



# The Royal College of Pathologists

## ***Guidelines on Autopsy Practice***

### **Scenario 1: Sudden death with likely cardiac pathology**

#### **The role of the autopsy**

To establish:

- whether the death is attributable to cardiac disease or to other causes of sudden natural death
- the nature of the cardiac disease
- whether an inherited cardiac condition is present, necessitating specific advice to the family
- that adequate histological material is retained and is available should review or referral be necessary
- the possibility of toxic/illicit drug abuse and other unnatural deaths.

#### **Pathology encountered at the autopsy**

Suggested sequential autopsy examination in sudden death investigation, encompassing the main causes (Sheppard and Davies, 1998)<sup>1</sup>

1. Consider natural death  
– *external examination, scene of death.*
2. Exclude non-cardiac natural death  
*e.g. haemorrhage (e.g. cerebral, aortic aneurysm, peptic ulcer), pulmonary embolism, bronchopneumonia in the elderly.*
3. Consider macroscopic cardiac disease  
*e.g. ischaemic heart disease (60% of sudden deaths in England, and 80% of sudden cardiac deaths),<sup>2</sup> valvular disease.*
4. Consider microscopic findings in myocardium  
*e.g. cardiomyopathies, myocarditis.*
5. Reappraise history, do toxicology screen  
*e.g. sudden adult death syndrome (SADS), illicit and psychiatric drugs, sudden unexpected death in epilepsy (SUDEP), alcoholic fatty liver.*

## Causes of sudden cardiac death<sup>1-5</sup>

- Coronary artery disease and ischaemic heart disease:
  - atherosclerosis
  - structural/congenital malformation (including anomalous origin)
  - Kawasaki's disease
  - myocardial bridging
  - coronary artery dissection
  - aortitis and secondary atherosclerosis
  - embolism into coronary arteries
  - fibromuscular dysplasia of intramyocardial artery
  - coronary artery spasm (regional infarction in absence of coronary lesion).
- Valve disease:
  - aortic stenosis
  - mitral valve prolapse
  - infective endocarditis.
- Myocardial disease:
  - myocarditis (including cardiac sarcoidosis)
  - cardiomyopathies
  - LV hypertrophy and hypertension
  - idiopathic myocardial fibrosis
  - amyloidosis
  - cardiac tumour – primary (myxoma) or metastatic.
- Structural conduction system abnormalities:
  - absence of atrial portion of AV node
  - bundle of His damage
  - nodal mesothelioma
  - atrioventricular nodal artery stenosis.
  - anomalous conduction pathways (e.g. Wolf-Parkinson-White syndrome)  
*(NB diagnosis relies on ECG evidence in life or positive family history. Serial sectioning of conduction system for routine diagnosis is unnecessary).*
- Drug toxicity:
  - cocaine
  - amphetamine and ecstasy
  - solvent abuse
  - marijuana<sup>6</sup>
  - antidepressants and anti-psychotics.<sup>7,8</sup>
- No morphological abnormalities (sudden adult death syndrome, SADS):<sup>2,9</sup>
  - functional conduction system abnormalities (long QT syndrome, Brugada syndrome)<sup>10</sup>
  - catecholaminergic polymorphic ventricular tachycardia
  - idiopathic ventricular fibrillation
  - blunt chest trauma (commotio cordis).

## Other clinical scenarios in which sudden cardiac death may occur

- Sudden death in athletes<sup>11,12</sup>
- SUDEP<sup>13</sup>
- Congenital heart disease (including surgically-corrected CHD)  
*(NB it is essential that in complex congenital heart disease +/- surgical correction, the heart is retained for expert referral)*

- Following cardiac surgery/interventions (*see future scenario*, ‘Autopsy following cardiac interventions/surgery’, *for more details*)
- Cardiac involvement in systemic disease (connective tissue disorders, sickle cell disease, metabolic and endocrine heart disease)
- Disseminated malignancy.

### Specific health and safety aspects

No specific infection hazards, but note that some pacemakers are defibrillators and can deliver a significant electric shock.

### Clinical information relevant to the autopsy

- Circumstances of death: date, time and place of death (e.g. at home, at rest or during exercise). Was the death witnessed? Were there any suspicious circumstances?
- Past medical history: general health status, previous significant illnesses, e.g. syncope, palpitations and respiratory disease.
- Previous surgical operations or interventions.
- Details of current medications, especially cardiac drugs.
- History of alcohol or other drug abuse.
- Family cardiac history: sudden premature death, palpitations.
- ECG, serum enzyme and troponin estimations, if done.
- Lipid profiles and related medication, if known.

### The autopsy procedure

- Check for implantable cardioverter defibrillator (ICD)/pacemaker; if defibrillator is *in situ*, see MDA Safety Notice 2002(35) for safe removal.<sup>14</sup>
- Check for recent intravenous access, intubation, ECG pads, defibrillator burns and drain sites.
- Establish body weight, to correlate with heart weight.
- Full autopsy, with sequential approach to sudden death investigation as suggested above.

### The standard examination of the heart<sup>15,16</sup>

1. Check pericardium for evidence of adhesions, effusion, exudates, haemopericardium.
2. Check anatomy of the great arteries before transecting them 3 cms above the aortic and pulmonary valves.
3. Check and divide the pulmonary veins; divide the SVC 2 cms above junction of crest of right atrial appendage and SVC (to preserve sinus node); divide IVC close to diaphragm.
4. Open the atria and inspect appendages for thrombi, and mitral and tricuspid valves from above. Check aorta, pulmonary artery and aortic and pulmonary valves from above.
5. Examine the coronary arteries for anatomy (‘dominance’), disease distribution and severity.
  - a) *In situ*: make multiple transverse cuts along the course of the main epicardial arteries.
  - b) Heavily calcified: either cut with sharp scissors, or ideally (if there is consent to retain tissues) remove, decalcify, cut transversely and sample focal lesions for histology.

- c) Check coronary arterial ostia and major branches such as the diagonals, obtuse marginals and the posterior descending branch of the right coronary artery. Ideally, summarise the findings on the American Heart Association (AHA) diagram of coronary artery anatomy, indicating the minimum luminal diameter of stenosed segments.
  - d) Stents: recently inserted – open vessel longitudinally by incising it longitudinally along the length of the stented segment and remove stent; previous insertion: cut across with sharp scissors to check patency. (*See future scenario, 'Autopsy following cardiac interventions/surgery', for further details.*)
7. Do complete transverse (short-axis) slices of ventricles at 1 cm intervals from apex to mid-ventricular level and assess carefully for symmetry, focal lesions, mural thrombus and cavity dimensions. Consider doing digital photography of a representative slice for the autopsy record if myocardial disease or SADS is suspected
  8. Once emptied of blood, weigh the entire specimen and assess for hypertrophy. Note body weight. Note that LV mass is determined by body build, weight and fitness and the sex of the individual.
    - a) Total heart weight: assess weight of heart against tables of normal weights by age, sex and body weight (comprehensively detailed in the reference texts given below).
    - b) Wall thickness: measure thickness of posterior LV and septum and relate to cavity diameters (mean of two planes).
    - c) Isolated ventricular weights when appropriate, using the Fulton technique for individual ventricular weights (mandatory for assessing right ventricular hypertrophy) may be done.
  9. Cut top half of the heart in the flow of blood and complete examination of atrial and ventricular septae, valves and ventricular outflow tracts. Measure mitral valve annulus (normal <11 cms).

#### Specific categorisation of sudden cardiac deaths (Davies criteria<sup>5</sup>)

- a) Coronary atheroma and clear evidence of coronary thrombosis and/or acute myocardial infarction – *very high probability of causing sudden death.*
- b) Coronary atheroma with at least one coronary artery <1 mm diameter and evidence of healed myocardial infarction – *moderate to high probability of causing sudden death.*
- c) Coronary atheroma with at least one coronary artery <1 mm diameter, but no evidence of healed myocardial infarction – *questionable probability of causing sudden death: depends on number of stenoses and circumstances of death.*
- d) No evidence of ischaemic heart disease, but evidence of congestive cardiac failure or significant left or right ventricular hypertrophy and/or dilatation – *moderate probability of causing sudden death; cardiomyopathies should be excluded.*
- e) No significant cardiac pathology / unexplained sudden cardiac death (SADS) – *histology and toxicology essential* if SADS is to be considered seriously.

#### Specific significant organ systems

- Examination of the major extra-cardiac arteries.
- Examination of the cranial cavity to search for cerebral haemorrhage.

## Organ retention

If no cause of death other than cardiac failure is identified and the heart appears grossly normal or involved by primary myocardial disease, consider retaining and fixing the heart for specialist referral as the final diagnosis may have genetic implications for the family.

If an expert cardiac opinion is required, it is important to ensure that the whole heart – or a representative mid-ventricular transverse slice, at the very least – is retained for referral and histological sampling, the subsequent fate of the heart being at the family's discretion once the diagnosis had been made. In these circumstances, a digital photograph of a representative mid-ventricular slice should be retained as part of the deceased's autopsy record, either by the pathologist conducting the autopsy or by the referral pathologist.

With prior warning, the referral pathologist may be able to ensure rapid turnaround of the heart, so detailed examination, digital photography of the gross specimen and comprehensive sampling for histology is done before the heart is returned to the family for interment.

The family should also be asked to consider agreeing to long-term retention of the tissue blocks for research, as many primary myocardial diseases and SADS cases are still being investigated and their genetic basis clarified; future access to pathology material for review is an important part of this process.

It may be helpful for coroners and their officers to know that a mid-ventricular slice accounts for only 15% of the total heart by weight and yields a maximum of ten tissue blocks. Permitting the referral pathologist to assess the slice for disease distribution and to take mapped blocks is a crucial step in reaching a diagnosis and counselling the family appropriately.<sup>2</sup>

## Recommended blocks for histological examination – best practice

- As a minimum, take mapped blocks of anterior, lateral and posterior left ventricle and septum from a representative transverse slice, right ventricular outflow tract and both atria. A connective tissue stain (elastic van Gieson or Masson's trichrome), as well as H&E, should be done as standard. Congo red (thick section, amyloid), Perl's Prussian blue (iron) and PAS/AB/PAS (storage disorders), immunohistochemistry for CD3, CD20, CD68, etc. (myocarditis) should be done as required.
- Lung (with connective tissue stain to assess vessels).
- Other relevant tissues as determined by the observed pathology.

## Other samples required

- If illicit drug use suspected, peripheral blood (see Scenario 3: *Suspected illicit drugs*).
- If acute anaphylaxis suspected, spun peripheral blood serum (see Scenario 4: *Autopsy for suspected acute anaphylaxis*).
- If early myocardial infarction is suspected but is not evident macroscopically, measurement of post-mortem peripheral blood cardiac troponin T may help confirm the diagnosis.<sup>17</sup>
- If a potentially inheritable disorder of the heart is suspected, blood and fresh spleen should be reserved (frozen) pending onward referral for genetic testing.

## The clinicopathological summary

Decide whether the pathology satisfactorily explains the clinical circumstances of the death.

1. Consider whether there are features indicating a familial disease, requiring screening and counselling of the next of kin.
2. If no satisfactory cause of death is identified, cardiac or otherwise, consider SADS in consultation with a cardiac pathologist.
3. If the final diagnosis is cardiomyopathy, SADS or SUDEP, consider recommending a support group such as The Sudden Adult Death Trust ([www.sadsuk.org](http://www.sadsuk.org)) to the family.

## Specimen cause of death opinions/statements

- 1a. Acute myocardial infarction
  - 1b. Coronary artery thrombosis
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- 1a. Acute cardiac failure
  - 1b. Old myocardial infarction and coronary artery atherosclerosis
- 
- 1a. Acute cardiac failure
  - 1b. Idiopathic myocardial fibrosis
- 
- 1a. Coronary artery ostia stenosis
  - 1b. Aortitis
  - 1c. Ankylosing spondylitis
- 
- 1a. Acute cardiac failure
  - 1b. Hypertrophic cardiomyopathy
- 
- 1a. Acute myocarditis (no pathogen identified)
- 
- 1a. Acute cardiac failure due to arrhythmia
  - 1b. Wolff-Parkinson-White syndrome (pre-mortem clinical diagnosis)
- 
- 1a. Sudden Adult Death Syndrome

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### **Good reference texts**

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### **The RCPATH Working Party on the Autopsy**

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