# A primer of Point of Care Blood Gas Testing for laboratorians

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**Purpose**
**This document serves as a general guide for Blood Gas Analysis (BGA) testing that can be useful for laboratory personnel who perform BGA. This document is not a comprehensive guide for interpretation of BGA for medical and treatment purposes.**

# Contents

# 1.   INTRODUCTION

Point-of-care testing (POCT) is performed in a variety of locations both within and outside of the laboratories. There has been a driving force for more testing to be performed outside of the laboratory as clinicians are demanding faster test turnaround closer to the patient.

Blood gas analysis (BGA) is a clinical laboratory test that is often performed at the point-of-care by healthcare professionals (respiratory therapists, nurses, physicians, physician assistants, anaesthesia technologists, cardiovascular perfusionists) other than the traditional medical laboratory scientists who usually operate in the core laboratory. BGA is usually performed with benchtop or portable blood gas analyzers. Healthcare providers have the option to select blood gas analyzers that offer combination of analytes and test menus to meet their clinical needs.

Arterial, venous, or capillary blood gas analysis is an important diagnostic tool for a variety of critical care conditions. The core analytes in BGA (typically $pO_2$, $pCO_2$, pH) and Hb can be used to assess oxygen uptake, oxygen carrying capacity, and the acid-base status of the patient.

While blood gas POCT has many advantages, there are challenges that need to be considered when implementing it; some of these challenges are listed below:

- Increased supervisory/management workload
- Errors due to lack of expertise and insufficient quality control
- Problems of comparability of results of different methods (laboratory versus non laboratory)
- Increased costs due to additional instrumentation, expensive reagents & enrolment in external quality assurance programs
- Inadequate documentation of results

The objective of this document is to provide up to date educational information on blood gas testing covering the following items:

- Selection of appropriate system
- Sample collection and handling
- Typical analytes on a blood gas analyzer and result interpretation
- Connectivity

## Quality control and eQA

- Competency

# 2.   BACKGROUND – SELECTION OF APPROPRIATE SYSTEM

Prior to acquiring any point-of-care equipment it is recommended that all stakeholders are part of the decision-making process. This includes medical staff, POCT coordinators, the staff who will be performing the testing and end users for advice on requirements. If all stakeholders are consulted, the equipment selected will be appropriate for the testing environment.

Selection of a blood gas instrument must address both the clinical context and the testing environment that it will be used in, since a variety of instruments and testing panels are available for different settings. If they will be used at the point-of-care, they will need to have features that will allow for their easy transport, have a smaller footprint, have QC lock out features and ideally have the capability to either send results wirelessly or via Ethernet to a data manager.

A list of organizational requirements to implementing POCT blood gas testing includes:

- Analysis of costs and benefits including eligibility for reimbursement
- Does the equipment need to be transported regularly?
- What space is available for equipment?
- Conduct a literature research for evaluations of appropriate instruments for clinical purpose
- Capability to evaluate appropriate equipment and reagents
- Ensure, if possible, electronic capture of results
- Ensure availability of technical support
- Availability of appropriate quality control and external proficiency material

# Instrument Menu

A number of analytes can be measured either directly or indirectly (through calculation) including pH, partial pressure of $CO_2$ ($pCO_2$), partial pressure of $O_2$ ($pO_2$), Hematocrit (Hct), sodium (Na), potassium (K), chloride  (Cl), ionized calcium (iCa), lactate, glucose, creatinine, ionized magnesium (iMg), bilirubin, % oxygen saturation ($sO_2$%, O2SAT), base excess, total carbon dioxide ($TCO_2$), bicarbonate ($HCO_3^-$), blood urea nitrogen (BUN), anion gap, co-oximetry (Hemoglobin fractions).

A decision has to be made whether some analytes are better measured directly as opposed to indirect measurement. For example, in surgical settings, hemoglobin is probably better measured directly rather than calculated from the hematocrit because if the patient is given a substantial amount of fluid as part of the procedure, it can alter the hematocrit and this will in turn affect the hemoglobin concentration (1). Measurement methods usually employed for the various analytes include amperometric, potentiometric, electrochemical, conductometric or photometric.

Reagents are in the form of disposable, single-use or multi-use electrodes or cartridges or microsensor cards that come in standard packages of 1, 25, 50, or more. The number of tests that can be performed per cartridge is important when determining cost.

Manufacturer storage requirements must be followed in order to obtain the reagent/microsensor stability claimed by manufacturer which typically ranges from a two week to 6 months.

# Calibrations and Quality Control

Blood gas analyzers utilize both 1 and 2-point calibration systems.   Furthermore, the application of internal monitoring systems allows for the detection, correction, and documentation of some system errors. The frequency of the calibration is either before every test or can be on an automated time schedule. Some instruments can allow interruption of the calibration to perform a STAT sample.

POCT blood gas analyzers can contain various QC functions which may be in the form of on- board liquid QC and/or internal monitoring systems; additionally some systems provide an external QC simulation device.

With the help of a data manager, comparable plot/monthly cumulative reports can be generated. Monthly reports can include a number of calculated statistics, e.g., number of measurements, mean, maximum, minimum and delta values.

# Specimen requirements

Blood gas analysis can be performed on arterial, venous or capillary samples; however an arterial sample is needed for information on oxygen uptake from the lungs. Heparin is the only appropriate anticoagulant. Proper handling is required to avoid pre-analytical errors (see pre-analytical error section).

The volume requirement of the specimen varies depending on the analyzer, the number of tests ordered as well as the design of the sampling device. Arterial and venous blood is typically collected on a syringe, but when sample volume is of critical importance, a capillary sample may be taken. The time to result from the moment the specimen is introduced into the analyzer depends on the particular test or panel and ranges from 35 seconds to 2 minutes.

## Warranty/service

The average life-expectancy for blood gas instruments is usually between 5-10 years. Some devices need to be sent to the manufacturer for servicing or replacement while others can have on-site service. It is important to explore the different types of warranty offered and whether a loaner device is provided.

## Cartridge Storage and Instrument Preparation

Always make sure to follow manufacturer instructions for storage of consumables such as sensors, cartridges, test cards, calibration solutions, QC materials etc.  Manufacturer instructions may change over time, so it is important to review current product instructions.   Also, always follow manufacturer's recommendation for installation and use of instrument.

# 3.  PRE-ANALYTICAL SOURCES OF ERROR

To get high quality results it is recommended to have a dedicated pre-analytical blood gas program at each institution to manage the entire process around blood gas testing, including continuous training and careful selection of both blood gas sampling devices and analyzers that minimizes the risk of pre-analytical errors.

According to a study by Carraro and Plebani, pre-analytical errors are responsible for up to 62% of all errors in laboratory medicine. The analytical phase accounts for 15% and the post analytical phase for 23% of errors (1). According to the Clinical and Laboratory Standards Institute (CLSI) (2) several aspects of blood pH and gas analysis are unique among clinical and laboratory determinations, and test results can have immediate impact on patient care. Also, as precisely described by Baird in a 2013 publication (3) *"The preanalytical steps in testing, from choosing the correct tests to ensuring the specimen is introduced into the instrument correctly, must be perfectly coordinated to ensure that the patient receives appropriate and timely therapy in response to the analytical results. While many of the pre-analytical steps in blood gas testing are common to all laboratory tests, such as accurate specimen labeling, some are unique to this testing because of the physicochemical properties of the analytes being measured"*.

The resources available to generate a dedicated pre-analytical blood gas program can be found in the literature, via guidelines and resources on the internet like webinars and videos, and most blood gas analyzer manufacturers also offer dedicated preanalytical training. For a list of recommended resources, **see APPENDIX A.**

## Sample collection

It is recommended to use sampling devices that are designed for safe blood gas sample collection (for both patient and operator) and for obtaining high quality results. Consider the following:

1. **For arterial blood sampling**:
   Choose short-beveled needles: they are easier to position inside the artery and reduce the risk of puncturing the opposite artery wall.

- This helps users to position the needle correctly and allows for the patient to experience a smoother sampling process with reduced pain. An audit on arterial blood gas sampling showed that half the patients (49% of n = 20) recalled pain levels of 5 and above on a visual analogue scale (0-10) (4). Use of arterial local anesthesia, such as lidocaine, for arterial blood sampling can also be considered but should be carefully evaluated before adopted in practice (5).

- Use self-filling syringes as they fill readily when puncturing the artery and aid in keeping the sample anaerobic thereby limiting interference from environmental air.
    - The bias introduced if a vein is accidentally punctured during arterial sampling will depend on the initial values of both the arterial and venous specimens, but the most impact is typically on $pO_2$ where the result will be a falsely low. In addition, blood gas specimens should be obtained anaerobically to avoid admixture with room air that can cause a bias on blood gas parameters.

2. Select pre-heparinized syringes with sufficient concentration of heparin to reduce the risk of clots.
    - Clots in a blood gas sample may lead to inaccurate patient test results and interfere with the analyzer, thus anticoagulation is needed to reduce the clotting of the sample. Heparin is the only anticoagulant recommended for blood gas analysis. Excessive (too high) levels of heparin concentration in the vacutainer tube may lead to bias on the patient test results; in contrast not enough heparin in the vacutainer test tube may lead to insufficient anticoagulation.

3. **Use blood gas syringes pre-heparinized with dry electrolyte-balanced heparin to reduce**:

    i. **The risk of electrolyte bias**
    - Due to its chelating properties, heparin will bind positively charged ions, leading to falsely low results. Bias from the use of heparin is most pronounced on the positively charged ions like $iCa^{2+}$ and sodium. Manufacturers have developed different solutions to compensate for this and it is recommended to consult manufacturer's documentation for specific product capability on reducing or eliminating heparin bias on test results.

    ii. **Sample dilution**
    - If the syringe is anticoagulated immediately before sampling via flushing of the syringe with liquid heparin, there is a risk of variation in the heparin concentration from sample to sample and dilution of the sample due to the leftover liquid heparin that can't be expelled, e.g. present in the tip. This can potentially lead to insufficient anticoagulation and risk of clots if heparin concentration is too low or bias on results if heparin concentration is too high (6)

4. **Employ procedures/processes to reduce the risk of patient-sample mix-ups**.
    - Incorrect or missing patient and sample IDs are some of the most frequent and critical pre-analytical errors. Correct identification of the patient is extremely important for subsequent clinical interpretation because an immediate action is often warranted following availability of blood gas results. Thus a process for correct identification should be easy to implement by operators.

    - Consider the following recommendations:
        - Use at least two patient identifiers when collecting arterial samples, e.g. patient's name and date of birth or an accession number
        - Make sure the arterial syringe has a patient ID label attached to it before you leave the patient
        - Always enter a patient ID into the analyzer before analysis

- Consider if specimen identification and blood gas syringe labeling can be automated, such as through bar-coded wristbands and pre-barcoded syringes to avoid transcription errors.

5. **Choose syringes that come with a tip cap that is vented to ensure the safe removal of air bubbles and to avoid contact with patient blood**.

6. **If available, use a protection device for the safe removal of needles**
   - Operator safety is a key focus area in the pre-analytical phase, and it is recommended to take organizational steps for developing and implementing a sharps injury prevention program that creates a safe environment for operator and patients. Safety engineered sampling devices are available on the market, and this should be taken into consideration when selecting a blood gas sampling device.

# Sample storage time, sample preparation and sample transport

In addition to the above listed considerations for selection of blood gas sampling device, also consider sample storage temperature and time, sample transport, and sample preparation before analysis. Parts of this will depend specifically on the sampling device used, and in any case, the manufacturer's recommendations should be always be adhered to initially. The following should be considered:

## Sample storage temperature and time

After sampling of a blood gas specimen, the metabolism will continue and is dependent on factors like storage temperature, time to analysis and the individual patient condition.

Glass and plastic samplers have different gas-diffusion characteristics affecting $pO_2$ and $pCO_2$ and it is known that sampling devices made of glass may be stored at colder temperatures. If plastic is used, room temperature is likely the right temperature.

The following changes may be caused by continued metabolism of heparinized arterial blood gas samples that are obtained anaerobically and stored at room temperature

| Parameter | Change | Biochemical reason |
|-----------|--------|--------------------|
| $pO_2$ | ↓ | The cells that utilize oxygen continue to do so in vitro |
| $pCO_2$ | ↑ | $CO_2$ is a product of the metabolism |
| pH | ↓ | Increase in $CO_2$ causes a fall in pH <br> Hydrogen-ion increase due to continued glycolysis |
| Glucose | ↓ | Due to continued glycolysis |
| Lactate | ↑ | Due to continued glycolysis |

*Table 2: Blood Gas Parameter Changes Due to Metabolism in Storage*

For individual blood gas samples, the degree of metabolism will vary with the leukocyte count and other factors (7).

Manufacturer recommendations should always be followed. Below a summary of factors to consider:
- Storage should in principle be avoided whenever possible or, at least, kept to a minimum. POCT should be considered to cut down storage time.
- If it is not possible to analyze the sample immediately, analyze it within 30 minutes after collection (8, 9, 10, 11, 12, 13, 14).
- Samples with expected high $pO_2$ values or for special studies (shunt studies) should be analyzed immediately or within 5 minutes. The use of glass syringes can also be considered (10, 12, 13)

- For some samples, the recommendations above do not apply and individual guidelines should be used or developed. Examples are samples with an increased leukocyte or platelet count, fetal scalp samples, samples with atypical metabolism, fast-clotting samples, etc. (14)
- Certain analytes are affected differently by storage periods, and manufacturer documentation should be consulted to determine the storage period that is acceptable for the tested analyte.

## Sample transport

Some hospitals transport samples to the central laboratory via a pneumatic tube transport system (PTS). Factors to be considered before PTS is used are:

- Is the sampling device designed and tested for PTS?
- If air bubbles are not removed before pneumatic tube transport, the bias effect on $pO_2$ test results will be increased significantly.

The topic of pneumatic tube transport and impact of presence of room air is discussed in various publications, and is summarized below:

- PTS has no effect on pH or $pCO_2$ (15-20)
- PTS does not affect $pO_2$ as long as $pO_2$ is close to that of ambient air (~20 kPa) (22)
- PTS can cause an increase in $pO_2$ for samples whose $pO_2$ is significantly less than 20 kPa, and a decrease in $pO_2$ for samples whose $pO_2$ is significantly greater than 20 kPa (22)
- The main cause of these changes in $pO_2$ induced by PTS is contaminating air (i.e. bubbles in syringe) (21,22)
- Clinically significant aberrant $pO_2$ results can occur if samples are not purged of air bubbles before transport via PTS (19,22,23)

The following are recommendations to avoid potentially erroneous $pO_2$ results due to pneumatic tube transport issues:

- If air can be reliably excluded from an arterial sample before transport, the changes in $pO_2$ induced by PTS would be clinically insignificant (19, 22, 23)
- Protocols aimed at purging air from arterial specimens are neither 100 % effective nor universally applied (19, 20, 22)
- The effect of PTS on $pO_2$ values can be ameliorated by reducing the speed at which samples are sent via PTS (22) and by sending samples in pressure-sealed containers (20 )

## Sample Preparation

Sample mixing is important to obtain reliable results, in particular for hemoglobin. The sampling device must be designed to ensure proper mixing, manually or automatically. Samples must be mixed immediately after collection and just prior to testing. Recent studies have highlighted the importance of proper mixing to ensure reliable and accurate hemoglobin results (24).
It is recommended to consult manufacturer's specifications for specific products capability of adequate mixing for homogeneous sample and correct test results. Also, the use of automatic mixing of samples to ensure a homogeneous sample should be considered.

# 4. TYPICAL ANALYTES ON A BLOOD GAS ANALYZER & RESULT INTERPRETATION

Examples of analytes that are measured as part of blood gas analysis are shown in Table 3.

| Analyte | Symbol | Description |
|---|---|---|
| Partial pressure of oxygen | $pO_2$ | Measurement of oxygen tension in blood; arterial $pO_2$ ($pO_2$ (a)) indicates oxygen uptake from the lungs to the blood |
| Partial pressure of carbon dioxide | $pCO_2$ | Measurement of carbon dioxide in blood; arterial $pCO_2$ ($pCO_2$(a)) indicates the adequacy of pulmonary ventilation |
| pH | pH | Negative logarithm of the hydrogen ion concentration; indicates acidity or alkalinity of blood |
| Bicarbonate | $HCO_3^-$ | Often calculated from pH and $pCO_2$ using the Henderson-Hasselbalch equation; standard bicarbonate uses a constant $pCO_2$ of 5.33 kPa (40 mmHg) whereas actual bicarbonate uses both the measured pH and $pCO_2$. Used as an aid in identifying the source of an acid-base disturbance. Standard $HCO_3^-$ is standardized with the aim to eliminate effects of the respiratory component on the $HCO_3^-$. $HCO_3^-$ is classified as the metabolic component of acid-base balance. |
| Sodium | $Na^+$ | Major extracellular cation; important in maintaining osmotic pressure and regulating water balance |
| Potassium | $K^+$ | Major intracellular cation; important in cardiac and neuromuscular function |
| Chloride | $Cl^-$ | Major anion in the extracellular fluid; important in maintaining osmotic pressure |
| Ionized calcium | $iCa^{2+}$ | Cation involved in bone homeostasis and blood coagulation |
| Ionized magnesium | $iMg^{2+}$ | Co-factor in more than 300 enzymatic reactions and involved in muscle function |
| Glucose | Glu | Measurement used to identify dysglycemia (hypoglycemia or hyperglycemia) |
| Lactate | Lac | Anion useful in assessing adequacy of tissue oxygenation (e.g., sepsis, trauma); waste product from anaerobic metabolism; early sensitive indicator imbalance between tissue oxygen demand and oxygen supply. |
| Creatinine | Cr | Endogenous waste product of muscle creatine; excreted in the kidneys and indicates renal function status |
| Blood urea nitrogen/urea | BUN/urea | End product of protein metabolism, used to indicate renal function status, often in conjunction with creatinine |
| Bilirubin, total | tBil | Product of hemoglobin metabolism; frequently used to monitor neonatal jaundice |
| Hemoglobin | Hb or tHb | Concentration of total hemoglobin (both functional and nonfunctional; $HHb+O_2Hb+COHb+MetHb$), the major carrier of oxygen in blood. |
| Hematocrit | Hct | Measurement of packed red cell volume, indirect indicator of hemoglobin concentration |
| Oxygen saturation of hemoglobin | $sO_2$ | Percentage of oxygenated hemoglobin relative to total functional hemoglobin; indicates the utilization of the currently available oxygen transport capacity |
| Oxyhemoglobin | $O_2Hb$ | Functional hemoglobin that is oxygenated |
| Deoxyhemoglobin (reduced) | HHb | Functional hemoglobin that is not oxygenated |
| Carboxyhemoglobin | COHb | Nonfunctional hemoglobin with bound carbon monoxide; elevated in smokers and carbon monoxide poisoning |
| Methemoglobin | MetHb | Nonfunctional hemoglobin with iron in the oxidized ferric state ($Fe^{3+}$); elevated concentrations may cause cyanosis; formed when blood is exposed to certain oxidizing agents; has a very low affinity to $O_2$ resulting in decreased oxygen-carrying capacity. |
| Fetal hemoglobin | HbF | Major hemoglobin moiety (50-80%) in neonates at birth. Less than 2% in adults; elevated in some hemoglobinopathies (sickle cell anemia) and neoplastic conditions (leukemia) |

*Table 3: Measured analytes on blood gas analysers*

Additionally, there are several calculated results associated with BGA, examples of which are shown in Table 4.

| Analyte | Symbol | Description |
|---|---|---|
| Anion Gap | AG | Difference between the measured cations (positively charged ions) and the measured anions (negatively charged ions). A high anion gap indicates metabolic acidosis. |
| Base Excess | BE | An estimate of the metabolic component of the acid-base balance. The base excess is defined as the amount of acid or alkali that would be required to return the pH of the blood to 7.35 if the $pCO_2$ were adjusted to normal; BE may help determine whether an acid/base disturbance is a respiratory, metabolic for mixed metabolic/respiratory problem<br><br>Base(Ecf) is independent from changes on $pCO_2$ and is also called "in-vivo base excess" or "standard base excess" (SBE). |

*Table 4: Examples of Calculated ABG Parameters*

# Guide to Results Interpretation

Understanding and interpreting BGA requires knowledge about the clinical condition of the patient. The laboratorian does not need to know all of the details of BGA but should understand the basics. There are a number of tools available for basic interpretation of BGA that laboratory staff should be familiar with. Some of these resources are listed in **APPENDIX B.**

It is vital that blood pH is maintained within the narrow range of 7.35-7.45. Even mild excursions outside of this range can have severe adverse effects and a pH of <6.8 or >7.8 is incompatible with life. The maintenance of blood pH is controlled by the concentration of bicarbonate and pCO₂ as per the Henderson-Hasselbalch equation below:

$$pH \propto \frac{[HCO_3^-]}{pCO_2}$$

This equation is essential for understanding and interpreting blood gas results. The pH will fall if either the pCO₂ is increased or if the bicarbonate is decreased and the pH will rise if either the pCO₂ is decreased or if the bicarbonate is increased. However, the pH will remain unchanged if both the pCO₂ and bicarbonate are increased or decreased by the same relative amount.

Disturbances in a patient's acid-base status are characterized by **one or more** of the three parameters (pH, pCO₂ and bicarbonate) being outside of the reference range.

At a very basic level, by using reference intervals to (classify a blood gas results as normal, elevated or depressed) and the following interpretative chart, it is possible to quickly classify a patient's acid/base disorder as being respiratory or metabolic in nature.

| Disorder | pH | pCO₂ | HCO₃⁻ | BE |
|---|---|---|---|---|
| Metabolic Acidosis | ↓ | - | ↓ | ↓ |
| Respiratory Acidosis | ↓ | ↑ | - | - |
| Metabolic Alkalosis | ↑ | - | ↑ | ↑ |
| Respiratory Alkalosis | ↑ | ↓ | - | - |

↓ = initially decreased, ↑ = initially increased, - = initially normal

*Table 5: Results Interpretation Chart*

# Reference intervals

Examples of representative reference intervals for the various analytes that may be available on a blood gas analyzer are listed below.

| ABG test | Units | Examples of reference interval |
|---|---|---|
| pH | pH | 7.35–7.45 |
| $pCO_2$(a) | mmHg (kPa) | M 35–48 (4.7-6.4)<br>F 32–45 (4.3–6.0) |
| Bicarbonate ($HCO_3^-$) | mmol/L | 18 -23 |
| Base excess (BE) | mmol/L | -4 - 2 |
| $pO_2$(a) | mmHg (kPa) | 83-108 (11.1-14.4) |
| $sO_2$(a) | % | 95-98 |
| Hemoglobin (Hb) | g/dL (mmol/L) | M 13.2 – 17.3 (132 – 173)<br>F 11.7 – 15.5 (117 – 155)) |
| $ctO_2$ | mmol/L | M 23.3-29.7<br>F 22.3-28.4 |
| $p50$ | mmHg (kPa) | 25–29 (3.3-3.9) |
| MetHb | % | 0–1.5 |
| COHb | % | 0.5-1.5 |
| Lactate | mg/dL (mmol/L) | 4.5–14.4 (0.5-1.6) |

*Table 6: Analyte Reference Intervals*

It could also be beneficial for laboratorians to have access to nomograms that assist in the interpretation of blood gasses. Two examples have been given below:
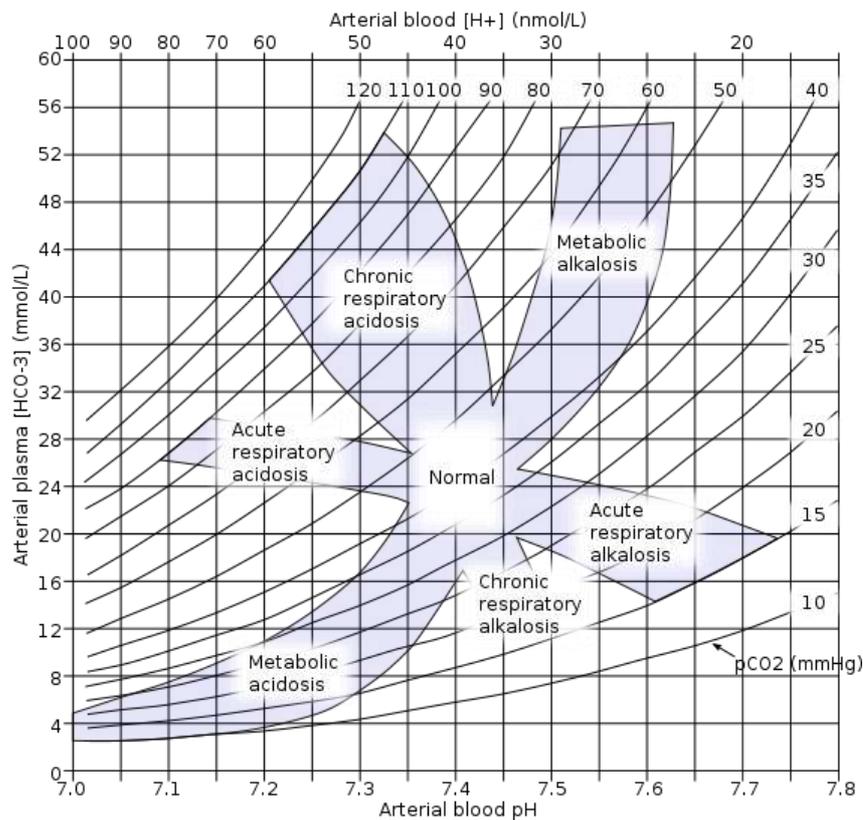


**Diagram 1: For use with pH and bicarbonate ($HCO_3^-$) results**
(Reproduced with permission from McGraw-Hill Medical Education, USA)
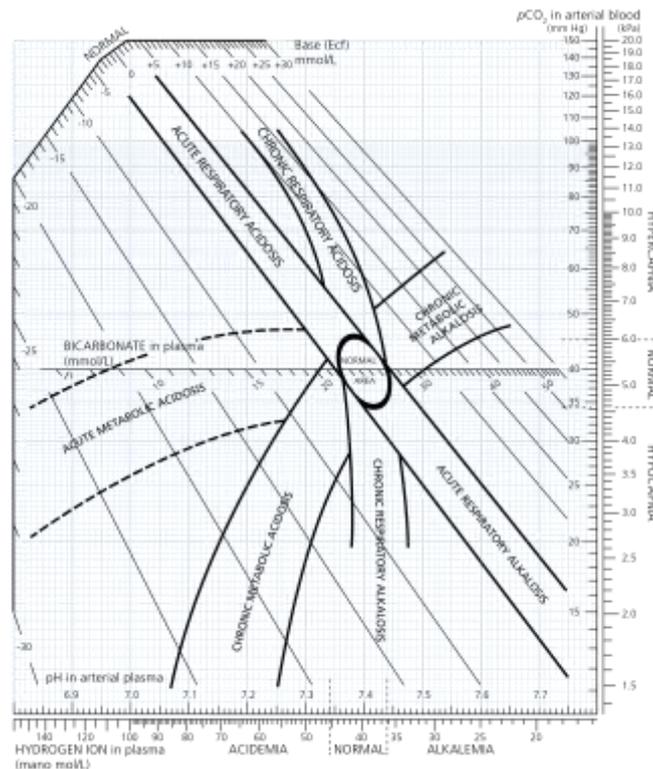
**Diagram 2**: Siggaard-Anderson Acid-Base Chart
(reproduced with permission from Radiometer Medical ApS, Denmark)
For use with pH and $pCO_2$ results.

# Clinical case studies

The information contained in this section can now be used to interpret blood gas results and investigate a clinical case study:

A patient underwent pulmonary endarterectomy. During the procedure their blood gas analysis at one time point was (reference intervals given in parenthesis):

| | | |
|---|---|---|
| pH | 7.31 | (7.35-7.45) |
| $HCO_3^-$ | 18 mmol/L | (22-28) |
| $pCO_2$ | 35 mmHg | (35-45) |

We can see that pH is low, as is $HCO_3^-$, whereas $pCO_2$ is normal. Using the given nomogram, this patient has metabolic acidosis. This is also supported by the Interpretive Chart and the Henderson-Hasselbalch equation.

$$\textbf{pH} \propto \frac{HCO_3^-}{pCO_2} \quad \rightarrow \quad \textbf{pH} \downarrow \propto \frac{HCO_3^- \downarrow}{pCO_2 \ (N)} \quad \rightarrow \quad \text{metabolic acidosis}$$

See APPENDIX C for more clinical case studies.

# 5.  CONNECTIVITY OF DEVICES

Getting blood gas results to the treating physician in a controlled, timely manner is vitally important. A well-designed and implemented connectivity solution can help direct results to into the correct patients' notes, and also provide the support required for efficient analyser and operator management.  Connectivity has become such an integral advantage to POCT programs that in many countries the main elements of a networked service are now required for POCT accreditation. Some of the benefits of a professional connectivity software solution are:

- Possible to see the current status of all the analyzers on the network
- Patient results can be reviewed by the Lab Manager prior to release to the treating physician
- Patient data can be automatically routed to the appropriate electronic patient record (EPR)
- Malfunctioning analyzers can put into a safe 'Do Not Use' state, until remedial action can be performed
- Allows for comprehensive Operator Identity system to limit usage to certified operators and maintain records of operator usage
    – Advantageous for medium to large hospitals where the number of trained blood gas analyzer operators can quickly run into hundreds with a significant turnover.
- Operator and patient data can be managed centrally and downloaded to the network without the need for manual entry.

Most blood gas analyzer manufacturers can supply a data manager software package that will organize the data generated by the analyzer. This allows data, such as QC results, to be displayed in a useful chart so that operators can manage the analyzer effectively. There are also third-party companies that can provide interfacing tools for connecting an analyzer to the LIS and/or HIS.

In most hospitals, information technology (IT) resources have developed over time and cover the many and varied requirements of the hospital with a 'patchwork' of interconnected systems. To enable these systems to cooperate and share data, communication standards have been developed to allow products from different suppliers to work together. POCT1-A is a Point of Care Testing specific standard and details how remote blood gas analyzers, and other POCT systems, should communicate with information management systems within hospital locations. LIS02-A2 and HL7 have been developed primarily for clinical laboratory analyzers, but still represent the standard way for instrumentation to communicate with the LIS, HIS and other systems.

Without connectivity, hospitals must rely on printed hard-copy form, which requires documentation to be hand carried to the physician. The printout is then included in the patient notes using staples or sticky tape. The same results may have to be manually transcribed onto a chart. Additionally, all the Quality Control results for each of the blood gas analyzers have to be manually transcribed into a QC tracking system.

The maintenance of these systems depends entirely on a suitably trained individual walking to each blood gas analyzer in turn, manually checking the status of all the consumables and reacting to any error codes that the analyser may have encountered since it was last checked.

# 6.  QUALITY CONTROL and EXTERNAL QUALITY ASSESSMENT

Performing quality control (QC) enables the user to assess the stability of the analytical aspect of the instrument, to differentiate between random and systematic error, and to ensure that the accuracy and precision of the instrument has not changed significantly to invalidate the results.

The frequency at which the QC testing should be performed is dependent on many factors and should be determined individually by each site. For example, a benchtop blood gas analyzer with a high throughput of samples would require more frequent QC testing compared to a portable blood gas analyzer that uses single test cartridges or test cards. The results of QC testing can be compared on-site to assigned values and limits for acceptable performance that are set for each QC.

After applying various statistical rules (i.e. Westgard rules) to the results, it is determined if the run is "in-control" and whether or not the patient results can be released. Additionally, Westgard Rules can be used to help determine the cause of any bias in results, and therefore the direction of the corrective action necessary to bring the system into control. Patient specimens should only be analyzed if the QC result is within the acceptable criteria established by the laboratory director or designee. If it fails, then troubleshooting should be initiated according to the manufacturer's instructions.

As was defined by the Clinical and Laboratory Standards Institute (CLSI) and incorporated into the US laboratory regulations (CLIA '88,) an analytical run for the purposes of quality control "is an interval (i.e., a period of time or series of measurements) within which the accuracy and precision of the measuring system is expected to be stable." However, the concept of run length does not exist with single use diagnostic testing devices where each test is a run unto itself. With instrument-based systems, every time a new cartridge, pack, strip, etc. is inserted into the base instrument a quasi-new test system is created. Therefore, quality control must take a different form with POCT devices.

Quality control has been integrated into various POCT instruments by incorporating:

- Automation of calibration function
- Encoding (via bar-code or microchip) of crucial quality control and
- Quality assurance information on the unit dose packages
- On-board liquid quality control
- Real time process monitoring
- Inclusion of calibration solution in unit use electrode-based systems

An analytical instrument can be divided into three main sections:

- Mechanical/ electronic
- Analytical
- Reagent/calibrants

With some blood gas POCT systems, the mechanical/electronic and analytical components have been completely separated from the reagent/ calibrant components. In some systems, the analytical components are individually packaged with the reagents and calibrants. With these latter devices, the only consistent part from test to test is the mechanical/electronic component. All biosensors, electrodes, reagents and calibrants are replaced with every analysis. By separating the QC testing of these two subsystems an effective QC program can be developed for a POCT program that utilizes multiple instruments. The functionality of the mechanical/ electronic component of each analytical device in operation should be tested on a predefined frequency, e.g. every 24 hours. However, this does not replace the internal QC testing or external quality assessment (eQA).

## External quality assessment (eQA)

eQA is a quality assurance process designed to test all phases of the testing process: pre-analytical, analytical and post-analytical, and verify that the performance of an individual laboratory is similar to others using the same analytical system. Materials of known concentration are analyzed by the blood gas analyzer and the results are sent to the facility that distributed the material. The result is compared with other laboratories that tested the same material, using either the peer mean, method specific mean, all methods mean or, for commutable material, an established target value and total allowable error limits for the measure and or up to a 3 standard deviations limit if a total

allowable error limit has not been established.  The laboratory must investigate all eQA results that are unacceptable, and document the investigation and, when applicable, resolution, and any risk-reduction activities taken as a result of the investigation (1,2).


# 7.   COMPETENCY

## Competency Assessment
The aim of competency assessment is to ensure that the healthcare worker can generate quality results consistently from the instrument, and can correctly manage them in the decision-making process.  The reader is advised to refer to their regional regulations pertaining to competency assessment. However, in their absence, the following is a list of skills that should be assessed:

1.   Direct observations of patient testing:
     a.   Using a specimen (previously analyzed specimen, external proficiency testing material, quality control material or calibrator)
     b.   Include any specimen handling and processing
2.   Recording and reporting test results.
3.   Direct observation of instrument maintenance and function checks.
4.   Assessment of problem solving skills (reviewing temperature and QC logs and troubleshooting failed QC; knowledge of common error messages; knowing who to contact for help).
5.   Achieve a satisfactory level in a written examination.

User competencies should be documented in their personnel file. The POCT department should also keep a copy for their records for audits and inspections. Some BGA instruments often have middleware that have capability to keep track of user competencies.

**Reference:**
Khan AI: Quality Requirements for Point of Care Testing when Traditional Systems Fail. In: Global Point of Care: Strategies for Disasters, Emergencies, and Public Health Resilience, Editors: GJ Kost & CM Curtis, AACC Press 2015.


# 8.   ANALYTICAL SOURCES OF ERROR

The following describes analytes that have been reported in the past to be affected by certain interfering substances. This edited summary is taken from the CLSI document: Blood gas and pH analysis and Related Measurements – approved guideline, Second Edition 2009. Technology is continuously improving and so the manufacturer's package insert /manual should be consulted to determine what substance can affect these analytes.


***$pO_2$***
Nitrous oxide, halothane and isofluroane have been shown to cause interferences. However, newer generations of $pO_2$ sensors do not have this problem.

***pH***
Glass pH sensors do not show any interference. Some of the cartridge-based sensors use polymeric sensors that can be affected by interference from synthetic oxygen carriers.

***Sodium, potassium and calcium***
Benzalkonium compounds used in antiseptics have been shown to cause interference with some of these analytes.

### Magnesium

Calcium ions and pH may interfere with iMg measurement; it is recommended to measure iCa and pH simultaneously.

### Chloride

Interference has been shown by salicylates, thiocyanates, bromide, iodide, due to chloride sensors being based on anion exchange technology.

### Glucose/Lactate

Depending on the type of biosensors used, ascorbic acid, salicylate, acetaminophen, dopamine, fluoride and oxalate may cause interference.

### Hematocrit

Conductivity-based hematocrit measurements can be affected by electrolyte concentrations, and abnormal protein levels. Hematocrit estimated from measuring total hemoglobin is calculated using the mean corpuscular hemoglobin concentration (MCHC). Medical conditions affecting the MCHC can cause an abnormal hematocrit.

### Hemoglobin

Hydroxocobalamin, used to treat cyanide poisoning, has been shown to interfere with all of the hemoglobin fractions (carboxyhemoglobin, methemoglobin, and oxyhemoglobin). Methylene blue, used to treat methemoglobinemia, interferes with hemoglobin measurements as well as lipid emulsions.

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# APPENDIX A: Additional resources on blood gas pre-analytics

Below please find references to further reading concerning blood gas preanalytics:

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Smajić J, Kadić D, Hasić S, Serdarević N. Effects of post-sampling analysis time, type of blood samples and collection tubes on values of blood gas testing. August 2015. https://www.ncbi.nlm.nih.gov/pubmed/26276646

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## Guidelines

Clinical and Laboratory Standards Institute (CLSI). Blood gas and pH analysis and related measurements. Approved Guidelines – second edition. CLSI document C46-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2009. https://clsi.org/

Clinical and Laboratory Standards Institute (CLSI). Procedures for the collection of arterial blood specimens; Approved Standard – Fourth edition. CLSI document GP43-A4 (ISBN 1-56238-545-3). Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2004. https://clsi.org/


AARC Clinical Practice Guideline: Blood Gas Analysis and Hemoximetry: 2013
Michael D Davis, Brian K Walsh, Steve E Sittig and Ruben D Restrepo
Respiratory Care October 2013, 58 (10) 1694-1703; DOI: http://dx.doi.org/10.4187/respcare. http://rc.rcjournal.com/content/58/10/1694.full

Lora Dukić, Lara Milevoj Kopčinović, Adrijana Dorotić, Ivana Baršić. Blood gas testing and related measurements: National recommendations on behalf of the Croatian Society of Medical Biochemistry and Laboratory Medicine. Biochemia Medica 2016;26(3):318-36. http://www.biochemia-medica.com/2016/26/318

# APPENDIX B: Interpretation of results

Below is a list of some resources that are available for blood gas analysis. They include links to webpages or articles that the reader can access. The webpages were accessed by the authors of this document on the day that is specified below the link – these webpages may periodically change.

## Peer-reviewed articles

**American Thoracic Society. David A Kaufman. Interpretation of Arterial Blood Gases (ABGs)**
https://www.thoracic.org/professionals/clinical-resources/critical-care/clinical-education/abgs.php
*(Last accessed on September 28, 2017)*
This is a section of the Clinical Education component of the American Thoracic Society, in which Dr. Kaufman provides basic information on the interpretation of BGA. He describes a 6-step approach for the identification of acidemia or alkalemia (metabolic or respiratory), the acid-base disorders and a basic interpretation of the anion gap. The enclosed tables provide useful information to the reader.

**Pramod Sood, Gunchan Paul, and Sandeep Puri. Interpretation of arterial blood gas.** *Indian J Crit Care Med.* **2010 Apr-Jun; 14(2): 57–64.**
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2936733/
*(Last accessed on September 28, 2017)*
This article provides some key factors in the interpretation of arterial blood gas (ABG) analysis. It is particularly useful for laboratorians since it addresses issues of pre-analytical errors (i.e. venous instead of arterial samples, air bubbles in the sample, choice of anticoagulant, and the effect on results of delayed analysis. The article continues with basic interpretation of the major ABG findings in clinical conditions where blood gas analysis is instrumental in diagnosis. Flow diagrams and tables help the reader navigate through these conditions. At the end, some rules for rapid clinical interpretation of ABG are presented.

**Arterial Blood Gas (ABG) interpretation for medical students, OSCEs and MRCP PACES**
http://www.oxfordmedicaleducation.com/abgs/abg-interpretation/
*(Last accessed on September 28, 2017)*
This is a section from Oxford Medical Education and it is targeted for medical students to help them understand the basics of blood gas analysis. It lists the basic components of the ABG with a short description on each and examples of the clinical conditions associated with abnormal results. It also provides some clinical examples.

**Jones M.  Basic interpretation of metabolic acidosis.** *Crit Care Nurse*. **2010 Oct;30(5):63-9;**
https://www.ncbi.nlm.nih.gov/pubmed/20889514
*(Last accessed on September 28, 2017)*
This article describes the basic concepts of acid-base balance and metabolic acidosis. It provides the pathophysiology and the role of the respiratory and renal system in acid-base disorders. Case studies (diabetic ketoacidosis, gastroenteritis, cardiopulmonary bypass) are presented to indicate the role of blood gas analysis in identifying metabolic acidosis and anion gap.

**Singh V, Khatana, S and Gupta P. Blood gas analysis for bedside diagnosis. Natl Maxillofac Surg. 2013 Jul-Dec; 4(2): 136-141**
https://www.ncbi.nlm.nih.gov/pubmed/24665166
*(Last accessed on September 28, 2017)*
The article provides a description of arterial blood gas analysis and its role in monitoring postoperative patients. It has sections on basic physiology and conditions that cause an acid-base imbalance. Practical tips are also described for obtaining an arterial sample and interpreting the blood gas analysis results.

## Useful Websites and apps

There are many resources online (websites or apps) with information about blood gases. Some of these resources serve as a tool for education and training, some offer the opportunity for the reporting of different calculations, provide a graphical presentation of the data, or even give diagnostic advises.

Below is a list of websites that the authors of this document have found informative.

**Apps**
Useful apps can be found online that aid in the learning and interpretation of blood gas results . Availability of app varies between geographical regions and app providers, and examples are not included here.

**Labtest online**
https://labtestsonline.org/

**Arterial Blood Gas (ABG) interpretation for medical students, OSCEs and MRCP PACES**
http://www.oxfordmedicaleducation.com/abgs/abg-interpretation/

**Calculation and graphical interpretation of the acid-base and oxygen status of the blood**
http://www.siggaard-andersen.dk/

# APPENDIX C: Case studies

## Clinical Cases

### Case 1
Patient underwent pulmonary endarterectomy. During the procedure their blood gas analysis at one time point was (reference intervals given in parenthesis):

$$pH \quad 7.31 \ (7.35\text{-}7.45)$$
$$HCO_3^- \quad 18 \ mmol/L \ (20\text{-}28)$$
$$pCO_2 \quad 35 \ mmHg \ (35\text{-}45)$$

Since,

$$pH \propto \frac{HCO_3^-}{pCO_2}$$

$$pH \downarrow \propto \frac{HCO_3^- \downarrow}{pCO_2 \ (N)}$$

In this case there is an uncompensated metabolic acidosis.

### Case 2
A 24 year old woman is admitted to hospital with drug overdose. Blood pressure is normal. She is breathing rapidly and was given oxygen by the ambulance attendant. BUN and blood sugar are normal. Initial studies of gases and electrolytes show the following:

$$pH \quad\quad = 7.14$$
$$pCO_2 \quad = 30.1 \ mm \ Hg$$
$$pO_2 \quad\quad = 121.6 \ mm \ Hg$$
$$Na \quad\quad = 142 \ mmol/L$$
$$Cl \quad\quad = 103 \ mmol/L$$
$$K \quad\quad = 3.6 \ mmol/L$$
$$CO_2 \quad\quad = 18 \ mmol/L$$
$$HCO_3^- \quad = 9.9 \ mEq/L$$
$$O_2Sat \quad = 96.2\%$$

**Questions**:
1. Is the patient acidemic, alkalemic or "neutral"?
2. Does she have increased anion gap?
3. What are likely causes of this acid-base abnormality?
   *See answers below*

### Case 3
A man with chronic obstructive lung disease has fever, leukocytosis and thick sputum. He is admitted to hospital, where initial laboratory work reveals the following:

$$pH \quad\quad = 7.17$$
$$pCO_2 \quad = 61.2 \ mm \ Hg$$
$$pO_2 \quad\quad = 52.4 \ mm \ Hg$$
$$HCO_3^- \quad = 21.4 \ mEq/L$$
$$O_2Sat \quad = 75.8\%$$
$$Na \quad\quad = 143 \ mmol/L$$
$$Cl \quad\quad = 106 \ mmol/L$$

K        = 4.1 mmol/L
CO$_2$      = 28 mmol/L

**Questions:**
1. Does the patient have acidemia or alkalemia?
2. Are the alveoli ventilating properly?
3. Why is the bicarbonate not higher?
4. Does the patient have increased anion gap?
   *See answers below*


## Case 4

An 18-year old boy had acute post-streptococcal glomerulonephritis at age 12.  His mother is overprotective and has been tutoring him out of school since.  He takes meprobamate, penicillin, and reserpine.  For the past year he has been having attacks of tetany.

pH       = 7.52
$p$CO$_2$     = 22 mm Hg
Na       = 138 mmol/L
Cl       = 108 mmol/
K        =  3.3 mmol/L
CO$_2$      = 18 mmol/L
BUN     = 13 mg/dL
Ca       = 9.9 mg/dL
Mg       = 1.9 mEq/L
P        = 2.1 mg/dL

**Questions:**
1. Does the patient have acidemia or alkalemia?
2. Is the cause of the trouble respiratory or metabolic?
3. Are the alveoli ventilating properly?
4. What is the most likely cause of the acid-base imbalance?
   *See answers below*


## Case 5

A 74 year old woman has profound weakness and areflexia. She is incoherent. Electrolyte and gas studies on admission show the following:

pH       = 7.58
$p$CO$_2$     = 49 mm Hg
CO$_2$      = 42 mmol/L
Na       = 147 mmol/L
Cl       = 88 mmol/L
K        = 1.7 mmol/L

**Questions**:
1. Does the patient have acidemia or alkalemia?
2. Is the major problem metabolic or respiratory?
3. What are the possible causes of the distress?
4. Would potassium gluconate be good therapy?
   *See answers below*

**Case 6**

An 80-year-old woman is complaining of abdominal pain which is severe and has been there for about 12 hours. She appears to be in distress her respiratory rate is 30, BP 110/50, pulse 110. Her abdomen is acutely tender with guarding and rigidity.

A Venous blood gas taken on admission reveals

pH = 7.2
Oxygen = 45 mm Hg
$CO_2$ = 25 mm Hg
$HCO_3$ = 27 mEq/L
Lactate = 5 mmol/L

**Questions:**
1. Is this an acidosis or alkalosis?
2. Why is the $CO_2$ low?
3. If the $CO_2$ is low why is the pH 7.2?
4. Where is the acid coming from?
5. Why is the $HCO_3$ not lower?
   *See answers below*

# Answers to Case 2 – 6 Questions

### Case 2
Question 1:    pH of 7.14 indicates acidemia.
Question 2:    103(Cl) + 18 ($CO_2$) = 121, 142(Na) - 121 = 21 (anion gap)
              Normal anion gap is less than 12; therefore, anion gap is increased.
Question 3:    Azotemia and diabetic ketoacidosis can be ruled out. With normal blood pressure and good oxygenation, it is unlikely that she has poor perfusion leading to lactic acidosis. It is most likely that the drug she took caused the increased anion gap and acidemia. In this case the drug was ethylene glycol.

### Case 3
Question 1:    Patient is acidemic.
Question 2:    The alveoli are not ventilating properly. $pCO_2$ reflects alveolar ventilation.
Question 3:    The bicarbonate is not higher because this patient has acute respiratory acidosis. When the problem is metabolic, the lungs react almost immediately to bring the pH back to normal. The kidneys, on the other hand, are slower and take a longer time to compensate. In this patient, the bicarbonate steadily crept upward and mechanical ventilation brought the $pCO_2$ down, so that pH eventually became normal.
Question 4:    The anion gap is normal. Anion gap is rarely of much use except in metabolic acidosis.

### Case 4
Question 1:    The patient is alkalemic.
Question 2:    The patient's problem is primarily respiratory. If he were alkalemic for metabolic reasons, you would expect elevated bicarbonate and $pCO_2$.
Question 3&4:  The patient's lungs are well if not over ventilated. Since there is no mention of having mechanical ventilation, this boy must have been hyperventilating which caused a respiratory alkalosis. Note that calcium is normal.

**Case 5**

Question 1:     Patient is alkalemic.

Question 2:     The cause is metabolic in origin.

Question 3:     To diagnose the cause one must have more information.  She could have been vomiting or have diuretic therapy, or she might have Cushing's syndrome plus any of a number of much less common disorders.

Question 4:     Gluconate is not useful. This patient needs adequate chloride supplies to accompany the potassium, which should be prescribed.


**Case 6**

Question 1:     Patient is acidemic.

Question 2:     She has a respiratory compensation hence the low $CO_2$ secondary to the high respiratory rate.

Question 3:     Because of the elevated lactate (metabolic acidosis).

Question 4:     This patient has a source of ischaemic tissue (Ischaemic bowel) and the high lactate is due to a large amount of tissue with inadequate oxygenation which is producing lactic acid.

Question 5:     The $HCO_3$ is not lower because it is a relatively long-standing (12 hours plus) condition and she has also been compensating by her renal system retaining more $HCO_3$ and excreting more hydrogen ions.