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See also ANALYTICAL METHODS, AUTOMATED; CELL COUNTERS, BLOOD; DIFFERENTIAL COUNTS, AUTOMATED.

BLOOD FLOW. See BLOOD RHEOLOGY; HEMODYNAMICS.

BLOOD GAS MEASUREMENTS

AHMAD ELSHARYDAH
RANDALL C. CORK
Louisiana State University
Shreveport, Louisiana

INTRODUCTION

Blood gas measurement—monitoring is essential to monitor gas exchange in critically ill patients in the intensive care units (1,2), and “standard of care” monitoring to deliver general anesthesia (3). It is a cornerstone in the diagnosis and management of the patient’s oxygenation and acid–base disorders (4). Moreover, it may indicate the onset or culmination of cardiopulmonary problems, and may help in evaluating the effectiveness of the applied therapy. Numerous studies and reports have shown the significance of utilizing blood gas analyses in preventing serious oxygenation and acid–base problems. This article gives a summarized explanation of the common methods and instruments used nowadays in blood gas measurements in clinical medicine. This explanation includes a brief history of the development of these methods and instruments, the principles of their operation, a general descrip-

tion of their designs, and some of their clinical uses, hazards, risks, limitations, and finally the direction in the future to improve these instruments or to invent new ones. Blood gas measurement in clinical medicine can be classified into two major groups: (1) Noninvasive blood gas measurement, which includes blood oxygen–carbon dioxide measurement—monitoring by using different types of pulse oximeters (including portable pulse oximeters), transcutaneous oxygen partial pressure–carbon dioxide partial pressure (PO_2/PCO_2) monitors, intrapartum fetal pulse oximetry, cerebral oximetry, capnometry, capnography, sublingual capnometry, and so on; (2) invasive blood gas measurement, which involves obtaining a blood sample to measure blood gases by utilizing blood gas analyzers (in a laboratory or by using a bedside instrument), or access to the vascular system to measure/monitor blood gases. Examples include, but not limited to, mixed venous oximetry (SvO_2) monitoring by utilizing pulmonary artery catheter or jugular vein (SvO_2) measurement (5); continuous fibroptic arterial blood gas monitoring, and so on. In this article, we will talk about some of these methods; others have been mentioned in other parts of this encyclopedia.

BASIC CONCEPTS IN INVASIVE AND NONINVASIVE BLOOD GAS MEASUREMENTS

The Gas Partial Pressure

Gases consist of multiple molecules in rapid, continuous, random motion. The kinetic energy of these molecules generate a force as the molecules collide with each other and bounce from one surface to another. The force per unit area of a gas is called pressure, and can be measured by a device called a manometer. In a mixture of gases (e.g., a mixture of O_2 , CO_2 , and water vapor), several types of gas molecules are present within this mixture, and each individual gas (e.g., O_2 or CO_2) in the mixture is responsible for a portion of the total pressure. This portion of pressure is called partial pressure (P). According to Dalton’s law, the total pressure is equal to the sum of partial pressures in a mixture of gases. Gases dissolve freely in liquids, and may or may not react with the liquid, depending on the nature of the gas and the liquid. However, all gases remain in a free gaseous phase to some extent within the liquid. Gas dissolution in liquids is a physical, not chemical, process. Therefore, gases (e.g., CO_2 , O_2) dissolved in liquid (blood) exist in two phases: liquid and gaseous phase. Henry’s law states that the partial pressure of a gas in the liquid phase equilibrates with the partial pressure of that gas in the gaseous phase (6,7).

BLOOD GAS ELECTRODES

Basic Electricity Terms

Electricity is a form of energy resulting from the flow of electrons through a substance (conductor). Those electrons flow from a negatively charged pole called Cathode, which has an excess of stored electrons, to a positively charged pole called Anode, which has a relative shortage

of electrons. The potential is the force responsible for pumping these electrons between the two poles. The greater the difference in electron concentration between these two poles, the greater is the potential. Volt is the potential measurement unit. The electrical current is the actual flow of electrons through a conductor. Ampere (amp) is the unit of measurement for the electrical current. Conductors display different degree of electrical resistance to the flow of the electrical current. The unit of the electrical resistance is ohm (Ω). Ohm's law states: voltage = current \times resistance.

The Principles of Blood Gas Electrodes

Blood gas electrodes are electrochemical devices used to measure directly pH and blood gases. These blood gas electrodes use electrochemical cells. The electrochemical cell is an apparatus that consists of two electrodes placed in an electrolyte solution. These cells usually incorporated together (one or more cells) to form an electrochemical cell system. These systems are used to measure specific chemical materials (e.g., PO_2 , PCO_2 and pH). The basic generic blood gas electrode consists of two electrode terminals, which are also called half-cells: one is called the working half-cell where the actual chemical analysis occurs, or electrochemical change is taken place; and the other one is called the reference half-cell. The electrochemical change occurring on the working terminal is compared to the reference terminal, and the difference is proportional to the amount of blood gas in the blood sample (6,7).

PO_2 Electrode

The PO_2 electrode basically consists of two terminals (1). The cathode, which usually made of platinum (negatively charged) and (2) the anode, which usually made of silver-silver chloride (positively charged). How does this unit measure PO_2 in the blood sample? As shown in Fig. 1,

the electricity source (battery or wall electricity) supplies the platinum cathode with energy (voltage of ~ 700 mV). This voltage attracts oxygen molecules to the cathode surface, where they react with water. This reaction consumes four electrons for every oxygen molecule reacts with water and produces four hydroxyl ions. The consumed four electrons, in turn, are replaced rapidly in the electrolyte solution as silver and chloride react at the anode. This continuous reaction leads to continuous flow of electrons from the anode to the cathode (electrical current). This electrical current is measured by using an ammeter (electrical current flow meter). The current generated is in direct proportion to the amount of dissolved oxygen in the blood sample, which in direct proportion to PO_2 in that sample.

Oxygen Polarography

The electrical current and PO_2 have a direct (linear) relationship when a specific voltage is applied to the cathode. Therefore, a specific voltage must be identified, to be used in PO_2 analysis. The polarogram is a graph that shows the relationship between voltage and current at a constant PO_2 . As shown in Fig. 2, when the negative voltage applied to the cathode is increased, the current increases initially, but soon it becomes saturated. In this plateau region of the polarogram, the reaction of oxygen at the cathode is so fast that the rate of reaction is limited by the diffusion of oxygen to the cathode surface. When the negative voltage is further increased, the current output of the electrode increases rapidly due to other reactions, mainly, the reduction of water to hydrogen. If a fixed voltage in the plateau region (e.g., -0.7 V) is applied to the cathode, the current output of the electrode can be linearly calibrated to the dissolved oxygen. Note that the current is proportional not to the actual concentration, but to the activity or equivalent partial pressure of dissolved oxygen. A fixed voltage between -0.6 and -0.8 V is usually selected as the

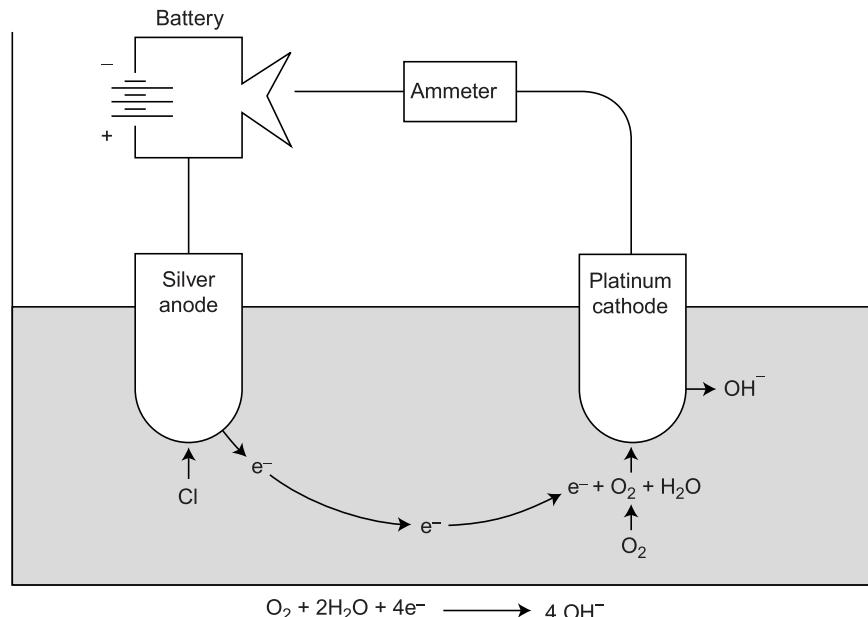


Figure 1. PO_2 electrode.

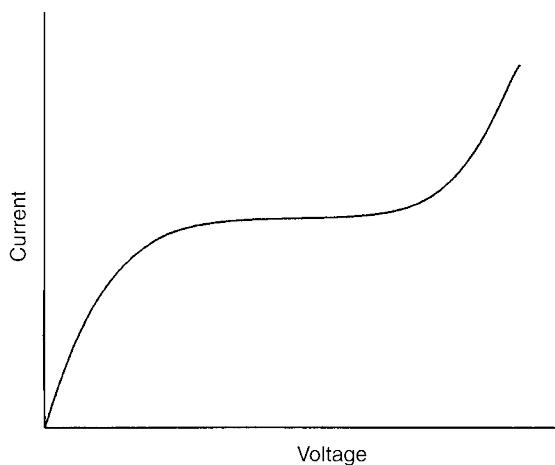


Figure 2. Polarogram.

polarization voltage when using Ag/AgCl as the reference electrode.

pH Electrode

The pH electrode uses voltage to measure pH, rather than actual current as in PO_2 electrode. It compares a voltage created through the blood sample (with unknown pH) to known reference voltage (in a solution with known pH). To make this possible, the pH electrode basically needs four electrode terminals (Fig. 3), rather than two terminals (as in the PO_2 electrode). Practically, one common pH-sensitive glass electrode terminal between the two solutions is adequate. This glass terminal allows the hydrogen ions to diffuse into it from each side. The difference in the hydrogen ions concentration across this glass terminal creates a net electrical potential (voltage). A specific equation is used to calculate the blood sample pH, using the reference fluid pH, the created voltage, and the fluid temperature.

PCO_2 Electrode

The PCO_2 electrode is a modified pH electrode. There are two major differences between this electrode and the pH

electrode. The first difference is that in this electrode, the blood sample comes in contact with a CO_2 permeable membrane (such as Teflon, Silicone rubber), rather than a pH-sensitive glass (in the pH electrode), as shown in Fig. 4. The CO_2 from the blood sample diffuses via the CO_2 permeable (silicone) membrane into a bicarbonate solution. The amount of the hydrogen ions produced by the hydrolysis process in the bicarbonate solution is proportional to the amount of the CO_2 diffused through the silicone membrane. The difference in the hydrogen ions concentration across the pH-sensitive glass terminal creates a voltage. The measured voltage (by voltmeter) can be converted to PCO_2 units. The other difference is that the CO_2 electrode has two similar electrode terminals (silver–silver chloride). However, the pH electrode has two different electrode terminals (silver–silver chloride and mercury–mercurous chloride).

BLOOD GAS PHYSIOLOGY (8,9)

Oxygen Transport

Oxygen is carried in the blood in two forms: A dissolved small amount and a much bigger, more important component combined with hemoglobin. Dissolved oxygen plays a small role in oxygen transport because its solubility is so low, 0.003 mL O_2 /100 mL blood per mmHg (133.32 Pa). Thus, normal arterial blood with a PO_2 of ~100 mmHg (13332.2 Pa) contains only 0.3 mL of dissolved oxygen per 100 mL of blood, whereas ~20 mL is combined with hemoglobin. Hemoglobin consists of heme, an iron-porphyrin compound, and globin, a protein that has four polypeptide chains. There are two types of chains, alpha and beta, and differences in their amino acid sequences give rise to different types of normal and abnormal human hemoglobin, such as, hemoglobin F (fetal) in the newborn, and hemoglobin S in the sickle cell anemia patient. The combination of oxygen (O_2) with hemoglobin (Hb) (to form oxyhemoglobin– HbO_2) is an easily reversible. Therefore, blood is able to transport large amounts of oxygen.

The relationship between the partial pressure of oxygen and the number of binding sites of the hemoglobin that have oxygen attached to it, is known as the oxygen dis-

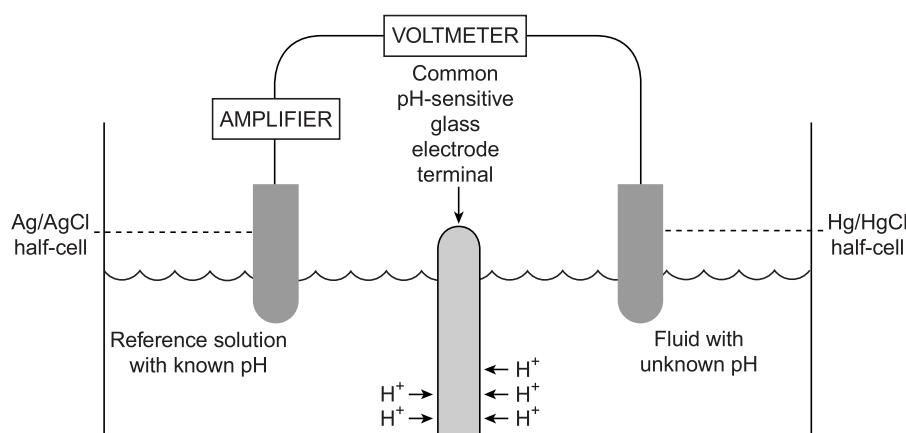


Figure 3. pH electrode.

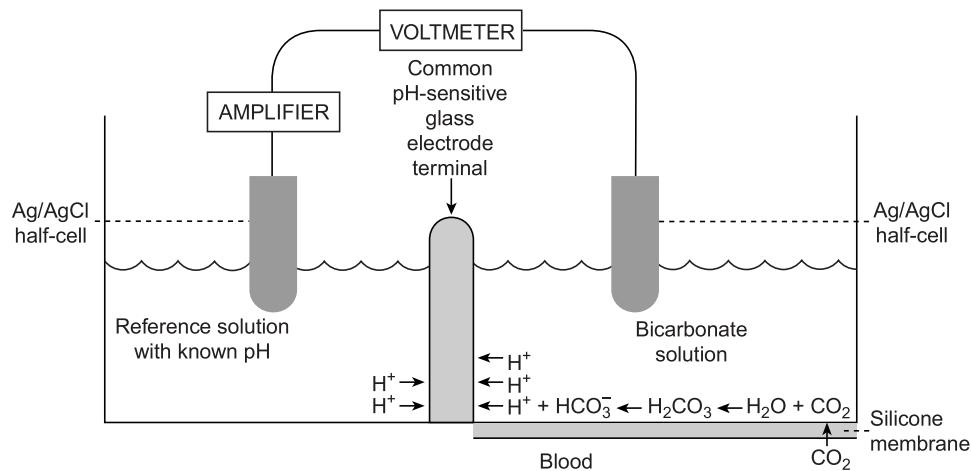


Figure 4. PCO_2 electrode.

sociation curve (Fig. 5). Each gram of pure hemoglobin can combine with 1.39 mL of oxygen, and because normal blood has $\sim 15 \text{ g Hb}/100 \text{ mL}$, the oxygen capacity (when all the binding sites are full) is $\sim 20.8 \text{ mL O}_2/100 \text{ mL}$ blood. The total oxygen concentration of a sample of blood, which includes the oxygen combined with Hb and the dissolved oxygen, is given by $(\text{Hb} \times 1.36 \times \text{SaO}_2) + (0.003 \times \text{PaO}_2)$. Hb is the hemoglobin concentration.

The characteristic shape of the oxygen dissociation curve has several advantages. The fact that the upper portion is almost flat means that a fall of 20–30 mmHg in arterial PO_2 in a healthy subject with an initially normal value (e.g., $\sim 100 \text{ mmHg}$ or 13332.2 Pa) causes only a minor reduction in arterial oxygen saturation. Another consequence of the flat upper part of the curve is that loading of oxygen in the pulmonary capillary is hastened. This results from the large partial pressure difference between alveolar gas and capillary blood that continues to exist even when most of the oxygen has been loaded. The steep lower part of the oxygen dissociation curve means that considerable amounts of oxygen can be unloaded to the peripheral tissues with only a relatively small drop in capillary PO_2 . This maintains a large partial pressure difference between the blood and the tissues, which assists in the diffusion process. Various factors affect the position of the oxygen dissociation curve, as shown in Fig. 5. It is shifted to the right by an increase of temperature, hydrogen ion concentration, PCO_2 , and concentration of 2,3-diphosphoglycerate in the red cell. A rightward shift indicates that the affinity of oxygen for hemoglobin is reduced. Most of the effect of the increased PCO_2 in reducing the oxygen affinity is due to the increased hydrogen concentration. This is called the Bohr effect, and it means that as peripheral blood loads carbon dioxide, the unloading of oxygen is assisted. A useful measure of the position of the dissociation curve is the PO_2 for 50% oxygen saturation; this is known as the P_{50} . The normal value for human blood is $\sim 27 \text{ mmHg}$ (3599.6 Pa).

Carbon Dioxide Transport

Carbon dioxide is transported in the blood in three forms: dissolved, as bicarbonate, and in combination with proteins

such as carbamino compounds (Fig. 6). Dissolved carbon dioxide obeys Henry's law (as mentioned above). Because carbon dioxide is some 24 times more soluble than oxygen in blood, dissolved carbon dioxide plays a much more significant role in its carriage compared to oxygen. For example, $\sim 10\%$ of the carbon dioxide that evolves into the alveolar gas from the mixed venous blood comes from the dissolved form. Bicarbonate is formed in blood by the following hydration reaction:



The hydration of carbon dioxide to carbonic acid (and vice versa) is catalyzed by the enzyme carbonic anhydrase (CA), which is present in high concentrations in the red cells, but is absent from the plasma. However, some carbonic anhydrase is apparently located on the surface of the endothelial cells of the pulmonary capillaries. Because of the presence of carbonic anhydrase in the red cell, most of the hydration of

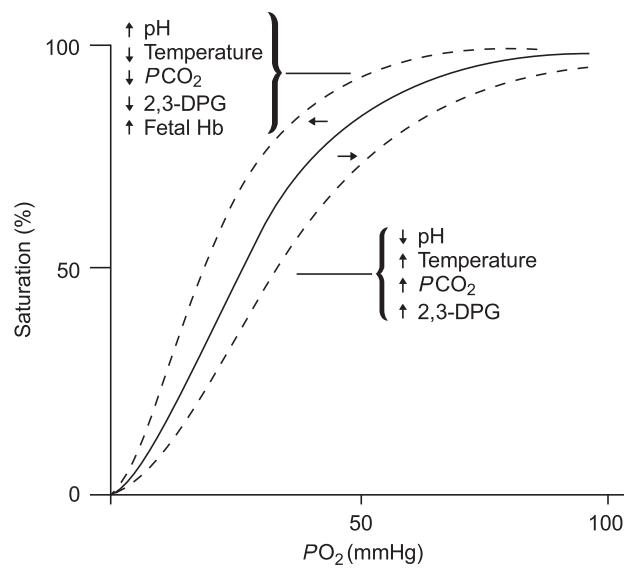


Figure 5. Oxygen dissociation curve and the effects of different factors on it.

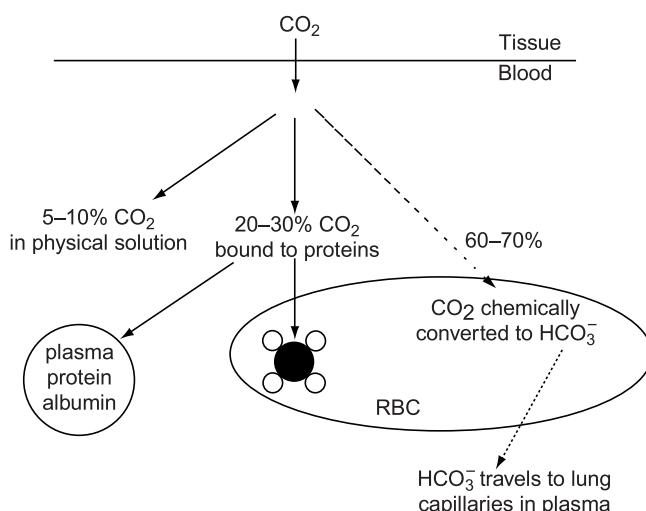


Figure 6. Carbon dioxide transport in blood.

carbon dioxide occurs there, and bicarbonate ion moves out of the red cell to be replaced by chloride ions to maintain electrical neutrality (chloride shift). Some of the hydrogen ions formed in the red cell are bound to Hb, and because reduced Hb is a better proton acceptor than the oxygenated form, deoxygenated blood can carry more carbon dioxide for a given PCO_2 than oxygenated blood can. This is known as the Haldane effect. Carbamino compounds are formed when carbon dioxide combines with the terminal amine groups of blood proteins. The most important protein is the globin of hemoglobin. Again, reduced hemoglobin can bind more carbon dioxide than oxygenated hemoglobin, so the unloading of oxygen in peripheral capillaries facilitates the loading of carbon dioxide, whereas oxygenation has the opposite effect. The carbon dioxide dissociation curve, as shown in Fig. 7, is the relationship between PCO_2 and total carbon dioxide concentration. Note that the curve is much more linear in its working range than the oxygen dissociation curve, and also that, as we have seen, the lower the saturation of hemoglobin with oxygen, the larger the carbon dioxide concentration for a given PCO_2 .

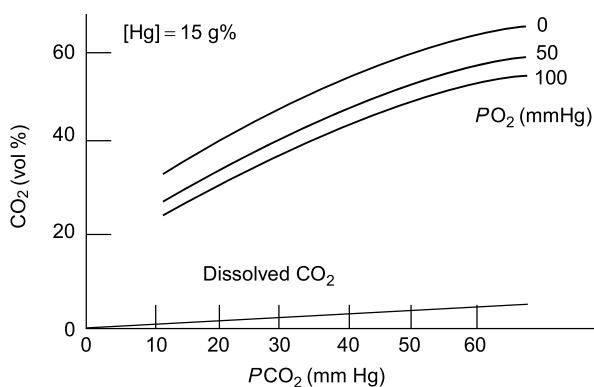


Figure 7. The carbon dioxide dissociation curve showing the effect of PO_2 variations.

OXIMETRY

Historical Development

Oximetry has its origins in the early 1860s (10), when Felix Hoppe-Seyler described the hemoglobin absorption of light using the spectroscope. He demonstrated that the light absorption was changed when blood was mixed with oxygen, and that hemoglobin and oxygen formed a compound called oxyhemoglobin. Soon after, George Gabriel Stokes reported that hemoglobin was in fact the carrier of oxygen in the blood. In 1929, Glen Allan Millikan (11), an American physiologist, began construction of a photoelectric blood oxygen saturation meter, which, used to measure color changes over time when desaturated hemoglobin solutions were mixed with oxygen solutions in an experimental setting. The use of photoelectric cells later proved to be crucial to the development of oximeters. In 1935, Kurt Kramer demonstrated, for the first time, *in vivo* measurement of blood oxygen saturation in animals. The same year, Karl Matthes introduced the ear oxygen saturation meter. This was the first instrument able to continuously monitor blood oxygen saturation in humans. In 1940, J.R. Squire introduced a two-channel oximeter that transmitted red and infrared (IR) light through the web of the hand. In 1940, Millikan and colleagues developed a functioning oximeter, and introduced the term “oximeter” to describe it. The instrument used an incandescent, battery-operated light and red and green filter. In 1948, Earl Wood of the Mayo Clinic made several improvements to Millikan’s oximeter, including the addition of a pressure capsule. Then, in the 1950s, Brinkman and Zijlstra of the Netherlands developed the reflectance oximetry. However, oximetry did not fully achieve clinical applicability until the 1970s.

Principles of Operation

It is important to understand some of the basic physics principles that led to the development of oximetry and pulse oximetry. This is a summary of these different physics principles and methods (7,12).

Spectrophotometry. The spectroscope is a device which was used initially to measure the exact wavelengths of light emitted from a light generator (bunsen burner) (10). Each substance studied with the spectroscope has its unique light emission spectrum, in other words, each substance absorbed and then emitted light of different wavelengths. The graph of the particular pattern of light absorption–emission of sequential light wavelengths called the absorption spectrum. Figure 8 reveals the absorption spectra of common forms of hemoglobin.

Colorimetry. Colorimetry is another method of qualitative analysis (10). In this method, the color of known substance is compared of that of unknown one. This method is not highly exact, because it depends on visual acuity and perception.

Photoelectric Effect. The photoelectric effect is the principle behind spectrophotometry. It is defined as the ability of light to release electrons from metals in proportion to the

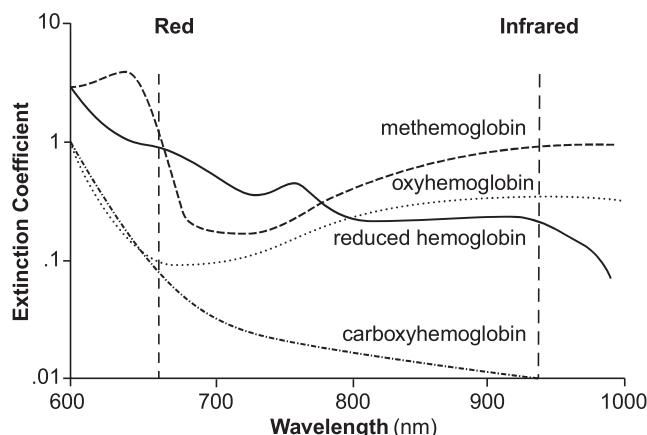


Figure 8. Absorption spectra of common forms of hemoglobin. Absorption spectra of oxyhemoglobin, deoxyhemoglobin, methemoglobin, carboxyhemoglobin.

intensity of the light. In spectrophotometry, light passes via a filter that converts the light into a specific wavelength. This light then passes through a container that contains the substance being analyzed. This substance absorbs part of this light and emits the remaining part, which goes through a special cell. This cell is connected to a photodetector, which detects and measures the emitting light (spectrophotometry). This method can be used for quantitative as well as qualitative analyses.

Lambert–Beer Law. This law combines the different factors that affect the light absorption of a substance:

$$\log 10 I_0/I_x = kcd$$

I_0 = intensity of light incident on the specimen

I_x = intensity of the transmitted light

I_0/I_x = optical density

As shown in the above formula, the concentration of absorbing substance, the path length of the absorbing medium (d) and the characteristics of the substance and the light wavelength (k = constant) all affect light absorption (12).

Transmission Versus Reflection Oximetry. When the light at a particular wavelength passes through a blood sample, which contains Hb, this light would be absorbed, transmitted, or reflected. The amount of the absorbed, transmitted, or reflected light at those particular wavelengths is determined by various factors, including the concentration (Lambert–Beer law) and the type of the Hb present in the blood sample. The amount of light transmitted through the blood sample at a given wavelength is related inversely to the amount of light absorbed or reflected. The transmission oximetry is a method to determine the arterial oxygen saturation (S_aO_2) value by measuring the amount of light transmitted at certain wavelengths. On the other side, in the reflection oximetry, measuring the amount of light reflected is used to determine the S_aO_2 value. The significant difference between these two methods is the location of the photodetector (Fig. 9). In the reflection method, the

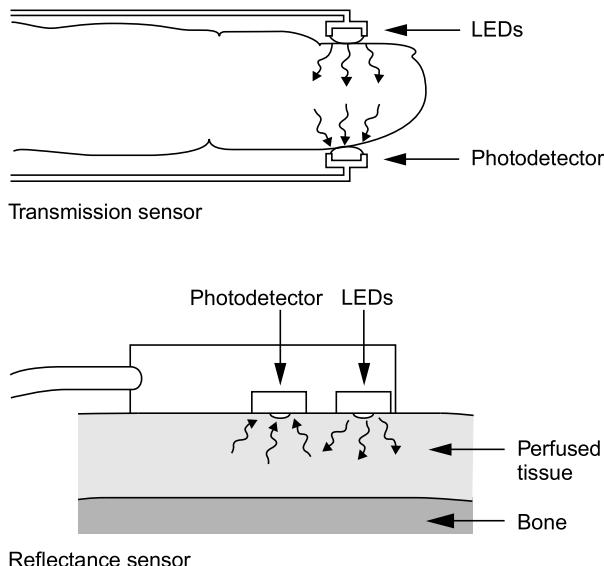


Figure 9. Major components of transmission and reflection oximeters.

photodetector is on the same side of the light source. However, in the transmission oximetry, it is on the opposite site side of the light source (7,12).

Oximetry Versus Cooximetry. Each form of hemoglobin (e.g., oxyhemoglobin, deoxygenated hemoglobin, carboxyhemoglobin, methemoglobin) has its own unique absorption–transmission–reflection spectrum. By plotting the relative absorbance to different light wavelengths for both oxyhemoglobin and deoxygenated Hb as shown in Fig. 10. It is clear that these two hemoglobins absorb light differently at different light wavelengths. This difference is big in some light wavelengths (e.g., 650 nm in the red region), and small or not existing in other light wavelengths. The isosbestic point (13) is the light wavelength at which there is no difference between these two hemoglobins in absorbing light (~ 805 nm near the IR region). The difference in these two wavelengths can be used to calculate the S_aO_2 .

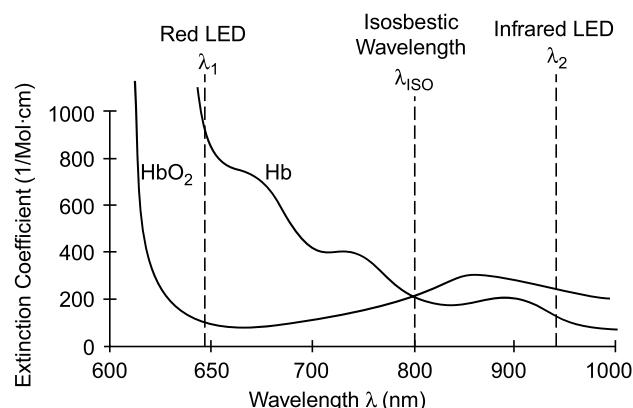


Figure 10. Light absorption spectra of oxygenated and deoxygenated hemoglobin.

However, these two hemoglobins are not only the hemoglobins exist in the patient's blood. There are other abnormal hemoglobins (dyshemoglobins) that can join these two hemoglobins in some abnormal conditions (such as carboxyhemoglobin and methemoglobin). Each one of these dyshemoglobins has its unique transmission-reflection-absorption spectrum. Some of these spectra are very close to the oxyhemoglobin spectrum at the routinely used two light wavelengths (see above). This makes these two wavelengths incapable in detecting those dyshemoglobins. Therefore, the use of regular oximeters in these conditions may lead to erroneous and false readings, which may lead to detrimental effects on the patient's care. To overcome this significant problem a special oximeter (cooximeter, i.e., cuvette oximeter) is needed when there is a suspicion of presence of high level of dyshemoglobins in the patient's blood. Functional S_aO_2 is the percentage of oxyhemoglobin compared to sum of oxy- and deoxyhemoglobins. Therefore, the abnormal hemoglobins are not directly considered in the measurement of functional S_aO_2 by using regular oximetry. Cooximetry uses four or more light wavelengths, and has the ability to measure carboxyhemoglobin and methemoglobin as well as normal hemoglobins. The fractional S_aO_2 measures the percentage of oxyhemoglobin to all hemoglobins (normal and abnormal) present in the blood sample (14,15).

EAR OXIMETRY

Historical Development

In 1935, Matthes (16,17) showed that transmission oximetry could be applied to the external ear. However, a major problem with noninvasive oximetry applied to the ear was the inability to differentiate light absorption due to arterial blood from that due to other ear tissue and blood. In the following years, two methods were tried to solve this problem. The first was increasing local perfusion by heating the ear, applying vasodilator, or rubbing the ear. The second was comparing the optical properties of a "bloodless" earlobe (by compressing it using a special device) to the optical properties of the perfused ear lobe. Arterial S_aO_2 was then determined from the difference in these different measurements. This step was a significant step toward an accurate noninvasive measurement of S_aO_2 . In 1976, Hewlett-Packard (18) used the collected knowledge about ear oximetry to that date to develop the model 47201A ear oximeter, Fig. 11.

HEWLETT-PACKARD EAR OXIMETER

This oximeter (18) is based on the measured light transmission at eight different wavelengths, which made this sensor less accurate and more complex than pulse oximeters. It used a high intensity tungsten lamp that generated a broad spectrum of light wave lengths. This light passes through light filters, then enters a fiberoptic cable, which carries the filtered light to the ear. A second fiberoptic cable carries the light pulses transmitted through the ear to the device for detection and analysis. The ear probe is relatively bulky ($\sim 10 \times 10$ cm) equipped with a tempera-



Figure 11. The Hewlett-Packard Model 47201A ear oximeter.

ture-controlled heater (to keep temperature of 41°C). It is attached to the antihelix after the ear has been rubbed briskly. This monitor is no longer manufactured because of its bulkiness and cost, and because of the development widely of a more accurate, smaller, and cost-effective monitor, the pulse oximeter.

PULSE OXIMETRY

Historical Development

In the early 1970s, Takuo Aoyagi (16,19,20), a Japanese physiological bioengineer, introduced pulse oximetry, the underlying concept of which had occurred to him while trying to cancel out the pulsatile signal of an earpiece densitometer with IR light. In early 1973, Dr. Susumu Nakajima, a Japanese surgeon, learned of the idea and ordered oximeter instruments from Nihon Kohden. After several prototypes were tested, Aoyagi and others delivered the **first commercial pulse oximeter in 1974**. This instrument was the OLV-5100 ear pulse oximeter, (Fig. 12). In 1977, the Minolta Camera Company

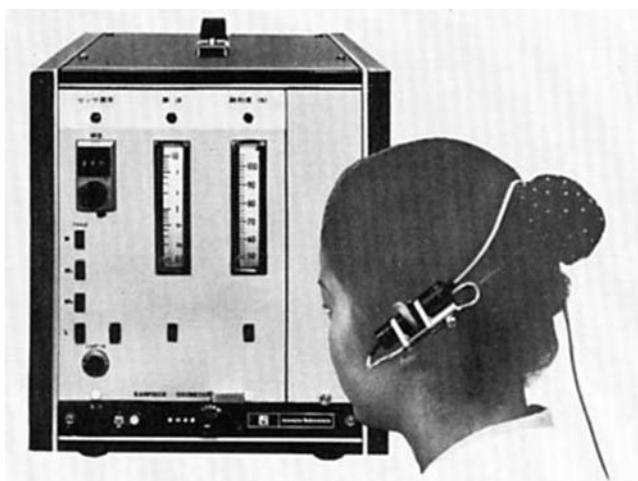


Figure 12. The OLV-5100 ear pulse oximeter, the first commercial pulse oximeter, it was introduced by Nihon Kohden in 1974.

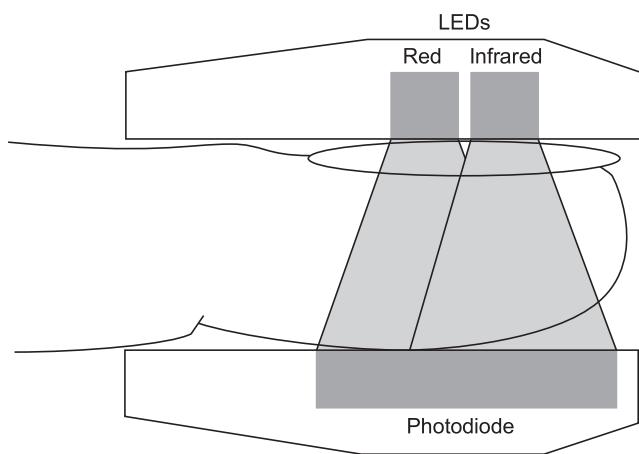


Figure 13. The basic components of a pulse oximeter sensor. Two LEDs with different wavelengths as light sources and a photodiode as receiver.

introduced the Oximet MET-1471 pulse oximeter with a fingertip probe and fiberoptic cables. Nakajima and others tested the Oximet MET-1471 and reported on it in 1979. In the years since, pulse oximetry has become widely used in a number of fields, including Anesthesia, intensive care, and neonatal care.

Principles of Operation

Pulse oximetry differs from the previously described oximetry in that it does not rely on absolute measurements, but rather on the pulsations of arterial blood. Oxygen saturation is determined by monitoring pulsations at two wavelengths and then comparing the absorption spectra of oxyhemoglobin and deoxygenated hemoglobin (20,21). Pulse oximetry uses a light emitter with red and infrared LEDs (light-emitting diodes) that shine through a reasonably translucent site with good blood flow (Fig. 13). Typical adult–pediatric sites are the finger, toe, pinna (top), or lobe of the ear. Infant sites are the foot or palm of the hand and the big toe or thumb. On the opposite side of the emitter is a photodetector that receives the light that passes through the measuring site. There are two methods of sending light through the measuring site (see above) (Fig. 9). The transmission method is the most common type used, and for this discussion the transmission method will be implied. After the transmitted red (R) and IR signals pass through the measuring site and are received at the photodetector, the R/IR ratio is calculated. The R/IR is compared to a “look-up” table (made up of empirical formulas) that converts the ratio to pulse oxygen saturation (S_pO_2) value. Most manufacturers have their own tables based on calibration curves derived from healthy subjects at various S_pO_2 levels. Typically, an R/IR ratio of 0.5 equates to approximately 100% S_pO_2 , a ratio of 1.0 to ~82% S_pO_2 , while a ratio of 2.0 equates to 0% S_pO_2 . The major change that occurred from the eight-wavelength Hewlett-Packard oximeters (see above) of the 1970s to the oximeters of today was the inclusion of arterial pulsation to differentiate the light absorption in the measuring site due

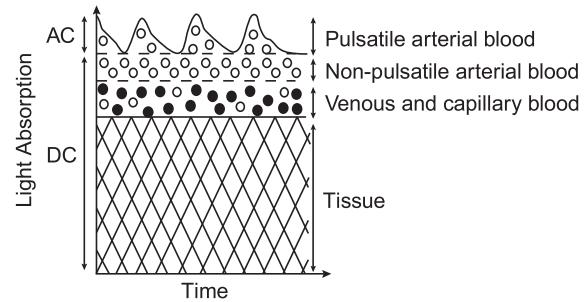


Figure 14. Schematic Representation of light absorption in adequately perfused tissue.

to skin, tissue, and venous blood from that of arterial blood. At the measuring site there are several light absorbers (some of them are constant) such as skin, tissue, venous blood, and the arterial blood (Fig. 14). However, with each heart beat the heart contracts and there is a surge of arterial blood, which momentarily increases arterial blood volume across the measuring site. This results in more light absorption during the surge. Light signals received at the photodetector are looked at as a waveform (peaks with each heartbeat and troughs between heartbeats). If the light absorption at the trough, which should include all the constant absorbers, is subtracted from the light absorption at the peak, then the resultants are the absorption characteristics due to added volume of blood only, which is arterial blood. Since peaks occur with each heartbeat or pulse, the term “pulse oximetry” was applied.

New Technologies

Conventional pulse oximetry accuracy degrades during motion and low perfusion. This makes it difficult to depend on these measurements when making medical decisions. Arterial blood gas tests have been and continue to be commonly used to supplement or validate pulse oximeter readings. Pulse oximetry has gone through many advances and developments since the Hewlett-Packard Model 47201A ear oximeter invention in 1976. There are several types of pulse oximeters manufactured by different companies available in the market nowadays. Different technologies have been used to improve pulse oximetry quality and decrease its limitations, which would lead eventually to better patient care. Figure 15 shows a modern pulse oximeter (Masimo Rad-9) designed by [Masimo](#) using the [Signal Extraction Technology \(Masimo SET\)](#) (22,23), is a software system composed of five parallel algorithms designed to eliminate nonarterial “noise” in a patient’s blood flow. This monitor display includes: S_pO_2 , pulse rate, alarm, trend, perfusion index (PI) (24), signal IQ, and plethysmographic waveform. Moreover, [Masimo](#) manufactures a handheld pulse oximeter by utilizing the same technology (Masimo SET) as shown in Fig. 16. Its small size (~15.7 × 7.6 × 3.5 cm) and broad catalog of features make it suited for hospital, transport, and home use. [Nellcor](#) (25) uses the OxiMax technology to produce a list of pulse oximetry monitors and sensors. These sensors have a small digital memory chip that transmits



Figure 15. Masimo Rad-9 pulse oximeter.

sensor-specific data to the monitor. These chips contain all the calibration and operating characteristics for that sensor design. This gives the monitor the flexibility to operate accurately with a diverse range of sensor designs without the need for calibrating each sensor to the specific monitors. This opens a new area of pulse oximetry innovations. Figure 17 reveals some of the Nellcor monitors and sensors available. Furthermore, Nellcor has designed a handheld pulse oximeter, as shown in Fig. 18, compatible with its line of OxiMax pulse oximetry sensors. Nellcor combines two advanced technologies in measuring blood gases: the Oxi-Max technology and Microstream CO₂ technology (see the section Capnography) to produce a S_pO_2 and end-tidal CO₂ partial pressure ($P_{ET}CO_2$) handheld capnograph-pulse oximeter to monitor both S_pO_2 and $P_{ET}CO_2$. Several additional parameters are now available on the modern oximeter, and they add additional functionality for these monitors and decrease their limitations. One of these parameters is called the “perfusion index” (PI) (24,26). This is a simple



Figure 17. Nellcor N-595 pulse oximeter.

measure of the change that has occurred in the tissue-under-test (e.g., the finger) over the cardiac cycle. When this parameter was first recognized as being something that a pulse oximeter could measure, it was difficult to imagine a value to the measurement because it is affected by so many different physiological and environmental variables, including systemic vascular resistance, volume status, blood pressure, and ambient temperature. But as time continues to pass since its introduction, more applications for PI have been found. The most obvious use for perfusion index is as an aid in sensor placement. It provides a means to quantify the validity of a given sensor site and, where desired, to maximize measurement accuracy. Perfusion index has also provided a simple and easy way test for sufficient collateral blood flow in the ulnar artery to allow for harvest of the radial artery for coronary artery bypass graft (CABG) surgery and for monitoring peripheral perfusion in critically ill patients.

Clinical Uses

Pulse oximeters are widely used in clinical practice (27–30). They are used extensively in the intensive care units to monitor oxygen saturation, and to detect and prevent hypoxemia. Monitoring oxygen saturation during anesthesia is a standard of care, which is almost always done by pulse oximeters. Pulse oximeters are very helpful in monitoring patients during procedures like bronchoscopy, endoscopy, cardiac catheterization, exercise testing,



Figure 16. Masimo Rad-5 handheld pulse oximeter.



Figure 18. Nellcor N-45 handheld pulse oximeter.



Figure 19. Portable Nonin Onyx 9500 pulse oximeter.

and sleep studies. Also, they are commonly used during labor and delivery for both the mother and infant. These sensors have no significant complications related to their use. There are several types of portable pulse oximeters on the market. These oximeters are small in size, useful for patients transport, and can be used at home. Figure 19 shows one of these pulse oximeters.

Accuracy and Limitations

The accuracy of pulse oximeters in measuring exact saturation has been shown to be $\sim \pm 4\%$ as compared to blood oximetry measurements. Several studies have shown that with low numbers of S_aO_2 , there is a decreased correlation between S_pO_2 and S_aO_2 , especially when $S_aO_2 < 70\%$ and in unsteady conditions (31). However, newer technologies have improved accuracy during these conditions substantially. Another factor that influences the accuracy of pulse-oximetry is the response time. There is a delay between a change in S_pO_2 and the display of this change. This delay ranges from 10 to 35 s. Pulse-oximeters have several limitations that may lead to inaccurate readings. One of its most significant limitations is that it estimates the S_aO_2 , not the arterial oxygen tension (P_aO_2). Another limitation is the difficulty these sensors have in detecting arterial pulsation in low perfusion states (low cardiac output, hypothermia etc.) (32). Furthermore, the presence of dyshemoglobins (e.g., methemoglobin, carboxyhemoglobin) (15) and diagnostic dyes (e.g., methylene blue, indocyanine green, and indigo carmine) (33) affects the accuracy of these monitors, leading to false readings. High carboxyhemoglobin levels will falsely elevate S_pO_2 readings, which may lead to a false sense of security regarding the patient's

oxygenation, and possible disastrous outcome. CO-oximetry should be used to measure S_aO_2 in every patient who is suspect for elevated carboxyhemoglobin (such as fire victims). Methemoglobinemia may lead to false $\sim 85\%$ saturation reading. The clinician should be alert to the potential causes and possibility of methemoglobinemia (e.g., nitrites, dapsone, and benzocaine). The CO-oximetry is also indicated in these patients. Vascular dyes may also affect the S_pO_2 readings significantly, especially methylene blue, which is also used in the treatment of methemoglobinemia. Brown, blue, and green nail polish may affect S_pO_2 too. Therefore, routine removal of this polish is recommended. The issue of skin pigmentations effect on S_pO_2 reading is still controversial. Motion artifacts are a common problem in using pulse oximeters, especially in the intensive care units.

Future Directions for Pulse Oximeters

As mentioned above, there are several limitations with the recent commercially available pulse oximeters. Pulse oximeters technology is working on decreasing those limitations and improving pulse oximeters function (34). In the future, techniques to filter out the noise component common to both R and IR signals, such as Masimo signal extraction, will significantly decrease false alarm frequency. Pulse oximeters employing more than two wavelengths of light and more sophisticated algorithms will be able to detect dyshemoglobins. Improvements in reflection oximetry, which detects backscatter of light from light-emitting diodes placed adjacent to detectors, will allow the probes to be placed on any body site. Scanning of the retinal blood using reflection oximetry can be used as an index of cerebral oxygenation. Combinations of reflectance oximetry and laser Doppler flowmetry may be used to measure microcirculatory oxygenation and flow.

Continuous Intravascular Blood Gas Monitoring (CIBM)

The current standard for blood gas analysis is intermittent blood gas sampling, with measurements performed *in vitro* in the laboratory or by using bedside blood gas analyzer. Recently, miniaturized fiberoptic devices have been developed that can be placed intravascularly to continuously measure changes in PO_2 , PCO_2 , and pH. These devices utilize two different technologies: Electrochemical sensors technology, based on a modified Clark electrode, and optode (photochemical/optical) technology (35,36).

Optode (Photochemical-Optical) Technology. An optode unit consists of optical fibers with fluorescent dyes encased in a semipermeable membrane. Each analyte, such as hydrogen ion, oxygen, or carbon dioxide, crosses the membrane and equilibrates with a specific chemical fluorescent dye to form a complex. As the degree of fluorescence changes with the concentration of the analyte, the absorbance of a light signal sent through the fiberoptic bundles changes, and a different intensity light signal is returned to the microprocessor. Optode technology has accuracy comparable to that of a standard laboratory blood gas analyzer. However, several reasons and problems, including the cost (see below) still limit the use of this monitor routinely.