



*Better health through
laboratory medicine.*

PEARLS OF LABORATORY MEDICINE

High-Sensitivity Cardiac Troponin

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Challenges in Cardiovascular Medicine

- **Acute Coronary Syndrome (ACS)**
 - Non-ST-elevation myocardial infarction (NSTEMI)
 - ST-elevation myocardial infarction (STEMI)
 - Unstable angina (UA)



Challenges in Cardiovascular Medicine

- Annually: 605,000 new and 200,000 recurrent acute myocardial infarctions (AMI)
 - Only ~18% have longstanding angina
- **2% to 5% myocardial infarctions are missed in the Emergency Department**
- Only 46% of patients arrive at the hospital within 2 hours of symptom onset

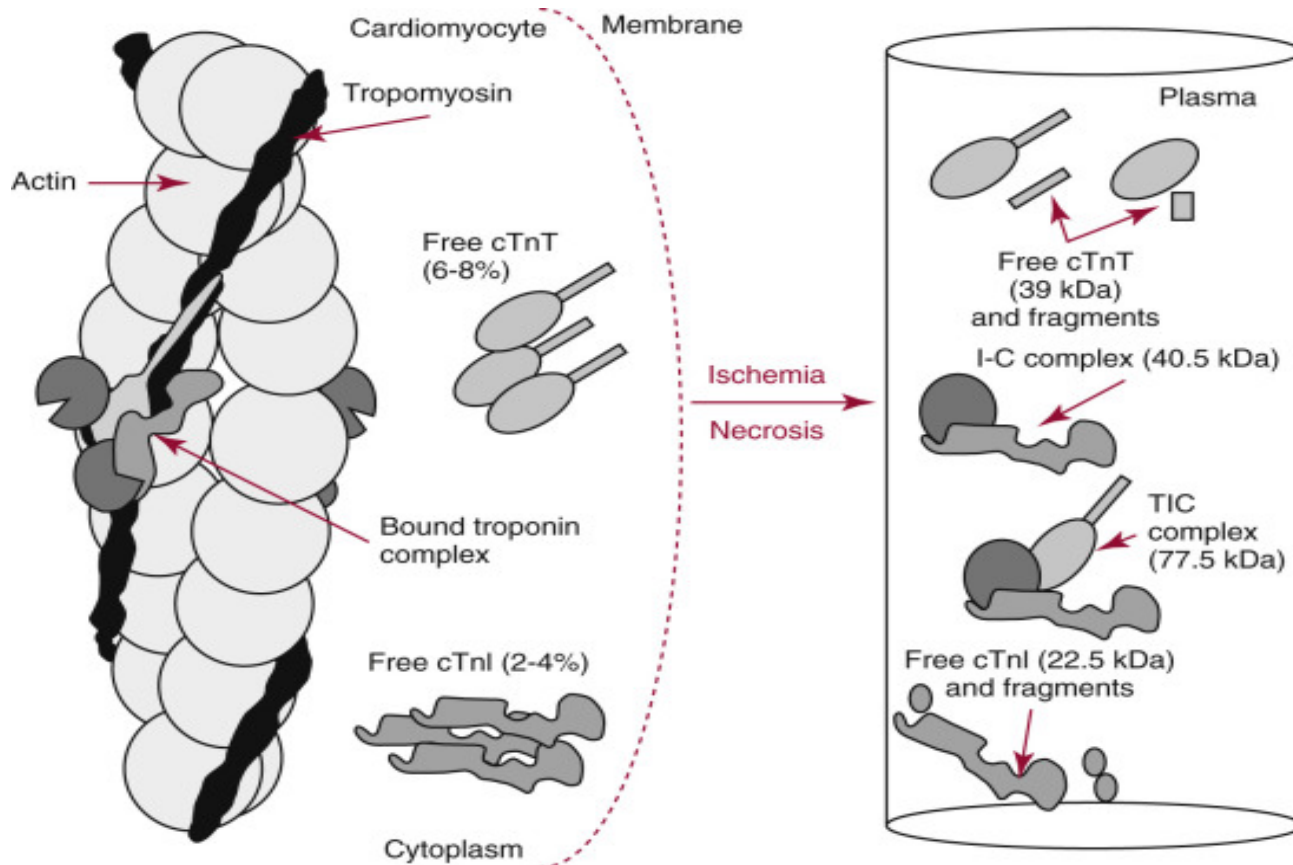


Challenges in Cardiovascular Medicine

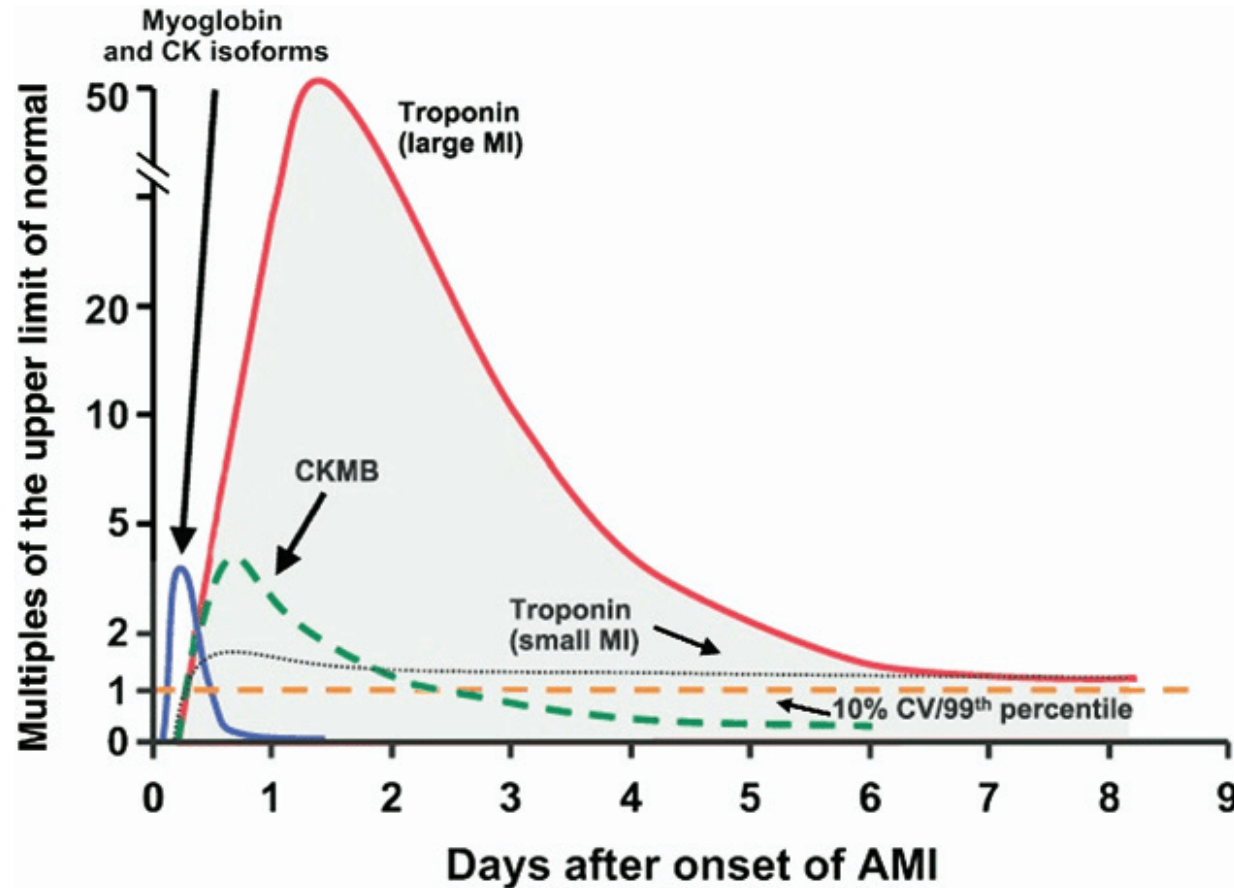
- AMI mortality rates (patients ≥ 45 years):
 - Within 1 year: 18% males, 23% females
 - Within 5 years: 36% males, 47% females
- **Appropriate triage and accurate diagnoses/treatment impact mortality downstream**



Cardiac Troponin Complex Consists of Three Regulatory Proteins



Troponin Elevations are Greater and Persist Over Longer Time Periods



*TnT elevations persist longer than TnI due to increased mass

Fourth Universal Definition of Myocardial Infarction

- Detection of a **rise and/or fall of cardiac biomarkers (preferably troponin)** with **at least 1 value above the 99th percentile upper reference limit (URL)** together with evidence of myocardial ischemia and at least 1 of the following:
 - Ischemic symptoms
 - ECG changes indicative of new ischemia
 - Pathological Q waves
 - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality
 - IC thrombus identified by angiography or autopsy
- Timing is essential, **serial testing recommended**

Myocardial Injury Differs From Acute Myocardial Infarction

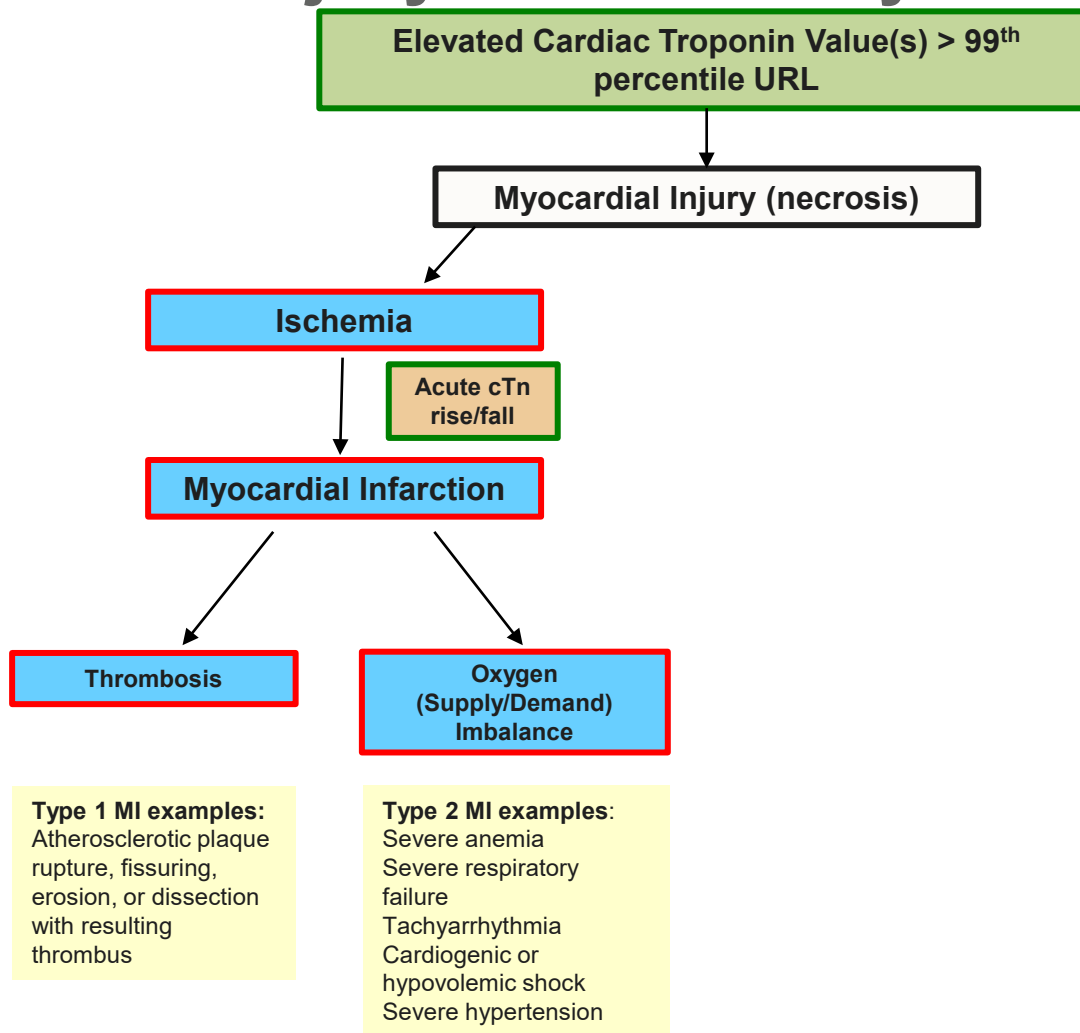
Criteria for Myocardial Injury

- The term **myocardial injury** should be used when there is evidence of elevated cTn values with at least one value $> 99^{\text{th}}$ percentile (sex-specific) URL (**new**)

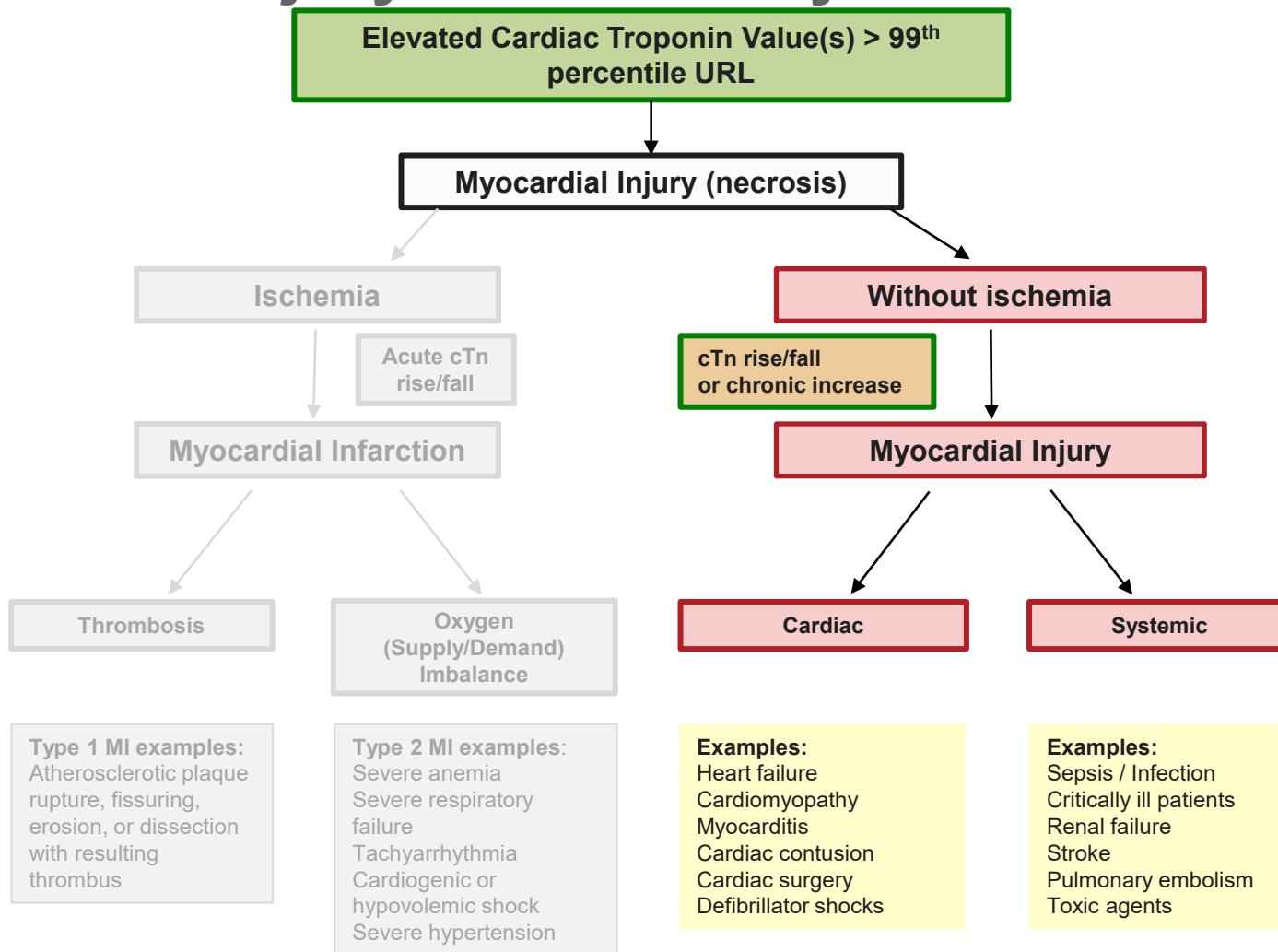
Criteria for Acute MI

- The term **acute MI** should be used when there is acute myocardial injury with clinical evidence (symptoms, ECG, imaging) of acute myocardial ischemia with detection of a rise and/or fall of cTn with at least one value $> 99^{\text{th}}$ sex-specific percentile used as the URL

Myocardial Injury vs. Acute Myocardial Infarction



Myocardial Injury vs. Acute Myocardial Infarction

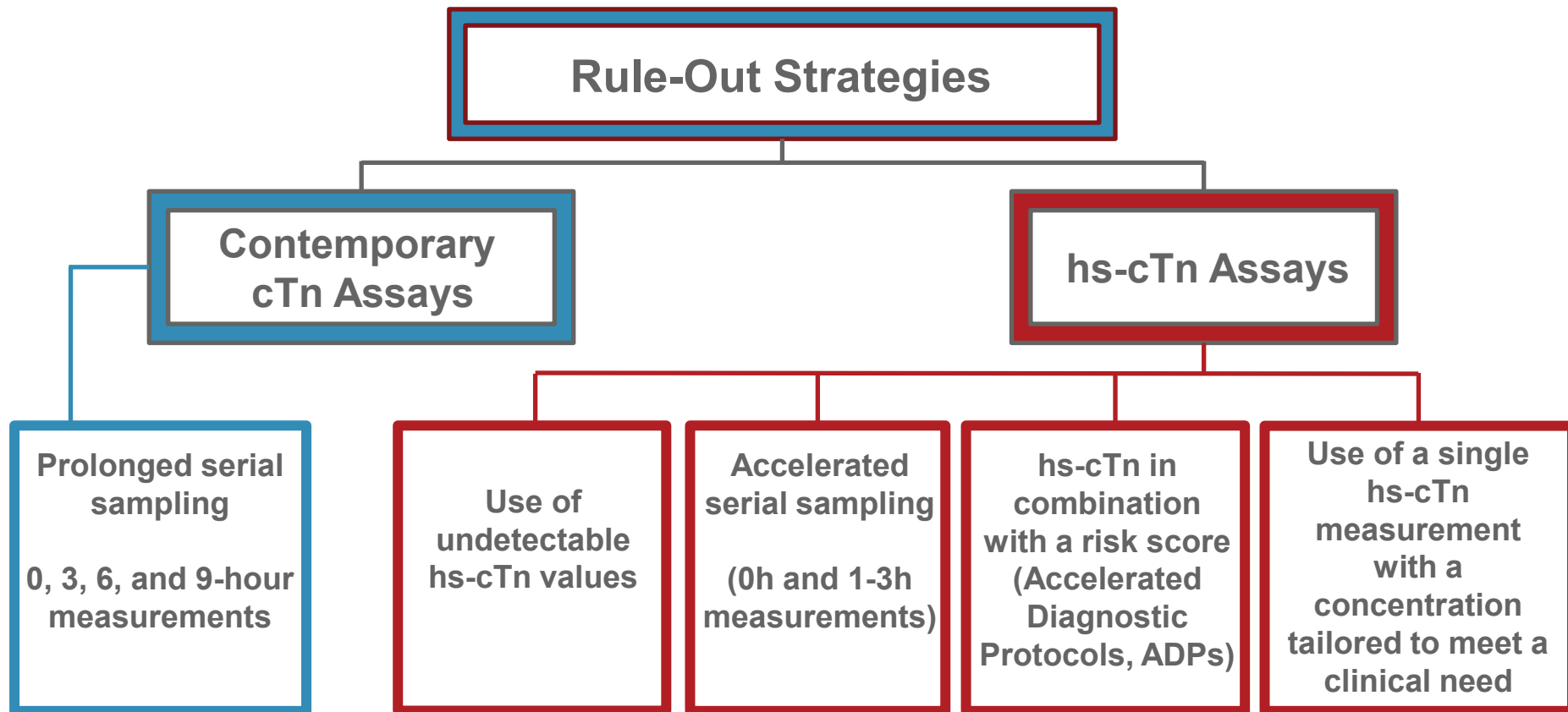


“High-Sensitivity” terminology reflects the analytical characteristics of the assay and NOT a difference in the cardiac troponin measured.

Acceptance Designation	Total Precision at 99 th Percentile
Guideline Acceptable	10%
Clinically Usable	>10 to ≤ 20%
Not Acceptable	> 20%
Assay Designation	Measurable Normal Values of Males and Females Below the 99 th Percentile
Level 4 - 3rd gen hs	≥ 95%
Level 3 - 2nd gen hs	75 to < 95%
Level 2 - 1st gen hs	50 to < 75%
Level 1 - Contemporary	< 50%



Rapid Rule-Out and Rule-In of Acute Myocardial Infarction is a Key Benefit of hs-cTn Assays



Report High-Sensitivity Troponin Results Using Whole Numbers (ng/L)

- A contemporary cTn assay result of **0.014 $\mu\text{g/L}$** will be **14 ng/L** for an hs-cTn assay
- This designation, as an expert opinion, has been supported by many Journals and is globally recognized as a way to distinguish hs-cTn assays from contemporary cTn assays



Use a Defined Reference Population to Establish 99th Percentile Concentrations with Sex-Specific Cutoffs

- Fourth Universal Definition of MI endorses sex-specific 99th percentiles, recognizing upper reference limits (URLs) are lower in women than men
- Minimum 300 males and 300 females required to define URL
- Minimum 20 males and 20 females required to verify URL
 - Use individuals representative of your geographic area
 - Ages distributed over 20y and greater
 - Ethnic and racial mix with population
- More rigorous criteria for defining/excluding normal subjects lowers the 99th percentile: a) comorbidities, b) medication use, c) surrogate biomarkers (eGFR, HbA1C, NT-proBNP/BNP)
- Statistical approach can influence 99th percentile (non-parametric, Harrel-Davis, robust)



High-Sensitivity Troponin Assays: Serial Sampling

- Serial monitoring aids in distinguishing myocardial infarction from myocardial injury
- Serial testing may provide a better means for diagnosis than use of a population-based 99th percentile
 - Fourth Universal Definition of MI supports serial 0 and 1/2/3h
 - Later times will not miss potential very early presenters
- Absolute changes, rather than relative (percent) changes, appear preferable for hs-cTn assays at low concentrations
- ADPs and rapid rule-out strategies relevant to implementation discussions
- Biological variation may influence interpretation of serial hs-cTn concentrations.
- Definition of a significant change (“delta”) is unclear and assay dependent



Report Results in ≤ 60 Minutes to Accelerate Clinical Diagnostic Decisions and Treatment Protocols

- Turnaround time ≤ 60 minutes from time specimen is received in the laboratory to reporting results in the electronic medical record
- Previous NACB (AACCC Academy) recommendations: <60 min from time of blood collection to reporting results
- There should be interdisciplinary efforts to continuously strive to improve hs-cTn turnaround times



Recommendations for Point-of-Care (POC) Cardiac Marker Testing

- Limited number of hs-cTn POC assays available
- If turnaround time goals cannot be met in the central lab, POC is only justified in the ED
 - Educate providers that current POC assays are substantially less analytically sensitive
 - POC and central lab cTn results are not interchangeable
 - Understand how hemolysis could affect cTn results
- Quantitative results should be reported
- POC testing may also be necessary in rural/small hospital settings to be able to provide 24 / 7 service

Proper interpretation of hs-cTn results requires an understanding of the assay used at your institution

- Distinguishing acute from chronic injury is one of the major challenges of using hs-cTn assays
 - Analytics become very important to interpret serial changes
 - Analytical characteristics (high-sensitivity, contemporary, POC)
 - Analytical interferences (hemolysis, biotin)
- <https://www.ifcc.org/ifcc-education-division/emd-committees/committee-on-clinical-applications-of-cardiac-bio-markers-c-cb/>



Points to Remember

- High-sensitivity troponin assays are defined by the analytical characteristics
- A single troponin result does not equal a diagnosis
 - Acute MI can be safely ruled-out within 3 hours (hs-cTn plus risk score/diagnostic pathways/ECG findings)
- Acute changes in troponin are essential for interpretation; serial changes are assay dependent
- Majority of cTn POC assays are not high-sensitivity
 - Less precise and less sensitive; results are not interchangeable with central lab cTn assays
- Education and multi-disciplinary collaboration are essential to define institutional testing practices/protocols with hs-cTn



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Disclosures/Potential Conflicts of Interest

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- **Expert Testimony:** No disclosures
- **Patents:** No disclosures

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