Understanding Blood Gases

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Blood gases are obtained in a variety of clinical situations, but they are obtained for two major reasons: (1) to determine if the patient is well oxygenated, and (2) to determine the acid-base status of the patient, concentrating on either the respiratory component, the metabolic (nonrespiratory) component, or most often, both respiratory and metabolic components of a patient's acid-base status. In the following discussion the term **nonrespiratory** will be used interchangeably with the term **metabolic.**

Most often blood gases are measured on arterial blood rather than on venous blood for two reasons.

1. Studying arterial blood is a good way to sample a mixture of blood that has come from various parts of the body. Blood obtained from a vein in an extremity gives information mostly about the extremity and can be quite misleading if the metabolism in the extremity differs from the metabolism of the body as a whole, as it often does. This difference is accentuated if the extremity is cold or underperfused as in a patient in shock, if the patient has done local exercise with the extremity such as opening and closing his fist, if there is local infection in the extremity, etc. Sometimes blood is sampled through a central venous catheter (CVP catheter) in hopes of getting mixed venous blood, but even in the superior vena cava or right atrium where a CVP catheter ends there is usually incomplete mixing of venous blood from various parts of the body. For complete mixing of the blood, one would have to obtain a blood sample from the pulmonary artery, through a Swan-Ganz catheter for example; and even then one would not get information about how well the lungs are oxygenating the blood.
2. The second reason for selecting arterial blood is that it gives the added information of how well the lungs are oxygenating the blood. Oxygen measurements of mixed venous blood can tell if the tissues are getting oxygenated, but cannot separate the contribution of heart from that of the lungs. In other words, if the mixed venous blood oxygen is low it means that either heart or lungs or both are at fault. So if mixed venous blood has a low oxygen concentration, it means either (a) that the lungs have not oxygenated the arterial blood well and that when the tissues extract their usual amount of oxygen from arterial blood, the resulting venous blood has a low oxygen concentration, or (b) that the heart is not circulating the blood well so that it is taking blood a long time to circulate through the tissues. The tissues, therefore, must extract more than the usual amount of oxygen from each cardiac cycle since the blood is flowing slowly. This produces a low venous O_2 concentration. If it is known that the arterial oxygen concentration is normal (indicating that the lungs are doing their job), but the mixed venous oxygen concentration is low, then one can infer that the heart and circulation are failing.

One advantage of using mixed venous blood instead of arterial blood is that if the oxygen concentration in mixed venous blood is normal, one can infer that the tissues are receiving enough oxygen. Usually this means that both ventilation and circulation are adequate.

OXYGEN

There are three ways to measure oxygen in blood: (1) oxygen content which is the number of ml of oxygen carried by 100 ml of blood, (2) the PO_2 or pressure exerted by oxygen dissolved in the plasma, and (3) the oxygen saturation of hemoglobin, which is a measure of the percentage of oxygen that hemoglobin is carrying related to the total amount the hemoglobin could carry, or

$$O_2\ Sat = \frac{\text{Amount of oxygen that hemoglobin is carrying}}{\text{Maximum amount of oxygen that hemoglobin can carry}} \times 100$$

The first of these three methods is the easiest to understand but the most difficult to measure, so it is not used routinely. The latter two methods which are used routinely are more understandable when compared to the first method in Table 1. Each gram of hemoglobin in 100 ml of blood can carry a maximum of 1.34 ml of oxygen, so if a patient has 15 gm Hgb /100 ml blood, then each 100 ml of blood can carry 15 × 1.34 cc or 20.1 cc of oxygen. If hemoglobin is only 97 percent saturated (carrying 97 percent of the total it is able to carry), then it carries 97 percent of 20.1 ml or 19.4 ml.

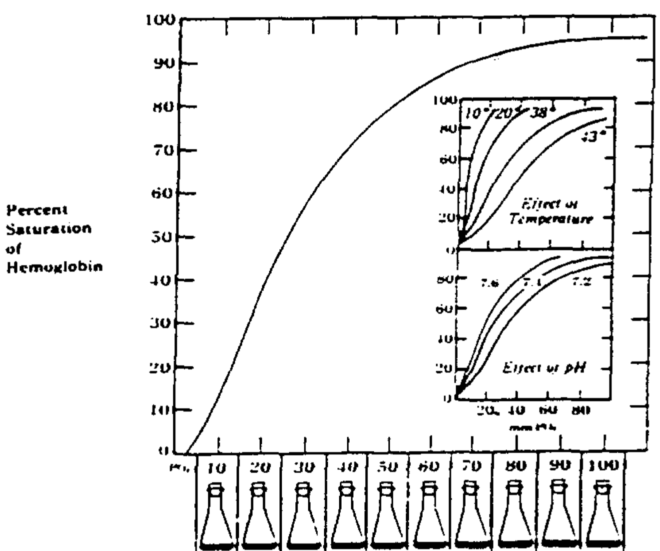
TABLE 1

HOW OXYGEN IS CARRIED IN BLOOD

Dissolved in plasma	0.3 ml/100 ml blood	Reflected by PO_2 by 90 mm Hg
Combined with Hgb	19.4 ml/100 ml blood	Reflected by O_2 Sat Hgb 97%
Total in whole blood	19.7 ml/100 ml blood	

The table reminds us that the majority of oxygen carried by the blood is carried by hemoglobin, and that a very small amount is dissolved in plasma. The percent saturation of hemoglobin with oxygen, then, gives a close estimate of the total amount of oxygen carried in blood. The PO_2 measurement, however, tells only of the pressure exerted by the small amount of oxygen that is dissolved in plasma. PO_2 is widely used and is valuable because PO_2 (pressure of oxygen dissolved in plasma) and O_2 Sat of Hgb (which is closely related to the total oxygen content of whole blood) are related to each other in a definitive fashion and the relationship has been charted—the oxyhemoglobin dissociation curve (Fig. 1). When the PO_2 in plasma is high, Hgb carries much oxygen. When the PO_2 is low, Hgb carries less oxygen. Once this relationship is known, PO_2 is just as valuable as a measurement of total O_2 content or the percentage of oxygen that hemoglobin is carrying. The relationship between PO_2 and O_2 saturation of hemoglobin is not a linear one, so that for a given rise or fall in PO_2 there is not always the same amount of rise or fall in O_2 saturation of hemoglobin. Instead, for a very low PO_2 a rise in PO_2 is associated with a more rapid rise in O_2 saturation; and for PO_2 in the normal range or higher, a rise in PO_2 is associated with a very small rise in O_2 saturation. This relationship is much easier to understand if one looks at the oxygen dissociation curve for hemoglobin. In simple terms, the dissociation curve indicates that in environments where the PO_2 is high, such as the capillaries of the lungs, hemoglobin combines with and carries a high percentage of the total oxygen it could carry; in environments where the PO_2 is low, such as the capillaries in the tissues, hemoglobin carries a lower percentage of the total oxygen it could carry, having given up the difference in oxygen for use by the tissues.

The dissociation curve presented applies only to normal [illegible]ditions. In the presence of acidosis or fever, the entire dissociation curve is shifted to the right, so that for a given oxygen saturation the PO_2 is greater than usual, and more oxygen is available for the tissues. In the presence of alkalosis, hemoglobin is more stingy and for a given oxygen saturation, the PO_2 is lower than usual. Certain abnormal types of hemoglobin may shift the dissociation curve to the right or the left, and the presence of certain compounds such as 2,3 diphosphoglycerate (2,3 DPG) may also shift the dissociation curve. Normal or high amounts of 2,3 DPG shift the curve to the right, thereby making more oxygen available to the tissues for a given O_2 Sat of Hgb, for 2,3 DPG decreases the affinity of hemoglobin for oxygen. Conversely, blood with low amounts of 2,3 DPG, such as transfused blood from a blood bank, has a left-shifted Hgb O_2 dissociation curve which makes less oxygen available to the tissues since this hemoglobin has a geater than normal affinity for oxygen. The measurement of P50 (partial pressure of oxygen when hemoglobin is exactly 50% saturated) allows one to detect the shifted oxyhemoglobin dissociation curve, so that P50 is greater than 27 when the curve is shifted to the right and less than 27 when it is shifted to the left.



		10	20	30	40	50	60	70	80	90	100
A	WHOLE BLOOD O_2 ml O_2/100 ml BLOOD	[illegible]	[illegible]	[illegible]	[illegible]	17.17	[illegible]	[illegible]	19.42	[illegible]	[illegible]
B	DISSOLVED O_2 ml O_2/100 ml BLOOD	[illegible]	[illegible]	[illegible]	0.12	[illegible]	0.18	0.21	0.24	[illegible]	0.30
C	O_2 COMBINED WITH Hb (A-B)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
D	% SAT. OF Hb $\frac{Hb\ O_2}{O_2\ CAPACITY} \times 100$	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Fig. 1. HbO_2 dissociation curves. The large graph shows a single dissociation curve, applicable when the pH of the blood is 7.40 and temperature 38° C. The blood O_2 tension and saturation of patients with CO_2 retention, acidosis, alkalosis, fever, or hypothermia will not fit this curve because the curve shifts to the right when temperature, pH, or PCO_2 is changed. Effects on the HbO_2 dissociation curve of change in temperature and in pH are shown in the smaller graphs. Reproduced with permission from Comroe, J.H., Jr.: *Physiology of Respiration, An Introductory Text*, 2nd edition. Copyright ©1974 by Year Book Medical Publishers, Inc., Chicago. (Data of J.W. Severinghaus: J. Appl. Physiol. 21:1108, 1966.)

One should always relate the oxygen content of blood to the FIO_2 (the fractional percentage of oxygen in the inspired air). For instance, an O_2 saturation of Hgb of 96 percent is normal if the patient is breathing room air which has an FIO_2 of .21, but is quite abnormal if the FIO_2 is .40. Some hospitals formally measure the A-a oxygen gradient (the difference between PO_2 in alveolar air and PO_2 in arterial blood), but much the same information can be obtained if one compares the PaO_2 or O_2 Sat of Hgb to the FIO_2. The normal range for A-a oxygen gradient increases with age. In young people the A-a oxygen gradient may normally be as high as 15 mm Hg and in elderly people it may be as high as 27 mm Hg.

The normal values for oxygen in arterial blood in Denver or any other place above sea level are lower than those at sea level because there is progressively lower PO_2 in the ambient air as one ascends (Table 2).

TABLE 2

ARTERIAL BLOOD O_2

	DENVER	SEA LEVEL
Oxygen content	18.9 cc O_2/100 cc of blood	19.7
PO_2	70 mm Hg (range 65–75)	>80 mm Hg
O_2 Saturation of Hgb	93% (range 92–94%)	>95%

In mixed venous blood the normal values for oxygen may be slightly lower in Denver than at sea level, but not enough lower to warrant remembering a second set of values (Table 3).

TABLE 3

MIXED VENOUS BLOOD O_2

Oxygen content	14–16 cc O_2/100 cc of blood
PO_2	35–40 mm Hg
O_2 saturation of Hgb	70–75%

Oxygen content refers to the total amount of oxygen that is present in blood in any form. Oxygen is carried in blood in just two ways: (1) dissolved in the plasma, and (2) combined with hemoglobin. By far the larger amount of oxygen is carried in combination with hemoglobin, and a very small amount is dissolved in plasma (Tables 4 and 5). Oxygen is not very soluble in plasma or water, so only a very small amount can dissolve in plasma. Oxygen content and O_2 saturation of hemoglobin are indicators of the amount of oxygen in blood or in the red blood cells respectively.

TABLE 4

HOW OXYGEN IS CARRIED IN BLOOD (DENVER)

	ARTERIAL	MIXED VENOUS
Dissolved in plasma	0.2 cc O_2/100 cc blood	0.1 cc O_2/100 cc blood
Combined with Hgb	18.7 cc O_2/100 cc blood	14.0 cc O_2/100 cc blood
Total oxygen content	18.9 cc O_2/100 cc blood	14.1 cc O_2/100 cc blood

TABLE 5

HOW OXYGEN IS CARRIED IN BLOOD (SEA LEVEL)

	ARTERIAL	MIXED VENOUS
Dissolved in plasma	0.3 cc O_2/100 cc blood	0.1 cc O_2/100 cc blood
Combined with Hgb	19.4 cc O_2/100 cc blood	15.4 cc O_2/100 cc blood
Total oxygen content	19.7 cc O_2/100 cc blood	15.5 cc O_2/100 cc blood

The oxygen that is combined with hemoglobin exerts no pressure, but the oxygen that is dissolved in plasma exerts a pressure or tension. The pressure or tension of O_2 dissolved in plasma can be readily measured and is known as PO_2. The hemoglobin-oxygen dissociation curve (Fig. 1) defines the relationship between the pressure exerted by dissolved O_2 and the amount of oxygen carried by hemoglobin. It should be made quite clear, though, that PO_2 is a measure of the **pressure or tension** exerted by dissolved oxygen, and PO_2 is **not** a measure of the **amount** of oxygen in blood.

An explanation of PO_2 must start with an explanation of barometric pressure. Barometric pressure may be thought of as the weight of the atmosphere or the pressure exerted by the atmosphere. At sea level barometric pressure is 760 mm Hg. We are not conscious of the weight or pressure exerted on us by the atmosphere, partly because the atmosphere is made up of gases. If we dive into water we are much more aware of the weight or pressure exerted on us by the water, and this pressure increases as we dive deeper because there is progressively more water above us. Just as in water, the deeper we are in the atmosphere the higher the barometric pressure. So, at the top of Pike's Peak (elevation 14,110 feet above sea level) we are near the top of the atmosphere and the barometric pressure is lower—425 mm Hg. The average barometric pressure in Denver is 625 mm Hg. (Of course, as weather fronts approach, the barometric pressure may fluctuate slightly even though the elevation is constant.) With high-pressure weather fronts, the barometric pressure may increase by 5 to 10 mm Hg, and with low-pressure fronts the barometric pressure may fall by 5 to 10 mm Hg. In blood gas laboratories a barometer is necessary for determining the barometric pressure each day.

If one takes a bottle in which a vacuum has been created and inverts this bottle in a pan of water, when the cork is removed from the bottle the water in the pan will rise in the bottle (Fig. 2). The force that makes the water rise in the bottle is the difference between the barometric pressure exerted on the pan and the absence of barometric pressure in the vacuum bottle. If we substitute a long tube for the bottle, create a vacuum in the tube, and invert the tube in a container of mercury instead of a pan of water, we have a barometer. Since the vacuum in the tube remains constant, the only factor influencing how high mercury rises in the tube is the barometric pressure (or weight of the atmosphere) pressing down on the mercury in the container.

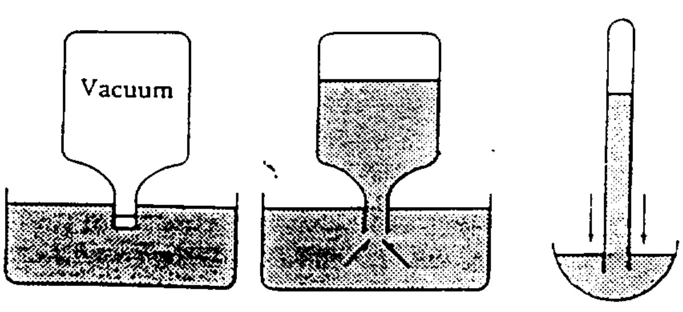


Fig. 2. Effects of barometric pressure.

Table 6 is a simplified explanation of why the arterial PO_2 in Denver is about 72 mm Hg and at sea level about 95 mm Hg.

It should be pointed out that the percentage of O_2 in the atmosphere is 21 percent (actually 20.93) everywhere in the atmosphere and that changes in PO_2 with altitude are due to changes in barometric pressure with altitude and not due to changes in the percentage of oxygen present.

TABLE 6

AT SEA LEVEL	AT DENVER	REMARKS
760	630 mm Hg	Average barometric pressure
−47	−47 mm Hg	Water vapor pressure at body temperature (subtracted because in the body this pressure is exerted by water vapor)
713	583 mm Hg	Corrected barometric pressure (in body or completely humidified air at body temperature)
× 21%	× 21%	Percent of oxygen in the atmosphere
150 mm Hg	123 mm Hg	PO_2 in air that is completely humidified
−40	−36	PCO_2 — pressure exerted by CO_2 in alveolus
110 mm Hg	87 mm Hg	PO_2 in alveolus
−5 mm Hg	−5 mm Hg	Gradient for diffusion of O_2 from alveolus into capillary
105 mm Hg	82 mm Hg	PO_2 in capillary blood in lungs
−10 mm Hg	−10 mm Hg	Due to venous shunting and mismatching of ventilation to perfusion
95 mm Hg	72 mm Hg	PO_2 in arterial blood

The percent saturation of hemoglobin is defined as the amount of O_2 that hemoglobin is carrying compared to the amount of O_2 that hemoglobin can carry, expressed as a percentage:

$$\text{Percent } O_2 \text{ saturation of Hgb} = \frac{\text{Amount } O_2 \text{ Hgb is carrying}}{\text{Amount } O_2 \text{ Hgb can carry}} \times 100$$

Since the amount of O_2 that Hgb can carry is a constant, 1.34 cc per gm of Hgb, then,

$$1.34 \text{ cc} \times \text{gm of Hgb} \times \% \text{ saturation of Hgb} = \text{cc of } O_2 \text{ that Hgb is carrying}$$

(It should be noted that there are rare abnormal types of hemoglobin that cannot carry 1.34 cc of O_2 per gm. There are also rare situations in which normal Hgb has been poisoned so that it cannot carry 1.34 cc of O_2 per gm—sulfhemoglobin or methemoglobin, for example.)

In 100 cc of blood { 1 gm of Hgb can carry 1.34 cc of O_2 ; 15 gm of Hgb can carry 15 × 1.34 cc of O_2 }

In arterial blood in Denver normal O_2 saturation of Hgb is 93 percent (i.e., Hgb is carrying 93 percent of the total amount of O_2 it **can** carry), then 93 percent of 20.1 cc equals 18.7 cc of O_2 carried by Hgb in Denver. At sea level, normal arterial O_2 saturation of Hgb is 97 percent, so Hgb is carrying 97 percent of 20.1 cc or 19.4 cc of oxygen.

The major factor which determines how much O_2 Hgb is carrying is the PO_2 that Hgb is exposed to. At high PO_2 Hgb carries more O_2; at low PO_2 Hgb carries less O_2. The exact relationship between the amount of O_2 that Hgb is carrying and the PO_2 is shown by the oxyhemoglobin dissociation curve, Fig. 1.

There are four pulmonary reasons why arterial blood may not be carrying the normal amount of oxygen (Fig. 3).

FIGURE 3

CAUSES OF HYPOXEMIA

Cause	
1. Alveolar hypoventilation.	associated with high PCO_2
2. Diffusion defect (at alveolar-capillary level). 3. Right-to-left shunt (in lung or heart). 4. Mismatching of ventilation and blood flow in the lungs. (Blood goes by alveoli that are poorly ventilated. This blood, as it passes through the lungs, picks up little oxygen. This poorly oxygenated blood then returns to the heart and is pumped out in the arteries to the body, therefore causing arterial blood to have less than the normal amount of oxygen.)	associated with low or normal PCO_2

The amount of oxygen that is transported to the tissues is more important than the PO_2. The PO_2 is a measure of intensity of pressure due to oxygen, and oxygen content is a measure of amount of oxygen.

OXYGEN TRANSPORT TO THE TISSUES = ARTERIAL O_2 CONTENT × CARDIAC OUTPUT

The oxygen transported to the tissues depends on (1) the amount of oxygen in arterial blood (arterial O_2 content), and (2) the ability of the heart to pump this blood containing oxygen around to the tissues.

The arterial O_2 content depends in turn on (1) how well the lungs are able to get oxygen from air into the blood, and (2) a normal amount of functioning hemoglobin to carry the oxygen.

In summary,

Oxygenation of the tissues depends on:	I. Arterial O_2 content, which depends on: 1. Lungs' ability to get O_2 into blood 2. Ability of hemoglobin to hold enough O_2	and II. Cardiac output (Circulation)

The pulmonary causes of tissue hypoxia have already been mentioned: (See Fig. 3)

The nonpulmonary causes of tissue hypoxia are: (1) reduced blood flow to the tissues (reduced cardiac output); (2) anemia—not enough hemoglobin to carry O_2; (3) nonfunctioning hemoglobin—enough hemoglobin but hemoglobin that exists cannot carry O_2 because it has been "poisoned"; and (4) right-to-left cardiac shunts—most frequently seen in cyanotic congenital heart disease.

1. Reduced blood flow to the tissues (reduced cardiac output) might be caused by:
   a. Myocardial infarction
   b. Abnormal cardiac rhythm
   c. Reduced cardiac function (other causes): congestive heart failure, valvular heart lesion, etc.
   d. Hypovolemia (intimately related to anemia)
2. Anemia: 1 gm of Hgb carries 1.34 cc O_2 and normally there are 15 gm of Hgb to carry 15 × 1.34 cc O_2 or 20.1 cc of O_2. If there is anemia so that only 7.5 gm of Hgb are present, then 7.5 × 1.34 cc O_2 ≈ 10 cc of O_2 are all that can be carried; if anemia is milder (between 7.5 and 15 gm Hgb) more O_2 can be carried; if anemia is more severe (less than 7.5 gm of Hgb) even less O_2 can be carried. Usually the body compensates for anemia by having the heart circulate faster the lesser amount of hemoglobin that is present.
3. Nonfunctioning hemoglobin: A few rare conditions exist in which there might be a normal amount of hemoglobin, but even this normal amount cannot function because it has been poisoned. Some examples of this are:
   a. Carbon monoxide poisoning
   b. Methemoglobinemia
   c. Sulfhemoglobinemia

   In each of these situations, something (carbon monoxide, for example) has combined with hemoglobin, making it hard for oxygen to combine with and be carried by this hemoglobin.
4. In right-to-left cardiac shunts, oxygen gets through the lungs normally into the bloodstream, there is enough functioning hemoglobin to carry the oxygen, and the heart is strong enough to circulate the oxygenated blood. However, some venous blood that never passes through the lungs to get oxygenated is shunted into the systemic arterial system, and the combination of oxygenated blood plus venous unoxygenated blood is carried through the arteries to the tissues, supplying them with less oxygen than they need.

The patient who is hypoxemic compensates for hypoxia in the following ways: (1) tachypnea (rapid breathing), (2) tachycardia (rapid heartbeat), and (3) erythrocytosis (high hemoglobin and hematocrit). The tachypnea and tachycardia represent extra energy expenditure by the patient. Erythrocytosis simply means increased production of red blood cells by the hypoxic patient's bone marrow in an attempt to get more O_2 to the tissues. If the fault is lack of enough red blood cells, this is useful. But if the fault is in getting enough O_2 through the lungs, increasing the number of red blood cells helps little or not at all. The hypoxemic patient tries all these means of compensating for hypoxemia and often all of them together are inadequate. Hypoxia often leads to pulmonary hypertension (high blood pressure in the arteries of the lungs), and this can lead to strain or failure of the right side of the heart.

If oxygen is administered to the patient to treat his hypoxemia, tachypnea and tachycardia do not occur, no erythrocytosis occurs, and pulmonary hypertension may go away. Complete compensation is possible with oxygen treatment; sometimes patient compensation is not complete. It can be seen that supplemental oxygen is rational treatment for the patient with hypoxemia, but long-term continuous oxygen is usually reserved for the patient who when completely stable has a PO_2 below 50 mm Hg (O_2 saturation below 85 percent) and who also has one or more of the following: (1) right heart failure which is difficult to manage with digitalis and iretics, (2) significant secondary erythrocytosis, and/or (3) a progressive downhill course with weight loss, progressive muscle wasting, or decreased mental function.

Often such a patient responds to nocturnal oxygen (oxygen for 8 hours at night), or if the patient is living at a high altitude a move to a lower altitude may make supplemental oxygen unnecessary.

Oxygen treatment may lead to CO_2 retention if the O_2 is not carefully controlled.

There are two major reflex stimuli to breathing: (1) CO_2 retention (hypercapnic stimulus to breathe), and (2) low PO_2 (hypoxic stimulus to breathe).

Small elevations of PCO_2 are a major stimulus to breathing. Increasing the PCO_2 by 4 mm Hg can cause a 100-percent increase in ventilation. Large elevations in PCO_2 may reduce the amount of ventilation by reducing all brain functions including function of the respiratory center. In patients with large elevation of PCO_2, hypoxemia may be the most important stimulus to breathe. If a patient who no longer has a hypercapnic stimulus to breathing is treated with oxygen, thereby eliminating the hypoxic stimulus to breathe, he may breathe even less, significantly worsening his condition. It has become apparent that giving a controlled amount of oxygen—just enough to raise the arterial PO_2 to approximately 60 mm Hg—allows the patient to benefit from the oxygen and usually does not reduce ventilation.

It should be clear that oxygen therapy, though often given in haphazard fashion, requires just as much understanding and precision in dosage as any other form of drug therapy.

NORMAL VALUES

Normal values for blood gases are given in Table 7. Following this the main emphasis will concern acid-base interpretation.

TABLE 7

NORMAL BLOOD GAS VALUES

	ARTERIAL BLOOD	MIXED VENOUS BLOOD
pH	7.40 (7.35–7.45)	7.38 (7.33–7.43)
PO_2	80–100 mm Hg	35–40 mm Hg
O_2 Sat	95% or greater	70–75%
PCO_2	35–45 mm Hg	41–51 mm Hg
HCO_2	22–26 mEq/L.	24–28 mEq/L.
Base Excess (B.E.)	−2 – +2	0 – +4

Note that in Table 7 only two measurements—PO_2 and PCO_2—are actually measurements of gases. However, all should be determined in blood gas analyses. It is imperative that a measure of the nonrespiratory (metabolic) component be included, and actual HCO_3 and Base Excess are most useful. Many other terms may be given on a blood gas report, but one need be concerned only with the ones listed in Table 7.

Older persons have values for PO_2 and O_2 saturation near the lower part of the normal range, and younger people tend to have high normal values. Normal values for mixed venous blood are more variable than for arterial blood but representative normals are given in Table 7. Because there is not much difference in normal values of HCO_3 and Base Excess between arterial and mixed venous blood and because venous blood is not often used, one does not need to remember a different set of values for venous blood.

An acid is any substance that can donate a hydrogen ion, H^+. H^+ can be thought of as the most important part of an acid.

TABLE 8

DEFINITIONS

Acid: A substance that can donate hydrogen ions, H^+. Example:

$$\underset{\text{(acid)}}{H_2CO_3} \longrightarrow H^+ + HCO_3^-$$

Base: A substance that can accept hydrogen ions, H^+. All bases are alkaline substances. Example:

$$\underset{\text{(base)}}{HCO_3^-} + H^+ \longrightarrow H_2CO_3$$

Many substances may include H in their chemical structure, but some cannot donate the H because it is too tightly bound. Only those substances that can give up their H^+ are acids.

Bases are substances that can accept or combine with H^+. The terms **base** and **alkali** are used interchangeably.

Each of the acid-base terms (Table 9) will now be discussed in more detail.

TABLE 9

ACID-BASE TERMS

pH measurement = Only way to tell if body is too acid or too alkaline
Acidemia = Acid condition of the blood - pH < 7.35
Alkalemia = Alkaline condition of the blood - pH > 7.45
Acidosis = Process causing acidemia
Alkalosis = Process causing alkalemia

The pH measurement is the only way to tell if the body is too acid or too alkaline. Low pH numbers (below 7.35) indicate an acid state, and high pH numbers (above 7.45) indicate an alkaline state.

If the numbers are lower than 7.35, there is acidemia, and if higher than 7.45, alkalemia. Acid**emia** refers to a condition in which the **blood** is too acid. Acid**osis** refers to the **process** in the patient which causes acidemia, and the adjective for the process would be acid**otic**. Alkal**osis** refers to the **process** in the patient which causes the alkal**emia**, and the adjective for this process is alkal**otic**.

This much time has been spent in defining the terms because later it will be seen that in a patient there may be more than one process occurring at the same time. For instance, if both an acidosis and an alkalosis are occurring at once, then the pH will tell us which is the stronger of the two processes. The pH will be below 7.35 if the acidosis is the stronger, above 7.45 if the alkalosis is the stronger and between 7.35 and 7.45 if the acidosis and alkalosis are of nearly equal strength. So the pH value of blood represents an average of the acidoses and alkaloses which may be occurring.

THE RESPIRATORY PARAMETER: PCO_2

The PCO_2 refers to the pressure or tension exerted by dissolved CO_2 gas in the blood (Table 10). The PCO_2 is influenced **only** by respiratory causes. Although, this is an oversimplification; still remember that PCO_2 is **influenced only by the lungs.**

Where does the CO_2 come from? It is present only in very tiny amounts in the air we breathe. It comes directly from foods we eat. As a result of metabolism for the production of energy, foods are converted by the body tissues to water and CO_2 gas. When the pressure of CO_2 in the cells exceeds 40 mm Hg (the normal arterial value), the CO_2 spills over from the cells into the plasma. In plasma, CO_2 may combine with H_2O to form H_2CO_3 (carbonic acid), but there is actually 800 times as much CO_2 in the form of dissolved gas in plasma as is converted to H_2CO_3.

TABLE 10

PCO_2, THE RESPIRATORY PARAMETER

PCO_2 = Pressure (tension) of dissolved CO_2 gas in blood
PCO_2 - Influenced only by respiratory causes

$$\text{Food} \xrightarrow[\text{by body}]{\text{converted}} H_2O + CO_2 + \text{energy}$$

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

Normal PCO_2 = normal ventilation
High PCO_2 = hypoventilation
Low PCO_2 = hyperventilation

You should consider CO_2 gas an acid substance because when it combines with water, an acid is formed—carbonic acid, H_2CO_3.

H_2CO_3 dissociates into hydrogen ion, H^+ and bicarbonate HCO_3^-. Much of the H^+ forms a loose association with the plasma proteins (is buffered), thus reducing the free H^+. The body has to get rid of the waste product, CO_2, and can do so in two ways:

1. The less important way is by converting the CO_2 gas to carbonic acid, H_2CO_3, which dissociates to H^+ and HCO_3^-. The H^+ can be excreted by the kidneys, mainly in the form of NH_4^+.
2. A much more important way is to have the lungs get rid of the CO_2.

Getting rid of CO_2 gas, then, is one of the main functions of the lungs, and a very important relationship exists between the amount of ventilation and the amount of PCO_2 in blood. If the PCO_2 in blood (i.e., the dissolved CO_2 gas in blood) is too high, it means that the lungs are not providing enough ventilation. This is called **hypoventilation.** Hypoventilation can thus be detected by finding high levels of PCO_2 in the blood. If the PCO_2 is too low, there is excessive ventilation by the lungs, or **hyperventilation,** and if the PCO_2 is normal, there is exactly the right amount of ventilation. This relationship between PCO_2 in blood and amount of ventilation is very important, PCO_2 being much more important than PO_2 in judging whether there is normal ventilation, hyperventilation, or hypoventilation, for there are other factors (such as shunting, diffusion abnormalities, etc.) which lower the PO_2 without reducing ventilation.

As seen in Table 11, there are only two abnormal conditions associated with abnormalities in PCO_2: respiratory acidosis (high PCO_2) and respiratory alkalosis (low PCO_2).

TABLE 11

RESPIRATORY ABNORMALITIES

PARAMETER	CONDITION	MECHANISM
↑PCO_2	Respiratory acidosis	Decreased elimination by lungs of CO_2 gas (Hypoventilation)
↓PCO_2	Respiratory alkalosis	Increased elimination by lungs of CO_2 gas (Hyperventilation)

The causes of respiratory acidosis (high PCO_2) are (1) obstructive lung disease (mainly chronic bronchitis, emphysema and occasionally asthma); (2) over sedation, head trauma, anesthesia, and other causes of reduced function of the respiratory center; (3) neuromuscular disorders such as myasthenia gravis or the Guillain-Barrè syndrome; (4) hypoventilation with a mechanical ventilator; and (5) other rarer causes of hypoventilation (such as the Pickwickian syndrome). It should be noted that **respiratory** acidosis may occur even with normal lungs if the respiratory center is depressed. The term **respiratory acidosis** means elevated PCO_2 due to hypoventilation.

TABLE 12

CAUSES OF RESPIRATORY ACIDOSIS (↑PCO_2)

1. Obstructive lung disease
2. Over sedation and other causes of reduced function of the respiratory center (even with normal lungs)
3. Neuromuscular disorders
4. Hypoventilation with mechanical ventilator
5. Other causes of hypoventilation, such as the hyperventilation-obesity (Pickwickian) syndrome

The causes of respiratory alkalosis (low PCO_2) are hypoxia, congestive heart failure, anxiety, pulmonary emboli, pulmonary fibrosis, pregnancy, hyperventilation with mechanical ventilator, gram negative septicemia, hepatic insufficiency, brain injury, salicylates, fever, asthma, and severe anemia. In gram negative septicemia, the hyperventilation may precede other evidence of septicemia. In patients with congestive heart failure, pneumonia, asthma, pulmonary emboli and pulmonary fibrosis, the hyperventilation (respiratory alkalosis) continues even if the hypoxia is corrected, so hypoxia is not the only cause in these conditions.

TABLE 13

CAUSES OF RESPIRATORY ALKALOSIS (↓PCO_2)

1. Hypoxia
2. Nervousness and anxiety
3. Pulmonary embolus, fibrosis, etc.
4. Pregnancy
5. Hyperventilation with mechanical ventilator
6. Brain injury
7. Salicylates
8. Fever
9. Gram negative septicemia
10. Hepatic insufficiency
11. Congestive heart failure
12. Asthma
13. Severe anemia

THE NONRESPIRATORY (METABOLIC) PARAMETERS: HCO_3 AND BASE EXCESS

Bicarbonate and Base Excess are influenced **only** by nonrespiratory causes, not by respiratory causes. Again, this is a simplification, but a very important fact to remember—**bicarbonate and Base Excess are influenced only by nonrespiratory processes.** We can define a **metabolic process** for our purposes as anything other than respiratory causes that affects the patient's acid-base status. Examples of common metabolic (nonrespiratory) processes would be diabetic acidosis and uremia. When a nonrespiratory process leads to the accumulation of acids in the body or losses of bicarbonate, bicarbonate values drop below the normal range and Base Excess values become negative. On the other hand, when a nonrespiratory process causes loss of acid or accumulation of excess bicarbonate, bicarbonate values rise above normal and Base Excess values become positive. Base Excess may be thought of as representing an excess of bicarbonate or other base. Bicarbonate, then, is base—or in other words, an alkaline substance. The term **Base Excess** refers principally to bicarbonate but also to the other bases in blood (mainly plasma proteins and hemoglobin).

As seen in Table 14, there are only two abnormal conditions associated with abnormalities in HCO_3 or Base Excess: metabolic alkalosis and metabolic acidosis. (Nonvolatile acid is any acid other than PCO_2 - H_2CO_3.)

TABLE 14

METABOLIC ABNORMALITIES

↑HCO_3 or B.E.	Nonrespiratory (metabolic) alkalosis	1. Nonvolatile acid is lost, or 2. HCO_3 is gained
↓HCO_3 or B.E.	Nonrespiratory (metabolic) acidosis	1. Nonvolatile acid is added (using up HCO_3) or 2. HCO_3 is lost

The causes of nonrespiratory (metabolic) alkalosis (increased HCO_3 and Base Excess) are: (1) loss of acid-containing fluid from the upper GI tract as by nasogastric suction or vomiting (this loss of acid from the stomach leaves the body with a relative excess of alkali), (2) rapid correction of chronic hypercapnia. It will take the body several days to correct its compensation for hypercapnia (accumulation of excess HCO_3) after the hypercapnia is suddenly relieved, (3) diuretic therapy with mercurial diuretics, ethacrynic acid, furosemide, and thiazide diuretics, (4) Cushing's disease, (5) treatment with corticosteroids, for example, prednisone or cortisone, (6) hyperaldosteronism, (7) severe potassium depletion, (8) excessive ingestion of licorice, (9) Bartter's syndrome, (10) alkali administration, and (11) nonparathyroid hypercalcemia.

TABLE 15

CAUSES OF NONRESPIRATORY (METABOLIC) ALKALOSIS (↑HCO_3)

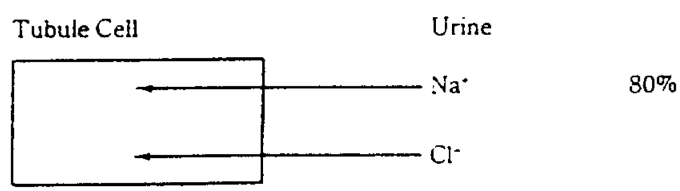
1. Fluid losses from upper GI tract-vomiting or N-G tube causing loss of acid
2. Rapid correction of chronic hypercapnia
3. Diuretic ℞-mercurial, ethacrynic acid (Edecrin), furosemide (Lasix), thiazides
4. Cushing's disease
5. ℞ with corticosteroids (prednisone, cortisone, etc.)
6. Hyperaldosteronism
7. Severe potassium depletion
8. Excessive ingestion of licorice
9. Bartter's syndrome
10. Alkali administration
11. Nonparathyroid hypercalcemia

The first three causes listed, i.e., fluid losses from stomach (vomiting or N-G drainage), rapid correction of chronic hypercapnia, and diuretic therapy, will all show correction of the alkalosis in response to administration of sodium chloride. Treatment with potassium chloride may be more reasonable if the potassium is low or if one is trying to prevent accumulation of salt and water. Treatment with two other diuretics, spironolactone (Aldactone) and triamterene (Dyrenium), does not cause metabolic alkalosis. With causes 4 through 9 in Table 15 the metabolic alkalosis cannot be corrected by administration of sodium chloride. With the last two causes listed the response of sodium chloride is variable.

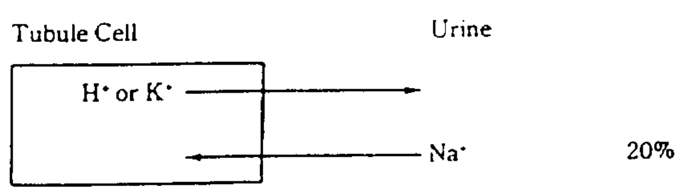
The following is an explanation of the relationship between hypokalemia (low K^+), hypochloremia (low Cl^-) and metabolic alkalosis. Normally in the kidney Na^+ and Cl^- pass from the blood into the urine at the glomerulus. Further along in the tubules of the kidney this Na^+, which is in the urine, must be reabsorbed from the urine into the kidney tubule cells and then into the blood.

Because Na^+ has a positive charge (+), when it is reabsorbed into the cells, the Na^+ must either:

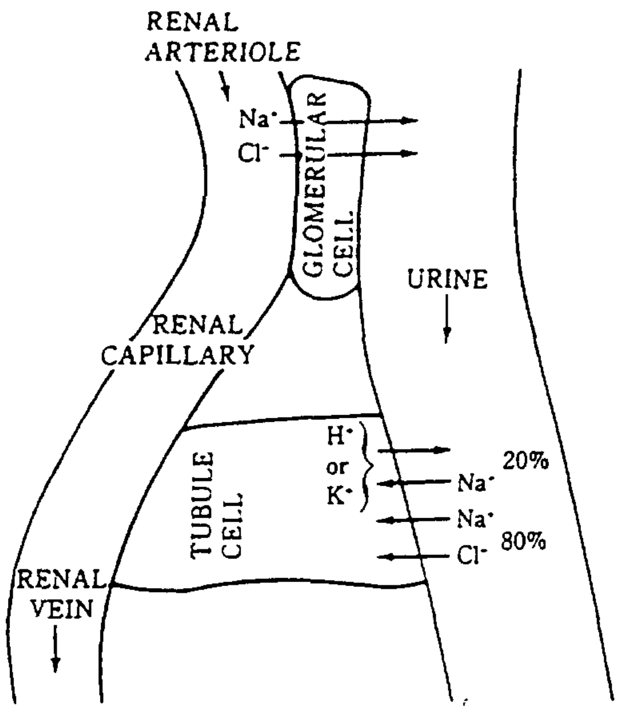
1. Be reabsorbed with something that has a negative charge (−) like Cl^- or



2. Enter the tubule cell in exchange for something else that has a positive charge, like K^+ or H^+ (which passes from the tubule cell to the urine).



LOW Cl^- & LOW K^+ CAN CAUSE METABOLIC ALKALOSIS



Normally, 80 percent of the Na^+ is reabsorbed while accompanied by Cl^- and 20 percent is exchanged for K^+ or [illegible].

When there is hypochloremia (↓Cl^-), the amount of Na^+ that is reabsorbed in the company of Cl^- is reduced and more Na^+ must be exchanged for K^+ or H^+. When Na^+ is exchanged for K^+ and H^+, the loss of H^+ represents a loss of acid, leaving the patient alkalotic—therefore a hypochloremic alkalosis.

When Na^+ is exchanged for K^+ or H^+, only a small amount of K^+ is available, and when this is used up the patient becomes hypokalemic and H^+ is lost. The loss of H^+ is a loss of acid, leaving the patient with an alkalosis-hypokalemic alkalosis.

A rare cause of nonrespiratory alkalosis, which unfortunately is not reflected by an elevated bicarbonate in the blood, is the intravenous infusion of phenytoin (Dilantin) which has a very alkaline pH. Infusion of this alkaline substance causes a short-lived alkalemia not associated with elevated HCO_3.

The causes of *nonrespiratory (metabolic) acidosis* (low HCO_3 and low Base Excess) can be divided into those causes in which there is an increase in the unspecified anions and those causes in which bicarbonate has been lost and there is no such increase in unspecified anions (Table 15). The normal value for unspecified anions is 12 ± 3. Substances which have a negative charge are attracted to an anode and are called anions. The anions that are normally measured (specified) are HCO_3 and Cl^-. The anions that are not regularly measured but are normally present in blood are called unspecified or unmeasured anions. They are phosphates, sulphates, creatinates, and proteinates.

When there is an increase in unspecified anions, it may be due to accumulation of phosphates, sulphates and creatinates as is seen in renal failure or the accumulation of an unusual negatively charged substance such as lactic acid, ketoacids, or the like. Often the unspecified anions are referred to as the anion gap. If one subtracts the sum of HCO_3 and Cl^- concentration from Na^+ concentration and finds a difference greater than 15, there is said to be an increase in unspecified anions (increased anion gap). Conditions causing this are diabetic ketoacidosis, alcoholic ketoacidosis, poisonings (salicylate, ethylene glycol, methyl alcohol, paraldehyde), lactic acidosis and renal failure. In these cases there is accumulation of or ingestion of an unusual acid. Conditions that cause a metabolic acidosis without an increase in unmeasured anions are associated with a high serum chloride. These conditions are diarrhea, drainage of pancreatic juice, ureterosigmoidostomy, obstructed ileal loop, treatment with acetazolamide (Diamox), renal tubular acidosis, treatment with ammonium chloride or with arginine HCL *and intravenous hyperalimentation*. In most of these latter conditions there is a deficit of bicarbonate, leaving relatively too much acid.

TABLE 16

CAUSES OF NONRESPIRATORY (METABOLIC) ACIDOSIS (↓HCO_3 AND ↓B.E.)

WITH INCREASE IN UNSPECIFIED ANIONS	WITHOUT INCREASE IN UNSPECIFIED ANIONS
Diabetic ketoacidosis	Diarrhea
Starvation ketoacidosis	Drainage of pancreatic juice
Alcoholic ketoacidosis	Ureterosigmoidostomy
Poisonings	*Obstructed ileal loop*
Salicylate	℞ with acetazolamide (Diamox)
Ethylene glycol	℞ with NH_4Cl
Methyl alcohol	Renal tubular acidosis
Paraldehyde (rarely)	Intravenous hyperalimentation (rarely)
Lactic acidosis	Dilutional acidosis
Renal failure	

In all of the conditions in the left-hand column there is an accumulation of an abnormal acid substance in blood which then reacts with and uses up some of the usual amount of bicarbonate, leaving the patient with reduced levels of bicarbonate and Base Excess.

One of the most important causes of metabolic acidosis is lactic acidosis. Whenever body tissues do not have enough oxygen they lose their ability to metabolize lactic acid which then accumulates in the blood. This lactic acid then combines with some of the normal amount of bicarbonate, using up the bicarbonate. In a cardiac arrest, we customarily administer bicarbonate, about 1 ampul (44.6 mEq.) every 5 minutes, to resupply the bicarbonate which is used up by combining with lactic acid. Other conditions besides cardiac arrest which *may be associated with lactic acidosis are shock, severe heart* failure and severe hypoxemia. Tissue hypoxia, seen in all of these conditions, leads to the lactate production.

If a patient has a metabolic acidosis with an anion gap of greater than 15, one can consult Table 16, left column, and ask the lab to measure whichever unspecified anion one guesses might be elevated; i.e., if patient is an uncontrolled diabetic, measure ketoacids; if patient is in shock, measure lactic acid.

To review (Table 17), PCO_2 is the respiratory parameter, is a gas, is an acid, and is regulated by the lungs. HCO_3 and Base Excess are nonrespiratory parameters, occur in solution, are bases (alkaline substances), and are regulated mainly by the kidneys (not by the lungs).

TABLE 17

PCO_2 — Respiratory Parameter
- Gas Acid
- Acid
- Regulated by the lungs

HCO_3 or Base Excess — Nonrespiratory Parameter
- Solution
- Base
- Regulated mainly by the kidneys

Where does the CO_2 content fit in this scheme? Determination of electrolytes consists of Na^+, K^+, Cl^-, and CO_2. In this case CO_2 is an abbreviation for CO_2 content which is composed mainly of bicarbonate; if the term CO_2 CONTENT were used it would improve understanding. Note that in conversation CO_2 is sometimes used to mean CO_2 content (mainly bicarbonate) and sometimes to mean CO_2 GAS. This double use of the term CO_2 is one of the main reasons understanding acid-base problems is hard. Use the terms CO_2 CONTENT and CO_2 GAS to avoid confusion. Better yet, some hospitals are reporting HCO_3 in place of CO_2 content when electrolytes are ordered.

Table 18 shows that CO_2 content is made up mainly of bicarbonate (HCO_3) and to a lesser extent, dissolved CO_2 gas. The normal value of CO_2 content, 25.2 mEq./*l*, consists of 24 mEq./*l* of HCO_3 and 1.2 mEq./*l* of dissolved CO_2 gas. The 1.2 mEq./*l* of dissolved CO_2 gas is expressed in different terminology, so PCO_2 of 40 mm Hg equals 1.2 mEq./*l*. To convert from mm Hg to mEq./*l*, the conversion factor is 0.03, so 40 mm Hg × 0.03 = 1.2 mEq./*l*.

TABLE 18

HCO_3	24 mEq./*l*	
Dissolved CO_2 gas	1.2 mEq./*l*	= 40 mm Hg PCO_2
CO_2 content	25.2 mEq./*l*	

In Table 18 you will note that the ratio of HCO_3 to PCO_2 is 24:1.2 or 20:1. The body always tries to keep this ratio of HCO_3 to PCO_2 stable at 20:1. That is, the ratio of alkali (HCO_3) to acid (PCO_2) is normally 20:1. As long as the ratio remains 20:1, the pH remains normal. If bicarbonate (HCO_3) or Base Excess increases, there is alkalosis causing the pH to rise. If HCO_3 or Base Excess falls, there is acidosis and the pH falls. IF THE pH CHANGE IS DUE MAINLY TO CHANGE IN BICARBONATE (OR BASE EXCESS), IT IS SAID TO BE DUE TO NONRESPIRATORY (METABOLIC) CAUSES.

Just the opposite happens with PCO_2 which, remember, is an acid substance. If the PCO_2 rises, there is an acidosis causing the pH to fall. If the PCO_2 falls, there is an alkalosis and the pH rises. IF THE pH CHANGE IS DUE MAINLY TO CHANGES IN PCO_2, IT IS SAID TO BE DUE TO RESPIRATORY CAUSES.

As seen in Table 19, acid-base abnormalities can be separated into just four categories to make understanding them easier. First they are divided by pH into either alkalemia or acidemia. Next they are subdivided into either nonrespiratory (metabolic) or respiratory causes. This is the procedure one uses in interpreting acid base abnormalities.

TABLE 19
CAUSES OF ALKALEMIA AND ACIDEMIA

CONDITION	TYPES	PRIMARY ABNORMALITY
Alkalemia (high pH)	Nonrespiratory (metabolic)	↑HCO_3
	Respiratory	↓PCO_2
Acidemia (low pH)	Nonrespiratory (metabolic)	↓HCO_3
	Respiratory	↑PCO_2

For example, if pH is high there is an alkalemia. There may be two types of alkalemia: (1) nonrespiratory, in which the primary abnormality is due to an increase in bicarbonate (example, a person who has taken too much bicarbonate or baking soda), and (2) respiratory, in which the primary abnormality is hyperventilation with loss of CO_2 gas. CO_2 gas is an acid substance; when CO_2 gas is lost (due to hyperventilation) an alkalemia occurs. (An example would be a nervous person having a hyperventilation attack.)

If the pH is low, there is an acidemia, and there are just two types of acidemia: (1) nonrespiratory, in which the primary abnormality is loss of HCO_3, usually due to reaction with excessive metabolic acids; (An example is diabetic acidosis in which ketoacids accumulate; these acids then react with the normal amount of HCO_3, using up HCO_3, and leaving HCO_3 and Base Excess levels low) and (2) respiratory, in which there is an accumulation of CO_2 gas (high PCO_2) which, you remember, is an acid substance (An example is a patient with acute respiratory failure who **hypoventilates** because his airways are obstructed by mucus). In respiratory acidosis there is an accumulation of volatile acid—CO_2 gas, but in nonrespiratory acidosis the acids which accumulate are not gases.

There may be more than one primary acid-base disturbance occurring at the same time. Occasionally two disturbances will be of equal magnitude and if one is an acidosis and the other an alkalosis, they will balance each other and the pH will remain normal. On another occasion there may be several acidoses, for instance, occurring at the same time, all adding their effects to make the pH more acidemic than one alone would.

There are two ways in which an abnormal pH may be returned toward normal: (1) compensation, and (2) correction (Table 20). In **compensation** , the system not primarily affected is responsible for returning the pH toward normal. For example, if there is respiratory acidosis (high PCO_2) the kidneys **compensate** by retaining bicarbonate to return the ratio of HCO_3 to PCO_2 toward 20:1, for when the ratio is 20:1, the pH is normal. Compensation is complete only in chronic respiratory alkalosis. In the other acid-base disorders the pH is returned nearly but not completely to normal because the compensation is not complete.

TABLE 20

COMPENSATION VS. CORRECTION OF ACID-BASE ABNORMALITIES

In both:	Abnormal pH is returned toward normal.
Compensation:	Abnormal pH is returned toward normal BY ALTERING THE COMPONENT NOT PRI-

MARILY AFFECTED, i.e., if PCO_2 is high, HCO_3 is retained to compensate.

Correction: Abnormal pH is returned toward normal BY ALTERING THE COMPONENT PRIMARILY AFFECTED, i.e., if PCO_2 is high, PCO_2 is lowered, correcting the abnormality.

In **correction,** the system primarily affected is repaired, returning the pH toward normal. For example, if there is respiratory acidosis (high PCO_2) vigorous bronchial hygiene and bronchodilators may improve ventilation and lower PCO_2, returning pH toward normal. In most cases, we as physicians, nurses, and paramedical persons are more interested in correcting the abnormality than in helping the body to compensate. In both compensation and correction the pH is returned toward normal. The body tries hard to maintain a normal pH, for the various enzyme systems in all organs function correctly only when the pH is normal. Using newer terminology the term **acute** respiratory acidosis means **uncompensated; chronic** respiratory acidosis means **compensated.**

Next we will discuss how the body compensates for the various acid-base abnormalities. Remember, the body compensates for abnormalities by trying to return the ratio of HCO_3 to PCO_2 to 20:1, for if this ratio is 20:1, the pH is normal. If the primary process is respiratory, then the compensating system is metabolic, and vice versa. When the lungs compensate for a nonrespiratory abnormality, compensation occurs in hours, but the kidneys take 2 to 4 days to compensate for a respiratory abnormality.

Remember, the PCO_2 in mm Hg must be converted to mEq./l by multiplying it by 0.03 before trying it in the 20:1 ratio mentioned above, e.g., PCO_2 of 40 mm Hg × 0.03 = 1.2 mEq./l.

In the following four examples the first column lists normal values for the parameters listed in the second column. The uncompensated state is listed in the third column, and the last column demonstrates how compensation takes place. The primary abnormality is enclosed in a box.

TABLE 21

COMPENSATION FOR RESPIRATORY ACIDOSIS

NORMAL		ABNORMAL	COMPENSATED
24	HCO_3, mEq./l	24	36
1.2	PCO_2, mEq./l	1.8	1.8
40	PCO_2, mm Hg	60	60
20:1	ratio	13:1	20:1
7.40	pH	7.23	7.40

In primary respiratory acidosis, characterized by elevated levels of PCO_2 (an acid), the system at fault is the respiratory system, and compensation occurs through metabolic processes. To compensate, the kidneys excrete more acid and excrete less HCO_3, thus allowing levels of HCO_3 to rise, returning the ratio of HCO_3 to PCO_2 toward 20:1 and therefore returning pH toward normal.

If the PCO_2 is high (respiratory acidosis) but the pH is normal, it means that the kidneys have had time to retain HCO_3 to compensate for the elevated PCO_2 and that the process is not acute (has been present at least a few days to give the kidneys time to compensate).

Usually the body does not fully compensate for respiratory acidosis.

TABLE 22

COMPENSATION FOR RESPIRATORY ALKALOSIS

NORMAL		ABNORMAL	COMPENSATED
0	B.E.	+2.5	-5
24	HCO_3, mEq./l	24	18
1.2	PCO_2, mEq./l	0.9	0.9
40	PCO_2, mm Hg	30	30
20:1	ratio	27:1	20:1
7.40	pH	7.52	7.40

In primary respiratory alkalosis, characterized by low PCO_2, compensation occurs through metabolic means. The kidneys compensate by excreting HCO_3, thus returning the ratio of HCO_3 to PCO_2 back toward 20:1, and this compensation by the kidneys takes 2 to 3 days. Of the 4 acid-base abnormalities, only in compensation for respiratory alkalosis is the body able to fully return the ratio to 20:1 and return of pH entirely to normal.

TABLE 23

COMPENSATION FOR METABOLIC (NON-RESPIRATORY) ACIDOSIS

NORMAL		ABNORMAL	COMPENSATED
0	B.E.	-17	-10
24	HCO_3, mEq./l	12	12
1.2	PCO_2, mEq./l	1.2	0.6
40	PCO_2, mm Hg	40	20
20:1	ratio	10:1	20:1
7.40	pH	7.11	7.40

In primary metabolic acidosis, the major abnormality is low HCO_3 or Base Excess. In most cases excess acids such as ketoacids in diabetic ketoacidosis have reacted with the normal amounts of HCO_3 using up some of the HCO_3 and leaving a low level of HCO_3. The body compensates by hyperventilating, thus lowering the PCO_2 so that the ratio of HCO_3 to PCO_2 returns toward 20:1. Because the compensating system is the lungs, compensation can occur in hours. However, if the nonrespiratory acidosis is severe, the lungs may not be able to blow off enough CO_2 gas to compensate fully. Actually, in metabolic acidosis the body never compensates fully (never gets the ratio back to 20:1 or the pH back to 7.40).

TABLE 24

COMPENSATION FOR METABOLIC (NONRESPIRATORY) ALKALOSIS

NORMAL		ABNORMAL	COMPENSATED
0	B.E.	+13	+9
24	HCO_3, mEq./*l*	36	36
1.2	PCO_2, mEq./*l*	1.2	1.8
40	PCO_2, mm Hg	40	60
20:1	ratio	30:1	20:1
7.40	pH	7.57	7.40

If the primary disturbance is nonrespiratory alkalosis (i.e., presence of excess HCO_3), the body compensates with the respiratory system by hypoventilating so that PCO_2 rises and the ratio of HCO_3 to PCO_2 is returned toward the normal of 20:1, therefore returning the pH toward normal. The body is usually unable to completely compensate for metabolic alkalosis.

In this instance respiratory compensation is by hypoventilation, and this occurs over one or several hours. Hypoventilation allows PCO_2 to rise only to a maximum of 50 to 60 mm Hg before other stimuli of ventilation such as hypoxia take over to prevent further hypoventilation. In compensating for one abnormality, high HCO_3, the body creates another abnormality, high PCO_2, but in doing so brings the ratio of HCO_3 to PCO_2 toward 20:1, allowing the pH to return toward normal in spite of two abnormalities. These two abnormalities balance each other.

It is important to realize that in each of these situations the body's compensation is only an effort to return the pH toward normal, and the primary abnormality is not corrected. The physician's definitive treatment is aimed at correcting the primary abnormality.

For instance, if the primary problem is excess HCO_3 (nonrespiratory alkalosis), treatment is directed toward getting rid of excess HCO_3 rather than just allowing PCO_2 to rise and normalize the ratio. Excess HCO_3 can be corrected by giving the patient acetazolamide (Diamox) to make his kidneys excrete more HCO_3, or more commonly by giving KCL to allow the kidneys to excrete K^+ and Cl^- rather than acids. Sometimes ammonium chloride (NH_4Cl), arginine monohydrochloride, or even hydrochloric acid (HCl) is given to react with the excessive HCO_3, thereby correcting the metabolic alkalosis.

Respiratory alkalosis (low PCO_2) is treated by getting the patient to stop hyperventilating.

Nonrespiratory acidosis, where excess acids have used up HCO_3 or HCO_3 has been lost, is treated by supplying HCO_3 in the form of $NaHCO_3$ orally or intravenously while also treating the cause of acid accumulation of HCO_3 loss. Multiplying the body weight (in kilograms) by the deficiency of HCO_3 (in mEq./*l*) by 0.3 gives a rough guide to the amount of $NaHCO_3$ (in mEq.) that should be administered. Thus a 60 kg. patient with an HCO_3 of 4 would be given 360 mEq. of $NaHCO_3$, or

$$24 - 4 = 20$$

$$(20 \times .3 \times 60 = 360)$$

Giving large doses of $NaHCO_3$ can give the patient a lar osmotic load which may be more detrimental than the acic mia, so metabolic acidosis is not usually treated wi $NaHCO_3$ unless the pH is below 7.25.

Respiratory acidosis (high PCO_2) is treated by increasi ventilation enabling the lungs to get rid of the CO_2. Althou **overtreatment** may occur, **overcompensation** by t body usually does not occur. In fact, complete compensati seldom occurs, so that instead of the ratio returning to 20:1 returns to nearly 20:1, and pH, instead of returning 7.40, returns almost to this point. (See Figure 4 and t explanation that goes with it.)

It is the fact that the pH usually does not return complete to 7.40 that allows us in some cases to decide just from bloc gas values which is the primary process and which is t compensating process. We first look at the pH to see whic side of 7.40 it is on. Even though it is in normal range, pH usually either above or below 7.40. If the pH is above 7.4 the primary process is probably alkalosis, and if below 7.4 the primary process is probably acidosis. For example:

pH 7.42
PCO_2 52 mm Hg.............Respiratory acidosis
HCO_3 33 mEq./*l*..............Metabolic alkalosis

Which is the primary process, respiratory acidosis o metabolic alkalosis? If one consults Figure 4, one finds tha these numbers can be interpreted in either of two ways, fo they fit into two 95% confidence bands, i.e., those for chroni (fully compensated) metabolic alkalosis and chronic (full compensated) respiratory acidosis. However, following ou rule, we see that the pH, though normal, is tending towar alkalemia. Therefore, the primary process is probabl alkalemia. So this is a metabolic alkalosis with nearly complete compensation. Often it is clinically obvious which is th primary abnormality, but sometimes this is not clinicall apparent.

It must be pointed out that there may be more than on **primary** acid-base abnormality; so, if there is both respiratory and a nonrespiratory acid-base abnormality, instead of one compensating for the other, both may b acidoses or both alkaloses in which case the pH deviate more from normal than if either of the two abnormalitie were present alone.

Here is an example of blood gases to interpret:

pH	7.24
PCO_2	38 mm Hg
HCO_3	15.5 mEq./*l*
B.E.	−11

Coronary care nurses deciphering an arrhythmia are taught to first find the P wave, and in trying to interpret an acid-base abnormality, one must look first at the **pH** to see if there is an alkalemia or an acidemia. Here we have an acidemia for the pH is low. Next look at the PCO_2 to see if there is a respiratory abnormality. There is no abnormality, for the PCO_2 is normal. Next, look at either HCO_3 or Base Excess to see if there is a metabolic abnormality. The HCO_3 and the Base Excess are low indicating a metabolic acidosis. So we have an acidemia caused by a metabolic acidosis. Consulting Figure 4, one sees that the example falls in the area labeled acute (uncompensated) metabolic acidosis.

Next is a tougher example:

pH	7.20
PCO_2	55 mm Hg
HCO_3	20.5 mEq/l
B.E.	-8

First, look at the pH to see if there is an alkalemia or an acidemia. Here the pH is low indicating an acidemia. Does the PCO_2 indicate a respiratory abnormality? Yes, PCO_2 is high, indicating respiratory acidosis. Does the HCO_3 or B.E. indicate a nonrespiratory abnormality? Yes, HCO_3 and Base Excess are low, indicating nonrespiratory (metabolic) acidosis. Therefore, this is an acidemia caused by combined respiratory and metabolic acidoses. Consulting Figure 4 one sees that this example falls in the area between acute metabolic acidosis and acute respiratory acidosis indicating that both are occurring.

The foregoing is all that is necessary to solve most acid-base problems. Some experts feel that the use of confidence limits is a big help or even a necessity in solving acid-base problems. This concept will be briefly discussed below and may help to explain some of the intricacies of acid-base problems. The use of a nomogram will also be presented.

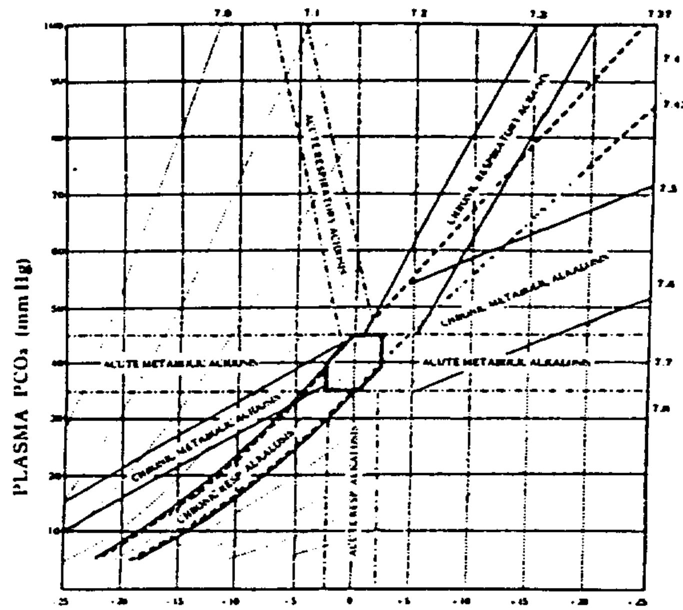
Some of the statements made above are true most of the time but not all of the time. For instance, because of the equation, $CO_2 + H_2O \rightleftharpoons HCO_3 + H^+$, it can be seen that elevations of PCO_2 will raise the HCO_3 just because of the chemical reaction. Later—several days later—the HCO_3 is elevated further because the kidneys excrete less HCO_3 in an effort to compensate.

Ninety-five percent confidence limits have been compiled so that if, for example, the primary problem is chronic respiratory acidosis (fully compensated respiratory acidosis), one can look up the level of HCO_3 that would be expected in 95 percent of the cases of chronic respiratory acidosis.

In Figure 4, Base Excess values are plotted on the horizontal axis and PCO_2 values are plotted on the vertical axis; pH isobars are the sweeping lines of small dots. Cohen, the author who produced this figure, prefers the narrow range of 7.37 to 7.43 for the normal pH range instead of 7.35 to 7.45. Cohen plotted 95% confidence bands for the acute and chronic (uncompensated and compensated) form of each of the 4 basic acid-base disturbances. If one knows any two of the three parameters (pH, PCO_2, B.E.), one can calculate the third and also name the process and determine whether it is acute or chronic (fully compensated) or somewhere in between. Without using the 95 percent confidence limits or consulting the nomogram, one may occasionally miss the less obvious part of a combined acid-base problem.

Figure 5

pH ISOBARS



BLOOD BASE EXCESS (mEq/l)

Ninety-five percent confidence limits of respiratory or metabolic compensation.

A computer program for acid-base interpretation based on Figure 4 has been developed.

APPENDIX

EFFECT OF ALTITUDE ON BLOOD GAS VALUES

The normal values for arterial blood gases are influenced by altitude, so an altitude of one mile above sea level—for instance in Denver—the arterial PO_2, O_2 saturation and PCO_2 are all lower. The PO_2 and O_2 saturation are lower because the ambient air has a lower oxygen tension and the PCO_2 is lower because of the slight hyperventilation that occurs at higher altitude.

Values in mixed venous blood are only minimally different from sea level values.

NORMAL BLOOD GAS VALUES AT ONE MILE ALTITUDE — DENVER

	ARTERIAL BLOOD	MIXED VENOUS BLOOD
pH	7.40 (7.35–7.45)	7.38 (7.33–7.43)
PO_2	65–75 mm Hg	35–40 mm Hg
O_2 saturation	92–94%	65–75%
PCO_2	32–40 mm Hg	38–46 mm Hg
HCO_3	18–26 mEq/l	19–27 mEq/l
B.E.	-4.5 – +0.5	-3.5 – +1.5

·'FINITIONS FOR ACID BASE DISTURBANCES

1. H^+: Hydrogen ion
2. $[H^+]$: Hydrogen ion concentration
3. pH: The negative log of the hydrogen ion concentration, or simply, a way of representing the free H^+ in a solution. The pH of a solution is inversely proportional to the concentration of H^+ in the solution.
4. Acid: A substance which can donate hydrogen ions, H^+. Example: $\underset{(acid)}{H_2CO_3} \longrightarrow H^+ + HCO_3^-$
5. Base: A substance which can accept hydrogen ions, H^+. All bases are alkaline substances.

   Examples: $OH^- + H^+ \longrightarrow H_2O$

   $\underset{(bases)}{HCO_3^-} + H^+ \longrightarrow H_2CO_3$
6. Acidemia: Arterial pH below 7.35
7. Alkalemia: Arterial pH greater than 7.45
8. PCO_2: The tension exerted by carbon dioxide gas. The P in PCO_2 stands for pressure or tension exerted by CO_2 gas. CO_2 written without the preceeding P does not refer to CO_2 gas, but usually refers to total CO_2 content. (Usually CO_2 gas is dissolved in a solution.) Any deviation from the normal carbon dioxide tension (PCO_2) reflects a respiratory acid-base disturbance, either primary or compensatory. CO_2 combines reversibly with water to form carbonic acid, H_2CO_3.

   $$CO_2 + H_2O \rightleftharpoons H_2CO_3$$

   In blood, there is 800 times as much CO_2 in the form of a gas, dissolved CO_2, as there is in the form of an acid, H_2CO_3. PCO_2 should be thought of as an acid. PCO_2 is inversely related to ventilation and so tells a lot about the lungs' function.
9. Base Excess: Expresses directly, in mEq/l, the amount of strong base (or acid) added per liter of blood with normal arbitrarily fixed at 0 (range of normal −2 to +2). Positive values express excess of base (or deficit of acid) and negative values express deficit of base (or excess of acid). Base Excess reflects mainly the concentration of bicarbonate and is affected only by metabolic processes. Positive values reflect metabolic alkalosis, and negative values reflect metabolic acidosis.
10. Standard bicarbonate: The actual bicarbonate concentration measured at 37° on blood that has been equilibrated to a high oxygen tension to completely saturate the hemoglobin and to a PCO_2 of 40 mm Hg, therefore correcting any respiratory abnormalities that might have existed in the patient when the blood was drawn. Any abnormality remaining in standard bicarbonate, then, is due to metabolic causes.
11. Actual bicarbonate: The actual amount of bicarbonate, HCO_3^- expressed in mEq/l of plasma as it existed in the patient. (If the patient had a PCO_2 of 40 mm Hg, completely saturated hemoglobin, and a temperature of 37°, then actual bicarbonate and standard bicarbonate are identical.)
12. Total CO_2 content (sometimes abbreviated as just CO_2): The amount of CO_2 gas extractable from plasma in the presence of a strong acid. Total CO_2 content consists of bicarbonate (HCO_3^-), carbonic acid (H_2CO_3), and dissolved carbon dioxide gas (PCO_2).

    $$HCO_3^- + \begin{array}{l}\text{dissolved } CO_2 \text{ gas}\\ \text{and } H_2CO_3\end{array} = \text{total } CO_2 \text{ content}$$

    Since there is 800 times as much dissolved CO_2 gas at equilibrium as H_2CO_3, and since CO_2 gas and H_2CO_3 are interchangeable anyway, dissolved CO_2 gas is used instead of H_2CO_3.

    $$HCO_3^- + \text{dissolved } CO_2 \text{ gas} = \text{total } CO_2 \text{ content}$$
    $$HCO_3^- + PCO_2 = \text{total } CO_2 \text{ content}$$

    (Capital P stands for the pressure or tension exerted by the dissolved gas.)

    To convert PCO_2 from mm Hg to mEq/l it is multiplied by 0.03

    $$HCO_3^- + (0.03 \times PCO_2) = \text{total } CO_2 \text{ content}$$

    Example: $24 \text{ mEq/l} + (0.03 \times 40 \text{ mm Hg}) = \text{total } CO_2 \text{ content}$

    $$24 \text{ mEq/l} + 1.2 \text{ mEq/l} = 25.2 \text{ mEq/l}$$

    In normal plasma, more than 95% of the total CO_2 content is contributed by HCO_3^-, the other 5% being contributed by dissolved CO_2 gas and H_2CO_3. Dissolved CO_2 gas (which is regulated by the lungs), therefore, contributes little to the total CO_2 content. Total CO_2 content gives little information about the lungs.
13. Buffer: A substance which minimizes any change in pH when either acid or base is added to a solution containing the buffer.

APPROXIMATE CONTRIBUTION OF INDIVIDUAL BUFFERS TO TOTAL BUFFERING IN WHOLE BLOOD

Individual Buffers	% Buffering in Whole Blood	
Hemoglobin & Oxyhemoglobin	35	Total non-bicarbonate—47%
Organic Phosphate	3	
Inorganic Phosphate	2	
Plasma Proteins	7	
Plasma bicarbonate	35	Total bicarbonate—53%
RBC bicarbonate	18	

14. Metabolic acidosis: An abnormal physiological process characterized by the primary gain of strong acid or primary loss of bicarbonate from the extracellular fluid.
15. Metabolic alkalosis: An abnormal physiological process characterized by primary gain of strong base (or loss of strong acid) or the primary gain of bicarbonate by the extracellular fluid.
16. Respiratory acidosis: An abnormal physiological process in which there is a primary reduction in the rate of alveolar ventilation relative to the rate of CO_2 production.
17. Respiratory alkalosis: An abnormal physiological process in which there is a primary increase in the rate of alveolar ventilation relative to the rate of CO_2 production.

18. Henderson-Hasselbalch equation:
(small "p" stands for negative logarithm of a number)

$$pH = pK + \log \frac{HCO_3}{\begin{bmatrix}\text{dissolved } CO_2 \text{ gas} \\ \text{and } H_2CO_3\end{bmatrix}}$$

Although the equation is usually written simply:

$$pH = pK + \log \frac{[HCO_3]}{[H_2CO_3]}$$

It is understood that most of the H_2CO_3 is in the form of dissolved CO_2 gas. In clinical practice we measure the pressure exerted by the dissolved CO_2 gas, so the equation could be rewritten:

(Capital "P" stands for pressure or tension exerted by dissolved gas.)

$$pH = pK + \log \frac{[HCO_3]}{[PCO_2 \text{ in mm Hg}]}$$

To convert PCO_2 from mm Hg to mEq/*l*, multiply by 0.03.

$$pH = pK + \log \frac{[HCO_3]}{[0.03 \times PCO_2]}$$

(pK is a constant 6.10)

$$\text{Example: } 7.40 = 6.10 + \log \frac{[24 \text{ mEq}/l]}{[0.03 \times 40]}$$

$$7.40 = 6.10 + \log \frac{24 \text{ mEq}/l}{1.2 \text{ mEq}/l}$$

$$7.40 = 6.10 + \log 20$$

(log of 20 is 1.30)

$$7.40 = 6.10 + 1.30$$

$$7.40 = 7.40$$

19. P_{50}: The partial pressure of oxygen (PO_2) when hemoglobin is exactly 50% saturated. This measurement is used to detect a shift in the oxyhemoglobin dissociation curve; i.e., if the P_{50} is greater than 27 the curve is shifted to the right and if the P_{50} is less than 27 the curve is shifted to the left.
20. Acute respiratory acidosis: uncompensated respiratory acidosis
21. Chronic respiratory acidosis: compensated respiratory acidosis
22. Acute metabolic acidosis: uncompensated respiratory acidosis
23. Chronic metabolic acidosis: compensated metabolic acidosis
24. **Fully** compensated: compensated to the greatest extent that the body can in 95% of the cases
25. **Completely** compensated: compensated to the extent that the pH is the normal range

PROCEDURE FOR DRAWING BLOOD FOR ARTERIAL BLOOD GAS ANALYSIS

A. Equipment

1. 5-cc. or 10-cc. glass syringe
2. 10-cc. bottle of heparin, 1000 units/cc. (reusable)
3. #21, #22 or even #25 disposable needle (short bevel)
4. Cork
5. Alcohol swab
6. Container of ice (emesis basis, cardboard milkshake cup, or plastic bag)
7. Request slip on which to write patient's clinical status, etc., including name, date, time, whether receiving O_2, and if so how much and by what route, whether in shock, recent bicarbonate ℞, etc. If on continuous ventilation: tidal volume, respiratory frequency, inspired oxygen concentration (FIO_2), amount of PEEP or CPAP.

B. Technique

1. Call the lab to notify them you plan to draw a blood gas sample so that they can be calibrating equipment for 15 to 30 minutes (not necessary in busy labs).
2. Patients should be in steady state for at least 15 minutes (no recent change in inspired O_2, etc.).
3. Brachial artery is generally preferred, though radial may be used after demonstrating that ulnar artery circulation is intact with Allen text. Femoral artery sometimes must be used in hypotensive patients but should be avoided if possible.
4. Elbow is **hyperextended** and arm is externally rotated (very important to have elbow **completely straight**—usually a folded towel or pillow uncer the elbow accomplishes this); for radial artery puncture, wrist is hyperextended after supporting lower arm on towels.
5. 1 cc. of heparin is aspirated into the syringe, barrel of the syringe is wet with heparin, and then the excess heparin is discarded through the needle, being careful that the hub of the needle is left full of heparin and there are no bubbles.
6. Brachial or radial artery is located by palpatation with index and long fingers, and point of maximum impulse is found.
7. Needle is inserted into the area of maximum pulsation. This is easiest with the syringe and needle approximately perpendicular to the skin; however, if the needle is inserted at a more acute angle (such as is used for venipunctures) there may be better hemostasis after the needle is removed.
8. Often the needle goes completely through both sides of the artery and only upon slowly withdrawing the needle does the blood gush up into the syringe.
9. The only way to be certain that **arterial** blood is obtained is the fact that the blood pumps up into the syringe under its own power. (If one has to aspirate blood by pulling on the plunger of syringe—as is sometimes required with a tighter fitting plastic syringe—it is impossible to be positive that blood is arterial.) **The blood gas results do not allow one to determine whether blood is arterial or venous.** If one suspects that blood may be venous, then draw another sample of obviously venous blood and compare the two samples. If the two samples are similar, then the first sample was also venous, but if the PO_2 and O_2 saturation on the second (obviously venous) sample are significantly lower than the first sample, then the first sample is probably arterial.