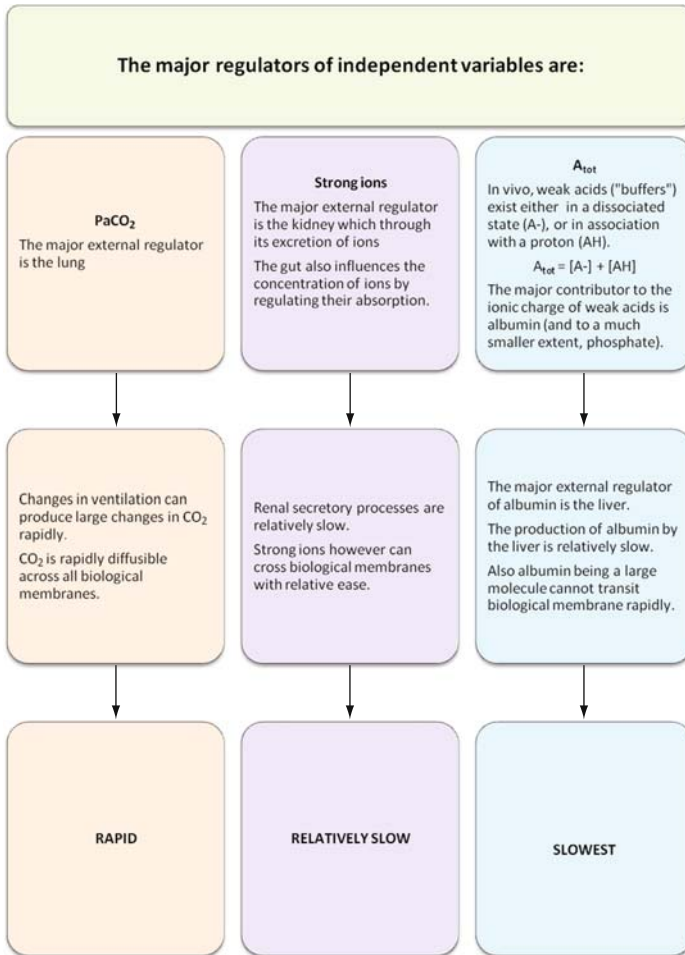
and the difference between the two (namely the strong ion gap) should be zero. In practice the above situation is exceptional. The Strong Ion Gap is the difference between the two ways of measuring the Strong Ion Difference; it is thus a quantification of unmeasured anions (both strong and weak).

$$SIG = SID_{app} - SID_{eff}$$

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



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

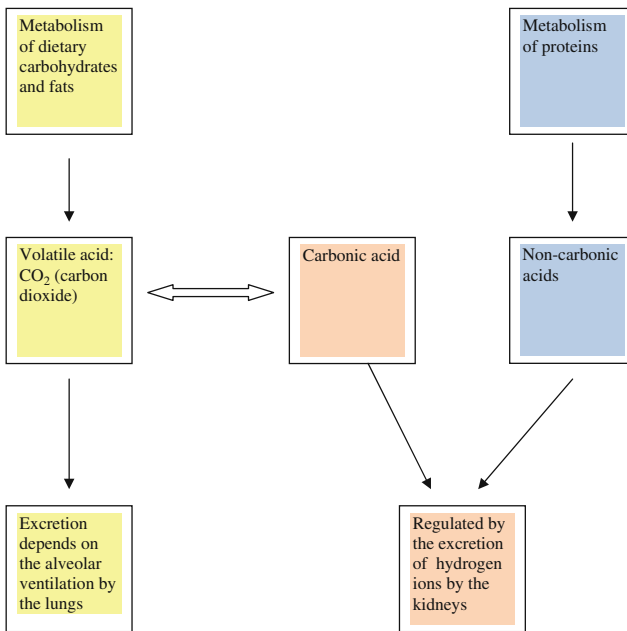
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5.1 The Generation of Acids

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 CO₂ production

Under basal conditions about 12,000 mmol of CO₂ are produced per day.
CO₂ production: about 200 ml per minute
i.e. $200 \times 60 \times 24 \text{ mL} = 288 \text{ liters per day}$
Since each gram-molecule of CO₂ takes up a volume of 22.4 liters at STP,
CO₂ production = 12 moles/day

With **usual** levels of activity CO₂ production ranges between 15,000 and 20,000 mmol/day

Changes in alveolar ventilation can rapidly alter intracellular pH.

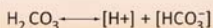
Being highly lipid-soluble, CO₂ can easily diffuse across biological membranes.

Large changes in alveolar ventilation can dramatically alter intracellular pH

CO₂ fluctuations can have an instantaneous and powerful effect on intracellular pH (and therefore on cellular metabolism) of all body tissues.

5.3 Disposal of Fixed Acids

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



The urinary loss of a single filtered HCO_3^- ion is equivalent to the gain of a proton.

Therefore all the filtered HCO_3^- (which is about 4300* mEq!) needs to be absorbed before the excretion of the daily dietary load of H^+ (50-100 mEq).

90% of the filtered bicarbonate is reabsorbed in the proximal convoluted tubule; the rest is absorbed by the distal convoluted tubules and the collecting ducts.

As mentioned, 50 to 100 mEq (average 70 mEq) of fixed acids are excreted daily through the urine. In states of increased acid production the kidney is capable of gradually stepping up the H^+ excretion to over 300 mEq per day. This is mainly achieved by NH_4 excretion. The renal response is slow and takes about 4 days to reach its maximum.

H^+ excretion in the urine is capable of a tenfold rise.

A urinary pH of as low as 4.5 can be achieved.

The H^+ gradient across the tubular membranes can increase up to x1000.

*Daily filtered bicarbonate = $\text{GFR} \times \text{plasma bicarbonate concentration}$
 = $180 \text{ L/day} \times 24 \text{ mmol/L}$
 = 4320 mmol/day (i.e., 4000 to 5000 mmol per day)

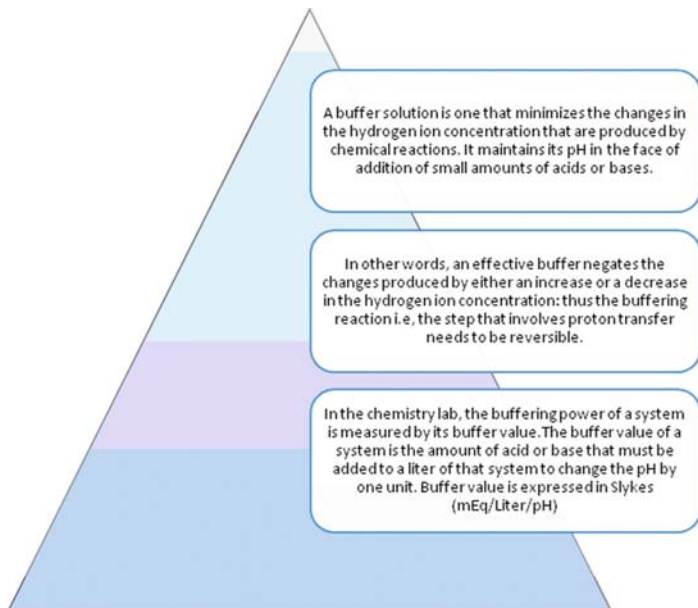
Malnic, G, Giebisch, G. Mechanism of renal hydrogen ion secretion. *Kidney Int* 1972; 1:280

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

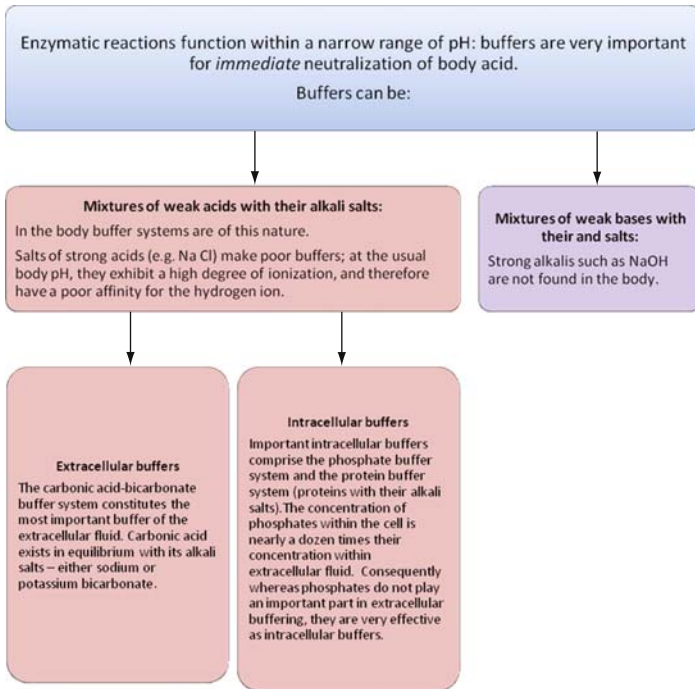
Grogono, AW. www.acid-base.com

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.



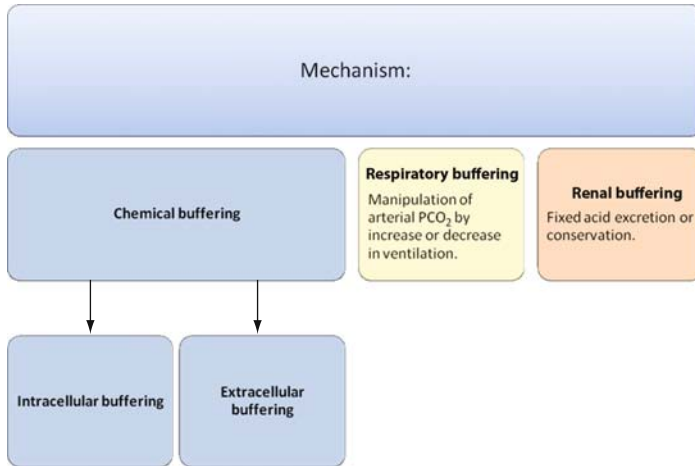
5.5 Buffers



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

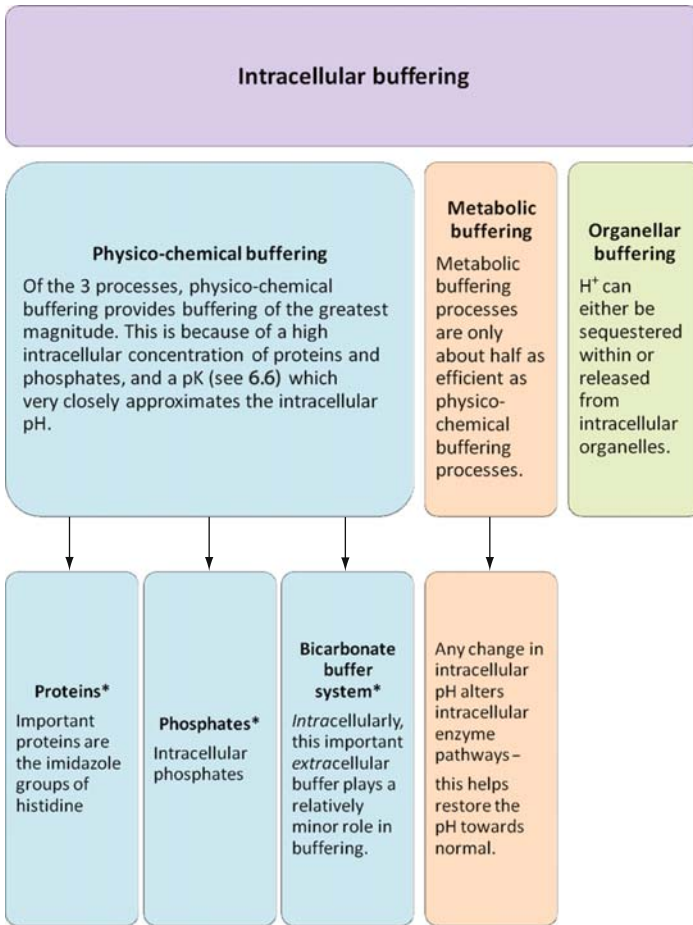


Hamm, LL, Simon, EE. Roles and mechanisms of urinary buffer excretion. *Am J Physiol* 1987; 253:F595

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

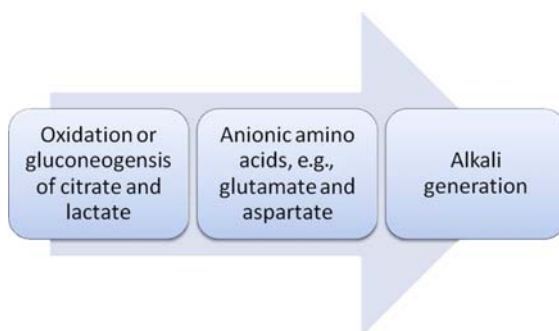
5.7 Intracellular Buffering

5



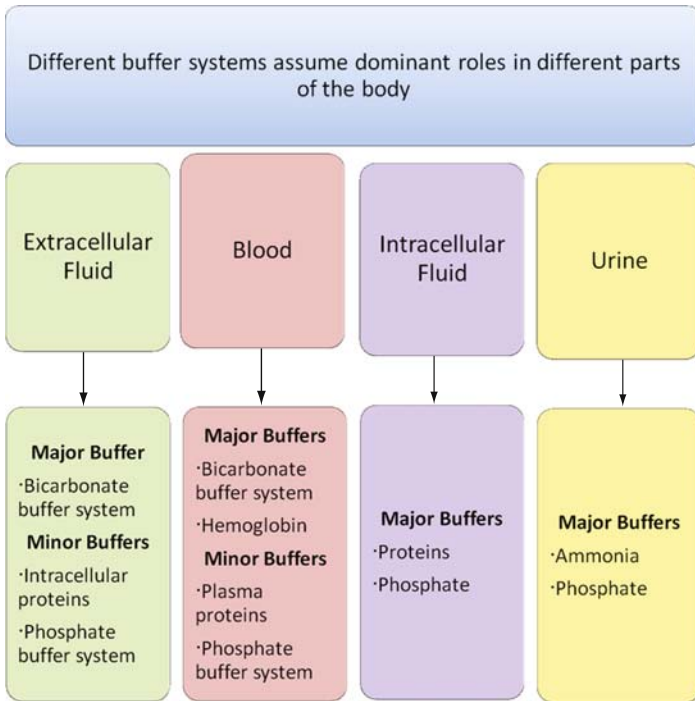
*Together, these 3 processes are responsible for virtually all the buffering that occurs in response to an acute acid load

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



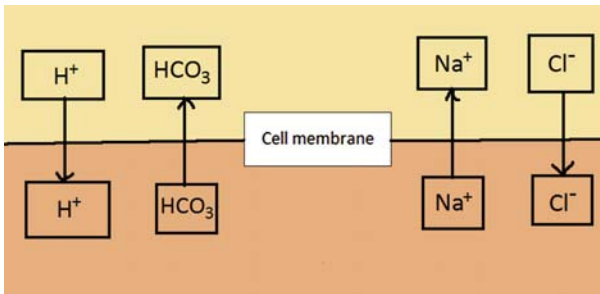
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Brandis, K. Acid-Base Physiology. www.anaesthesiaMCQ.com

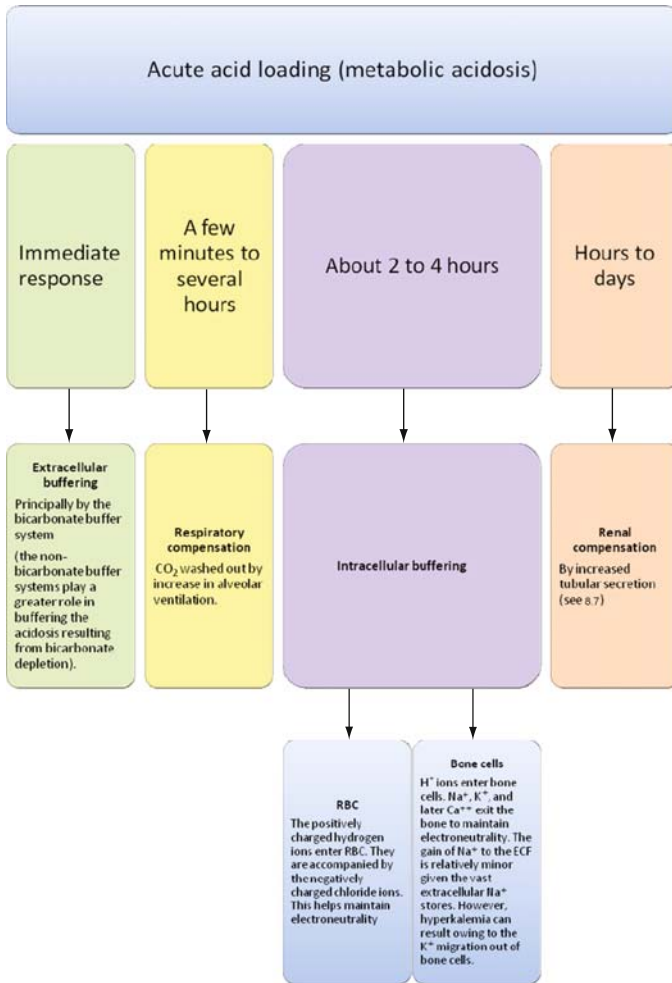
Madias, NE, Cohen, JJ. Acid-base chemistry and buffering. In: Acid / Base, Cohen, JJ, Kassirer, JP (Ed), Little, Brown, Boston, 1982

5.10 Transcellular Ion Shifts with Acute Acid Loading

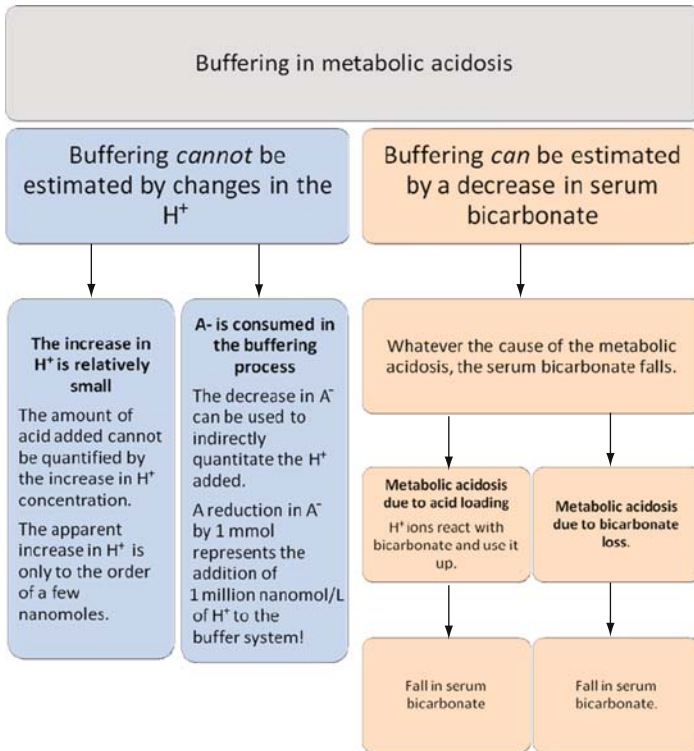
The maintenance of pH in the face of acid loading is on account of ion fluxes across the cell membrane. The coupled exchange of ions (H^+ for HCO_3^- and Na^+ for Cl^-) is an electroneutral process; this means that the membrane potential remains unaltered.



5.11 Time-frame of Compensatory Responses



5.12 Quantifying Metabolic Buffering

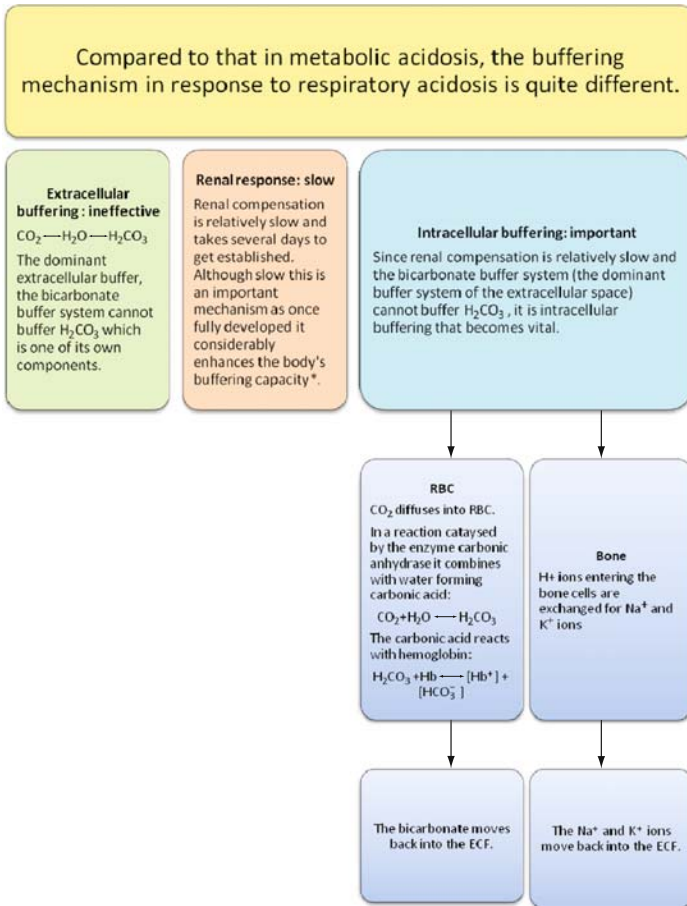


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Brandis, K. Acid-Base Physiology. www.anaesthesiaMCQ.com

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

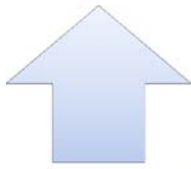


* Acutely the plasma HCO_3^- increases by 1 mmol/L for every 10 mmHg rise in PCO_2 ; later, once the renal response is established, it increases by about 3.5 mmol/L for a 10 mmHg increase in PCO_2 .

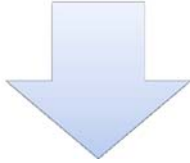
Pitts, RF. Physiology of the Kidney and Body Fluids. Year Book, Chicago, 1974, Chapter 11.

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

5.14 Buffering in Alkalosis



Generally speaking the opposite processes (to those in acidosis) are operative in alkalosis



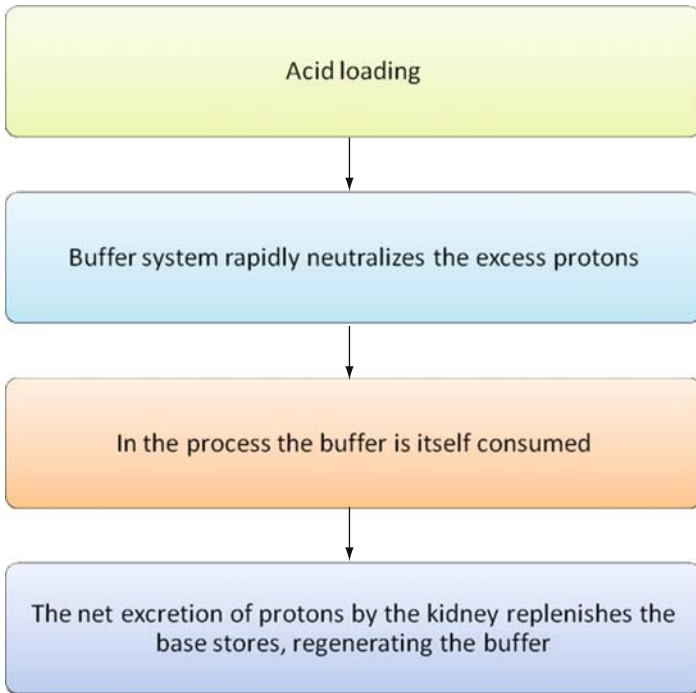
However, the proportion of buffering processes by the individual intracellular and extracellular buffers are different.

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

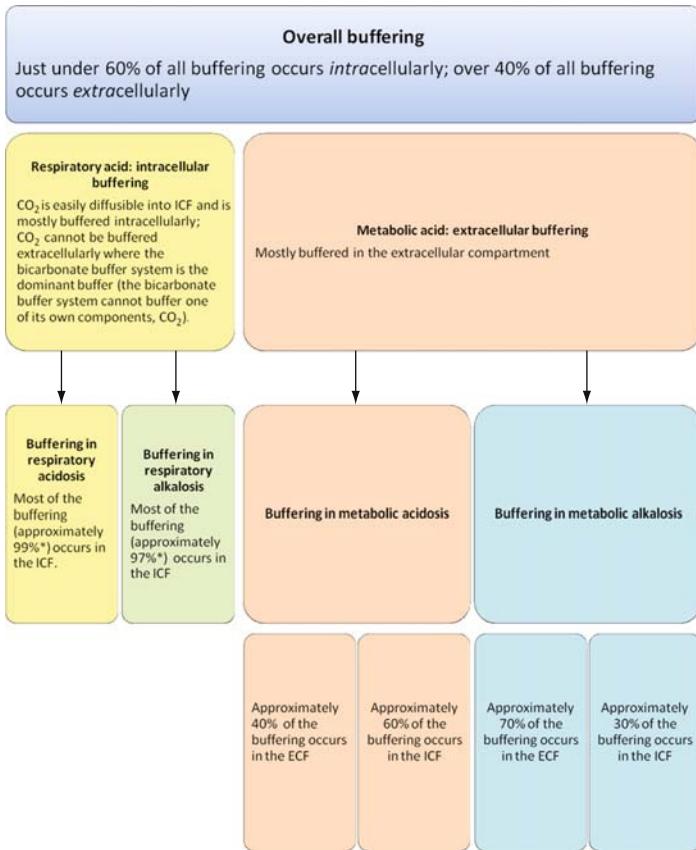
Rose, B, Post, T. 2000, www.utd.com; Buffers-II

5.15 Regeneration of the Buffer

5



5.16 Site Buffering



5

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

According to the isohydric principle all the buffer systems within the body exist in equilibrium with each other; therefore analysis of any one buffer systems of the body mirrors the state of all the other buffer systems.

The non-bicarbonate buffer system

The non bicarbonate buffer system is in reality an conglomeration of several different buffer systems.

Because of its inhomogeneity, it is difficult to measure.

The bicarbonate buffer system

The bicarbonate buffer system is the most convenient to measure. Its measurement effectively provides quantitative information about the other buffer systems of the body.

pH

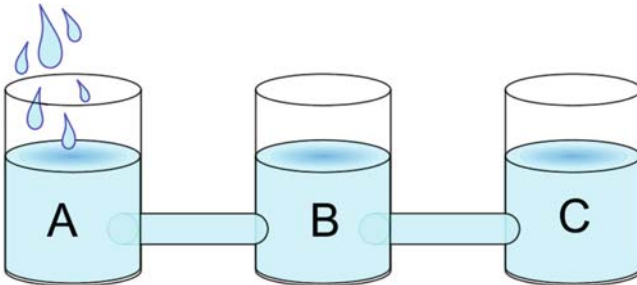
Measured by the ABG machine.

CO₂

Measured by the ABG machine

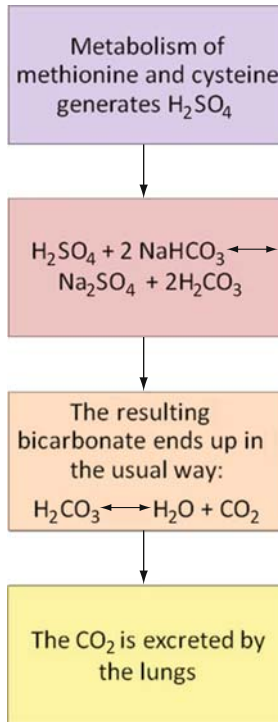
HCO₃

Calculated from Henderson-Hasselbach equation.



5.18 Isohydric Principle (cont'd)

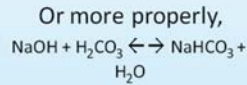
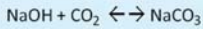
Even when the acid that is added to the blood is a non-bicarbonic acid, it can be converted into the latter and then eliminated by the lungs as CO_2 .



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,

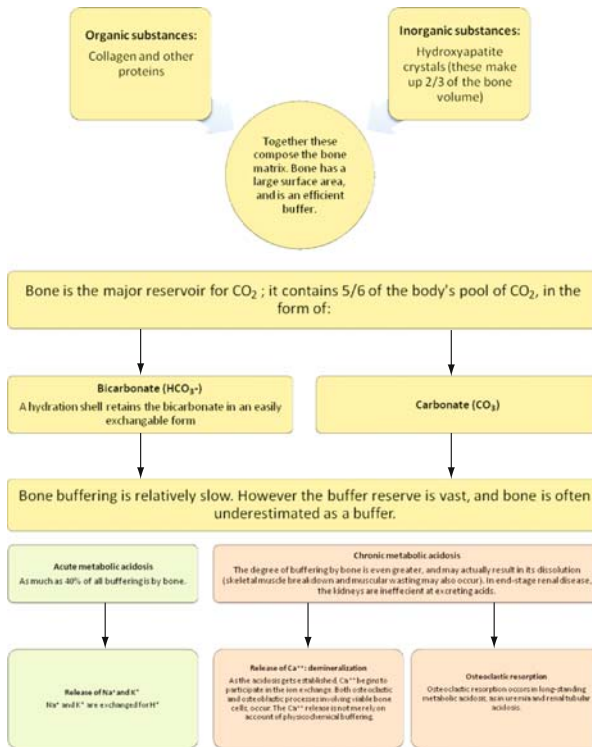
5



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

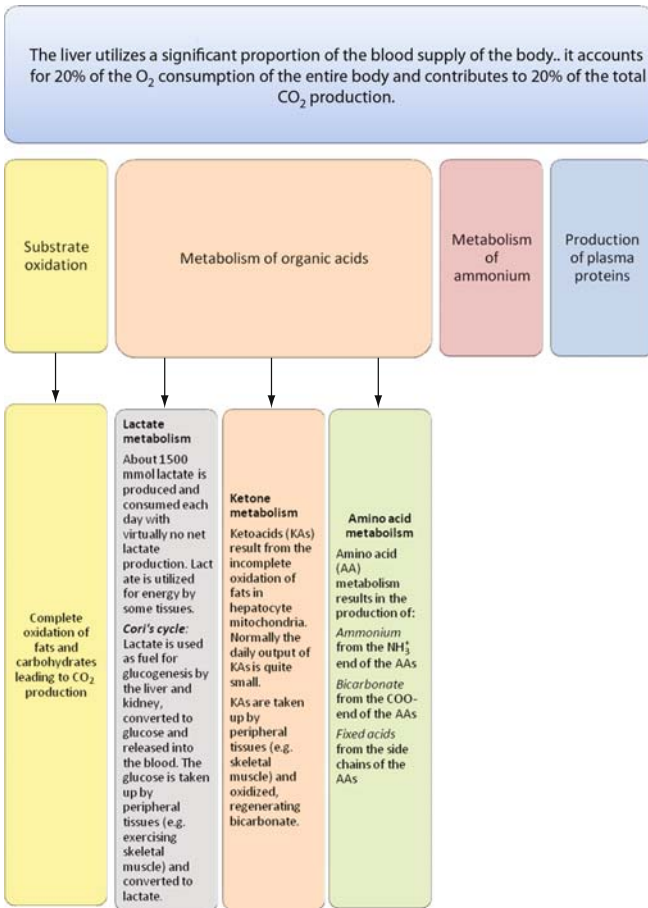
Chabala, JM, Levi-Setti, R, Bushinsky, DA. Alterations in surface ion composition of cultured bone during metabolic, but not respiratory, acidosis. *Am J Physiol* 1991; 261:F76

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

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6.1 Hydrogen Ion Activity

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

Concentration

The number of particles in solution.

Effective concentration (Activity)

The number of particles that appear to be present in solution.

6

The activity (**a**) of a substance (**s**) can be represented by the following equation:

$$a = q c$$

where,

a = activity of the substance **s** in solution

q = the activity coefficient of the substance **s**

c = the concentration of the substance **s** in solution



In an ideal solution, the effective concentration should equal the actual concentration.

$$a = c$$

$$a/c = q = 1$$

Which is a different way of saying that in an ideal solution, the activity coefficient should be 1.

In practice the activity coefficient of solutes is assumed to be one. The inaccuracies produced by this assumption are generally not clinically significant.

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

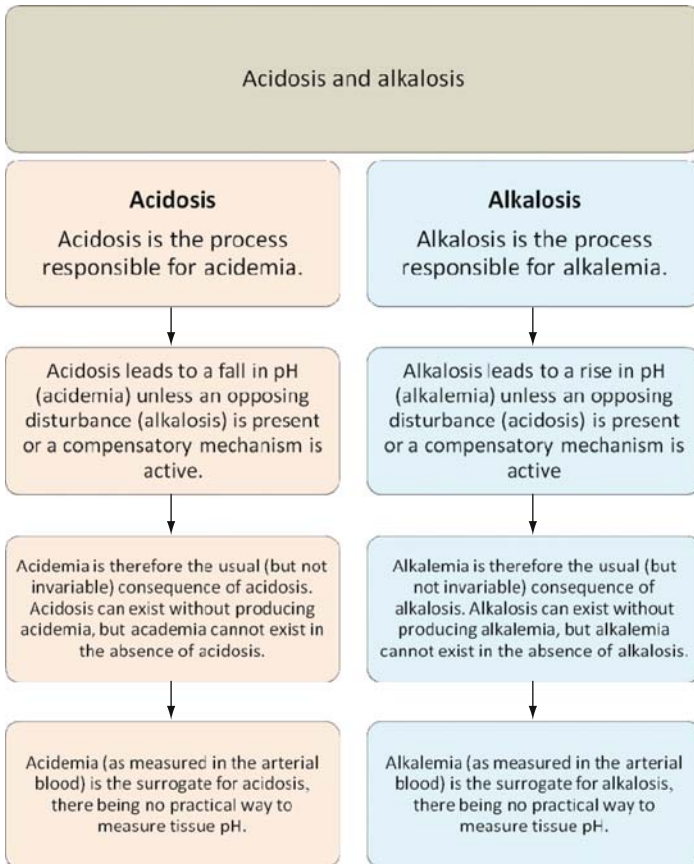
Cohen, JJ. Acid–base chemistry and buffering. In: Acid / Base, Cohen, JJ, Kassirer JP (Ed), Little, Brown, Boston, 1982

6.2 Definitions of Acid-Base Disorders

<p>Acidosis An abnormal process or condition which would lower arterial pH if there were no secondary changes in response to the primary etiological factor.</p>	<p>Alkalosis An abnormal process or condition which would raise arterial pH if there were no secondary changes in response to the primary etiological factor.</p>	<p>Simple (Acid-Base) Disorders Those (acid-base disorders) in which there is a single primary etiological acid-base disorder.</p>	<p>Mixed (Acid-Base) Disorders Those (acid-base disorders) in which two or more primary etiological disorders are present simultaneously.</p>	<p>Acidaemia Arterial pH < 7.36 (i.e. $[H^+] > 44$ nM)</p>	<p>Alkalaemia Arterial pH > 7.44 (i.e. $[H^+] < 36$ nM)</p>
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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



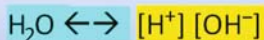
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Winters, RW. Terminology of acid–base disorders. *Ann Intern Med* 1965; 63:873

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.

For water, the law of mass action can be written as:



V_1 represents the velocity of the movement of this reaction to the right

$$V_1 = k_1[\text{H}_2\text{O}]$$

k_1 being the rate constant of the reaction

V_2 represents the velocity of the movement of this reaction to the left

$$V_2 = k_2[\text{H}^+] [\text{OH}^-]$$

k_2 being the rate constant of the reaction

At equilibrium,

$$V_1 = V_2$$

Or,

$$k_1[\text{H}_2\text{O}] = k_2[\text{H}^+] [\text{OH}^-]$$

A third constant can now be derived for H_2O when it is 50% dissociated into its component ions:

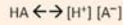
$$K = k_1/k_2 = [\text{H}^+] [\text{OH}^-] / [\text{H}_2\text{O}]$$

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:



Or,

$$K_a = \frac{[\text{H}^+] [\text{A}^-]}{[\text{HA}]}$$

Where K_a is the dissociation constant for that acid.

K_a , the dissociation constant

K_a , the dissociation constant is different for each acid system. For all practical purposes, the **value of K_a 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

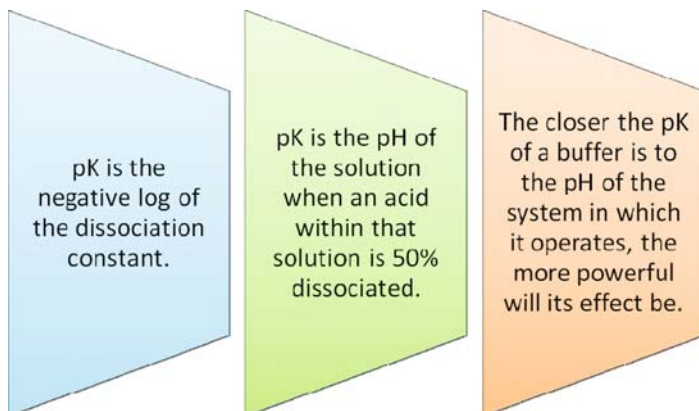
They tend to dissociate relatively less in solution.

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

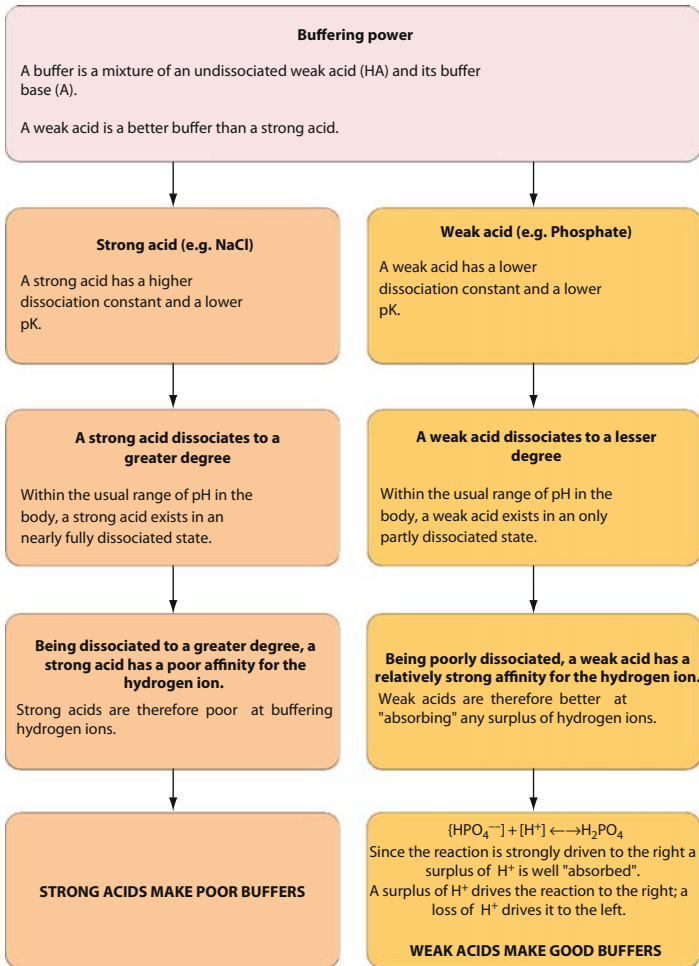
Gennari, FJ, Cohen, JJ, Kassirer, JP. Measurement of acid-base status. In: Acid / Base, Cohen, JJ, Kassirer, JP (Ed), Little, Brown, Boston, 1982

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.

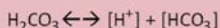
6.7 The Buffering Capacity of Acids



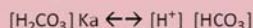
6.8 The Modified Henderson–Hasselbalch Equation

The law of mass action as applied to the carbonic acid system:

The following equation represents the dissociation of carbonic acid



Applying the law of mass action,



Or,

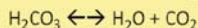
$$K_a = \frac{[\text{H}^+] [\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]}$$

Where K_a is the dissociation constant of carbonic acid

Rearranging,

$$\frac{K_a}{[\text{H}^+]} = \frac{[\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]}$$

The following equation represents the reaction between H_2O and CO_2 to reversibly form H_2CO_3



$$K_a = 2.72 \times 10^{-4}$$

$$[\text{H}^+] \text{ concentration} = 40 \times 10^{-9}$$

Inserting the above values into the equation,

$$\frac{[\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]} = \frac{2.72 \times 10^{-4}}{40 \times 10^{-9}}$$

i.e., $10^{-9} = 6800$

6800 molecules of HCO_3^- are present for every molecule of H_2CO_3 .

For the above reaction it can be shown that the dissociation constant is far to the right.

340 molecules of CO_2 are present for every molecule of H_2CO_3 .

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

Putting the two equations together,



Only 1 molecule of H_2CO_3 is present for 6800 molecules of HCO_3

Only 1 molecule of H_2CO_3 is present for 340 molecules of CO_2 .

Since it is present in relatively low concentrations, H_2CO_3 can be disregarded.

H_2O is being "constant" can also be disregarded.

The equation now becomes:



Rearranging,

$$K'a = \frac{[\text{H}^+] [\text{HCO}_3]}{[\text{CO}_2]}$$

Or

$$[\text{H}^+] = \frac{K'a [\text{CO}_2]}{[\text{HCO}_3]}$$

At 37°C (normal body temperature),

$K'a = 800 \times 10^9 \text{ nmol/L}$

$\text{pKa} = 6.10$

$$\text{Since } [\text{H}^+] = \frac{K'a [\text{CO}_2]}{[\text{HCO}_3]}$$

$$[\text{H}^+] = \frac{800 [\text{CO}_2]}{[\text{HCO}_3]}$$

Multiplying CO_2 by 0.03 (its solubility constant in the plasma)

$$[\text{H}^+] = 800 \times 0.03 / [\text{HCO}_3]$$

The equation now becomes:

$$[\text{H}^+] = \frac{24 \times [\text{CO}_2]}{[\text{HCO}_3]}$$

This is Kassirer and Bleich modification* of the Henderson–Hasselbach equation

*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

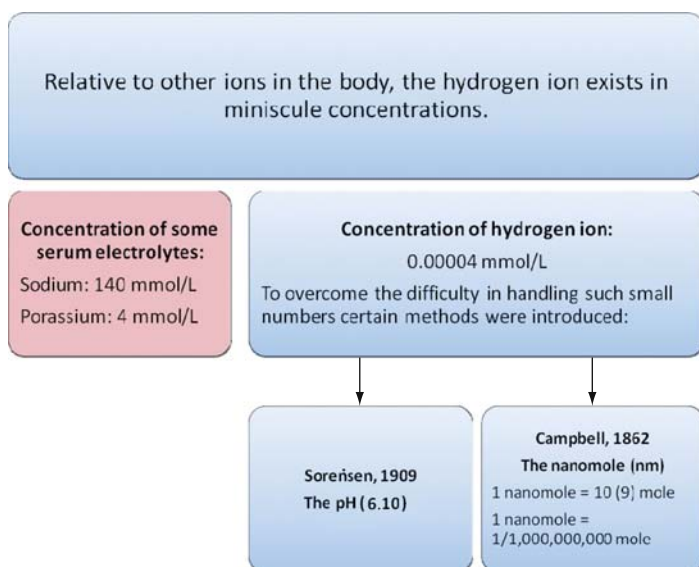
Kassirer, JP Serious Acid–Base Disorders. *N Engl J Med* 291, 773; 1974

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



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.

Mathematically,

10 can be expressed as 10^1 (1)
 100 can be expressed as 10^2 (2)
 1000 can be expressed as 10^3 (3)

And so forth.

Similarly,

$1/10$ can be expressed as 10^{-1}
 $1/100$ can be expressed as 10^{-2}
 $1/1000$ can be expressed as 10^{-3}

And so forth.

Sorensen 'used' these negative exponents to the base 10 to simplify handling of these numbers. He then discarded the negative sign from the power to which 10 was expressed, and called the number "pH", a short form for what he called the "Puissance hydrogen" or "Wasserstoffionexponent" or simply the "Potenz" ie "Potential" of hydrogen.

When the concentration of a substance is expressed as a negative power, the greater its negative power the lower the concentration is of that substance

Sorensen used this method to express the concentration of the hydrogenion.

Thus, a hydrogenion concentration of:

$0 = \text{pH } 1$
 $0.01 = \text{pH } 2$
 $0.001 = \text{pH } 3$

And so forth.

In Sorensen's new terminology, a molar solution of a strong acid having a hydrogen ion concentration of 0.01 (10^{-2}), had a pH of 2. Similarly, and a hydrogen ion concentration of 0.0000001 (10^{-7}) was expressed as having a pH of 7.

Thus pH is the negative logarithm of the H^+ ion concentration in moles per liter of solution. It has no units: it has been described as the "dimensionless representation of the $[H^+]$ " (Kellum, 2000)

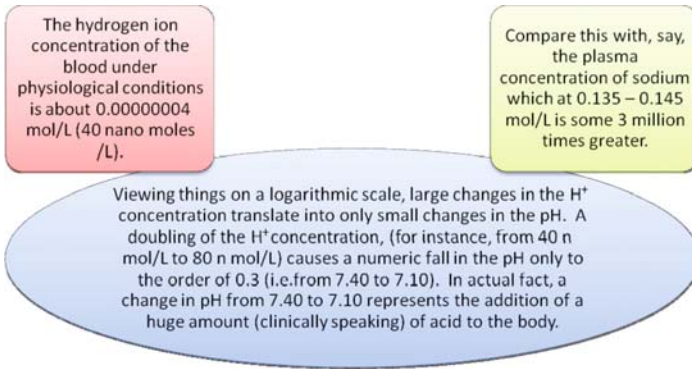
The lower the concentration of the hydrogen ion in solution, the greater is the pH of that solution.

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.

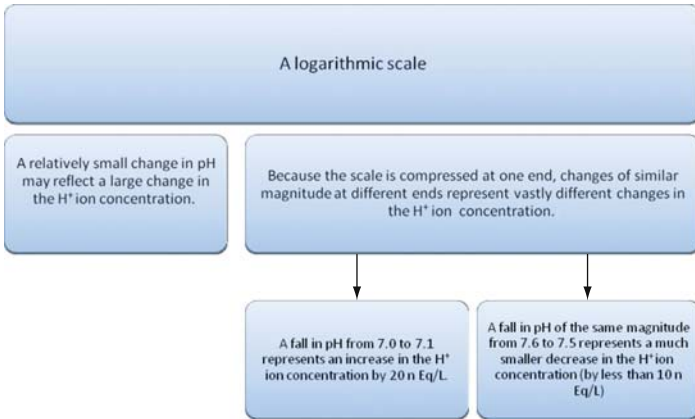
A similar calculation can also be used for checking if the data are reliable (see the first example in chapter 13)

6

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

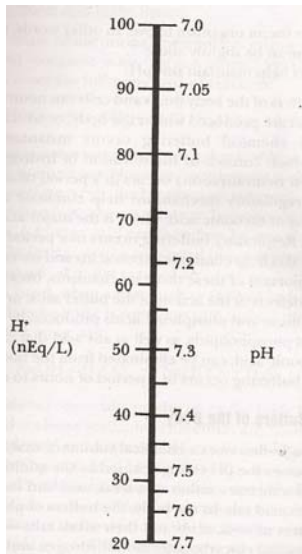
Kassirer JP, Bleich HL. Rapid estimation of plasma CO_2 from pH and total CO_2 content. *N Engl J Med* 1965; 272:1067

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



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.

In respect of the bicarbonate buffer system which is the primary buffer system of the extracellular space:

When the concentration of bicarbonate equals the concentration of carbonic acid

$$\text{Ratio of } \frac{\text{Bicarbonate}}{\text{Carbonic acid}} = \frac{1}{1} = 1$$

$$\text{pH} = \text{pK} + \log \frac{\text{Bicarbonate}}{\text{Carbonic acid}}$$

Since $\log 1 = 0$

The pK of the system is 6.1,

$$\text{pH} = 6.1 + 0$$

$$\text{pH} = 6.1$$

The pH of the system equals its pK

When the pH of the system equals its pK, the buffer system is functioning at its maximum efficiency.

In vivo, the concentration of bicarb substantially exceeds the concentration of carbonic acid

Bicarbonate = 27 mEq/L

Carbonic acid = 1.35 mEq/L

Ratio of Bicarbonate: Carbonic acid = 20

$$\text{pH} = 6.1 + \log \frac{27}{1.35}$$

$$\text{pH} = 6.1 + \log 20$$

Since $\log 20 = 1.3$

$$\text{pH} = 6.1 + 1.3$$

$$\text{pH} = 7.4$$

The pH of this system does not equal its pK

The pH of this system is very different from the pK of the bicarbonate buffer system. This would make for a poor buffer system were it not for the continuous removal of CO_2 by the lungs see (00.00).

6.15 Is the Carbonic Acid System an Ideal Buffer System?

Normal blood levels of HCO_3^- and CO_2

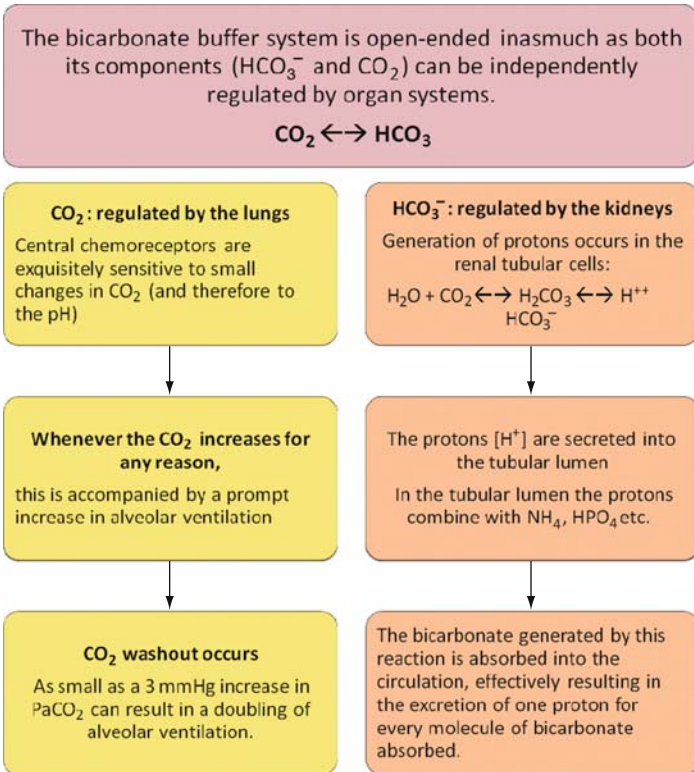
HCO_3^- : 22–26(24) mEq/L

CO_2 : 40 mmHg
 i.e.,
 $0.03 \times 40 = 1.2$ mEq/L
 (0.03 being the solubility coefficient of CO_2)

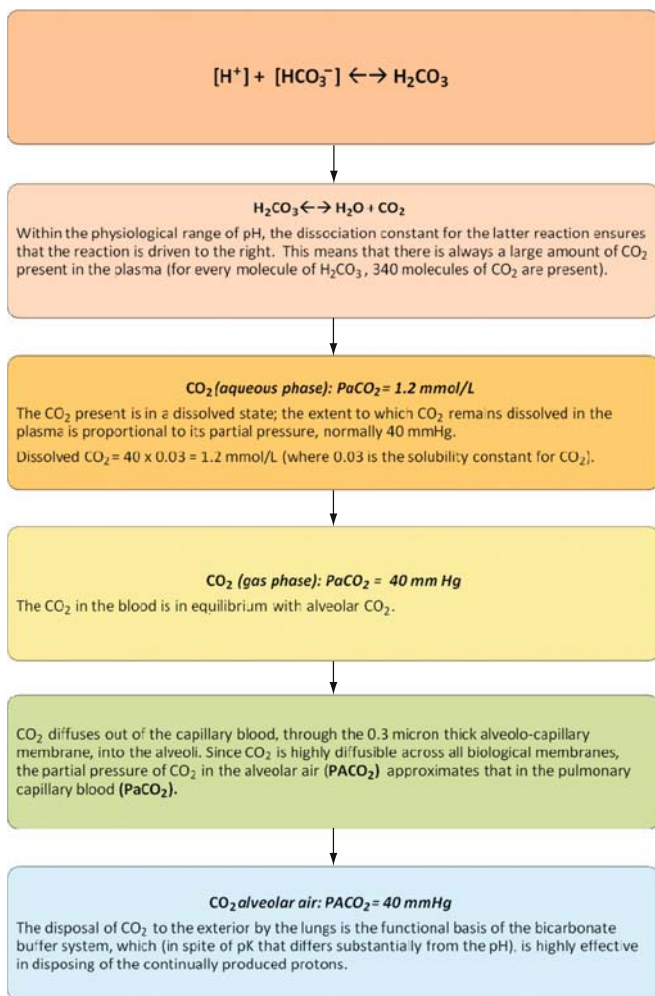
At the normal body pH of 7.4, the ratio of HCO_3^- : $\text{CO}_2 = 24:1.2$
 $= 20$

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.

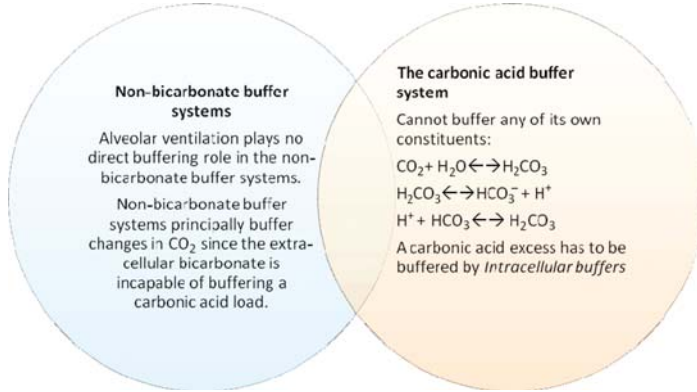
6.16 The Bicarbonate Buffer System is Open Ended



6.17 Importance of Alveolar Ventilation to the Bicarbonate Buffer System



6.18 Difference between the Bicarbonate and Non-bicarbonate Buffer Systems



6

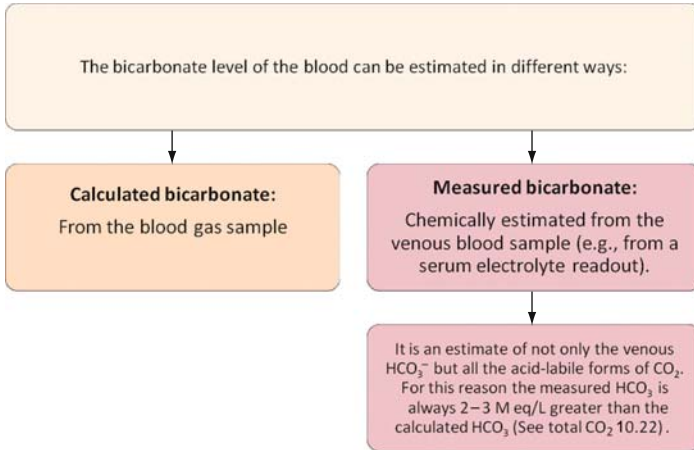
(see also isohydric principle 5.17)

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

When there is a discrepancy between the measured and calculated bicarbonate:

The venous HCO_3^- is actually the total CO_2 content which is a measure of all the acid-labile forms of carbon dioxide (plasma HCO_3^- constitutes about 95% of this). The measured venous HCO_3^- (total CO_2 content) normally exceeds the calculated arterial HCO_3^- by 2 to 3 mEq/L.

The pK of the bicarbonate buffer system may not be 6.1 in the critically ill: the calculated bicarbonate may therefore be erroneous.

Blood drawing by applying a tourniquet can result in a local lactic acidosis; this will lower the bicarbonate leading to a falsely low measured bicarbonate.

Usually, venous HCO_3^- samples are processed later than arterial blood gas samples. If the standing time of the venous sample is long, its bicarbonate content may become altered.

Chapter 7

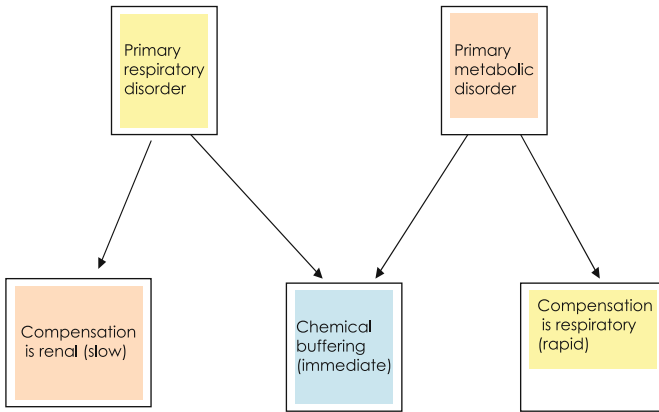
Acidosis and Alkalosis

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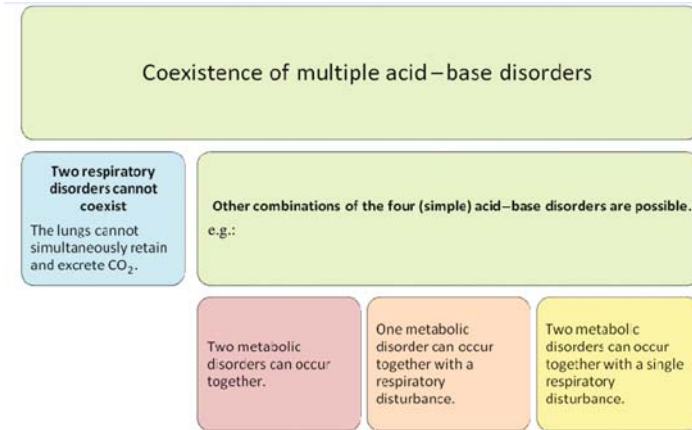
7.1 Compensation

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



7.2 Coexistence of Acid–Base Disorders

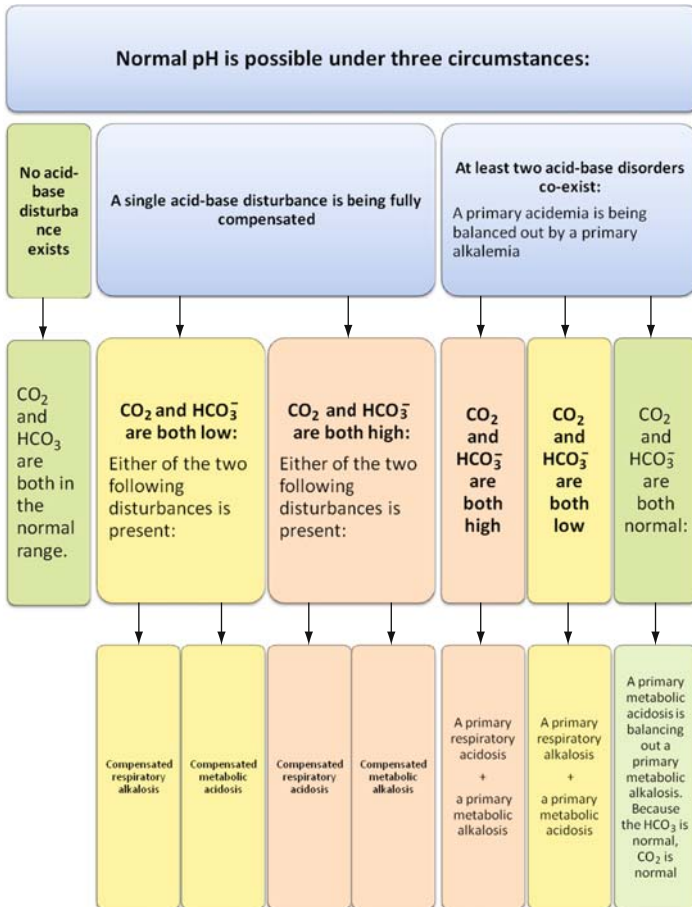
Frequently, two (sometimes three) acid–base disorders occur simultaneously.



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

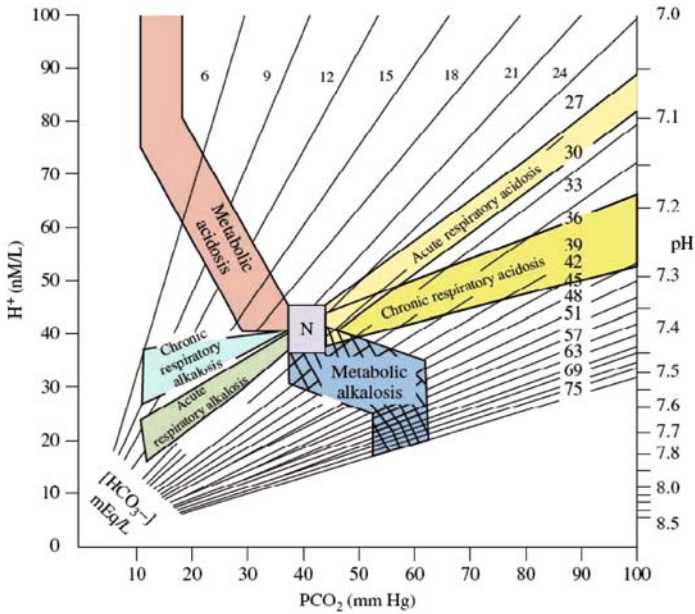
McCurdy, DK. Mixed metabolic and respiratory acid–base disturbances: diagnosis and treatment. *Chest* 1972; 63:355S

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.



7

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

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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).

Respiratory failure			
Type 1 (Hypoxemic respiratory failure) PaO ₂ is low (PaO ₂ < 50 mmHg) CO ₂ is not elevated (PaCO ₂ < 60 mmHg)	Type 2 (Hypercapnic respiratory failure) PaO ₂ is low (PaO ₂ < 50 mmHg) CO ₂ is elevated (PaCO ₂ > 60 mmHg)	Type 3 (Per-operative respiratory failure) FRC falls below closing volume as a result of atelectasis. Contributing factors: Supine posture General anesthesia Depressed cough reflex Splinting due to pain	Type 4 (shock with hypoperfusion) The proportion of the cardiac output to the respiratory muscles rises by as much as 10-fold when the work of breathing is high; this can seriously impair coronary perfusion during shock.

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

Polioomyelitis

Amiotrophic lateral sclerosis

Myasthenia gravis

Organophosphate poisoning

Botulism

Muscular relaxants

Dyselectrolytemias

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

Polioomyelitis

Dyselectrolytemias

Malnutrition

Chest wall

Kyphoscoliosis

Obesity

Thoracoplasty

Pleura

Chronic large effusions

Lung parenchyma

Long standing and severe ILD

Airways

Persistent asthma

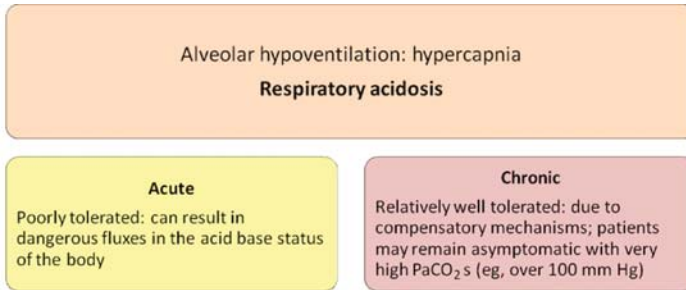
Severe COPD

Bronchiectasis

8.3 Acute Respiratory Acidosis: Clinical Effects

A rapid decrease in alveolar ventilation is poorly tolerated by the body.

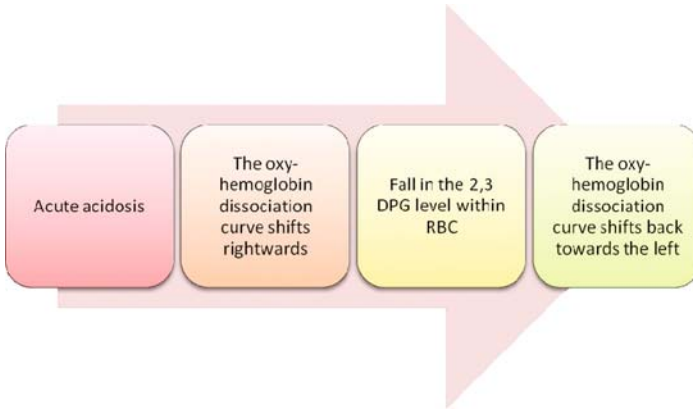
Both acute hypercapnia and acute hypoxemia can be extremely damaging. On the other hand, surprising degrees of hypercapnia and hypoxemia can be tolerated by the body when chronic.



Clinical features of hypercapnia.				
Sympathetic stimulation Tachycardia Arrhythmias Sweating Reflex peripheral vasoconstriction	Peripheral vasodilatation Occurs as a direct effect of hypercapnia. Headaches, hypotension (if hypercapnia is severe).	Central depression Occurs at very high CO ₂ levels. Drowsiness, flaps, coma.	Decreased diaphragmatic contractility & endurance	Cerebral vasodilatation: increased intracranial pressure Confusion, headache, loss of consciousness (if severe), hyperventilation

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.

Non-bicarbonate buffer systems

Non-bicarbonate buffer systems in the body play an important role in buffering changes in CO_2 .

Intracellular proteins and phosphates

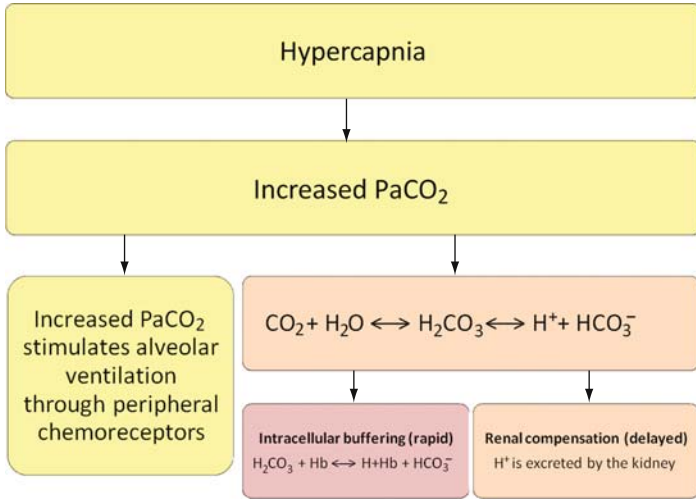
Almost all (about 99%) of the buffering occurs intracellularly, where the concentration of proteins is high.

Hemoglobin

Intracellular proteins

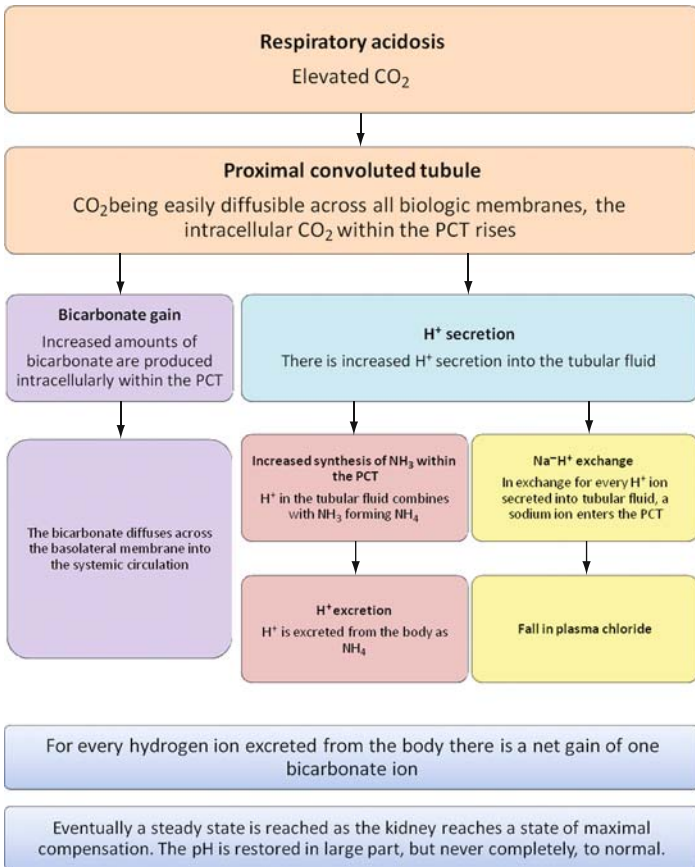
A minor component of buffering is carried out by intracellular proteins.

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)

- $\Delta\downarrow^*pH = 0.008 \times \Delta\uparrow PaCO_2$
- $\Delta H^+ = 0.8 \times \Delta PaCO_2$
- HCO_3^- increases by up to 0.1 mEq/L for every mmHg rise in CO_2
- $H^+ = (0.8 \times PaCO_2) + 8$

Chronic respiratory acidosis (>24 hours)

- $\Delta\downarrow pH = 0.003 \times \Delta\uparrow PaCO_2$
- $\Delta H^+ = 0.3 \times \Delta PaCO_2$
- HCO_3^- increases by up to 0.4 mEq/L for every mmHg rise in CO_2
- $H^+ = (0.3 \times PaCO_2) + 27$

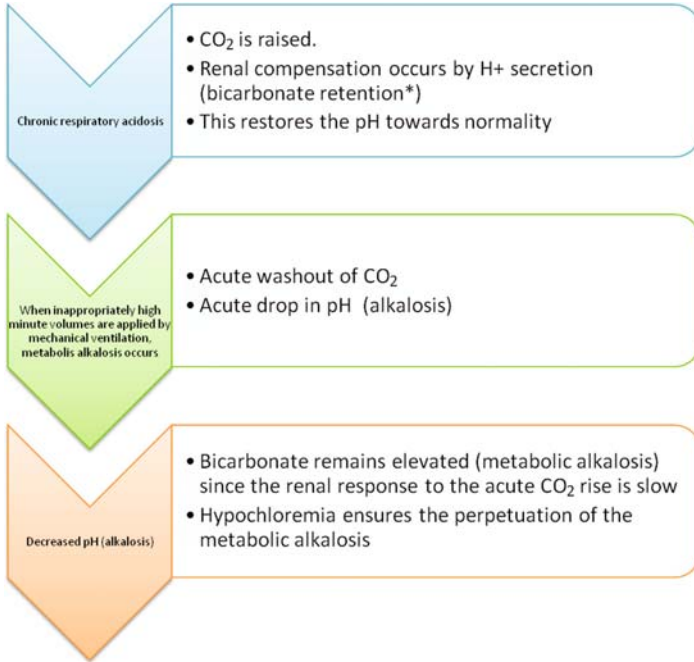
Limits of compensation for respiratory acidosis

- 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

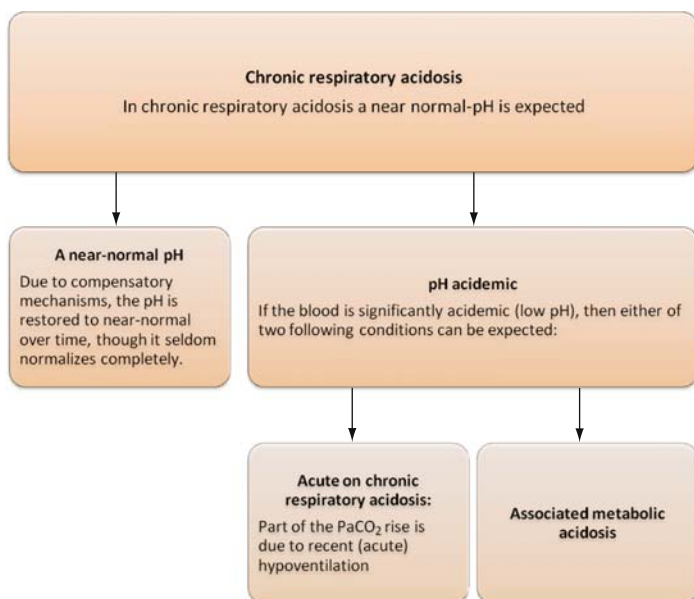
8.9 Post-Hypercapnic Metabolic Alkalosis

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

8.10 Acute on Chronic Respiratory Acidosis



8.11 Respiratory Acidosis: Acute or Chronic?

Using the modified Henderson–Hasselbach equation, $H^+ = 24 (PaCO_2/HCO_3)$ $H^+ = \text{normally } 40 \text{ nmol/L}$ The ratio $\Delta H^+ / \Delta CO_2$ differs in each of the following conditions:		
Acute respiratory acidosis: $\Delta H^+ / \Delta CO_2 = > 0.7$	Acute-on-chronic respiratory acidosis $\Delta H^+ / \Delta CO_2 = 0.3-0.7$	Chronic respiratory acidosis: $\Delta H^+ / \Delta CO_2 = < 0.3$
Case example: PaCO₂ = 80 mmHg; HCO₃ = 20 mEq/L $H^+ = 24 (PaCO_2 / HCO_3)$ Substituting, $H^+ = 24 (80 / 20)$ $H^+ = 24 \times 4 = 96$ Normal $H^+ = 40$; normal PaCO ₂ = 40 $\Delta H^+ / \Delta CO_2 = (96-40) / (80-40)$ $\Delta H^+ / \Delta CO_2 = 1.4$ i.e., the value falls above 0.7	Case example: PaCO₂ = 90 mmHg; HCO₃ = 30 mEq/L $H^+ = 24 (PaCO_2 / HCO_3)$ Substituting, $H^+ = 24 (90 / 30)$ $H^+ = 24 \times 3 = 72$ Normal $H^+ = 40$; normal PaCO ₂ = 40 $\Delta H^+ / \Delta CO_2 = (72-40) / (90-40)$ $\Delta H^+ / \Delta CO_2 = 0.44$ i.e., the value falls between 0.3 and 0.7	Case example: PaCO₂ = 90 mmHg; HCO₃ = 45 mEq/L $H^+ = 24 (PaCO_2 / HCO_3)$ Substituting, $H^+ = 24 (90 / 45)$ $H^+ = 24 \times 2 = 48$ Normal $H^+ = 40$; normal PaCO ₂ = 40 $\Delta H^+ / \Delta CO_2 = (48-40) / (90-40)$ $\Delta H^+ / \Delta CO_2 = 8 / 50 = 0.16,$ i.e., the value falls below 0.3

Chapter 9

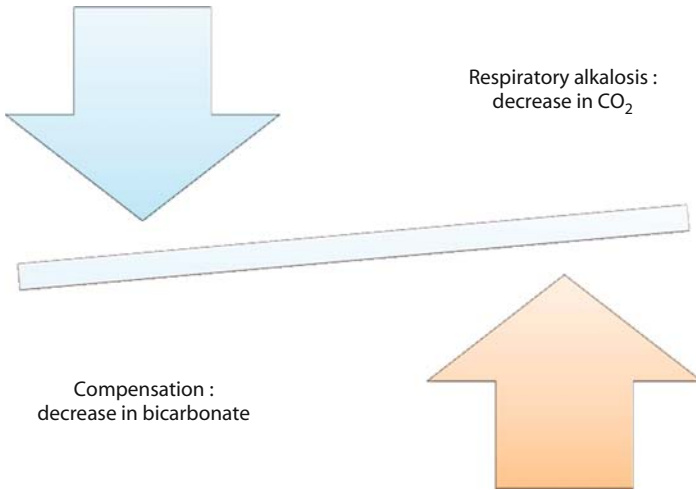
Respiratory Alkalosis

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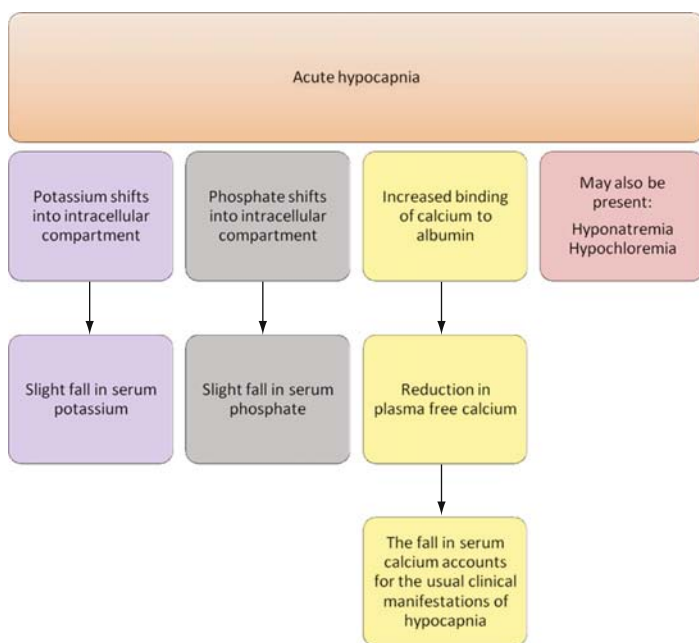
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9.1 Respiratory Alkalosis

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.

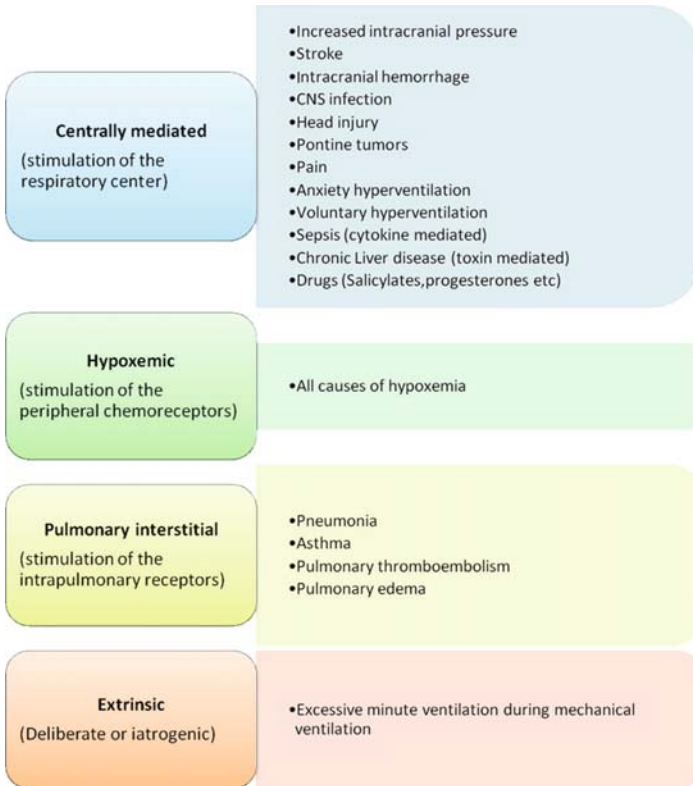


9.2 Electrolyte Shifts in Acute Respiratory Alkalosis

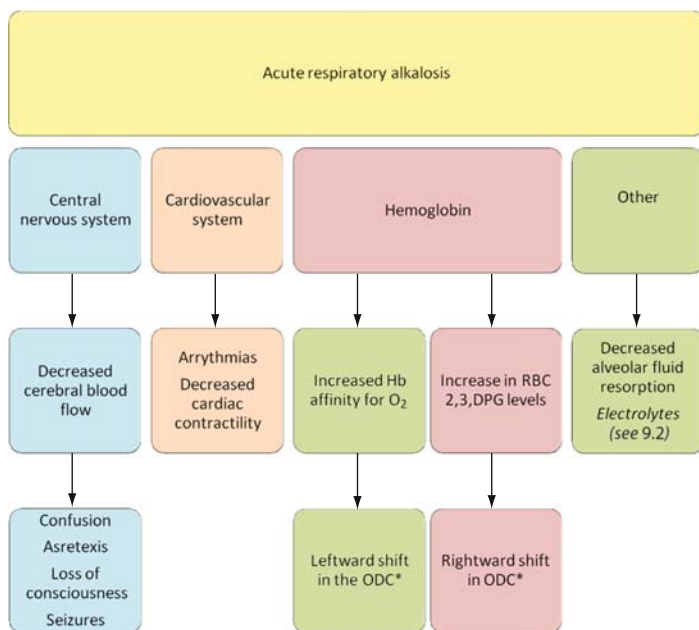


Wiseman, AC, Linas, S. Disorders of potassium and acid–base balance. *Am J Kidney Dis* 2005; 45(5): 941–9

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)	Chronic respiratory alkalosis (>12 hours)
<ul style="list-style-type: none"> • $\Delta \uparrow \text{pH} = 0.01 \times \Delta \downarrow \text{PaCO}_2^*$ • $\Delta \downarrow \text{H}^+ = 0.75 \times \Delta \downarrow \text{PaCO}_2$ • HCO_3^- falls by up to 0.2mEq/L for every mmHg fall in CO_2 • $\text{H}^+ = (0.75 \times \text{PaCO}_2) + 10$ 	<ul style="list-style-type: none"> • $\Delta \uparrow \text{pH} = 0.003 \times \Delta \downarrow \text{PaCO}_2$ • $\Delta \downarrow \text{H}^+ = 0.3 \times \Delta \downarrow \text{PaCO}_2$ • HCO_3^- falls by up to 0.5mEq/L for every mmHg fall in CO_2 • $\text{H}^+ = (0.3 \times \text{PaCO}_2) + 28$

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

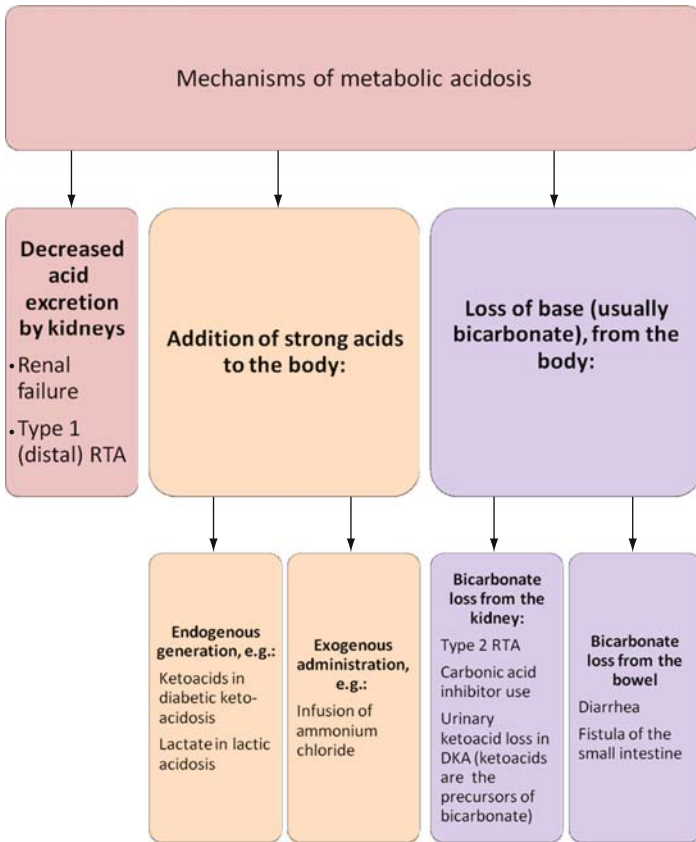
Metabolic Acidosis

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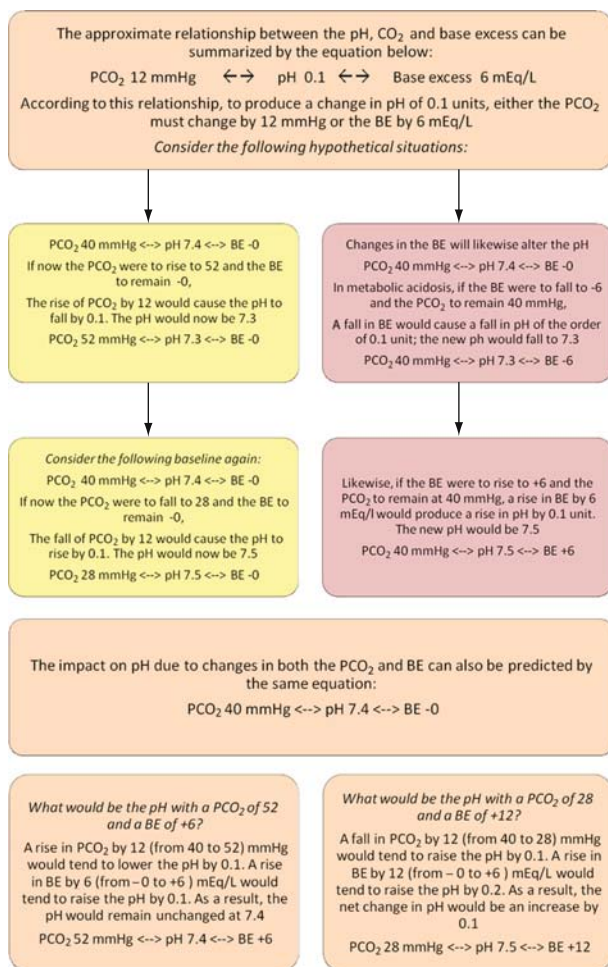
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10.1 The Pathogenesis of Metabolic Acidosis



10.2 Relationships



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.

In practice the measured ions are:

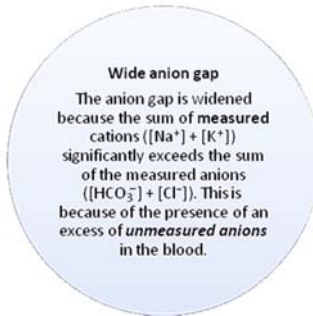
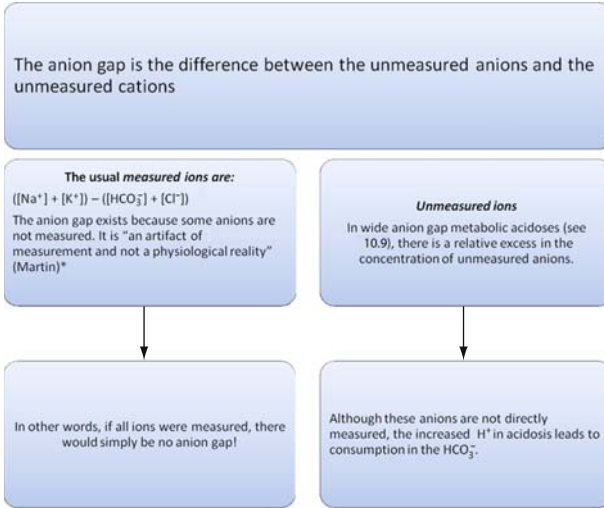
Anions, e.g.:

Sodium (Na^+) and Potassium (K^+)

Cations, e.g.:

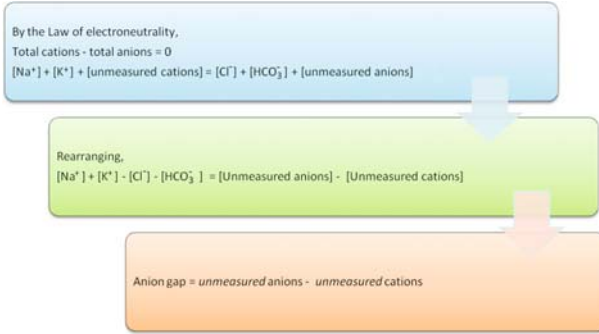
Bicarbonate (HCO_3^-) and Chloride (Cl^-)

10.4 The Anion Gap

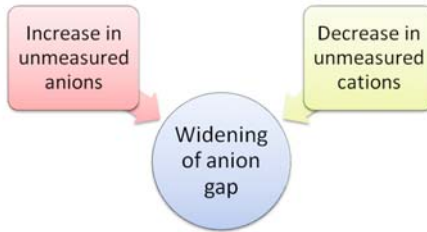


* Martin, L, All you Really Need to Know to Interpret Arterial Blood Gases. Lippincott, Williams and Wilkins, 1999

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:



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

The Law of Electroneutrality can also be written as follows:

Total cations (minus) total anions = 0

$$[\text{Na}^+] + [\text{k}^+] - [\text{Cl}^-] - [\text{HCO}_3^-] - [\text{A}^-] - [\text{unmeasured anions}] = 0$$

In the above equation,

$[\text{H}^+]$ is not taken into consideration since its concentration relative to other cations is miniscule

The concentration of the **unmeasured anions** (eg PO_4^- and SO_4^-) is only to the order of 1 to 3 mEq/L (average 2) mEq/L.

The symbol $[\text{A}^-]$ signifies the collective base pairs of the other weak acids: mostly the charged amino acid residues of plasma proteins.

$[\text{A}^-]$

These weak acids are 90% dissociated at the body pH of 7.4 (since their pK ranges from 6.6 to 6.8). **A(tot)** or the total concentration of these weak acids is 2.4 times (in mEq/L) the concentration of plasma proteins (in g/dL).

$$[\text{A}^-] = \text{A}(\text{tot}) \times 0.9$$

$$[\text{A}^-] = \text{Plasma protein concentration in gm/dL} \times 2.4 \times 0.9$$

$[\text{A}^-]$ now becomes quantifiable, and based on the normal range of plasma proteins, its normal range is seen to be 11-16

Substituting the normal values of the ions in the equation

$$[\text{Na}^+] + [\text{k}^+] - [\text{cl}^-] - [\text{HCO}_3^-] - [\text{A}^-] - [\text{unmeasured anions}] = 0$$

We have:

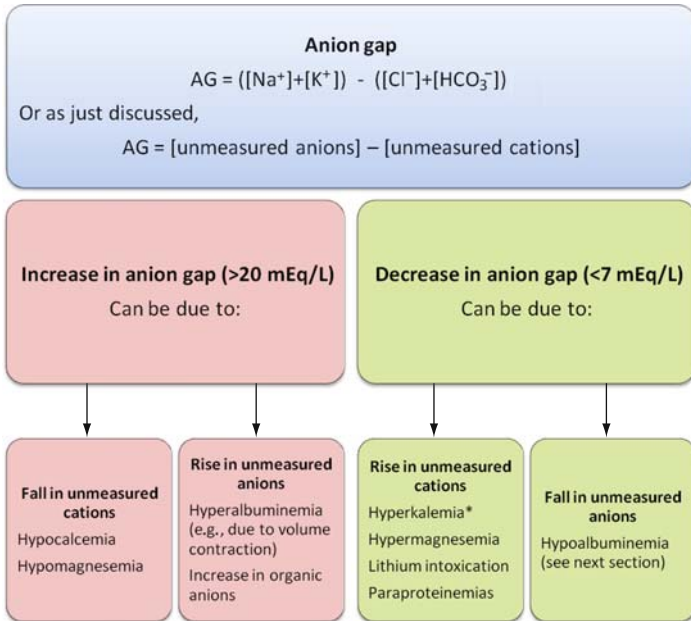
$$140 + 4 - 102 - 25 - 15 - 2 = 0$$

The normal range for the anion gap is 10–15

10.6 Electrolytes and the Anion Gap

Based on the Law of Electroneutrality:

$[Na^+] + [K^+] + [unmeasured\ cations] = [Cl^-] + [HCO_3^-] + [unmeasured\ anions]$, 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

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:

$$(\text{Na}^+) - ([\text{Cl}^-] + [\text{HCO}_3^-])$$

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

$$([\text{Na}^+] + [\text{K}^+]) - ([\text{Cl}^-] + [\text{HCO}_3^-])$$

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.

Either venous CO_2 or the arterial HCO_3 can be used in the formula:

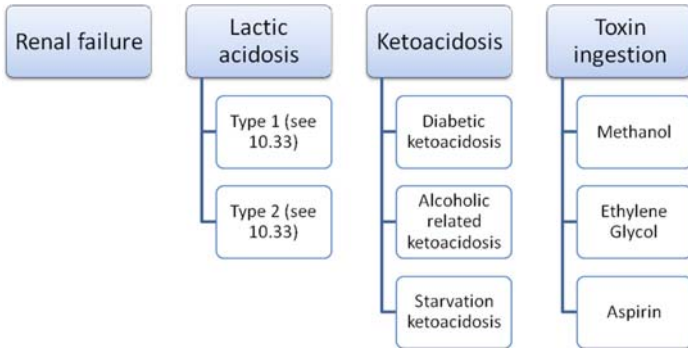
$$\text{AG} = [\text{Na}^+] - ([\text{Cl}^-] + [\text{venous } \text{CO}_2])$$

As far as possible the venous CO_2 should be used in the calculation; this is the preferred approach.

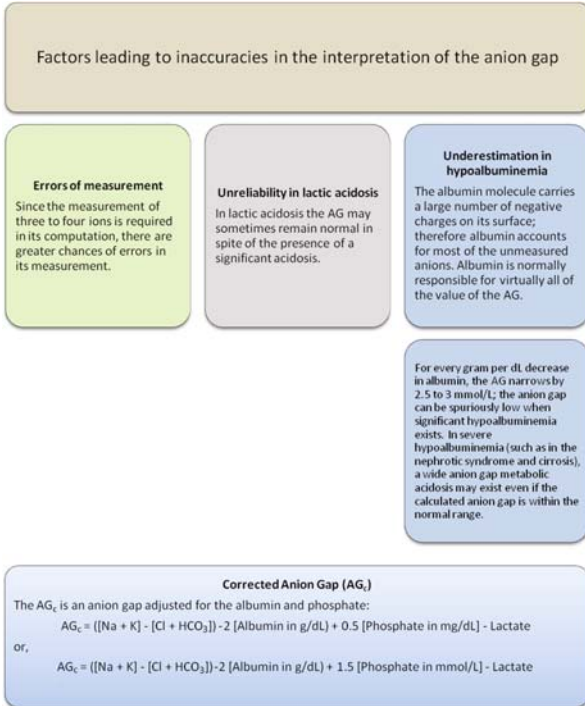
$$\text{AG} = [\text{Na}^+] - ([\text{Cl}^-] + [\text{HCO}_3^-])$$

However, since venous CO_2 roughly approximates the calculated arterial HCO_3 , the latter is often used in its place.

10.9 Causes of a Wide Anion Gap



10.10 Limitations of the Anion Gap: The Corrected Anion Gap

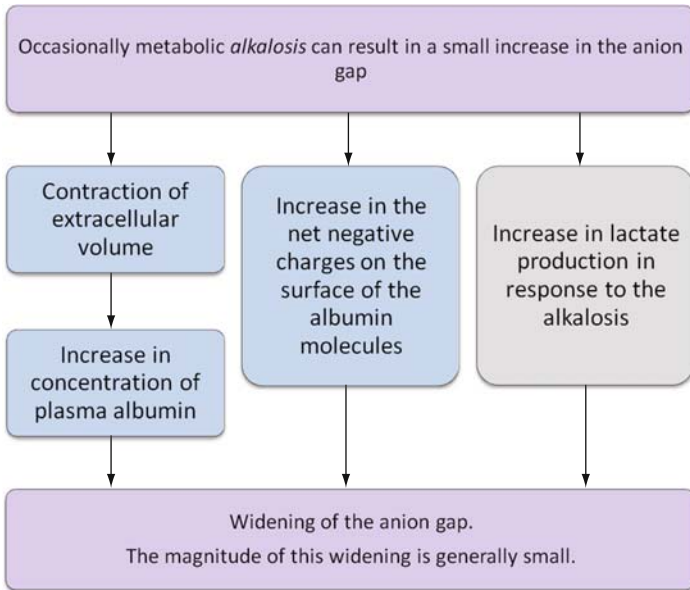


Gabow, PA. Disorders associated with an altered anion gap. *Kidney Int* 1985; 27:472

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

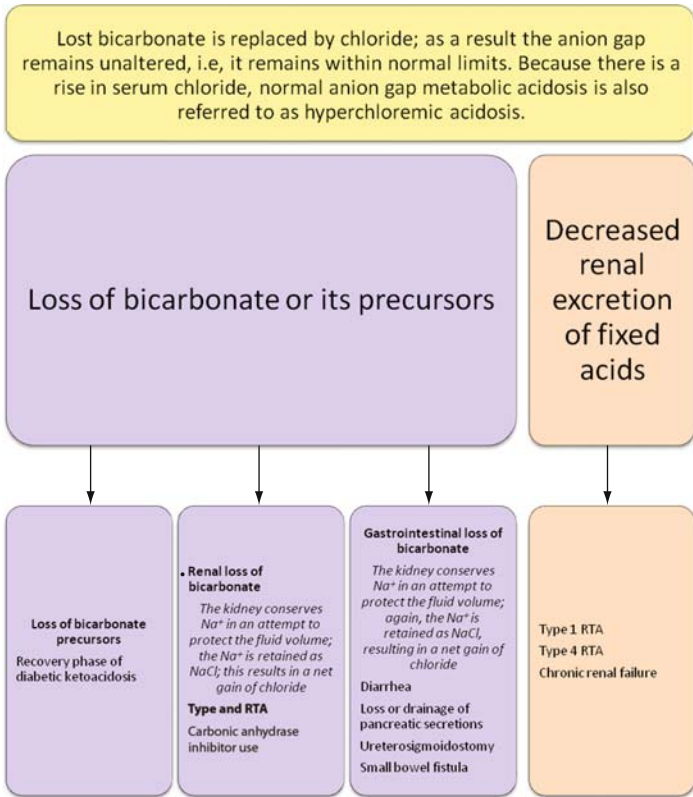
10.12 Wide Anion Gap in Metabolic alkalosis



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

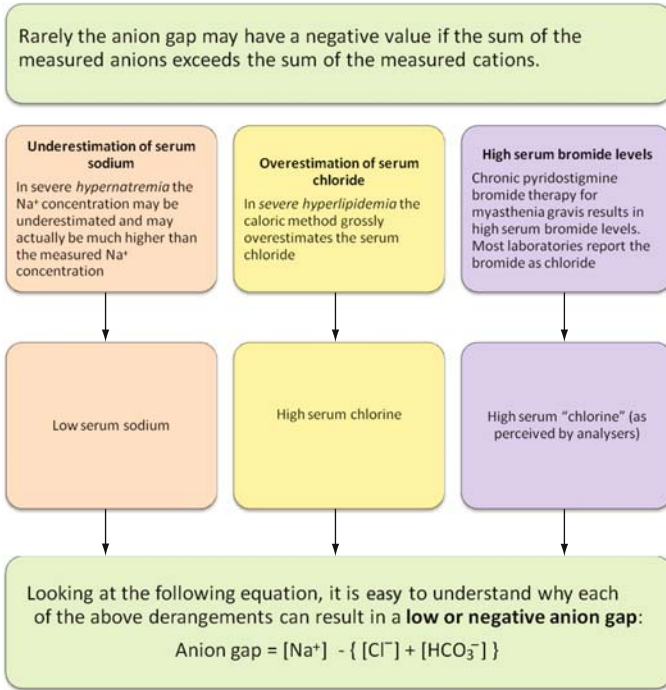
10.13 Normal Anion-Gap Metabolic Acidosis



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

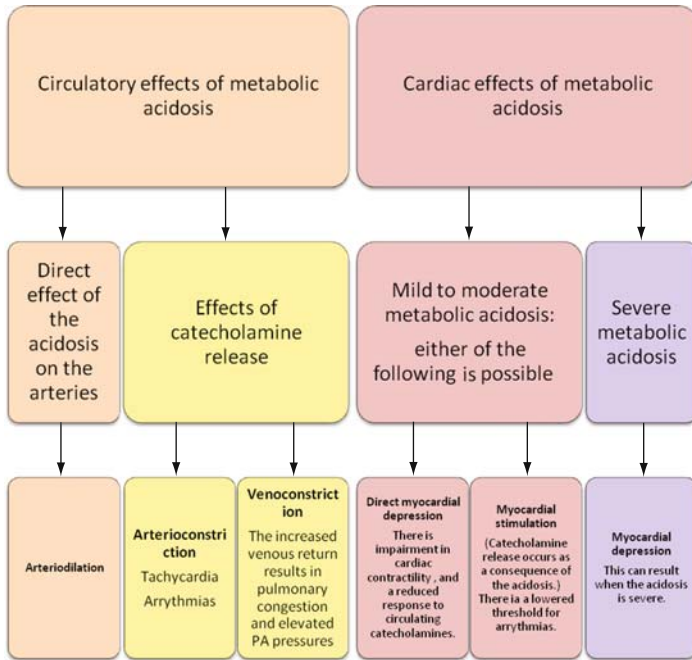


Kelleher, SP, Raciti, A, Arbeit, LA. Reduced or absent serum anion gap as a marker for severe lithium carbonate intoxication. Arch Intern Med 1986; 146:1839

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

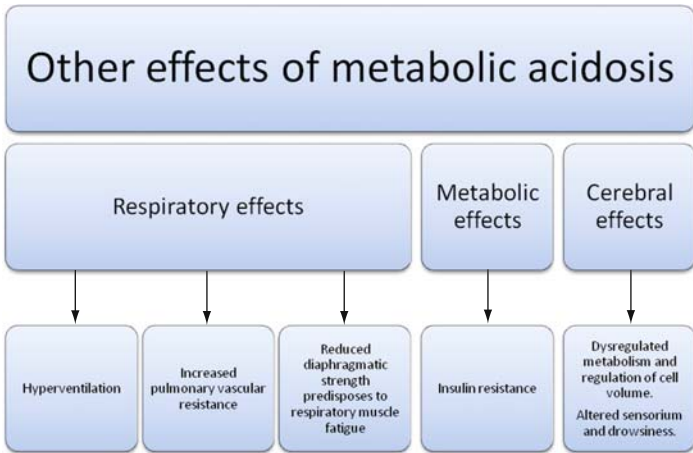
Winter's formula	ΔPCO_2	PCO_2 and pH
<p>The degree of compensation can be predicted by Winter's formula:</p> <p>Predicted $\text{PCO}_2 = (1.5 \times \text{HCO}_3^-) + 8 \pm 2$.</p> <p>Lower PCO_2 values than predicted indicate the presence of a coexisting respiratory alkalosis. Higher CO_2 values than predicted indicate a coexisting respiratory acidosis.</p>	<p>The change in PCO_2 $(\Delta\text{PCO}_2) = (1.1 - 1.3) \times \Delta\text{HCO}_3^-$</p>	<p>$\text{PCO}_2 =$ the last 2 digits of the pH</p>
<p>Limits of compensation for metabolic acidosis</p> <ul style="list-style-type: none"> • Although respiratory response to metabolic acidosis starts immediately, the overall compensatory response takes 12–24 hours to develop fully. • The lungs are capable of maximising ventilation such that the PCO_2 drops to a lower limit of about 10 mmHg. 		

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

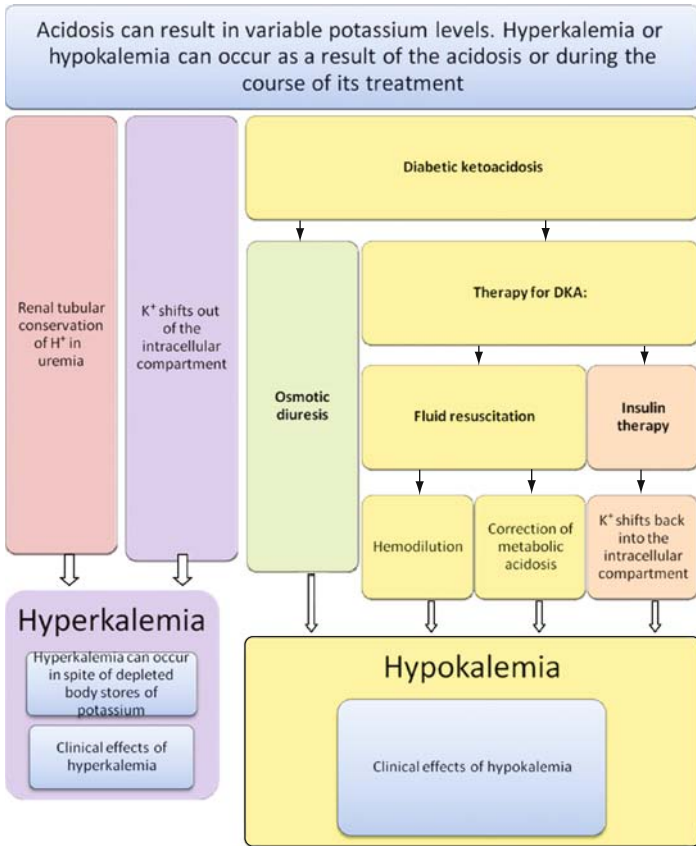
Albert, MS, Dell, RB, Winters, RW. Quantitative displacement of acid-base equilibrium in metabolic acidosis. Ann Intern Med 1967; 66:312–322

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

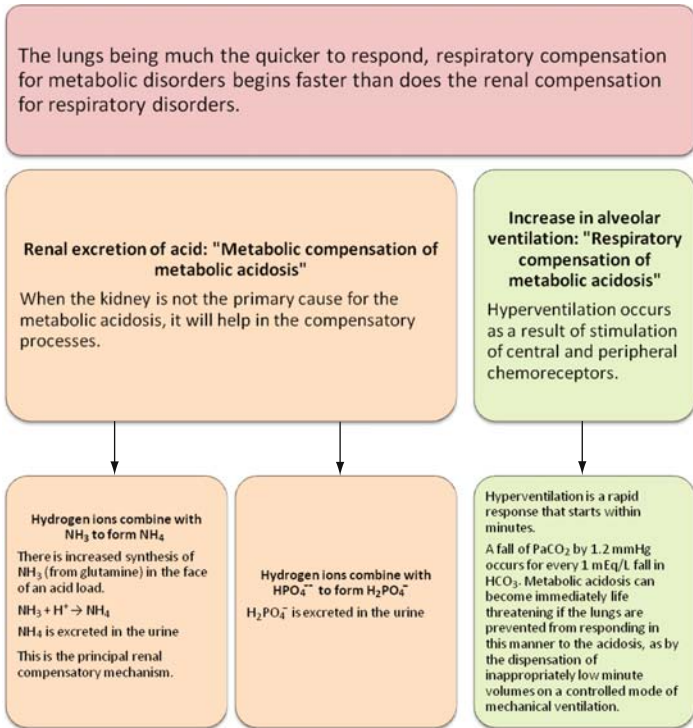


Wallia, R, Greenberg, AS, Piraino, B, et al. Serum electrolyte patterns in end-stage renal disease. *Am J Kidney Dis* 1986; 8:98

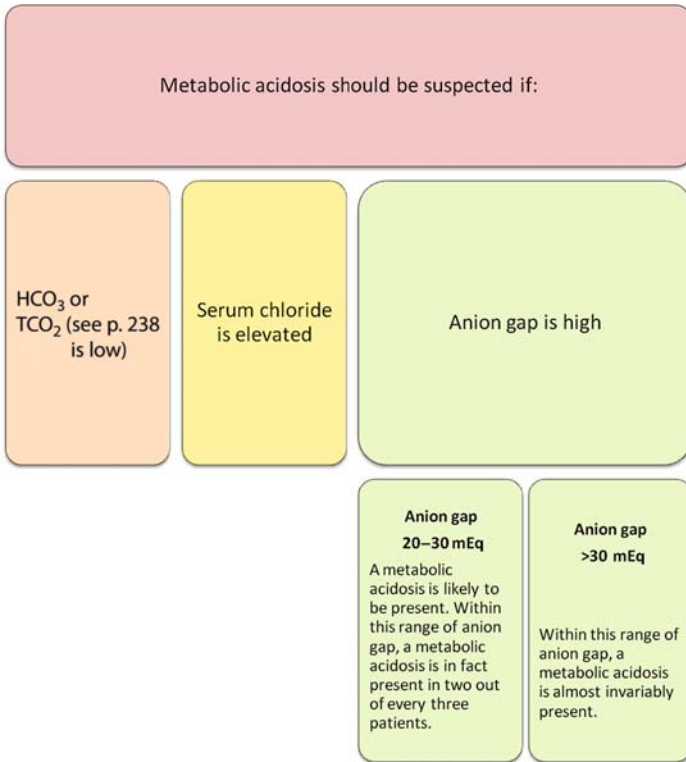
Wiederseiner, JM, Muser, J, Lutz, T, et al. Acute metabolic acidosis: Characterization and diagnosis of the disorder and the plasma potassium response. *J Am Soc Nephrol* 2004; 15:1589

10.19 Compensatory Response to Metabolic Acidosis

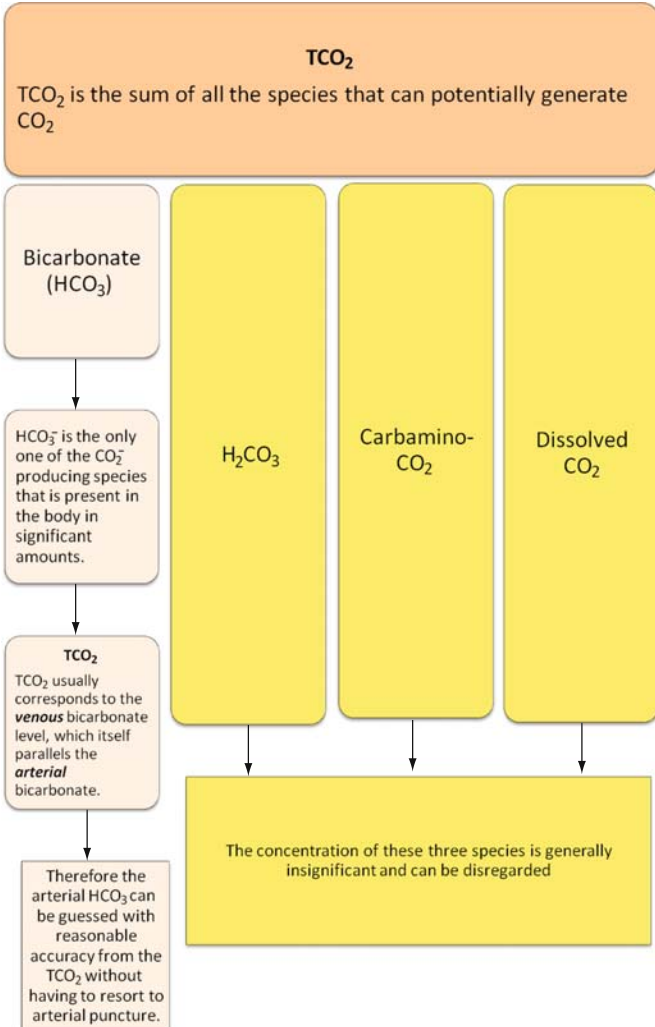
Rarely does a metabolic acidosis remain uncompensated (examples: presence of associated respiratory disease: a paralysed patient on ventilator who is being given inappropriately low minute volumes). In contrast to respiratory disorders which are well compensated by the kidney, compensation for metabolic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



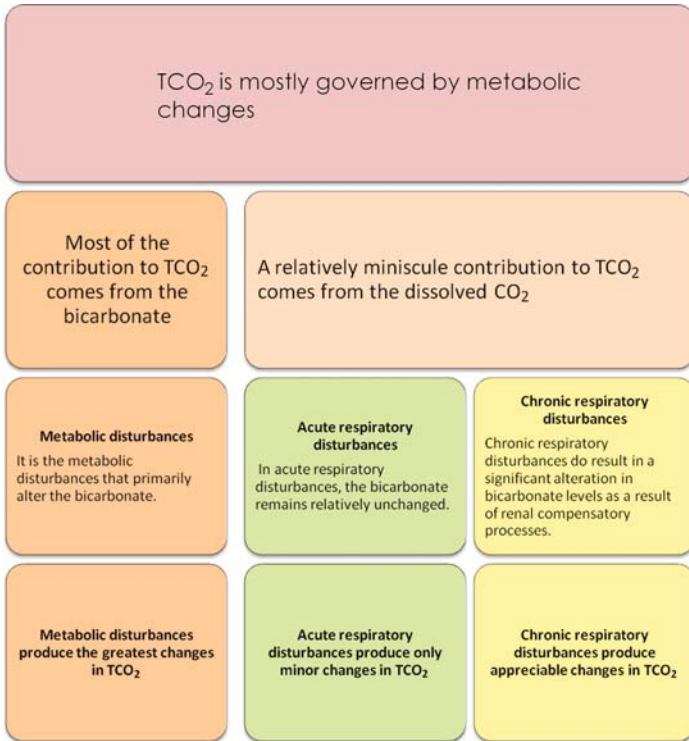
10.20 When to Suspect Metabolic Acidosis



10.21 Total CO₂ (TCO₂)



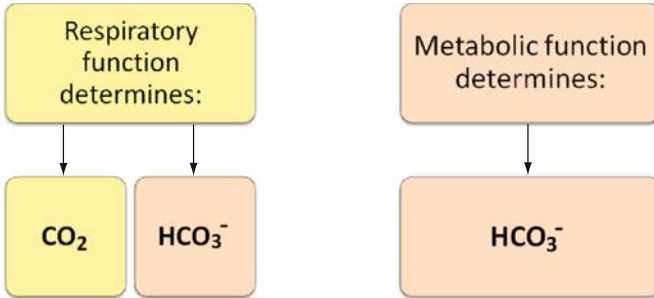
10.22 Clinical Utility of TCO₂



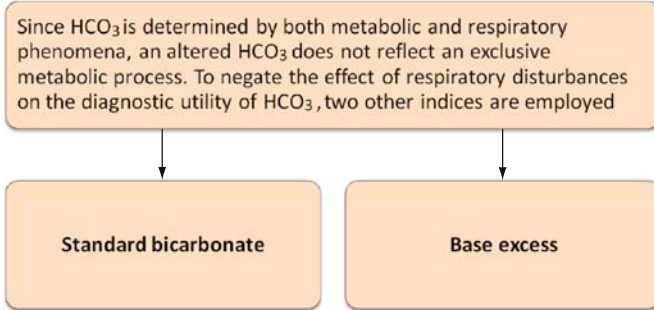
As mentioned earlier, at the usual body pH, the ratio of bicarbonate to carbonic acid is 20:1. This means that the TCO₂ is about 5% (or 2–3 mEq) higher than the serum bicarbonate. When the difference between the two is greater than this, a metabolic acidosis is usually present.

10.23 HCO_3^- in Metabolic & Respiratory Disorders

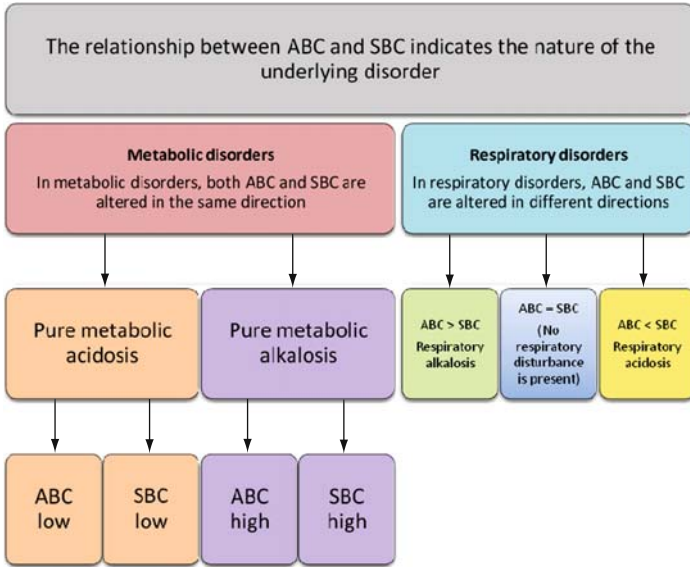
An altered HCO_3^- is not specific for metabolic derangements.



Although plasma bicarbonate is the most commonly used index of the *metabolic* status, it can also be altered in *respiratory* disturbances as well

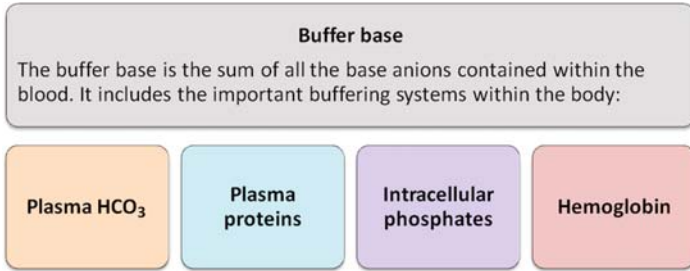


10.24 Relationship between ABC and SBC



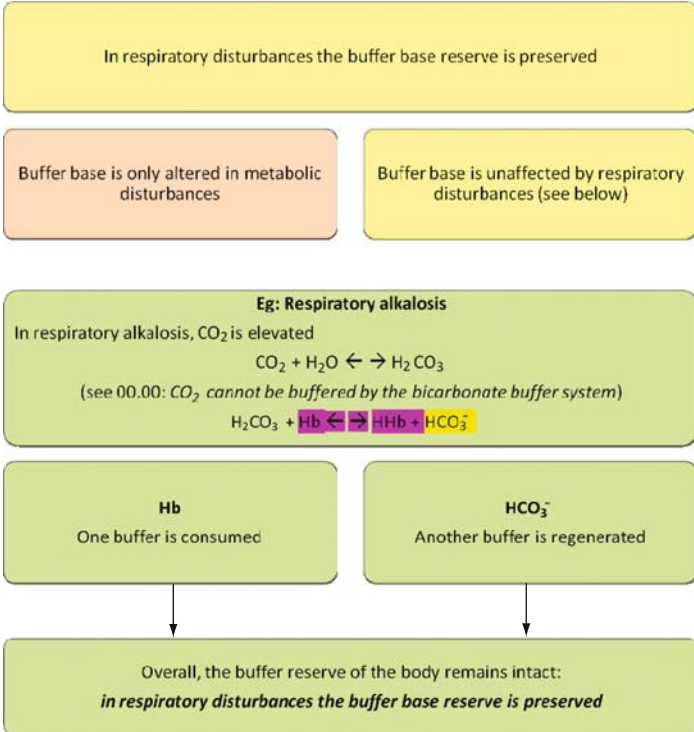
10.25 Buffer Base

“Whole buffer base” (Singer and Hastings, 1948).



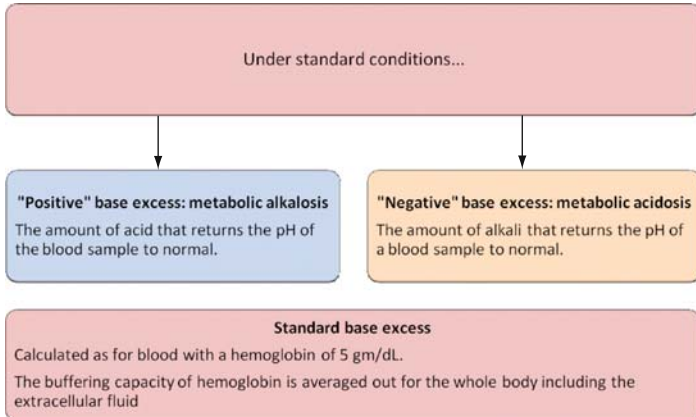
It may be that the buffer base mirrors electrolyte derangements the understanding of which may hold the key to this elusive concept.

10.26 Preservation of the Buffer Base in Respiratory Disturbances



10.27 Base Excess

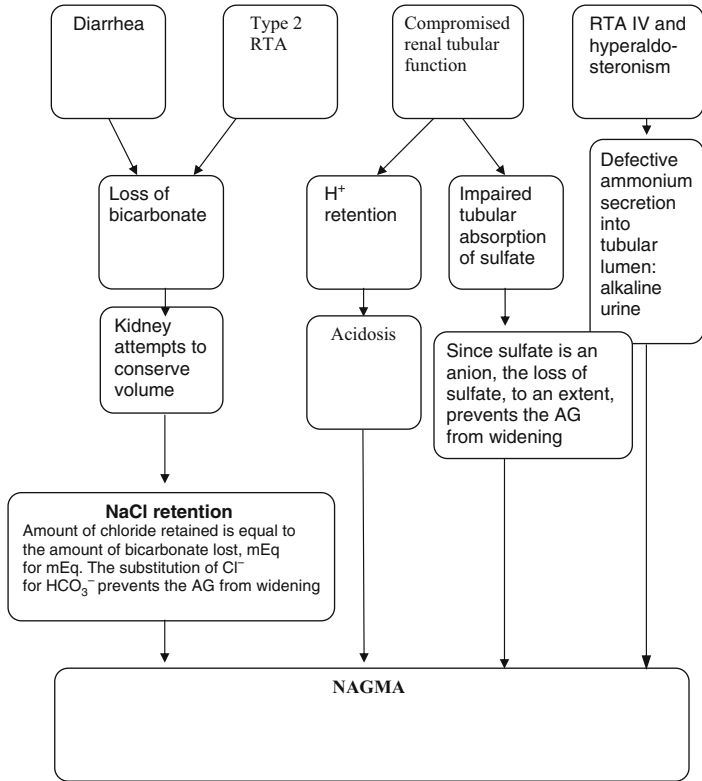
In 1958 Astrup and Siggard-Andersen described *Base Excess* as an improved indicator of *metabolic* acid–base disorders.



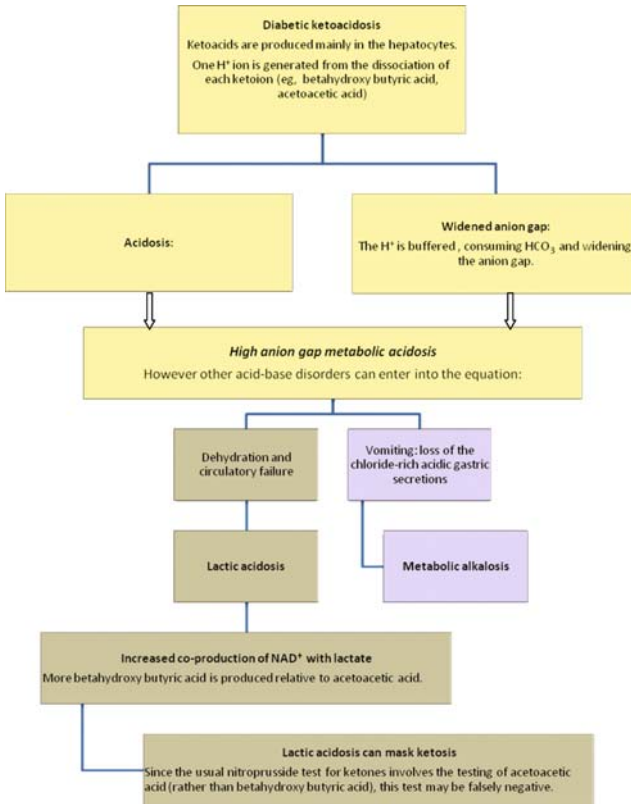
Schlichtig, R, Grogono, AW, Severinghaus, JW. Human PaCO₂ and standard base excess compensation for acid–base imbalance. *Crit Care Med* 1998; 26(7):1173–9

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



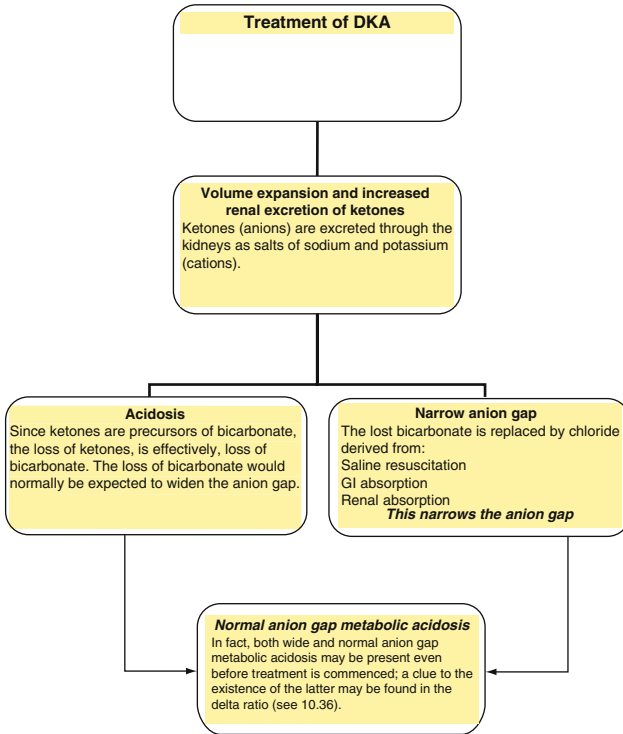
10

Adrogue, 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

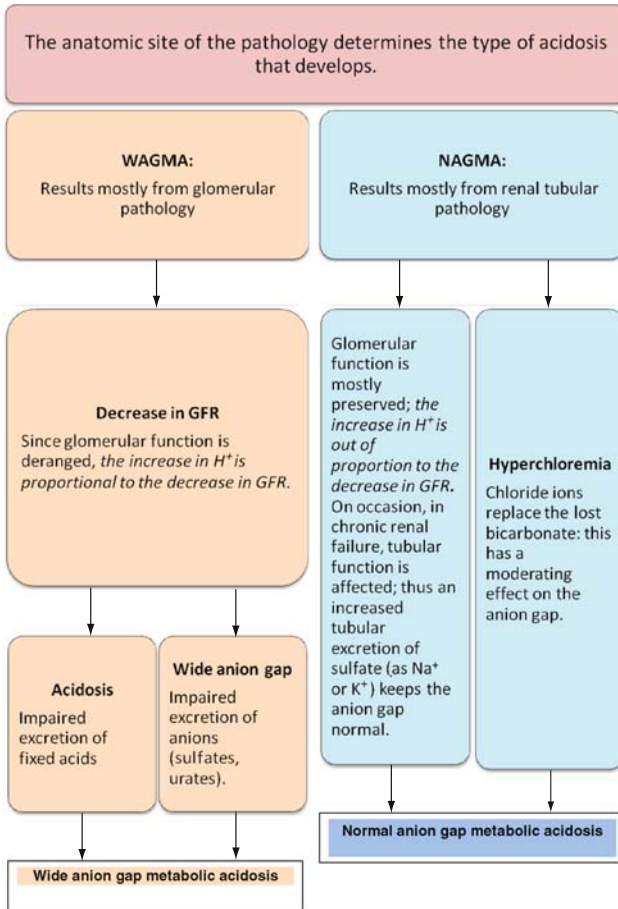
10.30 Normal Anion Gap Metabolic Acidosis During Treatment of DKA

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.

About 1 mEq/kg/hr lactate normally produced during glucose metabolism; it is utilized for gluconeogenesis by the liver.
 Normal serum lactate is generally ≤ 2 mEq/L. This can rise to about 4 mEq/L during exercise.

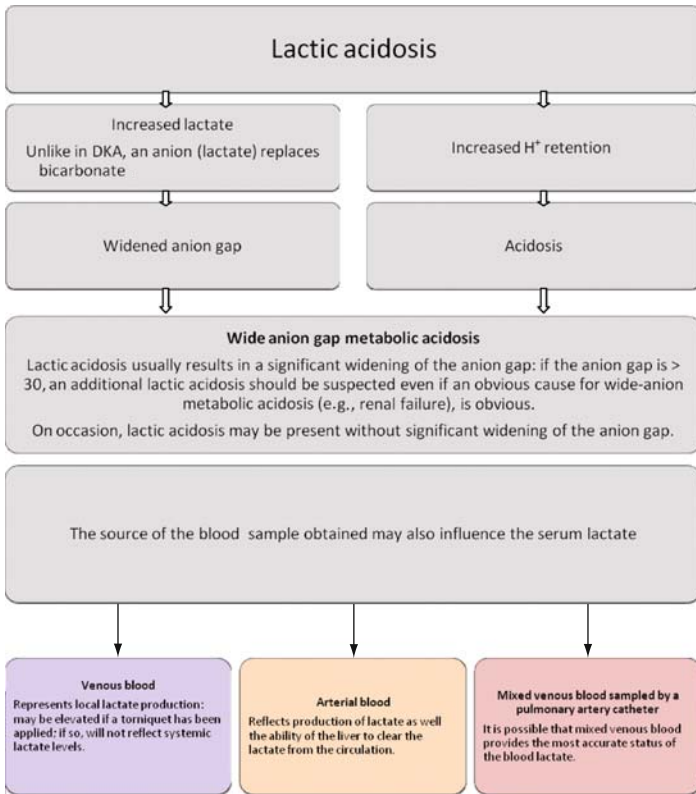
<p>L-lactic acidosis</p>	<p>D-Lactic acidosis</p> <p>D-lactate overproduction by intestinal bacteria.</p> <p><i>Occurs in the setting of:</i></p> <p>Intestinal obstruction Jejunioileal bypass</p> <p>A D-lactic acidosis must be suspected in the setting of unexplained metabolic acidosis especially if diarrhea is also present.</p> <p>The usual lab technique for the detection of blood lactate measures L-lactic acid, and special a test for D-lactic acid needs to be separately ordered.</p>
<p>Type A lactic acidosis occurs in states of tissue hypoperfusion</p> <p>Circulatory failure and shock Severe anemia Histotoxic hypoxia (CO or cyanide poisoning) Mitochondrial enzyme defects</p>	<p>Type B lactic acidosis occurs under aerobic conditions</p> <p>Hepatic failure Renal failure Diabetes mellitus Seizures Malignancies Infections (malaria, cholera) Drugs (biguanides, methanol, INH, AZT)</p>

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

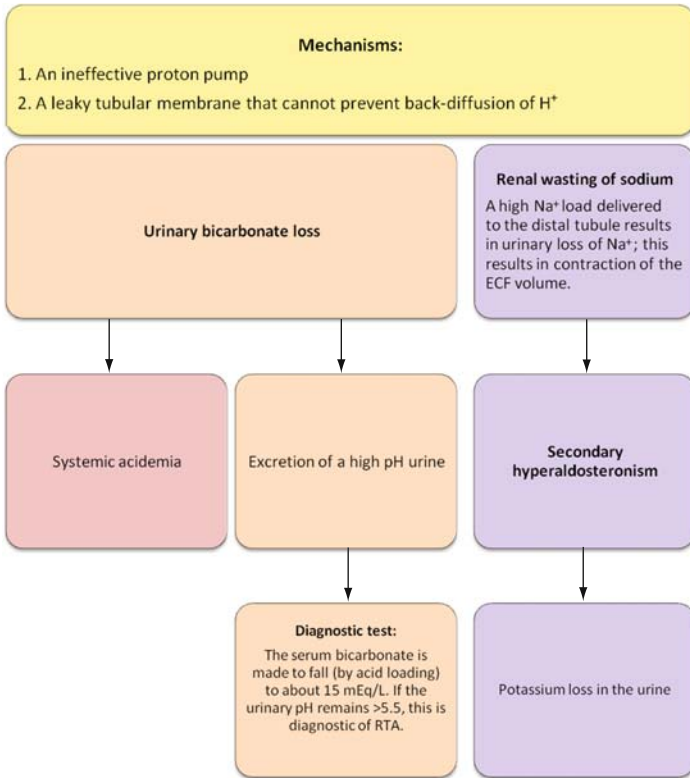


Weil, MH, Michaels, S, Rackow, EC. Comparison of blood lactate concentrations in central venous, pulmonary artery and arterial blood. Crit Care Med, 1987; 15:489–490

10.34 Distal RTA

Syn: Type I RTA, Classic RTA

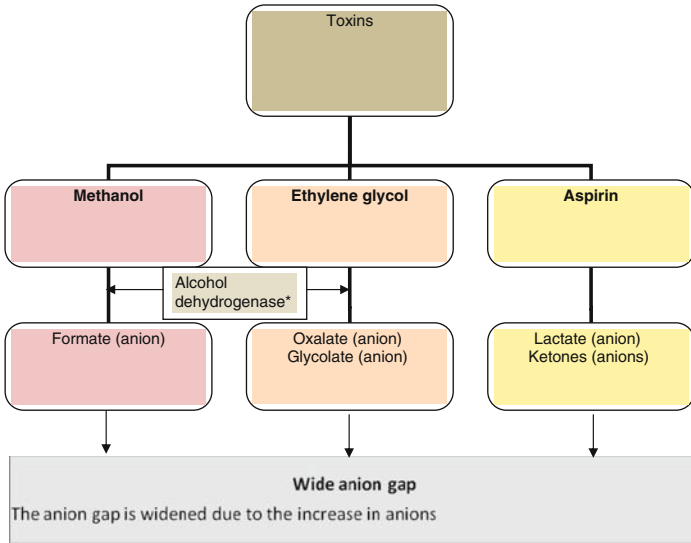
A urinary acidifying defect results in an alkaline urine remains (pH <5.5) in the face of severe acidemia. Distal RTA is generally more severe than proximal RTA.



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



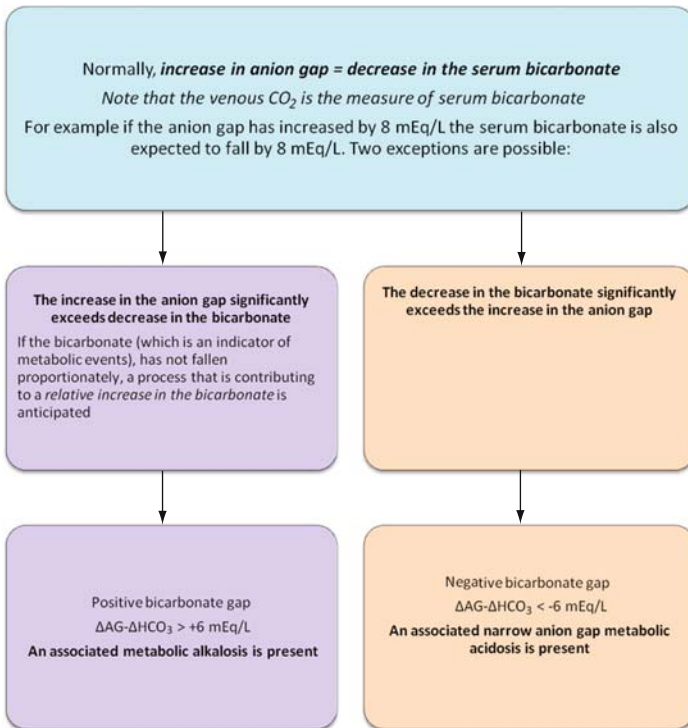
*The enzyme alcohol dehydrogenase helps in the catalysis of the reactions that lead to formation of the toxic metabolites. Co-ingested ethanol competes for the active sites on the enzyme alcohol dehydrogenase and so decreases the rate of formation of the methanol and ethylene glycol-induced toxic metabolites

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

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 (ΔHCO_3) is termed the bicarbonate gap.



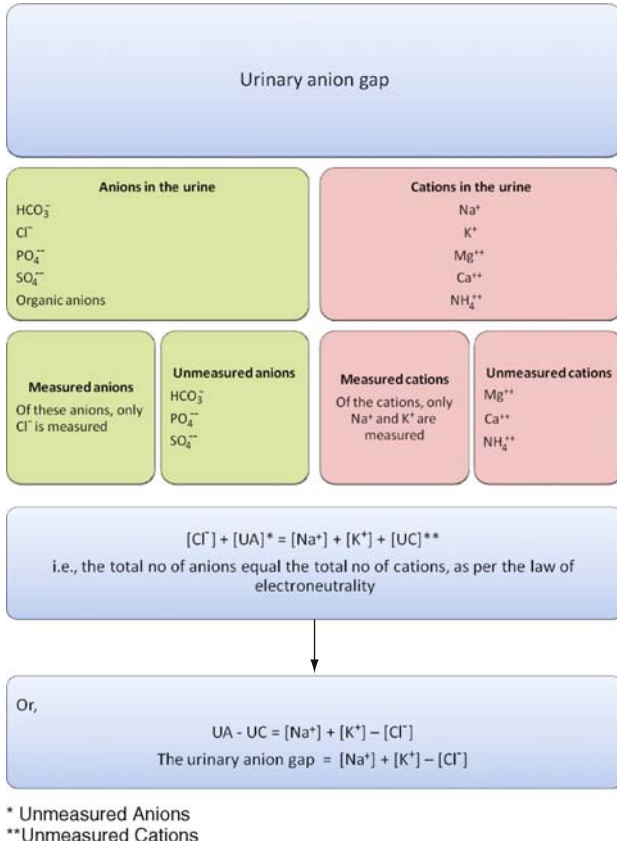
In a pure wide anion gap metabolic acidosis, the fall in the bicarbonate need not always exactly parallel the rise in the AG: although the bicarbonate is the principal extracellular buffer, it is not the only buffer; there are other buffer systems that are also participating in the buffering process.

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

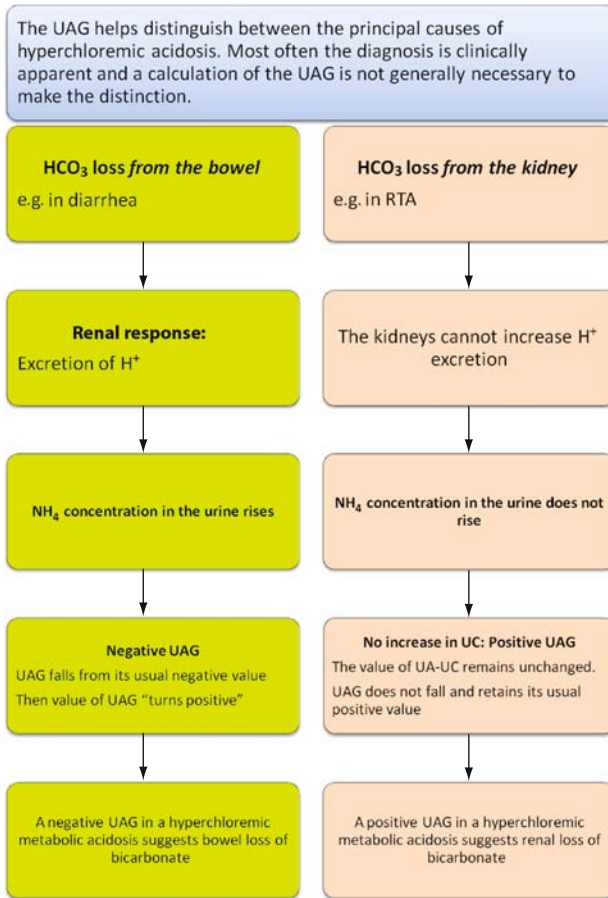
10.37 Urinary Anion Gap

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



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

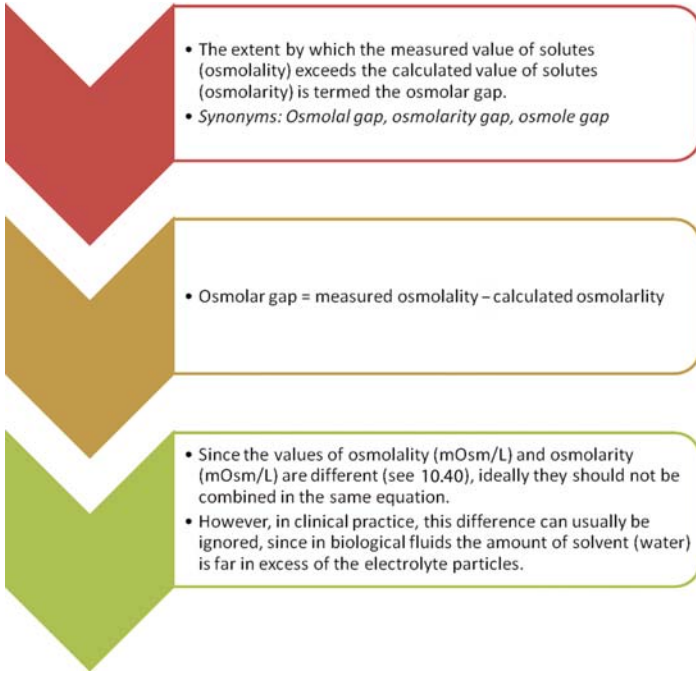
10.40 Osmolarity and Osmolality

<p>Osmolality Osmolality is the number of osmoles of solute per kilogram of solvent. It is the osmotic activity in relation to the weight of the solvent.</p>	<ul style="list-style-type: none"> • Osmolality is expressed in mOsm/kg of solute • It is measured in the lab by osmometers. 	
<p>Osmolarity The number of osmoles of solute per liter of solvent. It is the osmotic activity in relation to the volume of the solvent.</p>	<ul style="list-style-type: none"> • Osmolarity is expressed in mOsm/L. • It is a calculated value. 	
<p>Several formulae for the calculation of plasma osmolarity are available</p> $(2 \times \text{Na}) + \text{glucose}/18 + \text{BUN}/2.8$ $(2 \times \text{Na}) + \text{glucose}/18 + \text{BUN}/2.8 + 9$ $(2 \times \text{Na}) + \text{glucose}/18 + \text{BUN}/2.8 + \text{Ethanol}/4.6$		
<p>The factor of 2 is on account of the chloride that accompanies the Na^+</p>	<p>2.8 in the conversion factor for glucose (for the conversion of mg/dL to mmol/L)</p>	<p>18 in the conversion factor for blood urea nitrogen (for the conversion of mg/dL to mmol/L)</p>

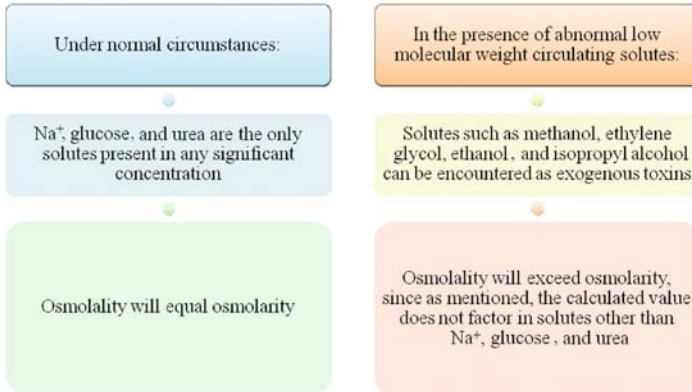
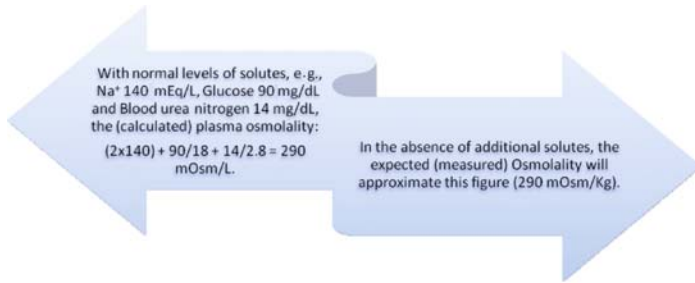
Rose, BD. Clinical Physiology of Acid–Base and Electrolyte Disorders, 4th ed, McGraw-Hill, New York, 1994, 567–568

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

10.41 The Osmolar Gap

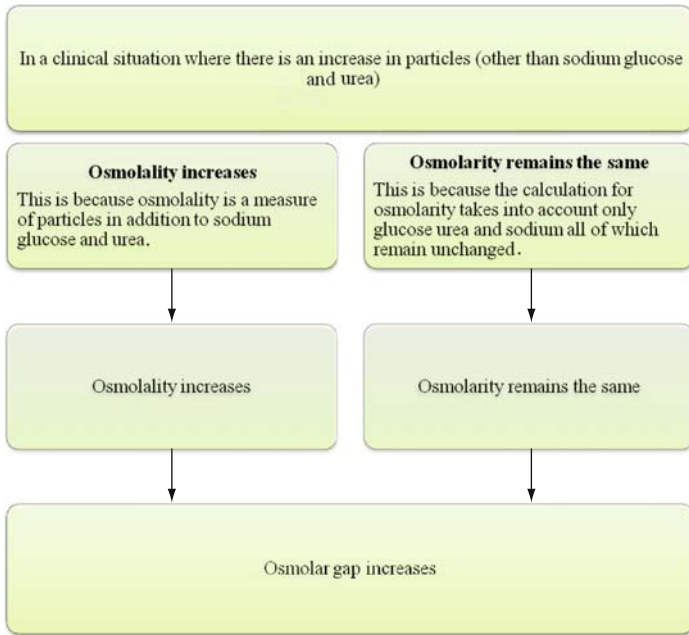


10.42 Detection of Abnormal Solutes



- 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*.

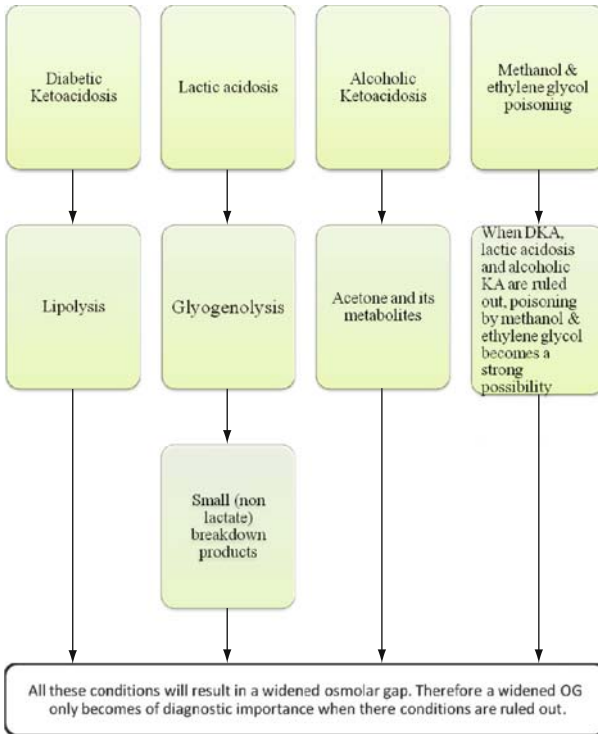
Walker, JA, Schwartzbard, A, Krauss, EA, et al. The missing gap: A pitfall in the diagnosis of alcohol intoxication by osmometry. Arch Intern Med 1986; 146:1843

*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:



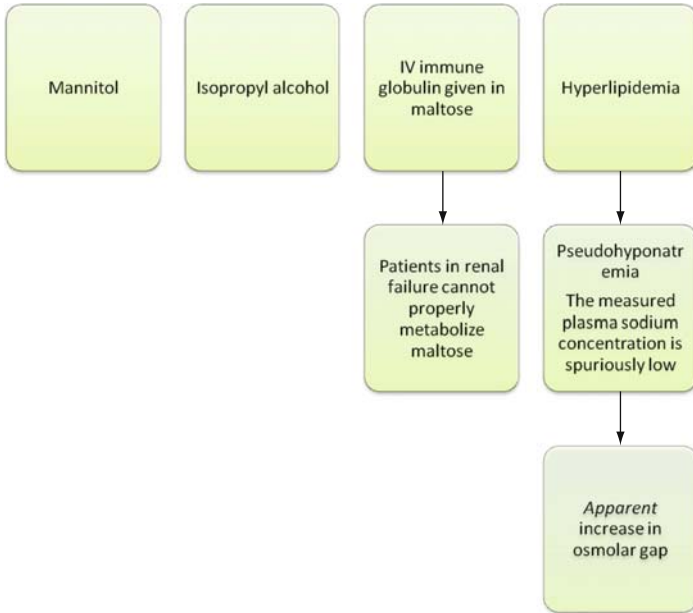
Sklar, AH, Linas, SL. The osmolal gap in renal failure. *Ann Intern Med* 1983; 98:481

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

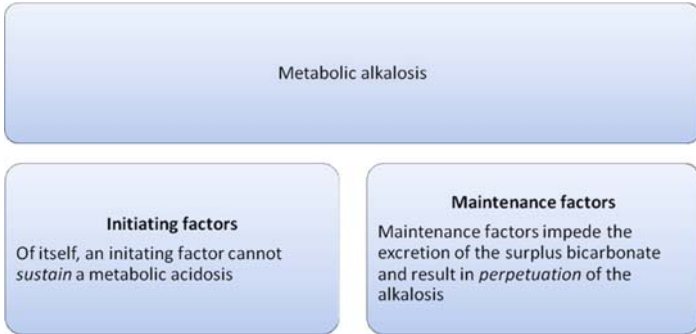
Metabolic Alkalosis

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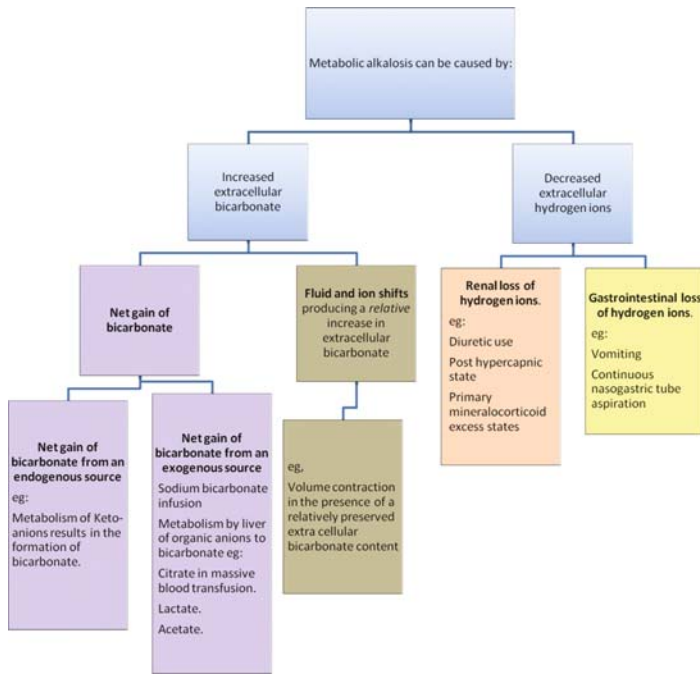
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11.1 The Pathogenesis of Metabolic Alkalosis

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



11.2 Metabolic Alkalosis: Etiology



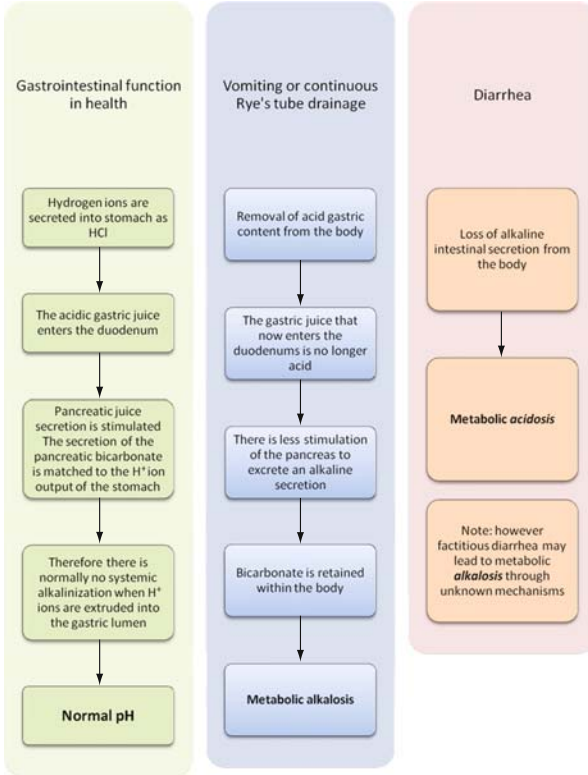
Galla, JH. Metabolic alkalosis. *J Am Soc Nephrol* 2000; 11:369

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

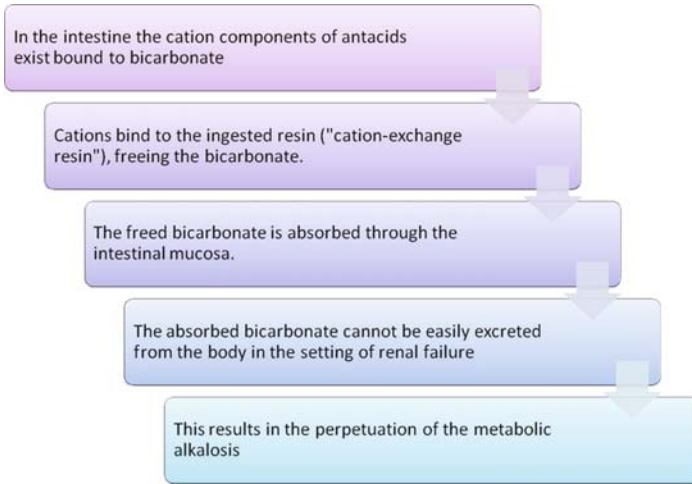


Kassirer, JP, Schwartz, WB. The response of normal man to selective depletion of hydrochloric acid. Factors in the genesis of persistent gastric alkalosis. *Am J Med* 1966; 40:10

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

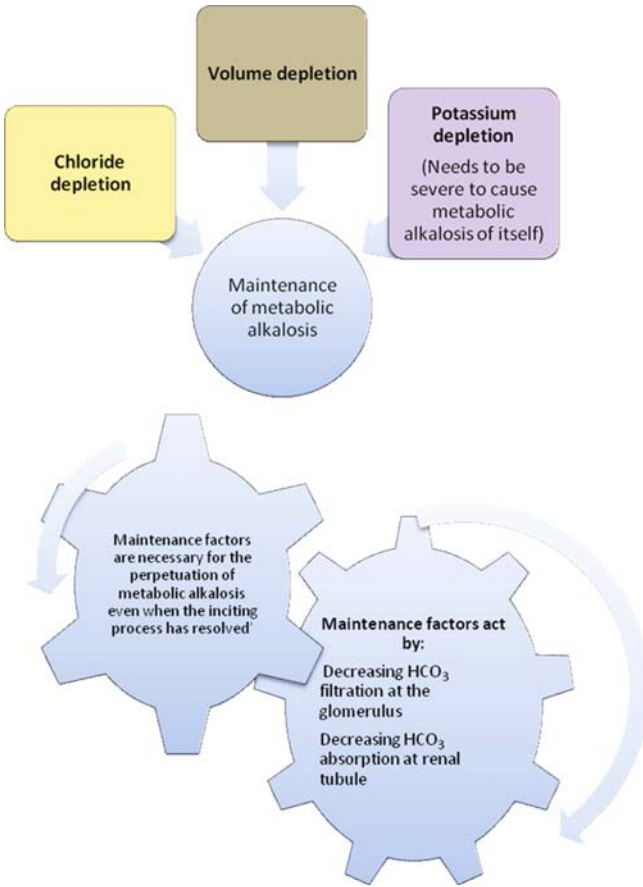
Cation exchange resins are used in the treatment of hyperkalemia.



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



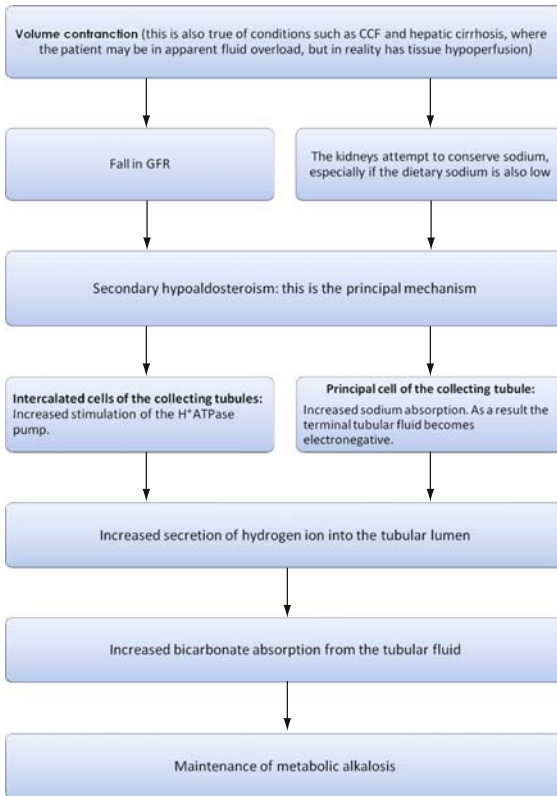
Sabatini, S, Kurtzman, NA. The maintenance of metabolic alkalosis: Factors which decrease bicarbonate excretion. *Kidney Int* 1984; 25:357

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

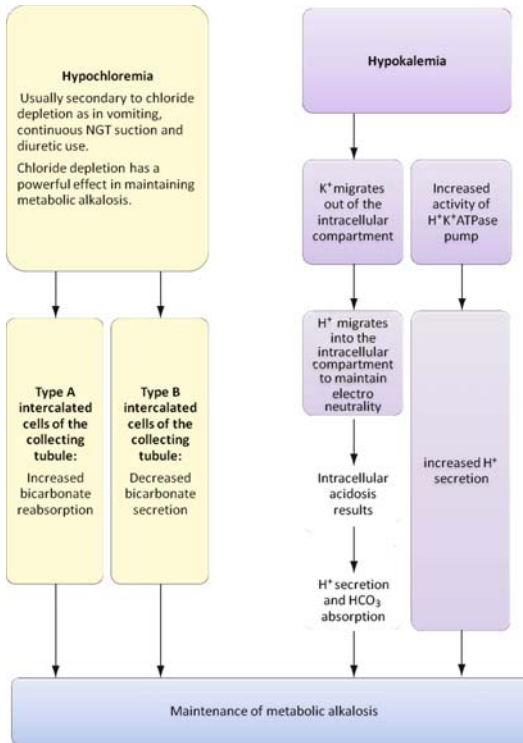
Bicarbonate absorption is increased by the following factors:

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

Predicted PCO₂

Predicted PCO₂ = (0.9 × HCO₃⁻) + 9
+/- 2.

Alternatively,
Predicted PCO₂ = (0.7 × HCO₃⁻) + 21

Lower PCO₂ values than predicted indicate the presence of a coexisting respiratory alkalosis.

Higher CO₂ values than predicted indicate a coexisting respiratory acidosis.

ΔPCO₂

The change in PCO₂.
(ΔPCO₂) = (0.6 - 0.8) × ΔHCO₃

Limits of compensation for metabolic alkalosis

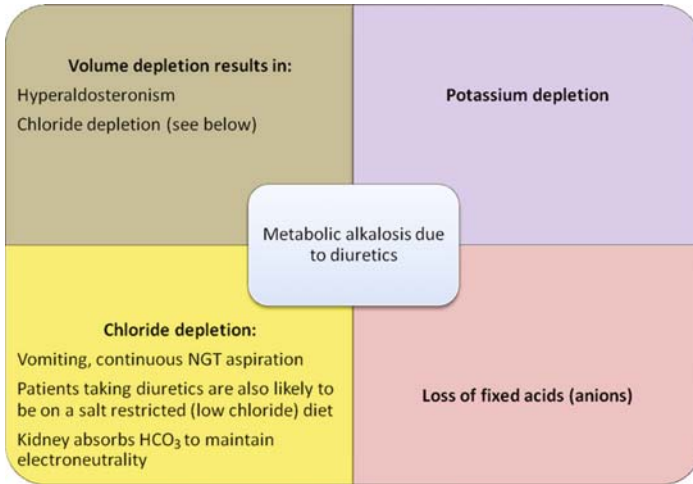
- The lungs are capable of hypoventilating such that the PCO₂ rises to a maximum of about 60 mmHg.
- PCO₂ levels in excess of this in primary respiratory acidosis may imply a coexistent primary metabolic alkalosis.

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:



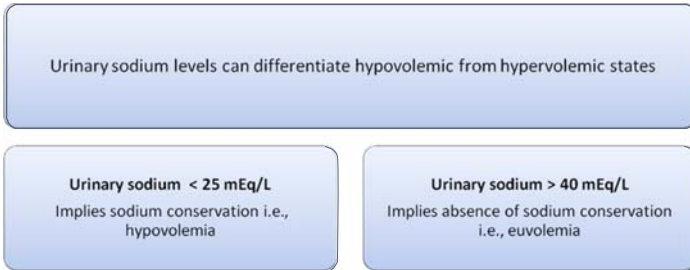
Garella, S, Chazan, JA, Cohen, JJ. Saline-resistant metabolic alkalosis or “chloride-wasting nephropathy”. *Ann Intern Med* 1970; 73:31

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

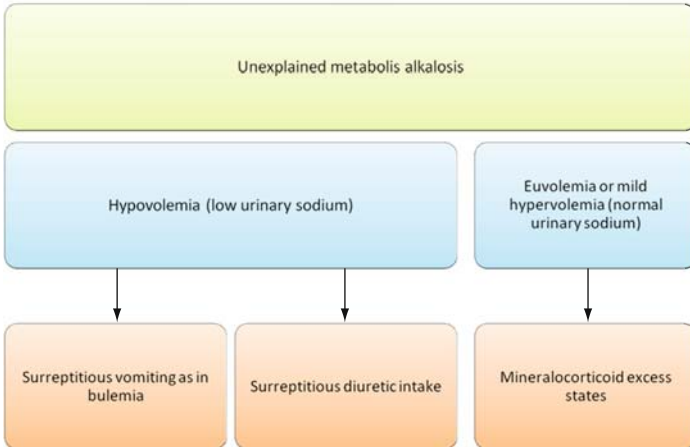
Cannon, PJ, Heinemann, HO, Albert, MS, et al. “Contraction” alkalosis after diuresis of edematous patients with ethacrynic acid. *Ann Intern Med* 1965; 62:979

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

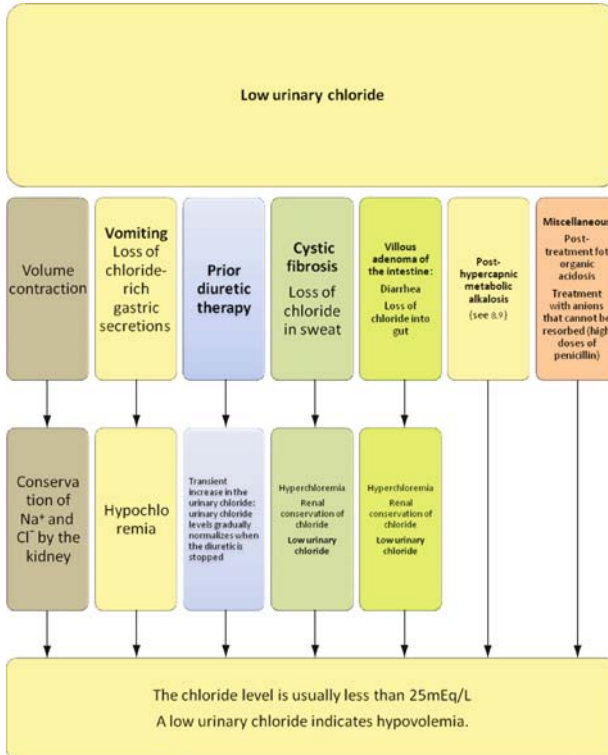


Rose, BD. Clinical Physiology of Acid–Base and Electrolyte Disorders, 4th ed, McGraw-Hill, New York, 1994, pp. 522–530

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

11.11 Urinary Chloride

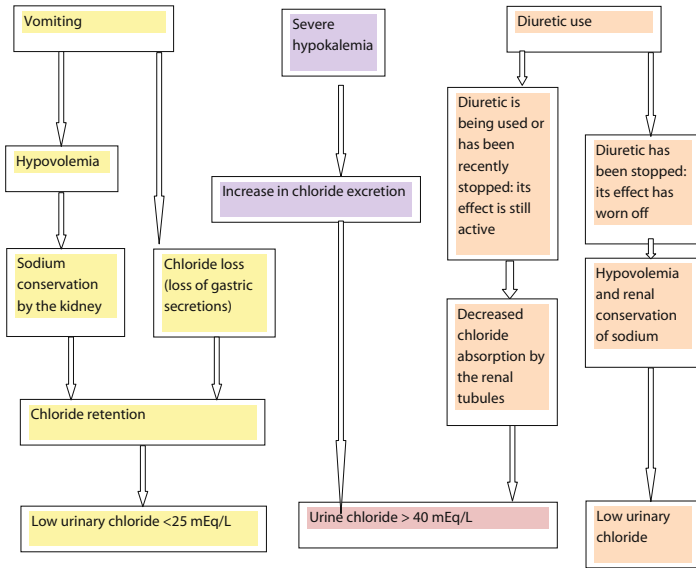
Sometimes, for several reasons, urinary *sodium* may prove to be unreliable as an indicator of the subject's volume status especially when there is significant bicarbonaturia ($\text{pH} > 7.0$). Urinary *chloride* estimation may more accurately reflect the patient's volume status.



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

A high urinary chloride may indicate the presence of the following conditions:

Ongoing diuretic therapy
Decreased chloride absorption

Bartter's syndrome

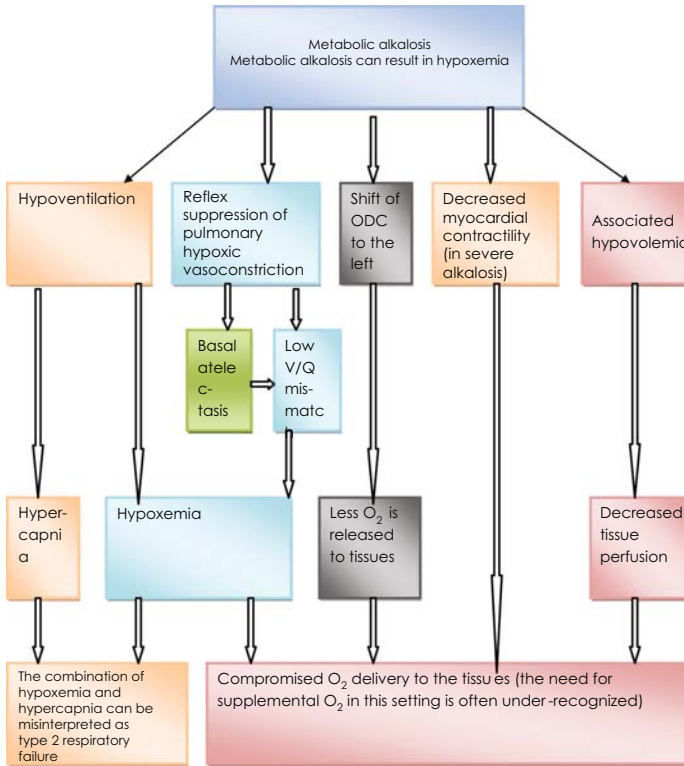
Gitelman's syndrome

Severe hypokalemia (<2 mEq/L)
Increased chloride excretion

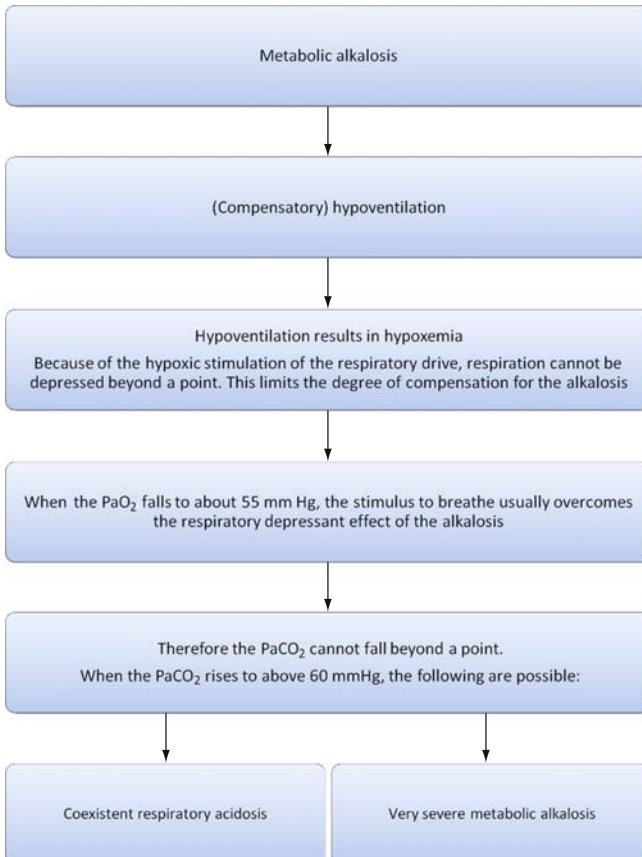
Rose, BD. *Clinical Physiology of Acid–Base and Electrolyte Disorders*, 4th ed, McGraw-Hill, New York, 1994, pp. 527–530

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. Metabolic 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

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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.

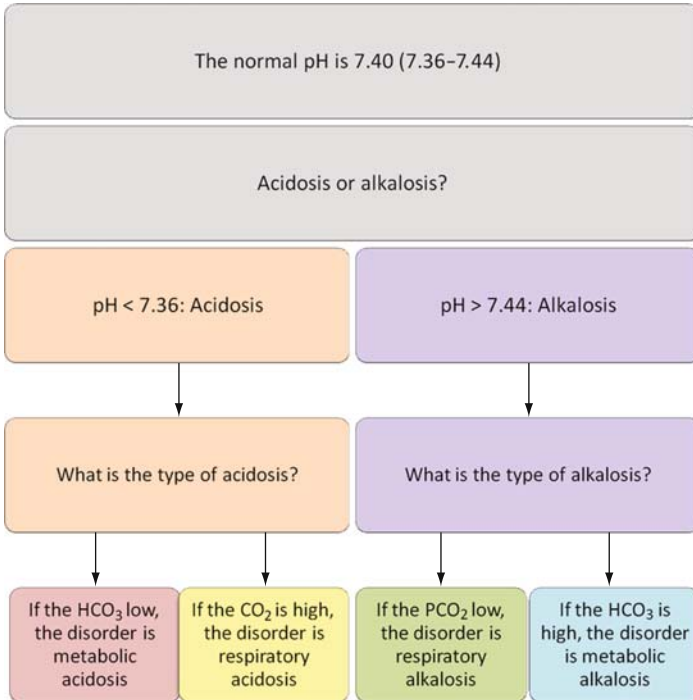
Is the following lab report authentic?
pH 7.32, PCO_2 32, HCO_3 16.

The modified Henderson-Hasselbach equation:
 $H^+ = [24 \times CO_2] / HCO_3$
 Inserting the values of CO_2 and HCO_3 ,
 $H^+ = [24 \times 32] / 16$
 $H^+ = 48$.

$H^+ = 48$.
 This value represents an excess of 8 nEq/L over the normal (Normal H^+ level = 40 nEq/L).

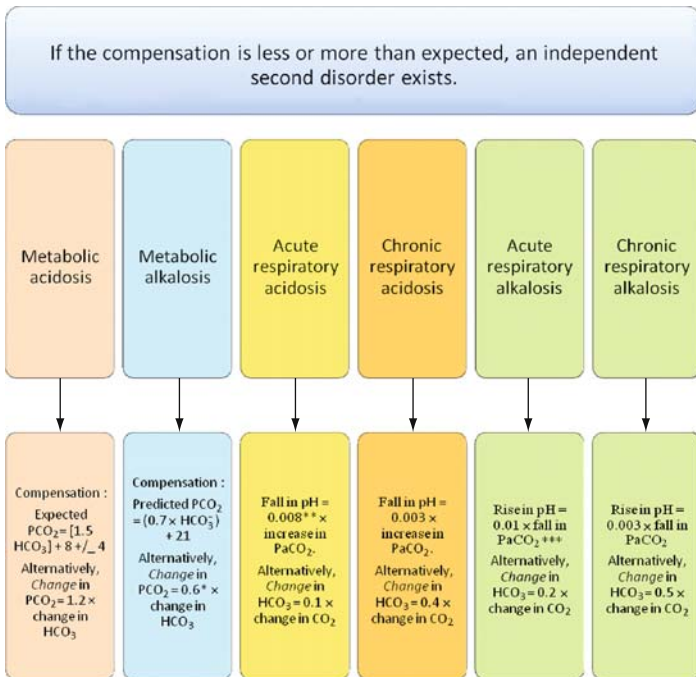
Expected fall in pH = $7.4 - [8 \times 0.01] = 7.32$
 The data are authentic.

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

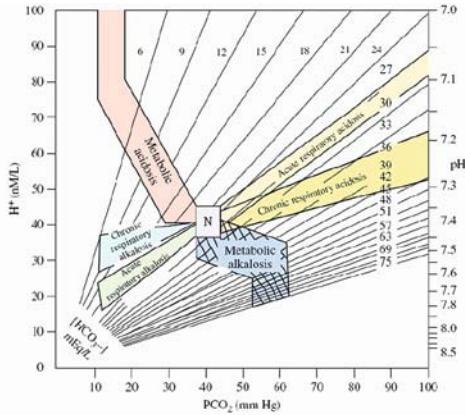
The alpha-numeric mnemonic

<p>Metabolic acidosis: The A-B-C approach</p>	<p>Respiratory disorders: The 1-2-(3)-4-5 approach</p>
<p>A = Check the Anion gap. This helps narrow down the differential diagnosis.</p> <p>B = If the anion gap is wide, check the Bicarbonate gap. This helps uncover the presence of another coexisting metabolic disorder.</p> <p>C = If the anion gap is unaccountably wide (DKA, lactic acidosis, uremia and salicylate poisoning have been ruled out), in the appropriate setting a widened osmole gap provides a clue to toxin ingestion. For want of a better term I have called it a Colloid gap (-- AH).</p> <p>Compensation for metabolic acidosis can be assessed and the coexistence of a primary respiratory disorder uncovered by using Winter's formula:</p> <p>Predicted $PCO_2 = (1.5 \times HCO_3^-) + 8 +/- 2$</p>	<p>The following formulae have been used to assess the compensation for respiratory disorders, and to uncover any associated primary metabolic disorder.</p> <p>Acute respiratory acidosis = The HCO_3 increases by 0.1 mEq/l for every 1 mmHg rise in CO_2</p> <p>Acute respiratory alkalosis = The HCO_3 decreases by 0.2 mEq/l for every 1 mmHg fall in CO_2</p> <p>(0.3*)</p> <p>Chronic respiratory acidosis = The HCO_3 increases by 0.4 mEq/l for every 1 mmHg rise in CO_2</p> <p>Chronic respiratory alkalosis = The HCO_3 falls by 0.5 mEq/l for every 1 mmHg fall in CO_2</p>

*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.

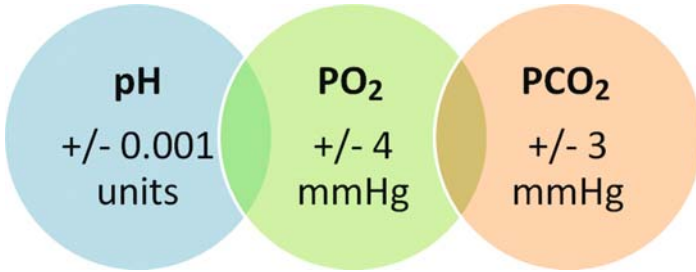
When a given patient's values fall upon any such band, a simple acid-base disorder corresponding to that band may be presumed; it is however not mandatory that a simple acid base disorder exists in such a patient.

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 systemic approach. JAMA

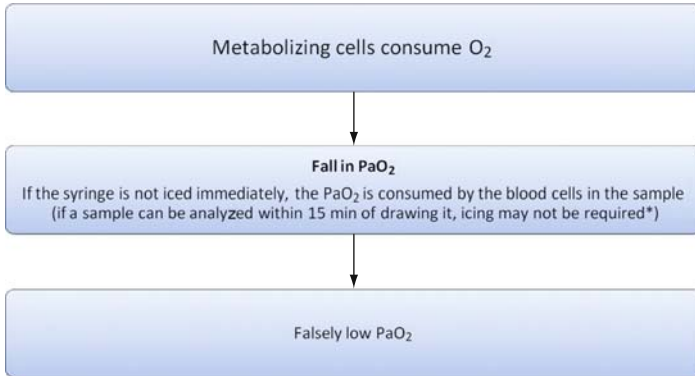
12.7 Accuracy of Blood Gas Values

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



Glaser, 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

Leucocytosis and thrombocytosis leads to increased O_2 consumption

When the leucocyte or thrombocyte count is abnormally high (as in leukemia or thrombocytosis), these blood cells can consume a large amount of O_2 within the sample, resulting in a drop in the PaO_2 . This can occur in spite of icing the sample.

Falsely low PaO_2

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

The leucocytes and thrombocytes may coat the surface of the electrode.

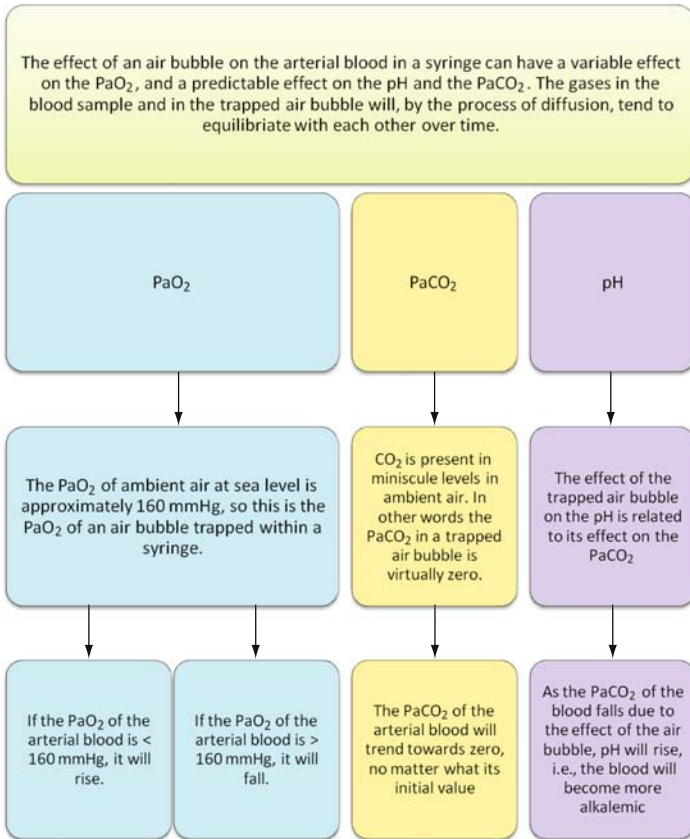
This possibly physically impedes the O_2 from gaining access to the electrode.

Prompt, centrifugation of the blood upon drawing the sample and analysis of the supernatant plasma prevents this problem.

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

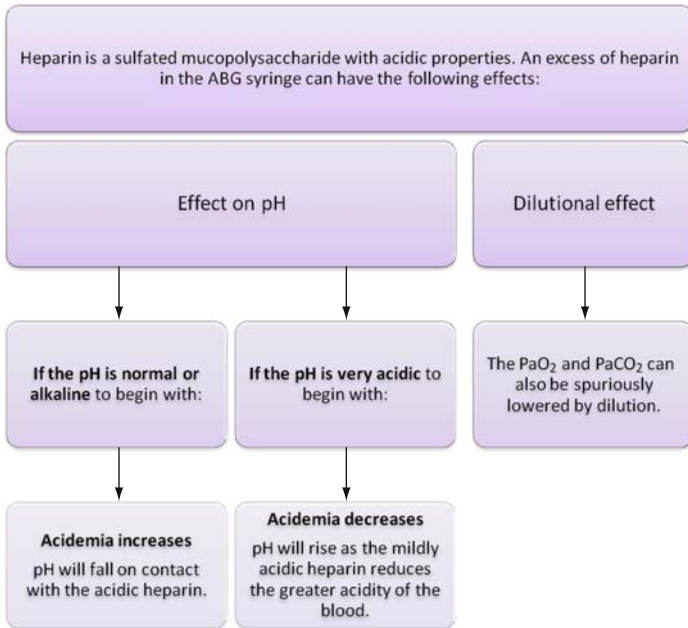
Charan, NB, Marks, M, Carvalho, P. Use of plasma for arterial blood gas analysis in leukemia. *Chest* 1994; 105:954–955

12.10 The Effect of an Air Bubble in the Syringe

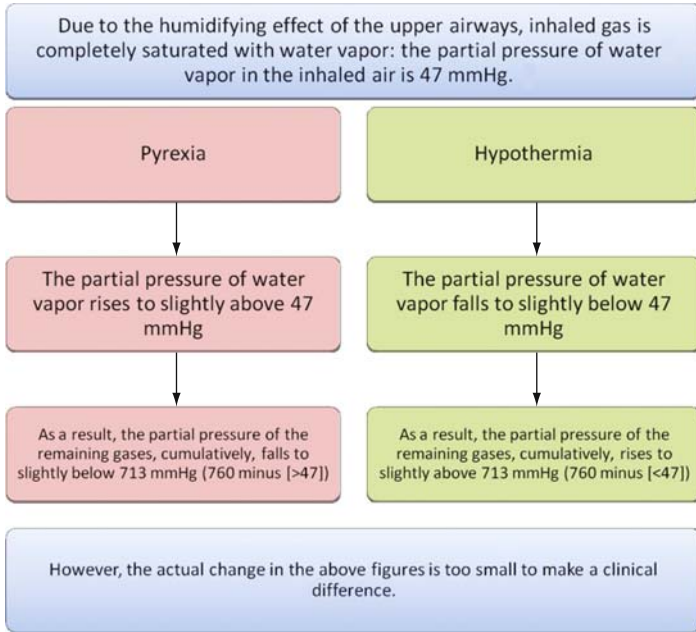


Mueller, RG, Lang, GE, Beam, JM. Bubbles in samples for blood gas determinations: A potential source of error. Am J Clin Pathol 1976; 65:242

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 SpO₂ and CaO₂ with a change in temperature***

With warming, gases are less soluble in the plasma. The levels of O ₂ and CO ₂ are liable to underestimation. With cooling, gases are more soluble in the plasma. The levels of O ₂ and CO ₂ are liable to overestimation.					
Pyrexia (esp >39°C)			Hypothermia		
O ₂ in a febrile patient (esp >39°C):	CO ₂ in a febrile patient (esp >39°C):	pH in a febrile patient	O ₂ in a hypothermic patient:	CO ₂ in a hypothermic patient:	pH in a hypothermic patient:
Decreased solubility of O ₂ in the blood with a rise in temperature	Decreased solubility of CO ₂ in the blood with a rise in temperature	As the temperature of the body rises, the pH falls	Increased solubility of O ₂ in the blood with a fall in temperature	Increased solubility of CO ₂ in the blood with a fall in temperature	As the temperature of the body falls, the pH rises
Overestimation of hypoxemia	Underestimation of acidosis	Overestimation of pH	Underestimation of hypoxemia	Overestimation of acidosis	Underestimation of pH
For every degree C over 37° rise in the patient's temperature, the PO ₂ should be increased by 7.2% (PaO ₂ will be shown about 5 mmHg lower than it actually is)	For every degree C over 37° rise in the patient's temperature, the PCO ₂ should be decreased by 4.4% (PaCO ₂ will be shown about 2 mmHg lower than it actually is)	For every degree C over 37° rise in the patient's temperature, the pH should be decreased by 0.015 units	For every degree C below 37° fall in the patient's temperature, the PO ₂ should be decreased by 7.2% (PaO ₂ will be shown about 5 mmHg higher than it actually is)	In vitro changes in acid-base status parallel those in vivo: correction of PCO ₂ is not required	In vitro changes in acid-base status parallel those in vivo: correction of pH is not required

*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

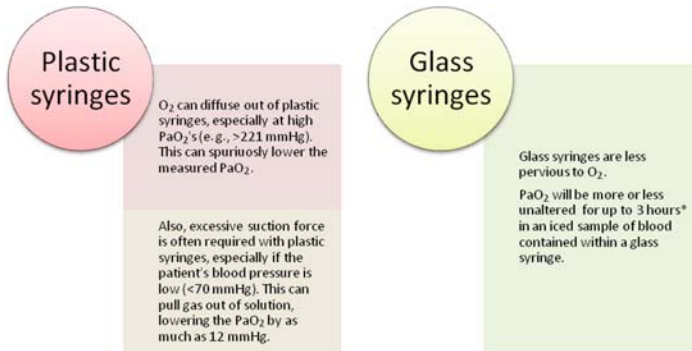
Shapiro, BA. Temperature correction of blood gas values. *Respir Care Clin N Am* 1995; 1:69

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. Hypothermia. *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

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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 correlative 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, PaCO₂: 26mmHg, PaO₂: 94mmHg,
Na⁺: 138mEq/L, k⁺: 4.0 mEq/L, Cl⁻: 103mEq/L,
HCO₃⁻: 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 mmHg 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

A 50-year-old woman is found to have a PaO_2 at 50 mmHg on room air. Supplemental oxygen is administered, and her PaO_2 rises to 100 mmHg. What is the change in the oxygen content of the blood given that her hemoglobin is 15 gm/dL?

Assuming no shift in the position of the oxy-hemoglobin dissociation curve, a PaO_2 of 50 mmHg corresponds approximately to a SpO_2 of 85%, and a PaO_2 of 100 mmHg to 98%.

$$CaO_2 = 1.34 \times SpO_2 \times Hb \text{ (see 00.00)}$$

CaO_2 on room air
 $CaO_2 = 1.34 \times 0.85 \times 15$
 $CaO_2 = 17 \text{ mL } O_2 / \text{dL}$

CaO_2 on supplemental oxygen
 $CaO_2 = 1.34 \times 0.98 \times 15$
 $CaO_2 = 19.7 \text{ mL } O_2 / \text{dL}$
 The CaO_2 has increased by about 14%.

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-a DO_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).

$$\text{A-aDO}_2 = \text{PAO}_2 - \text{PaO}_2.$$

$$\text{PAO}_2 = \text{FIO}_2 (\text{Pb} - \text{Pw}) - \text{PaCO}_2 / \text{R}$$

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

$$\text{PAO}_2 = [0.21(760 - 47)] - (20/0.8)$$

$$\text{PAO}_2 = 149 - 25$$

$$\text{PAO}_2 = 124$$

$$\text{A-aDO}_2 = \text{PAO}_2 - \text{PaO}_2 = 124 - 118$$

$$\text{A-aDO}_2 = 6 \text{ (normal } < 14 \text{ on room air)}$$

The A-a DO_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 PaO_2 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 (28×5). 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

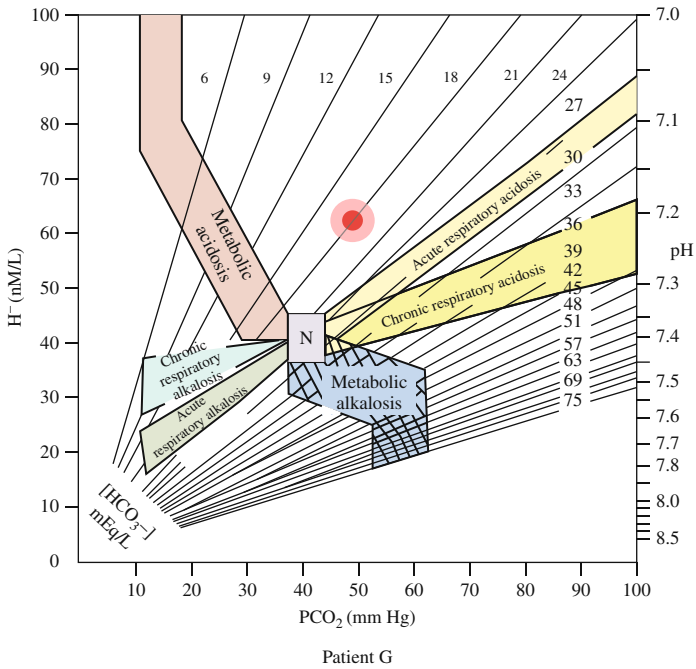
The SpO₂ of a 60-year-old man recovering in the ICU from an acute coronary syndrome, has fallen to 86% on supplemental oxygen. The chest X-ray shows possible mild interstitial pulmonary edema.

PH: 7.43, HCO₃⁻: 24mEq/L, PaCO₂: 37mmHg, PaO₂: 126 mmHg
on 35% oxygen by ventimask.

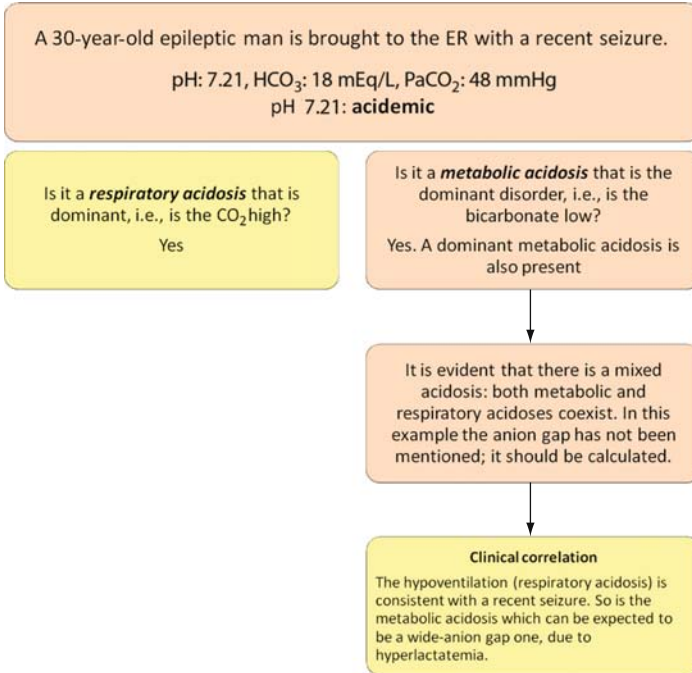
The PaO₂ seems slightly low for the FIO₂ being given, but can be accounted for by the recumbency and possible mild cardiogenic pulmonary edema. What is interesting is the disparity between the PaO₂ and SpO₂. The ABG shows no obvious acid-base disorder.

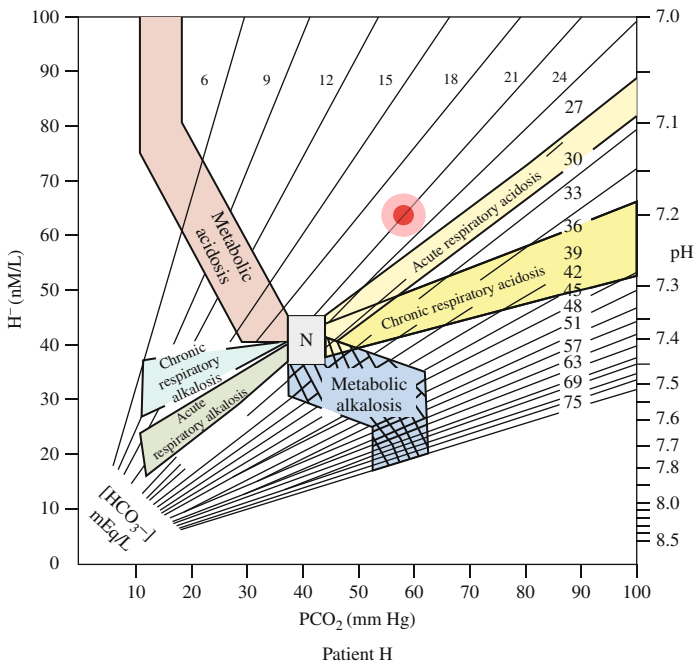
The clinical setting is that of an acute coronary artery syndrome, and it is safe to assume that the patient is on nitrates; the latter are commonly implicated in the genesis of methemoglobinemia.

Methemoglobinemia was later confirmed on CO-oximetry.



This patient's 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



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

An elderly male presents to the ER with opiate induced respiratory depression.

pH: 7.19, HCO_3^- : 20mEq/L, PaCO_2 : 56mmHg, PaO_2 : 115mmHg
on supplementary oxygen

pH 7.19: **acidemic**

Is it a **respiratory acidosis** that is dominant, i.e., is the CO_2 high?

Yes

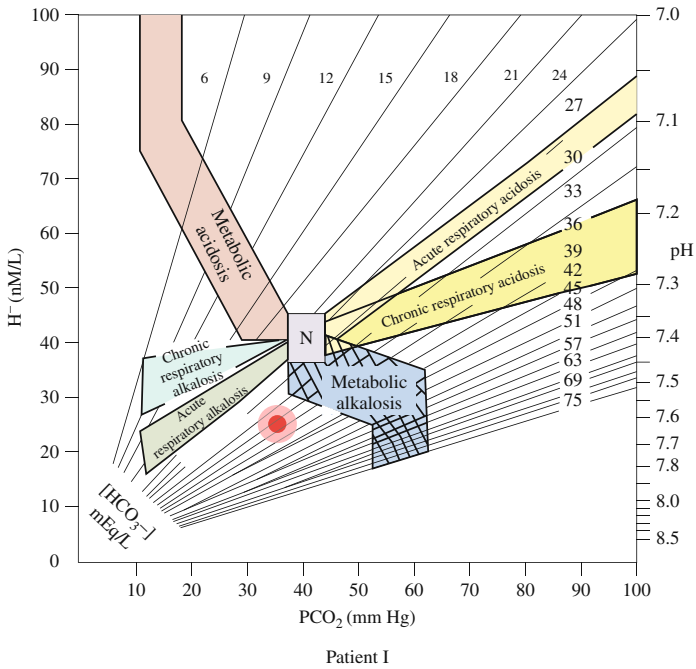
Is it a **metabolic acidosis** that is the dominant disorder, i.e., is the bicarbonate low?

Yes. A primary metabolic acidosis is also present

In this example data to calculate the anion gap has not been provided, but the anion gap and the delta ratio needs to be calculated to further characterize the metabolic acidosis.

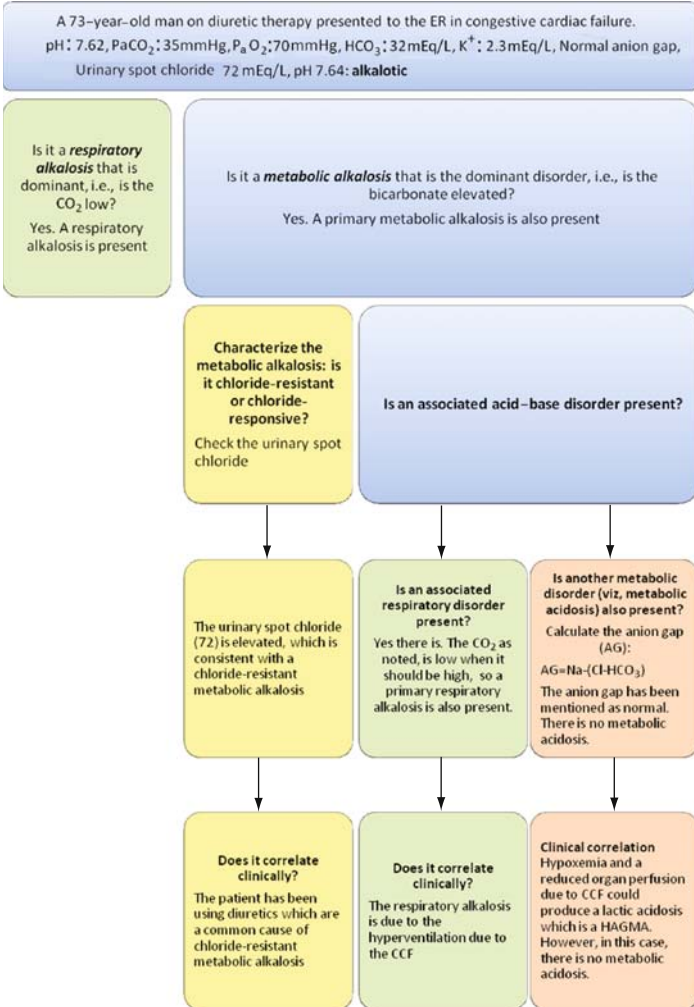
Clinical correlation

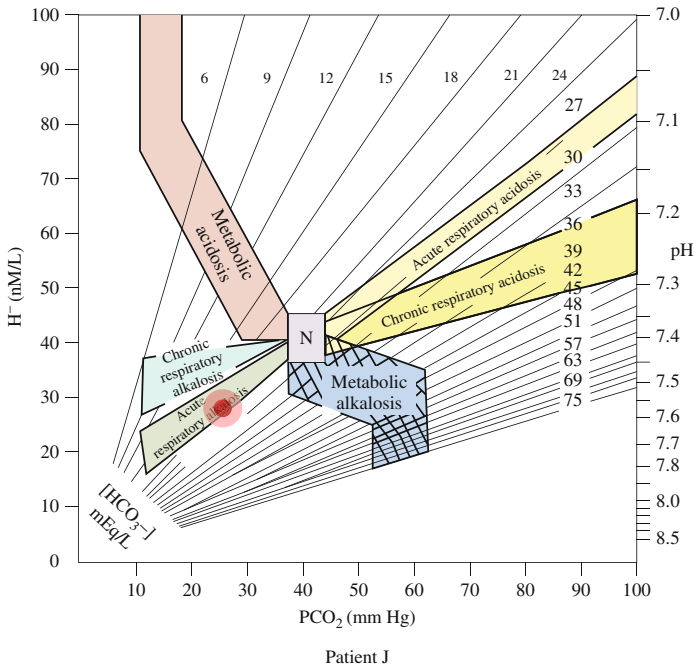
The respiratory acidosis is clearly due to respiratory depression by the sedative. A cause for the metabolic acidosis needs to be sought



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.

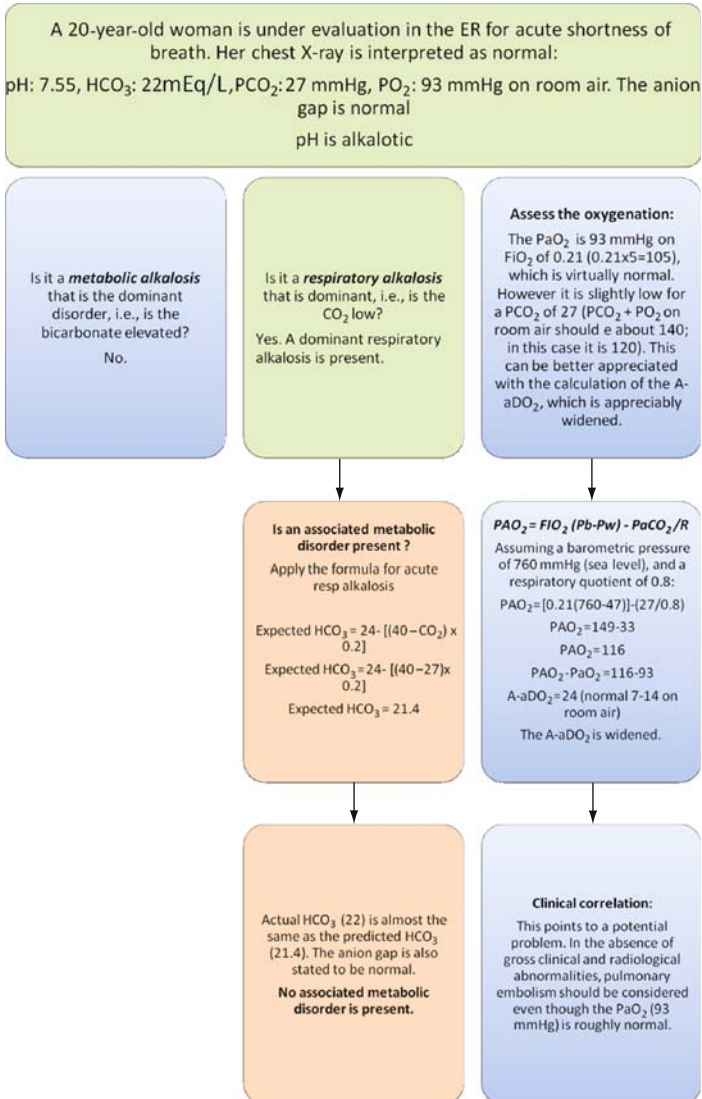
Patient I: A 73 year old man with congestive cardiac failure

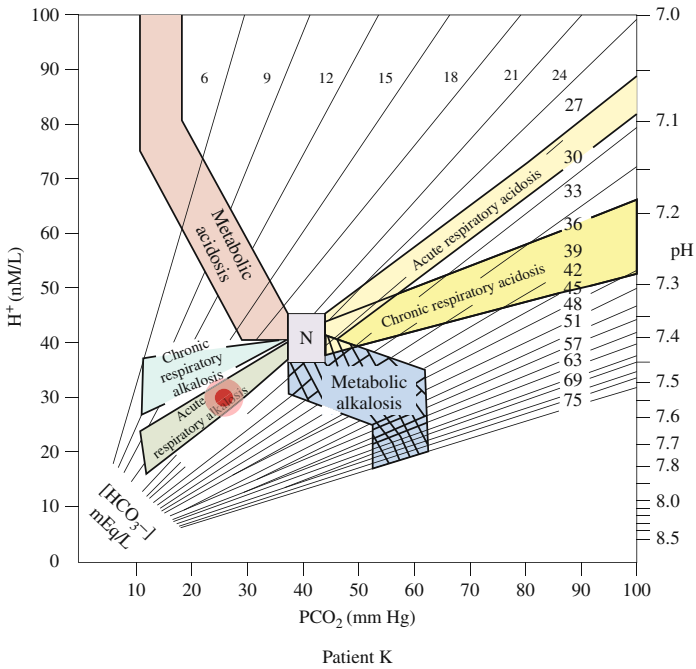




The patient's values fall on the band of acute respiratory alkalosis. As mentioned in (00.00), when a patient's values fall on any of the "95% confidence bands", a simple acid-base disorder is likely to be present, in this case, acute respiratory alkalosis.

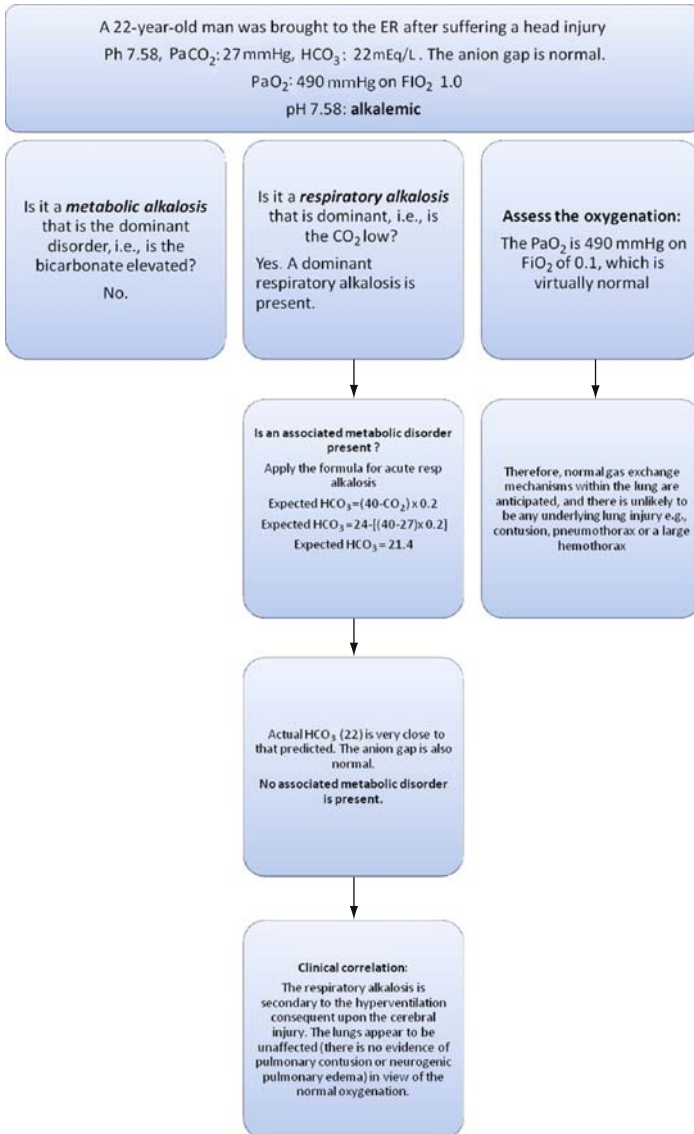
Patient J: A 20 year old woman with acute shortness of breath

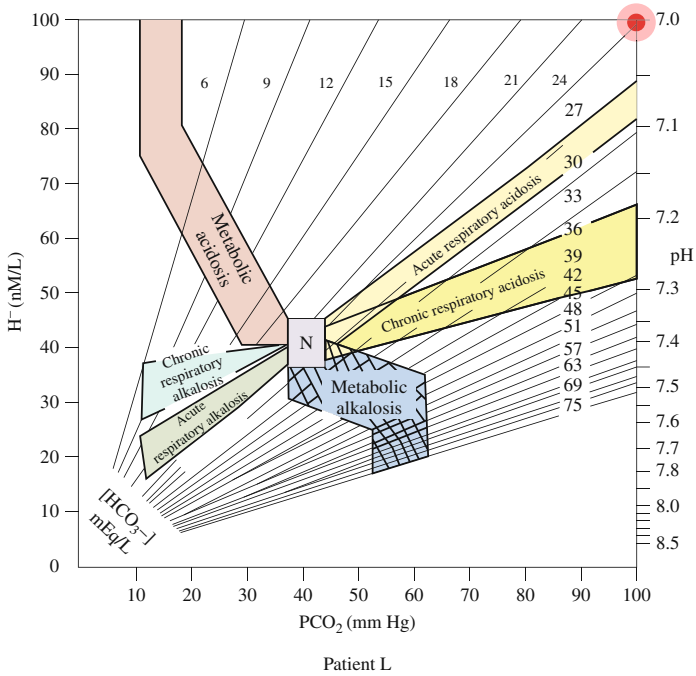




As in the preceding example, this patient's values fall squarely on the band that represents acute respiratory alkalosis. A simple acid-base disorder, acute respiratory alkalosis, is present.

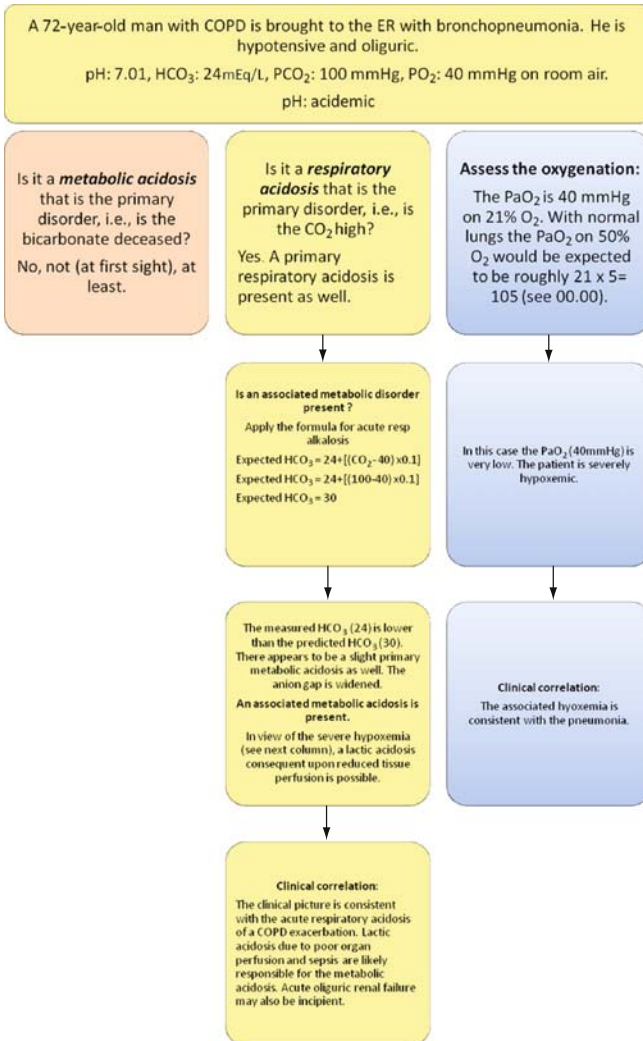
Patient K: A 22 year old man with a head injury

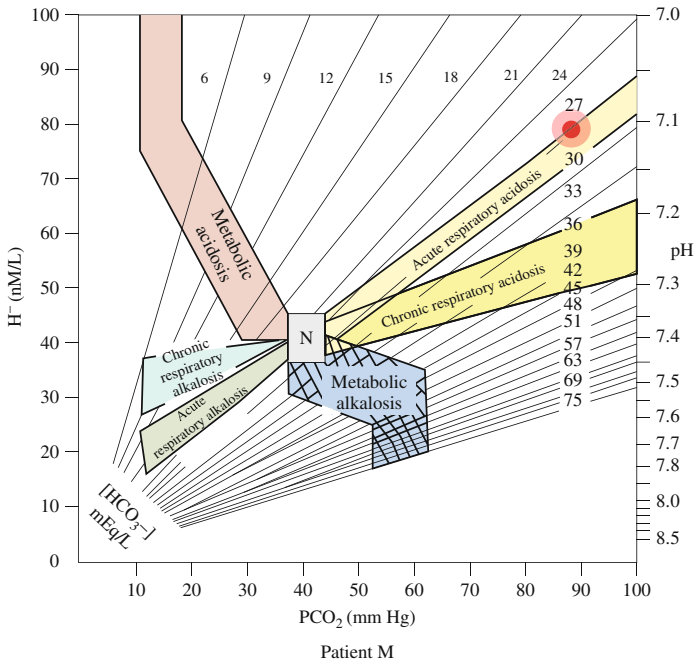




This patients values have been graphed between the bands representing acute respiratory acidosis and metabolic acidosis, both of which can be shown to be present (see algorithm opposite).

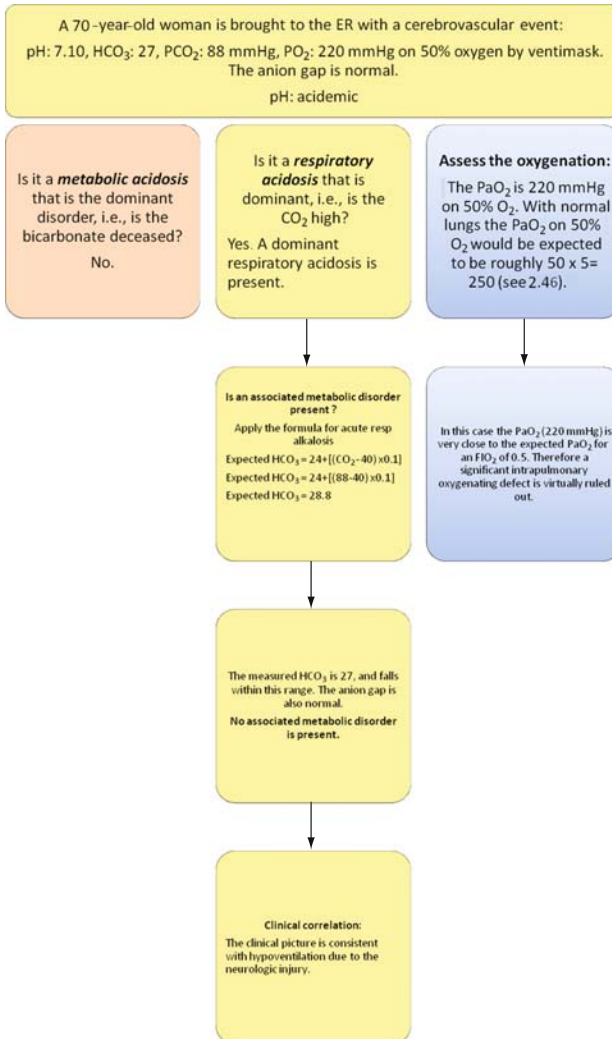
Patient L: A 72 year old man with bronchopneumonia

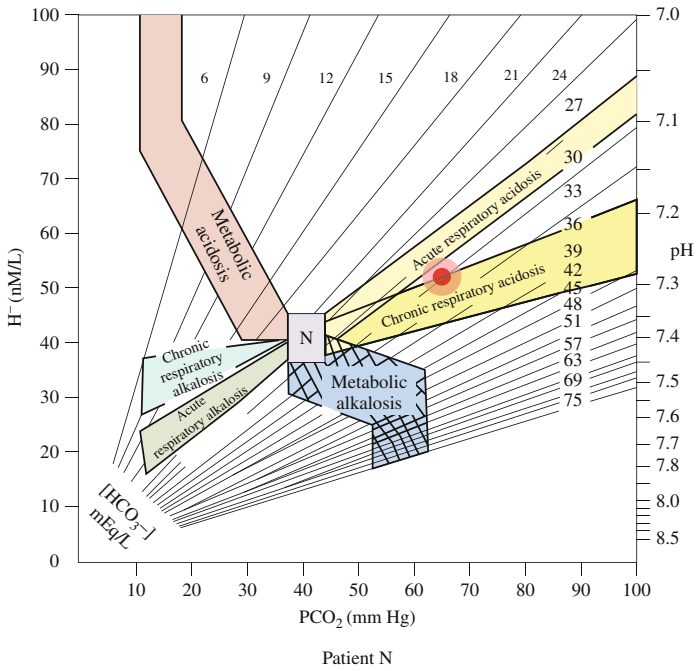




This patient's values fall on the band representing acute respiratory acidosis. No associate acid-base disorder appears to be present (see 00.00).

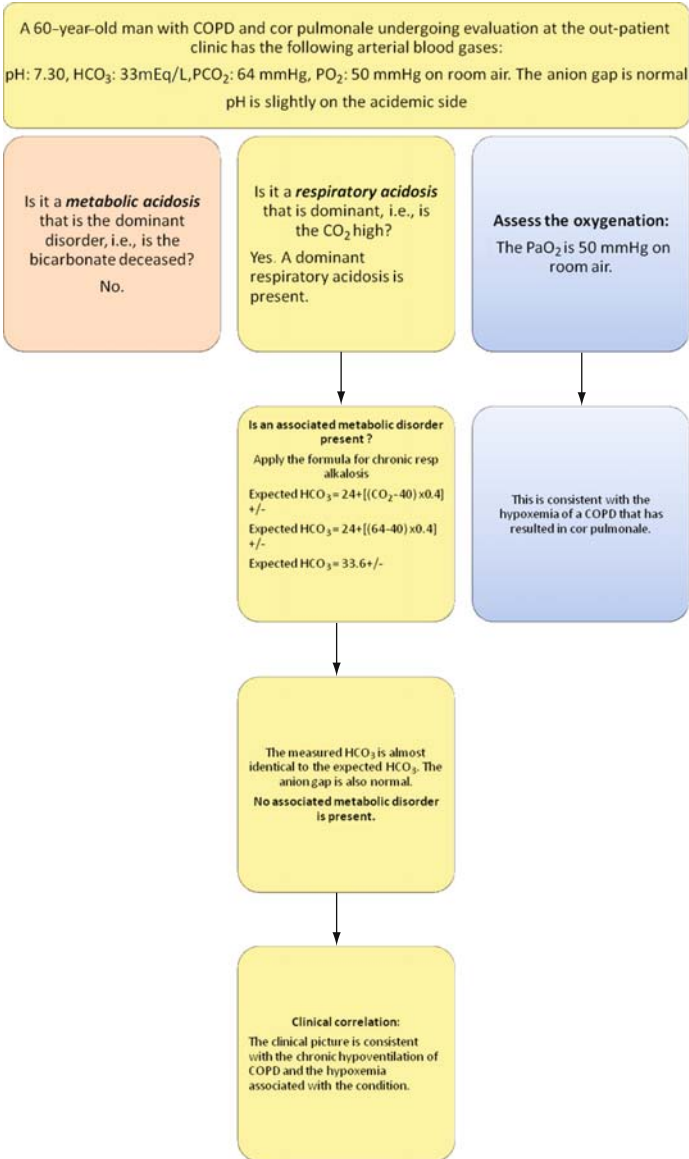
Patient M: A 70 year old woman with a stroke

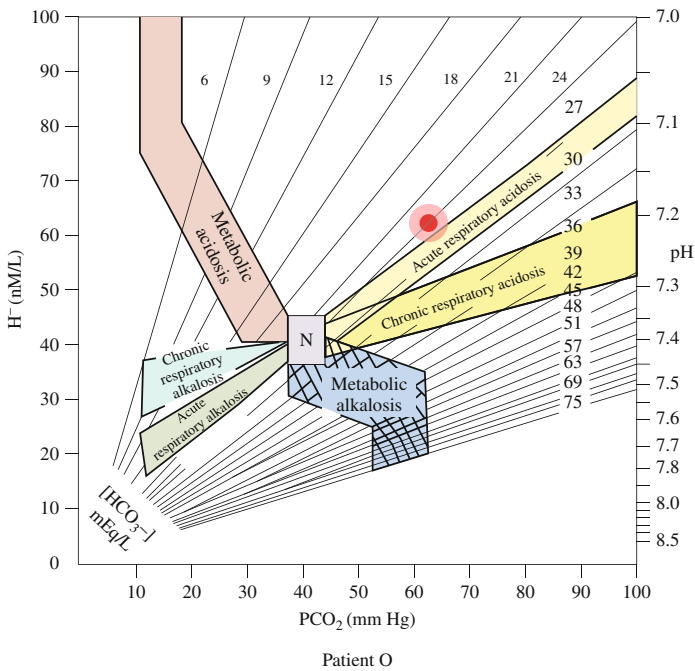




Chronic respiratory acidosis.

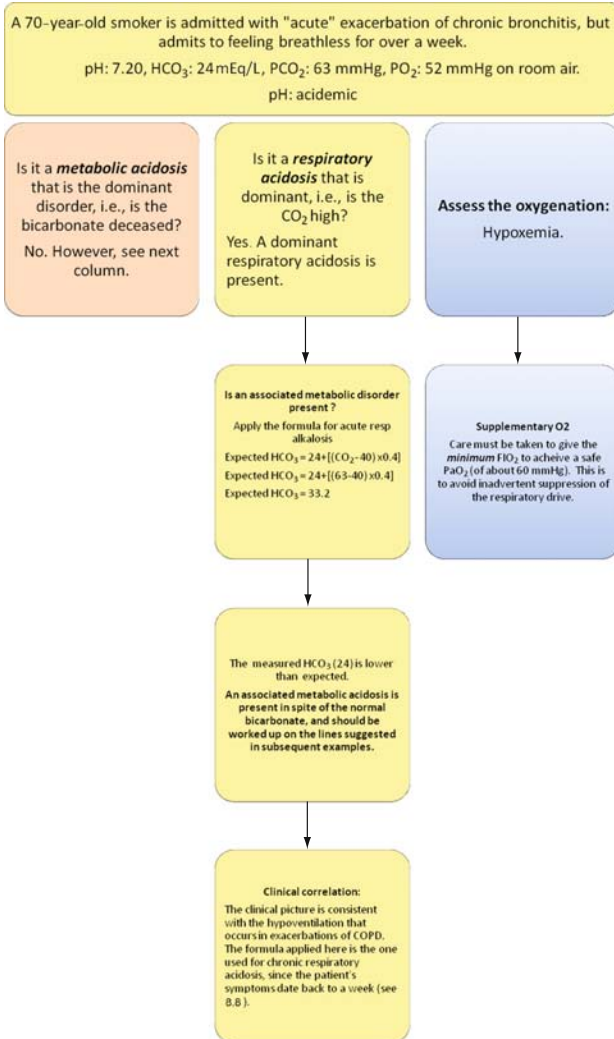
Patient N: A 60 year old male with stable COPD

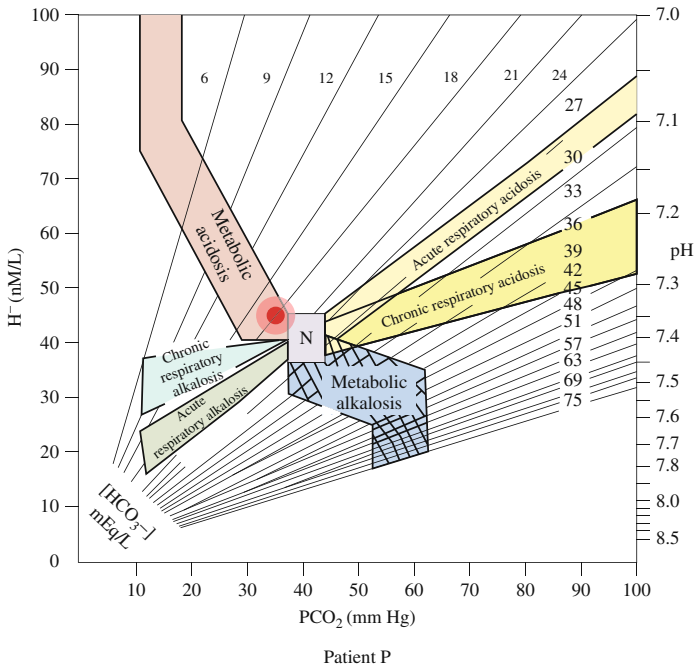




The point plotted on this graph is close to the band for respiratory acidosis—in fact it lies between this band and the band of metabolic acidosis. As the algorithm on the opposite page suggests, both respiratory acidosis and metabolic acidosis are present.

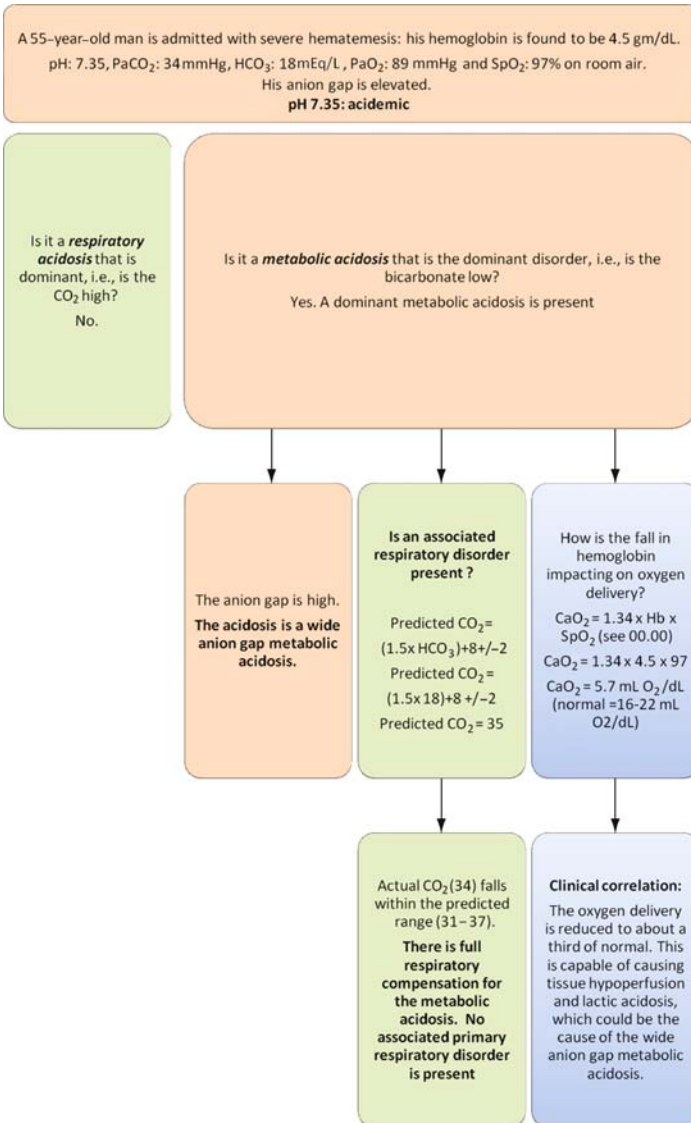
Patient O: A 70 year old smoker with AECB

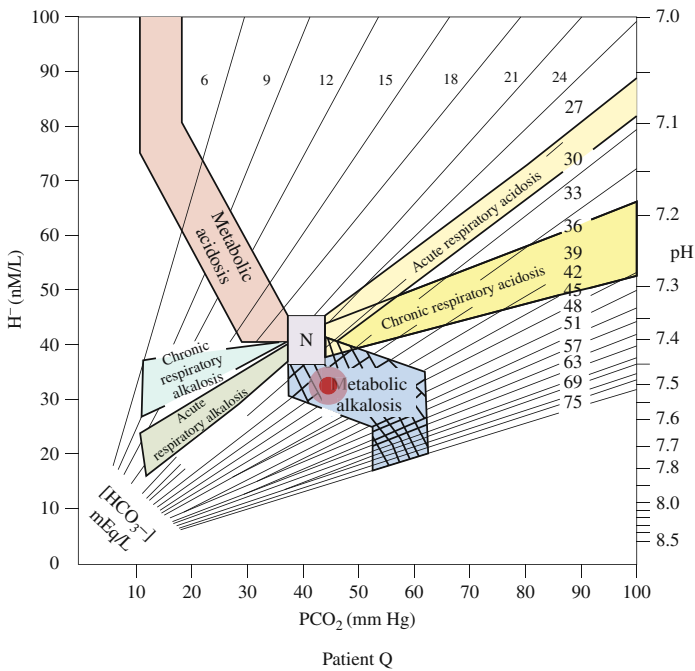




Metabolic acidosis.

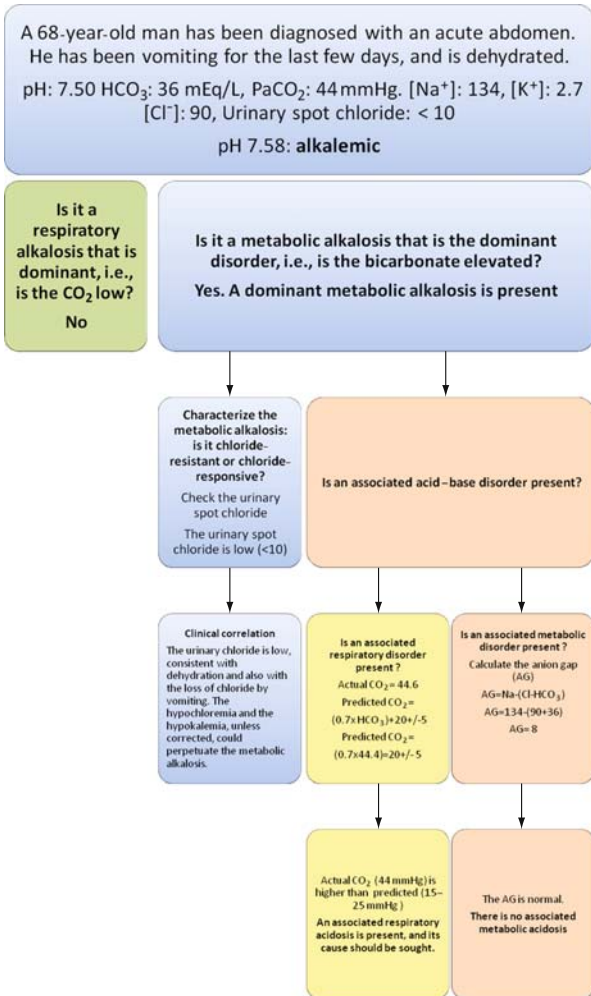
Patient P: A 55 year old man with hematemesis

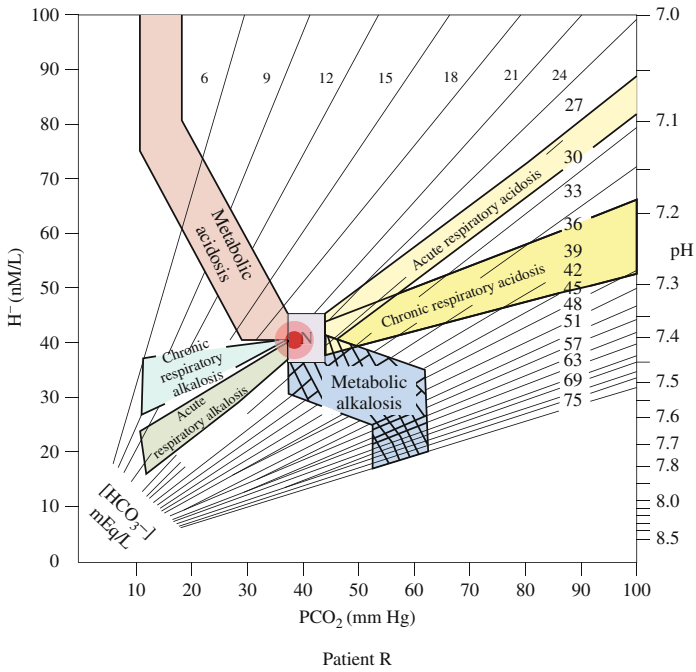




Metabolic alkalosis. Based on acid-base mapping alone, no other acid-base disturbance is expected to coexist. However the method is not infallible, and as the discussion on the facing page shows, an associated respiratory acidosis is in fact present.

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





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, PaCO₂: 39mmHg, HCO₃⁻: 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)

$$\text{Delta ratio} = \Delta AG - \Delta HCO_3$$

$$= (30 - 12) - (24 - 21)$$

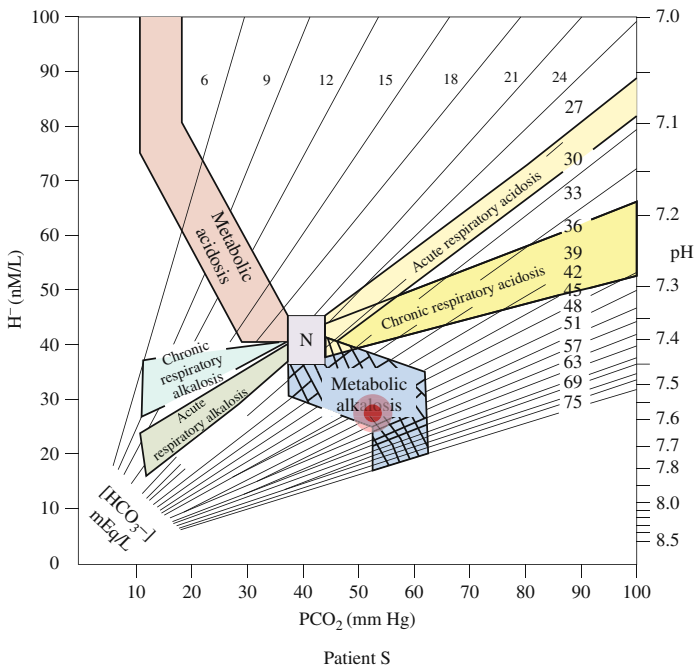
$$= 18 - 3$$

$$= 15 \text{ (normal } +6 \text{ to } -6)$$

There is a coexistent metabolic alkalosis

Clinical correlation:

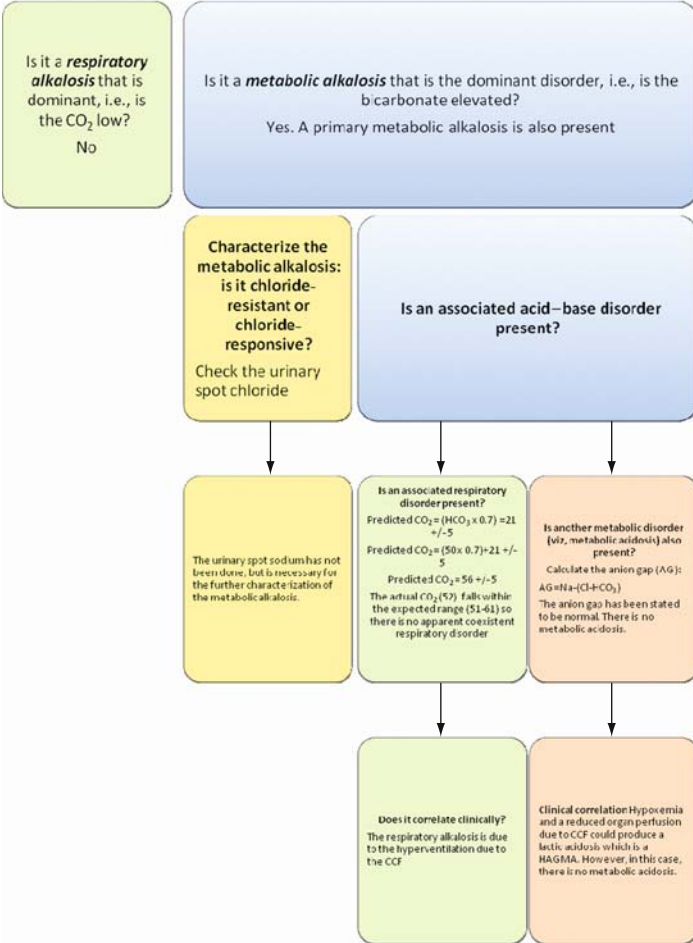
The metabolic acidosis is presumably on account of the hypoperfusion and a possible prerenal component. The metabolic alkalosis can be accounted for by the dehydration and volume contraction.

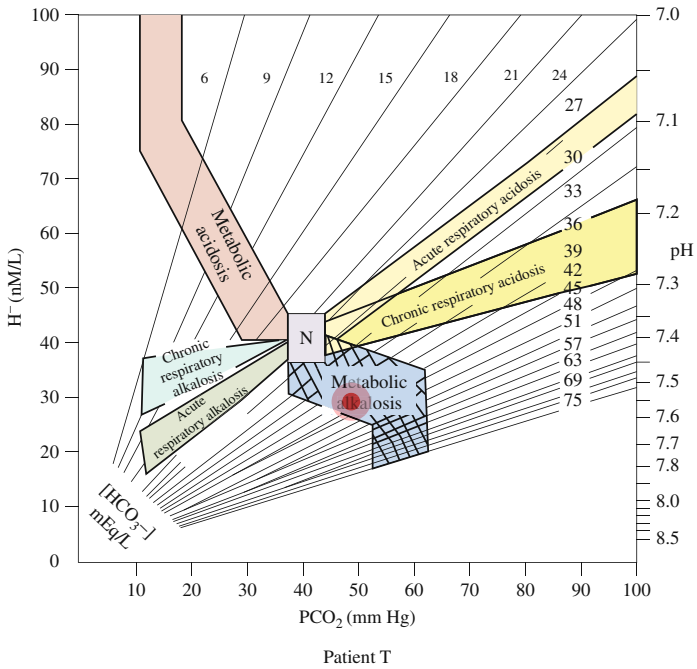


One of the limitations of the acid-base mapping is that it is not possible to diagnose a “triple disorder” by this method. Although the above patient’s values fall well within the band of metabolic alkalosis, there are two additional coexistent acid-base disturbances, as the algorithm on the opposite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

Patient S: A 50 year old woman with paralytic ileus

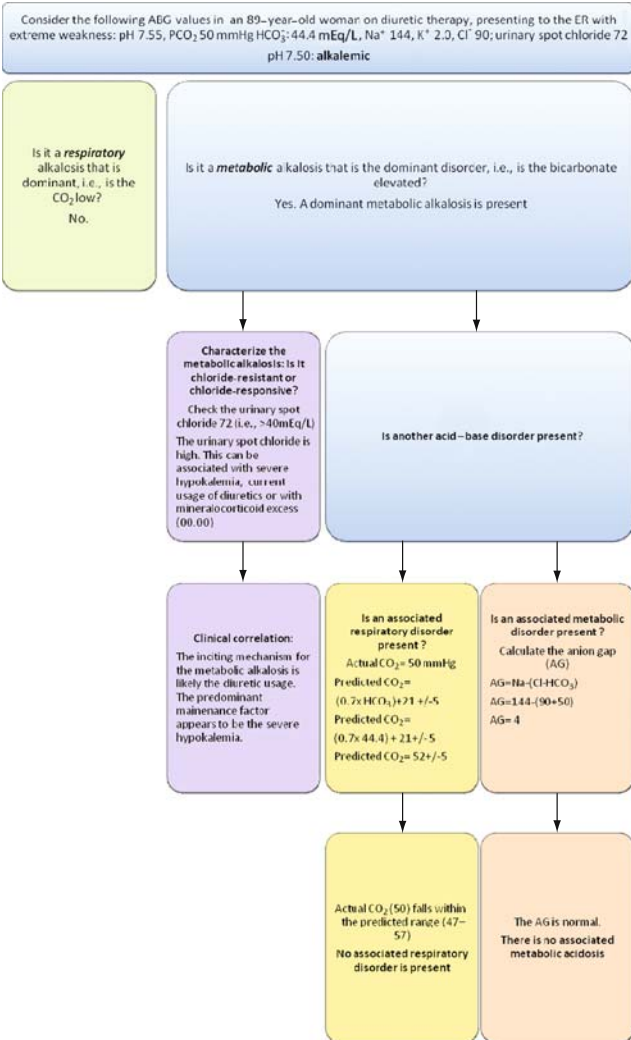
A 50-year-old woman with post-operative paralytic ileus has the following blood gases:
 pH: 7.58, HCO_3^- : 50mEq/L, PCO_2 : 52 mmHg. The anion gap is normal.
 pH 7.64: **alkalotic**

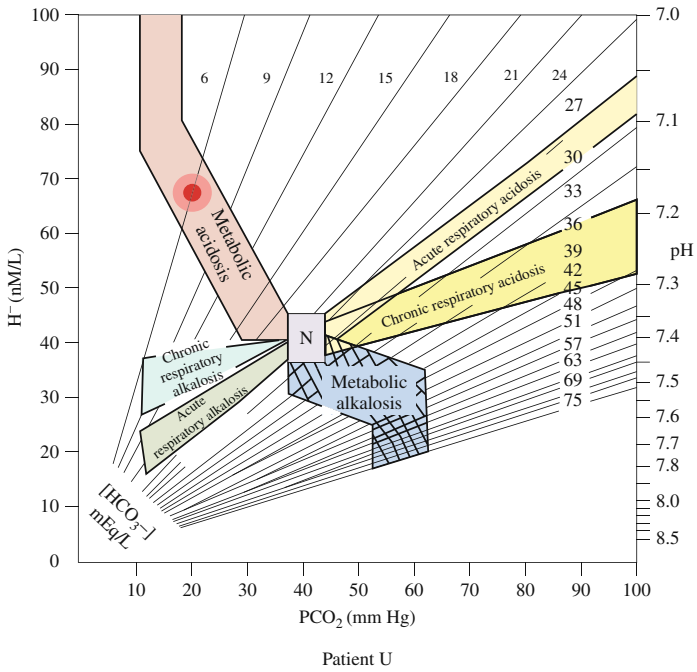




Metabolic alkalosis.

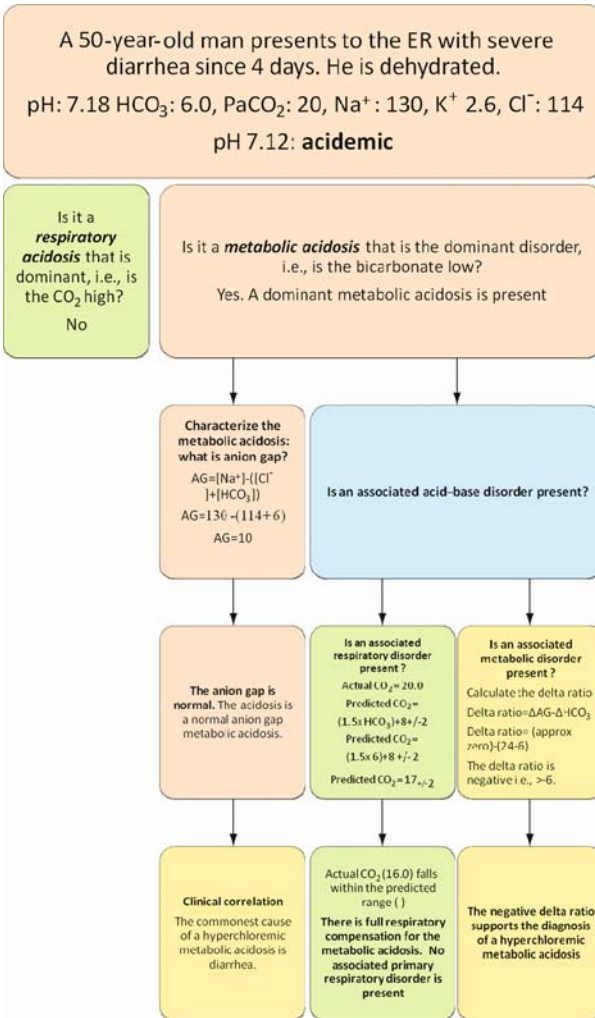
Patient T: An 89 year old woman on diuretic therapy

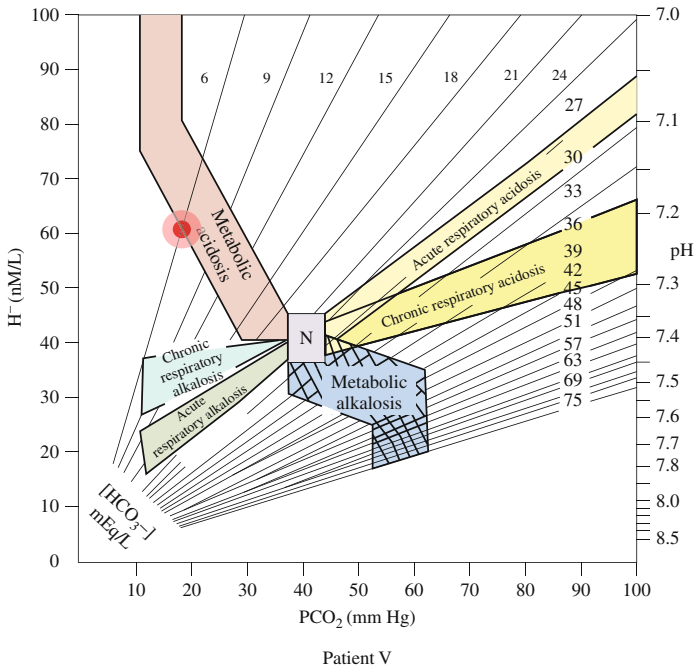




Metabolic acidosis.

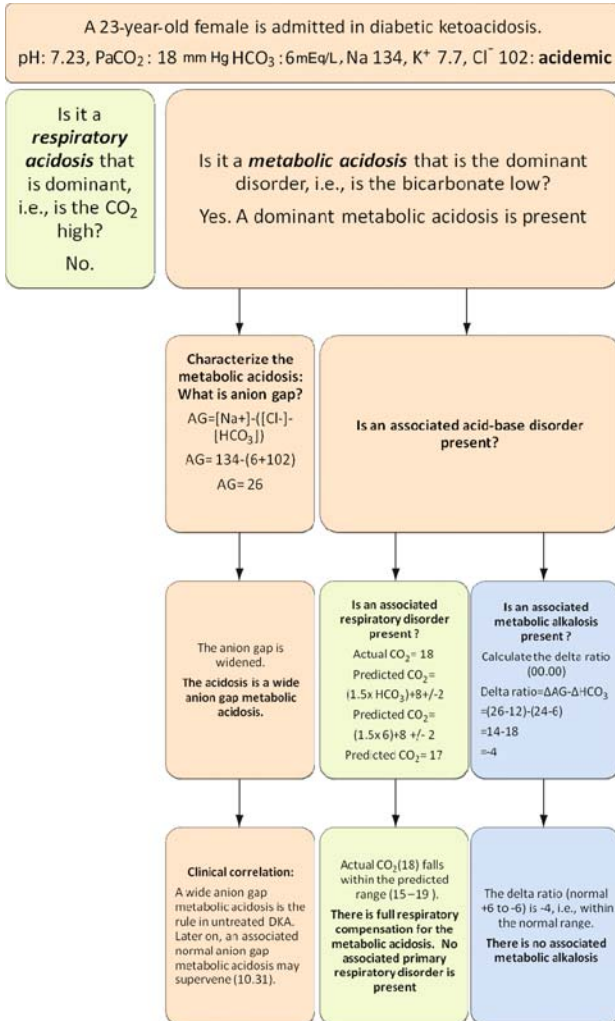
Patient U: A 50 year old man with severe diarrhea

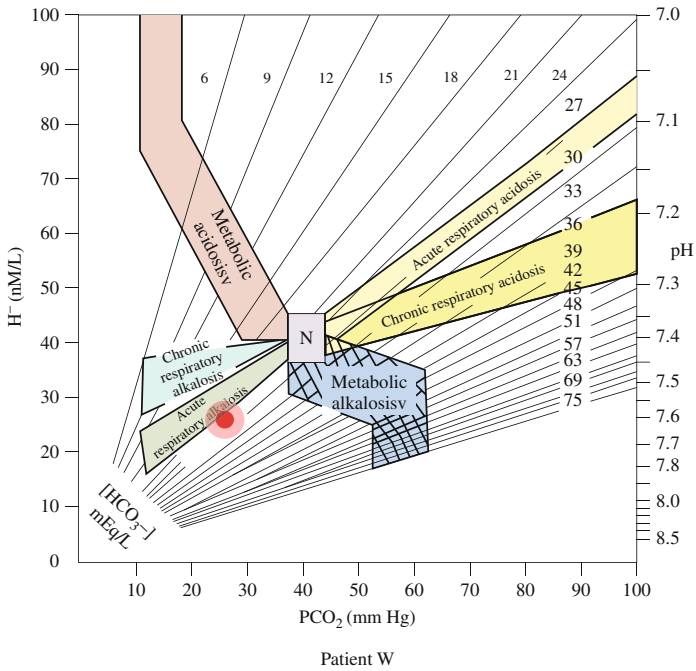




Metabolic acidosis.

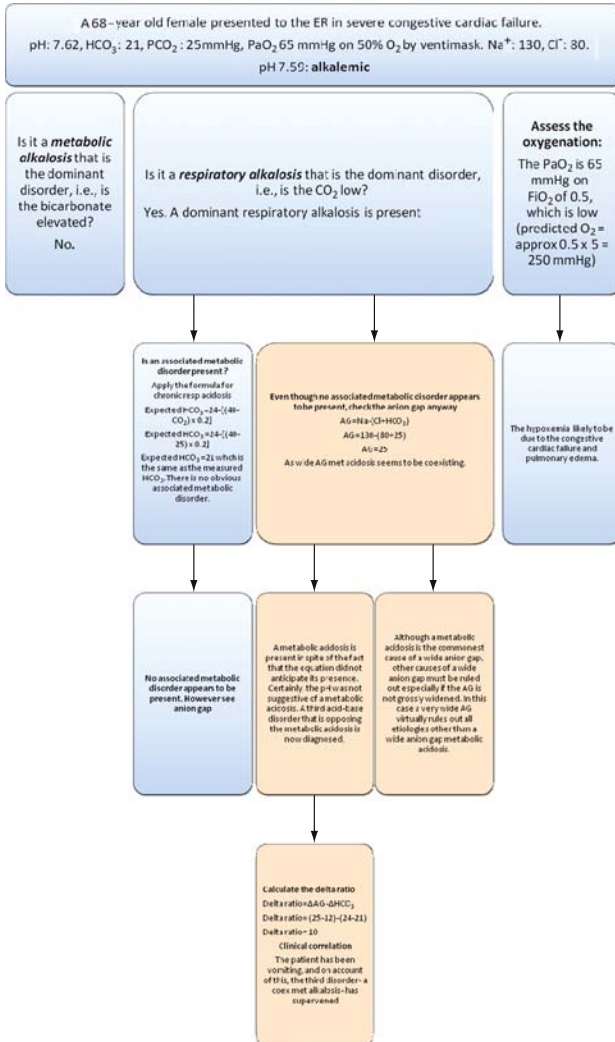
Patient V: A 23 year old female with diabetic ketoacidosis

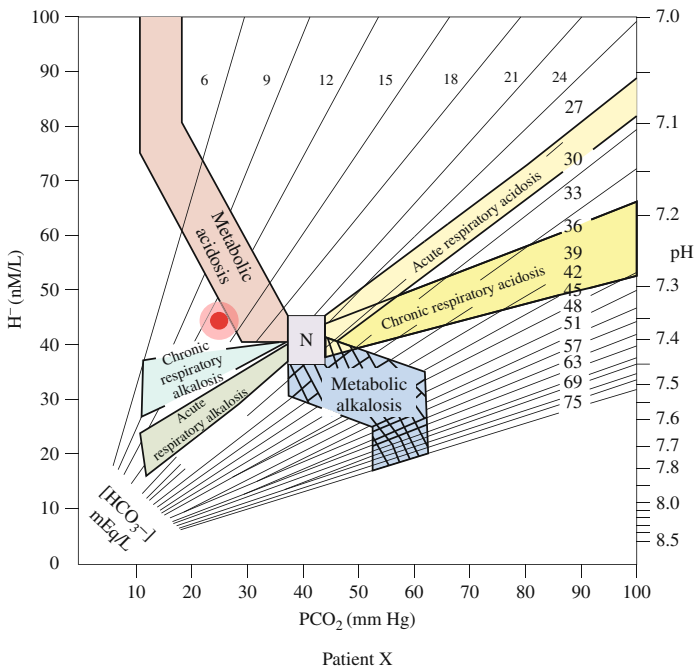




To all appearances, an acute respiratory alkalosis with a probable metabolic alkalosis is present. As in the case of patient S, this patient’s acid-base mapping has failed to reveal a triple disorder (see discussion opposite).

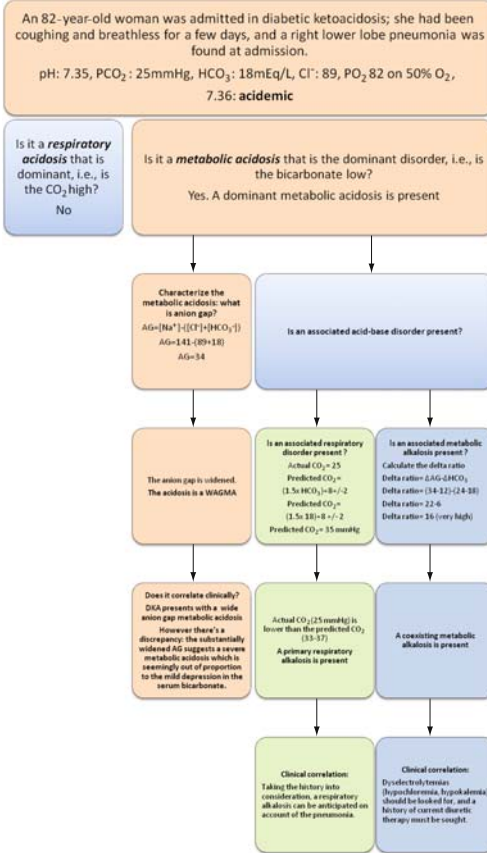
Patient W: A 68 year old woman in congestive heart failure

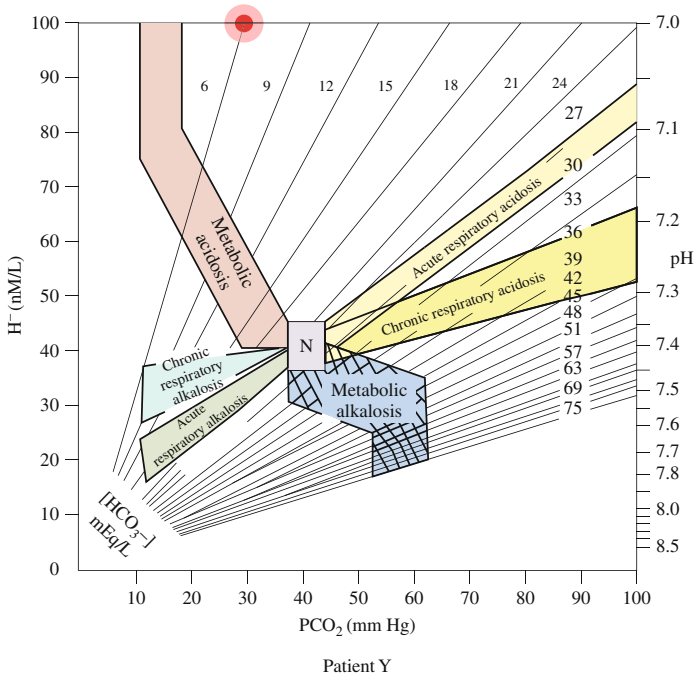




Impression: metabolic acidosis with chronic respiratory alkalosis. In fact, a triple disorder is present (see discussion opposite).

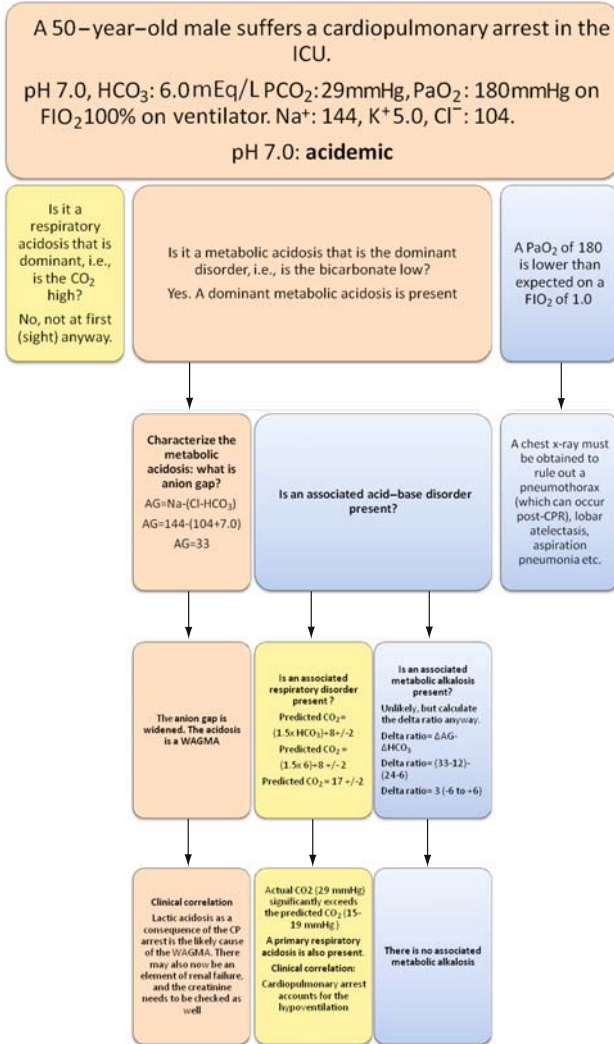
Patient X: An 82 year old diabetic woman with pneumonia

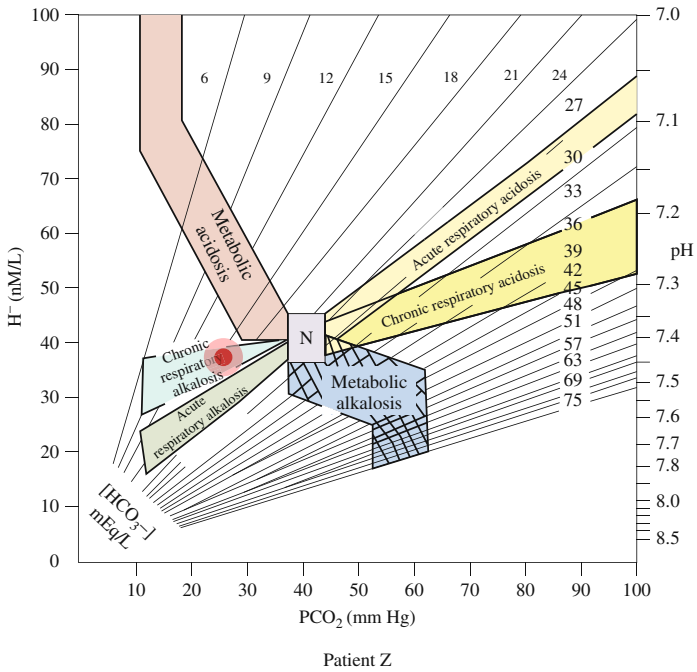




Severe metabolic acidosis with acute respiratory alkalosis.

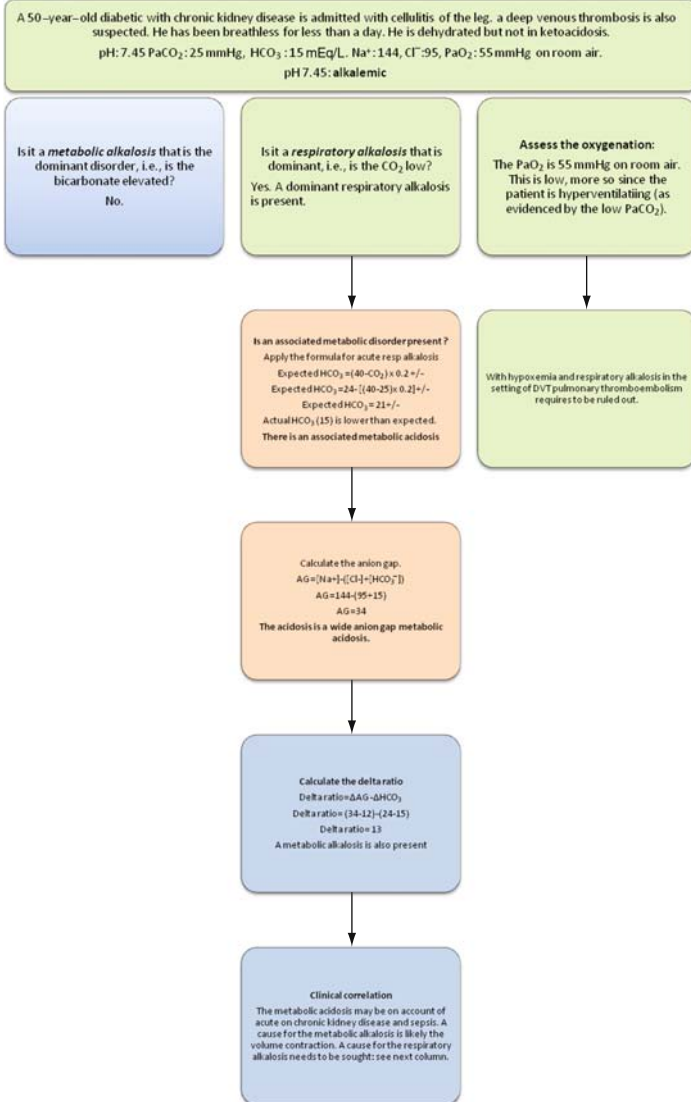
Patient Y: Cardiopulmonary arrest in a 50 year old male





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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