A Review on inherited cardiomyopathies, a research article on the detection of expanded triplet repeats in Huntington disease (HD) alleles, and a research article describing a novel detection method for the Chikungunya virus (CHIKV) were selected for the March 2013 JMD CME Program in Molecular Diagnostics. The authors of the referenced articles and the planning committee members and staff have no relevant financial relationships with commercial interests to disclose.


Upon completion of this month’s journal-based CME activity you will be able to:
- Discuss the genetic etiologies of inherited cardiomyopathies including hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), left ventricular noncompaction (LVNC), and restrictive cardiomyopathy (RCM).
- Describe diagnostic testing in the postgenomic era of HCM, DCM, ARVC, LVNC, and RCM.
- Describe the Chikungunya (CHIKV) virus and the diagnosis of CHIKV infection.
- Describe the detection of Huntington disease (HD) alleles.

1. Inherited cardiomyopathies are a group of cardiovascular disorders. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2013, 15:158-170.]

   a. Inherited cardiomyopathies are classified based on ventricular morphology and function.
   b. Therapeutic options for inherited cardiomyopathies are limited.
   c. Inherited cardiomyopathies include hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), left ventricular noncompaction (LVNC), and restrictive cardiomyopathy (RCM).
   d. DCM is the most common of the inherited cardiomyopathies.

2. HCM is characterized by left ventricular hypertrophy (LVH) in the absence of an underlying systemic condition or other cardiac disease, such as valvular heart disease or hypertension. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2013, 15:158-170.]

   a. The age at onset of HCM can range from infancy to old age.
   b. HCM manifestations usually do not appear before adolescence in carriers of a pathogenic variant.
   c. HCM is primarily inherited in an autosomal recessive pattern.
   d. HCM is traditionally diagnosed using cardiac imaging modalities such as echocardiography and cardiac magnetic resonance imaging.
3. DCM is defined by left ventricle (LV) dilatation and systolic dysfunction. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2013, 15:158-170.]

a. DCM is the most common indication for cardiac transplantation in the United States.
b. The spectrum of DCM clinical manifestations includes heart failure, thromboembolism, and sudden cardiac death (SCD).
c. DCM can be an end-stage presentation of other diseases or environmental exposures such as myocarditis and alcohol abuse.
d. DCM is mainly a disease of the sarcomere.

4. DCM shows a considerable degree of locus heterogeneity. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2013, 15:158-170.]

a. DCM is most commonly inherited in an autosomal dominant pattern.
b. Desmosomal genes, traditionally known to cause ARVC, may also be involved in the etiology of DCM.
c. Electrophysiologic manifestations of conduction disease, which are associated with variants of the titin gene (TTN), usually appear with the onset of DCM.
d. TTN may contribute up to 25% of familial and 18% of sporadic DCM cases, making it the most common mutated gene in DCM.

5. ARVC is defined by myocyte loss. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2013, 15:158-170.]

a. Fibrofatty infiltration of the myocardium in ARVC is associated with an increased susceptibility to arrhythmias.
b. ARVC accounts for a significant portion of sudden deaths in athletes and young adults.
c. Both the right ventricle and the LV can be affected in ARVC.
d. The prevalence of ARVC is estimated to be 1 in 500 individuals.

6. Isolated LVNC is characterized by a heavily trabeculated or spongy appearance of the LV myocardium. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2013, 15:158-170.]

a. Myocardial compaction arrest during the first trimester of embryonic development is widely believed to be a cause of LVNC.
b. LVNC is most frequently associated with Barth syndrome, an autosomal condition associated with mitochondrial disorders.
c. Patients with LVNC tend to have early-onset disease, with clinical expression varying from asymptomatic to progressively poor cardiac function, ventricular hypertrophy, increased thromboembolic events, and SCD.
d. Approximately 50% of patients with LVNC also have right ventricular involvement.

7. RCM is characterized by increased stiffness of the ventricular chambers. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2013, 15:158-170.]

a. RCM is characterized by increased ventricular wall thickness and decreased systolic function.
b. Most individuals with RCM develop heart failure and succumb to death within a few years.
c. A clinical overlap between RCM and HCM has been reported.
d. Missense variants in the desmin gene (DES) have been identified in several families with desmin-related myopathy, which can present with RCM.

8. The Chikungunya virus (CHIKV) is an arthropod-borne virus. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2013, 15:227-233.]

a. CHIKV has been responsible for numerous outbreaks of febrile arthralgia since its discovery in the early 1950s.
b. Chikungunya fever has been documented in nearly 12 countries.
c. From 2005 to 2006, a massive CHIKV outbreak occurred in La Réunion, France, with an estimated 266,000 CHIK cases and >250 deaths.
d. In India, it is estimated that >1.5 million people were infected in 2006 alone.

9. CHIKV belongs to the Alphavirus genus of the Togaviridae family. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2013, 15:227-233.]

a. The CHIKV virus possesses a linear, positive-sense, single-stranded RNA genome.
b. The CHIKV genome is approximately 11.8 kb in length.
c. The CHIKV genome encodes four non-structural proteins (nsP1 to nsP4).
d. The CHIKV genome encodes four structural proteins (C, E2, 6K, and E1) with organization as follows: 5’-cap-nsP1-nsP2-nsP3-nsP4-(junction region)-C-E2-6K-E1-poly(A)-3’.
10. Diagnosis of CHIKV infection is dependent on virus isolation, detection of virus-specific antibodies by enzyme-linked immunosorbent assay (ELISA), or genomic detection by RT-PCR. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2013, 15:227-233.]

a. Cell culture-based virus isolation is the gold standard for diagnosis of CHIKV infection.
b. Cell culture-based virus isolation requires specialized skills available only in some reference laboratories.
c. An RT-PCR assay was developed for the early detection of the CHIKV using 2,7-diamino-1,8-naphthyridine derivate (DANP)-labeled cytosine bulge hairpin primers to amplify the nsP3 gene of the CHIKV genome, with a detection limit of 0.03 plaque-forming units (PFUs) per reaction of CHIKV.
d. RT-PCR-based molecular assays are being increasingly used for rapid, early diagnosis, particularly during the acute phase of the illness.

11. Huntington disease (HD) is an autosomal dominant neurodegenerative disorder. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2013, 15:255-262.]

a. Abnormal expansions of the CAG repeat in the Huntington (HTT) gene on chromosome 4 are associated with HD.
b. Determination of the number of CAG trinucleotide repeats is routinely used in diagnostic and predictive testing of individuals symptomatic or at risk for HD.
c. The polymorphic CCG repeat in a locus adjacent to the CAG repeat region varies between 3 and 6 triplets in length.
d. The polymorphic CCG repeat includes an apparent CCT site that is usually two or rarely three repeats in length.

12. When a sample appears homozygous for a normal allele, additional HD testing is recommended to exclude the possibility that an expanded allele was not identified by PCR. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2013, 15:255-262.]

a. The authors described a chimeric PCR process to easily distinguish true homozygous alleles, making Southern blot analysis unnecessary in all cases.
b. Southern blot analysis is expensive, labor intensive, requires high concentrations of DNA, and can delay turnaround time.
c. Chimeric or triplet repeat primed PCR has been described in screening for fragile X premutations, screening for full mutations, and determination of mosaic fragile X samples.
d. Individuals with juvenile-onset HD usually have larger CAG repeat sizes than adult-onset cases.