Pre-Analytical Errors in Capillary Blood Gas Sampling

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SASKATOON HEALTH REGION

SASKATOON, SASKATCHEWAN, CANADA

Saskatoon Health Region

Where in the World is Saskatchewan?

+ Fall
+ Winter

Objectives

Discuss the unique challenges involved in the identification and collection of capillary blood specimens from neonates

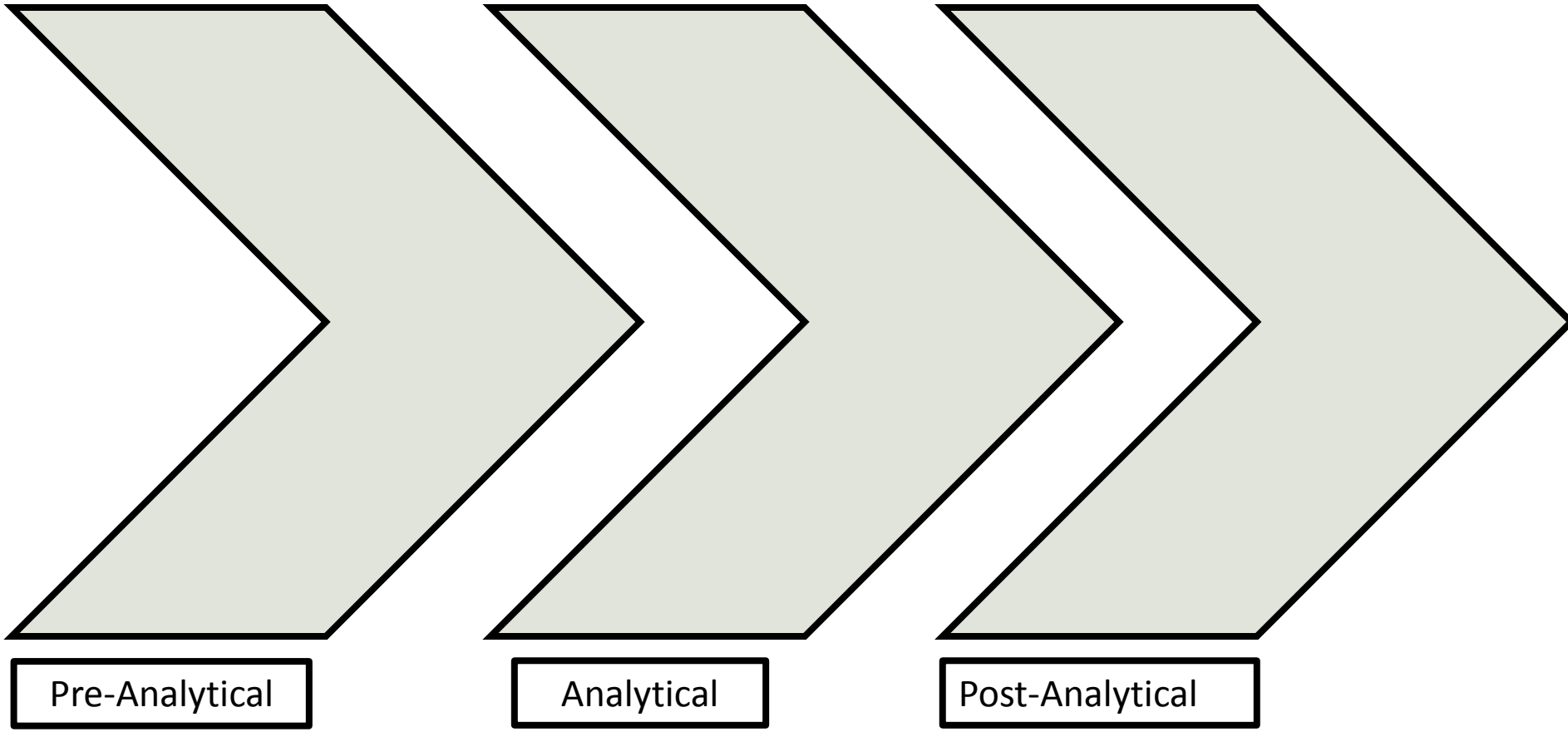
Describe the effect of body temperature, specifically hypothermia, on the measurement of blood gases

Analyze the limitations of arterialization of capillary blood specimens on the measurement of blood gases

Review the ways in which heparin based anticoagulants can influence the measurement of electrolytes, specifically ionized calcium

Assess the effect of small air bubbles and transporting blood through the pneumatic tube on the measurement of oxygen

Potential Errors in Obtaining and Reporting a Blood Gas Result



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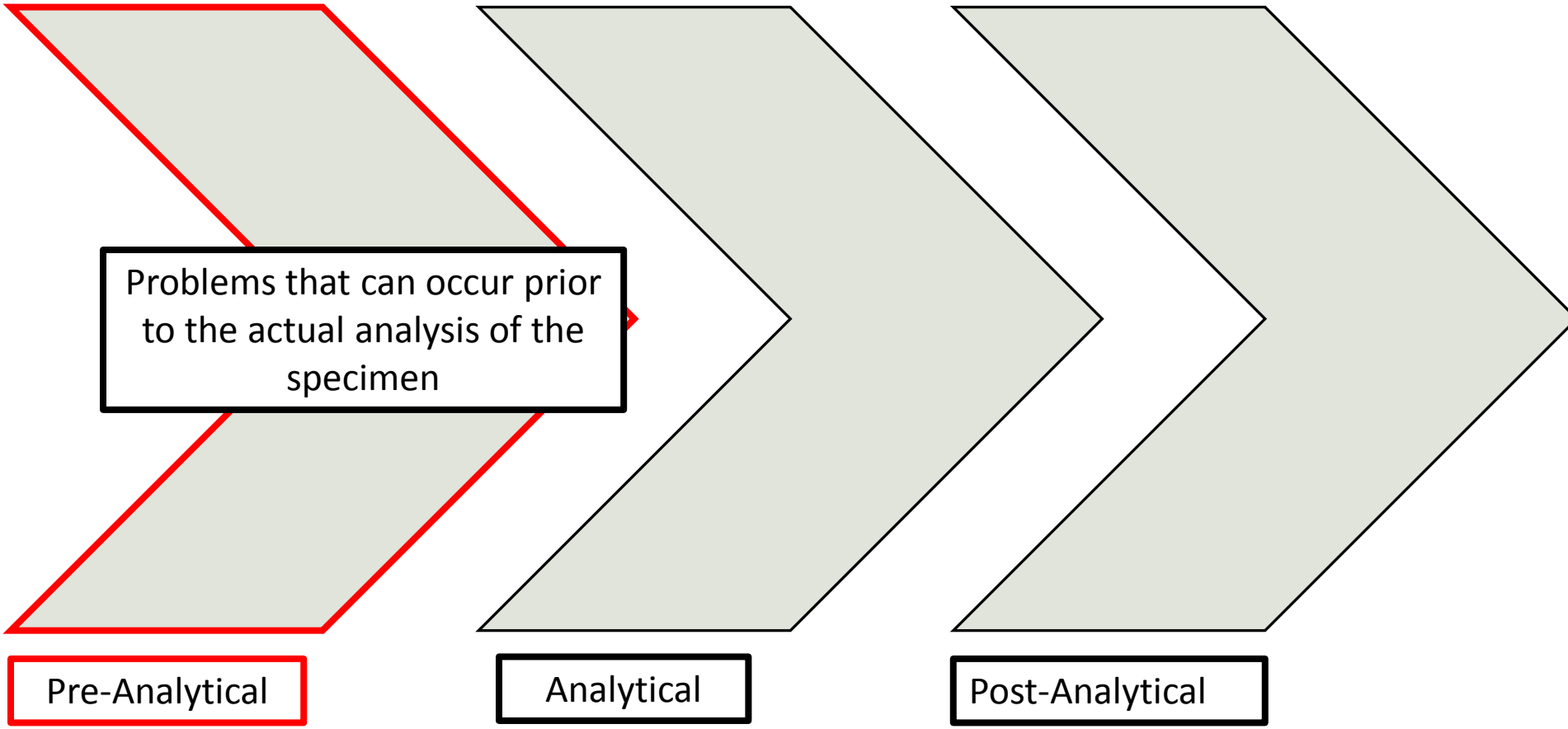

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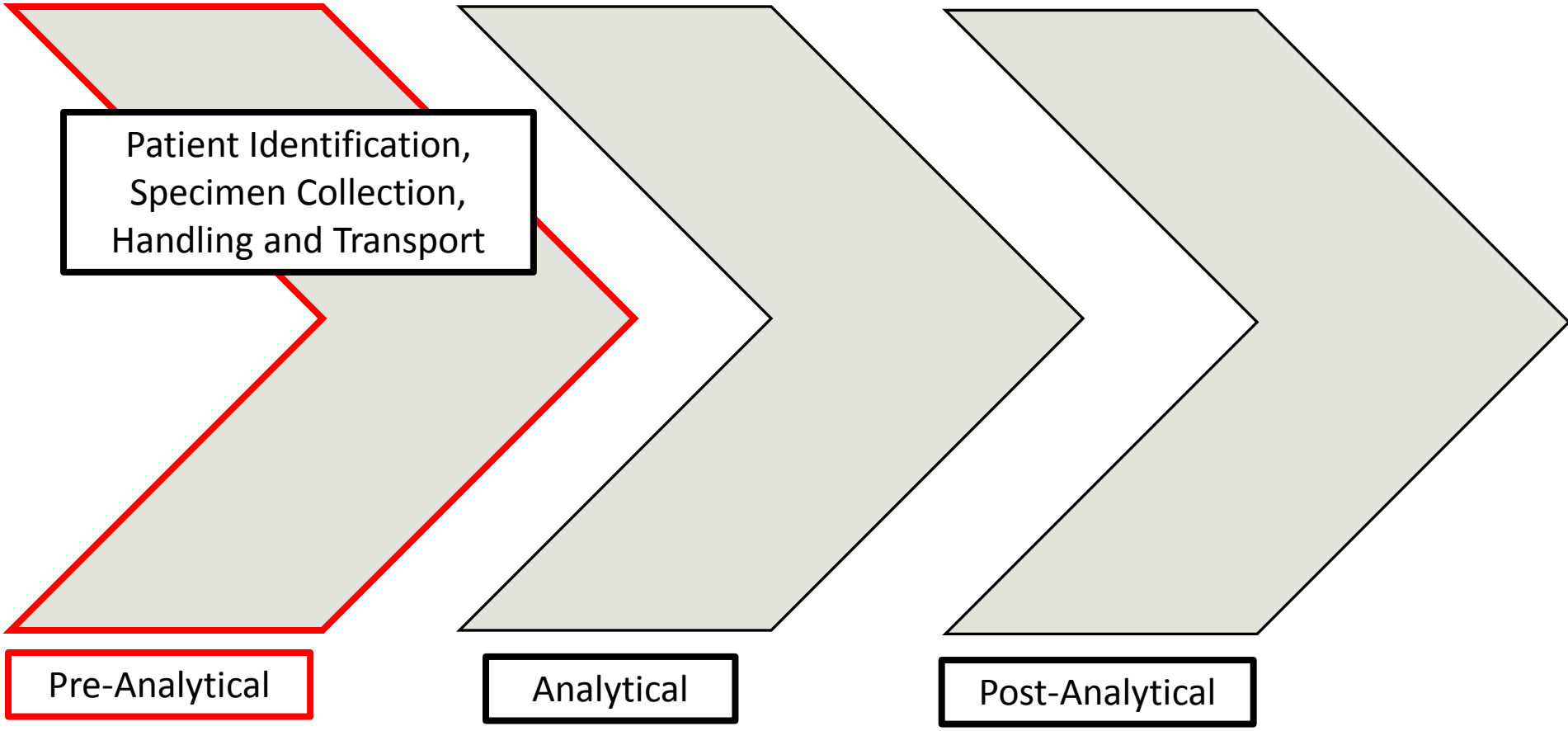

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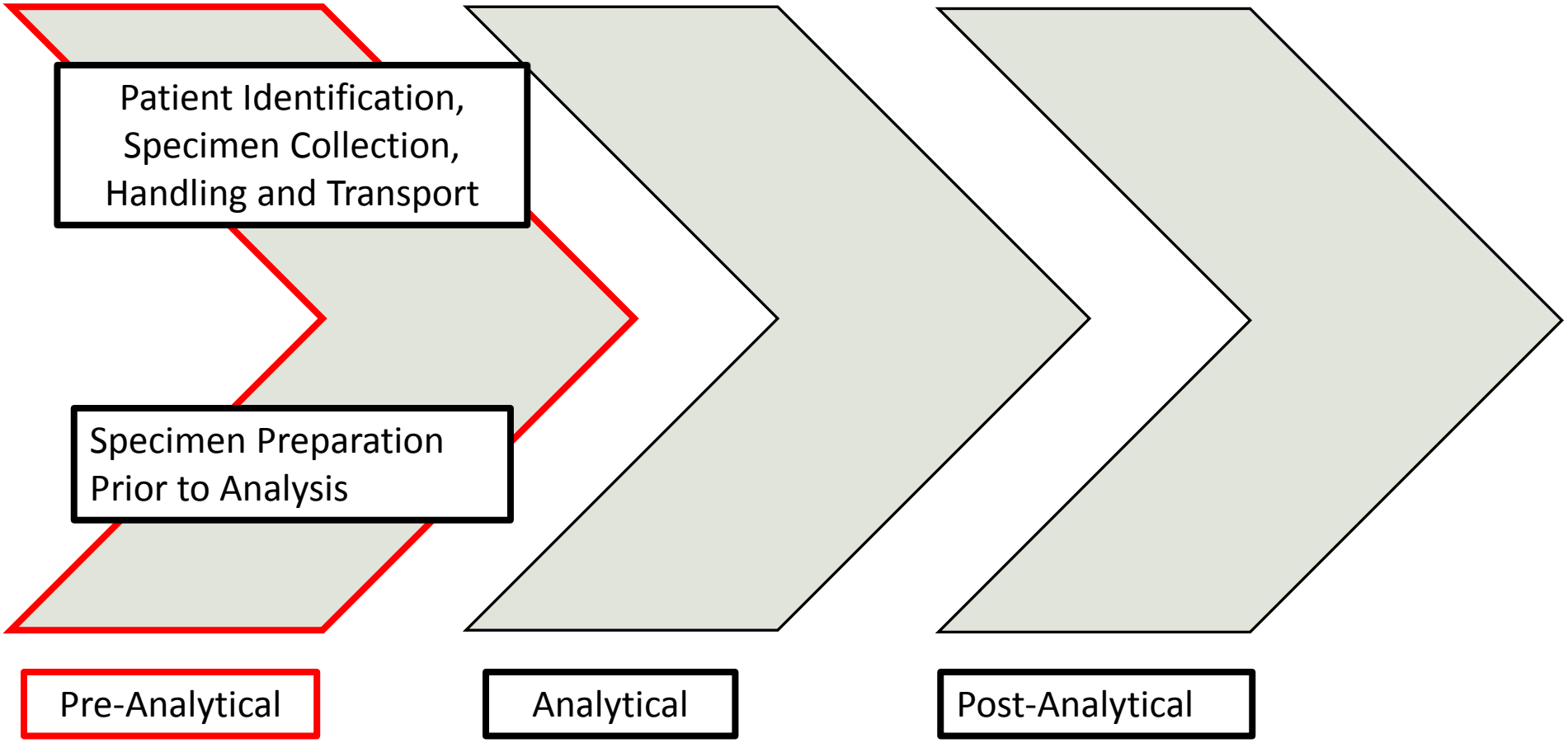

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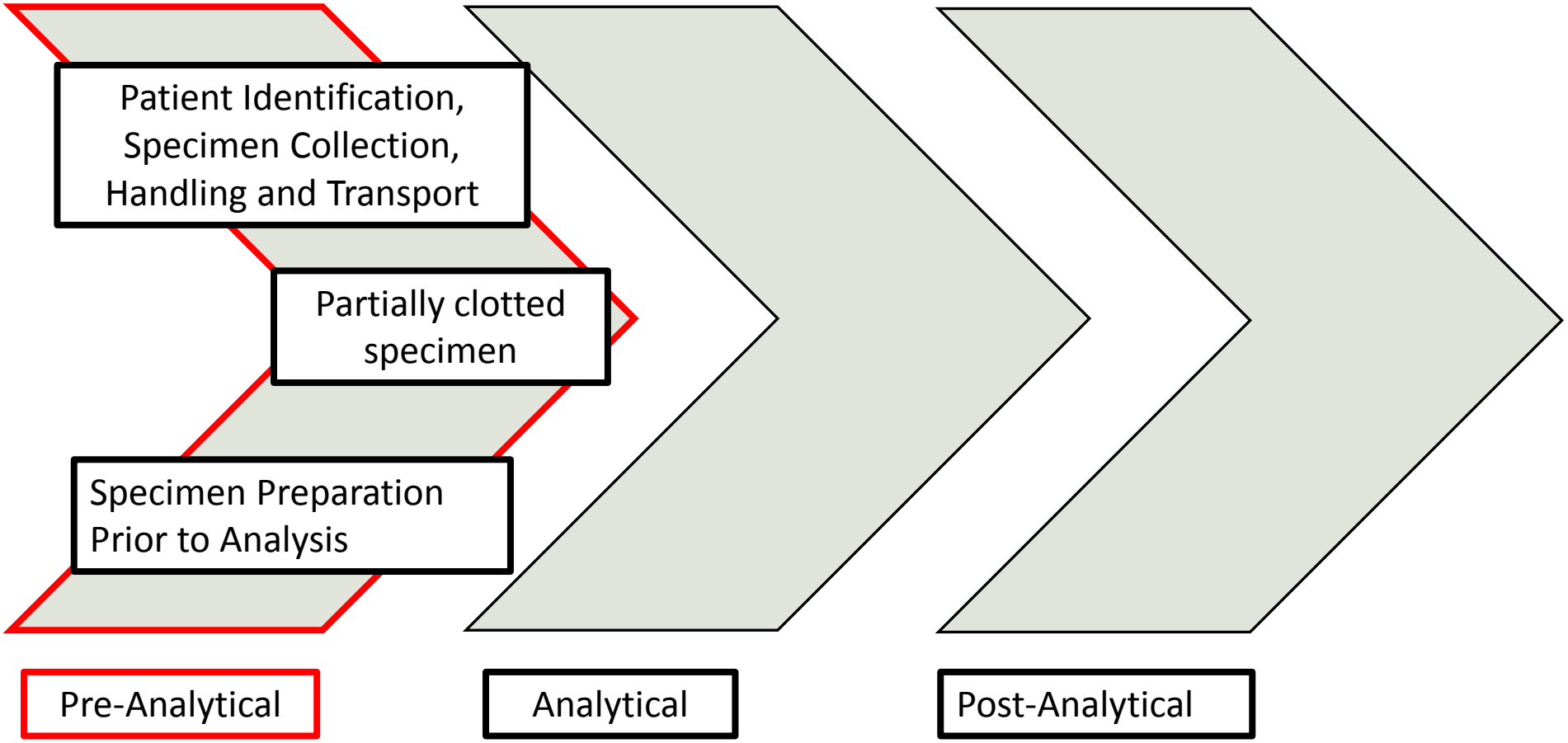

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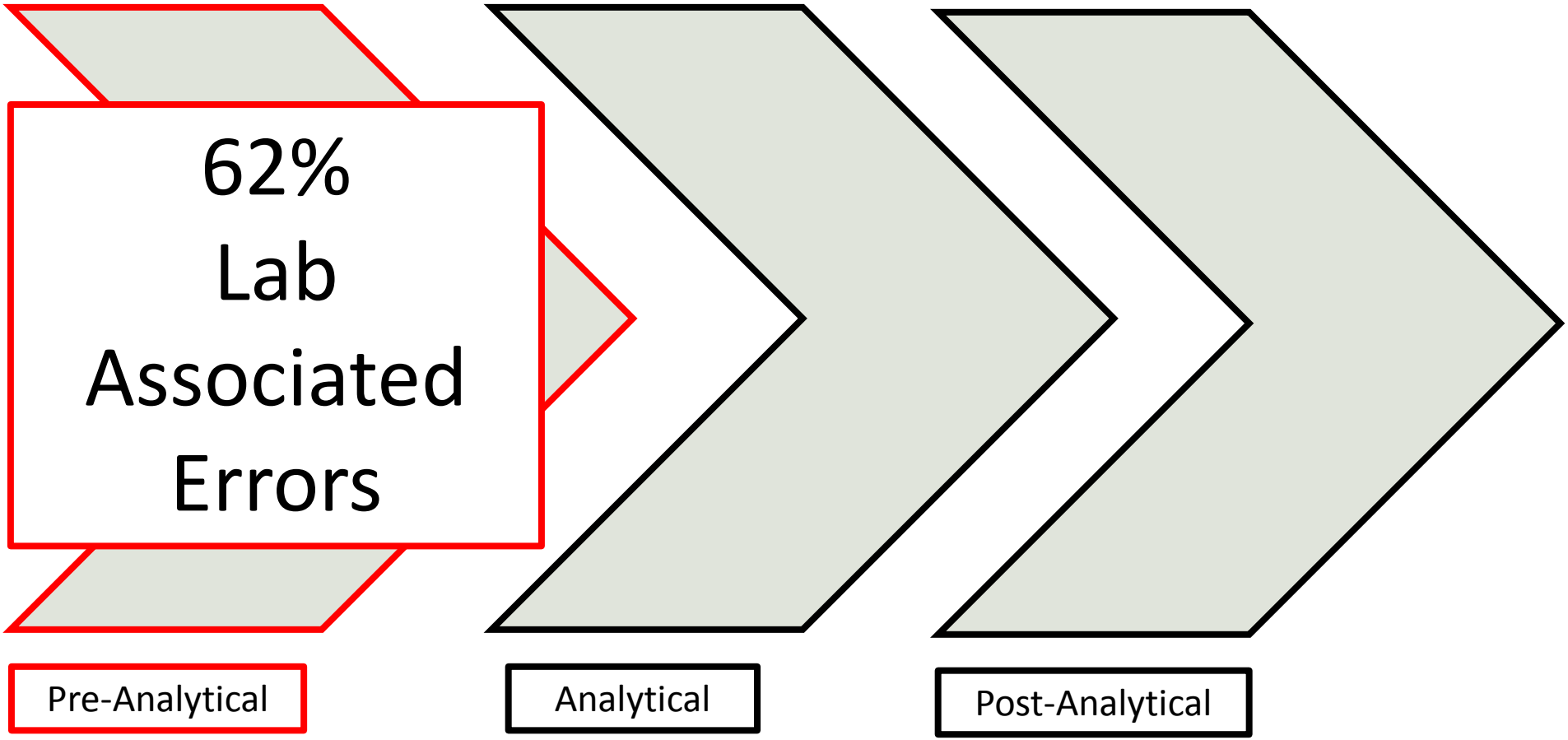

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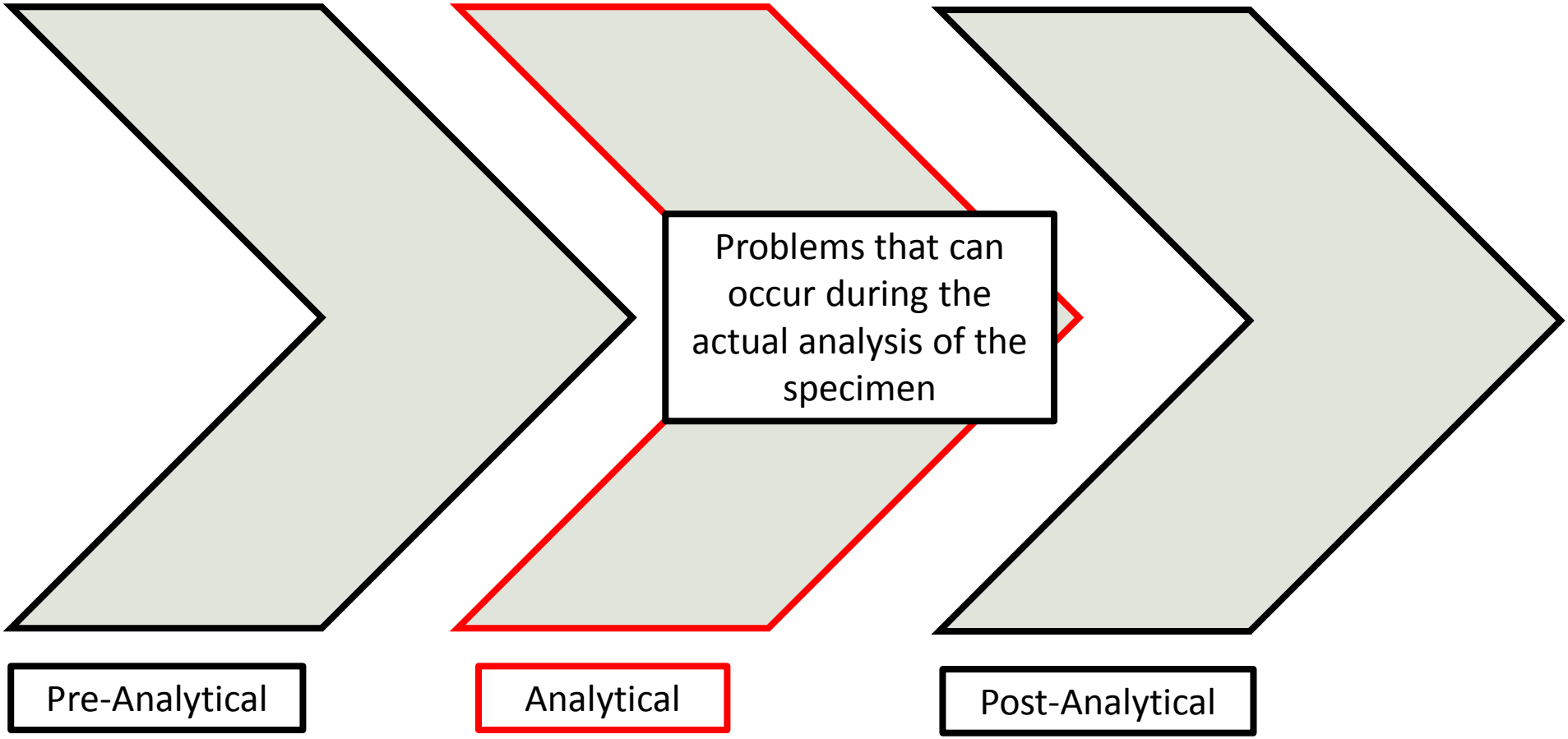

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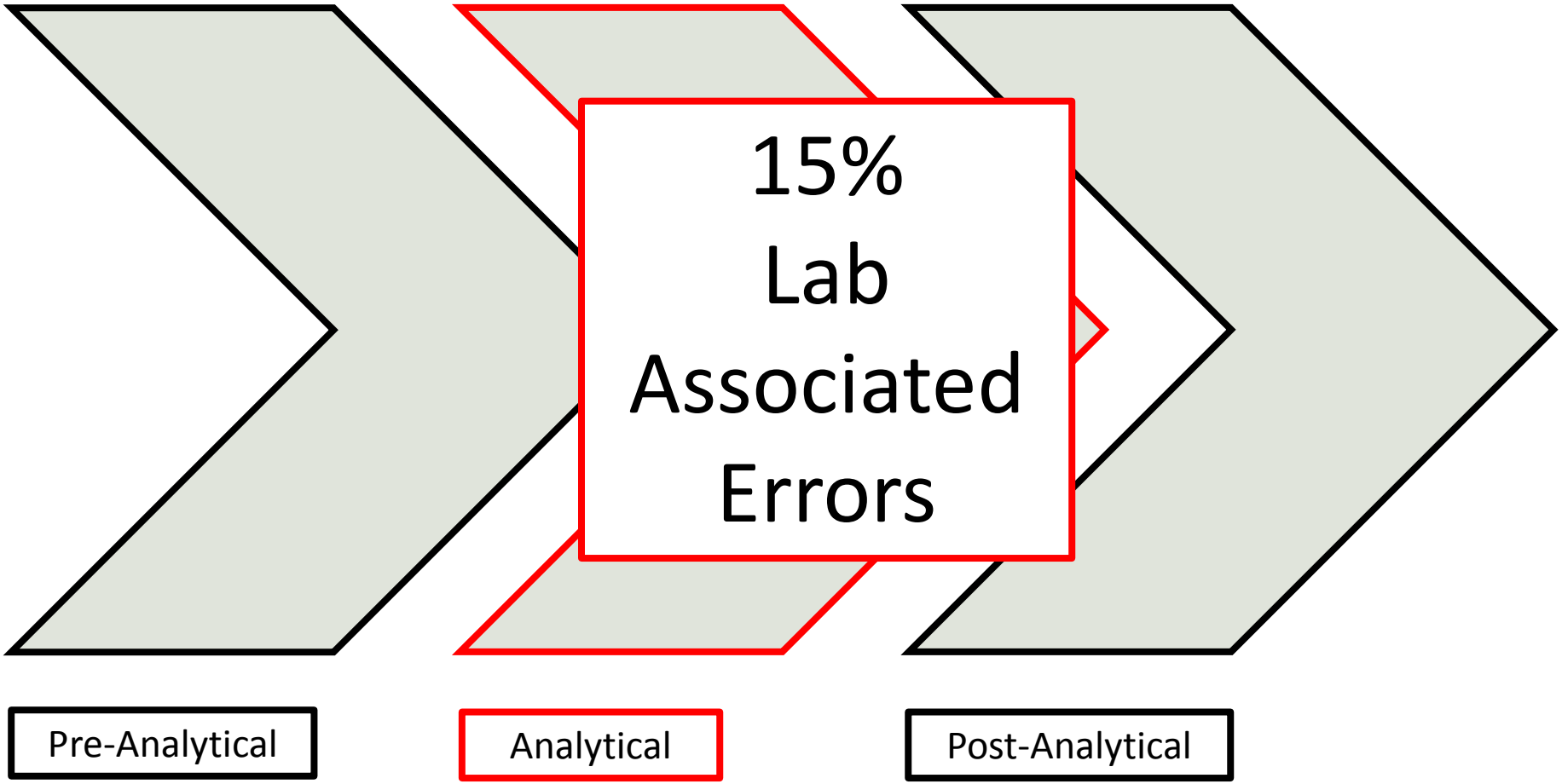

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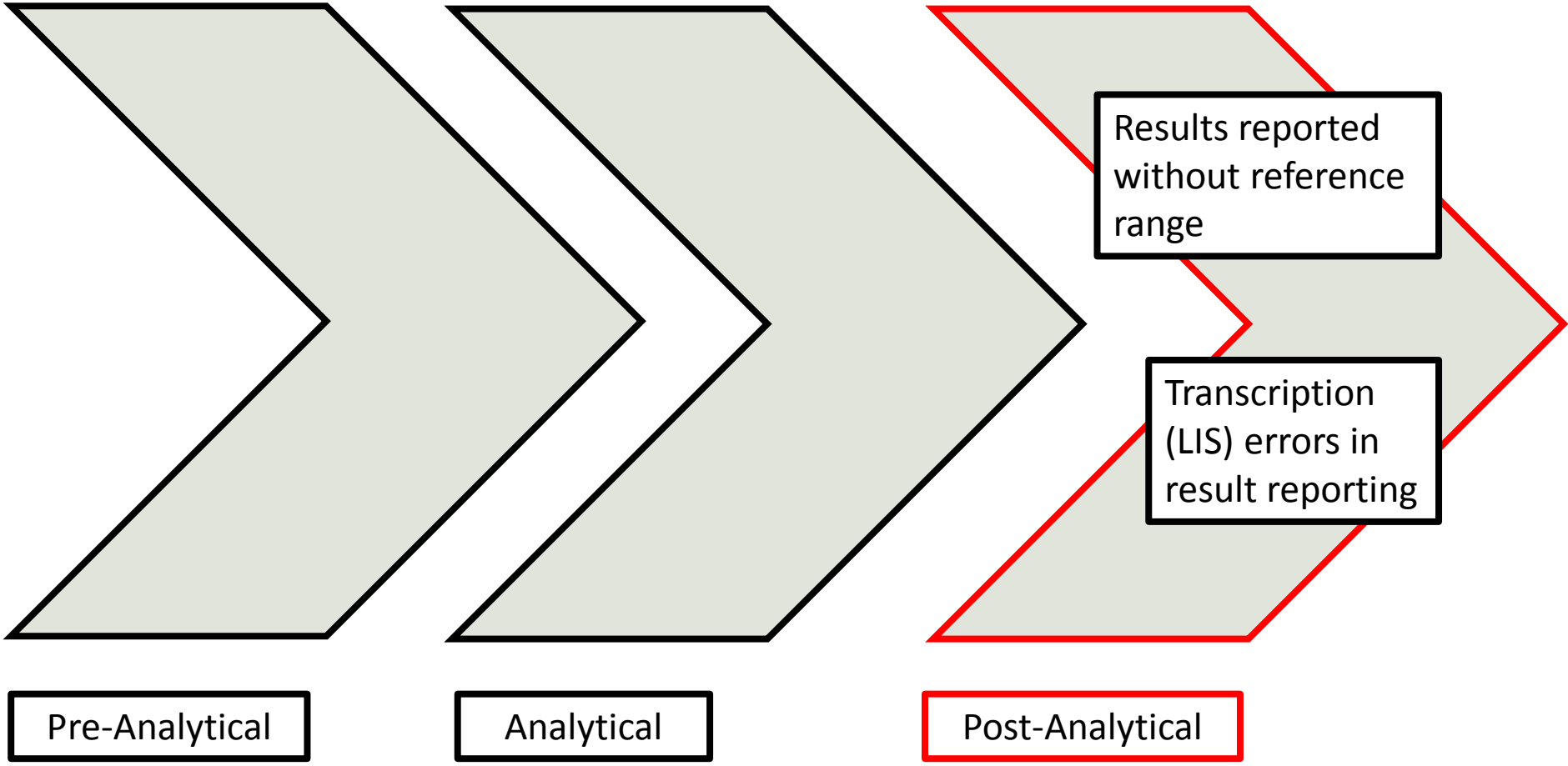

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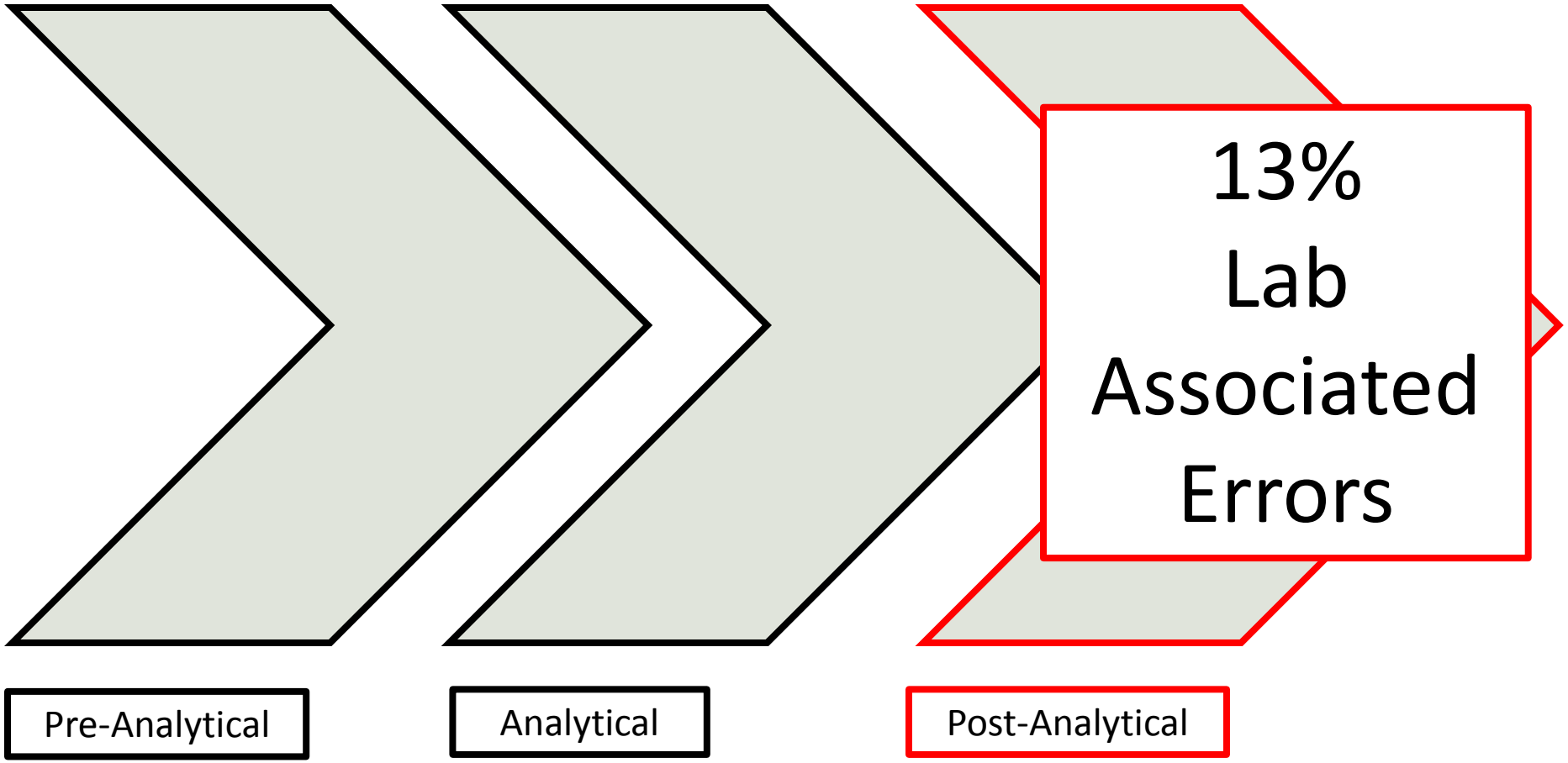

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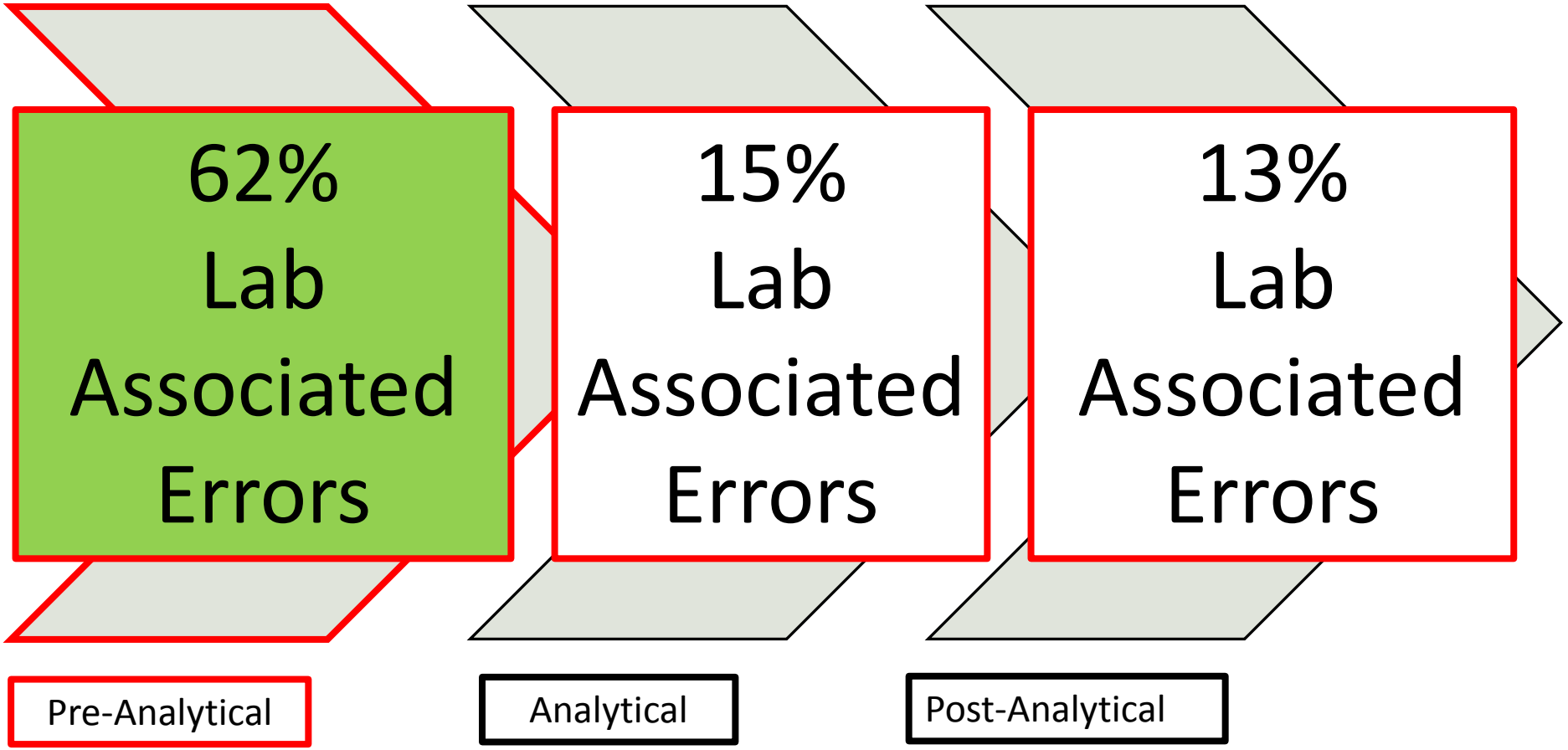

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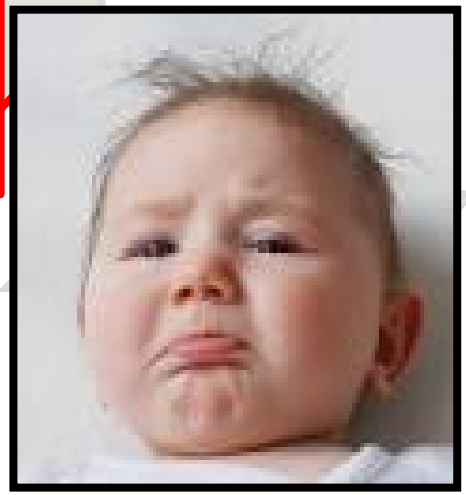
Potential Errors in Obtaining and Reporting a Blood Gas Result

62%
Lab
Associated
Errors

Pre-Analytical





Pre-Analytical Errors in Capillary Blood Gas Sampling

Special Emphasis on Neonates

Saskatoon Health Region

Survey 204 clinical labs Croatia (174:85%)

Objectives

1) Prevalence of CBS for different patient populations

2) Compliance of protocols with international guidelines

Nationwide survey of policies and practices related to capillary blood sampling in medical laboratories in Croatia

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Abstract

Introduction: Capillary sampling is increasingly used to obtain blood for laboratory tests in volumes as small as necessary and as non-invasively as possible. Whether capillary blood sampling is also frequent in Croatia, and whether it is performed according to international laboratory standards is unclear.

Materials and methods: All medical laboratories that participate in the Croatian National External Quality Assessment Program (N = 204) were surveyed on-line to collect information about the laboratory's parent institution, patient population, types and frequencies of laboratory tests based on capillary blood samples, choice of reference intervals, and policies and procedures specifically related to capillary sampling. Sampling practices were compared with guidelines from the Clinical and Laboratory Standards Institute (CLSI) and the World Health Organization (WHO).

Results: Of the 204 laboratories surveyed, 174 (85%) responded with complete questionnaires. Among the 174 respondents, 155 (89%) reported that they routinely perform capillary sampling, which is carried out by laboratory staff in 118 laboratories (76%). Nearly half of respondent laboratories (48%) do not have a written protocol including order of draw for multiple sampling. A single puncture site is used to provide capillary blood for up to two samples at 43% of laboratories that occasionally or regularly perform such sampling. Most respondents (88%) never perform arterialisation prior to capillary blood sampling.

Conclusions: Capillary blood sampling is highly prevalent in Croatia across different types of clinical facilities and patient populations. Capillary sampling procedures are not standardised in the country, and the rate of laboratory compliance with CLSI and WHO guidelines is low.

Key words: capillaries; blood specimen collection; standardisation; diagnostic techniques and procedures

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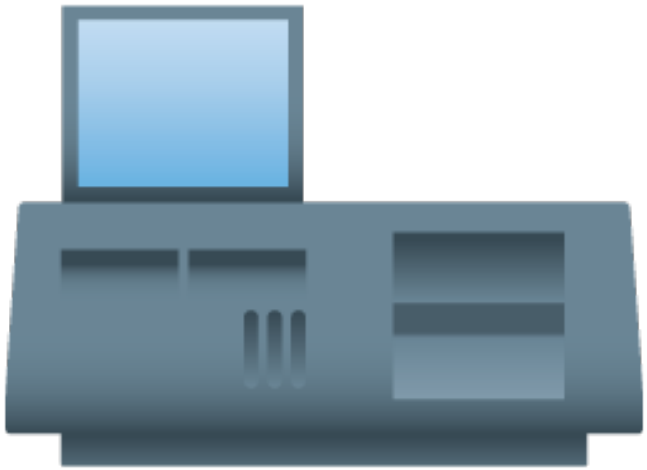
Introduction

Capillary blood sampling allows much smaller blood volumes to be drawn in a much less invasive manner than venous sampling. Capillary blood samples are primarily arterial blood, though they also contain unknown proportions of blood from venules, arterioles, and capillaries, as well as from interstitial and intracellular fluid (1). Together with technological advances that allow multiple blood tests to be performed quickly and easily with small sample volumes, capillary sampling is helping to drive the widespread use of point-of-care (POC) diagnostics. POC analyzers are meant to allow clinical staff, rather than laboratory staff, to perform a variety of tests quickly and easily in the ward rather than in the laboratory (2).

Although capillary blood sampling has several advantages over venous sampling, it also carries greater risk of giving incorrect test results. This is because hemolysis and lipemia cannot be detected in capillary-sampled blood, and both can significantly affect test results. In addition, analyte concentrations can differ between capillary and venous blood, potentially invalidating standard reference ranges based on venous blood. Indeed, differences between the two sampling methods mean that clinicians must be careful to perform

- 89% of labs performed CBS routinely or occasionally
- 75% CBS used for hematology (CBC); 24% blood gases
- 51% CBS performed in Pediatrics
- 78% of labs performing CBS had a written protocol; only 30% included order of draw for multiple specimens

Capillary Blood Gas Analysis



- Not just blood gases !
  - (pO_2, pCO_2, pH)
- Hemoglobin derivatives
  - (carboxy-Hb, met-Hb, oxy-Hb, and reduced Hb)
- Electrolytes
  - (Na^+, K^+, Cl^-, iCa^{2+}, iMg^{2+})
- Metabolites
  - (glucose, lactate, creatinine, TBIL)

Outline

Identification Issues

Patient Info
- Age
- Body Temp

Puncture Site
- Heel
- Earlobe

Arterialization

Anticoagulant

Method and Conditions of Specimen Transport

Sample Handling

Clinical Laboratory

Identification Issues

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"Voluntary Electronic Reporting of Laboratory Errors. An Analysis of 37,532 Laboratory Event Reports from 30 Health Care Organizations"

Snydman et al., *American Journal of Medical Quality*; 2012:27(2); 147-53

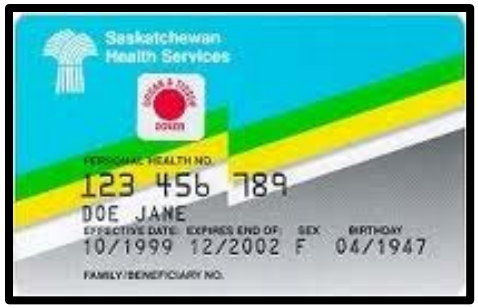
- Pre-analytical events were most commonly (81.1%) reported
  - 18.7% specimen not labelled
  - 16.3% specimen mislabelled
  - 13.2% improper collection

} Top 3 problems

Patient Identification

(CLSI GP33-A Accuracy in Patient and Sample Identification)

- Two unique patient identifiers
  - Full name
  - Assigned ID number
  - Date of Birth
  - Photo ID on government approved card (ie driver's licence)



Patient Identification – At Birth

- First ID band (mother's information)
- Within 1 hr of birth, baby issued with personal health number (second ID band)

When baby arrives in Post Partum – 2 ID bands

Patient Identification Normal Newborn Nursery

- First ID band (mother's information)
- Within 1 hr of birth, baby issued with personal health number (second ID band)
  - Date of Birth
  - No given name yet – will happen after birth registration forms filled out

Patient Identification Challenges

- Mother's surname (at birth) Father's surname (after birth registration)
- Identification of twins, triplets etc.
  - Twin A Baby Girl
  - Twin B Baby Boy

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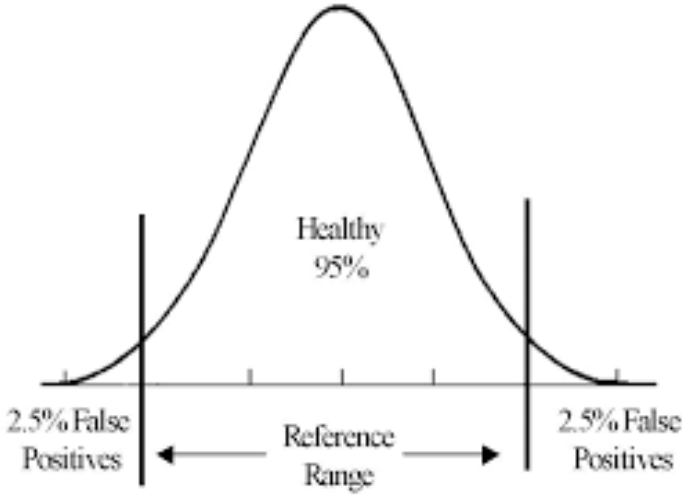
Patient Assessment Information (CLSI C46-A2)

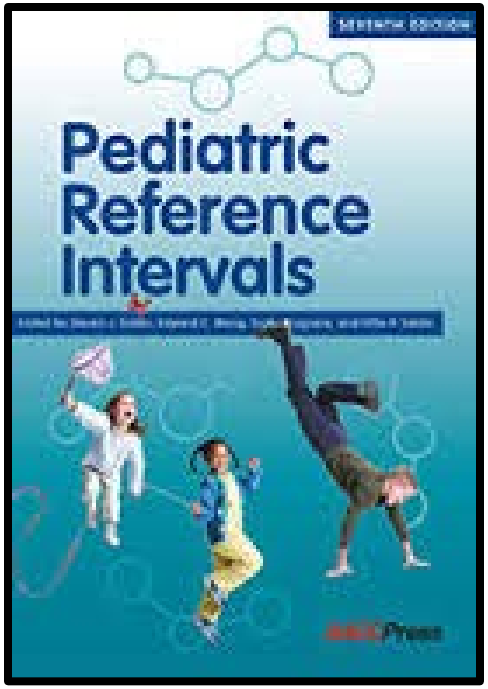
- "Steady state" ventilation (20-30 min acceptable for most patients post ventilator change)
- **Patient age** & Location
- **Body Temperature**
- Time of sampling
- FIO_2 or actual flow rate and method of delivery
- Ventilatory status (spontaneous breathing or assisted/controlled ventilation)
- Mode of Ventilation (pressure support)
- Site of Sampling
- Position and/or activity (rest, exercise)

Gestational & Post- Natal Age: Pre-analytical Error?

- Analysis of blood gases, basic biochemistry, coagulation, CBC, urinalysis and microbiology should be available in all units where babies are delivered
- Pediatric and Neonatal patients are not just little adults
- Acquiring Gestational Age (& Post-Natal Age) reference ranges is a huge challenge



Neonatology & Laboratory Medicine, Anne Green, Imogen Morgan and Jim Gray, 2003



PEDIATRIC AND
MATERNAL-FETAL
DIVISION

AACC
Better health through laboratory medicine.

Plasma Creatinine Concentration (µmol/L)				
Post-Natal Age	Gestational Age (28 weeks)	Gestational Age (32 weeks)	Gestational Age (36 weeks)	Gestational Age (40 weeks)
2 days	40 - 220	27 - 175	23 - 143	18 - 118
7 days	23 - 145	19 - 119	16 - 98	13 - 81
14 days	18 - 118	15 - 97	12 - 80	10 - 66
21 days	16 - 104	14 - 86	11 - 71	9 - 57
28 days	15 - 95	12 - 78	10 - 64	9 - 53

Neonatology & Laboratory Medicine, Anne Green, Imogen Morgan and Jim Gray, 2003, pg 303

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Body Temperature & Premature Babies

Robin Knobel, PhD, RN, assistant professor at the Duke University School of Nursing in Durham North Carolina, and a Robert Wood Johnson Foundation nurse faculty scholar, shared her research at the conference. In a telephone interview with Medscape Medical News*, she discussed what nurses can learn from this type of monitoring.*

Medscape: What prompted you to study temperature regulation in extremely low-birthweight infants?

Dr. Knobel: I worked as a NICU [neonatal intensive care unit] and a neonatal nurse practitioner. We did a lot of transport, and it would always impress me how cold the babies were when we would pick them up. Nurses would take care of everything — blood pressure, ventilation, all those vital things — but many times they would forget about the temperature.

Once I picked up a really cold baby who ended up dying because he was so hypothermic in the beginning. I also saw many hypothermic babies coming from the delivery room who would be cold from the delivery experience. I decided that I wanted to do something to improve temperatures for babies.

Body Temperature & Premature Babies

- All infants up to ~ 1 yr generate heat by non-shivering thermogenesis
  - Thermogenin
    - mitochondrial protein (brown adipose tissue)
    - Used to generate heat
- Infants < 32 wks do not warm themselves effectively (relative deficiency of thermogenin)

Henry's Law

- The partial pressure of a gas is proportional to its concentration at a given temperature and pressure

Hypothermia used as neuroprotective strategy for asphyxiated neonates

Hypothermia affect blood gas solubility

- Decrease temp
- Increase pH
- Decrease pCO_2

pCO_2 affects vascular tone & cerebral perfusion

COMMENTARY

Blood Gas Values During Hypothermia in Asphyxiated Term Neonates

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The authors have indicated they have no financial relationships relevant to this article to disclose.

HYPOTHERMIA HAS BECOME an important novel neuroprotective strategy for asphyxiated term neonates.[1] Most of these neonates will receive mechanical ventilation. Hypothermia affects blood gas parameters such as pH and P_{CO_2}. At lower temperatures pH increases and P_{CO_2} decreases. This is relevant, because P_{aCO_2} is known to affect vascular tone and, hence, cerebral perfusion.[2] In addition, cerebral blood flow decreases during hypothermia, which increases the risk of insufficient blood flow during hypocapnia.[3]

Most blood gas instruments, whether a central laboratory or point-of-care device, contain a temperature-controlled sample chamber specified to be 37°C. It is at that temperature that all measurements of pH and partial pressure of gases are performed. In the α-stat strategy, uncorrected values are used to keep the pH and P_{CO_2} close to the 37°C reference value.[4] However, most instruments can calculate and present temperature-corrected pH and P_{CO_2} values. In the so-called pH-stat method, the measured pH is corrected to the actual body temperature of the patient. Ventilator settings can be adjusted to keep the actual pH as close to 7.4 as possible.[4] At present, it is unclear whether the α-stat or pH-stat theory should be used in the neuroprotective strategy for asphyxiated term neonates.

In the 2 large randomized, controlled trials on therapeutic hypothermia in term neonates with perinatal asphyxia, attending physicians were advised to correct blood gases and pH for rectal temperature.[5,6] Here we will summarize the relevance of blood gas values in and the effects on cellular function during hypothermia.

HYPOTHERMIA, P_{CO_2}, AND pH

Physical laws determine that the solubility of a gas within a liquid decreases when lowering the temperature. During hypothermia, arterial P_{CO_2} decreases and pH increases compared with 37°C when measurements are made at the actual body temperature (Fig 1). In healthy subjects with a body temperature of 37°C, pH and P_{aCO_2} should approach 7.4 and 5.3 kPa (40 mm Hg), respectively. During hypothermia (33°C), pH will rise to 7.5 and P_{CO_2} will decrease to 4.5 kPa (34 mm Hg).

P_{aCO_2} AND CEREBRAL BLOOD FLOW

Under normal conditions, term neonates autoregulate their cerebral blood flow in response to changes in systemic arterial pressure, but this mechanism can be impaired during neonatal distress.[7] In particular, changes in P_{aCO_2} have a well-recognized effect on cerebral blood flow. Hypocapnia induces cerebral vasoconstriction and may decrease cerebral tissue high-energy phosphates.[8,9] This effect has been extensively investigated in experiments in neonatal animals.[9–11] In preterm neonates, profound hypocapnia below values of 4 kPa (30 mm Hg) was related to periventricular leukomalacia.[12] There is little reason to assume that hypocapnia could not damage the brain in the sick term neonate.[13] Klinger et al[14] reported that in asphyxiated term neonates early hypocapnia was independently associated with adverse outcome. Others have reported an association between neurodevelopmental sequelae and profound hypocapnia in infants who were referred for extracorporeal membrane oxygenation because of severe cardiopulmonary failure.[15] Substantial hypercapnia and, in particular, hypocapnia must therefore be considered to be potentially dangerous for the sick asphyxiated term infant.

pH AND CELLULAR ENZYMATIC PROCESSES

There is some evidence that intracellular pH changes with temperature such that the intracellular pH remains at or close to the pH of neutrality (the state when $[H^+] = [OH^-]$). Experimental work has shown that protein buffering, largely because of the imidazole group of histidine, is responsible for maintaining this temperature-pH relationship (aided by phosphate and bicarbonate buffering). The idea that the degree of dissociation (known as α) of imidazole remains constant despite changes in temperature is known as the "α-stat hypothesis."[4] The net charge on all proteins is kept constant despite changes in temperature. It is hypothesized that as a result, all proteins can function optimally despite temperature changes.[4] The α-stat strategy is often used for pediatric and adult cardiac surgery, although there are no good data to support this practice. In contrast, in the pH-stat strategy, pH and P_{aCO_2} are maintained at constant values during cooling such that in vivo hypothermic blood is at a pH of 7.40 and the P_{aCO_2} is 5.3 kPa (40 mm Hg), whereas the blood measured at 37°C is hypercapnic and acidotic. Studies of hypothermic circu-

Opinions expressed in these commentaries are those of the author and not necessarily those of the American Academy of Pediatrics or its Committees.

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

"During hypothermia, arterial pCO_2 decreases and pH increases compared with 37°C when measurements are made at the actual body temperature"

Intensive Care Med (2005) 31:24–27
DOI 10.1007/s00134-004-2369-3

PHYSIOLOGICAL NOTE

Andreas Bacher

Effects of body temperature on blood gases

Published online: 24 June 2004

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Abstract *Background:* Changes in body temperature have important impact on measurements of blood gases. In blood gas analyzers the samples are always kept constant at a temperature of exactly 37°C during the measurements, and therefore results are not correct if body temperature differs from 37°C. *Objective:* Lack of knowledge of the effects of body temperature on results of blood gas monitoring may lead to wrong and potentially harmful interpretations and decisions in the clinical setting. The following article elucidates alterations in monitoring of blood gases and oxyhemoglobin saturation (SO_2) that occur during changes in body temperature.

Keywords Blood gas monitoring · Oxyhemoglobin saturation · Hypothermia · Hyperthermia

Blood gas monitoring

Blood gases (oxygen and carbon dioxide) are usually reported as partial pressures (gas tensions) since according to Henry's law the partial pressure of a gas is proportional to its concentration at a given temperature and pressure. However, as temperature decreases, the solubility of oxygen and carbon dioxide in blood or any other fluid increases, which means that the relationship of partial pressure to the total content of oxygen or carbon dioxide in the fluid changes.

Carbon dioxide

If blood containing a given amount of carbon dioxide at a certain tension (PCO_2) at 37°C is cooled, with the possibility to equilibrate with air, the total content of CO_2 in this blood sample remains constant, whereas PCO_2 decreases due to the increased proportion of dissolved CO_2 at lower temperature. Since the PCO_2 of air or any inspired gas mixture is almost zero, no additional molecules of CO_2 diffuse into the blood. If a blood sample is rewarmed to 37°C in a blood gas analyzer under vacuum-sealed conditions, the previously increased dissolved proportion of CO_2 again contributes to PCO_2. The measured PCO_2 of this blood sample is the same as at 37°C.

Hypothermia reduces the metabolic rate and the rate of CO_2 production. To hold the arterial CO_2 content constant during cooling it is necessary to reduce CO_2 elimination (i.e., by reducing minute ventilation in anesthetized patients) equivalently to the decrease in CO_2 production. If this is performed, arterial carbon dioxide tension ($PaCO_2$) measured in a blood gas analyzer at 37°C remains at the same level as during normothermia. Blood gas analyzers are usually equipped with algorithms that enable the true $PaCO_2$ to be calculated at the actual body temperature (Fig. 1) [1]. True $PaCO_2$ corrected for current body temperature is of course lower during hypothermia than the $PaCO_2$ value measured at 37°C. The difference between these two values corresponds to the increase in CO_2 solubility during cooling. The concept of CO_2 management in which the PCO_2 obtained by measurement at 37°C is kept constant at 40 mmHg regardless of current body temperature is called alpha-stat. If the PCO_2 value corrected for current body temperature is held constant during cooling at the same level as during normothermia (37°C), the total amount of CO_2 increases during hypothermia because of the constant $PaCO_2$ and the increased proportion of CO_2 that is soluble in blood. In this case

" In conclusion, variations in body temperature significantly affect the results of important and frequently used monitoring techniques in intensive care, aesthesia and emergency medicine. The knowledge of physical and technical changes during hypothermia and hyperthermia is necessary to avoid pitfalls in monitoring of blood gases …."

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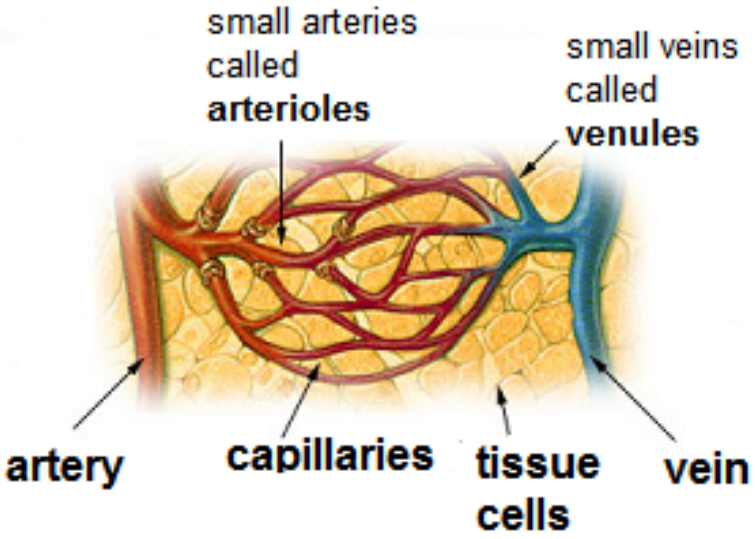
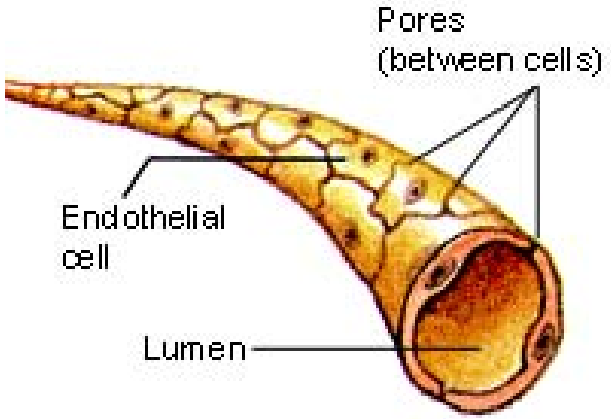
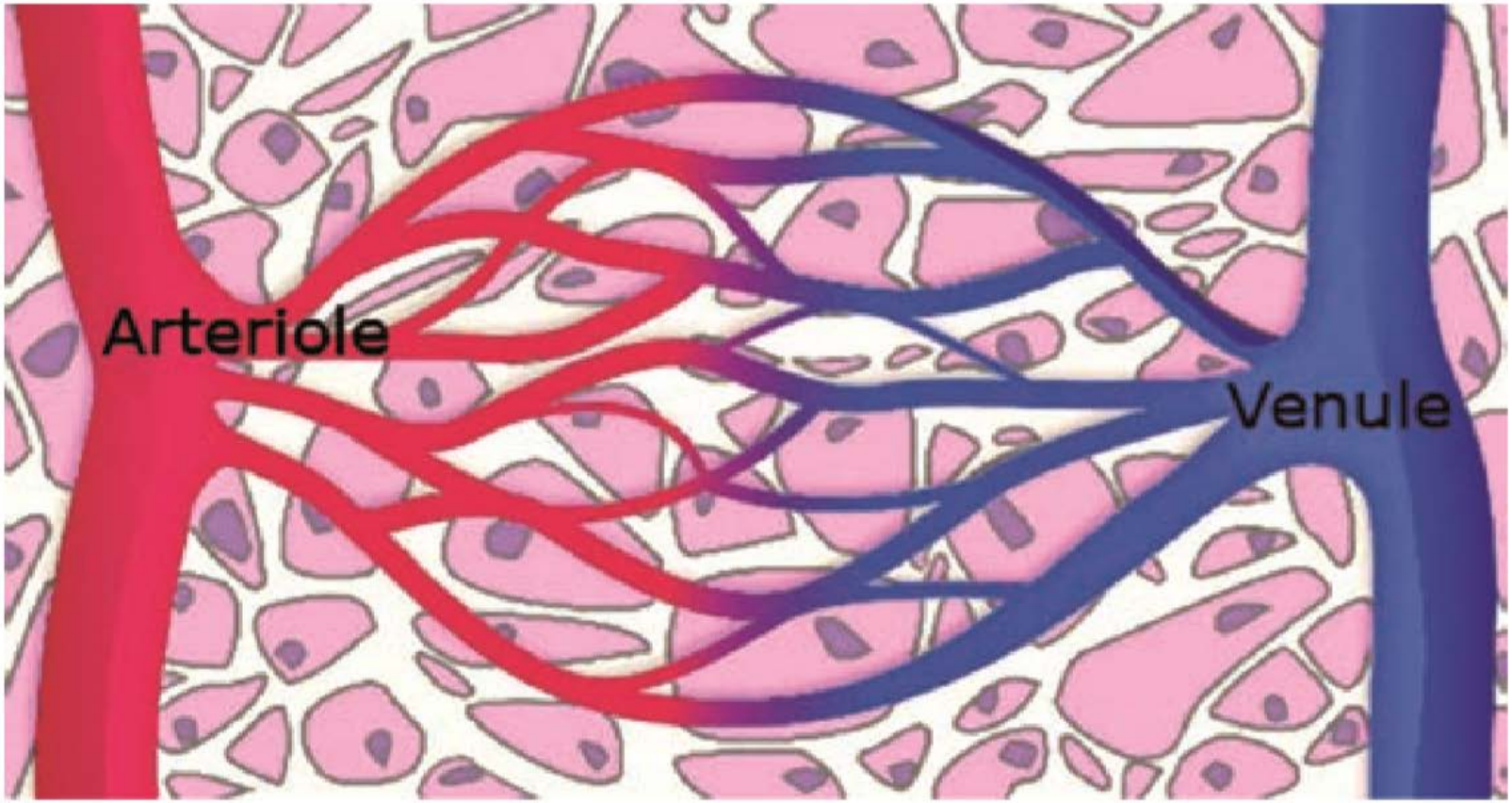




- Capillaries are the smallest blood vessel connecting arterioles and venules
- Capillary wall is a single cell thick which promotes the release of O_2 and nutrients and capture of CO_2 and waste
- Blood collected by skin puncture represents a mixture of arteriole, capillary and venule blood

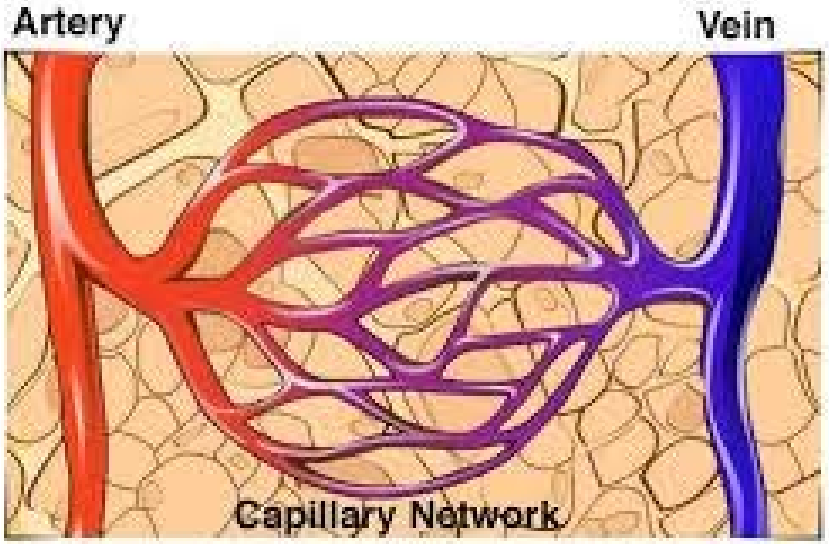
Figure 1: Capillary network



Arterial blood		AV Difference		Venous Blood	
pH	7.40	pH	0.2	pH	7.38
pCO_2	5.3 kPa	pCO_2	0.7	pCO_2	6.0
pO_2	13.0 kPa	pO_2	8.0	pO_2	5.0

Higgins C. Capillary-blood gases: To arterialize or not. MLO. November 2008:42-47

Differences between Arterial, Capillary and Venous Glucose Concentrations



- Arterial Glucose ~ Capillary Glucose
- Capillary Glucose > Venous Glucose

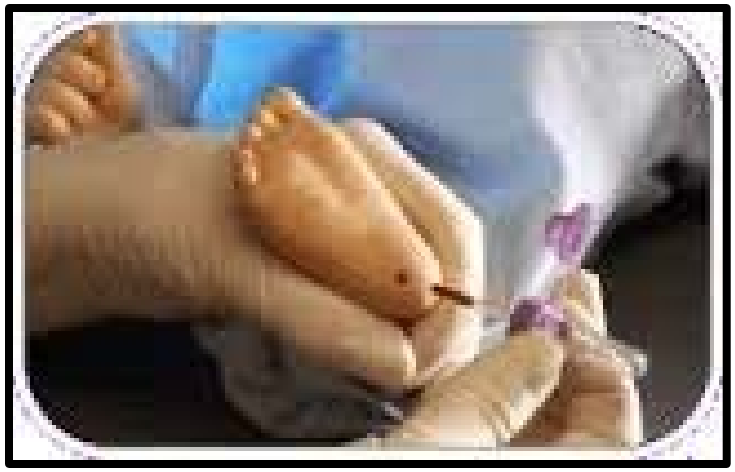
Venous glucose = capillary glucose (fasting specimens)

Capillary glucose can be up to 20 – 25% higher than venous glucose

- After a meal
- Glucose load
- Glucose clamping studies

GP 42-A6 Procedures and Devices for the Collection of Diagnostic Capillary Blood Specimens. Approved Standard- 6th Edition, Sept, 2008

WHO guidelines on drawing blood: best practices in phlebotomy, Geneva, Switzerland, 2010



- Single deep puncture
- Heel (< 1 y)
- Earlobe (> 1y)

Numerous Conditions where Capillary Blood Sampling is Unsuitable, including

- Dehydrated Patients
- Edematous Patients
- Poor peripheral perfusion

Do not “milk “ the puncture site

- May cause hemolysis
- Contamination with tissue fluid

Hemolysis in Serum Samples Drawn in the Emergency Department

Edward R. Burns, Noriko Yoshikawa
Department of Pathology, Albert Einstein College of Medicine and Montefiore Medical Center, New York, NY.

4,021 patients (ED = 2,992 Med Ward = 1,029)

Both collected by Laboratory Phlebotomists

Rates of hemolysis: 12.4% in ED
1.6% in a Medical Ward

Laboratory Medicine May 2002 vol. 33 no. 5; 378-380

How do we currently detect hemolysis?

- Visual inspection of plasma

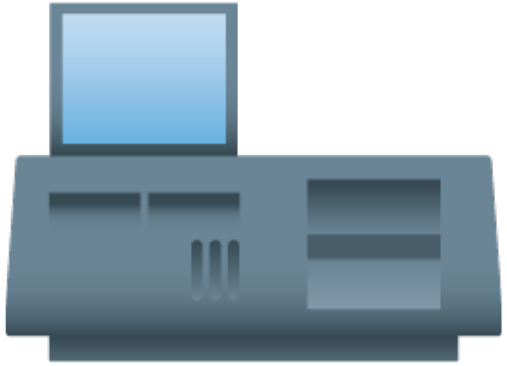
- Problems:
  - time consuming (requires centrifugation)
  - manual qualitative assessment
  - between observer variability

How do we currently detect hemolysis?

- Hemolysis Index (Automated Clinical Chemistry Systems)
- Spectrophotometric assessment
  - Blanked bichromatic measurements
    - 405 nm and 700nm
- Problems:
  - Some time consumed

Can we detect hemolysis in a whole blood specimen?

Not yet!



Distribution of H Index (NICU, Well Baby Nursery)

N= 852

Percentile	
0th	7 (minimum)
25th	53 (1st quartile)
50th	97 (median)
75th	158 (3rd quartile)
100th	1246 (maximum)

Distribution of H Index (NICU, Well Baby Nursery)

75-80% of all specimens are visually hemolyzed

N= 852

7	(minimum)
53	(1st quartile)
97	(median)
158	(3rd quartile)
1246	(maximum)

100th

Frequency

0 50 100 150 200 250 300 350 400 450 500

0 100 200 300 400 500 600 700 800 900 1000 1100 1200 1300

H Index

Effect of Hemolysis of Blood Gases and Electrolytes

pH (-.2%); *pO_2 (-4.9%); sO_2 (-4.9%); COHb (-11%); *Ca^{2+} (-7%)
*pCO_2 (+4.1%); HCO^{3-} (+1.4%); *K^+ (+152%)

* Clinically Meaningful Bias

Influence of spurious hemolysis on blood gas analysis. Clin Chem Lab Med. 2013 Aug;51(8):1651-4.

Identification Issues

Patient Info
- Age
- Body Temp

Puncture Site
- Heel
- Earlobe

Arterialization

Anticoagulant

Method and Conditions of Specimen Transport

Sample Handling

Clinical Laboratory

Arterial Blood = Gold Std Sample

Immerse heel in warm water
- 40-45° C
- 5-10 min

"The clinical value of capillary-blood gas results depends, however, on the extent to which pH, pCO2, and pO2 of capillary blood accurately reflect pH, pCO2, and pO2 of arterial blood"

Capillary-blood gases: To arterialize or not

By Chris Higgins

The gold-standard sample for blood-gas analysis is arterial blood obtained via an indwelling arterial catheter or by arterial puncture. For a number of reasons, capillary blood is an attractive substitute sample that is routinely used in some clinical settings. The purpose of this article is to examine the evidence that blood-gas parameter values (pH, pCO_2, and pO_2) obtained from a capillary-blood sample accurately reflect arterial blood. There is conflicting opinion that increasing local blood flow (by warming or application of vasodilating agent) prior to capillary-blood sampling is necessary for most accurate results and this controversial issue will be addressed. [***Note: The unit of pCO_2 and pO_2 measurement used in this article is kPa — to convert kPa to mmHg divide by 0.133.***]

Blood-gas analyzers measure blood pH, and the oxygen and carbon-dioxide tensions of blood (pCO_2 and pO_2). These measurements, along with parameters (bicarbonate, base excess, and so on) derived by calculation from these measurements, allow evaluation of acid-base status and adequacy of ventilation and oxygenation. Thus, blood-gas analysis is helpful for assessment and monitoring of patients suffering a range of metabolic disturbances and respiratory diseases, both acute and chronic. It is an important component of the physiological monitoring that critically ill patients, particularly those being mechanically ventilated, require.

The gold-standard sample for blood-gas analysis is arterial blood obtained anaerobically via an indwelling arterial catheter (most often sited at the radial artery in adults and the umbilical artery in neonates), or arterial puncture. In an intensive-care setting where patients may require frequent (perhaps two hourly) blood-g… because… arterial… Placing… technica… serious… thrombo… determi… placem… for only… sample… The… alternat… femoral artery in the groin. Although arterial puncture does not place patients at risk of the serious complications associated with arterial catheterization, it is potentially hazardous and certainly not risk free.[3] Furthermore, it is a procedure that is reported by patients to be significantly more painful than venous puncture.[4] Specialist training in arterial puncture is essential for patient safety and comfort; and, in many countries, obtaining arterial blood is the almost exclusive preserve of medically qualified staff.

Capillary blood can be obtained by near-painless[5] skin puncture using a lancet or automated incision device that punctures the skin to a depth of just 1 millimeter.[6,18] It is the least-invasive and safest blood-collecting technique, and can be performed by all healthcare personnel after minimal training.[9] The relative simplicity and safety profile of capillary-blood sampling and the necessity for only small volumes (100 µL to 150 µL) of blood for pH and gas analysis make capillary blood an attractive substitute for arterial blood, particularly among neonates and infants but also adults. The clinical value of capillary-blood gas results depends, however, on the extent to which pH, pCO_2, and pO_2 of capillary blood accurately reflect pH, pCO_2, and pO_2 of arterial blood.

Capillary and arterial blood: theoretical considerations

With a diameter of just 8 µm, capillaries are the smallest blood vessel. They are the connection between arterioles (the smallest artery) and venules (the smallest vein) and, thus, between the arterial and venous sides of the circulatory system. The capillary network (see Figure 1) is the site of nutrient and waste exchange between blood and tissue cells, made possible by the single-cell (1-µm) thickness of the capillary wall. Oxygenated arterial blood arriving via arterioles at the capillary network yields up its oxygen and other essential nutrients to tissue cells as carbon dioxide and other waste products of metabolism are …s and the …here is a …rk (from …fference. …13 kPa, …venules, …Pa.[7] The …der 0.02 …ly.[8] …rterioles …and pO_2 …arterial …ause blood obtained by skin puncture is not actually pure capillary blood but a mixture of blood from punctured arterioles, capillaries, and venules (along with a small but variable contribution of interstitial fluid and intracellular fluid from damaged tissue cells).[9] Due to the relative high pressure on the arterial side of

Continues on page 44

- Arterial pO_2 decreases so does the arterial capillary difference
- Arterial pO_2 increases so does the arterial capillary difference

Capillary pH was similar to Arterial pH
- <0.05 difference
- Clinically insignificant

Capillary pCO_2 was similar to Arterial pCO_2
- < 3-5 mmHg difference
- Clinically acceptable

Capillary pO_2 was different from Arterial pO_2
- 20 mmHg difference
- Clinically UNacceptable

“There is really no substitute for arterial blood if accuracy of pO2 measurement is important, for example, for the prescription of long-term oxygen therapy”

Higgins C. Capillary-blood gases: To arterialize or not. MLO. November 2008:42-47

Identification Issues

Patient Info
- Age
- Body Temp

Puncture Site
- Heel
- Earlobe

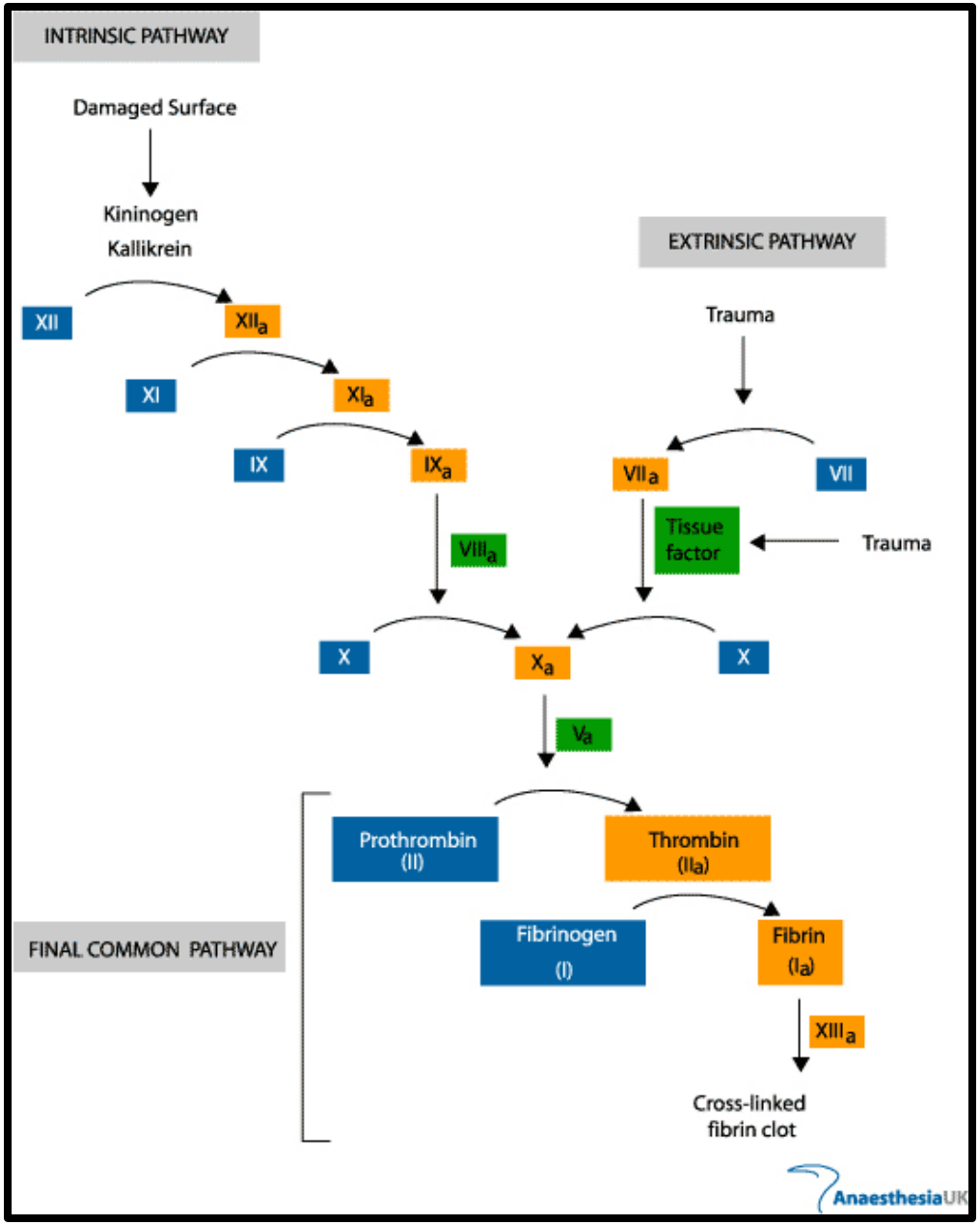
Arterialization

Anticoagulant

Method and Conditions of Specimen Transport

Sample Handling

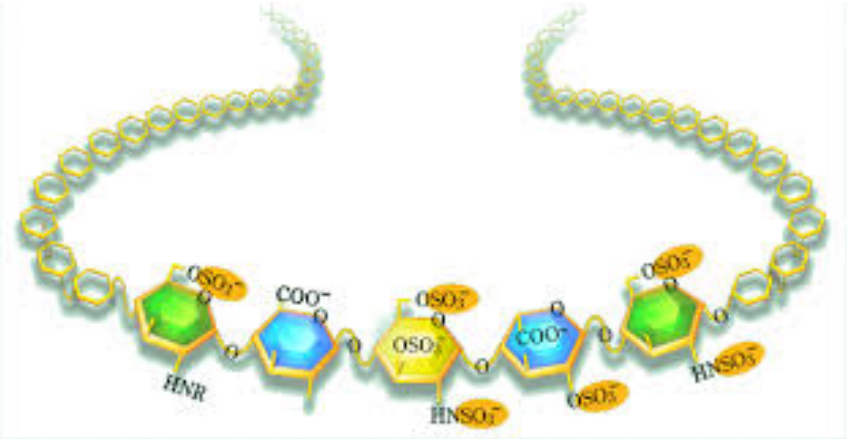
Clinical Laboratory



Anticoagulants

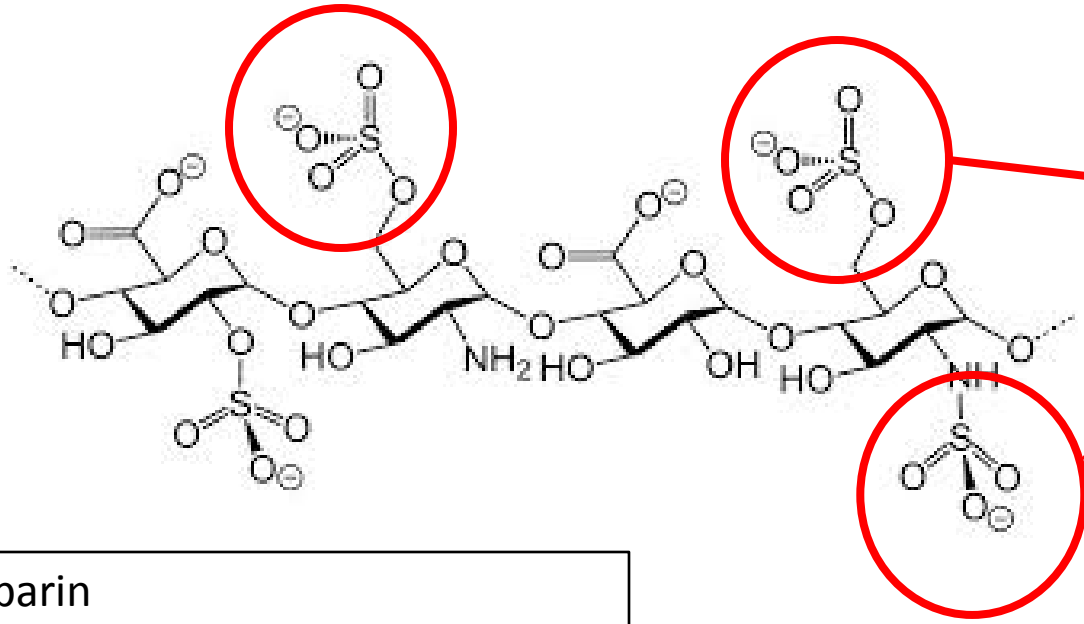
- Calcium chelators
  (ie. EDTA, Sodium Citrate)
- Vitamin K Antagonist
  (ie. Warfarin)
- Cofactor
  (ie. Heparin+antithrombin III)

Heparin



- Natural occurring polysaccharide
- Different sizes
- Different degrees of sulfation
- Different formulations

Different Formulations of Heparin



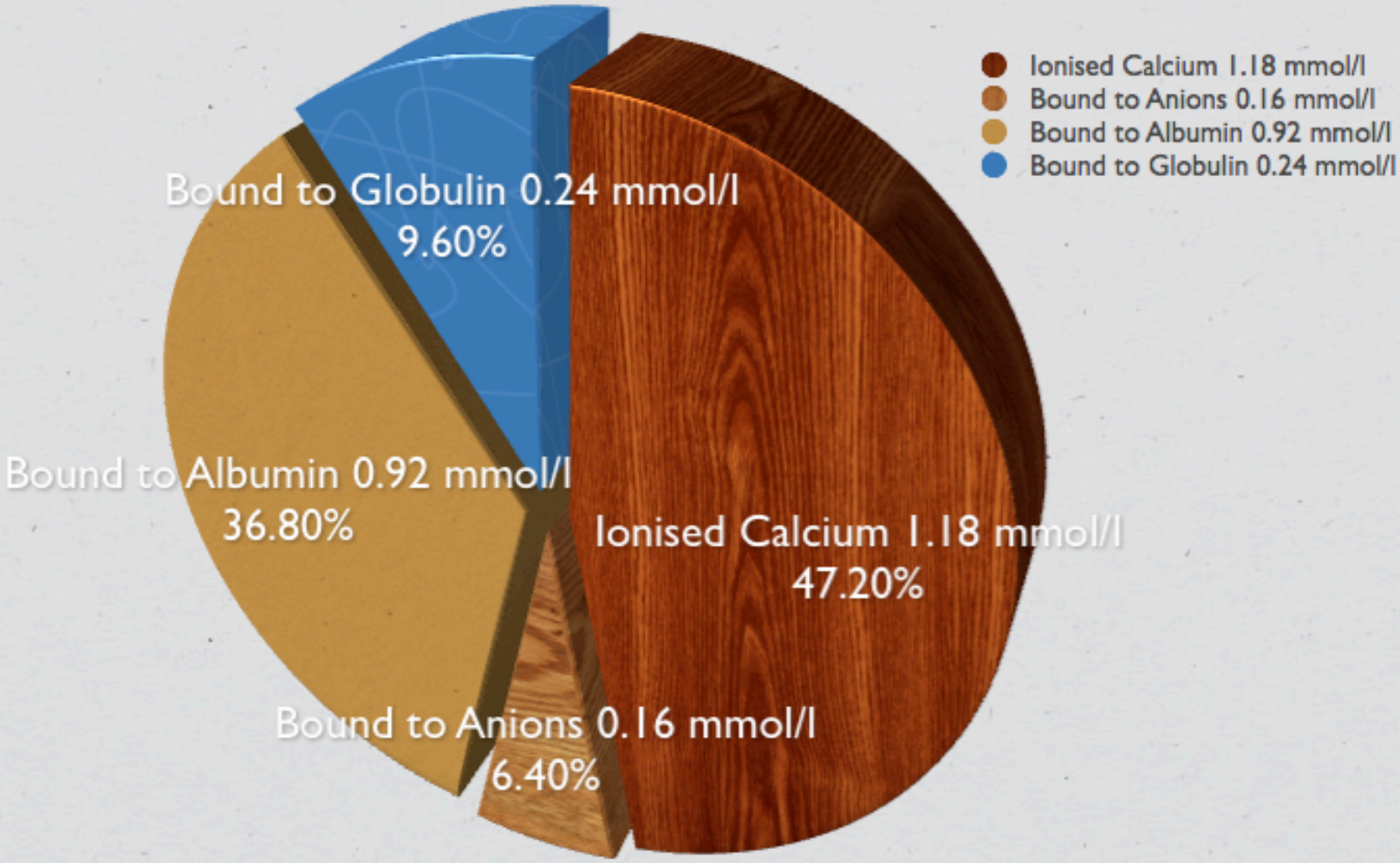
Potential binding sites for cations

Balanced Heparin

- Lithium and Zinc
- Lithium, Zinc and Calcium
- Lithium, Sodium, Potassium and Calcium

Depending upon formulation of heparin used, biases in the measurement of ionized calcium, ionized magnesium and sodium could be seen

Distribution of Calcium in Normal Human Plasma



The adult human body contains approx 1100gm (27.5mol) of Calcium. 99% of Calcium is in bones, Blood Calcium levels are normally 9-10.2mg/dL (2.25-2.55mmol/L)

Image by Dr Deepak Jagiasibava
deepak@jagiasi.com

Congenital Analbuminemia is rare

50 cases reported since 1954

12 local cases identified from First Nations Community near Saskatoon

CASE REPORT

Perinatal and childhood morbidity and mortality in congenital analbuminemia

Jennifer M Toye MD FRCPC MPH[1], Edmond G Lemire MD PhD FRCPC FCCMG FACMG[2], Krista L Baerg BSN MD FRCPC[2]

JM Toye, EG Lemire, KL Baerg. Perinatal and childhood morbidity and mortality in congenital analbuminemia. Paediatr Child Health 2012;17(6):e20-e23.

Albumin, a serum transport protein, provides 80% of colloid osmotic pressure. Congenital analbuminemia (CAA) is an autosomal recessive disorder characterized by absence of serum albumin. Fifty cases of CAA have been reported throughout the world; however, little is known about its clinical impact. Most reported cases have few clinical signs and symptoms. Twelve local cases from the northwestern central plains region in Saskatchewan were identified and reviewed to ascertain morbidity and mortality related with CAA. All the cases are from two remote First Nations communities. Cases had frequent hospital admissions and recurrent respiratory tract infections. Placental abnormalities included hydropic placentas, placental infarcts and microcalcifications. One-half of the cases were born preterm and one-quarter were small for their gestational age. There were three mortalities in the case series. The present case series suggests increased morbidity and mortality during infancy in patients with CAA. The long-term risks of CAA in this population are unknown and a longitudinal study is recommended.

Keywords: *Analbuminemia; Indians, North American; Infant; Intensive care; Low birth weight; Neonatal; Newborn; Oligohydramnios; Paediatric; Premature; Respiratory tract infections; Small for gestational age*

La morbidité et la mortalité pendant la période périnatale et pendant l'enfance en cas d'analbuminémie congénitale

L'albumine, une protéine du transport sérique, fournit 80 % de la pression colloïdo-osmotique. L'analbuminémie congénitale (AAC) est un trouble autosomique récessif caractérisé par l'absence d'albumine sérique. Cinquante cas d'AAC ont été signalés dans le monde, mais on ne sait pas grand-chose de ses répercussions cliniques. La plupart des cas déclarés s'associaient à peu de signes et symptômes cliniques. Les chercheurs ont dépisté 12 cas locaux, originaires de la région du nord-ouest des plaines centrales, en Saskatchewan, et les ont analysés afin de déterminer la morbidité et la mortalité liées à l'AAC. Tous les cas provenaient de deux communautés éloignées des Premières nations. Ils étaient souvent hospitalisés et avaient des infections respiratoires récurrentes. Les anomalies placentaires incluaient des placentas hydropiques, des infarctus placentaires et des microcalcifications. La moitié des cas étaient prématurés et le quart d'entre eux étaient petits par rapport à leur âge gestationnel. Trois mortalités ont été constatées. Cette série a démontré une augmentation de la morbidité et de la mortalité pendant l'enfance chez les patients ayant une AAC. On ne connaît pas les risques à long terme de l'AAC au sein de cette population. Une étude longitudinale est recommandée.

Congenital analbuminemia (CAA) is an autosomal recessive disorder characterized by very low, or absent, serum albumin in the absence of hepatic dysfunction, renal losses or gastrointestinal losses. Albumin maintains colloid osmotic pressure and is an important carrier protein of nutrients, wastes and hormones (1). Previously reported CAA cases describe individuals as being relatively asymptomatic, with the most frequently associated complications including lipodystrophy, hypercholesterolemia, frequent lower respiratory tract infections (LRTI) in children and low birth weight (1). Few reports have provided antenatal and maternal history, although it has been hypothesized that the low incidence of CAA may in part be due to affected fetuses creating an inhospitable in-utero environment (1,2).

CAA is a rare condition with 50 cases having been recorded since 1954, with an estimated frequency of 1 in 1,000,000 (3). Cases have been widely distributed throughout the world (3). Four cases of CAA from the northwestern central plains region in Saskatchewan have been previously reported (4-6). Two of these cases underwent molecular diagnostic testing of the albumin gene and were positive for the Kayseri defect (AT-nucleotide deletion in exon 3 leading to a premature stop codon and a nonfunctional truncated protein) (5). We have identified eight additional cases from the same region. All 12 cases are of Cree descent. Anthropological studies of this region report that between 1870 and 1960 the population was primarily sustained by within group marriages, suggesting that the elevated incidence of CAA in the region is due to a founder effect (6,7). The following case series will report on the morbidity and mortality associated with CAA.

METHODS

The present study was approved by the University of Saskatchewan (Saskatoon, Saskatchewan) Biomedical Research Ethics Board. Cases were identified by searching hospital health records for admissions coded for hypoalbuminemia (E88.0) between 2001 and 2009. These charts were reviewed to identify patients with CAA (defined as serum albumin levels <10 g/L or when measured with protein electrophoresis albumin levels approximately 0 g/L in the absence of secondary causes). Medical genetics files of cases and maternal health records were reviewed for additional medical history wherever possible. Twelve cases were identified and a total of 11 cases are included in the case series. Adequate records for the one excluded case could not be obtained.

Data collection included antenatal/obstetrical and birth histories, placental pathology, frequency of lower respiratory tract infections (LRTI), hospitalizations, comorbid conditions, laboratory investigations, clinical signs and symptoms suggestive of analbuminemia and cause of death.

[1]*Department of Pediatrics, Division of Neonatology, University of Alberta, Edmonton, Alberta;* [2]*Department of Pediatrics, University of Saskatchewan, Royal University Hospital, Saskatoon, Saskatchewan*

Correspondence: Dr Jennifer M Toye, Stollery Children's Hospital, 8440 – 112 Street, 3A3.13 Walter C Mackenzie Health Sciences Centre, Edmonton, Alberta T6G 2B7. Telephone 780-445-6472, e-mail jtoye@ualberta.ca

Accepted for publication February 14, 2012

Will the lack of albumin influence the measurement of ionized calcium?

Identification Issues

Patient Info
- Age
- Body Temp

Puncture Site
- Heel
- Earlobe

Arterialization

Anticoagulant

Method and Conditions of Specimen Transport

Sample Handling

Clinical Laboratory

Glass versus Plastic Syringe or Capillary Tube

Historical

Glass versus Plastic Syringes or Capillary Tube

Historical

1) Immediately place on ice slurry

Glass versus Plastic Syringes or Capillary Tube

Historical

1) Immediately place on ice slurry

2) Negligible permeability to oxygen and carbon dioxide (due to diffusion)

Glass versus Plastic Syringes Or Capillary Tube

- Cost
- Safety
- Convenience

New Standard

Glass versus Plastic Syringes or Capillary Tube

- Clinical Laboratory Standards Institute (CLSI) (C-46 A2)
  - Specimen collection devices
  - Sample handling
  - Specimen transport
  - Specimen storage

Recommendation:

Arterial specimens collected into a plastic syringe should be stored at room temperature and must be analyzed within 30 minutes

How do temperature and time affect ABG results with a plastic syringe?

- Clinical Laboratory Standards Institute (CLSI)
  - Specimen collection devices
  - Sample handling
  - Specimen transport
  - Specimen storage

Recommendation:

Arterial specimens collected into a plastic syringe should be stored at room temperature and must be analyzed within 30 minutes

CLIN. CHEM. 37/7, 1244–1248 (1991)

Changes in Oxygen Measurements When Whole Blood Is Stored in Iced Plastic Glass Syringes

John J. Mahoney, James A. Harvey, Ronald J. Wong, and Antonius L. Van Kessel[1]

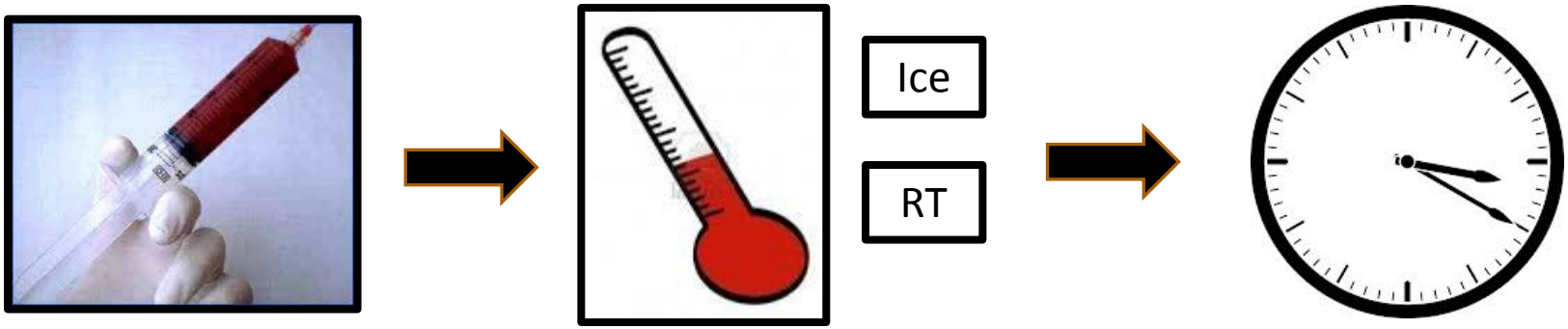


Table 1. Change in p_{O_2} of Whole Blood and Plasma in Glass Syringes after Storage in Ice Water

	Mean ± SD, p_{O_2}, mmHg (and kPa)		
n	Time 0	60 min	Delta
Whole blood			
10	103.3 ± 1.4 (13.77 ± 0.19)	102.9 ± 1.4 (13.72 ± 0.19)	−0.5 ± 1.1 (−0.07 ± 0.15)
10	41.1 ± 1.9 (5.48 ± 0.25)	41.8 ± 1.6 (5.57 ± 0.21)	0.7 ± 0.7 (0.09 ± 0.09)
Plasma			
10	110.2 ± 1.6 (14.69 ± 0.21)	111.4 ± 1.8 (14.85 ± 0.24)	1.2 ± 2.0 (0.16 ± 0.27)
8	64.3 ± 2.4 (8.57 ± 0.32)	66.4 ± 2.8 (8.85 ± 0.37)	2.1 ± 2.2 (0.28 ± 0.29)

CLIN. CHEM. 37/7, 1244–1248 (1991)

Changes in Oxygen Measurements When Whole Blood Is Stored in Iced Plastic Glass Syringes

John J. Mahoney, James A. Harvey, Ronald J. Wong, and Antonius L. Van Kessel[1]

Table 2. Change in p_{O_2} of Whole Blood and Plasma in Plastic Syringes after Storage in Ice Water

Mean ± SD, p_{O_2}, mmHg (and kPa)

Time 0	30 min	Delta	P
Whole blood (n = 10 each)			
101.0 ± 1.7	109.7 ± 4.1	8.4 ± 3.3	<0.0001
(13.46 ± 0.23)	(14.62 ± 0.55)	(1.12 ± 0.44)	
70.9 ± 1.3	71.7 ± 1.4	0.8 ± 0.6	<0.002
(9.45 ± 1.30)	(9.56 ± 0.19)	(0.11 ± 0.08)	
42.8 ± 0.8	43.1 ± 0.4	0.4 ± 0.5	NS
(5.71 ± 0.80)	(5.75 ± 0.05)	(0.05 ± 0.07)	
Plasma (n = 8 each)			
106.7 ± 2.2	119.3 ± 2.1	12.6 ± 2.4	<0.0001
(14.22 ± 0.29)	(15.90 ± 0.28)	(1.68 ± 0.32)	
79.1 ± 3.3	92.9 ± 2.2	13.8 ± 3.7	<0.0001
(10.54 ± 0.44)	(12.38 ± 0.29)	(1.84 ± 0.49)	
67.2 ± 3.7	88.1 ± 5.0	20.9 ± 2.3	<0.0001
(8.96 ± 0.49)	(11.74 ± 0.67)	(2.79 ± 0.31)	

Effect of small air bubbles on changes in blood pO_2 and blood gas parameters: calculated vs. measured effects

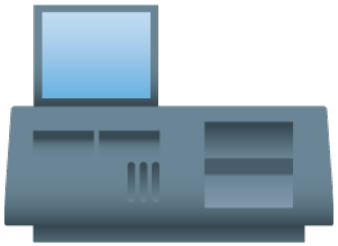
Jul 2012

John G. Toffaletti

Elizabeth H. McDonnell

- Background: Important to remove air bubbles from syringes (to avoid errors)
- Calculate expected theoretical changes in pO_2 (20 µL or 40 µL of air are added)
- Confirm validity of these calculations by measuring blood gas & Co-ox parameters (19 patients after equilibration with similar increments of air)

Remove Bubbles



Introduce air by visually pulling back on syringe plunger until tip was half full of air (20 uL) or completely full (40 uL)

Time	10:20	10:24	10:28	10:32	10:36	10:40
Bubble vol (µL)	0	40	80	120	160	200
pH	7.243	7.241	7.241	7.244	7.248	7.255
pCO_2 (mmHg)	34.5	34.1	33.7	32.9	32.0	30.9
pO_2 (mmHg)	69.4	85.1	105	127	159	183
ΔpO_2 (mmHg)	16	20	22	32	24	----
Hb (g/dL)	13.7	13.6	13.5	13.6	13.6	13.6
$\%O_2Hb$	89.7	93.3	95.0	95.8	96.1	96.2
sO_2 %	92.6	96.2	97.8	98.8	99.1	99.3
O_2 ct (mL/mL)	0.173	0.179	0.182	0.185	0.187	0.187

TABLE V: Blood gas and CO-oximetry measurements on a representative arterial blood sample as 40 µL increments of room air were added to 1.2 mL blood. The ΔpO_2 is the difference between the pO_2 values before and after addition of each 40 µL increment of air. O_2 ct = oxygen content.

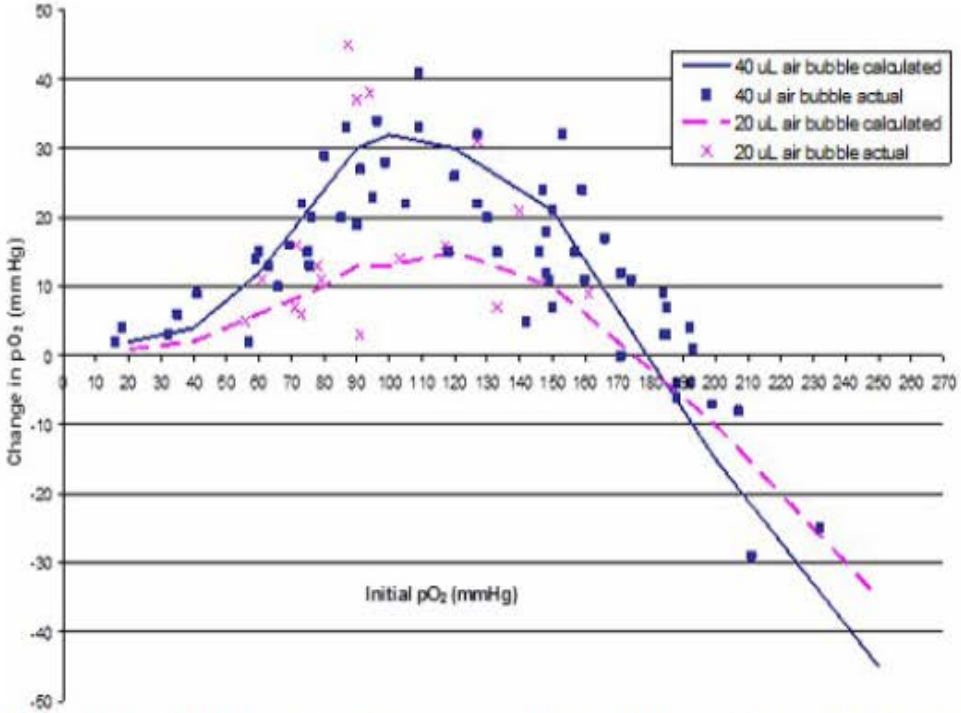


FIG. 1: Calculated and measured changes in blood pO_2 when 20 or 40 µL air (atmospheric pO_2) was added to blood. Data points are based on changes in pO_2 as measured on 19 blood specimens as air was sequentially introduced and equilibrated with the blood in a syringe.

Pneumatic Transport Exacerbates Interference of Room Air Contamination in Blood Gas Samples
Astles, J Rex;Lubarsky, David;Bounthon Loun;Sedor, Frank A;Toffaletti, John G
Archives of Pathology & Laboratory Medicine; Jul 1996; 120, 7; ProQuest
pg. 642

Purpose:
To characterize the potential interference to pO_2 measurement when blood contamination with air is sent through a pneumatic tube system

Pneumatic Transport Exacerbates Interference of Room Air Contamination in Blood Gas Samples

J. Rex Astles, PhD; David Lubarsky, MD; Bounthon Loun, PhD; Frank A. Sedor, PhD; John G. Toffaletti, PhD

Introduce air by visually pulling back on syringe plunger until tip was half full of air (20 uL) or completely full (40 uL)

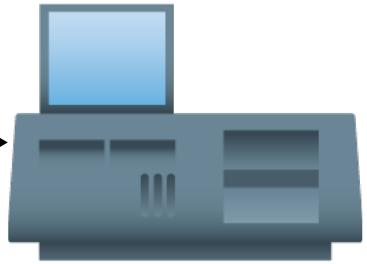


Table 1.—Effect of Pneumatic Transport on PO_2 (mm Hg) in tonometered Blood Transported With and Without a Tube Liner*

	7% O_2			12% O_2			20% O_2			50% O_2		
Bubble Size, mL:	**0**	**0.2**	**0.5**	**0**	**0.2**	**0.5**	**0**	**0.2**	**0.5**	**0**	**0.2**	**0.5**
PO_2, (mm Hg)												
Control	65	68	65	75	78	86	142	137	141	339	328	318
PTS transport–no liner	67	82	129	75	112	142	154	175	179	329	225	204
PTS transport—with liner	63	78	108	79	111	141	152	173	179	322	232	204

* Whole blood was tonometered at 37°C with either 7%, 12%, 20%, or 50% oxygen. Samples were sent at ambient temperature via PTS transpor either with or without a liner. The control sample was left undisturbed at ambient temperature for 2 minutes. Results are single determinations PTS indicates pneumatic tube system.

- Air contamination showed almost no effect on the control samples (walked to the lab for analysis)
- Specimens sent by PTS showed large erroneous increases in samples tonometered at 7% and 12%
- Specimens sent by PTS showed little interference in specimens tonometered at 20% oxygen
- Specimens sent by PTS showed large erroneous decreases in samples tonometered at 50% oxygen

Table 1.—Effect of Pneumatic Transport on PO_2 (mm Hg) in tonometered Blood Transported With and Without a Tube Liner*

	7% O_2			12% O_2			20% O_2			50% O_2		
Bubble Size, mL:	**0**	**0.2**	**0.5**	**0**	**0.2**	**0.5**	**0**	**0.2**	**0.5**	**0**	**0.2**	**0.5**
PO_2, (mm Hg)												
Control	65	68	65	75	78	86	142	137	141	339	328	318
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Identification Issues

Patient Info
- Age
- Body Temp

Puncture Site
- Heel
- Earlobe

Arterialization

Anticoagulant

Method and Conditions of Specimen Transport

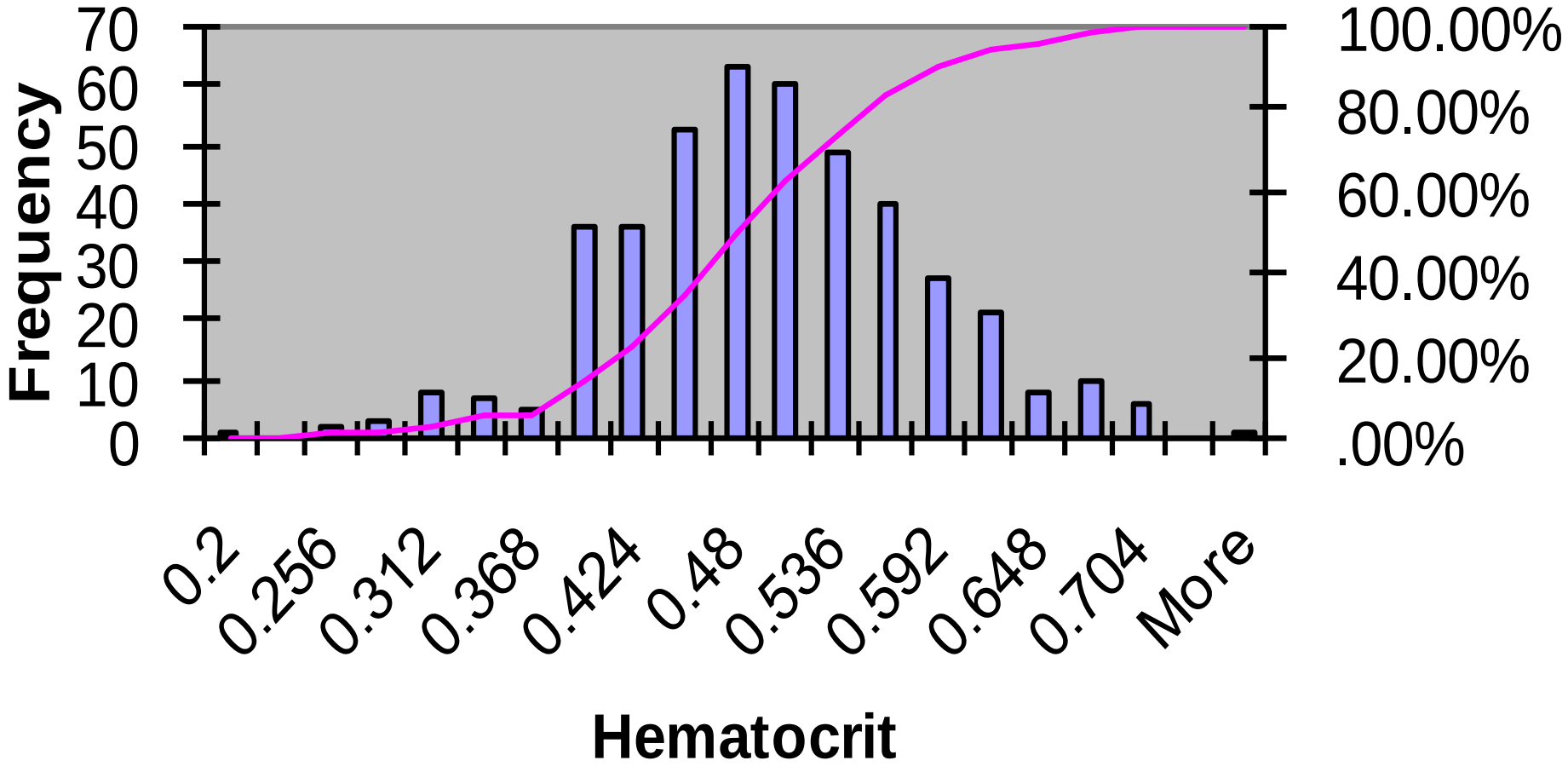
Sample Handling

Clinical Laboratory

Sample Handling

- Mixing necessary to dissolve heparin
- Necessary to achieve uniform distribution of RBCs
  - Hemoglobin measurement

Hematocrit in 434 In-patients <7d, October 2007, RRL



Clots may block the sample pathway of blood gas analyzers

Examined the magnitude of errors produced by clots on sensors for blood gases, pH and electrolytes

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Effects of Blood Clots on Electrochemical Sensors in Systems for Critical Care and Point-of-Care Testing.

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Abstract

Systems for whole blood analysis in critical care and point-of-care (POC) settings are frequently affected by the presence of blood clots in the sample. Partially coagulated blood may result from pre-analytical error or certain pathophysiological conditions. Miniaturized sensors and fluidic pathways, especially in systems for POC testing, increase the likelihood of trapping blood clots on sensors and interfering with sample analysis, often without knowledge of the user. The GEM® Premier™ 3000 critical care analyzer (Instrumentation Laboratory) measures pH, PCO_2, PO_2, Na^+, K^+, Ca^{++}, glucose, lactate and hematocrit in 150 mL of whole blood. Electrochemical sensors are incorporated in a disposable measurement cartridge for analysis of 75, 150, 300, 450 or 600 samples over a three-week period. Recently, Intelligent Quality Management (iQM™) has been added to the system. iQM is an active, real-time, quality-control system which includes checks for the presence of blood clots on sensors using failure-pattern recognition. Upon detecting a blood clot on a sensor, the system automatically begins corrective action, including vigorous rinsing of the sensor surface. If the clot is not immediately removed, the sensor becomes disabled and results for that channel suppressed until the system verifies removal of the clot. To demonstrate the importance of iQM in flagging errors due to clots, we evaluated the magnitude of errors produced by clots on sensors for blood gases, pH, and electrolytes. Clots were purposely formed by adding thrombogenic compounds to blood samples collected from healthy volunteers. Samples were analyzed on several GEM Premier 3000 instruments with iQM until a particular sensor was disabled. Then, blood samples without clots were analyzed both on the system with the disabled sensor and on a control system. Raw signals from the disabled sensor were retrieved and used to calculate what the reported result would have been, had the sensor not been disabled and the result reported while a clot was present on the sensor. Bias was calculated by comparison to the control instrument, and measured against total allowable error using CLIA 88 limits. The sensors with the largest clot-related errors were pH, PCO_2 and PO_2. For pH, 50% of the samples (range: 7.0 – 7.4); for PCO_2, 59% of the samples (range: 25 – 106 mmHg); and for PO_2, 89% of the samples (range: 26 – 46 mmHg) exceeded the allowable error. In the case of PCO_2 and PO_2, the magnitude and direction of the error indicate that the presence of clots interferes with diffusion of analyte across the outer sensor membrane, resulting in sluggish response. For pH, the direction and magnitude of the error are more complex. The presence of a clot not only causes sluggish response, but also appears to shift the local pH at the sensor in the alkaline direction. We conclude that the iQM system for the GEM Premier 3000 is effective in avoiding erroneous results due to the presence of blood clots on sensors, especially for pH and blood gases, the most important critical care analytes.

Introduction

Systems for whole blood analysis in critical care and POC settings are affected by the presence of blood clots in samples. Many traditional laboratory-based systems for critical-care analysis have built-in "clot catchers" to prevent clots from entering the systems fluidics. Clots which are not stopped by the clot catcher, or if a clot catcher is not present, may block fluidic lines and disable the system. The result is system down-time while the lines are removed and cleared by the user. Clots which are stopped by the clot catcher also result in increased maintenance while the clot catcher is replaced or cleaned. Miniaturized sensors and fluidics in unit-use and multi-use, cartridge-based systems for POC applications are particularly problematic in the presence of clots because often no user-performed maintenance is possible. If a clot causes cartridge fluidic problems, the cartridge must be discarded and replaced, a time-consuming and costly process. In addition to increased maintenance, system down-time, and expense, there is risk of incorrect reporting of analytical results if a clot becomes trapped on the surface of a sensor and the system has no mechanism for detecting or removing the clot. In this case, the clot may interfere with normal functioning of the sensor and the system may continue to report incorrect results

Sensors with largest clot related errors

- pH (50%)
- pCO_2 (59%)
- pO_2 (89%)

Exceeded total allowable error using CLIA 88 limits

Magnitude & direction of the error with pCO_2 & pO_2 showed that clots interfere with the diffusion of analyte across the outer sensor membrane (sluggish response)

Conclusions

- Pre-analytical phase of the blood gas testing process represents unique challenges for the neonatal population

- Capillary blood sampling is a common method used to collect a blood specimen in neonates

Thank you for your time

Questions ?

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