

Accounting for Pre-analytical Variables in POCT



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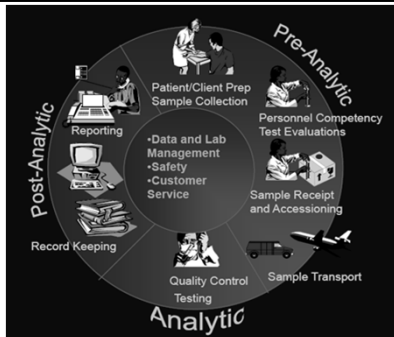
Point of Care Testing (POCT)

- Integral part of modern medical practice.
- Part of healthcare landscape transformation.
- Tremendous impact on operational efficiency and patient care.
- Dx market value growth rate of 9.3% and 27.5 billion by 2018.
- Large expansion on POCT usage

Point of Care Testing (POCT)

- Prone to errors as a part of over all health care system.
- Raises concern over the reliability of test results.
- Appears deceptively simple.
- Quality error rates associated with POCT may be considerably higher than those of central lab tests
» Kane et al 2011, Clin Chem 47:9
- Lack of Understanding, training, test limitations and misuse.

Total testing process starts and ends with the patient.



Pre analytical Phase

- Occurs before the specimen is analyzed.
- Complex and dynamic process
- Cause random errors undetectable by QC
- Often unknown to testing personnel and clinicians.

Pre analytical Variables

(What causes abnormal results (besides disease))

- **Physiologic:**
 - Age, Sex, time, Diurnal Variation, Seasonal, Altitude, Life style, pregnancy
- **Specimen Collection:**
 - Fasting, time of collection, posture, duration of tourniquet application, infusion, exercise, anticoag-blood ratio, stabilizing additives
- **Influence or Interference factors**
 - Circulating Abs etc

Preanalytical Phase in POCT

- Patient misidentification
- Hemolysis of RBC
- Heparin concentration
- Air contamination
- Incomplete/ Poor sample preparation
- Wrong storage condition
- Mixture of Venous and Arterial blood during venipuncture
- Finger Stick
- Test interferences, cross reactivity's, standardizations

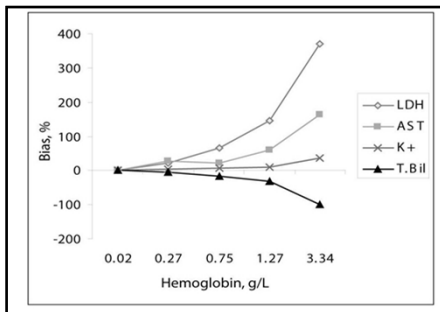
Patient misidentification

- Frequently Occurred
- Failure to provide proper, appropriate and immediate care.
- Financial implications
- Positive Patient Identification
- Barcode readers

Hemolysis

- Most common
- Not Visible
- Syringe drawn specimen (19%)
- Releases intracellular components
 - Biased results
 - Possible misdiagnosis
 - Possible errors in treatment/ lack of treatment.

Hemolysis



Koseoglu et al. Effects of hemolysis interference on routine biochemistry parameters. Biochemia Medica 2011;21(1):79-85

Effect of hemolysis on Cardiac TnI and T (Renze Bais, Clin Chem. 2010;56:1357-59)

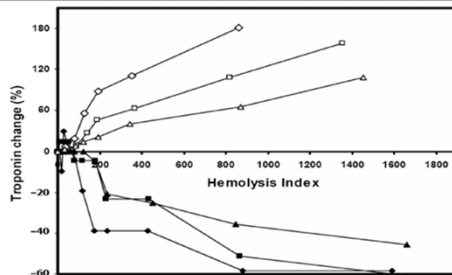


Fig. 1. Effect of increasing added hemolysis on the Ortho Clinical Diagnostics TnI ES assay (open symbols) and the Roche TnI assay (closed symbols). A 20% change was considered clinically significant. The 3 cTnI concentrations were 24 ng/L (○), 36 ng/L (□), and 49 ng/L (△), and the 3 cTnI concentrations were 6 ng/L (●), 12 ng/L (■), and 23 ng/L (▲). (Note that the negative and positive scales are not equal.)

Inappropriate/Poor sample collection

- Inadequate mixing
 - Dilutional Bias
 - Clot formation
- Insufficient sampling
 - poor lancing technique
 - Mixing with Anticoagulants
- Inadequate removal of flush solution in a-lines prior to blood collection.
- Air contamination (Air bubbles)

Arterial Blood Gases (ABG)

- Anticoagulants
 - Whole Blood Heparin is challenging.
 - Dry heparin
 - Calcium titrated heparin
- Sampling from Catheters
- Hemolysis
- Storage
 - Evaporation
 - Air contamination

Arterial Blood Gases (ABG)

- **Patient Stabilization**
 - Stable condition of ventilation for at least 5 minutes
 - Keeping breathing aids unchanged for at least 20 minutes
 - Minimize anxiety for arterial collection.



Finger stick blood testing

- Commonly used in POCT assays
- Capillary POC Blood Glucose is becoming increasingly controversial.
 - Use one of several enzymes for Glucose testing.
 - Number of drug interferences
 - Ascorbic acid, dopamine, acetaminophen, mannitol, Maltose (old meters)
 - <http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/PublicHealthNotifications/ucm176992.htm>

Possible sources of error of POC blood glucose testing

- **Operator errors**
 - Incorrect specimen collection
 - Poor lancing technique
 - Finger stick site on the same side as Peripheral IV with dextrose or insulin
 - Using previously punctured site
 - Milking the puncture site to obtain blood drop
 - Use of first drop if cleansing with alcohol
 - Venous/ arterial sample taken from clotted blood or inappropriate tubes.
 - Inaccurate timing relation to meals or insulin dose.
 - Failure to understand limitations of technology
 - Errors in meter maintenance and cleaning
 - Improper storage or handling the meter, test strips.

Possible sources of error of POC blood glucose testing

- **Reagent or test strip errors**
 - Expired or damaged strips
 - Multiple lots of strips available at a given time
 - Failure to prevent deterioration (Keeping strips dry)
- **Environmental (Device or Human factors)**
 - High patient to meter ratio
 - Temperature, humidity, high altitude
 - Hypo/ Hyper baric conditions

Possible sources of error of POC blood glucose testing

- **Clinical Factors**
 - Patient with peripheral vascular disease or conditions that impairs/ decreases circulation to the periphery.
 - Patient is dehydrated, hypoxia, DKA.
 - Shock.
 - Severe edema, finger edema.
 - Hypotensive.
 - Interference from other sugars.

Hemoglobin A1C

- Routine measurement of POCT A1C has become essential component of standard care for patients with diabetes.
- POC testing is accurate, but there can be substantial variations in results between POC and Lab A1C tests.
- In accuracies may be more marked in these with very high A1C readings

Coagulation Testing: PT/INR

- Monitor patients response to Warfarin
 - Wide range of clot detection technologies
 - Different reagents/ ISI calibrators
 - Cold hand, poor circulation
 - Milking finger
 - Contaminated , Bruised, Swollen finger
 - Resticking the same site
 - Smear blood on strip
 - Under/ over filling tubes
 - Device is not flat and vibration free: High INR
- Diseases: Liver disease, Hypo/ Hyperthyroidism, HF, Fever, Obesity
- Drugs: Anticoagulants, antiplatelet agents, NSAID and Serotonin reuptake inhibitors, inhibitors and inducers of CYP450
- Bilirubin, Hemolysis, Lipemia, Low or elevated HCT, Fibrinogen >7 g/L.
- Foods:

Coagulation Testing

- ACT devices
 - Different manufacturers results are not interchangeable.
 - Reference ranges and therapeutic targets vary considerably between instruments
 - Some devices even target ACT is not well defined.
 - Values are higher with Heparin using Celite A510 tubes on Hemochron compared to Medtronic ACT Plus. With Argatroban anticoagulants opposite patterns are seen.
 - Platelet counts, function, factor deficiencies, hypothermia, hemodilution, Lupus anticoagulants

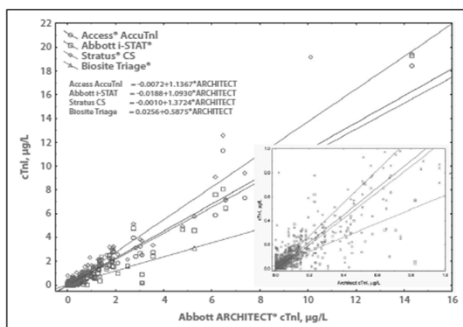
Cardiac Markers

- Expedited evaluation & treatment for ED Chest pain patients.
- Measurements Cardiac Troponins.
- Variations in sensitivity and specificity
- Lack of standardization
 - Presence of modified cTnI/cTnT in serum.
 - Antibody cross reactivity

Cardiac Markers

- POC Tn assays struggle to identify normal levels at 99 percentile.
 - High correlation with lab based assays
 - Near the decision limits there are number of exceptions.
- Mild hemolysis may reduce Tn values
- POCT for baseline measurement with subsequent monitoring by a conventional lab based should be avoided.

Figure 5. Comparison of POC assays with contemporary laboratory assays for predictive purposes generally shows a high correlation, although there are exceptions near the decision limits.



Per Venge et al. European Heart Journal: Acute Cardiovascular Care 2014, Vol. 3(S1) 1–18

POCT HIV testing

- Patients receiving ART may produce false Positive test results.
- Individuals with Toxoplasma IGG, HAMA, RHF, Herpes, hospitalized cancer patients.
- Clots, air bubbles, hemolysis, Lipemia
- Not validated for children < 12 years of age
- Card should be read within a specific amount of time
- Pouch is opened > 2 hrs – Cards can not be used.

POCT Pregnancy Tests

- False Negatives:
 - Very early in pregnancy- below the device limit of detection
 - Hook effect
 - Presence of HCG variants
 - Some POC assays may not detect certain variants and some may not detect at all.
 - Some has Poor sensitivity to hyperglycosylated HCG
 - Gronowski, Grenache, Griffley and others discussed exclusively in the literature.

Clinical Chemistry 55:7
1389–1394 (2009) Endocrinology and Metabolism

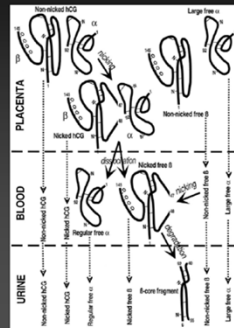
False-Negative Results in Point-of-Care Qualitative Human Chorionic Gonadotropin (hCG) Devices Due to Excess hCG β Core Fragment

Ann M. Gronowski,^{1*} Mark Cervinski,¹ Ulf-Håkan Stenman,² Allison Woodworth,³ Lori Ashby,⁴ and Mitchell G. Scott¹

This is the first report, to our knowledge, that hCG variants occurring at high concentration in pregnancy urine cause a false-negative result in POC qualitative hCG devices. Caution should be used when hCG devices in which hCG β cf causes negative interference are used to test women who are pregnant beyond 5–8 weeks' gestation, as false-negative results may occur. Devices used for this purpose should be tested to identify this problem.

hCG Heterogeneity

- Numerous molecular forms of hCG present in pregnancy serum
 - Dissociated or degraded molecules with no biological activity
- Key β -containing isoforms
 - Intact hCG
 - Nicked hCG
 - Free β subunit
 - Nicked free β subunit
 - β -core fragment (urine)



Cole, L.A. Clin Chem 1997;43:2233-2243

In Summary

- More than devices, gadgets for performing analyses rapidly.
- Oversimplification to conclude that each variable will always produce a specific effect.
- Awareness of the many factors occurring outside lab in and around the patient that may effect the test result before the sample is collected and tested.
- Can be minimized, when there is a good communication between Healthcare staff, POCT and central laboratory staff.