Recognition and Prevention of Pre-analytical Error in Blood Gases:

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Werfen Group
The Institute of Medicine in 1999 reported that medical errors may result in as many as 98,000 patient deaths annually in the United States at a cost of $17-29 billion.

JCAHO STATED GOAL:
Eliminate laboratory errors that lead to adverse patient outcomes
JCAHO, CAP, CLIA, Hospitals invest effort and resources to reduce medical error
Report Card- Medical Deaths US & Canada

98,000 Institute of Medicine (To Err is Human, 1999)

198,000 Newsweek 2005

250,000 (AMA) St. Louis Post Dispatch 2009

Canadian Medical Association Report

9000-24000 medical error deaths per year

Medicare Study on Medical Error

Medical Harm

- **134,000** Medicare beneficiaries experience harm from medical error each month (1 in 7)
- **1.6** million harmed each year

Mortality

- **15,000** or 1.5% die from causes associated medical error each month
- **180,000** deaths each year (nearly 500/day)
Lab Errors

Approximately 80% of clinical treatments are based upon lab test results

Reduction in lab errors will help reduce medical errors
Reducing Laboratory Error: Blood Gases
Arguably the most critical of lab results

- Critically ill patients
- Right results needed quickly
- Interventions often applied immediately
- Little margin for error
Reducing Laboratory Error

Total Error Concept

- Pre-analytical
- Analytical
- Post analytical
How important is Pre-analytical Error?

- Historically, most effort, regulations and expense on related to analytical QC.

- However, 75% of error in blood gases from preanalytical factors

Pre-analytical Error in Blood Gases

- Diverse level of skill and knowledge in staff obtaining and analyzing BG samples

- Blood cells metabolize – values will change

- Extra care required if Blood Gas sample analysis will be delayed
Pre-analytical Error in Blood Gases

Error chance higher with larger menus
- $K^+$, $Na^+$, $Cl^-$, $Ca^{++}$, Hct
- Lactate, Glucose,
- CO-Oximetry

Regulatory emphasis increased on pre-analytic component
Pre-analytical error and correlation

Correlation is part of new instrument verification process.

- Pre-analytical error introduces bias and imprecision that is not related to analytic correlation and can compromise studies
- Multi-analyte (Blood Gas, electrolyte, metabolite & CO-Oximetry) analyzers require extra vigilance in preventing pre-analytic error
Pre-analytical Error
Whole Blood

- Living tissue

- Active metabolism continues after blood draw
  - Leukocytes, thrombocytes & reticulocytes
    - Consume oxygen, glucose
    - Produce carbon dioxide & $H^+$
  - RBCs produce lactate and $H^+$ via anaerobic glycolysis
Pre-analytical Error
Whole Blood

Sample handling can cause significant error for:

- Blood gases
- Electrolytes
- Metabolites
- CO-Oximetry
Sources of BG Pre-analytical Errors

- Post-draw metabolism
- Steady state
- Heparin
- Air contamination
- Venous admixture
- Storage/Transport
- Abnormal cell count

- Pneumatic tube
- Catheter flush
- PAL placement & withdrawal rate
- Specimen mixing
- Temperature correction
Post-draw metabolism

Blood cells continue metabolism after draw

- Aerobic metabolism
  - White cells
  - Thrombocytes
  - Reticulocytes (immature RBCs)

- Lactate metabolism
  - Red blood cells
Post-draw metabolism

Pre-analytic changes affected by:

- Time and ambient temperature
- Cellular composition of sample RBC/WBC
Pre-analytical error in Blood Gases

Steady state

Wait time for ABG draw after $O_2$ therapy and/or ventilator/CPAP changes

- 20-30 minutes for steady state*
- Particularly in COPD and other conditions with abnormal V/Q ratios*

Pre-analytical Error

- **Heparin**
  
  Final concentration should be < 20 IU/ml (if reporting iCa)

- Liquid (Na heparin)
- Dry (Li Heparin)
- Dry balanced (Li Heparin)
Heparin

Liquid Heparin (pH as low as 6.5)

- Small blood sample, results in error
- pH, $pO_2$, $pCO_2$
- $Na^+$, $K^+$, $Ca^{++}$ (dilution error)
Liquid Heparin

0.05ml liquid heparin in 1.0ml sample dilutes plasma phase by ≈10% (50% Hct)

- ↓ pH
- Na, K, iCa, Cl
<table>
<thead>
<tr>
<th>1.0 ml <strong>whole blood sample</strong></th>
<th>0.5 ml <strong>whole blood sample</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hct 50%</td>
<td>Hct 50%</td>
</tr>
<tr>
<td>Liquid heparin 0.05 ml</td>
<td>Liquid heparin 0.05 ml</td>
</tr>
<tr>
<td>Plasma 0.5 ml</td>
<td>Plasma 0.25 ml</td>
</tr>
<tr>
<td>Hep + plasma 0.55 ml</td>
<td>Hep + plasma 0.30 ml</td>
</tr>
<tr>
<td>Dilution ≈10%</td>
<td>Dilution ≈20%</td>
</tr>
<tr>
<td>Blood cells 0.5 ml</td>
<td>Blood cells 0.25 ml</td>
</tr>
</tbody>
</table>

Liq. Heparin = 0.05 mL

Heparin + plasma = 0.55 mL

Dilution = 10%

Blood cells = 0.50 mL
Heparin

Dry Lithium Heparin including:
Balanced and Low heparin formulations

- **Eliminates liquid heparin pH/dilution error**
- Reduces Na error (no added sodium)
- May not mix as readily liquid heparin

- Use “mixing flea” for cap samples?
Heparin Recommendations

- Don’t use liquid
- Use balanced heparin or low heparin if reporting electrolytes
- Gently and thoroughly mix sample (30 sec.) in two planes (Rock & Roll)
- **Remember**: heparin prevents, but doesn’t reverse hemostasis
- Longer mix times for longer delays from draw to analysis (hemoglobin/Hct)
Air Bubble Contamination

* Double Bubble, Toil and Trouble

Air bubbles contain room air

- \( pO_2 \approx 150 \text{ mmHg at sea level} \)
  - 147 in Cleveland, 125 in Denver, 130 in Kamloops
  - May falsely lower or increase \( pO_2 \)

- \( pCO_2 = 0 \text{ mmHg} \)
  - Slight decrease in \( pCO_2 \)
  - Slight increase in pH

* from Macbeth- William Shakespeare
# Air Contamination

(0.1 ml in 1.0 ml sample)

<table>
<thead>
<tr>
<th></th>
<th>No Air</th>
<th>Air Bubble</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.53</td>
<td>7.54</td>
</tr>
<tr>
<td>$pCO_2$</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>$pO_2$</td>
<td>325</td>
<td>326</td>
</tr>
<tr>
<td></td>
<td>7.53</td>
<td>7.53</td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>322</td>
<td>304</td>
</tr>
</tbody>
</table>
Air Contamination
(0.1 ml air in 1.0 ml sample)

<table>
<thead>
<tr>
<th></th>
<th>No Air</th>
<th>Air Bubble</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.38</td>
<td>7.38</td>
</tr>
<tr>
<td>(p\text{CO}_2)</td>
<td>53</td>
<td>53</td>
</tr>
<tr>
<td>(p\text{O}_2)</td>
<td>78</td>
<td>79</td>
</tr>
</tbody>
</table>
Air Contamination
Will cause **error**, magnitude is **unpredictable**

- Volume of air/volume of blood
- Number/size of bubbles (surface area effect)
- Time of exposure
- Temperature iced/non-iced
- Initial $pO_2$
- Hb/HbO$_2$%
  - Oxygen buffering effect of Hb
What’s the Story?

ABG @ 0715

pH        7.37
pCO₂ 47 mmHg
pO₂ 48 mmHg
SpO₂ 96%

ABG redraw @ 0740

pH        7.40
pCO₂ 44 mmHg
pO₂ 88
SpO₂ 96%
# Venous Admixture

<table>
<thead>
<tr>
<th>Blood</th>
<th>Volume (ml)</th>
<th>$pO_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial</td>
<td>4.5</td>
<td>86</td>
</tr>
<tr>
<td>Venous</td>
<td>0.5</td>
<td>31</td>
</tr>
<tr>
<td>Mixed</td>
<td>5.0</td>
<td>56</td>
</tr>
</tbody>
</table>

Venous Admixture

- The addition of 10% of venous blood to an arterial sample can produce $\geq 25\%$ drop in $pO_2$
- Increased probability on femoral artery punctures
- Suspect venous contamination if condition & ABG results do not correspond
- Pulse oximetry can be helpful
Capillary Blood Gas Sampling

- Properly “arterialized” sample will yield pH and $pCO_2$ that are close to ABG and $pO_2$ that is somewhat lower
- Site should be pre-warmed up to (42°C), increases flow up to 7X
- Free-flowing sample
  - “milking” introduces venous blood and interstitial fluid
- Completely filled, air free tubes, with sealed ends
- Should be analyzed within 15 minutes

Adapted from:
AARC Clinical Practice Guideline: Capillary Blood Gas Sampling for Neonatal and Pediatric Patients
Storage/Transportation

Iced/Non-iced
- Ice slurry (metabolic inhibition)
  - Helps preserve pH, $pCO_2$, $pO_2$, glucose & lactate
  - $pO_2$ might increase in plastic syringes
  - May increase K, decrease Na
- Non-iced
  - Must analyze quickly
  - No change in K
  - ↓ Glucose 9 mg/dL/Hr
  - ↑ Lactate 0.5 mmol/L/Hr
Ice slurry: pro-con

**Pro**

- Minimizes metabolic changes
  \[ pO_2 \downarrow, pCO_2 \uparrow, pH \downarrow, glucose \downarrow, lactate \uparrow \]
  
  WBCs & thrombocytes oxidative metabolism
  \[ pO_2 \downarrow, pCO_2 \uparrow, pH \downarrow, glucose \]

  RBCs anaerobic metabolism
  \[ lactate \uparrow, pH \downarrow, glucose \downarrow \]
Ice slurry: pro-con

**Con**

- Possibility of enhanced “syringe hole” effect
- Inhibition of Na/K pump
- Cell membranes rupture more readily
  - Hemolysis, falsely elevates K
Hole Effect

“Plastic syringes are holes surrounded by plastic”

Kevin Fallon, PhD  Director (retired) Scientific Affairs, Instrumentation Laboratory

- Syringes are somewhat porous to gases
- Hole effect is enhanced by exposure to ice water
  - At 4° O₂ solubility nearly doubles
  - Oxyhemoglobin curve shifts to left
  - On analysis at 37° “Increased” pO₂
Ice slurry storage- plastic syringes

- Iced storage - iced vs. 22° C storage: over time, iced samples showed 1/3 of changes in pH, $pCO_2$ and $pO_2$ from post-draw metabolism
- Rapid increase in $pO_2$ in 20-250 mmHg range
- Samples with $pO_2 > 250$ showed decrease over time
- Change in $pO_2$ effected by HbO$_2$ capacity
- Conclusion: ice stored samples should be analyzed within 30 minutes

Iced Plastic Syringes “Hole Effect”

Ice Slurry

- Icing virtually stops metabolism
- Leukocythemia is an exception
  - Leukocyte larceny
Leukocyte Larceny

- Leukocytes consume $O_2$ at rapid rate
  - Icing normally slows $O_2$ consumption
- Samples with very high WBC may consume significant $O_2$ before sample cools
Leukocyte Larceny

Normal WBC

Leukocythemia

A. Van Kessel
Pneumatic Tube Transport (PT)

Study conclusions:

- pH and $pCO_2$ not significantly affected by PT, regardless of use of sealed/non-sealed tubes
- $pO_2$ significantly altered in non-sealed tubes
- $pO_2$ not significantly different if sent in pressure sealed tubes (if there is no trapped air)

Whole Blood Collection & Storage for Blood Gas and Electrolytes

- Expel air immediately and completely
- Measure < 30 minutes - room temperature*
- Measure > 30 minutes - ice/water slurry*
- Measure immediately- 100,000 white count

Catheter Flush (discard volume)

- Arterial and venous catheters must be adequately flushed prior to sampling

- Inadequate flush volume will bias sample with contents of flush solution

- Appropriate discard volume dependent upon deadspace volume of catheter
Discard Volume Study* (catheter flush)

- 84 critically ill patients, 504 total samples
- 20-gauge A-Line
- 6 samples each with discard volumes of 1, 1.5, 2, 2.3, 3.6 and 5.5 times deadspace

# Catheter flush discard volume

<table>
<thead>
<tr>
<th>Deadspace Multiple</th>
<th>1</th>
<th>2</th>
<th>5.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.403</td>
<td>7.418</td>
<td>7.424</td>
</tr>
<tr>
<td>$pCO_2$</td>
<td>35.9</td>
<td>38.8</td>
<td>39.6</td>
</tr>
<tr>
<td>$pO_2$</td>
<td>102.7</td>
<td>98.3</td>
<td>97.8</td>
</tr>
<tr>
<td>Na</td>
<td>145.6</td>
<td>142.1</td>
<td>141</td>
</tr>
<tr>
<td>K</td>
<td>3.44</td>
<td>3.95</td>
<td>4.12</td>
</tr>
</tbody>
</table>

Adapted from: *Critical Care Med* 2003 Vol. 31, No. 6 pp 1654-1658
Catheter flush discard volume

Conclusion:
- Nearly all samples showed bias
- Discard volume 2X deadspace gives clinically acceptable values
- Catheter deadspace can vary with catheter type or manufacturer
Catheter Deadspace Volume
Pulmonary Artery Line (PAL)

- Source for mixed venous blood
- Often drawn with ABG for a-v O\textsubscript{2} content gradient
- Accurate Hb and %HbO\textsubscript{2} critical for a-v gradient

Results compromised if
- Line inadvertently wedged
- Sample withdrawn too quickly
- Improperly mixed
- Insufficient discard volume drawn
Pulmonary Artery Catheter Placement
Is There a Problem?

<table>
<thead>
<tr>
<th></th>
<th>Radial Artery</th>
<th>Pulm. Artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.31</td>
<td>7.38</td>
</tr>
<tr>
<td>$pCO_2$</td>
<td>35</td>
<td>32</td>
</tr>
<tr>
<td>$pO_2$</td>
<td>51</td>
<td>128</td>
</tr>
</tbody>
</table>
Proper PAL Placement

<table>
<thead>
<tr>
<th></th>
<th>Radial Artery</th>
<th>Pulm. Artery Redraw</th>
<th>Pulm. Artery Wedged</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.31</td>
<td>7.26</td>
<td>7.38</td>
</tr>
<tr>
<td>$pCO_2$</td>
<td>35</td>
<td>41</td>
<td>32</td>
</tr>
<tr>
<td>$pO_2$</td>
<td>51</td>
<td>31</td>
<td>128</td>
</tr>
</tbody>
</table>
PAL precautions-Erroneous Results

Catheter wedged or sample drawn too quickly

- PAL draws from “right heart or mixed venous”
- Wedged position draws from “left heart or arterial”
- Wedged samples reflects local V/Q (ventilation/perfusion)
  - $pO_2$ can be higher than arterial value
- Wedged sample $\uparrow$ pH, $\downarrow pCO_2$, $\uparrow pO_2$ compared to PAL sample
PAL precautions

- Draw 2 x deadspace: otherwise, line fluid will contaminate sample

- Draw must be slow (1ml/5sec) for PA sample or mixed venous can be contaminated with “arterialized” blood

- PA sample drawn from inadvertently wedged catheter will be contaminated with “arterialized” blood

- Wedged samples must have balloon inflated
Now What’s Wrong?

<table>
<thead>
<tr>
<th></th>
<th>Arterial</th>
<th>Mixed Ven.</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.45</td>
<td>7.29</td>
</tr>
<tr>
<td>$pCO_2$</td>
<td>30</td>
<td>44</td>
</tr>
<tr>
<td>$pO_2$</td>
<td>168</td>
<td>35</td>
</tr>
<tr>
<td>Hb g/dL</td>
<td>9.4 (94g/L)</td>
<td>14.5 (145g/L)</td>
</tr>
<tr>
<td>Hct</td>
<td>28</td>
<td>44</td>
</tr>
</tbody>
</table>
Specimen Mixing

- Whole blood samples must be mixed thoroughly (particularly for Hb/Hct accuracy)

Recommendation
- 15 second minimum (or longer)
- Mix in two planes (rock & roll)
- Be gentle (prevent hemolysis, very important for K)
Temperature Adjustment

Blood gas analyzers measure at 37° C

Patient temp correction algorithms:

- Temp adjusted pH reciprocal to temperature
  0.015 per C° (7.40 at 37° = 7.36 at 40°)
- $pCO_2$ increase/decrease with temperature
  5% per C° (40 mmHg at 37° = 46 at 40°)
- $pO_2$ increase/decrease with temperature
  6% per C° (50 mmHg at 37° = 59 at 40°)
## Temperature Adjustment

<table>
<thead>
<tr>
<th>Temp.</th>
<th>37</th>
<th>39</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.40</td>
<td>7.37</td>
<td>7.50</td>
</tr>
<tr>
<td>$\rho CO_2$</td>
<td>40</td>
<td>44</td>
<td>30</td>
</tr>
<tr>
<td>$\rho O_2$</td>
<td>80</td>
<td>90</td>
<td>54</td>
</tr>
</tbody>
</table>

Temperature Adjustment

Routine temperature adjustment not recommended

- Reference range is at 37°C
- Wrong clinical decision?
  - Should not evaluate temp adjusted values vs. 37°C reference range
- How accurate are patient temperatures?
  - Oral, axial, elsewhere?
  - When was temp taken?
- Increases error probability
  - Comparing serial ABGs
- Role in rescue hypothermia/Bypass Surgery?
What could possibly be wrong???

<table>
<thead>
<tr>
<th></th>
<th>#1</th>
<th>Repeat</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.52</td>
<td>7.18</td>
</tr>
<tr>
<td>$\rho$CO$_2$</td>
<td>115</td>
<td>35</td>
</tr>
<tr>
<td>$\rho$O$_2$</td>
<td>9</td>
<td>219</td>
</tr>
<tr>
<td>Na</td>
<td>200</td>
<td>145</td>
</tr>
<tr>
<td>K</td>
<td>2.6</td>
<td>3.0</td>
</tr>
<tr>
<td>Ca</td>
<td>2.6</td>
<td>1.5</td>
</tr>
<tr>
<td>Hb</td>
<td>6.7 (67)</td>
<td>5.2 (52)</td>
</tr>
<tr>
<td>Hct</td>
<td>20</td>
<td>15</td>
</tr>
</tbody>
</table>
Patient Resuscitation

Infusion line in Rt. Femoral vein

Sample #1 drawn from Rt. Femoral

Repeat sample drawn from Lt. Femoral
In Summary: AVERT

Air in the sample
Venous sampling or admixture
Excessive or improper anticoagulation
Rate of metabolism
Temperature alterations

Pre-analytic Error Prevention

- Awareness
- Prevention
  - Policy/procedure
  - Training & competency
  - Monitoring compliance
- Reduced error = improved care/ better patient outcome
References/Resources

Clinical Blood Gases Assessment and Intervention, 2nd Edition
William J. Malley
Elsevier Saunders, St. Louis, MO

Preventing pre-analytical error in blood gas analysis
(3-part series)
Focus, 2006 Mar/Apr, Jul/Aug, Nov/Dec
John J. Ancy

Blood Gases and Pre-analytic Error Prevention
RT for Decision Makers, Feb. 2012
John J. Ancy