


USE OF MOLECULAR AUTOPSY IN CASES OF SUSPECTED ARVC

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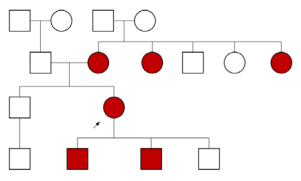
OBJECTIVES

- Case examples
- Background
 - ARVC
 - Molecular autopsy
- Molecular autopsy screen



ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY

- ARVC is an inherited cardiac disease
- Fibrofatty replacement of the myocardium that predisposes to ventricular tachycardia and sudden death in young individuals and athletes
- Autosomal dominant inheritance



MOLECULAR AUTOPSY

- The use of genetic testing to help determine a decedent's cause of death
- NAME Position Paper (2013): Retaining Postmortem Samples for Genetic Testing
 - Good sources for testing include:
 - Blood in EDTA***
 - Cardiac tissue
 - Skin tissue
 - Formalin-fixed tissue***

National Association of Medical Examiners Position Paper: Retaining Postmortem Samples for Genetic Testing

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Christina Honeywell MSc CCGC, Jeff Jantzen MD, Frank Miller MD,
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ABSTRACT: Sudden unexpected death is typically diagnosed in infants, children, teenagers, and young adults following completion of an autopsy that fails to identify a cause of death or when autopsy suggests a potentially genetic cause of death in an individual less than 40, such as cardiomyopathy or aneurysm. Such deaths may be a result of genetic abnormalities that are unable to be diagnosed by gross or microscopic inspection, but may be detectable by molecular studies. Unfortunately, the ability to perform postmortem genetic testing is frequently hindered by lack of an appropriate specimen following completion of an autopsy. This paper provides recommendations developed by the National Association of Medical Examiners with the assistance of genetic counselors. The recommendations establish procedures to facilitate postmortem genetic testing and DNA banking by health care professionals assisting families who have experienced sudden death in young relatives by clarifying proper sample acquisition and storage. Additionally, recommendations for discussion with surviving family members and test planning are provided. The objective of these recommendations is to ensure that postmortem samples suitable for DNA banking are retained, allowing at risk family members improved detection of potentially treatable genetic diseases.



WHEN TO COLLECT:

- At a minimum, samples should be saved from individuals 40 years of age and younger who die suddenly and unexpectedly and whose deaths remain unexplained at the completion of the autopsy.

- 1) Drowning, particularly in the case of a sober or experienced swimmer.
- 2) Single motor vehicle accidents when no mitigating factors are present (e.g., toxicology negative, favorable road conditions);
- 3) An unexplained seizure in a young person;
- 4) Cardiomyopathy or aneurysm identified on autopsy;
- 5) An unexplained death of an individual with a family history of sudden death or inherited heart disease, such as a cardiomyopathy, thoracic aneurysm or known genetic cardiac diagnosis;
- 6) All deaths that are sudden and unexplained where cause of death is not clear at autopsy.

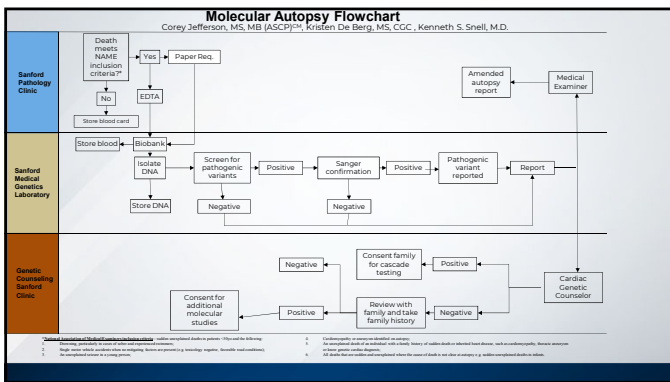
SANFORD CHIP

The Sanford CHIP is a laboratory developed test which is clinically validated by the Sanford Medical Genetics Laboratory to return two main classes of results:

SANFORD CHIP CLINICAL RESULTS

- 1 PHARMACOGENETICS:**
Returns genetic variants known to impact an individual's ability to metabolize certain medications.
- 2 DISEASE PREDISPOSITION:**
Returns genetic variants from a set of genes defined by the ACMG known to increase risk for conditions known to have medical actionability.

All positive results are confirmed with an alternate method.



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Genotyping

OR

Sequencing

CONCLUSIONS

- Presented two cases that had appeared to have an underlying cardiac death
- Genetic testing revealed etiology and provided management guidelines for family
- Sanford has helped develop a genetic screen to help diagnose underlying hereditary cardiac conditions



QUESTIONS?



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