



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

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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.

**KEYWORDS:** Forensic pathology, Autopsy, Postmortem samples, Genetic testing, Death investigation

## INTRODUCTION

The American Heart Association estimates that there are approximately 295,000 emergency medical services (EMS)-assessed out-of-hospital cardiac arrests each year in the U.S., with an estimated 92% of these individuals dying prior to subsequent hospital discharge when a rhythm is recorded during initial resuscitative efforts (1). Some studies indicate that in up to 30% of these cases in which autopsy is subsequently performed, there are no abnormalities found in the heart (2). Sudden cardiac death in individuals under the age of 40 is often caused by underlying genetic conditions such as long QT syndrome or hypertrophic cardiomyopathy. Recent studies suggest that genetic testing may help identify

inherited cardiac disease in either the decedent or surviving family as much as 40% of the time when young sudden cardiac death (SCD) occurs (3, 4). These studies also show that clinical cardiovascular screening (i.e., electrocardiogram, echocardiogram) may identify at risk relatives and permits strategies to reduce the likelihood of SCD in another family member. Other genetic conditions must also be considered with sudden unexpected death. However, sometimes genetic diagnoses can only be made through testing of a deceased individual as a result of decreased penetrance and variable expressivity, making it difficult, if not impossible, to confirm a diagnosis in a living relative. Unfortunately, specimens acquired at autopsy are often no longer available when such testing is considered, as recommenda-

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Acad Forensic Pathol  
2013 3 (2): 191-194

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tions do not currently exist in the United States for the saving of samples that are useful for genetic testing and/or DNA banking. Disease specific genetic testing recommendations are evolving rapidly and are detailed in other references, but are beyond the scope of this paper (5, 6). This publication establishes recommendations for appropriate specimen collection and retention in deaths with medical examiner/coroner (ME/C) involvement to facilitate genetic studies when appropriate and assist clinicians and genetic counselors with their duties.

## DISCUSSION AND RECOMMENDATIONS

Leadership members of the National Association of Medical Examiners (NAME) were approached by genetic counselors to consider developing recommendations for specimen collection and retention to accommodate genetic studies for a decedent and surviving family members. The task was delegated to the NAME ad hoc Molecular Biology Committee, which worked in conjunction with genetic counselors. Collaboration consisted of review and discussion of various drafts via a series of electronic communications. The ad hoc Molecular Biology Committee, with the assistance of genetic counselors, then drafted a manuscript based upon the proposed recommendations. The proposal was submitted for public review by the general NAME membership prior to endorsement by the NAME Board of Directors, with revisions incorporated as deemed necessary. A companion article providing additional information about the role of genetic counselors can be found in this issue of *Academic Forensic Pathology* (7). The current work represents the product of the collaboration, with the following recommendations:

### 1. When to Save a Sample

Ideally, a specimen should be saved in all ME/C cases in which an autopsy is performed; however, many offices function within systems where space, equipment, and financial considerations will prohibit achieving this practice. 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. As this determination is usually not known until the completion of autopsy and toxicology testing, an extra sample can be collected along with other routine samples during the autopsy procedure. Circumstances that should be considered suspicious for a possible genetic etiology include, but are not limited to:

- 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.

Triggers for sudden death can include exercise, emotional stress (including fright and anger), and acoustic stimuli. Overall, a low threshold should be observed for saving an appropriate sample. If there is a young or sudden death, or a suspicion that the death may have a genetic cause, the foresight to save a sample at autopsy can greatly assist with subsequent genetic testing.

### 2. Type of Sample, Storage, and Retention

Current NAME Autopsy Performance Standards include routine collection and preservation of blood, urine, and vitreous specimens (8). Similarly, NAME Accreditation Standards require policies for appropriate specimen collection and retention (9). However, collection and retention standards specific to the variety of individual testing options available, including genetic studies, do not exist. For the purpose of potential genetic testing and/or DNA banking, an appropriate sample is 5-10 mL of blood collected at autopsy or as part of an external examination that is preserved with K<sub>2</sub>EDTA (usually a purple top tube). If the sample is to be stored short term (less than four weeks after autopsy) the sample should be kept in a refrigerator (4°C). For storage of months to years, samples should ideally be moved to a -20°C to -70°C freezer and remain there until they can either be shipped to an appropriate laboratory when requested or properly disposed of at the termination of a retention schedule. Specific storage conditions may be tailored for a given death investigation office when it tends to refer such testing to a specific laboratory based upon that laboratory's preferences. The retention schedule for these specimens should provide ample opportunity for families and their health care providers to initiate genetic testing and/or DNA banking when indicated, but must be balanced with the overall capabilities of the ME/C facility.

### 3. Shipping of Sample

Once a family decides to pursue genetic testing, specimens should be shipped directly to the chosen genetic testing laboratory directly from the ME/C facility to ensure proper chain of custody. When such testing is initiated by an agency outside of the investigating ME/C, shipping materials and costs of delivery should be provided through the coordination of the receiving laboratory and the requesting health care agency. Once a sample is frozen after autopsy, it should not be thawed until arriving in the genetic testing laboratory. DNA quality is just as dependent on the manner in which a sample is sent as the type of sample from which it is extracted. To prevent thawing, all frozen samples should be packed in a Styrofoam container packed tightly with dry ice. Fresh samples may be shipped at room temperature. All samples, frozen and fresh, should be packaged according to hazardous material guidelines and shipped overnight by a courier or reliable shipping company to either a DNA bank or clinical genetic testing laboratory according to the decision of the family or healthcare professional.

### 4. Informed Consent

In the event that the results of genetic testing are considered crucial to the accurate outcome of a death investigation, the ME/C may elect to pursue testing without family consent according to local statutory authority. When not initiating genetic testing, the ME/C should alert family members of the potential for a genetic disease and recommend consultation with their primary care physicians. The informed consent process in sudden cardiac death cases can present unique challenges; therefore, a multidisciplinary approach is suggested. A genetic counselor, clinical physician, or both, can ensure that the family receives all of the critical information needed to make an informed decision about potential testing. Family members need to be notified regarding the option for postmortem genetic testing and informed consent for such testing needs to be obtained from the family by a professional who is well versed in the complexities of this process. Genetic testing may not be reimbursed by medical insurance companies in many cases, and therefore it is important to explore the financial responsibility of testing with the family. If genetic testing is not possible due to either financial hardship or diagnostic uncertainty, but family indicates a desire to pursue such testing, DNA banking may be a more financially reasonable option for the family to pursue. Doing so would provide families the possibility of testing the sample in either the near future or in the remote future as scientific knowledge advances.

### 5. Ethical Issues

Postmortem samples retained during standard autopsy procedure for other specific evaluations such as toxicology should be released for genetic testing if deemed necessary by the ME/C or if family indicates they would like to pursue such testing on their own, assuming all foreseeable toxicology testing is completed, that relinquishment of the specimen would not hinder the death investigation or subsequent legal proceedings, and no alternative specimen was initially saved specifically for this purpose. Families with religious or cultural objections to retaining specimens should be entitled to forfeiture of potential genetic testing and/or DNA banking at their insistence, depending upon local death investigation statutes and the circumstances of the death, despite the potential loss of important diagnostic material. The National Association of Medical Examiners has previously released a position statement supporting the retention of biological specimens (10). Specimens saved for potential genetic testing are only to be used for clinical testing and not for research purposes unless permission to do so is specifically granted by the appropriate family representatives. Due to the delay in receiving genetic test results (usually four to ten weeks) in suspicious cases, it is recommended that relatives be informed of their potential risk of sudden death and the availability of cardiac evaluation while they await results or even prior to consultation, if an inheritable genetic cardiac disease is of valid concern for a given sudden unexplained death.

### 6. Communication

Medical examiners/coroners should notify the next of kin and/or the primary care physician/pediatrician of autopsy results as soon as possible if a genetic condition is suspected. If possible, it is recommended to involve a genetic counselor in these cases. Some clinics combine the services of specialists such as cardiologists and geneticists. Health care professionals can find genetic counselors quickly through various websites, such as that of the National Society of Genetic Counselors, if counselors are not immediately available in their practice setting (11). ME/C familiarity of recommendations for cardiologists to screen at risk relatives for cardiac genetic conditions may facilitate discussion between the ME/C and family when recommending consultation (5, 6, 12, 13). Highest sensitivity should be practiced in discussion of retained samples with surviving family members, but these discussions should not be postponed. When testing is performed on a decedent's samples, the results should be made available to the ME/C.

**CONCLUSION**

Medical examiners and coroners not only have the responsibility of determining cause and manner of death, but also function as stewards of public health promotion and monitoring. With that role comes a responsibility to collect adequate specimens for genetic disease testing. Although some offices will face varying degrees of space, equipment, or funding barriers to implement these recommendations, procedures should be created to allow for potential genetic testing, while working within defined jurisdictional statutes. Through the collaborative efforts detailed in these recommendations, the National Association of Medical Examiners strives to provide a level of best practice that not only accomplishes the mission of death investigation, but also preventative medicine.

**DISCLOSURES**

Dr. Baxter is employed by GeneDx, a for-profit genetic testing laboratory. Dr. Jentzen provides expert testimony and retains consultant fees and royalties. Dr. Stacy receives cases from other counties for which the fees are billed and tracked by the University of Missouri. Dr. Pinckard is the Editor-in-Chief of *Academic Forensic Pathology*.

The opinions and conclusions of this paper have been reviewed and approved by the National Association of Medical Examiners Board of Directors and as such are endorsed by NAME. These opinions and positions are based on a consensus of the current literature, knowledge, and prevailing theories on this topic. As scientific knowledge and experience grow, NAME reserves the right to revise or update these opinions. The process by which NAME position papers are initiated, written, reviewed, and approved is publicly available at <https://netforum.avectra.com/temp/ClientImages/NAME/2c26a527-f992-4f70-9d03-7941bff5319d.pdf>. All scientific position papers endorsed by the National Association of Medical Examiners automatically expire five years after publication unless reaffirmed, revised, or retired at or before that time. This work is a product of NAME and as such was not subjected to *Academic Forensic Pathology* Journal editorial review.

The editors and publication staff do not report any relevant conflicts of interest.

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