AACC | Better health through laboratory medicine.

Accounting for Pre-analytical Variables in POCT

L.V. Rao, PhD

Senior Clinical Laboratory Director

Associate Professor, Pathology

UMass Memorial Medical Center (Worcester, MA)

Senior Scientific Director

Quest Diagnostics (Marlborough, MA)

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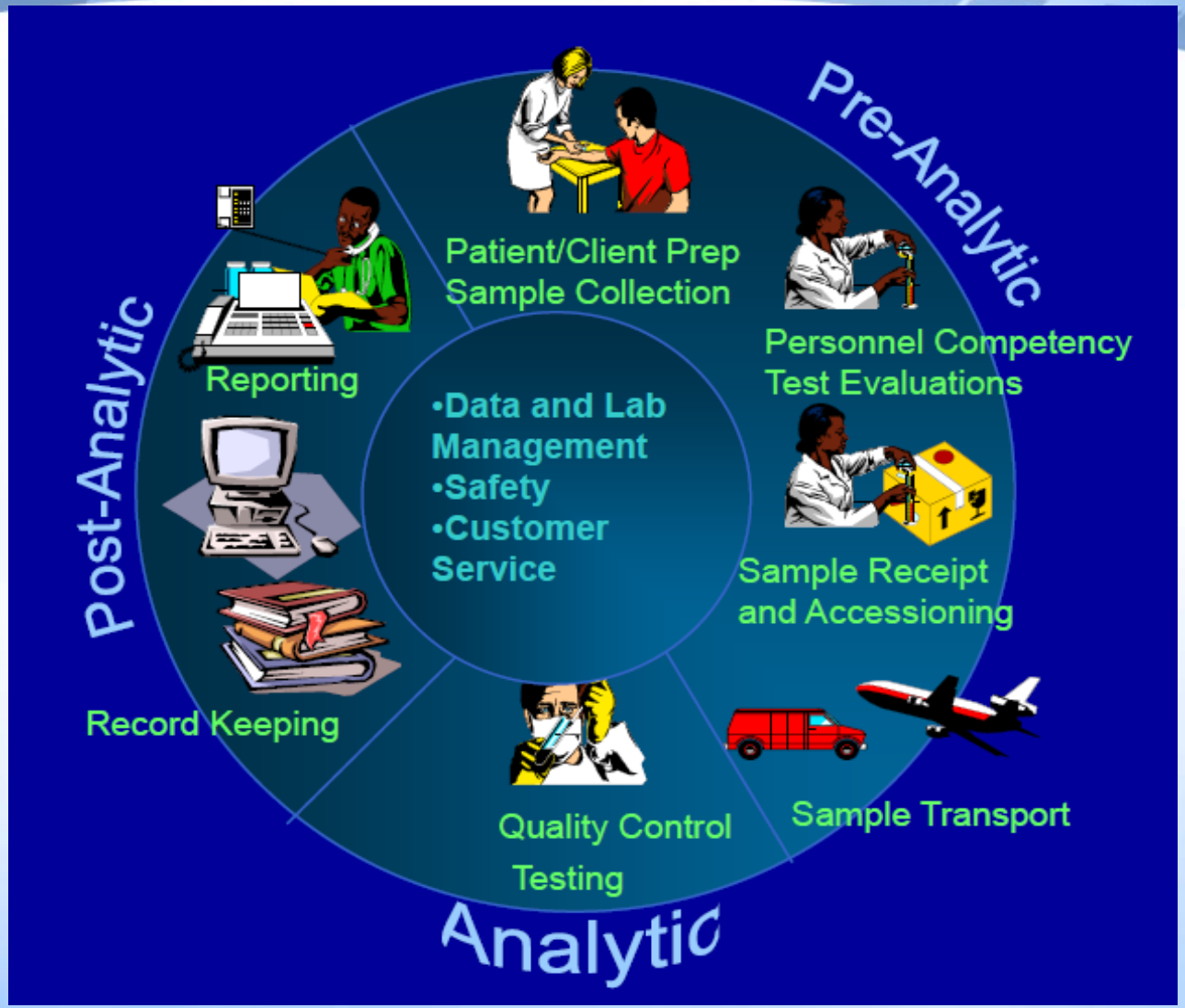
Point of Care Testing (POCT)

- 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

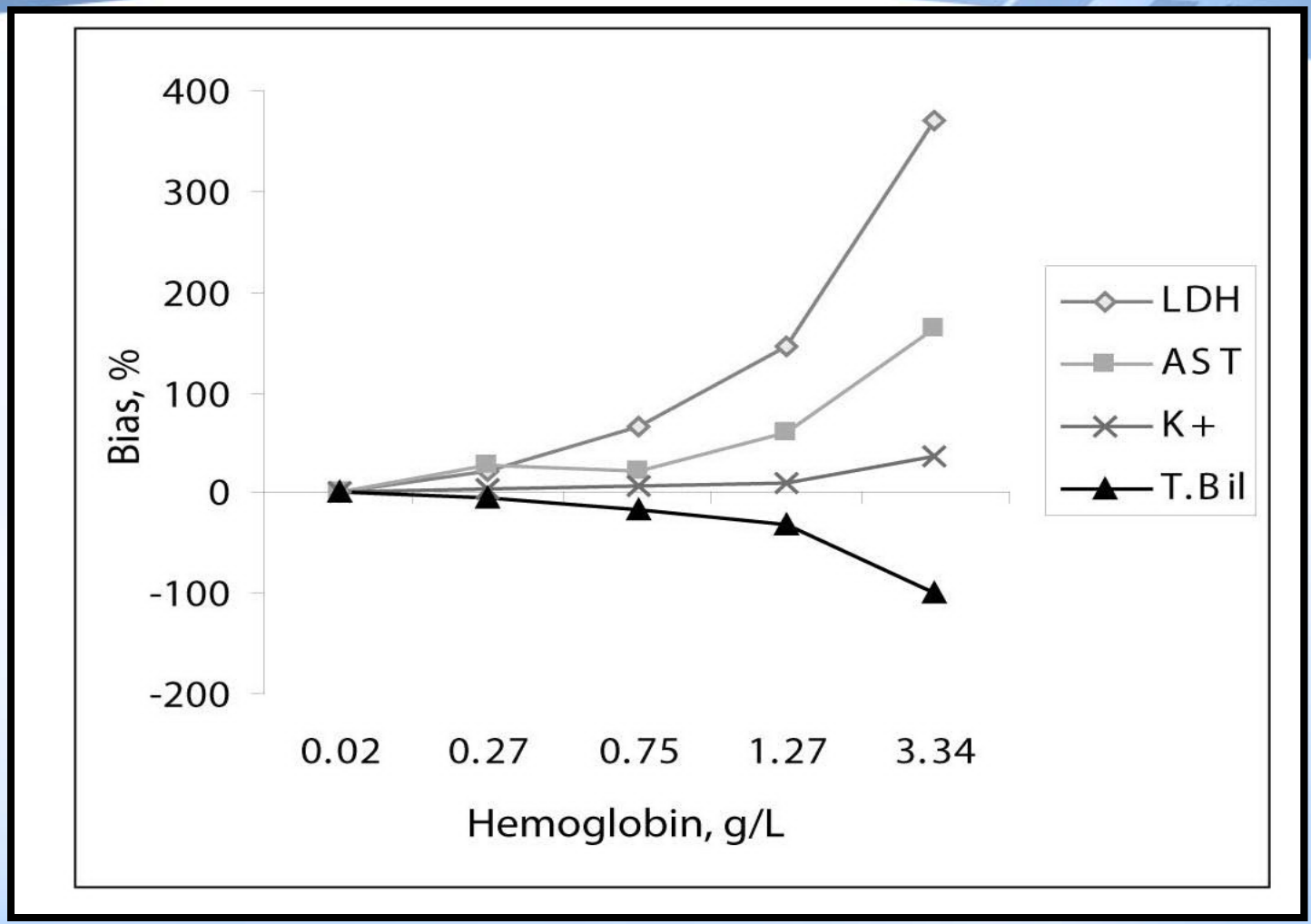
- Frequently Occurred
- Failure to provide proper, appropriate and immediate care.
- Financial implications

- 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)

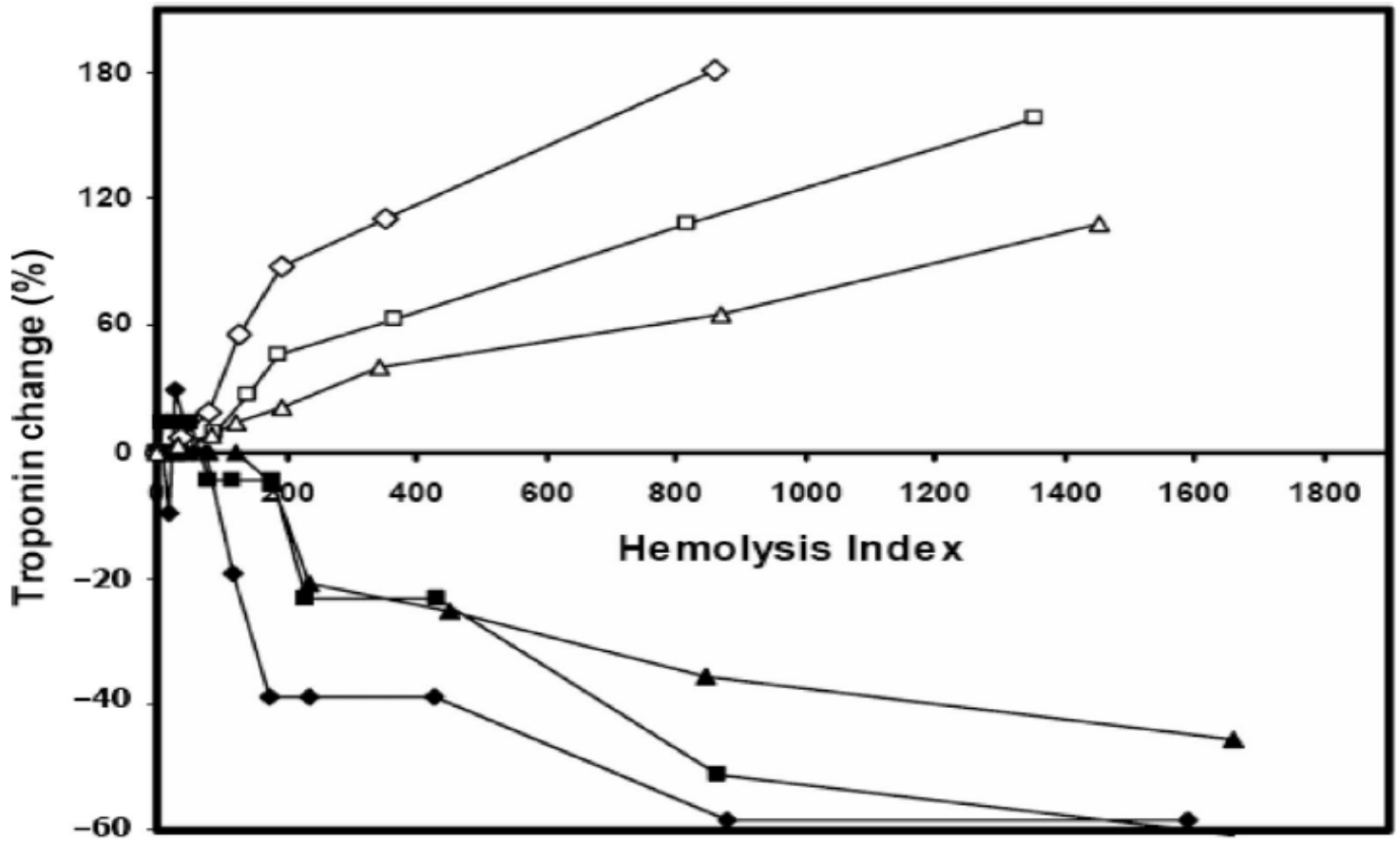


Fig. 1. Effect of increasing added hemolysis on the Ortho Clinical Diagnostics TnI ES assay (open symbols) and the Roche TnT hs assay (closed symbols).

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 cTnT 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
- In adequate 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
  - Devise 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 induces 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, hemodilu tion, Lupus anticoagulants

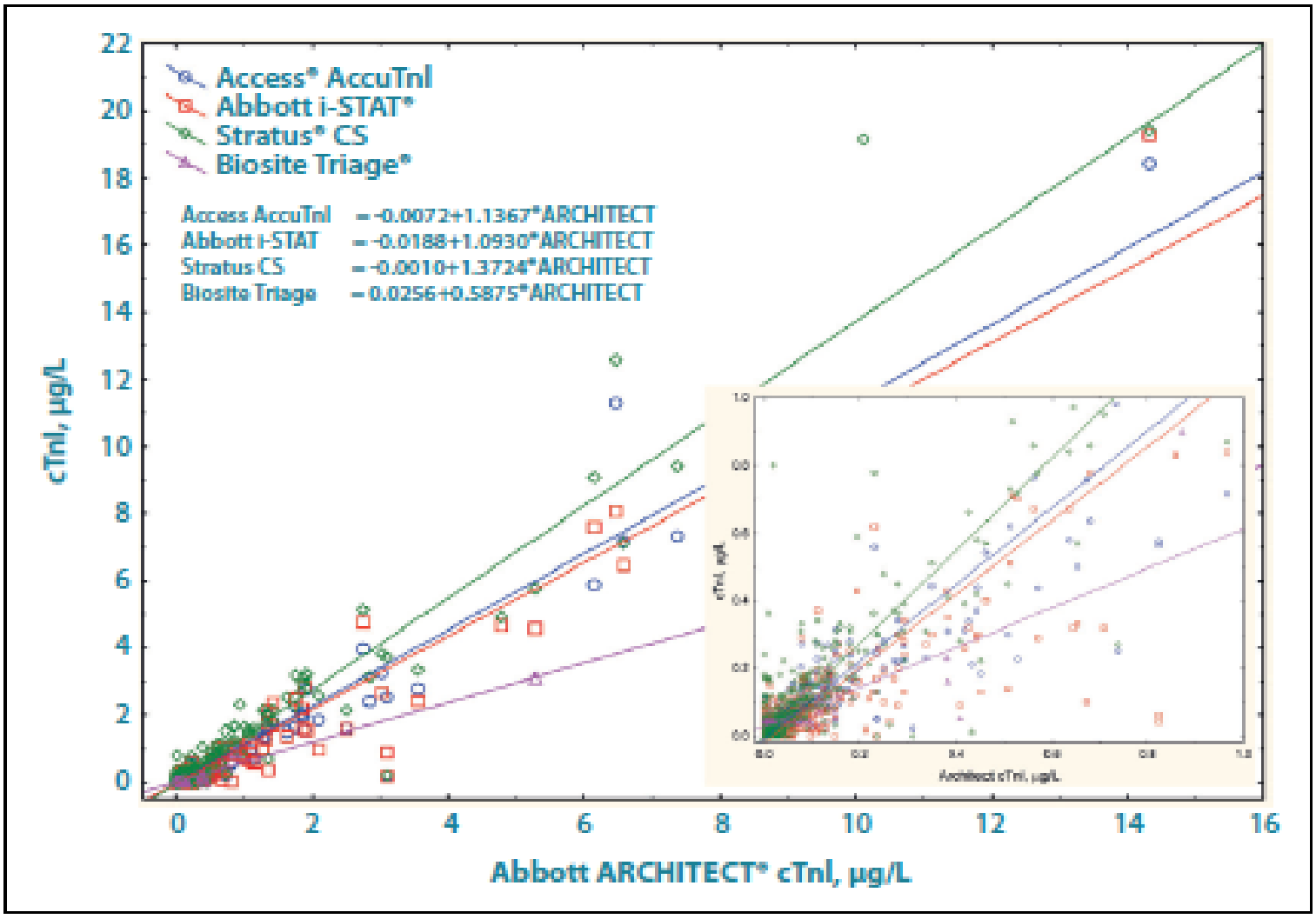
Cardiac Markers

- 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)

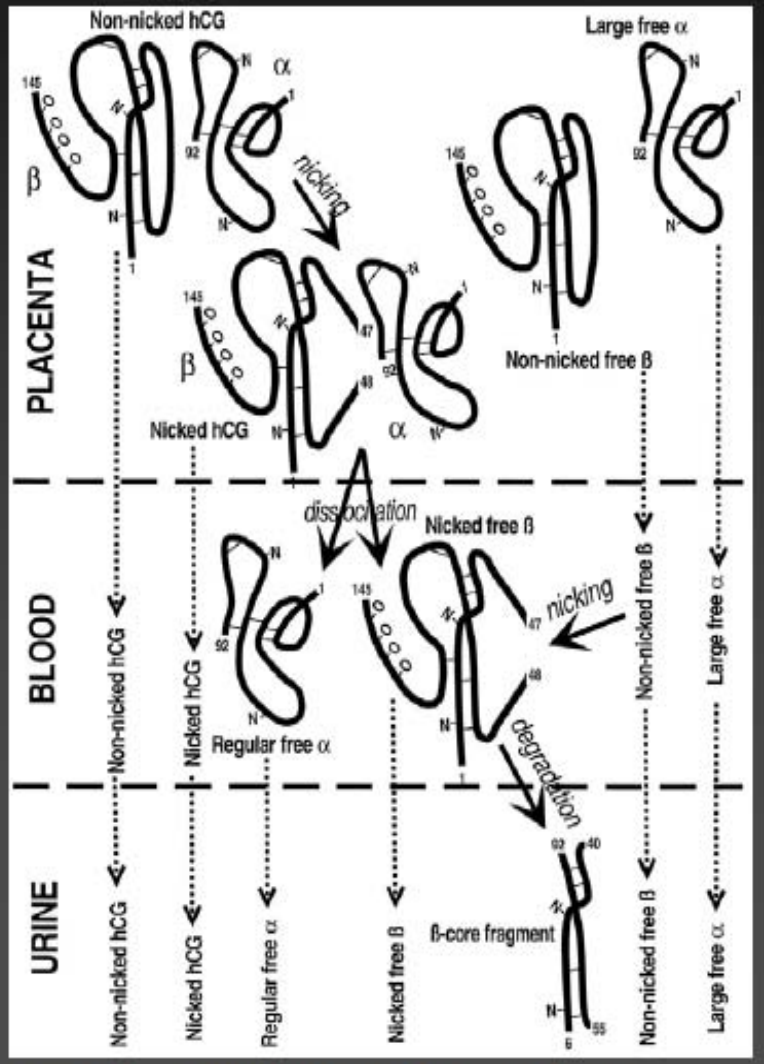
False-Negative Results in Point-of-Care Qualitative Human Chorionic Gonadotropin (hCG) Devices Due to Excess hCGβ Core Fragment

Ann M. Gronowski,[1*] Mark Cervinski,[1] Ulf-Håkan Stenman,[2] Alison Woodworth,[3] Lori Ashby,[4] and Mitchell G. Scott[1]

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 hCGβcf 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, LA. *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.

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Thank you for attending!

Please join Dr. Rao in the networking lounge for an online Q&A chat.

Visit the Resource Room to get the CE code for this session.