CHAPTER

6

Blood Gas and Critical Care Analyte Analysis

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CHAPTER OBJECTIVES

1. List the types of samples that can be analyzed for blood gas and analyte concentrations.
2. Describe the three phases of analysis.
3. Explain the types of errors that can occur with blood gas analysis.
4. Calculate oxygen content.
5. Define Westgard rules.
6. Distinguish between shift and drift.
7. Describe the QC process for a point-of-care testing device.

KEY TERMS

Acid
Amperometry
Analyte
Anode
Base
Buffer
Cathode
CO oximetry
Electrochemical cell
Electrode
Oxidation
Partial pressure of oxygen (pO_2)
Potentiometric
Pulse oximetry
Reduction

Introduction

Blood gas analysis provides critical information to healthcare providers that assists in the diagnosis and treatment of a variety of metabolic and respiratory disorders. Historically, clinical laboratory testing was performed by medical laboratory scientists and medical laboratory technicians. Today, blood gas analysis is performed by trained personnel not only in the central or core laboratory, but by respiratory therapists[1] in satellite laboratories or with portable devices at the point of care (POC) in critical care areas such as the emergency department, neonatal and adult medical intensive care units, surgical intensive care units, and the operating room.[2]

The collection and analysis by portable or standard blood gas machines at or near the point of care minimizes the time needed to obtain and report laboratory values, which facilitates timely evaluation of results and prompt intervention.[3] Although the basic principles of operation for blood gas analyzers haven't changed significantly from earlier units, the components were notably adapted in 2005. At that time, self-contained cartridges were introduced into several analytical systems, paving the way for point-of-care testing and compact units. During this innovative period, additional **analytes** were incorporated into the testing menus. Today, healthcare facilities have the option of selecting analyzers to meet a variety of clinical needs and testing menus.[4]

Early blood gas analyzers were high maintenance and temperamental instruments that required operator-generated maintenance, calibration, and quality control. These units only measured the pH, partial pressure of oxygen (pO_2), and partial pressure of carbon dioxide (pCO_2) and provided calculated or derived values for other parameters. Today, auto-calibration and verification modes provide a more predictable testing atmosphere for the measurement of pH, pO_2, pCO_2, hemoglobin, electrolytes, and metabolites such as glucose, lactate, and creatinine.[5] Of course, calibration and quality control remain paramount in the accurate

measurement and reporting of all values obtained from blood gas analyzers.

Percutaneous arterial puncture or arterial sampling from an indwelling catheter with measurement by a point of care or standard analyzer remains the "gold standard" for analysis. Fiber-optic catheters may be used for invasive in vivo analysis of pH, pCO_2, and pO_2. The indwelling catheters and analysis system allow for continuous blood gas monitoring with minimal blood loss.[6] Continuous monitoring of pCO_2, pO_2, and oxygen saturation can be accomplished through noninvasive methods by transcutaneous monitors and **pulse oximeters**, respectively. Noninvasive methods involve minimal risk to the patient and require no specimen; a continuous measurement is obtained by placing **electrodes** or probes on the body.

Common Nomenclature for Blood Gases and Analytes

Nomenclature and reference ranges for analytes and arterial blood gas parameters are summarized in **Tables 6-1** and **6-2**, respectively. Reference ranges may vary slightly and are based on the methodology, age of the patient, and reference values the particular healthcare facility adopts.[7] The reference ranges listed in this chapter are a guide. Blood gas instruments directly measure the pH, pO_2, and pCO_2; other parameters, such as the bicarbonate, oxygen saturation, and base excess, are derived or calculated values. Direct measurements are more accurate and reliable; the parameters automatically calculated by the analyzer may be subject to variables that are not accounted for, contributing to error.

Common Abbreviating Symbols and Acronyms

Symbols for electrolytes and analytes are summarized in **Table 6-1**. The testing of these analytes is described later in the chapter. **Table 6-3** summarizes common symbols and acronyms used in blood gas testing.

Specimen Type and Origin Symbols

Blood gases can be analyzed on a variety of specimen types, including arterial, venous, and capillary samples. The collection site is based on the patient's diagnostic needs and clinical condition. In general, collection of an arterial specimen by percutaneous puncture or indwelling catheter is recommended. Heparin is the preferred anticoagulant used in the syringe for specimen collection.[8,9] Venous specimens may be suitable if pH, pCO_2, and bicarbonate values are needed. Results from venous specimens are affected by metabolism and peripheral circulation. Arterialized capillary samples can be collected from the earlobe, finger, toe, or heel. When collecting capillary blood from the heel, the site should first be massaged or carefully warmed. Heel collection is not suitable once an infant has reached 2 to 3 months of age. Capillary specimens are collected into heparinized micro-collection tubes.

TABLE 6-1
Analyte Nomenclature and Symbols

Analyte	Symbol	Reference Range	Comments
Potassium	K^+	3.5–5.1 mmol/L	Major intracellular cation
Sodium	Na^+	136–145 mmol/L	Major extracellular cation; important in maintaining osmotic pressure
Chloride	Cl^-	98–107 mmol/L	Major extracellular anion
Calcium	Ca^{2+}	8.8–10.2 mg/dL (total)	Occurs in three forms: bound to plasma proteins, complexed with ions such as bicarbonate, and ionized or free, which is the physiologically active form
Magnesium	Mg^{2+}	1.6–2.6 mg/dL	Role in many cellular enzymes for metabolism
Glucose		75–105 mg/dL	Increased in hyperglycemia and diabetes mellitus; decreased values termed hypoglycemia
Creatinine		0.5–1.5 mg/dL	Index of renal function and glomerular filtration
Blood urea nitrogen	BUN	6–20 mg/dL	Major nitrogen-containing end product of protein metabolism
Lactate		4.5–14.5 mg/dL (venous plasma) < 11.3 mg/dL (arterial blood in heparin)	Lactic acidosis may be hypoxic (shock, hypovolemia) or metabolic (diabetes mellitus, hepatic disease, neoplasms)

TABLE 6-2
Nomenclature and Symbols for Arterial Blood Gas Parameters

Parameter	Description	Reference Range	Comments
pH	Negative logarithm of the hydrogen ion concentration; measure of acid–base balance of blood.	7.35–7.45	Direct measure by pH (Sanz) electrode
pO_2	Partial pressure of oxygen in arterial blood. Also written as paO_2.	80–110 mm Hg	Direct measure by pO_2 (Clark) electrode
pCO_2	Partial pressure of carbon dioxide in arterial blood; mainly regulated by respiratory system. Also written as $paCO_2$.	35–55 mm Hg	Direct measure by pCO_2 (Stowe-Severinghaus) electrode
HCO_3	Bicarbonate; includes true bicarbonate, bicarbonate, and dissolved free CO_2.	21–28 mmol/L serum; 18–23 mmol/L arterial	Actual bicarbonate is a derived measurement calculated from the pH and pCO_2 of an aerobically drawn arterial specimen. Standard bicarbonate is derived from the Henderson-Hasselbalch equation and indicates the bicarbonate level in an oxygenated plasma specimen at 98.6°F (37°C) and pCO_2 of 40 mm Hg.
sO_2	Oxygen saturation of hemoglobin	95–100%	Derived value calculated using $sO_2\% = cO_2Hb/(cO_2Hb + cHHb) \times 100$. Calculated value does not account for other hemoglobins or actual pCO_2. Oxyhemoglobin is directly measured using oximetry.
P_{50}	pO_2 at which hemoglobin is 50% saturated with oxygen.		Calculated parameter
Buffer base	Total of all anionic buffers in the blood; includes hemoglobin, bicarbonate, inorganic phosphate, and proteins with a negative charge.	44–48 mmol/L	Calculated parameter; should not be affected by respiratory disorders.
Base excess	Number of millimoles of strong acid needed to titrate a blood sample to pH 7.4 at pCO_2 40 mm Hg.		Calculated parameter; should not be affected by respiratory disorders.

cHHb = content of deoxygenated hemoglobin; cO_2Hb = content of oxygenated hemoglobin

Introduction to General Measurement Concepts

Gas Tension

Gas tension is the partial pressure of a gas in blood. Partial pressure refers to the pressure exerted by a single gas in a mixture of gases or in a liquid. The pressure of the gas is related to the concentration of the gas to the total pressure of the mixture. For example, the concentration of oxygen in the atmosphere is 0.21. Atmospheric pressure is 760 mm Hg (at sea level). The **partial pressure of oxygen** in the atmosphere can be calculated by multiplying the concentration of this gas in the atmosphere (0.21) by atmospheric pressure (760 mm Hg).[10]

Gas tension of oxygen in the atmosphere = 0.21 × 760 mm Hg = 160 mm Hg

pO_2 refers to the partial pressure or tension of oxygen; it may also be written as PO_2, PO_2, and pO_2.The reference range of pO_2 in arterial blood is 80–110 mmol/L. pCO_2 refers to the partial pressure or tension of carbon dioxide; it may also be written as PCO_2, PCO_2, or pCO_2. The reference range of pCO_2 for arterial blood is 35–45 mm Hg.

pH

The pH is a measure of the acidity or alkalinity of a solution and ranges from 1–14. Values less than 7.0 are acidic and greater than 7.0 are alkaline. An **acid** is a substance that produces or donates hydrogen ions [H^+] when dissolved in water, whereas a **base** or alkaline substance is one that produces or donates hydroxyl ions [OH^-] when dissolved in water. When there are equal numbers of [H^+] and [OH^-] ions, the

TABLE 6-3
Common Symbols and Acronyms Related to Blood Gas Testing

Symbol	Meaning
pO_2	Partial pressure of oxygen; also written as PO_2, pO_2, or PO_2
pCO_2	Partial pressure of carbon dioxide; also written as PCO_2, pCO_2, or PCO_2
$[H^+]$	Hydrogen ion concentration
$[OH^-]$	Hydroxyl ion concentration
Hb	Hemoglobin
COHb	Carboxyhemoglobin
HHb	Reduced or deoxygenated hemoglobin
O_2Hb	Oxygenated hemoglobin or oxyhemoglobin
THb	Total hemoglobin
sO_2	Oxygen saturation of hemoglobin
P_{50}	pO_2 at which 50% of hemoglobin is saturated
ctO_2	Oxygen content
QA	Quality assurance
QC	Quality control

solution is neutral and the pH is 7.0, as shown in the following equation:[10]

$$H^+ + OH^- \longleftrightarrow H_2O$$

Relationship Between pH and H^+

The pH is the negative logarithm of the hydrogen ion concentration $[H^+]$ in moles/liter. For example, a pH of 6, a slightly acidic solution, would have an $[H^+]$ of 1.0×10^{-6}. Conversely, if a solution has an $[H^+]$ concentration of 1×10^{-12}, the pH of this solution would be 12, which is very alkaline.

The pH is measured in arterial blood to determine the degree of acidity or alkalinity. The acid–base balance of body fluids, including blood, is maintained through the hydrogen ion concentration. The reference range for the pH of arterial blood is 7.35–7.45.[10] **Buffers** are weak acids or bases that resist changes in pH when a strong acid or base is added. The body has several buffering mechanisms.

Sensors and Measurement Concepts

pH Electrode and Reference Electrode

Glass electrodes are commonly used to measure pH. The pH measurement system uses the Sanz electrode, which consists of two half cells connected by a potassium chloride (KCl) bridge. The measurement half cell or electrode has a glass membrane with layers of hydrated and nonhydrated glass. It is permeable or sensitive to hydrogen $[H^+]$ ions. This measurement electrode consists of silver-silver chloride (Ag-AgCl), which is then placed into a phosphate buffer of pH 6.840, and thus has a known $[H^+]$ concentration. The reference half cell or electrode consists of mercury and mercurous chloride (Hg-HgCl) or calomel. This calomel electrode is placed into a solution of saturated KCl.[11]

The reference electrode provides steady voltage while the measuring electrode responds to the ions of interest in the sample. Thus, the reference electrode provides a baseline voltage against which the voltage measured by the measuring electrode is compared. A pH meter or voltmeter measures this potential difference, known as ΔE, between the two electrodes. This relationship is shown in the following equation:

$$\Delta E = \Delta E^0 + 0.05916/n \log a_1 \text{ at } 25°C$$

where:

ΔE = Potential difference
ΔE^0 = Standard potential of **electrochemical cell**
n = charge of analyte ion
a_1 = activity of ion

There is a change of + 59.16 millivolts (mV) at 25°C for a 10-fold increase in $[H^+]$ activity and a decrease in pH units. At 37°C, the change in one pH unit causes a 61.5 mV change in the electrical potential.[12]

Functional Requirements and Characteristics of the pH System

It is postulated that sodium ions in the hydrated glass drift out and are replaced by the smaller hydrogen ions that are present in the sample. This results in a net increase in the external membrane potential, which travels through the thin, dry membrane to the inner hydrated glass surface. Chloride ions in the buffer solution migrate to the internal glass layer, creating a potential difference at the pH electrode that, in turn, signals the external reference electrode. The difference in voltage is converted and displayed as the pH.

pCO_2 Electrode System

Functional Requirements and Characteristics of the pCO_2 Electrode

The pCO_2 electrode is a modified pH electrode that was first described by Stowe and later by Severinghaus;[13] today it is known as a Stowe-Severinghaus electrode. The electrode has an outer semipermeable membrane consisting of Teflon or silicon elastic (Silastic). CO_2 diffuses into an electrolyte layer; a bicarbonate buffer covers the electrode glass. When CO_2 reacts with the buffer, carbonic acid forms, which then dissociates into a bicarbonate ion [HCO_3^-] and hydrogen ions [H^+].[14]

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

The hydrogen ions diffuse across the glass electrode and the change in [H^+] activity is measured using the same principle as for the pH electrode. The pCO_2 is determined from the pH value using the Henderson-Hasselbalch equation:

$$pH = pk + \log [HCO_3^-]/pCO_2$$

pO_2 Electrode System

Functional Requirements and Characteristics of the pO_2 Electrode

The partial pressure of oxygen (pO_2) is measured using the Clark electrode, which is a complete electrical cell. The Clark electrode consists of a small platinum **cathode** and a silver-silver chloride (Ag-$AgCl_2$) **anode** immersed in a phosphate buffer that contains additional potassium chloride. The platinum electrode is covered with a small layer of electrolyte and a thin gas-permeable membrane made of a material such as polypropylene. The membrane separates the test specimen from the electrode and is selectively permeable to oxygen, which diffuses into the electrolyte to contact the cathode. The cathode potential is adjusted to a constant voltage potential of −0.65 volts (V). When there is no oxygen present in the solution, the cathode is polarized and the current is approximately equal to 0 volts. When oxygen is present in the test specimen, a current is produced and oxygen diffuses from the sample solution and then through the membrane, where it is reduced.[15] Electrons are drawn from the anode surface to the cathode to reduce the oxygen. The current is proportional to the pO_2 of the test solution.

The sensitivity of the pO_2electrode is related to the thickness of the membrane and the size of the cathode area. A micro-ampmeter measures movement of electrons between the anode and cathode, which forms the electrical current. There are four electrons drawn for each mole of O_2 that is reduced. The reaction at the cathode is summarized as follows:

$$O_2 + 4e^- \rightarrow 2\ O^-$$

$$2\ O^- + 2\ H_2O \rightarrow 4\ OH^-$$

Next, elemental silver present at the anode is oxidized and then ionized, forming four electrons before combining with chloride to form silver chloride. The reaction at the anode is summarized as follows:

$$4\ Ag \rightarrow 4\ Ag^+ + 4\ e^-$$

$$4\ Ag^+ + Cl^- \rightarrow 4\ AgCl$$

Other gases may pass through the membrane, but the degree of the polarizing voltage does not permit them to be reduced at the cathode. The membrane prevents proteins and other oxidizing agents from reaching the cathode surface. Protein build-up on the membrane is an important source of measurement error; proteins may alter the diffusion of the gases and hinder the electrode response. The sensitivity of the electrode is related to the thickness of the membrane and the size of the cathode area.

Calculated Values

Hemoglobin/Oxygen Saturation

Oxygen saturation of hemoglobin is the percentage of oxygenated hemoglobin divided by total hemoglobin present capable of binding with oxygen. Oxygen saturation (sO_2) is calculated using the following equation:

$$sO_2\% = cO_2Hb/(cO_2Hb + cHHb) \times 100$$

where cO_2Hb is the concentration of oxyhemoglobin and $cHHb$ is the concentration of reduced or deoxyhemoglobin; the sum of oxy- and deoxyhemoglobin represents the total functional hemoglobin. Oxygen saturation is a derived value for most blood gas analyzers. It is only measured by analyzers that have hemoximetry capabilities. A hemoximeter directly measures the amount of hemoglobin present and capable of binding with oxygen.[16] Therefore, the microprocessors of analyzers that calculate sO_2 assume normal O_2 affinity of the hemoglobin. It is important for the clinician to recognize this

calculation may be approximate and should be interpreted with caution.

Oxygen saturation may also be calculated using the following formula:

$$sO_2\% = cO_2Hb/ctHb \times 100\%$$

where *ct*HB includes the carboxyhemoglobin, methemoglobin, and sulfhemoglobin fractions. Using this equation, the sO_2% will never reach 100% if any of these nonfunctional hemoglobin fractions are present. This calculation should not be used because the dishemoglobins, mentioned above, are present in the blood and the findings may be misleading. For example, if a patient had 10% carboxyhemoglobin, the sO_2 could not be any higher than 90%, even in fully saturated blood, which might indicate an increase in oxygen shunting to the lungs, which would not be accurate.[10]

Total Hemoglobin Measurement: Oxyhemoglobin and Dishemoglobinemias

Total hemoglobin (*ct*Hb or tHb) must be measured because the value is needed to calculate several other blood gas values. Total hemoglobin is a measure of all of the hemoglobin fractions detected by the spectrophotometer of the analyzer. The hemoglobin molecule that is bound to oxygen is known as oxyhemoglobin, whereas deoxyhemoglobin or reduced refers to a hemoglobin molecule that does not contain oxygen. Carboxyhemoglobin contains bound carbon monoxide instead of oxygen, and methemoglobin is a hemoglobin fraction that contains iron in the ferric (Fe^{3+}) form. These fractions are summarized in **Table 6-4**.

Blood gas analyzers measure total hemoglobin spectrophotometrically.[17] Once in the analyzer, the hemolyzer unit hemolyzes or ruptures the red blood cells in an aliquot of the specimen. A portion of the hemolyzed sample is transferred to a measuring chamber, also known as a cuvette. A tungsten halogen lamp or other light source provides polychromatic light, which is directed toward the sample in the cuvette. Depending on the concentration of hemoglobin in the sample, light is transmitted through the hemolyzed sample and toward the spectrophotometer. The specific wavelengths that transmit the color of each hemoglobin fraction are selected through a monochromater. Transmitted light contacts photodetectors that produce a voltage that corresponds to the amount of light transmitted and photons of light produced. The microprocessor converts the voltage through calculations into the hemoglobin

TABLE 6-4
Hemoglobin Fractions

Hemoglobin Fraction	Abbreviation	Description	Comments
Total hemoglobin	ctHb or tHb	Concentration of total hemoglobin or all fractions measured by spectrophotometer	
Oxyhemoglobin or fraction of oxyhemoglobin	O_2Hb or FO_2Hb	Concentration of hemoglobin that is oxygenated	Normal adult hemoglobin includes 1.5–3.5% HbA_2, less than 2% HbF, and ~95% HbA, which is the major adult hemoglobin
Deoxyhemoglobin or fraction of deoxyhemoglobin	HHb or FHHb	Concentration of hemoglobin that is deoxygenated and is not bound to oxygen	
Carboxyhemoglobin or fraction of carboxyhemoglobin	COHb or FCOHb	Concentration of hemoglobin that is combined with carbon monoxide	Hb affinity for CO is 200 times higher than for O_2; increased in city dwellers and smokers; extreme elevation and anoxia in carbon monoxide poisoning
Methemoglobin or fraction of methemoglobin	MetHb or FMetHb	Concentration of hemoglobin that contains iron in its ferric (Fe^{3+}) state	MetHb cannot bind oxygen; normally less than 1.5% of total Hb; increased in cyanosis and hypoxia; causes include exposure to nitrates and/or benzocaine products
Fetal hemoglobin or fraction of fetal hemoglobin	HbF or FHbF	Concentration of hemoglobin F or fetal hemoglobin; HbF can bind oxygen very tightly	Makes up 50–80% of total hemoglobin at birth and less than 2% in adults; the concentration of HbF is increased in some hemoglobinopathies and in some cases of hypoplastic anemia, pernicious anemia, and leukemia
Sulfhemoglobin or fraction of sulfhemoglobin	SulfHb or FSulfHb	Sulfur molecule attaches to hemoglobin and oxygen cannot be transported; may combine with CO to form carboxysulfhemoglobin	Normally less than 2.0%; cyanosis when increased; occupational exposure to sulfur compounds and pollutants

concentrations or fractions. Most blood gas analyzers detect oxyhemoglobin, as well as deoxyhemoglobin, carboxyhemoglobin, and methemoglobin fractions.

The hemoglobin unit must be calibrated using a known total hemoglobin standard. A calibration curve is electronically developed based on the voltage produced and is sent to the microprocessor. Sample results cannot be reported if the analyzer fails to calibrate successfully. Also, quality control using two different levels of a hemoglobin control must be performed with acceptable results before reporting patient values.[18]

Hematocrit Measurement

The hematocrit formerly was known as the packed cell volume (PCV). When a whole blood specimen is centrifuged, the red blood cells sediment to the bottom, the white blood cells and platelets form a middle layer, and plasma forms the upper layer. The percentage of red blood cells in the whole blood specimen is known as the hematocrit.

Bicarbonate Content

Bicarbonate constitutes a large fraction of the ions in plasma. Bicarbonate includes true bicarbonate, carbonate, and CO_2 bound in plasma carbamino compounds. True bicarbonates are the largest contributor to bicarbonate content.

Oxygen Content

Oxygen content can be measured directly or calculated by the oxygen content equation.

$$ctO_2 = (Hb \times 1.36 \times sO_2)\ (0.003 \times pO_2)$$

where

ctO_2 is the oxygen content
Hb is the hemoglobin in g/dL
sO_2 is the oxygen saturation in %
pO_2 is the partial pressure of oxygen in mm Hg

However, the tO_2 can be determined with results obtained from an arterial blood sample using the **CO-oximetry** test panel, which includes fractional concentration of oxyhemoglobin, reduced hemoglobin, carboxyhemoglobin, and methemoglobin. The sum total of these hemoglobin derivatives yields the total hemoglobin concentration. Many current blood gas analyzers either measure or calculate all variables needed to calculate the ctO_2.

Base Excess

Base excess can be defined as the concentration of titratable base when a fluid is titrated to a pH of 7.40 at a pCO_2 of 40 mm Hg. However, in practical terms, the base excess is calculated using a nomogram or with the Van Slyke equation.[19] The base excess is useful in evaluating the patient's acid–base balance in metabolic disorders. A positive base excess occurs when there is a surplus of HCO_3^- and a negative base excess when there is a deficit of HCO_3^-. The calculation of base excess requires the hemoglobin value, pCO_2, and HCO_3^-; the base excess at pH of 7.40, pCO_2 of 40 mm Hg, and Hb of 15 g/dL at a temperature of 37°C is zero.

$$\text{Base excess} = (1.0 - 0.0143\ Hb)(HCO_3^-) - (9.5 + 1.63\ Hb)(7.4\ pH) - 24$$

Today, this value is automatically calculated by the microprocessor in the blood gas analyzer.[20] The reference range for base excess in adults is from – 2 to + 3.

Biosensors and Methods Used in the Measurement of Analytes

Whole blood can be analyzed for many analytes, including the electrolytes potassium (K^+), sodium (Na^+), and calcium (Ca^{2+}) and metabolites such as glucose, lactate, blood urea nitrogen (BUN), and creatinine. The sensors used for these measurements are ion-specific or ion-selective electrodes (ISE).These sensors are membrane-based electrochemical transducers that respond to a specific ion. Biosensors are used in analyzers in the traditional clinical laboratory, but also in point-of-care (POC) testing devices. Biosensors use biologically sensitive material that contacts the appropriate transducer responsible for converting the biochemical signal into an electrical signal (**Figure 6-1**).

Electrolytes are determined by **potentiometric** measurements, a form of electrochemical analysis.[21] In potentiometry, the potential or voltage is measured between two electrodes in a solution. These potentials can also be produced when a metal and ions of that metal are present in a solution. By using a membrane that is semipermeable to the ion, different concentrations of the ion can be separated. These systems use a reference and a measuring electrode. A constant voltage is applied to the reference electrode; the difference in voltage between the reference and measuring electrode is used to calculate the concentration of the ion in solution.

Ion-selective electrodes are based on a modification of the principal of potentiometry.[21] The potential difference or electron flow is created by selectively transferring the ion to be measured from the sample solution to the membrane phase. The ISE measures the free ion concentration of the desired analyte on a selectively produced membrane. Membranes have a complex composition and contain organic solvents, inert polymers, plasticizers, and ionophors. Ionophors are molecules that increase the membrane's permeability to the specific ion.

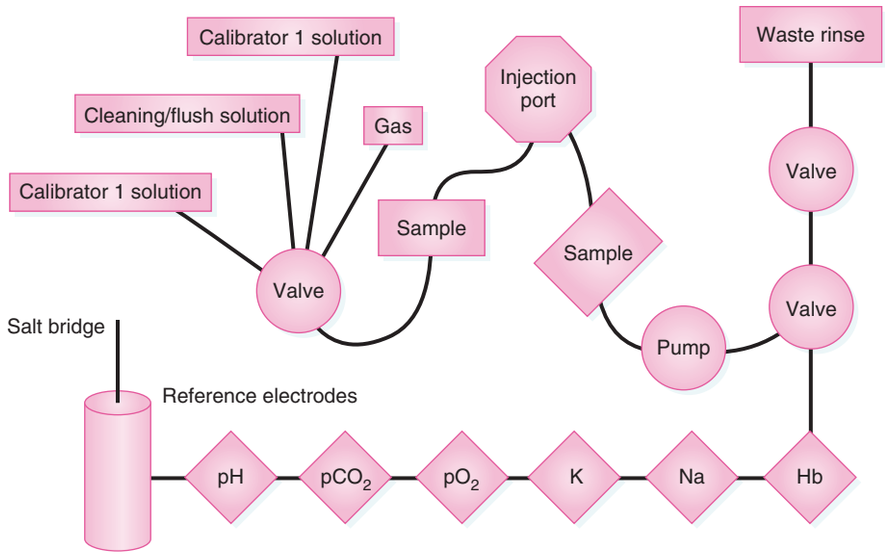

FIGURE 6-1 Schematic of a typical analyzer used to measure blood gas and electrolytes.

Because ISEs produce a direct measurement, there is no need for reagents or the production of a standard curve. Results are precise, accurate, sensitive, and specific for the analyte that is being tested. Ion-selective electrodes are also cost effective, have a rapid analysis time, and are easily maintained and adapted toward automation.

The corresponding membrane component is unique for a specific ISE membrane. For example, the sodium ISE membrane contains silicate in glass; the potassium ISE membrane contains valinomycin; the chloride ISE membrane contains solvent polymeric membranes. ISEs are also available for chloride (Cl^-), calcium (Ca^{2+}), magnesium (Mg^{2+}), and lithium (Li^+).

Amperometric methods measure the current flow produced from **oxidation-reduction** reactions. Types of **amperometry** include enzyme electrodes, such as the glucose oxidase method and the Clark pO_2 electrode, previously discussed. These types of designs are known as biosensors and are adaptable for testing in the clinical laboratory as well as for point-of-care (POC) testing.

Enzyme-based biosensor technology was first developed to measure blood glucose. A solution of glucose oxidase is placed between the gas-permeable membrane of the pO_2 electrode and an outer membrane that is semipermeable.[22] Glucose in the blood diffuses through the semipermeable membrane and reacts with the glucose oxidase. Glucose is converted by glucose oxidase to hydrogen peroxide and gluconic acid. A polarizing voltage is applied to the electrode, which oxidizes the hydrogen peroxide and contributes to the loss of electrons. Oxygen is consumed near the surface of the pO_2 electrode and its rate of consumption is measured. The loss of electrons and rate of decrease in pO_2 is directly proportional to the glucose concentration in the sample. Enzyme-based biosensors are also used to measure cholesterol, creatinine, and pyruvate.

There are also enzyme-based biosensors with potentiometric and conductimetric detection methods.[23] Conductimetric methods utilize chemical reactions that produce or consume ionic substances and alter the electrical conductivity of a solution. In this technology, polymembrane ion-selective electrodes are used. Blood urea nitrogen (BUN), glucose, and creatinine may be measured using this technology. The BUN biosensor immobilizes the enzyme urease at the surface of an ammonium ISE; the urease catalyzes the breakdown of urea to ammonia (NH_3) and CO_2. Subsequently the ammonia forms ammonium, which is detected by the ISE. The signal produced by the ISE is related to the concentration of blood urea nitrogen in the sample.

Biosensor systems can also use optical detection to measure glucose, bilirubin, and other analytes. The sensors include immobilized enzymes and indicator dyes and may be detected using spectrophotometer, fluorescence, reflectance, or luminescence.[24]

Phases of Analysis

Within the test setting, control of variables that may affect the three phases of analysis must be evaluated. Preanalytical test variables that may alter patient results include correct patient identification, turnaround time, transcription errors, patient preparation, specimen collection, and specimen transport. There are many individuals involved in the preanalytical testing phase; therefore, a coordinated effort among the healthcare providers involved in the process is essential. Following specimen collection and transport, the sample must be correctly processed or maintained prior to analysis.

The analytical stage includes the actual testing of the specimen. A specific testing protocol with standard operating procedures (SOPs) for each analyzer is

needed. This includes criteria to accept or reject specimens. All specimens must be analyzed consistently by the testing personnel, who must follow the specific procedure directions outlined in the procedure manual. The process that occurs during sample analysis is provided in **Figure 6-2**. Quality control (QC) is a very significant component to assess the quality of the analytical testing phase. Quality control is used to monitor and assess the accuracy of specimen analysis. QC uses samples with known values of each analyte with a range of acceptable values given. In the postanalytical phase, the results are evaluated for error and proximity to normal limits.

Of course, technical competence is a requirement for all testing phases. Proper training of personnel who perform the analysis is essential and should include education standards, learning objectives, an evaluation of technical competence, in-services, and continuing education. Work quality must be evaluated and corrective actions suggested if needed.

Preanalysis Phase: Specimen Handling and Special Considerations

Arterial blood collection begins by confirming the identification and location of the patient. The test order, or requisition, and patient identification must agree. Any identification discrepancies must be resolved and corrected before proceeding to collect the specimen. Correct specimen collection and transport are essential to ensure accurate results for the patient. Failure to properly collect or transport the sample can lead to erroneous results that may affect the diagnosis, treatment regimen, and clinical outcome.[25] Arterial blood gas specimens are most often collected using a single percutaneous needle puncture from the radial artery, although specimens may also be collected from brachial, femoral, or pedis arteries. The temporal artery may also be used for collection in newborns. Capillary blood gas collections from the heel or earlobe of infants are also acceptable for analysis; however, reference

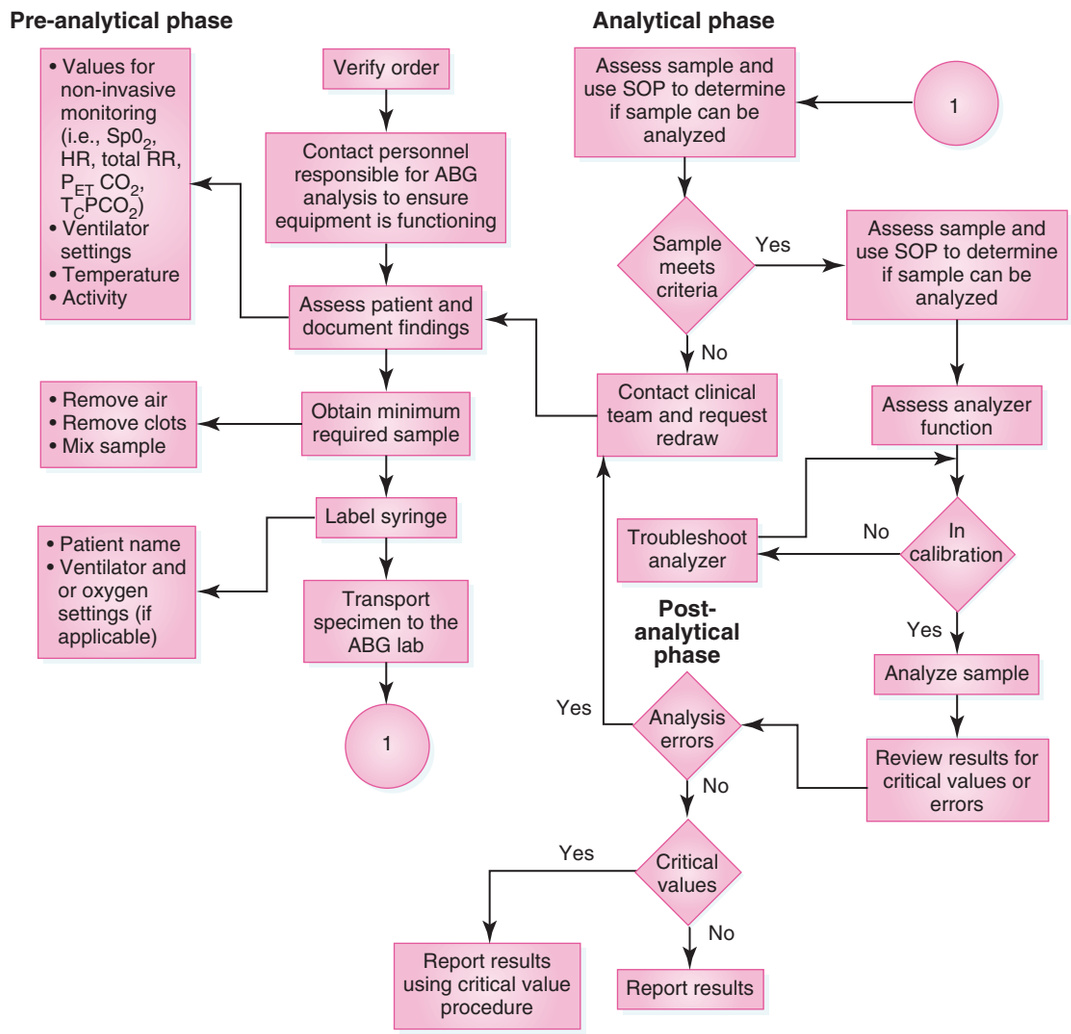

FIGURE 6-2 Process flow for the three phases of blood gas and analyte measurement.

ranges and results differ from arterial samples. Venous specimens are commonly used for venous pH, pCO_2, and bicarbonate testing. Attempts should be made to keep sample sizes as small as is technically feasible to limit blood loss, particularly in neonates.[2] Once collected, the specimen must be accurately labeled with the patient's name, identification number, location, F_IO_2, and temperature as well as the collector's initials, date, and time of collection.[2] Specimen labeling must occur even in cases where the individual collecting the specimen also performs the analysis.[26]

Following collection of percutaneous samples, all air bubbles must be immediately removed by gently tapping the side of the syringe. The syringe should not be agitated. Significant error may occur when even a small amount of air bubbles is found in the sample.[27]

When collecting specimens from indwelling arterial catheters, first remove 1–2 mL of blood from adults and 0.2–0.5 mL from infants. Flush the cannula with sterile, physiologic saline to prevent clotting in the cannula. Saline and heparin in catheter lines can dilute the sample and falsely decrease the pCO_2 and hemoglobin.[28,29]

Temperature Correction for Blood Gas Values

Patient temperature affects blood gas values. Blood gas analyzers assume the patient's temperature is 98.6°F (37°C). In cases of hypothermia due to surgery or prolonged exposure to cold, where the body temperature may be significantly lower than 98.6°F (37°C), or hyperthermia due to fever, the patient's actual body temperature may be manually entered into the analyzer so that temperature-corrected pH, pCO_2, and pO_2 values can be calculated.[30] The algorithms used for these calculations are generally found in the instrument operator's manual. The use of the temperature correction is not standardized, and there is a lack of agreement in the literature regarding its use. Some report corrected values provide a more correct indication of the acid–base balance and oxygenation state of the patient. For example, pO_2 changes approximately 7% for each 1°C deviation from 37°C. Thus, it is advisable to perform temperature corrections for measured pO_2 even for a 1°C deviation. Both the pO_2 value measured under the standard temperature of 98.6°F (37°C) and the temperature-corrected value should be reported.[31] It is generally accepted that it is not necessary to correct the pH and pCO_2 for hyperthermia and they are generally reported only when requested by the physician.[32] A temperature correction does not affect the calculated HCO_3^-.

Key Points for Specimen Collection/ Preparation for Analysis

Blood gas specimens must not be exposed to room air during collection, transport, or measurement. Room air has a pO_2 of approximately 150 mm Hg, which can affect the value of oxygen in the sample. Specimens must be transported for analysis within 10 minutes of collection when held at room temperature. Specimens that cannot be analyzed immediately must be placed within an ice slurry and maintained at a temperature of 32–39.2°F (0–4°C) for no longer than 30 minutes. Specimens should not be held in ice alone because the sample may freeze and red cells may hemolyze. Oxygen may be metabolized by white blood cells after specimen collection, especially if the patient has an elevated white blood cell count. Delays in transport may also increase diffusion of gases through the plastic syringe and increase the likelihood of potassium diffusion from the red cells. Preanalytical error may lead to measurement error and improper medical diagnosis.

Prior to analysis, gently mix the specimen to obtain a homogeneous sample; this can be accomplished by gently inverting the sample or by rolling the syringe in the palms of the hands. Never shake the specimen because this may hemolyze the red cells, releasing potassium and altering the results.

Preanalysis Phase: Calibration Principles

High and low calibration is required for all measured and reported laboratory analytes in order to verify the analyzer is operating correctly. Today, most blood gas analyzers are self-calibrating, controlled through the microprocessor and monitored constantly. The frequency and type of calibration that is programmed into the instrument varies and is based on the manufacturer, accreditation standards, and the facility's operation schedule.

A one-point calibration uses only one calibration standard; the electrical output is adjusted to a single standard. A one-point calibration of pO_2 and pCO_2 is generally automatically performed every 30 minutes. One-point calibrations should be manually performed prior to sample analysis. In a two-point calibration, the response of the electrode is measured against known values for both a high and low standard. The values are plotted and a linear calibration curve is derived; all subsequent measurements are compared against the calibration line. Most blood gas analyzers automatically perform a two-point calibration every 8 hours.

Functional Requirements of Calibration

The pH system is calibrated against primary calibration buffers that are phosphate solutions and that must meet the standards of the National Institute of Standards and Technology (NIST). These calibrators are prepared from standard reference materials—potassium dihydrogen phosphate and disodium monohydrogen phosphate—according to a specific protocol to produce two buffer solutions. The first has a pH of 6.841 at 98.6°F (37°C) and the second has a pH of 7.383 at 98.6°F (37°C). The buffers must meet NIST specifications; they are commercially available and manufactured to a size

and shape to fit into the reservoirs of the analyzer. The tolerance for calibrators should be ± 0.003 in order to achieve standard deviations of ± 0.005 to ± 0.01.

The calibration of the gas system requires known concentrations of O_2 and CO_2 gases to be introduced into the measurement chamber. Pure O_2, CO_2, and N_2 can be purchased as compressed gases with a certificate of analysis provided by the manufacturer and then mixed into the required composition, or they can be purchased commercially in the appropriate calibration mixture. The low gas mixture calibrator and high gas mixture calibrator compositions are shown in **Table 6-5**. Calibration using these mixtures will provide a calibration range of 0–152 mm Hg for O_2 and 38–80 mm Hg for CO_2. The pO_2 electrode can be calibrated using "no atmosphere" air as the low calibrator and "room air" as the other calibrator. Today, gas calibrators are included in the testing cartridges for most blood gas analyzers.

During calibration of the gas system, gas released from the tanks is pumped into the calibration buffers. The solutions are mixed, warmed to 98.6°F (37°C), and a small aliquot moved to make contact with the surface of the pO_2 and pCO_2 electrodes. A voltage measurement is taken, which is corrected for the barometric pressure; the microprocessor analyzes the values and derives a calibration curve for pH, pO_2, and pCO_2. Some analyzers have an internal barometer or transducer so that the barometric pressure value is known to the microprocessor, which then calculates the pO_2 and pCO_2 based on Dalton's law. Other models require that the operator manually enter the barometric pressure.

Analysis Phase: Laboratory Blood Gas Analyzers

Principles of Operation

The basic principles of operation for laboratory blood gas analyzers are the previously described electrodes for pH, pCO_2, and pO_2; spectrophotometric analysis of hemoglobin; and ion-specific electrodes for the measurement of electrolytes. The principle of operation is shown in **Figure 6-3**. Approximately 50–120 µL of a well-mixed arterial blood sample are injected through the inlet and sample probe into the measuring chamber. The specimen contacts the surface of each electrode for several seconds.

Calibration

Calibrator gases and buffers enter through the valve to the chamber area maintained in a fluid and metal bath at a constant temperature of 98.6°F (37°C) ± 0.1°C. The measuring and reference electrodes are located in this chamber. The high pH and low pH calibrators enter in alternating mode into the chamber, generating electrical responses for the upper and lower pH limits

TABLE 6-5
Gas Calibration Mixtures

	pO_2 (%)	O_2 (mm Hg)	pCO_2 (%)	CO_2 (mm Hg)	N_2 (%)
Low gas mixture	0	0	5	59	95
High gas mixture	20	150 mm Hg	10	80 mm Hg	70

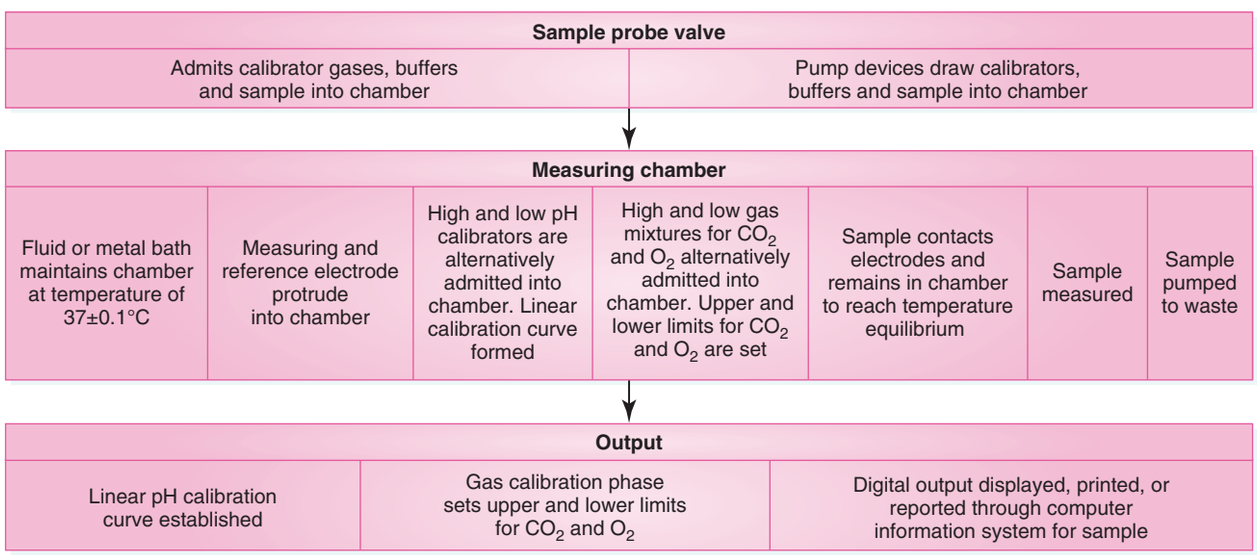

FIGURE 6-3 Process that occurs during the analysis of whole blood for gas and analyte measurement.

and producing a linear pH curve. The high and low gas calibrators for pO_2 alternatively enter the chamber, the electrical responses are measured, and a standardized linear curve is generated. The same process also occurs for pCO_2 with the high and low calibrator gases entering the measuring chamber, generating voltages, and producing a linear calibration curve. After an acceptable calibration, the blood sample is introduced and analyzed. The electrodes have a threaded neck with a leak-proof fit and the sample contacts the tip of each electrode. The pH electrode has glass that is sensitive to $[H^+]$ ions.

An electrical output is generated for each parameter of the sample and then sent to the microprocessor; the results are sent to the computer screen or printer. A report is generated, which can be sent through the laboratory information system to the patient's location or healthcare provider. Patient demographics, sample type, F_IO_2, and temperature are entered by the operator prior to sample analysis.

Analysis Phase: Sources of Measurement Error

Most errors in blood gas analysis occur in the preanalytical phase, including specimen collection and handling. Insufficient sample and/or inadequate mixing of the blood specimen prior to analysis may lead to a nonhomogeneous distribution of red blood cells across the electrode junction. Analytical errors such as problems with maintaining the temperature control can lead to measurement error if the sample does not reach 98.6°F (37°C) ± 0.1°C. The analysis process is outlined in **Figure 6-3**. Temperature control errors may result from pinched or clogged tubing within the analyzer or from clogs or spaces in the sample stream. Point-of-care testing devices may be more vulnerable to analytical errors and have a higher rate of error when compared to analyzers in a core or satellite laboratory.[33] Sources of error associated with blood gas analysis are summarized in **Table 6-6**.

Postanalysis Phase: Quality Control and Reporting Principles

Assessment of Analyzer Performance

Total quality management (TQM) is a management process designed to improve quality of care, maintain patient safety, and control the cost of care. In terms of laboratory analysis, TQM includes quality assurance (QA) and quality control (QC). Quality assurance deals with the wider measures of laboratory performance, such as turnaround time, specimen and patient identification, and appropriate test utilization. Through QA processes, problems are identified and solutions provided to mitigate the problem.

Analyzers must be maintained to ensure proper performance; careful maintenance of the analyzer and specimen quality are important in providing accurate and timely results. The microprocessor of the analyzer displays the diagnostic maintenance routine required

TABLE 6-6
Sources of Error Associated with Blood Gas Analysis

Preanalytical Errors	Analytical Errors	Postanalytical Errors
Wrong patient drawn	Insufficient sample	Reporting incorrect result to clinician
Poor drawing technique	Calibration set points not accurate	Transcription errors
Failure to follow protocol for specimen collection	Quality control not run or out of control	Failure to recognize and interpret flags and instrument errors
Failure to mix heparin sufficiently with sample	Maintenance not performed	
Air introduced into syringe	Failure to run calibration	
Specimen exposed to air	Temperature control errors	
Delay in transportation for testing		
Sample not kept cold during transport		
Failure to mix sample adequately before analysis		
All air bubbles are not removed from the sample		
Presence of fibrin clots in the sample		
Analysis of a clotted specimen		

by the manufacturer and also displays warnings or indicators of problems that must be addressed and corrected. Regular maintenance in accordance with the manufacturer's recommendations is required for all blood gas analyzers; the schedule should be adjusted to the needs of the particular facility. This includes routine maintenance, which is performed on a daily, weekly, or monthly basis.

Corrective maintenance is required if there are problems with quality control or performance concerns with the analyzer. The instrument manual provides specific guidelines for routine, preventative, and corrective maintenance requirements for each analyzer. In general, frequency of maintenance is directly related to the number of blood gas analyses performed on the instrument.

It is important to maintain a clean sample chamber and path. Although automatic flushing to clean the sample chamber and pathway is an element of most blood gas analyzers, it may still be necessary to manually clean these areas with implements or solutions recommended by the manufacturer. Fibrin strands or small clots may be present in samples or may develop in the sample as it is warmed in the temperature chamber. Fibrin and clots will alter calibrations and measurements by affecting the contact of blood, gases, or buffers with electrode membranes.

Quality control is a required component of laboratory analysis. It is not only necessary to ensure that the analyzer is operating correctly and producing accurate results, but also required for accreditation by agencies, including the College of American Pathologists, and to comply with the Clinical Laboratory Improvement Act of 1988.[1]

Proficiency testing is an external quality assessment process in which simulated patient specimens are produced from a common pool and analyzed by participating laboratories. The purpose is to evaluate each laboratory's performance on specific analytes. Target values are established for each tested parameter as well as for the method of analysis. Typically, proficiency testing occurs in three cycles per year; there are five specimens required for each specific analyte. For laboratories to be graded "successful" in most clinical laboratory areas, including chemistry, correct results must be produced for that analyte on four out of the five specimens. A minimal score of 80% must be achieved in three consecutive cycles. All unacceptable performances must be assessed and an explanation provided for the measurement error. Of course, the problem causing the error must be identified and corrected. As a component of the laboratory accreditation process, proficiency testing is mandatory.[1]

Quality control materials should be analyzed after a successful calibration, following completion of routine maintenance procedures, and after completing any corrective maintenance or troubleshooting of the analyzer. State and federal accreditation agencies require that three levels (low, normal, and elevated) of each analyte must be tested in each 24-hour period. Most facilities analyze all three levels in each 8-hour shift.

Postanalytical variables, the third stage of analysis, include the accurate recording and reporting of results. Results must be correctly reported to the appropriate healthcare provider in a timely manner. Patient results not within the reference range, and in particular critical values, must be reported to and documented with the healthcare provider.

Reporting Values

Reference ranges for some common parameters are summarized in **Table 6-7**. Results must be reported through the information system, electronic medical record, or instrument interface in a timely manner.

Importance of/Rationale for Critical Values for Blood Gases and Analytes

Critical values, also known as panic values, are those testing results that present a life-threatening situation for the patient.[34] Timely and accurate reporting of critical values to licensed medical professionals is required by laboratory accrediting bodies and is recognized as an important patient safety initiative.[35] Critical limits may vary with the laboratory and the medical facility. **Table 6-8** shows the upper and lower limits for pertinent clinical chemistry laboratory tests.[36]

Assessment of Analyzer Performance: Quality Control

It is essential to only report patient results that are accurate and precise so that the healthcare provider can make a reliable diagnosis and treatment regimen. Error refers to deviations from the true value. Testing errors are categorized as either random/wild or systematic. All test systems attempt to identify and minimize measurement errors. Systematic error occurs in some predictable manner. The measurement value is either overestimated or underestimated, but not both. It is controlled through proper calibration and quality control of the testing system. Systematic error is explainable and has a correctable cause. Systematic error may be caused by an inaccurate calibrator or standard, improper handling of samples or reagents, or instrument malfunction. It can generally be identified and corrected through quality control by identifying shifts, trends, and violations of the Westgard Rules (see more on these rules later in this section).[37] By contrast, random error is unpredictable and results from uncontrollable factors. It is introduced by chance and can be minimized, but never eliminated. Random errors may appear on both the high and low sides of the true value.

TABLE 6-7
Reference Values

Test	Specimen Type	Reference Range
Blood Gases		
pH	Arterial	7.35–7.45
pH (newborn)	Arterial	7.25–7.45
pCO_2	Arterial	35–45 mm Hg
pCO_2 (newborn)	Arterial	27–40 mm Hg
pO_2*	Arterial	83–108 mm Hg
pO_2 (newborn)	Arterial	55–90 mm Hg
HCO_3	Arterial	21–28 mmol/L
HCO_3 (newborn)	Arterial	17–24 mmol/L
T CO_2	Venous	22–29 mmol/L
T CO_2 (newborn)	Venous	13–22 mmol/L
sO_2	Arterial	95–98%
sO_2 (newborn)	Arterial	40–90%
Base excess	Arterial	–2 to +3
Base excess (infant)	Arterial	–10 to –2
Chemistry		
Glucose (adult: fasting)	Whole blood, serum, or plasma	60–95 mg/dL
Glucose (infant and child)	Whole blood, serum, or plasma	70–100 mg/dL
Glucose (newborn)	Whole blood, serum, or plasma	50–80 mg/dL
Potassium	Whole blood, serum, or plasma	3.5–5.1 mmol/L
Potassium (newborn)	Whole blood, serum, or plasma	3.0–5.8 mmol/L
Sodium	Whole blood, serum, or plasma	136–145 mmol/L
Sodium (infant)	Whole blood, serum, or plasma	139–146 mmol/L
Chloride	Whole blood, serum, or plasma	98–107 mmol/L
Chloride (newborn)	Whole blood, serum, or plasma	98–113 mmol/L
Hematology		
Hemoglobin (male)	Whole blood	13.5–17.5 g/dL
Hemoglobin (female)	Whole blood	12.0–16.0 g/dL
Hemoglobin (newborn)	Whole blood	10.0–17.0 g/dL
Hematocrit (male)	Whole blood	37–48%
Hematocrit (female)	Whole blood	35–45%

* pO_2 decreases with age and high altitude.

TABLE 6-8
Critical Values for Some Common Laboratory Analytes

Test	Specimen Type	Lower Limit	Upper Limit
Blood Gases			
pH	Arterial and capillary	7.20	7.60
pCO_2	Arterial and capillary	20 mm Hg	70 mm Hg
pO_2	Arterial	40 mm Hg	
HCO_3	Arterial and capillary	10 mmol/L	40 mmol/L
Chemistry			
Glucose (adult)	Whole blood, serum, or plasma	40 mg/dL	450 mg/dL
Glucose (infant < 1 year)	Whole blood, serum, or plasma	40 mg/dL	400 mg/dL
Glucose (newborn)	Whole blood, serum, or plasma	30 mg/dL	200 mg/dL
Potassium	Whole blood, serum, or plasma	2.8 mmol/L	6.2 mmol/L
Potassium (newborn)	Whole blood, serum, or plasma	2.8 mmol/L	6.5 mmol/L
Sodium	Whole blood, serum, or plasma	120 mmol/L	160 mmol/L
Sodium (infant)	Whole blood, serum, or plasma	125 mmol/L	150 mmol/L
Hematology			
Hemoglobin (adult)	Whole blood	6 g/dL	20 g/dL
Hemoglobin (newborn)	Whole blood	10 g/dL	20 g/dL

Their effect can be reduced by producing repeated measures of the same quality. Random error exhibits a Gaussian or normal data distribution, which enables us to make probability statements about measurement accuracy. An outlier is a value that is found outside of the normally distributed data.

Quality control (QC) should be performed at least once per shift. Electronic QC, which is a feature of many analyzers, uses an analyzer signal that mimics a sample. It is economical, easy to run, and reliable; however, it does not evaluate the operator or all systems within the analyzer. Thus, it is essential when appropriate to also analyze commercially available QC materials. The frequency of QC analysis depends on the instrument, its stability, and the manufacturer's specification, as well as government regulations and the policy of the healthcare system. Daily instrument setup involves calibration and running QC. Normal and abnormal QC with known results are analyzed and compared to known ranges. The result rarely perfectly matches the mean value every time. Limits of variation are established. If QC results are within the limits, we can assume that patient results are also acceptable and reportable.

Repeated measures of a given analyte on a given instrument will cluster around the mean. Plotting the frequency of each result against the concentration or amount of the analyte should produce a normal, Gaussian distribution. Based on the analysis of the QC material, parameters are established for results that are plus or minus 1 standard deviation (± 1 SD), plus or minus 2 standard deviations (± 2 SD), and plus or minus 3 standard deviations (± 3 SD) from the mean. Laboratory limits are generally set to ± 2 SD, which means that based on the Gaussian distribution, 95.0% of the QC results will be within 2 SDs of the mean. Thus, 5% or 1 out of 20 QC results will fall outside of the limits as a result of random error.

Levey-Jennings plots are used to track QC performance over a period of time. This process assists in identification of shifts and trends that alert the operator to possible problems in the testing system. A shift shows that the results are biased and "shifted" in one direction. The values are all shifting either above or below the mean. Shifts are sudden and show an abrupt change in consecutive results. Shifts are most often attributable to instrument malfunction or errors in operator technique. A Levey-Jennings plot showing a shift is provided in **Figure 6-4**.

By contrast, a trend is a gradual change in consecutive control results with all results going upward or downward. A trend results from systematic drift due to

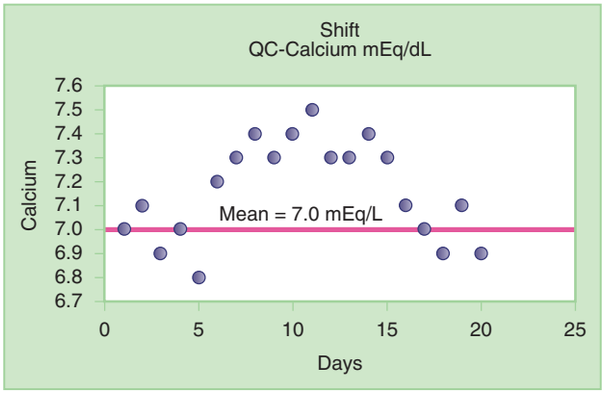

FIGURE 6-4 Shift.

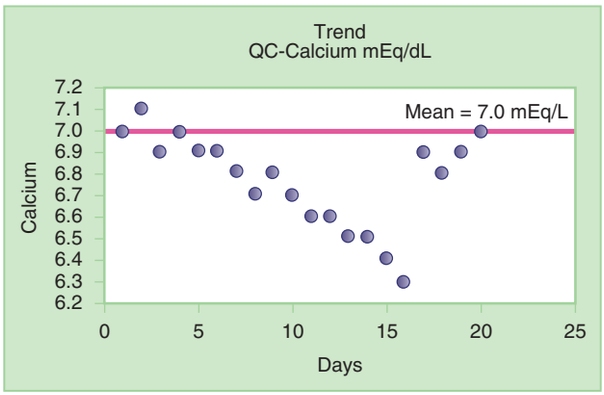

FIGURE 6-5 Trend.

deterioration of a reagent or control material. Trends may also be caused by failure of a component within the analyzer. An example of a trend is shown in the Levey-Jennings plot in **Figure 6-5**.

A high level of precision indicates reproducible measurements; precise results are reproducible, reliable, and consistent. They are most affected by random error. The greater the random error, the less precise is the measurement. Precision is enhanced by the use of standardized measurement methods, which include training and certification of the operator.[38] Poor precision results from poor technique. Precision is also enhanced by refining instruments through automation and by repeating the measure to reproduce the results.

Accuracy is the degree to which the test system measures the analyte of interest. Accuracy refers to agreement with the true value. It is most affected by systematic error; the greater the systematic error, the less accurate is the result. Accuracy is assessed by comparing the results to the "gold standard" of testing, or the reference technique considered to be the most accurate for a laboratory parameter. Accuracy is affected by both specificity and sensitivity. Tests with high specificity detect and measure only the characteristic of interest whereas tests with low specificity will detect the characteristic when it is not present. Thus, test systems with low specificity will have a high percentage of false positive results. Sensitivity is the ability to detect small amounts of the characteristic of interest; highly sensitive tests will detect small amounts of the analyte and will also differentiate between small amounts of different amounts of the analyte. Tests with poor sensitivity will produce a high percentage of false negatives; the phenomenon is not detected when it is indeed present. In a perfect test setting, all methods would achieve 100% sensitivity and 100% specificity; because the parameters are inversely related, this of course is not possible. Thus, test systems that are at least 90% sensitive and 90% specific are recommended. Screening tests generally promote a higher level of sensitivity and a lower level of specificity, so as to not miss a characteristic or condition. This generally prompts follow-up testing that is more specific, but perhaps less sensitive. Calibration that fails or quality control values that are not within control limits must be investigated and corrective action taken. All corrective measures must be documented.

In summary, internal quality control requires that controls are a part of internal QC and it should be run as often as specified by the instrument manufacturer. It should also be run whenever there is concern about results or the quality of the testing system. Of course, QC should be rerun if previous controls were not in control. It is important to emphasize that the operator cannot report patient results if QC results are not within control.

The Westgard Rules are six rules used to examine quality control charts to determine possible problems.[39] The type of error, random or systematic, can be identified. At least two levels of control must be run. If any of the six rules are broken, patient results cannot be reported. Once the problem is identified and corrective action taken and documented, it may be necessary to reanalyze patient samples from previous testing, especially if a systematic error is identified. Laboratories may choose to use all or some of the Westgard rules; however, they must use at least one for random and one for systematic error detection.

The 1_{2s} rule is a warning rule that describes random error; it states that there is a problem if one QC value falls more than 2 SD above or below the mean. Random error is also associated with violations of the 1_{3s} and R_{4s} rules; violation of either of these rules requires that the run be rejected. The 1_{3s} rule violation occurs when one result falls outside of the 3 SD limit; the R_{4s} rule violation occurs if the difference between the highest and lowest results exceeds a total range of 4 SD. Systematic error is associated with violations of the 2_{2s}, 4_{1s}, and 10_{x}; in each case the run should be rejected. The 2_{2s} violation occurs when two consecutive controls exceed either the +2 SD or –2 SD limits; the 4_{1s} violation occurs when four consecutive controls exceed either the +1 SD

TABLE 6-9
Westgard Rules

Rule	Description	Type of Error
1_{2s}	At least one QC value falls more than 2 SD above or below the mean. Warning.	Random
1_{3s}	Result falls outside of 3 SD limit. Reject Run.	Random
2_{2s}	Two consecutive controls exceed the +2 SD or –2 SD limit. Reject Run.	Systematic
R_{4s}	Difference between highest and lowest result of a run exceeds 4 SD. Reject Run.	Random
4_{1s}	Four consecutive controls exceed the +1 SD or –1 SD limit. Reject Run.	Systematic
10_{x}	Ten consecutive controls fall on the same side of the mean. Reject Run.	Systematic

or –1 SD limits. When 10 consecutive controls fall on the same side of the mean, the 10_x rule is violated. The Westgard rules are summarized in **Table 6-9**.

Emerging Technology: Point-of-Care Analyzers

Point-of-care testing is a rapidly growing part of healthcare and takes place in critical care units, surgery, the emergency department, cardiac care units, and neonatal and pediatric units. Other uses for POC testing include interfacility transport and physician office testing. Benefits of POC include rapid turnaround time and enhanced patient management. The goal of POC testing is to offer a test whose result provides a more rapid, yet still accurate result to the healthcare provider that leads to a more timely medical decision and the initiation of appropriate care.

POC technologies are built on principles similar to those of clinical laboratory analyzers. Electrochemistry has been developed for the POC analysis of glucose, pH, blood gases, electrolytes, BUN, and creatinine. Lateral flow-immunoassay is used to identify infectious agents such as group A streptococcus (*Streptococcus pyogenes*), viruses such as influenza, human chorionic gonadotropin (hCG) for pregnancy, and certain cardiac markers. These methods were first developed for qualitative testing, or to identify the presence of an analyte or compound, but now have quantitative capabilities when combined with a detection system. The test system consists of layers of a porous material that contains reagents specific to react with the analyte to be tested. The top layer contains a semipermeable membrane that will trap red blood cells and other larger molecules that may interfere with the test. As the sample diffuses through the membrane, if present, the analyte will react with the reagents and form a chromogen, or colored compound. The color intensity is proportional to the amount of analyte present. This can be quantitated using principles of light scattering, reflectometry, electrochemistry, or turbimetric methods.

Biological sensors or immunosensors have been developed to measure troponin, infectious agents, and antibodies to identify an immunologic response to infectious agents. In this type of flow-through technology, a gold-labeled antibody is bound to a porous surface matrix. If the sample contains the analyte to be tested for, the analyte binds to the antibody. Next, a second antibody is added that is labeled with biotin or another measureable compound, forming a sandwich containing the first antibody, the analyte, and then the second antibody. This complex is trapped on the membrane, but can travel laterally along the membrane until it reaches the "capture area," where the compound streptavidin is bound to a solid, nonmovable phase. Biotin in the antibody binds to the streptavidin, which immobilizes the complex. It is visualized as a colored band, which is measured and then quantitated using the reflectometer.

Other technologies adapted to POC testing include light scattering, used in coagulation testing; spectrophotometry for bilirubin, hemoglobin, and chemistry analytes; electrical impedance for hematology blood cell counts, and fluorescence for C-reactive protein (CRP), cardiac markers, and drugs.

POC blood gas analyzers permit in vitro analysis at the patient's bedside, in the emergency room, or in the intensive care unit. These units use solid state sensors with fluorescence or thin-film electrodes. The microchips, reagents, calibrators, and a sampling device are all contained within a disposable cartridge system for single analysis. Healthcare facilities can select cartridges with additional test options, including potassium, glucose, BUN, and lactate. These are usually battery operated, but some also offer the advantage of operating using an electrical output. Manufacturers provide a range of flexibility as to the number of tests per cartridge (single or multiple) and test menu based on the needs of the facility.

The standard components of most POC units include an operator interface, a bar code device to easily identify the type of test being performed, a sample delivery method, a reaction cell, sensors, quality control, data management, storage, and a retrieval system.

Advantages of POC devices include their ease of use and rapid results—most results can be available in minutes. Because whole blood can be tested, minimal specimen processing is needed; the sample does not have to centrifuged and the plasma separated from the red blood cells prior to testing. There are minimal operating steps and the units are small and portable. The reagent cartridges eliminate the need to prepare reagents and there are flexible test menus that can be aligned with the needs of the unit. Calibration and quality control are integrated into the unit, which eliminates the need for separate calibrators and QC material. The calibration and QC, however, cannot be overridden, so the operator cannot report a patient result if the calibration fails or if the QC is out of control.

There are, however, potential concerns with POC testing. With diverse testing personnel from a variety of education, or lack of education, backgrounds, testing may not be performed correctly. Preanalytical errors involving sample identification, collection, and input are also possible concerns. Those who are not educated on the importance of sample collection and testing protocol may perform tests incorrectly and report invalid results. These results may negatively impact patient care. Therefore, problems with training and competency of operators remain a large concern. Quality control and a proficiency testing protocol with corrective actions and documentation need to be provided for any instrument malfunctions or out of control situations. Although some testing devices provide auto-verification and prevent reporting of patient results when calibration or quality control fails, other analyzers permit the operator to override and report the results. There may be problems with the accurate and timely recording of data, including QC, calibration, and patient results. Because some operators are not trained sufficiently to learn the importance of laboratory testing, significant errors may occur in each phase of testing. The desire to turn out a result, any result—accurate or not—may be the overriding goal because the operator has other responsibilities to their patient. Some POC devices are not electronically interfaced into the patient's medical record and may not be compatible with the laboratory's information management system. In these cases, results need to be manually entered into the medical record or laboratory information management system, increasing the propensity for transcription error. Transcription errors can compromise patient care, especially if the error goes unrecognized and the patient is treated on erroneous results.

There may also be duplication in testing, which is costly and not efficient. Patients may have specimens collected and tested in the core laboratory while having the same or similar tests performed via POC. POC testing, although convenient, uses many consumable cartridges and supplies, which can add cost to the facility and to the patient. Duplicate testing systems for the same analyte add cost to the facility and to the laboratory when considering the cost to purchase or rent the analyzer as well as costs for supplies, reagents, and maintenance. Finally, POC testing does not always completely correlate with values obtained on traditional laboratory analyzers, due to specimen type and methodology. Thus, the healthcare provider must be cognizant of the type of analysis performed before altering a diagnosis or treatment regimen. Even with broader menu flexibility, POC testing does not offer the comprehensive testing menu of the core clinical laboratory. Yet POC testing fulfills important and critical healthcare needs of patients and providers, and is indeed here to stay. Future developments in the area of POC testing will most likely continue.

Current Blood Gas Technology

Prior to 2005, blood gas analyzers directly measured pH, pO_2, and pCO_2 and provided calculated parameters for HCO_3^-, percent oxygen saturation, and base excess. These were large analyzers with gas tanks and manual quality control. Sampling was more cumbersome and specimens could be easily exposed to air during collection and sample analysis. Today's analyzers provide a variety of test menus, which may include electrolytes and other measured analytes and self-contained reagent cartridge systems. Quality control is electronically generated and there are features for auto-calibration and auto-verification. Manufacturers offer a complete testing approach that includes a corresponding sample collection device, methods of analysis, and reporting of results, which often can be directly entered into the patient's electronic medical record. Rear-venting syringes with lyophilized heparin improve the sample collection by reducing exposure to oxygen and minimizing the fibrin clot formation.

Matching Analyzer Type to Clinical Setting

Today's blood analyzers used in POC settings with low- to medium-volume testing use self-contained reagent cartridges. Single-use cartridges contain the calibration solution and miniaturized electrochemical sensors that are needed for analysis. These single-use systems are portable and easy to transport. They are recommended for settings with a test volume of less than 10 samples per day. Sensor electrodes in single-use cartridge systems are self-calibrating and can flag calibration errors. The analyzer and electrodes require little, if any, maintenance and a calibration is performed before any measurement is released. In the event of a calibration error, the calibration is flagged and the results are suppressed. Problems due to blockage from fibrin clots are confined to the cassette in use. The cartridge containing the

waste, blood, and calibration fluid is removed from the analyzer and disposed of in a biohazard container.

In settings with medium- to high-volume sample testing, a multiuse cartridge system is used. These cartridges can be customized to the specific analyte menu and to the volume of testing. The number of samples measured on a cartridge may vary from 25 to 750. Once loaded onto the analyzer, the cartridge has an in-use life of between 14 and 30 days. For cost effectiveness, the appropriate size cartridge is selected to meet the unit's workload volume.

There are also larger analyzers that provide sensor electrodes and reagents, such as calibrators, wash solutions, and quality control materials in either a modular format or as individual reagent containers. These systems include a closed waste system and feature reduced downtime compared with earlier models. These larger analyzers may require more maintenance to replace or to remembrane sensor electrodes, replace tubing or peristaltic pumps, or replace a gas cartridge when compared to the smaller volume analyzers. Thus, the larger analyzers may require additional technical support and expertise.

As discussed previously in this chapter, modern analyzers utilize a variety of technologies to measure and report results. These include potentiometry, amperometry, and fluorescence. Ion-selective electrodes are used to measure the electrolytes, Na^+, K^+, Ca^{2+}, Cl^-, and Mg^{2+}. The hematocrit is measured using conductivity, and hemoglobin is measured using spectrophotometry. CO-oximetry measurement is based on optical measurements of analytes at a number of wavelengths of light.

Laboratory Processes: Calibration and Quality Control

Calibration allows the analyzer responses to be set and adjusted to a known standard reference. Newer analyzers use aqueous tonometered solutions for calibration. These are available in sealed units. A one-point calibration adjusts the electrode to one level, either high or low. It is frequently performed and is automatically conducted by some analyzers before each measurement is released. A two-point calibration adjusts the electrode at two levels, high and low, and is set by the operator at intervals ranging from every 2 to every 24 hours. Calibrations can be preset at scheduled intervals.

Internal quality control is designed to detect and monitor errors in the testing procedure, but will not detect errors in sample collection and handling. Internal QC assures the operator that the reagents and analyzer are operating correctly; it will identify many analytical errors. The frequency of QC depends on the level of testing done and the specifications of the manufacturer and standards of the accrediting agencies. Internal QC may also be conducted manually using individual gas ampules that contain aqueous control solutions that are equilibrated with gas mixtures. Today, most analyzers utilize automatic on-board quality control materials that simplify the process and reduce operator workload, while producing a more consistent quality control program. Electronic QC requires no user input and automatically detects, corrects, and monitors the status of the analyzer's internal electronics.

Because QC can be automatically scheduled into the analyzer, it doesn't get delayed if the healthcare provider is attending to patient care issues. The automatic QC can be scheduled to run three levels at three times a day; the operator must still verify the results. Further, operators cannot attempt to analyze expired QC or incorrect QC materials, another concern with older testing systems. In the past, operators may have had to rerun a calibration or QC to obtain values that are accepted or are in range. This practice delayed patient care and perhaps compromised patient results, and also added to the cost of the test.

Currently Available Analyzers and Units Used for Blood Gas Analysis

In the early days of blood gas analysis, there were four major equipment manufacturers: Corning (now Siemens), Instrument Laboratories (IL), Nova Biomedical, and Radiometer. These four manufacturers still exist, and there are several other vendors worldwide, including Roche.

Each manufacturer has product lines that meet the needs of the testing facility, based on the volume of testing, test menu, and speed of analysis. There is also flexibility when choosing the degree of operator-initiated and internal quality control, calibration, and verification. Whereas surgery requires a POC analyzer that produces fast and accurate results, the needs of the neonatal ICU are directed more toward trending, and what the patient's results are from day to day. For example, smaller critical care units may opt for a bench top unit, such as Siemen's 405, which offers tests for blood gases, glucose, hemoglobin, hematocrit, calcium, electrolytes, and a full co-oximeter panel. The QC is automatically run by the analyzer, but does require operator verification. Larger volume critical care units may choose larger analyzers that can accommodate a higher test volume, such as the Siemens 1265. Adult medical and surgical critical care units may rely primarily on specific parameters, such as the blood gases, whereas pediatric testing in neonatal units often requires a broader test menu. There is also flexibility in the cartridge size; for example, Siemens offers a 450-specimen and a 700-specimen cartridge for the 405 series analyzers. Again, a facility can choose the more cost-effective and appropriate cartridge for its testing setting.

Larger volume analyzers generally require increased maintenance, which includes checking the electrodes, calibrating the barometer, and deproteinizing the electrodes. Linearity studies, calibration verification, and other surveys required by the College of American Pathology (CAP) are also required throughout the year. However, even large-volume modern blood gas analyzers require significantly less manual maintenance than did their predecessors. Whereas older analyzers required pathways to identify the problem, today's analyzers offer more self-maintenance. The testing cartridge contains the reagents and components, in place of reagent bottles and ampules that would have to be replaced. Cartridge-based systems provide flexibility in the test menu and can be selected based on the testing volume. Because cartridges last 2 to 4 weeks, the menu and type of cartridge can be adjusted to meet the needs of the facility. The electrode module is similar to that of earlier units, and therefore requires appropriate maintenance.

By choosing the same manufacturer, units can be selected that meet the needs of the core laboratory, critical care units, surgery, neonatal care units, and emergency room. Consolidation to a single vendor as compared to using different analyzers and vendors for different departments is both cost effective and beneficial for inventory management. There are less items to inventory and to order and less products to be knowledgeable about. Further, there is consistency in the results from the POC units to the larger units that may be used in the respiratory department or laboratory. The ability to communicate with one vendor and to become familiar with its products minimizes issues with testing. Further, there is a greater agreement with patient values when the same product line or methodology is used.

The Siemens products also interface into the laboratory's information system, so that the operator can review historical data, tracking, test ordering and canceling, and quality audits.

The Instrument Laboratory (IL) also offers products with POC and traditional central core laboratory capabilities. The GEM 3000 series provides self-contained plug-in cartridges, eliminating the need to prepare reagents and to pump in the gas mixtures. There are also important quality control features, including IL's proprietary Intelligent Quality Management (IQM) System. Quality control between the central laboratory and POC is more consistent and standardized through the IQM system. Auto-validation is another feature of the IL analyzers; the system runs a fully automated QC sequence immediately after the aspiration of each patient sample and before test results are released. In the past, it was necessary to aspirate blood gases two times in a row to determine precision. Other features of the IL system include enhanced clot detection, low sample warning flags, and detection of biosensor malfunctions. However, because of these technology checks, the analysis time is extended from 1 minute to approximately 4 minutes from aspiration to result. The IL analyzers run over 100 QC each day on average, which further assists with compliance and consistency of results.

Other advantages of modern analyzers include the concept that the instrument is continuously up and running. Clogged aspiration probes, electrode drift, or replacing electrode membranes used to be labor-intensive procedures requiring a skilled professional. Upon completion of such tasks, a calibration and full QC were required, which often led to instrument down time and delays for patient results.

Less staff time is needed to test daily QC and to install and recalibrate gas cylinders, and there is a more efficient mechanism to document errors. For IL analyzers, new electrodes are included in each GEM cartridge, so there is no need to remembrane or replace failed electrodes. Other advantages include integrated sample collection devices. For example, the GEM systems use a flexible heparin tube for pediatric patients whose volume is sufficient to perform blood gases, and also electrolytes and other analytes.

The GEM system also offers an add-on module for CO-oximetry analysis (GEM-OPL), which is interfaced into the main testing unit. The GEM-OPL uses six wavelengths of light, but does not require hemolysis of the sample. It uses thin-slide translucency technology that requires only 50 µL of blood and a disposable cuvette. The full CO-oximetry panel is reported within 10 seconds.

Roche's line of analyzers includes the cobas b 221, which is also a multiparameter analyzer for blood gases, CO-oximetry, electrolytes, and metabolites. It is designed to be a high-volume analyzer, and is not considered to be a portable unit. These units also use reagents to generate the gases, eliminating metal tanks for O_2 and CO_2. Roche's cobas b 123 is a POC system that features a mobile blood gas analyzer with a selection of 15 parameters. The system uses a patented thick-film sensor technology and a broad test menu with results within 2 minutes. Another feature of the cobas b 123 is its four-level clot protection system as well as automatic linearity testing and calibration. Roche's Electronic Quality Assurance Program (eQAP) assists with QC, regulatory compliance, and the ability to participate in peer review and benchmarking of quality control.

Radiometer, manufacturer of the ABL line of analyzers, patented its "First Automatic" technology, designed to improve workflow by improving sample collection, processing, analysis, and reporting. Its goal is to provide a system with fewer preanalytical errors; better identification of patient, sample, and results; and less paperwork. Radiometer's ABL 800 Flex analyzer offers a comprehensive test menu of 18 analytes and rapid

TABLE 6-10
Currently Available Analyzers

Manufacturer	Model	Category	Measured Analytes				Volume	Features
			Blood Gas	Electrolytes	Metabolites and Other Tests	CO-Oximetry		
Siemens	RAPIDLab 1200 Systems	POC	pH, pCO_2, pO_2	Sodium (Na^+), Potassium (K^+), Calcuim (Ca^{2+}), Chloride (Cl^-)	Glucose, lactate, neonatal total bilirubin	Total hemoglobin (tHb), deoxyhemoglobin (HHb), oxyhemoglobin (O_2Hb), Oxygen saturation (sO_2), Carboxyhemoglobin (COHb), Methhemoglobin (MetHb)	Medium to high	Clot detection and clearance sampling system, automatic QC, comprehensive menu
	RAPIDPoint 350	POC	pH, pCO_2, pO_2	Na^+, K^+, Ca^{2+}, Cl^-	Hematocrit		Low to medium	Single reagent cartridge; dialysate mode; 75–120 µL sample
	RAPIDPoint 340	POC	pH, pCO_2, pO_2				Low to medium	Single reagent cartridge; dialysate mode; 75–120 µL sample
	RAPIDLab 248	Critical care	pH, pCO_2, pO_2				Critical care testing	Small sample size, 50–95 µL; analysis in 45 seconds
	RAPIDLab 348	Critical care	pH, pCO_2, pO_2	Na^+, K^+, Ca^{2+}, Cl^-	Hematocrit		Critical care testing	Small sample size, 50–95 µL; analysis in 50 seconds
	RAPIDLab 348	POC	pH, pCO_2, pO_2	Na^+, K^+, Ca^{2+}, Cl^-	Hematocrit			Dialysate mode; low volume; enhanced operator features
	RAPIDPoint 500	POC	pH, pCO_2, pO_2	Na^+, K^+, Ca^{2+}, Cl^-	Glucose, lactate	tHb, HHb, O_2Hb, sO_2, COHb, MetHb, neonatal total bilirubin		Data management system
Instrument Laboratory (IL)	GEM Premier 4000	POC	pH, pCO_2, pO_2	Na^+, K^+, Ca^{2+}, Cl^-	Glucose, lactate, neonatal total bilirubin, hematocrit	tHb, HHb, O_2Hb, sO_2, COHb, MetHb		Self-contained, multiuse cartridges, Intelligent Quality Management (IQM) System

(*continues*)

TABLE 6-10
Currently Available Analyzers (*Continued*)

Manufacturer	Model	Category	Measured Analytes				Volume	Features
			Blood Gas	Electrolytes	Metabolites and Other Tests	CO-Oximetry		
Instrument Laboratory (IL)	GEM Premier 3500	POC	pH, pCO_2, pO_2	Na^+, K^+, Ca^{2+}, Cl^-	Glucose, lactate, hematocrit			Self-contained, multiuse cartridges, IQM
	GEM Premier 3000	POC and centralized testing	pH, pCO_2, pO_2	Na^+, K^+, Ca^{2+}, Cl^-	Glucose, lactate, hematocrit, prothrombin time (PT), activated partial thromboplastin time (APTT), activated clotting time (ACT), activated clotting—time low range (ACT-LR)	tHb, HHb, O_2Hb, sO_2, COHb, MetHb	Large volume	Comprehensive test menu; customizable cartridges; can add coagulation and CO-oximetry units
Roche	cobas b 123 POC	Critical care	pH, pCO_2, pO_2	Na^+, K^+, Ca^{2+}, Cl^-	Glucose, lactate, hematocrit	tHb, HHb, O_2Hb, sO_2, COHb, MetHb	Medium to small volume	Results within 2 minutes; thick-film sensor technology
	cobas b 121	Critical care	pH, pCO_2, pO_2					Small sample size
	cobas b 221 system	Critical care	pH, pCO_2, pO_2	Na^+, K^+, Ca^{2+}, Cl^-	Glucose, lactate, hematocrit, BUN, bilirubin	tHb, HHb, O_2Hb, sO_2, COHb, MetHb	Medium to high	
Radiometer	ABL 800 FLEX	POC and centralized testing	pH, pCO_2, pO_2	Na^+, K^+, Ca^{2+}, Cl^-	Glucose, lactate, creatinine, bilirubin	tHb, HHb, O_2Hb, sO_2, COHb, MetHb	Medium to high volume	First automatic and FlexQ features
	ABL 90 FLEX	Acute care	pH, pCO_2, pO_2	Na^+, K^+, Ca^{2+}	Glucose, lactate, bilirubin	tHb, HHb, O_2Hb, sO_2, COHb, MetHb	Medium volume	Comprehensive acute care panel, 35-second turnaround time
	ABL 80 FLEX		pH, pCO_2, pO_2	Na^+, K^+, Ca^{2+}, Cl^-	Glucose, hematocrit	tHb, HHb, O_2Hb, sO_2, COHb, MetHb	Medium to low volume	

Note: Table is not comprehensive and includes only measured, not derived, parameters.

analysis. Its FLEXQ module automatically identifies, mixes, and measures up to three samples in succession.

Although some blood gas systems permit the integration of POC results into the electronic medical record, other systems have this capability only for the centralized laboratory or respiratory care unit. Concerns continue with the ability of some analyzers to handle fibrin clots, which relates to the expertise of the individual drawing the arterial blood sample. Cleaning the arterial line to avoid diluted samples and avoiding clots within the specimen are dependent upon each person's training. Although the newer analyzers can detect clots and bubbles, a clot will still cause problems with the system until it is removed.

Today many hospitals use POC instruments in conjunction with stand-alone instruments to verify results obtained on POC analyzers. Both POC and stand-alone analyzers are subject to Clinical Laboratory Improvement Amendments of 1988 (CLIA) regulations. Some of the currently available analyzers are summarized in **Table 6-10**.

The accuracy and precision of results are related to the degree of technology, but equally important is the expertise of the testing personnel. Testing in the central laboratory is conducted by appropriately educated laboratory professionals who maintain regulatory compliance. Nonlaboratory personnel who use POC systems may not be fully cognizant of the influence of physiologic and analytical factors on the final result, which could lead to improper treatment decisions. Up to 68% of errors in blood gas measurements in point-of-care are related to sample collection, handling, and preparation that invalidate the results regardless of the technology of the analyzer.

References

1. Department of Health and Human Services, Health Care Financing Administration, Public Health Service. Clinical laboratory improvement amendments of 1988; final rule. *Federal Register.* 1992 February 28. Available at: https://www.federalregister.gov/clinical-laboratory-improvement-program. Accessed June 14, 2014.
2. National Committee for Clinical Laboratory Standards (NCCLS). Procedures for the collection of arterial blood specimens, 1999. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC87384. Accessed June 26, 2014.
3. Browning JA, Kaiser DL, Durbin CG Jr. The effect of guidelines on the appropriate use of arterial blood gas analysis in the intensive care unit. *Respir Care.* 1989;34(4):269-276.
4. Jordan A. Blood gas: A brief anecdotal history by one who has been there. MLO-online. 2012. Available at http://www.mlo-online.com/articles/201209/blood-gas-a-brief-anecdotal-history-by-one-who-has-been-there.php. Accessed July 10, 2014.
5. Paxton A. Blood gas analyzers—the old and the new. CAP Today. August 2007. Available at: http://www.cap.org/apps/portlets/contentViewer. Accessed June 25, 2014.
6. Shapiro BA, Mahutte CK, Cane RD, Gilmour IJ. Clinical performance of a blood gas monitor: A prospective, multicenter trial. *Crit Care Med*. 1993;21(4):487-494.
7. Klæstrup E, Trydal T, Pedersen JF, Larsen JM, Lundbye-Christensen S, Kristensen SR. Reference intervals and age and gender dependency for arterial blood gases and electrolytes in adults. *Clin Chem Lab Med.* 2011;49(9):1495-1500.
8. Crockett AJ, McIntyre E, Ruffin R, Alpers JH. Evaluation of lyophilized heparin syringes for the collection of arterial blood for acid base analysis. *Anaesth Intensive Care.*1981;9(1):40-42.
9. Thomson JM. Blood collection and preparation techniques: Pre-analytical variation. In: Jespersen J, Bertina RM, Haverkate F, eds. *EACT Assay Procedures: A Manual of Laboratory Techniques.* Dordrecht, Netherlands: Kluwer Academic; 1992:13-20.
10. Pruden EL, Siggaard-Andeson L, Tietz NW. Blood bases and pH. In: Burtis CA, Ashwood ER, eds. *Tietz Fundamentals of Clinical Chemistry.* Philadelphia: WB Saunders; 1996:211-223.
11. Adams AP, Morgan-Hughes JO, Sykes MK. pH and blood-gas analysis. Methods of measurement and sources of error using electrode systems. *Anaesthesia*. 1967;22(4):575-597.
12. Beetham R. A review of blood pH and blood-gas analysis. *Ann Clin Biochem*. 1982;19(Pt 4):198-213.
13. Severinghaus JW, Astrup PB. History of blood gas analysis. I. The development of electrochemistry. *J Clin Monit.* 1985;1(3):180-192.
14. Severinghaus JW, Astrup PB. History of blood gas analysis. III. Carbon dioxide tension. *J Clin Monit*. 1986;2(1):60-73.
15. Reynafarje B, Costa LE, Lehninger AL. O_2 solubility in aqueous media determined by a kinetic method. *Anal Biochem*. 1985;145(2):406-418.
16. Gehring H, Duembgen L, Peterlein M, Hagelberg S, Dibbelt L. Hemoximetry as the "gold standard"? Error assessment based on differences among identical blood gas analyzer devices of five manufacturers. *Anesth Analg.* 2007;105(6 Suppl):S24-S30.
17. Toobiak S, Sher EA, Shaklai M, Shaklai N. Precise quantification of haemoglobin in erythroid precursors and plasma. *Int J Lab Hematol*. 2011;33(6):645-650.
18. Kazmierczak SC. Laboratory quality control: Using patient data to assess analytical performance. *Clin Chem Lab Med*. 2003;41(5):617-627.
19. Siggaard-Andersen O. The van Slyke equation. *Scand J Clin Lab Invest Suppl.* 1977;146:15-20.
20. Lang W, Zander R. The accuracy of calculated base excess in blood. *Clin Chem Lab Med*. 2002;40(4):404-410.
21. Albert V, Subramanian A, Rangarajan K, Pandey RM. Agreement of two different laboratory methods used to measure electrolytes. *J Lab Physicians.*2011;3(2):104-109.
22. Ronkainen NJ, Halsall HB, Heineman WR. Electrochemical biosensors. *Chem Soc Rev.* 2010;39(5):1747-1763.
23. D'Orazio P. Biosensors in clinical chemistry. *Clin Chim Acta*. 2003;334(1–2):41-69.
24. Borisov SM, Wolfbeis OS. Optical biosensors. *Chem Rev*. 2008;108(2):423-461.
25. Carraro P, Plebani M. Errors in a stat laboratory: Types and frequencies 10 years later. *Clin Chem*. 2007;53(7):1338-1342.
26. Bonini P, Plebani M, Ceriotti F, Rubboli F. Errors in laboratory medicine. *Clin Chem*. 2002;48(5):691-698.
27. Biswas CK, Ramos JM, Agroyannis B, Kerr DN. Blood gas analysis: Effect of air bubbles in syringe and delay in estimation. *Br Med J (Clin Res Ed)*. 1982;284(6320):923-927.
28. Davies MW, Mehr S, Morley CJ. The effect of draw-up volume on the accuracy of electrolyte measurements from neonatal arterial lines. *J Paediatr Child Health.*2000;36(2):122-124.
29. Weibley RE, Riggs CD. Evaluation of an improved sampling method for blood gas analysis from indwelling arterial catheters. *Crit Care Med.* 1989;17(8):803-805.
30. National Committee for Clinical Laboratory Standards (NCCLS). C46-P Blood gas and pH analysis and related measurements. 2000. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC87384. Accessed June 26, 2014.

31. Bisson J, Younker J. Correcting arterial blood gases for temperature: (When) is it clinically significant? *Nurs Crit Care*. 2006;11(5):232-238.
32. Westgard JO, Klee GG. Quality management. In: Burtis CA, Ashwood ER, eds. *Tietz fundamentals of clinical chemistry*, Philadelphia: WB Saunders; 1996:211-223.
33. O'Kane MJ, McManus P, McGowan N, Lynch PL. Quality error rates in point-of-care testing. *Clin Chem*. 2011;57(9):1267-1271.
34. Piva E, Plebani M. Interpretative reports and critical values. *Clin Chim Acta*. 2009;404(1):52-58.
35. Rensburg MA, Nutt L, Zemlin AE, Erasmus RT. An audit on the reporting of critical results in a tertiary institute. *Ann Clin Biochem*. 2009;46(Pt 2):162-164.
36. Kost CJ. Critical limits for urgent clinical notification of US medical centers. *JAMA*. 1990;263(5):704-707.
37. Schoenmakers CH, Naus AJ, Vermeer HJ, van Loon D, Steen G. Practical application of Sigma Metrics QC procedures in clinical chemistry. *Clin Chem Lab Med*. 2011;49(11):1837-1843.
38. Harel O, Schisterman EF, Vexler A, Ruopp MD. Monitoring quality control: Can we get better data? *Epidemiology*. 2008; 19(4):621-627.
39. Westgard JO. Internal quality control: Planning and implementation strategies. *Ann Clin Biochem*. 2003;40(Pt 6):593-611.