

In this issue

Revolutionizing Group B Streptococcus Detection using Rapid PCR

FREELITE™ - A timely new tool to meet the challenges in diagnosis and management of Myeloma and related disease.

Clinical Implications of Measured versus Estimated Oxygen Saturation

Are You Being Over Exposed?

Revolutionizing Group B Streptococcus Detection using Rapid PCR

Group B Streptococcus (GBS) transmitted from the birth canal during delivery is the most common cause of sepsis (blood infection), meningitis (infection of the fluid and lining surrounding the brain) and pneumonia in newborns. Health care costs to support these infants are phenomenal, but in the worst of cases GBS has been the tragic cause of mortality in otherwise healthy babies. The emotional cost to families that suffer this loss of life is immeasurable.

In the 1980's, clinical trials demonstrated that administering antibiotic drugs during labour to women at risk of transmitting GBS to their newborns could prevent invasive disease in the first week of life. In 1996, the Centre for Disease Control (CDC) recommended guidelines for administration of antibiotics based on either a list of risk factors associated with delivering a GBS baby or the mother's positive group B strep culture screen performed at 37 weeks. Although both of these recommendations resulted in a striking reduction in babies born with GBS, gaps continue to prevail.

Studies have shown that risk factors alone will miss up to 18% of colonized mothers and although culture based screening was demonstrated to be >50% more effective than risk factors, culture is limited in the time to results (typically 2-3 days) and the possibility of condition change.

Even when used together there are uncertainties in the mother's true GBS status at time of actual delivery. For example:

- Mothers may become colonized or "positive" for GBS between the 35-37 week screening time and actual delivery
- Mothers may deliver premature with no 35-37 week screening result taken
- Mothers may have no screening test done and exhibit no risk factors
- Mothers may deliver at hospitals other than where their results were sent
- Mothers may not have results available or charted at delivery time

Rather than chance a GBS infection, these uncertainties often result in empiric treatment raising significant likelihood and concern for massive and unnecessary newborn antibiotic exposure. Alternatively many could be at risk of a missed GBS threat.

Continued on Page 2



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Revolutionizing Group B Streptococcus Detection using Rapid PCR.... cont'd

Now the 2002 Centre for Disease Control guidelines have recognized that a rapid test for detection of GBS colonization at the time of delivery or at rupture of membranes might obviate the need for prenatal culture based screening or the reliance on broad based risk factors if the sensitivity and specificity of a rapid test were comparable to culture in selective broth media. This could much more accurately direct prophylactic therapy by identifying true GBS risk.

The good news - Health Canada and the FDA have recently authorized such a test. A new and unique DNA based diagnostic tool for

detecting the presence of Group B streptococcus colonization has been developed by a Canadian company; Infectio Diagnostic (IDI). Their breakthrough real-time PCR assay provides GBS results in less than 1 hour with a sensitivity of 94% and a specificity of 96%. This rapid and highly sensitive platform allows the ability to detect the presence of GBS during labour to accurately assess the need for immediate antibiotic therapy for the prevention of GBS disease and just as importantly reduce the needless administration of antibiotics to healthy infants with no risk of infection.

Efforts to date have substantially reduced infant morbidity and mortality caused by GBS however death and disability continue to occur. These new advancements in technology and genomic innovation to support the detection of GBS among pregnant women will bring society closer to eliminating this heartbreaking and preventable disease.

Reference: Centers for Disease Control and Prevention. Prevention of Perinatal Group B Streptococcal Disease: Revised Guidelines from CDC. Morbidity and Mortality Weekly Report August 16, 2002; 51 (No. RR-11)

FREELITE™ - A timely new tool to meet the challenges in diagnosis and management of Myeloma and related disease.



The diagnostic laboratory screening protocols for monoclonal gammopathies rely upon serum protein electrophoresis (SPE), 24-hour urine electrophoresis (UPE) and immunofixation (IFE) of any suspicious samples. As failure to diagnose Multiple Myeloma at first presentation may have severe consequences in terms of renal failure, amyloidosis, fractures and paralysis from spinal collapse, it is important to have available the diagnostic tools which aid in establishing a diagnosis early in the onset of disease. In particular, certain diseases are more difficult to diagnose early, as only a slight increase on the production of free light chains by the plasma cells is apparent.

In a major development, The Binding Site has developed FREELITE™, a quantitative assay measuring free light chains (flc) in serum on automated nephelometric/turbidimetric systems. This test may be used in conjunction with electrophoretic testing and as an aid in the diagnosis and subsequent monitoring of certain diseases as described below.

Light Chain Multiple Myeloma (LCMM)

LCMM accounts for approximately 15% of all multiple myeloma (MM) cases. Low levels of flc are not easily identified by SPE so the usual laboratory procedure is to perform UPE or IFE on samples that may have been concentrated. In a recent study, serum flc was measured in 224 LCMM patients entered into the UK MRC myeloma trials. All 120 k and 104 l patients had highly elevated serum flc

concentrations. This finding indicates that the abnormal production of flc in the serum is a further diagnostic marker for this group of patients.

In addition, LCMM samples were studied during chemotherapy and both serum and urine flc concentrations decreased in parallel during treatment. A number of patients had undetectable levels of flc in the urine, while serum levels remained elevated, thereby in this case serum concentrations provided a further marker of complete remission.

Nonsecretory Myeloma (NSM)

Patients with NSM, by definition, have no detectable monoclonal proteins in their serum or urine by conventional electrophoresis techniques and account for 1-4% of all MM patients. Serum flc have been measured in 28 such patients and 20 were found to have flc concentrations above the normal range, and many had grossly distorted k/l ratios.

The clinical utility of serum flc was assessed in 6 of the 28 NSM patients during follow up. The sera showed elevated flc concentrations at presentation, reduced levels during plateau phase and raised levels again at relapse. This indicated that serum flc measurements could be of use in the management of many patients with NSM and should reduce the need for bone marrow biopsies that are currently required for tumour assessment.

The disease states described above are just 2 of several being investigated for the diagnostic utility of FREELITE™. Others include primary amyloidosis and light chain deposition disease where serum flc concentrations have proven useful for identifying and monitoring patients, particularly since changes in the concentration of flc predicted clinical outcome. Serial quantification of flc may allow early assessment of responses to chemotherapy and permit precise tailoring of treatment regimes for individual patients.

FREELITE™ assays have been shown to be specific, sensitive and quantitative, and offer considerable benefits in terms of clinical and laboratory practice, including:

- **Convenience of serum as a test medium**
- **Numerical results for disease monitoring**
- **Identification of primary amyloidosis and NSM patients that have no detectable monoclonal proteins by conventional tests.**
- **An accurate marker for assessing complete remission**
- **Short half-life marker for assessing treatment responses.**

Further details on the applications and utilization of FREELITE™ can be accessed through Somagen™ Diagnostics.

Clinical Implications of Measured versus Estimated Oxygen Saturation



Ateriole blood gases are an important diagnostic tool for the evaluation of both oxygenation status and acid-base balance of the patient. The test is used to evaluate respiratory conditions that affect the lungs, determine the effectiveness of oxygen therapy and give information on how well the kidneys are functioning.

It has been clearly understood by clinicians that oxygen saturation is a major part of the necessary clinical perspective. Oxygen saturation is the amount of oxyhemoglobin in blood expressed as a fraction (%) of the total amount of hemoglobin able to bind oxygen (oxyhemoglobin plus deoxyhemoglobin). What has been frequently unrecognized has been the role that the technology of determining these quantities can play in the validity of any clinical interpretation of numeric results.

Most Blood gas analyzers only measure PO₂, PCO₂ and pH and estimate the oxygen saturation (SO₂) based on assumptions of a normal oxygen-hemoglobin dissociation curve (ODC) and assuming that all of the hemoglobin is available to bind with O₂. Although it is possible to estimate this value, the assumptions, which are made in the estimation, can cause significant errors in the resulting values for those patients who are in the most critical clinical state. Listed below are cases where abnormal amounts of dyshemoglobins (carboxy-, met- and sulf-hemoglobins) exist and can lead to inaccurate SO₂ values.

- **Inhalation of carbon monoxide, i.e. fires, car exhaust and smokers**
- **Drug induced increases of methemoglobin, i.e. dapson or primaquine**
- **Monitoring of methemoglobin in patients treated with nitrous oxide**
- **Drug induced increases in sulfhemoglobin**

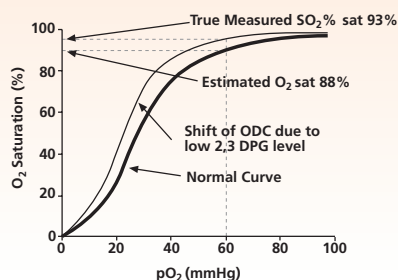
Other factors, which are known to affect this curve, include: pH, PCO₂, temperature and 2,3 diphosphoglycerate (2,3 DPG) content. The clinical case below illustrates the advantage of Measured SO₂% compared to Estimated O₂ saturation.

CLINICAL CASE

A patient who has undergone extensive abdominal surgery and received 7 units of stored blood has the following post-operative blood gas results:

pH	7.32
PCO ₂	45 mmHg
PO ₂	61 mmHg
Estimated O ₂ sat.	88 %
Measured SO ₂ %	93 %

The discrepancy in the saturation results is due to the low 2,3 DPG levels in the stored blood given to the patient. Low 2,3 DPG levels shift the ODC to the left. Estimated O₂ sat from the normal ODC is therefore lower than the true result given by the directly measured SO₂%.



Integrating direct measurement of SO₂% into a blood gas analyzer provides a more accurate result than estimated saturation in clinical situations where changes in pH, PCO₂, temperature, 2,3 DPG levels and hemoglobin species may be present. With the OPTI CCA Blood Gas Analyzer, measured oxygen saturation (SO₂%) is determined from direct measurement of oxyhemoglobin (O₂Hb) and deoxyhemoglobin (HHb), it is not dependent upon the position of the oxygen dissociation curve.

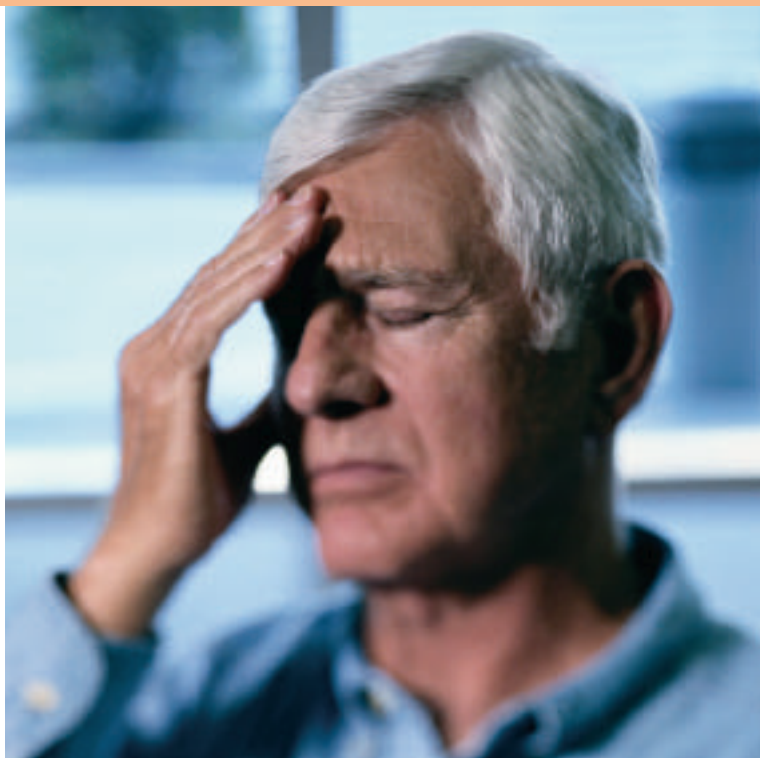
Summary

Now that direct measurement of oxygen saturation is available on instruments such as the OPTI CCA, it is generally agreed that the use of estimated oxygen saturation is, at best, misleading. Considering these facts, integrating direct measurement of SO₂% into a blood gas analyzer becomes an important consideration when purchasing new equipment.

For more information on the OPTI CCA, please contact Brian Roskewich, Point of Care Specialist at ext. 9532.

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“Some blood gas analyzers estimate oxygen saturation from a measured PO₂ and an assumed normal oxyhemoglobin dissociation curve. These results can differ significantly from direct measurement, especially if pH and PCO₂ are not adjusted and if 2,3 DPG is unknown and /or not adjusted for and is abnormal. Clinically significant errors can result from incorporation of this calculated value in further calculations, such as shunt fraction, or by assuming that the value obtained is equivalent to the oxyhemoglobin fraction.”



Are You Being Over Exposed?

Effectively utilized in the Pathology Laboratory to “fix” or halt the metabolic process within tissues, formalin has limited value when exposed to healthy “live” tissue. In addition to its chemical reaction with human protein, formalin is a very potent irritant to the eyes, nose, throat, and sinuses. It has been documented to cause neuro-toxic effects such as headaches, excessive fatigue, malaise, and lethargy. It may also cause skin rash on contact and inflammatory reactions in tissue, particularly the respiratory airways in humans.

It is no surprise that regulatory agencies such as OSHA (Occupational Health and Safety), NIOSH and AGCIH have developed specific guidelines that establish safe or reasonable limits for formalin and similarly dangerous chemical exposures in the workplace.

To be assured of OSHA compliance and confidence for staff, exposure levels must be measured in the following ways:

TWA: Time Weighted Average - taken over 8 hr period

STEL: Short Term Exposure Limit - taken over 15 min of high exposure activity

Current acceptable formalin exposure levels for each limit are:

TWA – 0.75 ppm
STEL – 2.0 ppm

Monitoring for compliance for both of these levels cannot be stressed enough. Some laboratory duties require exposure to formalin at higher levels for short periods of time over the day (for example changing reagents on tissue processors, grossing tissues where there is limited ventilation). Using only TWA as an overall measure may result in overexposure diluted over time to a falsely acceptable outcome. A false sense of security is not a measure of success and the consequences of overexposure are far worse than the fix.



Establishing a program to accurately monitor and document contact with formalin can be accomplished with a sensitive dosimeter badge program that will comprehensively measure both the TWA and STEL as well as analyze and report results. Sensors™ Medical Compliance Products has developed a badge system that can be integrated into any laboratory chemical monitoring program as the first line system or as a regular QC to ensure ongoing compliance and peace of mind for laboratory staff. In addition to formalin monitoring, Sensors™ Chemicals has dosimeter badges with the capability to monitor personal exposure to a variety of laboratory chemicals including xylene, toluene, glutaraldehyde and nitrous oxide. Please share this with your Occupational Health and Safety Officer, it is a positive step to ensure the health of your tissue.

More information on hazardous chemical monitoring and reducing formalin exposure is available through Somagen™ Diagnostics Inc. in conjunction with the Somagen™ Chemical Safety Monitoring Program.

Past issues of the Somagen Laboratory Quarterly are available on our website.

Visit our website at www.somagen.com

