British Heart Foundation

NHS England and NHS Improvement

Pathology Protocol

NHS and Coronial Sudden Unexpected Death (NHS-C-SUD) Programme

VERSION 1.6

Contents

1. Background to the project

Cardiac pathology, post-mortem genetic testing and clinical familial evaluation are the three primary components of the comprehensive personalised medical management of families who have suffered sudden unexpected deaths (SUD) due to potential genetic cardiac causes. The aim is to test the optimum pathway that identify a cause of death and diagnose and treat relatives who are also potentially at risk of a genetic cardiac condition. The delivery of appropriate patient pathways is, however, highly heterogeneous across the nation and requires close working between the NHS and coronial services. There is an opportunity now with the implementation of Genomic Laboratory Hubs and the Genetic Medicine Service Alliances across England to explore the systematic introduction of post-mortem genetic testing for SUD.

2. Introduction to this paper

This protocol has been developed in the context of the NHS and Coronial Sudden Unexpected Death project, set up in 2021, to standardise the end-to-end process carried out by the pathologist within each region taking part in the project.

Standardising this process should improve the experience for bereaved families, manage costs and optimise the potential to assess the surviving immediate relatives. It is assumed that the post-mortem examination will be completed in line with the Royal College of Pathologists Guidelines on Autopsy Practice: Sudden death with likely cardiac pathology

The protocol has been developed based on the following assumptions about access to specialist pathology within the 7 regions:

Table 2.0

There is not a specialist cardiac pathologist within this region	There is a specialist cardiac pathologist within this region
Manchester	Sheffield
Leicester	Birmingham
North-East London	South-East London
Bristol	

The charity CRY has kindly agreed to continue to support those services without access to specialist cardiac pathology within their region. Therefore, the CRY funded centre will accept what is anticipated to be a modest increase in referrals from the North-East London, Manchester, Leicester and Bristol pilot sites. This is an interim arrangement which will be in place during the pilot lifecycle.

Regions that have access to a local specialist pathologist should continue as they do now.
NHSE&I is currently working with the Royal College of Pathologists to address a longer-term solution.

We anticipate that each senior coroner will deal with no more than 3-4 cases per month that will meet the inclusion criteria.

3. Case inclusion criteria for this project

All sudden unexpected death cases, aged 1-60 years, reported to HM Coroners in the participating sites will be included provided a cardiac genetic cause is suspected. Deaths occurring that remain unexplained despite a full coronial and expert cardiac post- mortem examination and toxicological testing (Sudden Arrhythmic Death Syndrome) will also be included. Decedents older than one year where resuscitation has failed or there is no recovery despite an initially successful resuscitation may also be included.

The pathologist will retain cardiac tissue blocks and tissue suitable for DNA extraction and flag up the case to the coroner's officer following autopsy of a sudden death case where the following findings are present:

1. Unascertained cause of death*:
    a. Morphologically normal heart. Sudden arrhythmic/adult death syndrome (SADS)
    b. Equivocal/uncertain/borderline findings
2. A dilated, thin walled, hypertrophied, scarred or fatty heart with normal or unobstructed coronary arteries:
    a. Hypertrophic cardiomyopathy (HCM)
    b. Dilated cardiomyopathy (DCM)
    c. Arrhythmogenic cardiomyopathy (ACM)/arrhythmogenic right ventricular cardiomyopathy
    d. Unexplained cardiac hypertrophy
    e. Unexplained cardiac scarring/ fibrosis
3. Severe mitral valve prolapse with myxomatous degenerative valvular disease (<40 years**)
4. Thoracic aortic aneurysm +/- dissection/rupture (<40 years**)
5. Others – i.e. idiopathic calcification of infancy, possible metabolic/storage cardiomyopathy

* Toxicology will be required and will only likely be available at a later stage.
** If there is additional family history of sudden death or similar heart disease then older cases may be included.
NB cases where a non-cardiac cause of death was indicated (e.g. trauma) but a genetic heart disease has been identified incidentally will be included.

4. Alignment with the Child Death Review process

This project is aligned with the Child Death Review process for unexplained deaths in children. Alongside the review process, the case will be referred to the coroner and the coronial pathologist will take forward the initial post-mortem examination. The pathologist will specifically address potential paediatric causes of sudden unexpected death such as inborn errors of metabolism. If the result of the post-mortem examination indicates that the cause of death is likely to be a genetic cardiac condition or unexplained, the case will be included in the pilot. In other words, the coroner's office should signpost the parents of the child to the local clinic for inherited heart conditions and ensure retention of tissue.

Of course, if the post-mortem examination indicates a cause of death that is unrelated to inherited heart disease, the case should not be included in this pilot.

5. Managing the process within each region

5.1 Allocation of cases to the pathologists and specialist cardiac pathologists within each region

a) The coroner should continue to allocate the case to the local pathologist through the existing allocation process/system (no change to existing process required). Some coroners may choose to allocate cases automatically to the local specialist cardiac pathologist where the circumstances of death or the deceased's history indicates from the outset that a genetic cause of death is highly likely. If so, click here to read the criteria that would indicate a genetic cardiac cause of death prior to the post-mortem examination being carried out.
b) If the pathologist carrying out the initial post-mortem examination is satisfied based on their initial examination that the cause of death is a genetic cardiac condition, there is no need for further specialist examination unless that pathologist believes it would be of benefit.
c) However, if the pathologist concludes that a specialist cardiac post-mortem examination is

required, the case should be referred to the cardiac pathologist providing a service for that region (see table 2.0 on page 2) as quickly as possible.

d) If the case is being referred to the CRY funded specialist pathologist centre at St George's, more information on that process can be found in appendix A. Tissue suitable for DNA extraction should be stored locally and not sent to the CRY funded centre at St George's for the lifetime of the pilot. The post-mortem examination should be carried out in accordance with relevant guidelines (see Royal College of Pathologists Guidelines on Autopsy Practice: Sudden death with likely cardiac pathology)

e) Ideally the heart should be returned to the family within 2 weeks of the death to allow the funeral to take place (depending on local testing reporting timelines and family arrangements).

5.2 Reporting findings

a) Following completion of specialist pathology examination, the report detailing the findings should be provided to the coronial service investigating the death.

b) In cases where a genetic cardiac cause is the suspected cause of death, the specialist pathologist should highlight this at the front of the report and indicate the need for family and genetic investigation. This will act as a prompt for coroner's officer to advise the family of the need for specialist follow up in an ICC service and for tissue to be retained to support the assessment of the family.

c) Suggested wording: *In view of the above diagnosis and negative toxicology, I would advise that the immediate blood family are screened by a cardiologist at an inherited cardiac condition centre. Retention of tissue suitable for DNA extraction and future genetic testing is strongly recommended (if not already given).*

5.3 Capturing consent to retention of tissue after the coroner's purposes are complete.

a) Consent for retention of tissue after the coroner's purposes are complete should be captured in accordance with the Human Tissue Act and using the agreed standardisation consent forms developed for this project (Histology Tissue Retention Consent Form)

b) Consent should be captured by the coroner's officer.

c) The coroner's officer will be supported to do this as outlined in section 5.6

d) The coroner's officer should inform the pathologist and/or specialist pathologist whether consent has been captured to retain the tissue so that it can be either stored or disposed of appropriately.

5.4 Retention of tissue

Provided consent has been captured to retain tissue after the coroner's purposes are complete, the following samples should be retained depending on the availability of suitable -80 degrees Centigrade freezers at the mortuary:

- Cardiac blocks (FFPE at room temperature)
- Tissue for DNA extraction
    - Blood (frozen)
    - 1 cubic centimetre Spleen tissue (0.5cm x 0.5cm x 0.5cm) Spleen or liver (taken at time of initial autopsy frozen or placed in tube of pre filled RNALater solution at room temperature)

Where no mortuary freezer is accessible, RNALater solution is the recommended storage medium. Tissue should be taken and added to this solution at the point of initial autopsy to

maximise tissue quality for DNA extraction. Tissue added to RNA solution should be stored at room temperature or preferably in a refrigerator prior to transport to lab.

Where tissue has been frozen, please allow to thaw prior to adding to RNA solution.

Please avoid fixing spleen in formalin to avoid rendering sample suitable for genetic analysis.

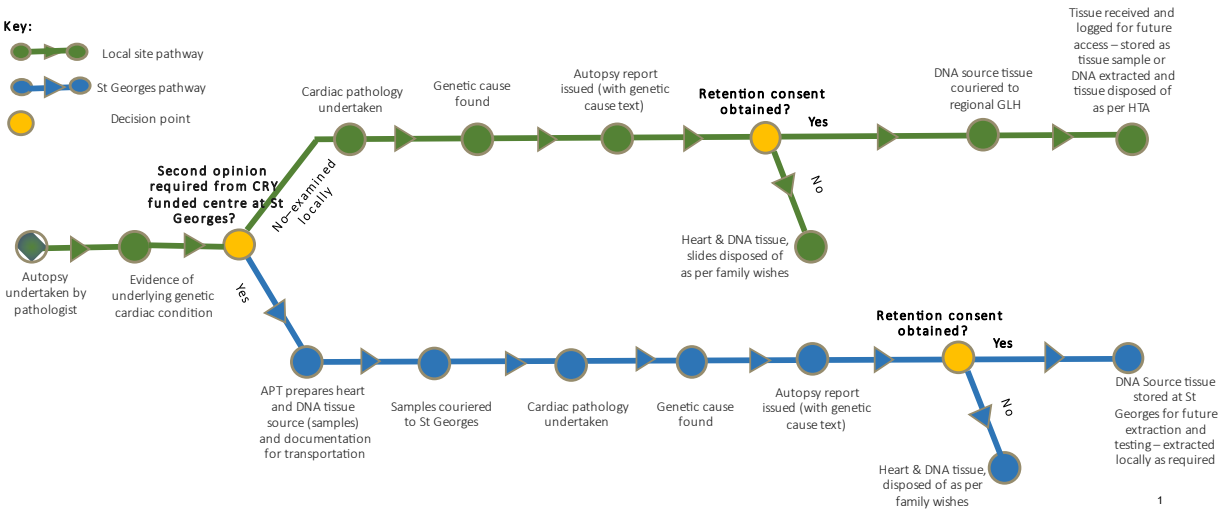
5.5 Storage of Tissue

a) Where cardiac pathology has been undertaken locally or sent to the CRY funded centre at St George's, locally stored tissue suitable for DNA extraction should be transported to the regional Genomic Laboratory Hub (GLH) for processing and storage according to existing developed practice. Each regional pathologist should liaise with their local GLH to finalise arrangements for transport of the tissue and storage arrangements thereafter or either that tissue or the extracted DNA.

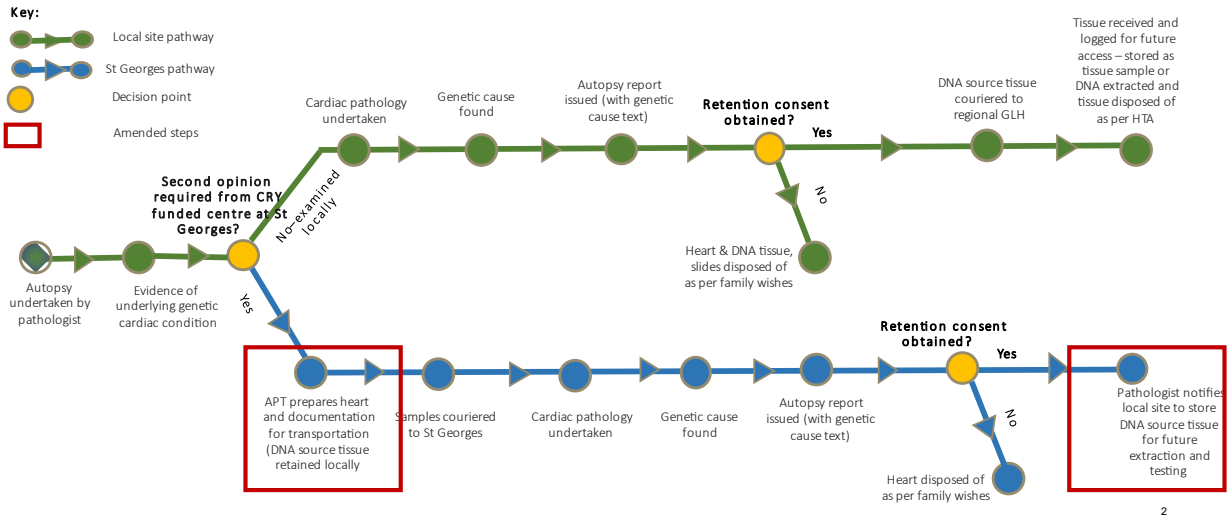
b) Where cardiac pathology has been undertaken at the CRY Funded centre at St George's and examination indicates a genetic cardiac cause of death, the CRY pathologist will advise that locally held tissue suitable for DNA extraction should be processed for storage as outlined in 5.5(a), above.

c) The arrangements for each region should be shared with the coroners' officers (See diagrams below. The first diagram outlines pathways prior to the pilot programme. The second diagram outlines the pathway during the programme lifetime. Ideally, the location should be notified to the relevant ICC coordinator during the signposting with consent process

Cardiac Pathology exemplar– Existing pathway



Cardiac Pathology exemplar– Pilot programme pathway



5.6 Training and support for the coroner's officer

a) Coroners' officers within each area taking part in the project should undergo the training arranged by the British Heart Foundation to ensure they understand the end-to-end process and have the appropriate level of knowledge to support the families at this early stage of the pathway.

b) They should also be aware of the support information offered by charities such as Cardiac Risk in the Young (CRY) so they can signpost the families to them. See the leaflet on 'Supporting families following a sudden unexpected death'