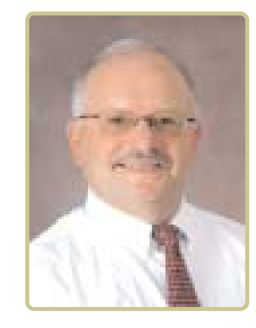
PREVENTING PRE-ANALYTICAL ERROR IN BLOOD GAS ANALYSIS

by John Ancy MA RRT



In recent years, significant attention has been given to the dire consequences of medical errors. Most estimates of unnecessary hospital patient deaths are in the 100000/year range. For example, in 1999 the Institute of Medicine reported that medical errors might result in as many as 98000 patient deaths annually, at a cost of 17 to 29 billion dollars. Hospitals, health insurers, JCAHO, CMS and numerous state agencies are focusing major efforts on reduction of unnecessary patient mortality and injury. Errors in blood gas analysis and reporting certainly have a potential to cause injury, unnecessary or inappropriate interventions and in extreme cases, patient death. A good blood gas laboratory employs a "Total Error Concept" quality assurance program, which seeks to reduce the potential error in all aspects of testing. This method uses sound quality control practices to assure analytical performance, while providing appropriate practices in the preanalytical (sample procurement, transport and storage) and postanalytical components (reporting).

Considerable expense, attention and effort are invested in blood gas quality control. As a consequence, analytical performance, defined as accuracy and precision is generally quite good. However, the same attention and consideration are often not afforded to preanalytical practices. This is evidenced by a 2002 article in Clinical Chemistry by Bonini, et al that cited that 75% of blood gas errors were due to preanalytical errors. Obviously, increased effort should be given to understanding and minimizing preanalytical error. In addition to blood gas analysis and oximetry, modern multi-analyte systems may offer electrolyte, glucose, lactate, creatinine and BUN capabilities. The ever-expanding menu of available tests on newer blood gas analyzers, while offering diagnostic flexibility, also presents wider challenges in handling samples prior to analysis. This article along with two follow up articles will focus on understanding and preventing preanalytical error in blood gas, oximetry and other common analytes testing.

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In whole blood testing, as practiced in blood gases analysis, there are numerous sources of preanalytical error, some of which are: air contamination, post draw metabolism, abnormal cell count, liquid heparin dilution, venous admixture, specimen mixing and catheter flush. Air bubble entrapment in samples is a common source of preanalytical error that can cause significant inaccuracy in reported blood gas values. Room air has a PO2 of approximately 150 mmHg and a PCO2 that is practically 0 mmHg. Blood in a syringe with a trapped air bubble will move toward equilibration with the air (Henry's law). Thus, an arterial sample having a PaO2 of 100 mmHg and a PaCO2 of 40 mmHg will exhibit an increase in PO2 and a decrease in PCO2, with a slight increase in pH. The change in PO2 is much more pronounced than the change in PCO2, which is most likely due to the solubility differences of oxygen and carbon dioxide. The degree of change in PO2 is affected by many factors. The size of the air bubble relative to the volume of blood, temperature, time of exposure and agitation are important factors. It should be noted that air trapped as froth has a much greater potential to alter PO2, due the greater surface area presented by the very small bubbles. Somewhat in contradiction to Henry's law, a sample that has a PO2 of 100 mmHg will show a greater increase when exposed to air than a sample with a PO2 of 50 mmHg. Hemoglobin in the sample with a PO2 of 100 mmHg is nearly 100% saturated. Most of the oxygen that migrates from trapped air stays in the plasma phase, the state that blood gas analyzers measure partial pressure. Whereas, in a sample with a PO2 of 50, much of the oxygen readily combines with available sites on hemoglobin, leaving PO2 relatively unaffected. The solution to prevent air contamination error is to remove air immediately.

Blood is a living tissue and cells continue metabolizing after removal from the body. Blood gas results should reflect the physiologic state in the body at the time of the draw and not value changes that have occurred in the sample due to improper handling. Appropriate sample handling can minimize post draw metabolic changes and hence reduce the potential for preanalytical error. There are two simple and widely accepted techniques for minimizing metabolic changes in blood gas samples. Immediate sample analysis or placing a blood gas samples in ice slurry are very simple and effective practices. These practices are not only effective in reducing post draw value changes in blood gases, but also can help to minimize changes in electrolyte and metabolite values. Quick sample analysis is usually the best practice to reduce the potential for preanalytic change. Icing samples has some limitations and precautions, which will become evident upon further explanation.

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Post draw O_2 and glucose consumption and CO_2 and lactate production in the sample can significantly alter blood gas and pH results. The major factors that influence post sampling metabolism are analysis delay, sample temperature, and metabolically active cell count (white cells and thrombocytes). Immediate sample analysis reduces time available for post draw cell metabolism. When immediate sampling is not an option, samples should be iced to minimize potential changes through reduction of metabolic rate. In essence, the higher the temperature of the sample and the longer the delay in analysis, the greater metabolic change that will occur. The third factor in post draw metabolism is the percentage of red and white cells. Oddly enough, in spite of the availability of ample oxygen, erythrocytes employ anaerobic glycolysis and produce lactate. Leukocytes, reticulocytes and thrombocytes employ oxidative metabolism and are capable of consuming considerable amounts of glucose and oxygen. In samples with normal blood count and a PaO_2 of 100mmHg, the post analytic decrease at room temperature is only about 10mmHg per hour. However, in samples from patients with leukocytosis, the elevated number of white cells can cause considerable post draw oxygen consumption. For example, Fox, et al reported a sample with a white count of 276000 (normal 6000 to 10000 cells/mm3) that exhibited a PaO_2 reduction from 130 to 58 mmHg in two minutes post draw. Post draw oxygen consumption by white cells has been termed "leukocyte larceny". In samples with extremely elevated white counts, icing is only marginally effective in preventing under-reporting of PaO_2. While the example cited may be extreme, leukocyte larceny is real and certainly has potential to cause erroneous interpretation of oxygenation status. In this particular case, if the PaO_2 had been reported as 58mmHg, interpretation would have been moderate hypoxemia, rather than the appropriate interpretation, overcorrected oxygenation. Leukocyte larceny should be considered as a potential culprit in cases in which blood gases indicate hypoxemia, but clinical condition and pulse oximetry indicate otherwise.

While placing samples in ice slurry minimizes metabolic change in most samples, there is actually a potential for increase in PO_2 from ice storage. There are three primary reasons for this seemingly unreasonable occurrence. Plastic syringes are not impermeable to oxygen diffusion. Secondly, the reduced temperature from the ice slurry, nearly doubles the oxygen solubility in blood. Finally, the lower temperature shifts the oxyhemoglobin curve to the left increasing the amount of oxygen combining with hemoglobin. When the sample is reheated in the blood gas analyzer, the additional oxygen is released to the plasma and measured as a falsely elevated PO_2.

In summary, immediate removal of air bubbles and prompt sample analysis is the best practice and can greatly reduce the potential for preanalytical error. If immediate sample analysis is not an option, storage of an anaerobic sample in ice slurry offers reasonable but not guaranteed maintenance of sample integrity.