

112 mono-components from more than 50 allergen sources. Nanotechnology benefits paediatric diagnosis, because it requires very little blood to do a comprehensive allergen profile. It is mainly indicated for patients with multiple food and inhalant allergies. Its main drawbacks are onerous validation procedures and the risk of overdiagnosis; it requires specialist knowledge to prevent misinterpretation of the complex results of these tests.⁷

Ongoing research is required to improve the ability of laboratory tests to assess the presence and severity of food allergy and to predict prognosis and resolution of disease.

Summary (Fig. 4)

- Commence investigation of food allergy with a detailed allergy-focused medical history and examination.
- Select the appropriate allergens and co-allergens for sIgE or SPTs to confirm or exclude IgE-mediated allergy.
- Confirm equivocal findings with an OFC test.
- Monitor development of tolerance with sIgE (in children) and confirm with an OFC test.
- Allergy tests should only be undertaken by healthcare professionals who are competent to perform and interpret them.
- SPTs and OFC tests should only be undertaken where there are facilities to deal with an anaphylactic reaction.
- CRDs employing recombinant allergens and comprehensive allergen profiles using microarray nanotechnology offer complementary diagnostic tools for the allergy specialist.

Further reading and references available at www.cmej.org.za

Troponins and acute coronary syndrome

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Cardiac muscle injury is defined as the disruption of normal cardiac myocyte membrane integrity resulting in the loss of intracellular constituents such as troponin, creatine kinase, and myoglobin into the extracellular space. The mechanism of injury includes trauma, toxins and viral infections, but ischaemia or infarction – due to an imbalance between the supply and demand of oxygen – is the most common cause.¹

Acute coronary syndrome (ACS) constitutes a large spectrum of clinical conditions, ranging from unstable angina pectoris to acute myocardial infarction (AMI).

Diagnosis of acute myocardial infarction

The diagnosis of AMI was traditionally made using the combination of chest pain, electrocardiographic (ECG) manifestations, and elevations in serum or plasma of cardiac biomarkers. The biomarkers traditionally requested are troponins and creatine kinase – MB fraction (CK-MB). Clinical symptoms such as chest pain are frequently atypical or absent, and ECG changes may be nonspecific or absent. This has resulted in the diagnosis of AMI becoming more dependent on the measurement of biomarkers.

Because of their greater sensitivity and specificity,¹ cardiac troponins (cTn) are the biomarkers of choice for the evaluation and management of patients with ACS, and in the diagnosis of AMI. Guidelines set in 2007 by the National Academy of Clinical Biochemistry and the European Society of Cardiology/American College of Cardiology stated that ‘in the presence

of a clinical history suggestive of ACS, the following is considered indicative of myocardial necrosis consistent with myocardial infarction: an elevation in cTn concentrations above the 99th percentile of a healthy population, accompanied by an assay imprecision of $\leq 10\%$...^{2,3} In addition, a rising and/or falling troponin pattern is an important component of the universal definition of AMI.³

Troponin biochemistry

Cardiac troponins consist of three proteins known as cTnC, cTnI and cTnT based on their function: C for calcium-binding, I for inhibition of actin-myosin interactions, and T for tropomyosin binding to facilitate contraction.^{2,3} cTn is released in the setting of irreversible damage to the myocyte and starts rising in blood 4 - 6 hours after cell death, peaks at approximately 18 - 24 hours and remains detectable for up to 14 days. This time frame is observed when using non-high-sensitivity cTn assays.¹

‘Highly sensitive’ cTn

The ever-increasing sensitivity of cTn assays has led to the development of ‘highly sensitive’ cTn (hsTn) assays, capable of measuring cTn levels below the 99th percentile in a healthy population. Use of these hsTn assays makes it possible to detect low levels of cTn even in healthy subjects.⁴ A rise in cTn can be observed 2 - 3 hours after the onset of an AMI, leading to earlier diagnosis and therapeutic intervention.¹ Serial changes documented by a second measurement will help to differentiate acute cardiac disorders (showing a rise and/or fall) from chronic cardiac disease, which will usually exhibit constant cTn levels.⁵ The improved sensitivity involves sacrificing reduced specificity, leading to additional diagnostic challenges for clinicians.⁶ With the increased use of hsTn assays and the application of the 99th percentile as the decision limit for AMI, a substantial increase in detection of patients with elevated cTn levels will be observed, and a high percentage of patients will be misclassified. It should be emphasised that AMI is not the only cause of myocyte necrosis, and therefore non-ischaemic causes of troponin elevation should be kept in mind.³ The high

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sensitivity of cTn, even in the presence of minimal cardiac myocyte necrosis, means that these markers may become 'positive' even in the absence of thrombotic ACS. Below is a list of causes of elevated cTn in the absence of ACS.

Causes of elevated cTn other than ACS¹

- Cardiac causes
 - . cardiac contusion (trauma)
 - . cardiac surgery
 - . cardioversion
 - . endomyocardial biopsy
 - . acute and chronic heart failure
 - . aortic dissection
 - . aortic valve disease
 - . hypertrophic cardiomyopathy
 - . myocarditis
 - . endocarditis
 - . coronary vasospasm
 - . post-cardiac transplantation
 - . post-percutaneous coronary inter-vention
 - . tachyarrhythmia
- . bradyarrhythmia
- . rhabdomyolysis with myocyte necrosis.
- Non-cardiac causes
 - . critically ill patients
 - . pulmonary embolism
 - . severe pulmonary hypertension
 - . renal failure
 - . stroke
 - . subarachnoid haemorrhage
 - . cardiotoxic drugs, e.g. amiodarone
 - . sepsis
 - . extensive burns
 - . extreme exertion
 - . infiltrative disease, e.g. amyloidosis.
- False-positive
 - . heterophilic antibodies
 - . rheumatoid factors
 - . fibrin clots
 - . microparticles
 - . analyser malfunction.

Ongoing research is in the process of best defining algorithms on how to interpret data

from hsTn assays in clinical practice. These include development of rule-out and rule-in algorithms as well as optimising the timing of the second measurement.⁵

Potential uses for hsTn

- Earlier diagnosis of patient with ACS, especially AMI.
- Risk stratification of patients with stable coronary artery disease; the higher the hsTn level, the higher the incidence of cardiovascular events.⁵
- Detection of non-ischaemic causes of elevated cTn.

Summary

- Correlate biochemical marker levels with the clinical scenario (e.g. chest pain, ECG).
- Observe cTn kinetics – a rise and/or fall in levels.
- Take note of the non-ischaemic causes of elevated cTn levels.
- hsTn can be a useful cardiac biomarker.

References available at www.cmej.org.za

SINGLE SUTURE

3D blood vessels could aid artificial organs

Growing artificial organs might help solve the transplantation shortage, but one major hurdle still exists: it is difficult to get blood vessels to grow all the way through a large organ. A gel that allows blood vessels to grow in precise shapes and respond to human cells in a manner similar to natural vessels might help jumpstart that process.

Ying Zheng and colleagues at the University of Washington in Seattle injected human endothelial cells – which line blood vessels – into tiny channels within a collagen gel.

The endothelial cells spread throughout the channels, which were only micrometres in width, and formed hollow, three-dimensional tubes, or microvessels. When the researchers pumped blood into the system, it moved through the microvessels without sticking. It could even flow smoothly around 90 degree bends.

The researchers then added a series of proteins involved in inflammation. They found that the proteins caused the blood to clot inside the microvessels, just as it would in the body. Because the system reacted to these stimuli in the same way as a natural vascular system would, Zheng says, it might one day be useful for screening drugs.

When the group injected human brain and muscle cells into the gel, along with proteins that stimulate blood vessel growth, the microvessels showed that they could branch and integrate with the two types of tissue.

Because the channels can be directed into any shape, bioengineer Linda Griffith of Massachusetts Institute of Technology is hopeful that the system can model complex vascular systems such as the blood-brain barrier, which is difficult to study in living animals. Additionally, she adds, researchers could study how cancers metastasise by putting other cell types, such as bone or liver cells, into the channels along with cancerous cells.

Zheng says that the next step is to use the system as a starting point for an artificial organ. Drawing the channels in the right shape will allow the organ to have an adequate blood supply throughout.

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