The blood gas handbook
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Introduction

In the evaluation of the critically ill patient, the blood gas status plays a key role. Evaluation of blood gas parameters can be divided into subgroups of oxygen status, related metabolic parameters and acid-base status. Because each subgroup consists of several parameters, the amount of data to interpret may be overwhelming. It is not only the blood gas status, but all organ systems that need a careful evaluation related to the specific patient and the specific situation. It is therefore often helpful to have an easy-to-use guide to assist with some parts of the evaluation.

Part One of this handbook offers guidance to the evaluation of arterial oxygen status based on comprehensive blood gas analysis (i.e., including oximetry) and a closely related metabolic parameter, lactate. Some important general considerations related to blood sampling are also presented.

Part Two of the handbook describes parameters available from Radiometer’s blood gas analyzers, including blood gas and acid-base parameters, metabolic parameters and electrolytes as well as guides to evaluation of the parameters not included in Part One.

Although such a guide always has to be used with caution, as not every possible detail or condition can be covered, it can help the clinician make decisions with regard to the need for further tests and therapeutic interventions.

Kaare E Lundstrøm, MD
Sampling and sample handling

Radiometer recommends a structured approach to the analytical process of blood gas measurement, involving three phases:

- **In the preanalytical phase**, the decision to collect a sample is made, the sample is collected and, in some cases, stored and transported.

- **In the analytical phase**, the sample is analyzed. The performance of blood gas analyzers should be verified with a quality assurance plan to ensure that the analyzer is in control. This part is described in the relevant operator manuals and is not treated further here.

- **In the postanalytical phase**, correct interpretation of the data and subsequent treatment of the patient are facilitated by customized data management and reporting.
The preanalytical phase – before the sample is transferred to the analyzer – is the largest contributor of bias to blood gas measurement and therefore the weak link in the analytical process of blood gas measurements. Inappropriate sampling devices and improper handling can cause crucial inaccuracies in blood gas analysis as stated by NCCLS [6].

“Collection of a blood specimen, as well as its handling and transport, are key factors in the accuracy of clinical laboratory analysis and ultimately in delivering quality patient care... In blood gas and pH analysis incorrect results can often be worse for the patient than no result at all.”
The preanalytical phase

By following a few straightforward recommendations outlined here, preanalytical errors can be reduced.

Before sampling
The time of the sampling should be planned with the staff responsible for the treatment. In order to get a true picture of the patient’s condition, it is extremely important to record the exact status at the time of sampling, and the blood gas test should preferably be taken when the patient is stable. In general, it must always be remembered that a blood sample represents the status at the moment of sampling. This is extremely important especially when dealing with blood gas analyses, as many of the measured parameters can change significantly within seconds. It is therefore recommended to relate the blood gas values from a blood sample to the continuously monitored respiratory and circulatory parameters; these values must be recorded at the moment of sampling.

The blood sampler should contain sufficient heparin to prevent coagulation. Clots form in samplers with inadequate heparin and may block the analyzer or lead to inaccurate $p$CO$_2$, pH and hemoglobin measurements.

It is recommended to use preheparinized blood samplers with dry heparin. Liquid heparin dilutes the sample and causes errors that decrease the true value, often by more than 10%. If electrolytes are measured, electrolyte-balanced heparin should be used to prevent bias of the results. Non-electrolyte-balanced heparin will interfere with electrolyte measurements as the heparin will bind with cations, e.g., calcium or potassium.
Immediately after sampling
If air bubbles have formed in the syringe, cover the tip of the syringe with a piece of gauze, tap the syringe while holding it vertically, and expel the air bubbles.

When the air bubbles have been expelled, the sample should be closed with a tip cap and mixed thoroughly to dissolve the heparin. Failure to do so may lead to the formation of micro clots, which in turn can bias results and damage the analyzer. A patient ID label should be placed on the sampler barrel together with other information such as collection time, sampling site and type of sample, patient temperature, ventilator setting, etc. The temperature and $F_O_2 (I)$ affects the interpretation of the blood gas analysis and it is therefore important to record the patient’s temperature. If the patient temperature is entered into the blood gas instrument when analyzing the sample, the analyzer will be able to display temperature corrected results. $F_O_2 (I)$ is needed for correct calculation of $F_{shunt}$.

Storage and transport
In general, samples should be analyzed as quickly as possible to minimize the effects of continued metabolism, diffusion of oxygen through the plastic sampler and potassium leakage from red blood cells. If it is not possible to analyze the sample immediately, analyze it within 30 minutes after collection. The recommended storage temperature is room temperature. For more detailed information, please see [26].

Just before analysis
It is very important to ensure that the part of the sample that is transferred to the analyzer is homogeneous and representative of the whole sample. If not, significant errors can occur, particularly on the hemoglobin parameters. Therefore, it is important to mix the sample thoroughly by repeatedly
inverting it and rolling it horizontally. A sample that has been stored for 30 minutes may have settled completely, requiring a very thorough mixing.

The first few drops of blood from the tip of the syringe are often coagulated and not representative of the whole sample. Consequently, a few drops of blood should always be expelled, e.g., on a piece of gauze, before transferring the sample to the analyzer.

The postanalytical phase

When reporting results, it should be considered whether the results have been biased, particularly if they differ from the general assessment of the patient’s condition. If there is any suspicion of bias, it should be reported with the results and taken into account in the clinical decision-making.
Type of samples

Arterial samples
Arterial samples can be collected either by arterial puncture or by aspiration from an indwelling arterial catheter. Both methods have advantages and disadvantages.

Advantages

- Less risk of bias than arterial-line and capillaries if performed correctly
- Can be carried out in an emergency situation
- No catheter needed
- Requires less blood volume than catheter sampling

- Easy to obtain samples because of indwelling line
- Not painful to the patient
- Elimination of risk associated with multiple punctures
Disadvantages

- Painful to the patient, hyperventilation can potentially change blood gas values
- It can be difficult to locate arteries
- Risk of complications for the patient, not always advisable to perform arterial puncture
- User safety – risk of needle stick accidents
- Requires trained/authorized personnel

- Risk of infection with invasive catheter
- Risk of clotting leading to thromboses or emboli
- Risk of anemia because too much blood is removed (typically 5–6 mL per sample including waste)
- Risk of locally diminished or blocked blood flow leading to necrosis
- Risk of air contamination from catheter connections, etc.
- Risk of dilution errors if catheter is flushed insufficiently
Capillary samples
Capillary samples are often used for blood gas analysis, especially in neonatal and pediatric intensive care. However, this method has to be used with caution as several potential errors exist.

- The method is difficult to master in a way to eliminate the risk of false results, and it should only be performed by skilled personnel.
- Aeration of the sample is frequent and can cause significant changes in all respiratory parameters.
- Dependent on the peripheral circulation, capillary $pO_2$ often differs significantly from arterial values. Measures of oxygen status obtained from a capillary sample must always be interpreted with caution.
- There is risk of hemolysis causing changes in electrolyte status.

Venous samples
Peripheral venous samples are not recommended for blood gas analysis as they provide little or no information on the general status of the patient.

Samples obtained from central venous catheters can be used to evaluate mixed venous oxygen status. Misleading results can however be obtained if the sample is collected primarily from either the superior or the inferior vascular beds, or if cardiac left-to-right shunt on arterial level is present.

Oxygen status in mixed venous blood collected from a catheter placed with the tip in the pulmonary artery, is a useful tool to evaluate respiratory, metabolic and circulatory status of the patient. A low mixed venous oxygen content is a sign of impaired oxygen supply due to either low arterial oxygen availability or circulatory insufficiency with increased oxygen extraction.
As the ctO₂ may be low, aeration of a mixed venous sample may cause a relatively higher change in oxygen parameters than a similar aeration of an arterial sample.
Arterial oxygen status

General considerations
A major goal in intensive care medicine is to ensure sufficient oxygen supply to the organ systems. Oxygen supply is influenced by many factors, among which organ specific and systemic circulation, and oxygen status of the arterial blood are the most important. To optimally evaluate the oxygen supply, information concerning cardiac output and organ specific perfusion as well as arterial and truly mixed (not just central) venous oxygen status is required. Of major importance is also an estimation of the adequacy of the oxidative metabolism, typically provided by measurement of the lactate concentration in the blood.

However, all these parameters are not always available in the clinical situation. It is often necessary for the clinician to evaluate the general oxygen status primarily by the results of an arterial blood sample. Therefore, evaluation and optimization of the oxygen status of the arterial blood play a key role in the care of the critically ill patient.

The oxygen status of a patient may often be evaluated by looking at the partial pressure of oxygen ($pO_2$) and the oxygen saturation ($sO_2$) of arterial blood. However, although both are important parameters, $pO_2$ primarily reflects only the oxygen uptake in the lungs and $sO_2$ indicates only the utilization of the actual transport capacity of arterial blood. Despite normal $pO_2$ and $sO_2$, oxygen availability from the arterial blood may still be impaired. To get a more complete picture of the oxygen status, several parameters, not just $pO_2$ and $sO_2$, are required.
Based on documented physiology, the parameters related to the arterial oxygen status can be divided into three groups: oxygen uptake, oxygen transport and oxygen release.

Oxygen uptake in the lungs depends primarily on:

- The alveolar oxygen tension, which is primarily influenced by the ambient pressure, the $FO_2(I)$ and, though much less, by $pCO_2(a)$.
- The degree of intra- and extrapulmonary shunting ($FShunt$).
- The diffusion capacity of the lung tissue.

Other factors such as the content of hemoglobin in the blood ($ctHb$) and the oxygen affinity to hemoglobin ($p50$) also influence oxygen uptake. However, they are more important in other parts of the total arterial oxygen status and are therefore described later. The key parameter used for evaluating the adequacy of oxygen uptake is $pO_2(a)$. 
Oxygen transport, defined as the amount of oxygen being transported per liter of arterial blood, depends primarily on:

- The concentration of hemoglobin in the blood (ctHb)
- The concentration of dyshemoglobins
- The arterial oxygen tension ($pO_2(a)$)
- The arterial oxygen saturation ($sO_2(a)$), which again is determined by $pO_2(a)$ and $p50$

The key parameter used for evaluating the actual oxygen transport is the total content of oxygen in the arterial blood, ctO$_2(a)$.

It is not sufficient to use $sO_2$ as the only indicator of oxygen transport. An example of this is the patient with $sO_2$ of 97 % but a ctHb of 3.0 mmol/L and 20 % FCOHb.

Oxygen release depends primarily on:

- The arterial and end-capillary oxygen tensions and ctO$_2(a)$.
- The oxygen affinity to hemoglobin.

The release of oxygen is determined by the hemoglobin-oxygen affinity, which again is influenced by several factors (see later). The hemoglobin-oxygen affinity is expressed by the oxygen dissociation curve (ODC), the position of which is expressed by the value $p50$. 
Notes
Strategy for evaluation

The parameters $pO_2$, $ctO_2$ and $p50$ can be said to comprise the respiratory and hematological parts of the oxygen supply to the tissues. These are therefore the key parameters to focus on when arterial oxygen availability is evaluated. However, the interactions between the parameters are rather complex, and it is often difficult to predict the consequence of one or more of the parameters being too high or too low. Changes in one parameter may be completely or partially compensated for by the two other parameters. An example of this is the patient with hypoxemia, $pO_2(a)$ of 56 mmHg (7.5 kPa) and $sO_2$ of 79%. If the hemoglobin concentration is elevated, the patient may have normal arterial oxygen availability. On the other hand, the patient with the same $pO_2(a)$ of 56 mmHg (7.5 kPa) but $sO_2$ equal to 94% may have a significantly impaired oxygen availability if the hemoglobin concentration is low, or dyshemoglobins are present. In the clinical situation, the results of these kinds of interactions, though clinically of crucial importance, may be difficult to predict.

It is therefore imperative to evaluate both the oxygen uptake and the oxygen transport as well as the oxygen release to get the necessary information for adequate treatment. To ensure optimal use of all the information provided by an arterial blood gas status, a systematical approach to the evaluation of the parameters is needed.
Flow-chart for evaluation of oxygen status

The flowchart indicates the changes in the situation when arterial oxygen availability is impaired. It shows how deviations in parameters interact.

Many of the parameters influence each other to a certain degree, and some parameters not mentioned in the flowchart may also have some influence. However, to make the flowchart usable in the clinical situation, only the most clinically relevant parameters and interactions are included.

The user of the flowchart must not rely solely on the value of one parameter being in the expected range. All relevant parameters must be evaluated carefully along with the patient.

It is recommended to use the conventional indicators of oxygen uptake ($\rho O_2$), transport ($ctO_2$) and release ($p50$) initially as the three key parameters to focus on.
The flowchart is used as follows:
The parameters in the flowchart have levels of priority related
to order of evaluation. The key parameters \((pO_2, ctO_2, p50)\)
have the highest priority, and the level of priority decreases
to the right. In the column with the key parameters, the level
of priority decreases from top to bottom.

1. The first key parameter to evaluate is \(pO_2\)
2. When this is acceptable, the next key
   parameter is \(ctO_2\)
3. The third key parameter is \(p50\)

If the key parameter being evaluated deviates from the
expected range, you should focus next on the columns to
the right of that parameter. Here you will find the param-
eters influencing your key parameter. One or more of these
are possibly causing the deviation, and by manipulating these
parameters, it may be possible to optimize the key parameter.
Having done so, you continue with the next of the three key
parameters to be evaluated.

The arterial oxygen status can not be regarded as sufficiently
evaluated and optimized unless all three key parameters have
been considered in this way.
**Arterial oxygen status**

### Oxygen uptake

- $pO_2$
  - Increasing value
  - Decreasing value
  - (83-108 mmHg)
  - (11.1-14.4 kPa)

- $F O_2(I)$
- $F Shunt$
  - (1-10 %)

- $F CO_2$
  - (32-48 mmHg)
  - (4.3-6.3 kPa)

- Ambient pressure

### Oxygen transport

- $ctO_2$
  - Increasing value
  - Decreasing value
  - (7.1-9.9 mmol/L)
  - (15.9-22.4 mL/dL)

- $ctHb$
  - (7.4-10.9 mmol/L)
  - (12.0-17.5 g/dL)

- $F O_2Hb$
  - (94-98 %)

### Oxygen release

- $p50$
  - Increasing value
  - Decreasing value
  - (25-29 mmHg)
  - (3.3-3.9 kPa)

- $pH$
  - (7.35-7.45)

- $p CO_2$
  - (32-48 mmHg)
  - (4.3-6.4 kPa)

- Temp

- $c2.3$-DPG

- $F COHb$
  - (0.5-1.5 %)

- $F HbF$
Pulmonary disease
Cardiac right to left shunt
Low alveolar ventilation

True anemia
Hemodilution

\[ sO_2 \quad (95-99\%) \]
\[ FC0Hb \quad (0.5-1.5\%) \]
\[ FMetHb \quad (0-1.5\%) \]

\[ pO_2 \quad (see \ above) \]
\[ p50 \quad (see \ below) \]

Smoke or gas poisoning
Toxic effects

Metabolic alkalosis
Respiratory alkalosis
Hyperventilation

Hypophosphatemia
Smoke or gas poisoning
Neonates, hematological disorders
Example

Patient with low $pO_2$. $F_{Shunt}$ is found to be high and ventilator settings are changed to minimize the pulmonary shunt. This improves $pO_2$. Next, $ctO_2$ is evaluated and found also to be low. $sO_2$ is normal, but $ctHb$ is low and blood transfusion needed. Finally, $p50$ is evaluated and found to be low, expressing a leftshift of the ODC. This is due to a metabolic alkalosis and a slightly elevated concentration of carboxyhemoglobin. To improve oxygen release to the tissues, the left shift of the ODC is also corrected.
Evaluation of the three key parameters

1. $pO_2(a)$

Normal $pO_2$
Normal $pO_2$ indicates an adequate pulmonary oxygen uptake, and changes in ventilatory pattern will normally not be needed.

High $pO_2$
High $pO_2$ bears the risk of oxygen toxicity, and unless the high levels are specifically desired, action should be taken to reduce the high $pO_2$.

Low $pO_2$
If $pO_2$ is too low, it indicates an inadequacy of the oxygen uptake from the lungs. Check $F_{Shunt}$ as well as other measures of the pulmonary status (i.e. chest X-ray and pulmonary function test). Changes in $FO_2(I)$ and/or ventilator settings may be indicated as well as, if possible, specific treatment of the pulmonary or cardiac changes causing the hypoxemia.

2. $ctO_2(a)$

Normal $ctO_2$
Normal $ctO_2$ indicates adequate oxygen concentration in the arterial blood.
High ctO₂
High ctO₂ despite normal pO₂ can only be caused by high ctHb. This may increase the cardiac load inadvertently and hemodilution may be indicated.

Low ctO₂
If ctO₂ is too low and pO₂ is normal, it may be caused by low ctHb or the presence of dyshemoglobins. Rarely, an extreme right shift of the ODC as indicated by a high p50 can cause low ctO₂. Treatment of low ctO₂ despite normal pO₂(a) is typically red cell transfusion if ctHb is low or treatment of dyshemoglobinemia if present.

3. p50
When pO₂ and ctO₂ have been considered, p50 should be evaluated. This parameter describes the position of the ODC, which is essential for the oxygen release to the tissues. Physiologically, p50 is altered secondary to changes in several other parameters, and potentially harmful effects are thereby avoided. If necessary, it is often possible to influence the position of ODC by therapeutical interventions. Depending on the clinical situation, a low, a normal or a high p50 value (corresponding to a left shift, a normal position or a right shift of the ODC) can be the goal of interventions.
The general rules are:
A right-shift of ODC, e.g. caused by acidosis, facilitates oxygen release to the tissues.

A left-shift of ODC, e.g. caused by FHbF, facilitates oxygen uptake in the lungs (or in placenta), especially in situations with low $pO_2$.

Figure of ODC including factors shifting it to the left and the right.
Associated parameters in blood gas evaluation

Many factors influencing the arterial oxygen availability interact, and deviations in one parameter will often be totally or partially compensated for by opposite changes in another parameter.

In basic physiology, this is seen in fetal life where the major part of the hemoglobin is fetal hemoglobin with a high oxygen affinity. High concentrations of fetal hemoglobin shift the ODC to the left, ensuring a high oxygen binding capacity in the placental milieu with very low $pO_2$ values.

A more acute situation is the example of tissue acidosis during circulatory insufficiency. This shifts the ODC to the right, which again increases oxygen release to the tissue.

The effects of the interactions and compensatory mechanisms are highly relevant to the clinician.

Another important issue is to evaluate if tissue oxygenation is actually adequate for maintaining an oxidative metabolism. Despite a normal arterial oxygen availability, the oxygen delivery may be compromised due to poor circulation, poor oxygen availability may be compensated for by increased tissue perfusion, or metabolic changes may interfere with the oxidative metabolism.

There are two specific parameters which can help the clinician in the interpretation of the arterial blood gas status and the adequacy of oxygen supply: $p_x$ and concentration of lactate. These two parameters are therefore described in more detail.
$p_x$

$p_x$ is a measure of the oxygen extractivity of the arterial blood, reflecting the combined effect of $pO_2$, $ctO_2$ and $p50$. $p_x$ is defined as the oxygen tension after extraction of 2.3 mmol oxygen/L from the arterial blood at a constant pH and $pCO_2$, thereby reflecting the end-capillary $pO_2$, assuming standard conditions. The $p_x$ value must however not be interpreted as the mixed venous tension, as major differences between these two parameters may exist (see below).

The driving force for the oxygen diffusion is the pressure gradient between the capillary and the tissue cell; the end-capillary $pO_2$ is therefore important. Oxygen supply, especially to the brain, may be compromised if $p_x$ decreases below a certain point (about 5 kPa) and compensatory mechanisms (which are difficult or impossible to evaluate sufficiently in the clinical situation) are inadequate.

$p_x$ indicates the level of end-capillary $pO_2$ given a normal tissue perfusion and a normal oxygen demand. During such standard conditions, the normal oxygen extraction is 2.3 mmol/L. Oxygen release can be compromised if $p_x$ is below the normal range. Sufficient oxygen supply will, in this situation, often depend on an increased oxygen extraction, an increased tissue perfusion, or a decreased metabolic rate. Despite a normal venous oxygen tension, $p_x$ may be low if compensation for the impaired oxygen availability has taken place. On the other hand, $p_x$ may be normal and mixed venous tension very low if the circulatory status is compromised and oxygen extraction is increased.
In summary, $p_x$ reflects the adequacy of the arterial blood’s contribution to the oxygen supply to the cells. $p_x$ can be seen as the conclusion of the information available from one arterial blood sample regarding oxygen status. It provides, however, no information on the circulatory and metabolic status. Introducing a new parameter may seem to cause more confusion than clarification, as the number of parameters is already high, but this parameter actually simplifies the evaluation of arterial oxygen status. Though it is a calculated and theoretical parameter, with limitations due to this, $p_x$ is an easy-to-use tool for understanding the complexity of interactions in the arterial oxygen status.

$p_x$ is a theoretical and calculated parameter based on the determination of the ODC, which is quite sensitive to the quality of the measurements, especially if the ODC is based upon high $sO_2$ values; close to 97%. The information provided by $p_x$ must be interpreted with this in mind.
Interpretation of $p_x$-values

**Normal $p_x$**
The oxygen availability from arterial blood can be regarded as acceptable if $p_x$ is normal.

If, however, the cardiac output is low despite adequate therapy, or the oxygen demand is supranormal, further evaluation of the parameters influencing the $p_x$ value may show the way to improve the oxygen status, i.e. increase the $p_x$ value to supranormal levels (see below).

It is possible to reduce $FO_2(I)$ and ultimately mechanical ventilation to avoid adverse effects like oxygen toxicity and volu- or barotrauma to the lungs as long as $p_x$ is monitored and kept within the normal range.

**High $p_x$**
If $p_x$ is above the reference interval and the clinical situation suggests a normal oxygen demand and a normal cardiac output, then the oxygen supply may be unnecessarily high, indicating a risk of oxygen toxicity. In this situation, the oxygen tension ($pO_2$) typically is too high. If so, the risk of oxygen toxicity indicates interventions to reduce $pO_2$. Other causes of elevated $p_x$ could be high hemoglobin concentration, extreme acidosis, or too vigorous ventilation.

**Low $p_x$**
If $p_x$ is below the reference interval, it indicates inadequate oxygen availability from the arterial blood. $pO_2$, $ctO_2$ and $p50$ will be the primary foci of further evaluation\(^1\).

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\(^1\) For more detailed information of $p_x$, please see ref. [17]
Lactate

Inadequate oxygen supply will, in most cells of the body, cause production of excessive amounts of lactate. A critical degree of cellular hypoxia causes a shift from normal aerobic to anaerobic metabolism where lactate is produced. Lactate thus serves as a marker of critical imbalance between tissue oxygen demand and oxygen supply. In most situations, elevated blood lactate will be caused by hypoperfusion, severely impaired arterial oxygen supply, or a combination of the two. The overall goal of monitoring arterial blood gas status is to ensure an optimal arterial oxygen availability. Though not specific for arterial oxygen availability, lactate as a monitor of the adequacy of tissue oxygenation is a natural part of the arterial oxygen status evaluation.

In general, an elevated or increasing concentration of lactate should alert the clinician. Decreasing or persistently low levels of blood lactate (cLactate(P)) during critical illness signal successful treatment. Monitoring of cLactate(P) is a mean to monitor the adequacy of treatment of the critically ill patient.
Interpretation of cLactate(P)

Low or decreasing cLactate(P)
Treatment seems adequate, but if arterial oxygen availability is impaired, measures should be taken to improve it. However, extreme interventions with the risk of side effects may not be necessary. Examples of such could be treatment of low $pO_2$ by an increase of $FO_2(I)$ to levels possibly toxic to lung tissue, or treatment of high $FShunt$ by more aggressive ventilatory support, giving risk of volu- and barotrauma. Instead, blood gas status and cLactate(P) could be closely monitored.

High or increasing cLactate(P)
If arterial oxygen availability is impaired, measures to improve it must of course be taken. At the same time, the other parameters in the same column (circulatory and metabolic status) must be evaluated.

During circulatory impairment, it may be indicated to increase the arterial oxygen availability to levels in the upper normal range, or even higher, to compensate for the circulatory impairment causing the hyperlactatemia. In such situations it is important to be aware of the risk of oxygen toxicity.
Use of lactate and $p_x$ in relation to blood gas evaluation

Both $p_x$ and lactate are interpreted most easily when added to the previously described flowchart. The system of the flowchart is still that the parameters in the column to the right influence the parameter in focus, while the related parameter in the column to the left shows the effect of the deviation in the parameter in focus.

The use of the flowchart is as follows:

First evaluate the primary key parameter, typically $pO_2$. If this parameter is acceptable, continue by evaluating the next key parameter ($ctO_2$) in the column and then the next ($p50$). When all key parameters are within the normal range, $p_x$ should be evaluated next, as interactions between key parameters in normal range may cause deviations in $p_x$. If a key parameter is found to be deviating from expected or normal range (low $pO_2$, low $ctO_2$ or unwanted change of $p50$), $p_x$ should be evaluated as the next parameter.

If $p_x$ is within the normal range, the change in the key parameter has been compensated for by changes in one of the other key parameters. Whether or not intervention is required depends on the adequacy of the compensation and the clinical situation. The two other key parameters should therefore be evaluated before intervention.
Example 1
Low $pO_2$. One step to the left shows $p_x$, which is found to be normal. The hypoxemia is compensated and may not need correction. The other parameters in the same column as $pO_2$, as well as the next column of parameters, should be evaluated afterwards to find the compensation. In turn, the compensation should be evaluated for having inadvertent effects, as well as the cause of the low $pO_2$. In our example, there could be a compensatory slight increase in $cTO_2$. Analyzing the next column of parameters could then reveal an increase in $cTHb$ which increases the viscosity of the blood and thereby increases the load on the heart. This could be critical in a situation with impaired cardiac contractility.

If both the evaluated key parameter and $p_x$ are deviating from normal range, the situation is likely to require intervention. A guide to the intervention needed can be found by looking at the parameters in the column to the right of the key parameter.

Example 2
Low $pO_2$. One step to the left shows $p_x$, which is found to be low. The oxygen availability is thereby impaired. To the right is found a high $FShunt$, causing the hypoxemia. One step further to the right is the examination for pulmonary disease which, in this situation, could reveal a low compliance and diffusion impairment in the lungs (ARDS). Increase in PEEP pressure and thereby mean airway pressure may in that situation minimize $FShunt$, and can thereby be a better way to increase $pO_2$ and $p_x$, than just an increase in $FO_2(I)$. 
When all the key parameters of arterial oxygen status, and thereby $p_x$, are considered, $cLactate(P)$ should be evaluated.

If $cLactate$ is the first parameter to look at and it is found too high, the next step will be to look at the parameters in the column to the right to reveal the cause of the high lactate concentration.
General Oxygen Status

Circulatory status

- \( p_{O_2} \) (83-108 mmHg) (11.1-14.4 kPa)
- \( p_X \) (32-41 mmHg) (4.2-5.5 kPa)
- \( c_tO_2 \) (7.1-9.9 mmol/L) (15.9-22.3 mL/dL)
- \( p_{50} \) (25-29 mmHg) (3.3-3.9 kPa)

Metabolic status

- cLactate(P) (0.5-1.6 mmol/L) (4.5-14.4 mg/dL)
- Arterial oxygen availability

See page 24
Notes


Parameter description

All parameters in Part Two are described according to the following structure:

- Reference range
- Definition
- What does the parameter tell you
- Clinical interpretation
- Considerations

Reference ranges are defined as adult values if not stated otherwise [18].
**pO_2(a)**

**Arterial oxygen tension**

\[ pO_2(a) \text{ reference range (adult):} \]
\[ 83 – 108 \text{ mmHg (11.1 – 14.4 kPa)} \]

**Definition**

\( pO_2 \) is the oxygen partial pressure (or tension) in a gas phase in equilibrium with the blood. High and low \( pO_2 \) values of arterial blood indicate hyperoxemia and hypoxemia, respectively. Depending on the sample, the systematic symbol may be \( pO_2(a) \) for arterial blood or \( pO_2(v^-) \) for mixed venous blood. The analyzer symbol may be \( pO_2 \).

**What does \( pO_2 \) tell you?**

The arterial oxygen tension is an indicator of the oxygen uptake in the lungs. See Part One, arterial oxygen status.

**Clinical interpretation**

See Part One.

**Considerations**

For information on low arterial \( pO_2 \), see Part One, oxygen status.

It is important to notice that high \( pO_2 \) can be toxic due to the production of free oxygen radicals. This is especially important in neonates, and even more so in preterm infants. In the latter, arterial \( pO_2 \) should not be above 75 mmHg (10.0 kPa).
Concentration of total hemoglobin

cT(Hb) reference range (adult):
male: 8.4 – 10.9 mmol/L (13.5 – 17.5 g/dL)
female: 7.4 – 9.9 mmol/L (12.0 – 16.0 g/dL)

Definition

cT(Hb) is the concentration of total hemoglobin in blood. Total hemoglobin, in principle, includes all types of hemoglobin, such as deoxy-, oxy-, carboxy-, met-, and sulphemoglobin. In most oximeters, the very rare and non-oxygen carrying sulphemoglobin is not included in the reported cT(Hb).

\[ cT(Hb) = cO_2Hb + cHHb + cCOHb + cMetHb \]

The systematic symbol for arterial blood is cT(Hb)(a). The analyzer symbol may be tHb or cT(Hb).

What does cT(Hb) tell you?

cT(Hb) is a measure of the potential oxygen-carrying capacity, whereas the actual oxygen capacity is defined by the effective hemoglobin (cT(Hb) minus the dyshemoglobins). The arterial blood’s oxygen transport properties are in turn determined by the amount of hemoglobin (cT(Hb)), the fraction of oxygenated hemoglobin (\( F_{O_2}Hb \)) and the oxygen tension (\( pO_2 \)).
Clinical interpretation

High ctHb
High values of ctHb typically indicate a high blood viscosity, which increases the afterload to the heart and thereby can cause forward failure. In extreme cases, the microcirculation can be impaired.

Common causes of high values of ctHb (polycythemia):

Primary:
• polycythemia vera

Secondary:
• dehydration
• chronic lung disease
• chronic heart disease
• living at high altitude
• trained athletes

Low ctHb
Low concentrations of total hemoglobin or effective hemoglobin imply a risk of tissue hypoxia because of the lowered arterial oxygen content (ctO₂).

Physiological compensatory mechanisms for a low total concentration of hemoglobin are to increase cardiac output and to increase red blood cell production. An increase in cardiac output may be inexpedient in the case of ischemic heart disease or impossible in the case of impaired myocardial contractility or flow obstruction.
Common causes of low values ctHb (anemia):

Primary:
- impaired red cell production

Secondary:
- hemolysis
- bleeding
- dilution (overhydration)
- multiple blood samples (neonates)

Considerations
A normal total concentration of hemoglobin does not guarantee a normal oxygen transport capacity. If dyshemoglobins are present in high concentrations, the effective transport capacity will be significantly reduced. The figure below demonstrates the effect of ctHb on oxygen content.
Fraction of oxyhemoglobin

$FO_2Hb(a)$ reference range (adult): 94 – 98% (0.94 – 0.98)

Definition

$FO_2Hb$ is defined as the ratio between the concentrations of $O_2Hb$ and $tHb$ ($cO_2Hb/ctHb$). It is calculated as follows:

$$FO_2Hb = \frac{cO_2Hb}{cO_2Hb + cHHb + cCOHb + cMetHb}$$

The systematic symbol for arterial blood is $FO_2Hb(a)$. The analyzer symbol may be $O_2Hb$ or $FO_2Hb$.

What does $FO_2Hb$ tell you?

The fraction of oxygenated hemoglobin is a measure of the utilization of the potential oxygen transport capacity; that is the fraction of oxygenated hemoglobin in relation to all hemoglobins present ($tHb$) including dyshemoglobins:

Clinical interpretation

High (normal) $FO_2Hb$

- Sufficient utilization of oxygen transport capacity
- Potential risk of hyperoxia (see $pO_2$)
Low $\text{FO}_2\text{Hb}$

Common causes of low $\text{FO}_2\text{Hb}$:
- Impaired oxygen uptake (see Part One)
- Presence of dyshemoglobins
- Right-shift of ODC

Considerations

$\text{FO}_2\text{Hb}$ is sometimes erroneously called »oxygen saturation« or »fractional saturation«, two terms which should be avoided. The relation between $\text{FO}_2\text{Hb}$ and $s_{O_2}$ is:

$$\text{FO}_2\text{Hb} = s_{O_2} \times (1 - F_{COHb} - F_{MetHb})$$

It is important to know that ‘oxygen saturation’ as measured by pulse oximeters is not $\text{FO}_2\text{Hb}$ but $s_{O_2}$. The equation given above expresses the relationship between $\text{FO}_2\text{Hb}$ and $s_{O_2}$. Thus, if no dyshemoglobins are present, the fraction of oxygenated hemoglobin equals the oxygen saturation, expressed as a fraction. The difference between the two can be seen from the example below. Note that this primarily is useful when used in relation to ctHb.

<table>
<thead>
<tr>
<th>ctHb</th>
<th>10 mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>cHHb</td>
<td>0.2 mmol/L</td>
</tr>
<tr>
<td>cCOHb</td>
<td>3 mmol/L ~ 30%</td>
</tr>
<tr>
<td>cO$_2$Hb</td>
<td>6.8 mmol/L</td>
</tr>
</tbody>
</table>

$$\text{FO}_2\text{Hb} = \frac{6.8}{6.8 + 0.2 + 3.0} \cdot 100\% = 68\%$$

$$s_{O_2} = \frac{6.8}{6.8 + 0.2} \cdot 100\% = 97\%$$
Notes
Arterial oxygen saturation

\(sO_2(a)\) normal range (adult): 95–99% (0.95–0.99)

Definition

\(sO_2\) is called oxygen saturation and is defined as the ratio between the concentrations of \(O_2Hb\) and \(HHb+O_2Hb\):

\[
sO_2 = \frac{cO_2Hb}{cHHb + cO_2Hb}
\]

The systematic symbol for arterial blood is \(sO_2(a)\).

The analyzer symbol may be \(sO_2\).

What does \(sO_2\) tell you?

\(sO_2\) is the percentage of oxygenated hemoglobin in relation to the amount of hemoglobin capable of carrying oxygen. \(sO_2\) allows evaluation of oxygenation and dissociation of oxy-hemoglobin as expressed in the ODC.

Clinical interpretation

High (normal) \(sO_2\)

Sufficient utilization of actual oxygen transport capacity.

Potential risk of hyperoxia (see \(pO_2\)).
Low $sO_2$
Common causes of low $sO_2$:
• Impaired oxygen uptake (see Part One)
• Right-shift of ODC

Considerations
Dyshemoglobins and low hemoglobin concentrations resulting in decreased oxygen content, may be present even with normal values of oxygen saturation. This should be taken into consideration prior to monitoring respiratory function by means of the $sO_2$.

Note that this parameter provides the most information when used in relation to ctHb. See also $F_{O_2}Hb$. 
Fraction of carboxyhemoglobin

$F_{COHb}(a)$ reference range (adult): 0.5–1.5% (0.005–0.015)

Definition

$F_{COHb}$ is the ratio between the concentrations of COHb and tHb:

$$F_{COHb} = \frac{c_{COHb}}{c_{tHb}}$$

The systematic symbol for arterial blood is $F_{COHb}(a)$. The analyzer symbol may be COHb or $F_{COHb}$.

What does $F_{COHb}$ tell you?

Carbon monoxide binds reversibly with the heme group ferrous ions, but the affinity of hemoglobin for carbon monoxide is 200 to 250 times as great as the affinity for oxygen. Carboxyhemoglobin is incapable of transporting oxygen and furthermore increases the affinity for oxygen of the remaining binding sites. This results in a decreased oxygen transport capacity along with an impaired peripheral oxygen release due to the left-shift of the ODC.
Clinical interpretation
Carboxyhemoglobin levels are normally below 2 %, but heavy smokers may have up to 9–10 %. Newborns may present up to 10–12 % of carboxyhemoglobin because of an increased hemoglobin turnover combined with a less developed respiratory system.

In the acute exposition, headache, nausea, dizziness and chest pain occur with 10–30 %. Severe headache, general weakness, vomiting, dyspnea and tachycardia occur at 30–50 %. Above 50 %, seizures, coma and death occur.

Considerations
Exposition time is important when clinically evaluating these patients, as patients with a long exposition time may be severely affected at relatively low concentrations of carboxyhemoglobin. If carboxyhemoglobinemia is suspected, 100 % oxygen should be given and hyperbaric oxygen therapy considered in accordance with history and neuro-psychiatric symptoms.
**FMetHb(a)**

**Fraction of methemoglobin**

*FMetHb(a) reference range (adult): 0–1.5% (0–0.015)*

**Definition**

*FMetHb* is the ratio between the concentration of MetHb and tHb:

\[
FMetHb = \frac{c\text{MetHb}}{c\text{tHb}}
\]

The systematic symbol for arterial blood is *FMetHb(a)*. The analyzer symbol may be *MetHb* or *FMetHb*.

**What does FMetHb tell you?**

Methemoglobin is formed when the ferrous ion (Fe++) in the heme groups is oxidized to the ferric state (Fe+++). Methemoglobin is unable to combine with oxygen, resulting in a decreased oxygen-carrying capacity of the blood. Formation of metheme groups increases the affinity to oxygen of the remaining binding sites.

**Clinical interpretation**

Methemoglobin levels above 10–15% can result in pseudocyanosis. Methemoglobinemia may cause headache and dyspnea at levels above 30% and may be fatal, especially in levels above 70%.
Considerations
Most cases of methemoglobinemia are acquired from drugs or chemicals containing nitro- and aminogroups. Newborns can get methemoglobinemia from intake of well water containing nitrate.

Methemoglobinemia, if excessive, can be treated by giving methylene blue intravenously or red cell transfusion.
Fraction of fetal hemoglobin

FHbF reference value (neonatal): ≈ 80%

Definition

FHbF is the ratio between concentrations of HbF and tHb:

\[
FHbF = \frac{cHbF}{ctHb}
\]

The systematic symbol for arterial blood is FHbF(a). The analyzer symbol may be FHbF.

What does FHbF tell you?

Fetal hemoglobin consists of two α-chains and two β-chains, and has a higher oxygen affinity than adult Hb. It is also less sensitive to 2,3-DPG influence than adult Hb. Therefore the ODC is left-shifted when high concentrations of HbF are present. During fetal life this ensures oxygen uptake in the placenta, and despite the left-shift of the ODC more than half of the oxygen bound will be released into the fetal tissue as the oxygen levels there are low. However, after birth the oxygen levels change and high FHbF may compromise peripheral oxygen release.
Clinical interpretation
No strict guidelines for measurement of FHbF exist as it has not been easily available.

Measured before and after a red cell transfusion it can be used for the estimation of a total blood volume, and during exchange transfusions it may help in determining the amount of blood exchanged. The determination of the concentration of HbF is needed for accurate determination of $p_{50}$.

Considerations
FHbF may be increased in children and adults with some hematological diseases (for example: sickle cell anemia, thalassemias and some leucemias).
Arterial concentration of total oxygen

**Definition**

c\(_{tO2}(a)\) is the concentration of the total oxygen in the blood. ctO\(_2\) is the sum of the concentration of hemoglobin-bound oxygen and the concentration of physically dissolved oxygen:

\[
ctO_2 = sO_2 \times (1 - FCOHb - FMetHb) \times ctHb + \alpha O_2 \times pO_2
\]

It is also called the »O\(_2\) content«. The systematic symbol for arterial blood is ctO\(_2\)(a). The analyzer symbol may be tO\(_2\) or ctO\(_2\).

**What does ctO\(_2\) tell you?**

The oxygen content of the blood is an expression of the oxygen transport properties of the blood. It reflects the integrated effects of changes in the arterial \(pO_2\), the effective hemoglobin concentration, and the hemoglobin affinity for oxygen as expressed in the \(p50\).
**ODC and ctO₂ curve**

Low values of ctO₂(a) imply a risk of decreased oxygen delivery to the tissue and thus tissue hypoxia, unless it is compensated for by an increase in cardiac output. It is therefore good practice to look at the lactate level in cases of low oxygen content.

**Clinical interpretation and considerations**

See Part One.

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**The hemoglobin oxygen dissociation curve (ODC)**

**The blood oxygen binding curve**
Oxygen tension at 50% saturation of blood

$p50(a)$ reference value (adult): 25–29 mmHg (3.3–3.9 kPa)

Definition
$p50$ is the oxygen tension at half saturation (50%) of blood and is calculated from the measured oxygen tension and oxygen saturation by extrapolation along the oxygen dissociation curve to 50% saturation. The systematic symbol for $p50$ determined from arterial blood is $p50(a)$. The analyzer symbol may be $p50$ or $p50$. The analyzer symbol may be $p50$ or $p50$.

What does $p50$ tell you?
The $p50$ is the $pO_2$ at half saturation (50%) and reflects the affinity of hemoglobin for oxygen. The position of the oxygen dissociation curve is dependent primarily on the pH, but several physical and chemical changes may affect hemoglobin affinity for oxygen.
Clinical interpretation
See Part One.

Considerations
When $p50$ is calculated from one arterial blood sample, the parameter is quite sensitive to the quality of the measurements, especially at high $sO_2$ values; close to 97%. Calculation of $p50$ is less reliable when $sO_2 > 97%$. 

Left shift
- c2.3-DPG
- Temp.
- $pCO_2$
- pH
- $FHbF$
- $FCOHb$
- $FMetHb$

Right shift
- c2.3-DPG
- Temp.
- $pCO_2$
- pH
- $FSHb$
$pO_2(x)$ or $p_x$

**Arterial oxygen extraction tension**

$pO_2(x)$ or $p_x$ reference value (adult) [16]:

- **male:** 35 – 41 mmHg (4.6 – 5.5 kPa)
- **female:** 32 – 39 mmHg (4.2 – 5.2 kPa)

**Definition**

$pO_2(x)$ or $p_x$, as referred to from now on, is termed the oxygen extraction tension of arterial blood. It is a parameter that reflects the integrated effects of changes in the arterial $pO_2$, oxygen concentration, and changes in the hemoglobin-oxygen affinity on the ability of arterial blood to deliver oxygen to the tissues. $p_x$ is defined as the oxygen tension measured in arterial blood after extraction of 2.3 mmol of oxygen per liter of blood (at constant pH and $pCO_2$), which corresponds to the normal arterio-venous difference in the total oxygen concentration. The systematic symbol for the arterial oxygen extraction tension is $pO_2(x)$. The analyzer symbol may be $p_x$ or $pO_2(x)$.

**What does $p_x$ tell you?**

The purpose of the oxygen extraction tension is to determine whether or not a hypoxemia, an anemia, or an abnormally increased hemoglobin-oxygen affinity is compensated or not (see Part One).
Clinical interpretation and considerations

$p_x$ is a theoretical and calculated parameter based on the determination of the ODC. ODC is quite sensitive to the quality of the measurements, especially if the ODC is based upon high $sO_2$ values; close to 97%. Calculation of $p_x$ is less reliable when $sO_2 > 97\%$. The information provided by $p_x$ must be interpreted with this in mind. (See also Part One).
Concentration of extractable oxygen

\( c_x \) reference value (adult): \( \approx 2.3 \text{ mmol/L} \)

**Definition**

\( \text{ctO}_2(x) \) or \( c_x \), as referred to from now on, is defined as the amount of oxygen which can be extracted per liter of arterial blood when the oxygen tension is decreased to 38 mmHg (5.1 kPa), at constant pH and \( p\text{CO}_2 \).

The systematic symbol for the concentration of extractable oxygen is \( \text{ctO}_2(x) \). The analyzer symbol may be \( c_x \) or \( \text{ctO}_2(x) \).

**What does \( c_x \) tell you?**

\( c_x \) below the normal range (value) indicates a decreased ability of the arterial blood to release oxygen to the tissue.

**Clinical interpretation**

If the oxygen consumption is normal, low \( c_x \) often indicates that the mixed venous tension is low and/or cardiac output is increased.

**Considerations**

\( c_x \) is a theoretical and calculated parameter based on the determination of the ODC. ODC is quite sensitive to the quality of the measurements, especially if the ODC is based upon high \( s\text{O}_2 \) values; close to 97%. Calculation of \( c_x \) is less reliable when \( s\text{O}_2 > 97\% \). The information provided by \( c_x \) must be interpreted with this in mind.
Notes
Arterial oxygen compensation factor

Qx reference value (adult): ≈ 1

Definition
Qx is the factor by which the cardiac output has to increase to maintain a mixed venous tension of 38 mmHg (5.1 kPa) at an a-v difference of 2.3 mmol oxygen/L blood.

The systematic symbol for the arterial oxygen compensation factor is Qx. The analyzer symbol may be Qx.

What does Qx tell you?
A high oxygen compensation factor indicates that the arterial blood is inadequate for proper O₂ supply to the tissues.

Clinical interpretation
High Qx indicates that cardiac output may be increased and/or mixed venous oxygen tension decreased to compensate for the inadequate arterial oxygen supply.

Considerations
Qx is a theoretical and calculated parameter based on the determination of the ODC. ODC is quite sensitive to the quality of the measurements, especially if the ODC is based upon high sO₂ values; close to 97%. Calculation of Qx is less reliable when sO₂ > 97%. The information provided by Qx must be interpreted with this in mind. Qx, like pₓ, is very sensitive to the quality of the measurements.
Notes
Relative physiological shunt

*FShunt reference range (adult) [16]: 1 – 10% (0.01 – 0.10)*

**Definition**

*FShunt* is calculated as the ratio between the alveoliarterial difference and the arterio-venous difference in total oxygen concentration. If no mixed venous sample is measured, *FShunt* is estimated by assuming the arterio-venous difference to be 2.3 mmol/L. The total oxygen concentration of alveolar blood is calculated from the alveolar oxygen tension, obtained from the alveolar air equation. The systematic symbol for the relative physiological shunt is *FShunt*. The analyzer symbol may be *Shunt* or *FShunt*.

**What does *FShunt* tell you?**

*FShunt* \((Q_{\text{shunt} } / Q_{\text{total}})\) is the percentage or fraction of the venous blood not oxygenated during passage through the pulmonary capillaries. That is, the ratio between the shunted cardiac output and the total cardiac output,

\[
\text{Shunt} = \frac{Q_s}{Q_t} = \frac{c_tO_2(pc) - c_tO_2(a)}{c_tO_2(pc) - c_tO_2(v)}
\]

Shunt can arise in two ways:

1) True shunt, where passage from the right to the left side of the heart is without gas-exchange, e.g., heart-septum defects or,
2) ventilation-perfusion disturbance, where oxygenation is incomplete, e.g., lung diseases with inflammation or edema.

Clinical interpretation
In the absence of extrapulmonary shunting, \( F_{\text{Shunt}} \) provides information about the intrapulmonary component of hypoxemia.

A high \( F_{\text{Shunt}} \) indicates a pulmonary mismatch between ventilation and perfusion, e.g., perfusion of non-ventilated areas.

Considerations
Even when estimated from just an arterial sample, \( F_{\text{Shunt}} \) presents the most comprehensive information on the lung function available from arterial blood gas analysis.
Arterial blood pH

\( \text{pH(a)} \) reference range (adult): 7.35–7.45

**Definition**

pH indicates the acidity or alkalinity of the sample. Depending on the sample, the systematic symbol may be \( \text{pH(a)} \) for arterial blood or \( \text{pH(v)} \) for mixed venous blood. The analyzer symbol may be \( \text{pH} \).

pH is the negative logarithm of the hydrogen ion activity \( (\text{pH} = - \log_{10} [H^+] ) \).

**What does pH tell you?**

pH is the indispensable measure of acidemia or alkalemia and is therefore an essential part of the pH blood gas measurement. The normal function of many metabolic processes requires a pH to be within a relatively narrow range.

**Clinical interpretation**

If pH as related to \( p\text{CO}_2 \), is considered to be the respiratory component, and plasma bicarbonate concentration \( (\text{cHCO}_3^-) \), or the standard base excess (SBE), is considered to be the metabolic components, it is possible to distinguish between respiratory and metabolic disturbances.

Plotting the values of pH, \( p\text{CO}_2 \) and bicarbonate measurements in the diagram below can usually provide information about the type of acid-base disturbance.
Respiratory acidosis is characterized by low pH, high $p$CO$_2$ and normal SBE. If the condition persists, bicarbonate excretion in the kidneys will decrease and acidosis will be partly or totally compensated for by increased bicarbonate concentration in the blood. Compensated respiratory acidosis is characterized by only slightly low pH, high $p$CO$_2$ and high bicarbonate concentration.
Metabolic acidosis is characterized by low pH, low bicarbonate concentration and normal or low pCO₂. If the patient is spontaneously breathing, this condition is usually partly compensated for by hyperventilation which result in low pCO₂.

Respiratory alkalosis is characterized by high pH and low pCO₂.

Metabolic alkalosis is characterized by high pH and high bicarbonate concentration. Spontaneously breathing patients may decrease their alveolar ventilation slightly to compensate the alkalosis with a slightly increased pCO₂.

Common causes of low pH (acidosis):

A. Respiratory acidosis:
   - Alveolar hypoventilation
   - Increased metabolic rate

B. Metabolic acidosis:
   - Circulatory impairment
   - Renal failure
   - Diabetic ketoacidosis
   - Gastro-intestinal loss of bicarbonate (diarrhea)
Common causes of high pH (alkalosis):

A. Respiratory alkalosis:
   • Alveolar hyperventilation

B. Metabolic alkalosis:
   • Diuretics
   • Gastrointestinal loss of acid (vomiting)
   • Hypokalemia (low cK +)

Considerations
Before treating acidemia that occurs with concomitant oxygenation problems, it should be considered whether an acidemia might be beneficial for tissue oxygenation, due to the right-shift of the ODC.

Because of the compensatory mechanisms, a near-normal pH value does not exclude the presence of an acid-base imbalance. To evaluate the acid-base balance, even when pH is normal, \( p\text{CO}_2 \) together with \( c\text{HCO}_3^- \), BE or SBE must be evaluated.
Carbon dioxide tension

\( p\text{CO}_2(a) \) reference range (adult):

- **male**: 35 – 48 mmHg (4.67 – 6.40 kPa)
- **female**: 32 – 45 mmHg (4.27 – 6.00 kPa)

Definition

\( p\text{CO}_2 \) is defined as the carbon dioxide partial pressure (or tension) in a gas phase in equilibrium with the blood. High and low values of \( p\text{CO}_2 \) in arterial blood indicate blood hypercapnia and hypocapnia, respectively. Depending on the sample, the systematic symbol may be \( p\text{CO}_2(a) \) for arterial blood or \( p\text{CO}_2(\bar{v}) \) for mixed venous blood. The analyzer symbol may be \( p\text{CO}_2 \).

What does \( p\text{CO}_2 \) tell you?

Carbon dioxide readily diffuses across cell membranes and can be considered to be zero in normal inspired air. Therefore, \( p\text{CO}_2 \) is a direct reflection of the adequacy of alveolar ventilation in relation to the metabolic rate.

Clinical interpretation

**A. Low \( p\text{CO}_2 \)** Alveolar hyperventilation (hypocapnia):

Common causes of alveolar hyperventilation:

Primary:
- Aggressive ventilator treatment.
- Psychogenic hyperventilation.
Secondary:
• Compensatory to metabolic acidosis.
• Secondary to central nervous system affection.
• Secondary to hypoxia

B. High $pCO_2$ Alveolar hypoventilation (hypercapnia):

Common causes of alveolar hypoventilation:
• Lung disease.
• Central nervous system depression, either primary, or secondary to sedation or analgesics.
• Ventilator treatment, either with strategy of permissive hypercapnia or with too low alveolar ventilation.

Considerations
$pCO_2$ reflects the adequacy of pulmonary ventilation. Therefore, it is possible to distinguish between respiratory problems that are primarily of ventilatory origin or problems of oxygenation. The severity of ventilatory failure as well as the chronicity can be judged by the accompanying changes in acid-base status (see pH).

It is often part of the therapeutic strategy to accept or aim for values that are lower or higher than the reference range. In these situations, it is important to be aware of the effects of changes in $pCO_2(a)$.

Hypercapnia or hypocapnia are important causes of change in the arterial $pO_2$. Decreasing $pCO_2(a)$ causes pulmonary vasodilatation and vasoconstriction in several parts of the systemic circulation including the cerebral vasculature. The low alveolar $pCO_2$ increases the alveolar $pO_2$, and the alkalosis causes a left-shift of the ODC; both effects facilitate
oxygen uptake in the lungs. However, the systemic circulatory effects, as well as the impairment of oxygen release to the tissues caused by the left-shift of the ODC, may counteract these effects. The net result of decreasing \( p\text{CO}_2 \) may therefore be the impairment of oxygenation. Though the systemic vasoconstriction is compensated within minutes or hours, it may cause organ hypoperfusion and result in ischemia, especially in the cerebrum.

Increasing \( p\text{CO}_2(a) \) causes hypoxemia because the alveolar oxygen tension falls according to the alveolar gas equation. In addition, the rightward shift of the ODC, induced by acute respiratory acidosis, reduces the arterial \( c_t\text{O}_2 \), but facilitates the \( O_2 \) release. On the other hand, increasing \( p\text{CO}_2 \) may result in increased cardiac output and facilitated oxygen release to the tissues.

In conclusion, the effects of changes in \( p\text{CO}_2 \) are very complex and not yet completely understood. Evaluation of the arterial \( p\text{CO}_2 \) is therefore dependent of the specific clinical situation.
Notes
Actual bicarbonate

cHCO₃(aP) reference range (adult): 21 – 28 mmol/L

Definition
cHCO₃ is the concentration of bicarbonate (hydrogen carbonate) in the plasma of the sample. It is calculated using the measured pH and pCO₂ values. The systematic symbol for arterial blood is cHCO₃(aP). The analyzer symbol may be HCO₃⁻ or cHCO₃(P).

What does cHCO₃ tell you?
The actual bicarbonate is calculated by entering the measured values of pH and pCO₂ in the Henderson-Hasselbalch equation. An increased level of HCO₃⁻ may be due to a metabolic alkalosis or a compensatory response in respiratory acidosis. Decreased levels of HCO₃⁻ are seen in metabolic acidosis and as a compensatory mechanism in respiratory alkalosis.

Clinical interpretation and considerations
Bicarbonate should always be interpreted in relation to pCO₂ and pH. See pH.
cHCO₃(aP)

Notes
Standard bicarbonate

$cHCO_3^-(aP,st)$ reference range (adult) [24]:

- male: 22.5 – 26.9 mmol/L
- female: 21.8 – 26.2 mmol/L

Definition

Standard bicarbonate ($cHCO_3^-(B,st)$) is the concentration of hydrogen carbonate in plasma from blood which is equilibrated with a gas mixture with $pCO_2 = 40$ mmHg (5.3 kPa) and $pO_2 = 100$ mmHg (13.3 kPa) at 37 °C. The systematic symbol for arterial blood is $cHCO_3^-(aP,st)$. The analyzer symbol may be SBC or $cHCO_3^- (P,st)$.

What does $cHCO_3^-(P,st)$ tell you?

The equilibration of fully oxygenated blood with a $pCO_2$ of 40 mmHg (5.3 kPa) is an attempt to eliminate the respiratory component in the acid-base status. In these circumstances, a low standard bicarbonate indicates a metabolic acidosis, and an elevated standard bicarbonate indicates a metabolic alkalosis.

Clinical interpretation

SBC should always be interpreted in relation to $pCO_2$ and pH. See pH.
Actual base excess

cBase(B) reference range (adult): -2–(+) 3 mmol/L

Definition
 Actual base excess is the concentration of titratable base when the blood is titrated with a strong base or acid to a plasma pH of 7.40 at a $pCO_2$ of 40 mmHg (5.3 kPa) and 37 °C at the actual oxygen saturation. It is often abbreviated and symbolized as BE. The systematic symbol for actual base excess for arterial blood is $c_{Base(a)}$. The analyzer symbol may be ABE or $c_{Base(B)}$.

What does cBase(B) tell you?
 Base excess is the deviation in mmol/L of the buffer base amount from the normal level in blood. Buffer base represents the total buffer capacity in the blood, comprised of bicarbonate, hemoglobin, plasma proteins and phosphate. The normal total buffer base level is 48 +/- 2 mmol/L.

Clinical interpretation and considerations
 BE should always be interpreted in relation to $pCO_2$ and pH. See pH.
Notes
Standard base excess

cBase(Ecf) reference range (adult) [24]:
male: -1.5 – (+) 3.0 mmol/L
female: -3.0 – (+) 2.0 mmol/L

Definition
Standard base excess is an in vivo expression of base excess. It refers to a model of the extra cellular fluid (one part of the blood is diluted by two parts of its own plasma) and is calculated using one third of the ctHb for blood in the formula. Alternatively, a standard value for the hemoglobin concentration of the total extracellular fluid (including blood) of 3 mmol/L can be used,

cBase(Ecf) = cBase(B) for ctHb = 3 mmol/L.

The systematic symbol for standard base excess is cBase(Ecf). The analyzer symbol may be SBE or cBase (Ecf).

What does cBase(Ecf) tell you?
cBase(Ecf) is the base excess in the total extracellular fluids, of which blood represents approximately one third. Buffering capacities differ in the extra-cellular compartments, which makes the cBase(Ecf) more representative of the in vivo base excess compared to actual BE.
Clinical interpretation and considerations
Standard base excess (or deficit) is independent of the actual $pCO_2$ in the sample and is a useful reflection of changes in the non-respiratory components in acid-base status. SBE should always be interpreted in relation to $pCO_2$ and pH. See pH.
Anion Gap(K⁺)

Anion Gap(K⁺) reference range (adult): 10–20 mmol/L

Definition
Anion Gap(K⁺) is the concentration difference between the cations, sodium and potassium, and the measured anions, chloride and bicarbonate,

\[
\text{Anion Gap}(K^+) = cNa^+ + cK^+ - cCl^- - c\text{HCO}_3^-.
\]

The systematic symbol is Anion Gap(K⁺). The analyzer symbol may be Anion Gap(K⁺).

What does Anion Gap(K⁺) tell you?
Anion Gap(K⁺) is a reflection of the unmeasured anions in the plasma, e.g., proteins, organic acids, sulfates and phosphates (although changes in plasma calcium and magnesium also affect the Anion Gap(K⁺)).

Anion Gap(K⁺) may be an aid in the differential diagnosis of metabolic acidosis. Metabolic acidosis can be classified in two groups:

1. Those with an increase in the Anion Gap(K⁺), thus implying the presence of increased amounts of organic acid.
2. Those with normal Anion Gap(K⁺), due to loss of bicarbonate.
Clinical interpretation

A. Decreased Anion Gap(K+) can be caused by:
   • decrease in plasma proteins
   • hyponatriemia
   • increase in unmeasured cations

B. Increased Anion Gap(K+) can be caused by:
   • ketoacidosis
   • lactoacidosis
   • renal failure
   • intoxication with: salicylate, methanol and ethylene glycol

C. Metabolic acidosis with a normal Anion Gap(K+):
   • diarrhea
   • uremic acidosis of recent onset
   • renal tubular acidosis
   • ureterosigmoideostomia
Lactate concentration

cLactate(aP) reference range (adult): 0.5 – 1.6 mmol/L (4.5 – 14.4 mg/dL)

Definition

cLactate(P) is the concentration of lactate in plasma. The systematic symbol for arterial blood is cLactate(aP). The analyzer symbol may be cLac.

Clinical interpretation

In relation to oxygen status or circulatory impairment, see Part One.

With the exceptions mentioned below, an elevated lactate concentration has been shown to be a good predictor of patient outcome [2,21].

Probability of hospital mortality as related to blood lactate concentration in critically ill patients. (Adapted from references [2] and [21]).
Considerations
In addition to their presence during severe illness, elevated lactate concentrations can be found during and after seizures and physical exercise. In rare cases of congenital errors of metabolism, very high values can also be found. In these situations, the interpretation of lactate values can not be made as recommended in patients with acute severe illness.

Lactate concentrations in blood samples obtained from capillary or peripheral vascular beds may not be representative for the general status.

In many analyzers interference from several both endogene and exogene substances can influence the measurement of lactate. The measurement performed using the Radiometer lactate electrode is interference free from commonly seen oxidazable substances.
concentration of bilirubin

Reference ranges:
- < 24 hours premature 17 – 137 µmol/L (1 – 8 mg/dL)
- < 24 hours full-term 34 – 103 µmol/L (2 – 6 mg/dL)
- < 48 hours premature 103 – 205 µmol/L (6 – 12 mg/dL)
- < 48 hours full-term 103 – 171 µmol/L (6 – 10 mg/dL)
- 3 – 5 days premature 171 – 239 µmol/L (10 – 14 mg/dL)
- 3 – 5 days full-term 68 – 137 µmol/L (4 – 8 mg/dL)
- > 1 month 3.4 – 17 µmol/L (0.2 – 1.0 mg/dL)

Definition

cBilirubin is the total concentration of bilirubin in plasma.
The systematic symbol for arterial blood is cBilirubin(aP)
The analyzer symbol may be ctBil.

What does ctBil tell you?

Bilirubin is formed as a result of the catabolism of haem. Typically, the major part of bilirubin in plasma comes from the breakdown of red cells. Most of the initially produced unconjugated bilirubin is in plasma reversibly bound to albumin, but the unbound part is toxic. In children and adults the bilirubin is conjugated in the hepatocytes to the water-soluble, non-toxic conjugated bilirubin which is excreted in the bile. Neonates have an increased breakdown of haemoglobin, limited hepatic function and low concentrations of albumin. In neonates with jaundice the concentration of free, unconjugated bilirubin is therefore relatively high with risk of neurotoxicity (kernicterus). If the concentration of bilirubin in neonates exceeds defined levels it requires specific therapy (see below).
If cBilirubin exceeds 30–40 µmol/L it causes a yellow-coloring of the skin, i.e. jaundice.

Clinical interpretation
Hyperbilirubinemia is due to increased production, decreased elimination, or a combination of both.

A. Increased production:
Hemolysis.
Common causes
• infection
• chemical-toxical reaction
• immunisation (auto-immune disease or iso-immunisation)
• hereditary disease

B. Decreased elimination:
Intrahepatic cholestasis.
Common causes
• viral infection (hepatitis of any kind)
• primary biliary cirrhosis
• toxic reactions (medicaments)

Extrahepatic cholestasis
Common causes
• gallstones
• cholecystitis
• cancer
• biliary atresia
Considerations
In children and adults, jaundice will, in almost all cases, be due to conjugated bilirubin. The hyperbilirubinaemia itself is only a symptom and the treatment will be directed towards the cause of the hyperbilirubinaemia.

In newborns hyperbilirubinaemia is typically caused by unconjugated bilirubin and, therefore, requires specific treatment. The treatment modalities are:
- Phototherapy
- Exchange transfusion

The concentration of bilirubin indicating treatment varies depending on the gestational age and weight as well as the general condition of the baby. The more premature and the more ill the baby, the lower the action limit for therapy.

Several diseases in the newborn, i.e. immunization, infection, hypothyroidism, biliary atresia and galactosaemia, may cause hyperbilirubinaemia and, although in most cases this is simple hyperbilirubinaemia, the clinician has to be aware of underlying disease. Signs of such are high cBilirubin in cord blood, early (<24 hrs.) hyperbilirubinaemia, steep increase in cBilirubin and prolonged hyperbilirubinaemia.
cBilirubin

Notes
Glucose concentration

cGlucose(aP) reference range (adult):
3.89 – 5.83 mmol/L (70 – 105 mg/dL)

Definition

cGlucose(P) is the concentration of glucose in plasma. The systematic symbol for arterial blood is cGlucose(aP). The analyzer symbol may be cGlu.

Clinical interpretation

As both hyper- and hypoglycemia can produce neurological damage, aggressive treatment of deviations in cGlu is warranted.

Considerations

The measurement of glucose should be performed as soon as possible after sample collection to avoid metabolism in the sample causing false values of cGlu.

In many analyzers interference from several substances both endogene and exogene can influence the measurement of glucose. The measurement performed using the Radiometer glucose electrode is interference free from commonly seen oxidazable substances.
Potassium concentration

$cK^+(aP)$ reference range (adult): 3.4–4.5 mmol/L

Definition
c$K^+(P)$ is the concentration of potassium ($K^+$) in plasma. The systematic symbol for arterial blood is $cK^+(aP)$. The analyzer symbol may be $K^+$ or $cK^+$.

Clinical interpretation

A. Low $cK+$ can be caused by:
   - Diuretics
   - Diarrhea
   - Vomiting
   - Respiratory or metabolic baseosis
   - Hyperaldosteronism

B. High $cK+$ can be caused by:
   - Renal failure
   - Metabolic acidosis
   - Toxic acidosis (salicylate, methanol, etc.)

Considerations
High values of $cK^+$ can be caused by hemolysis of the red cells in a blood sample. This is typically seen following too vigorous aspiration and in capillary samples (poor sampling technique).
Sodium concentration

cNa\(^+\)(aP) reference range (adult): 136–146 mmol/L

Definition
cNa\(^+\)(P) is the concentration of sodium (Na\(^+\)) in plasma. The systematic symbol for arterial blood is cNa\(^+\)(aP). The analyzer symbol may be Na\(^+\) or cNa\(^+\).

Clinical interpretation
A. Low values of cNa\(^+\) can be caused by:
   - Water intoxication
   - Renal failure
   - Heart failure
   - Liver failure
   - Increased ADH secretion
   - Diuretics
   - Nephrotic syndrome

B. High values of cNa\(^+\) can be caused by:
   - Increased Na-load
   - Steroids
   - Vomiting
   - Diarrhea
   - Excessive sweating
   - Osmotic diuresis

Considerations
Regional oedema at the site of capillary sampling can cause false low values of cNa\(^+\).
Chloride concentration

$cCl^- (aP)$ reference range (adult): 98–106 mmol/L

**Definition**
cCl$^- (P)$ is the concentration of chloride ($Cl^-$) in plasma. The systematic symbol for arterial blood is $cCl^- (aP)$. The analyzer symbol may be $Cl^-$ or $cCl^-$. 

**Clinical interpretation**
cCl$^-$ itself as a single parameter in most settings is of minor importance. However, low values can cause muscle seizures, apathy and anorexia.

**Considerations**
The major importance of cCl$^-$ is in relation to calculation of anion gap. See anion gap.
Notes
**Calcium concentration**

\( c\text{Ca}^{2+}(aP) \) reference range (adult): \(1.15 – 1.29 \text{ mmol/L} \)

**Definition**

\( c\text{Ca}^{2+}(P) \) is the concentration of ionized calcium (\( \text{Ca}^{2+} \)) in plasma. The systematic symbol for arterial blood is \( c\text{Ca}^{2+}(aP) \). The analyzer symbol may be \( \text{Ca}^{2+} \) or \( c\text{Ca}^{2+} \).

**Clinical interpretation**

A. Low values of \( c\text{Ca}^{2+} \) can be caused by:
   - Baseosis
   - Renal failure
   - Acute circulatory insufficiency
   - Lack of vitamin D
   - Hypoparathyroidism

B. High values of \( c\text{Ca}^{2+} \) can be caused by:
   - Malignancies
   - Thyreotoxicosis
   - Pancreatitis
   - Immobilization
   - Hyperparathyroidism

**Considerations**

\( c\text{Ca}^{2+} \) is the electrolyte parameter most sensitive to the use of non-electrolyte balanced heparin. When measuring \( c\text{Ca}^{2+} \), it is therefore recommended always to use electrolyte-balanced heparin.
Notes
ACUTE CARE TESTING