Post-mortem in sudden unexpected death in the young:

Guidelines on autopsy practice

Prepared by the members of Trans-Tasman Response AGAinst sudden Death in the Young (TRAGADY)

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Abbreviations – Heritable cardiac conditions causing sudden death in the young

ARVC - Arrhythmogenic Right Ventricular Cardiomyopathy. A common cause of sudden cardiac death in athletes. Can cause death yet have normal or near normal cardiac examination, before and after death.

Brugada syndrome - A cardiac ion channelopathy with a characteristic ECG signature. Typically causes sudden death during sleep. More common in males, especially some Asian ethnic groups. Heart is structurally and histologically normal.

CPVT - Catecholaminergic Polymorphic Ventricular Tachycardia. Normal ECG in life. Sudden death during exertion or excitement. Heart is structurally and histologically normal.

DCM - Dilated Cardiomyopathy. Can be familial. Also commonly post-viral. Metabolic causes commoner in young children.

Long QT syndrome - A group of cardiac ion channelopathies characterised by prolongation of the QT interval. Sudden death typically occurs with exertion (especially swimming), excitement, but also at rest. Heart is structurally and histologically normal.

HCM – Hypertrophic Cardiomyopathy. Common cause of sudden death in athletes. Usually familial. Metabolic causes commoner in young children.

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Background

Inherited cardiac diseases that predispose to sudden and unexpected death in young people are being increasingly recognised and managed with life-saving interventions. The impetus for this document arises from ongoing evidence of inadequate or inconsistent investigation of young sudden deaths, which results in failure to identify potentially fatal, yet treatable familial disease. The document has also been prompted by the collective experiences of family support groups in many regions, which reveal that surviving relatives find the post-mortem process hard to understand and that the communications between family members and medical and legal professionals are frequently inadequate from their perspective

This document aims to assist pathologists and coroners in the delivery of good medical practice when faced with the challenge of investigating sudden and unexpected deaths, especially of young people. Local practice will vary in accordance with local legal ethical and cultural frameworks, particularly regarding issues such as consent, the retention of tissue or organs, and arranging genetic investigations. Parts of this document overlap with existing best practice guidelines for the investigation of sudden unexpected death in infancy (SUDI), in which the tests for metabolic, respiratory and infectious causes are more extensively described. Cross-reference with these documents is important, particularly for deaths occurring before the age of 2 years.

An adequately detailed investigation of sudden death in children and young adults can identify inherited cardiac disease in more than 40% of cases.[1,2] For each of these diagnosed cases, an average of 9-10 high-risk relatives are identified. Increasingly, effective screening and therapy are available, which has the potential to reduce greatly the risk of future sudden deaths in this high risk group.[2-4] However, the recognition of these disorders in the sudden death victim depends primarily on a detailed and thorough post-mortem examination, followed by expert evaluation of first degree relatives,[1,2,5-7], which may include analysis of DNA[2,8-10] The inclusion of a mechanism to record and evaluate a high quality family history enables recognition of several conditions that typically escape detection during life but which can cause sudden death. These include long QT syndrome,[11,12]

Brugada syndrome[13,14] and catecholaminergic polymorphic VT (CPVT).[15,16], all of which may have a negative standard post mortem examination result.

Cases presenting with sudden unexpected death, particularly among those younger than 40 years of age, have an increased likelihood of an underlying major familial susceptibility.[5,7] Medical practitioners and coroners, who may be under great pressure to avoid a post-mortem, must now respond to evidence that failure to identify these inherited disorders may result in missed opportunities to avert future premature deaths among other family members.

The process should aim to:

1. Examine all cases of sudden unexpected or unexplained death in the young (particularly in the age group of 0-40 yrs)
2. Investigate the possibility of familial disease
3. Educate, inform and communicate with the family in an open and timely manner.
4. Save DNA or other tissue to allow greater diagnostic accuracy either currently or in the future.
5. Preserve data and tissue to facilitate the prospect of future clinical diagnosis and research into causes of sudden death in accordance with local legal, ethical and cultural frameworks
6. Use a multidisciplinary approach, which utilises the requisite specialist skills of allied clinical and scientific disciplines, to evaluate all available information likely to identify the underlying factor(s) responsible for the sudden and unexpected death.
7. Record sufficient diagnostic data from which the incidence of sudden death and related health trends can be determined.

Definition of sudden unexpected death

A death occurring suddenly, in an individual in whom death was unexpected.[17]

"Sudden" implies death usually within 24 hours of the first symptom, or those resuscitated from cardiac arrest and dying during the same hospital admission. Most such deaths occur over a few seconds or minutes.

"Unexpected". This refers to prior circumstances, particularly of someone who was believed to have been in good health or who had a stable chronic condition (e.g. hypertrophic or dilated cardiomyopathy, a neurological condition such as epilepsy, or a respiratory condition such as asthma), in whom sudden death was not expected. It also includes a sudden death occurring in the presence of an illness which would not be expected to cause death.

Aims of investigation of sudden death victims

To establish the cause and mechanism and manner of death, and in particular to:

1. Exclude an unnatural death[2]
2. Ascertain the likely cause of death, for both accurate diagnostic coding and the information of surviving relatives
3. Identify any familial condition, if present, which might lead to the prevention of future premature deaths among other family members.
4. Provide accurate data for the inquiries into the incidence of remedial factors around sudden unexplained/unexpected deaths.

Who should lead the investigation?

The investigation, under the jurisdiction of the State and/or local Coroners, should be led by a pathologist with experience in the investigation of sudden death who has access to the infrastructure outlined below. This will *usually* be a forensic pathologist, but may also be an anatomical or other pathologist with appropriate forensic autopsy experience. In rural practice, liaison with a specialist centre is necessary to achieve a high diagnostic yield, and since findings may have important implications for surviving relatives, this liaison is strongly recommended. In cases of sudden unexpected death in children, involvement of a pathologist with paediatric experience is essential.

Where should the post mortem investigation be performed?

Where possible, the body should be transported to a specialist forensic pathology centre for investigation. If this is not possible, protocols should be established so that tissue samples are

[2] It is important to remember that some unnatural deaths (e.g.: motor vehicle accidents, experienced swimmers drowning), could be triggered by an arrhythmia.

retained for future specialist examination, and as a minimum a 10-20ml blood sample in a plain tube kept in a freezer to -20º C for subsequent molecular or biochemical analysis. Alternatively a refrigerated sample in an EDTA tube can also be used to extract DNA from later. The pathologist should be familiar with local blood and tissue storage practices prior to dealing with such cases.

Principles of the investigation

1. All cases of sudden unexpected death in young people (0-40years) should have an autopsy, and be examined and investigated under the same principles.[3]
2. A full post-mortem examination should be completed (i.e. not limited to the heart.)
3. The investigation, ideally led by the pathologist, involves a team approach, including as a minimum:
    3.1 A person designated to liaise with the family
    3.2 Specialist cardiology[4] involvement with the family when non-cardiac causes are excluded.[5]
    3.3 Laboratories with molecular genetics, toxicology and metabolic expertise.
4. A detailed antecedent clinical history must be obtained.
5. A detailed and relevant family history must be obtained.
4. Liaison with the family should be established early and be ongoing until a cause of death is ascertained.
5. Skilled macroscopic and microscopic examination of the organs is required particularly of the heart (especially right ventricular muscle), and the brain. This may require some specimens to be examined by others.
6. Adequate histological material for review or referral if necessary must be obtained.
7. Tissue or blood suitable for DNA extraction must be obtained.[6]
8. Results, including photography must be clearly documented.
9. Results must be described and annotated in a standard fashion which will allow epidemiological data gathering.

[3] To achieve this aim it may be necessary to explain to the next of kin potential benefits of a post mortem, including the detection of familial conditions, in cases where coronial investigation has not been ordered. Under these circumstances, a limited post mortem may be appropriate, along with securing a sample of blood or tissue adequate for DNA extraction.
[4] Specialist cardiology involvement will be a multidisciplinary team with expertise in inherited cardiac disease, clinical and molecular genetics and cardiac arrhythmias; henceforth "Cardiac Genetic Service"- (CGS).
[5] Consultation with other specialist physicians or paediatricians, i.e. neurologists/clinical geneticists/SIDS experts is also encouraged according to findings from the clinical or family history, or the post mortem itself.

10. *In cases where no cause is f*ound, there is no standardised nomenclature to ascribe as the cause of death. However, "presumed cardiac arrhythmia" may fulfil legal and family requirements while leaving the option for later genetic and family investigation and diagnosis of conditions which may have implications for the family.

Suggested sequential autopsy examination

1. Obtain initial history including copies of witness, police, medical staff and ambulance reports.
2. Obtain further detailed history including details of the presenting event, relevant family and previous medical history.
3. Consider pre-autopsy imaging (CXR/CT/MRI/photography)
4. Carry out external examination
5. Exclude non-cardiac natural death (cerebral haemorrhage, aortic aneurysm, peptic ulcer, and pneumothorax)
6. Exclude macroscopic heart disease (ischaemic, valvular, cardiomyopathy, congenital anomalies, the origin and course of coronary arteries, and evidence of ARVC).
7. Obtain samples of myocardium and blood or spleen (frozen) suitable for DNA analysis (and also suitable for viral PCR). These are critical if post mortem is negative and if a potentially inherited disease is found.
8. Obtain blood and urine for toxicology screen (as a minimum)
9. If post mortem-negative or a cardiomyopathy is found, refer the family for specialist cardiological investigation and guided DNA investigations.[7] [2,6]
10. In cases where a metabolic condition is considered likely (e.g. preceding viral illness, period of starvation, nocturnal death, possibly with positive findings such as fatty liver), particularly in children under 2 years of age, further tissues should be preserved. Pathologists should be aware of their local centre policy for the investigation of potential metabolic disease and of sudden infant death syndrome, and be guided by this. Samples usually include blood on a newborn screening card, urine, and skin for fibroblast culture.

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[6] Such samples will allow genetic diagnostic tests either currently available or available in the future as a consequence of ongoing research. The length of time this tissue is preserved will depend on the local legal/ethical and cultural issues, and issues of consent. The coroner may instruct tissue is returned to the family, *but the advantages of long term retention should be explained to the family prior to this occurring*.

[7] Aims in 9 and 10 can both be achieved by referral to CGS.

Clinical information relevant to the autopsy

A detailed clinical history and family history are an essential part of the investigation of sudden young death. The history taken by the police at the scene should be recorded with the aid of a structured questionnaire. As it is uncommon for police officers to have experience with recording these histories a recommended structured questionnaire is included in the appendix. This initial police report may be supplemented later by additional details obtained by a clinician or specially trained health assistant, or from medical records. A phone call to the deceased's GP may also provide valuable information.

The key features to document

Circumstances of the death - Detailed review, date, time, place, and activity (at home, at rest or during exercise or emotional excitement). Document associated seizures, prodromal symptoms. Was the death witnessed? Were there any suspicious circumstances?

Past medical history - General health status such as previous significant illness or events, particularly seizures, epilepsy, faints, syncope, palpitations and respiratory or neurological disease. Review of medical history of deceased from family and/or physician. Retrieval of results of any investigations e.g. ECG, EEG, CT, MRI. Many patients with prior syncopal episode have been routed down a cardiac or a neurological investigation path.

Previous surgical procedures or interventions

Details of current medications, including cardiac drugs, but remember that many non-cardiac drugs are pro-arrhythmogenic (see: www.qtdrugs.org)

A history of competitive or habitual sport should be ascertained given that "athlete's heart" may need to be considered as a cause of abnormal right and left ventricular morphology.[18]

Family history of sudden premature death, or familial epilepsy, fainting or syncope (**long QT syndrome, catecholamine polymorphic VT, and familial cardiomyopathy, amongst other cardiac conditions, have all been misdiagnosed as epilepsy**)

ECG, serum enzymes, troponin estimations if done in life

Lipid profiles and related medication if known

Autopsy procedure-special points pertaining to sudden unexpected death

Pre-autopsy

Consider imaging e.g. CXR, CT, MRI. (Any suggestion of pneumothorax?) As a minimum, total body X-Ray of:

a) All infants and children <2 years;

b) Trauma related deaths.

Weigh the heart and index to height/weight/aged (Index Table 1). Measure ventricular wall thickness- at least maximal septum, maximal posterior wall, LV mid cavity dimension (immediately basal to the anterior superior papillary muscle- and reference values to normative data (Index Tables 2-5); view and report valvular morphology and size, specific comment re aortic and mitral valve (e.g. MV prolapse) meticulous documentation of coronary arteries (origin, course, dominance, disease). Consider photography of heart even if "normal".

If no macroscopic heart disease is found, as a minimum the samples described below should be retained. Formalin should be buffered with 10% phosphate to reduce the acidity which both degrades DNA, RNA and viral particles. Buffering also prevents formation of formalin pigment in the sections.

Microscopy/Histology

Histology results are often equivocal e.g. myocarditis, hypertrophic cardiomyopathy and ARVC[19-21] may be over or under-diagnosed. **In the diagnosis of inherited heart disease, molecular cardiology and family investigation may take primacy in achieving a final diagnosis.**

Histology sections

Left and right atria[8]

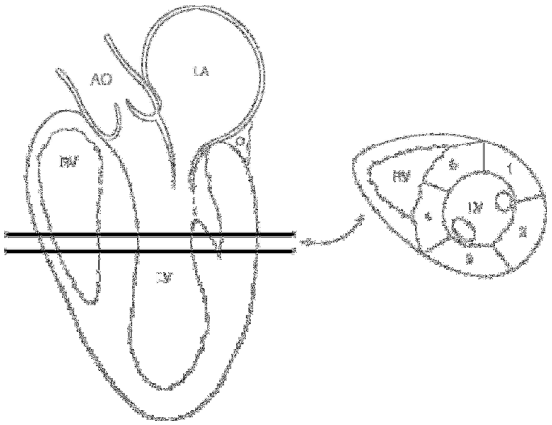
Mitral valve - if it appears abnormal [See footnote[8]]

Left ventricle - mapped blocks of the anterior, lateral, septal and posterior regions.

Right ventricular outflow and anterior free wall

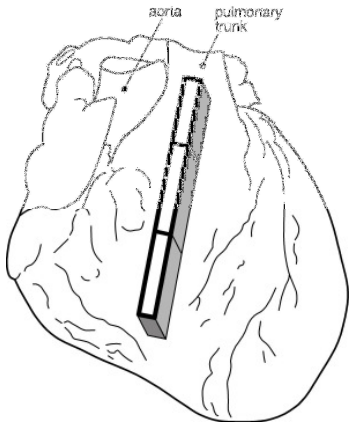
Conduction system - The pathologist should at least retain the AV node region.[22]

Pulmonary histology to exclude pulmonary hypertension



Suggested sampling site for LV and IVS sections

Optimally, an entire ring of ventricular myocardium should be sampled, preferably at the level immediately caudal to the insertion of the papillary muscles. Additionally, grossly abnormal areas of myocardium, valves and coronary arteries should be sampled as a matter of course.



Suggested sampling site for RV sections

A strip of right ventricular myocardium, extending along the anterior wall of the RV from the pulmonary valve to the apex. Generally, there should be 3 to 4 sections of RV myocardium, which can be placed together in a single cassette.

H and E staining should be done as standard. Depending on what is seen, further stains may be appropriate, for example connective tissue stains (such as elastic van Gieson or Movat pentachrome) as well as Congo red (thick section) for amyloid, perls's prussian blue for iron and PAS/AB/PAS for storage disorders. If histology is suggestive of myocarditis, but results are inconclusive, the tissue should be referred for review and specialised tests (such as immunohistochemistry (CD3, CD20, CD68, etc)) at a specialist centre.

Note recent evidence that viral myocarditis and dilated cardiomyopathy can occur without histological evidence of viral infection, particularly with Parvovirus and Adenovirus.[26-29] Viral PCR of myocardium is therefore recommended in every case when the heart is apparently normal- particularly when there is an antecedent history consistent with a recent viral infection, when

[8] A section can be taken by cutting vertically through the left atrium, through the atrioventricular groove to the posterior wall of the left ventricle to include the mitral valve. Similarly, a

histology is suspicious for myocarditis, and with dilated cardiomyopathies, looking for locally prevalent viruses, in particular Parvovirus B19, enterovirus and adenovirus. Other viruses to consider include respiratory viruses (Influenza, parainfluenza, RSV) or human herpes viruses (EBV, CMV, HHV6 etc..)

Fresh cardiac tissue should be obtained at autopsy for investigation of possible viral myocarditis. Optimal specimen is approximately 0.3cm cube of ventricular tissue placed in a vial of aqueous tissue storage reagent capable of rapidly permeating tissues to stabilize and protect cellular RNA, such as RNA*later*®[23] and sent immediately to the virus reference laboratory. Ideally tissue should be kept at 4ºC and shipped chilled. If the history or pulmonary pathology suggests respiratory infection, take a piece of lung and put into same solution (different bottle!). Any ante-mortem blood should be kept and an EDTA tube full of blood should also be sent for viral studies.

If no cardiac (or other cause) is found at the time of autopsy, strongly consider a formal neuropathological examination.

DNA

Some blood or tissue must be saved for possible DNA extraction.

Suitable samples include blood (whole frozen blood in a plain tube, or EDTA sample) myocardium and spleen or liver samples (snap deep frozen (-80º C)) or preserved in a tissue storage solution capable of protecting cellular RNA ("RNA later").[23] Blood spots on a neonatal (Guthrie) screening card may be insufficient. **Formalin fixed paraffin embedded tissue blocks may not be suitable for DNA extraction and should not be relied upon as the sole source of DNA.** [25]

Blood

If ante mortem blood is available (e.g. taken during resuscitation) this is preferable, and efforts should be made early to ensure it is not destroyed (which often occurs 72 hours after the sample was

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section can be taken from the right atrium through the right ventricle at the infundibulum. This will likely include at least one section with an epicardial coronary artery.

received). If early myocardial infarction is suspected, consider cardiac troponin T (if death less than 6 hours prior).

Toxicology (comprehensive) - biochemistry may be helpful with a history or family history of diabetes or coronary artery disease/atheroma.

Post Autopsy

Provisional results should be communicated early to family.

Referral of family to an appropriate medical speciality team

This will often be a cardiac genetic service (CGS) led by an experienced adult or paediatric cardiologist/ electrophysiologist. A strong professional liaison between pathologist and cardiologist or other physician aids the process of gathering all relevant details, as well as offering effective support and management for the surviving relatives. The medical team ideally should have strong professional links with a regional clinical genetics service, where available, or have a person within the team with genetic counseling experience.6

The pathologist should expect the CGS to take on the responsibility of coordinating appropriate clinical evaluation of relatives of the deceased. This may include arranging for mutation screening within specific genes on a DNA sample from the deceased after consultation with the pathologist and, if required, also with the coroner. It is strongly recommended that close family members understand the rationale for the proposed genetic investigations before they are ordered, and that the test outcomes, particularly the clinical interpretation of abnormal or equivocal results, are discussed directly with designated family member(s). The discussion of genetic results with relatives will be the responsibility of the clinician or pathologist who arranged the genetic investigation. As with all other specialist services, the family GP(s) should also be informed of the diagnostic process as it occurs, invited to add further medical or social history, as appropriate, as well as being included in the delivery of any follow-up support that may be required.

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Table 1: Predicted normal heart weights (grams) as a function of body weight, subjects aged less than 20 years old. [24]

Body mass	Females			Males		
(kg)	L95	Mean	U95	L95	Mean	U95
3	13	19	29	11	16	24
4	16	24	37	14	21	31
5	19	29	44	18	26	38
6	22	33	51	21	30	45
7	25	38	58	24	35	51
8	28	42	64	27	39	58
9	30	46	71	30	44	64
10	33	50	77	33	48	71
12	43	66	101	39	57	83
14	48	74	113	45	65	96
16	53	81	124	50	74	108
18	58	88	135	56	82	120
20	62	95	146	61	90	132
22	67	102	156	67	98	143
24	71	109	166	72	106	155
26	76	116	177	78	114	167
28	80	122	188	83	122	178
30	84	129	197	89	130	190
32	88	135	207	94	137	201
34	93	142	216	99	145	212
36	97	148	226	104	153	223
38	101	154	236	110	160	235
40	105	160	245	115	168	246
42	109	166	254	120	175	257
44	113	172	264	125	183	268
46	117	179	273	130	190	279
48	121	184	282	135	198	295
50	125	190	291	140	205	300
55	130	199	304	153	224	327
60	140	214	326	165	242	354
65	149	228	348	178	260	380
70	158	242	370	190	278	406
75	167	256	391	202	295	432
80	176	269	412	214	315	458
85	185	283	432	226	331	481
90	194	296	453	238	348	509
95	202	309	473	250	365	535
100	211	322	493	262	383	560

Table 2: Predicted normal heart weights (g) as a function of body height in 100 female and 100 male subjects younger than 20 years old*.

Body Height		Females			Males		
(cm)	(in)	L95	P	U95	L95	P	U95
40	16	8	12	19	8	14	26
45	18	10	15	24	10	18	32
50	20	12	19	29	12	22	39
55	22	14	24	35	14	26	46
60	24	17	27	42	17	30	54
65	26	20	31	48	20	35	63
70	28	23	36	56	23	40	72
75	30	26	41	64	26	46	81
80	31	30	46	72	29	51	92
85	33	33	52	81	32	58	103
90	35	37	58	90	36	64	114
95	37	41	64	100	40	71	126
100	39	45	71	111	44	78	138
105	41	50	78	122	48	85	151
110	43	55	85	133	52	93	165
115	45	59	93	145	56	100	179
120	47	64	101	157	61	109	194
125	49	70	109	170	66	117	209
130	51	75	117	183	71	126	224
135	53	81	126	197	76	135	240
140	55	87	135	211	81	144	257
145	57	93	145	226	86	154	274
150	59	99	154	241	92	164	292
155	61	105	165	257	98	174	310
160	63	112	175	273	103	184	329
165	65	119	185	290	109	195	348
170	67	126	196	307	116	206	367
175	69	133	208	324	122	217	388
180	71	140	219	342	128	229	408
185	73	148	231	361	135	241	429
190	75	156	243	380	142	253	451
195	77	164	256	399	149	265	473
200	79	172	268	419	156	278	495

*P = predicted normal heart weight; L95 = lower 95% confidence limit; U95= upper 95% confidence limit.

Table 3: Predicted normal ventricular wall thickness (cm) as a function of age in 100 female subjects younger than 20 years old*.

Age (yr)	Right ventricle			Left ventricle			Ventricular septum		
	L95	P	U95	L95	P	U95	L95	P	U95
0	0.05	0.20	0.34	0.25	0.51	0.78	0.30	0.62	0.93
1	0.08	0.25	0.38	0.38	0.72	0.92	0.42	0.74	1.06
2	0.10	0.25	0.39	0.46	0.72	0.99	0.48	0.80	1.12
3	0.11	0.26	0.41	0.51	0.77	1.04	0.52	0.84	1.17
4	0.12	0.27	0.41	0.55	0.81	1.08	0.56	0.88	1.20
5	0.13	0.27	0.42	0.58	0.84	1.11	0.58	0.90	1.23
6	0.13	0.28	0.43	0.60	0.87	1.14	0.60	0.93	1.25
7	0.14	0.28	0.43	0.63	0.89	1.16	0.62	0.95	1.27
8	0.14	0.29	0.44	0.65	0.91	1.18	0.64	0.96	1.28
9	0.15	0.29	0.44	0.66	0.93	1.20	0.65	0.98	1.30
10	0.15	0.30	0.45	0.68	0.95	1.21	0.67	0.99	1.31
11	0.15	0.30	0.45	0.69	0.96	1.23	0.68	1.00	1.33
12	0.16	0.30	0.45	0.71	0.97	1.24	0.69	1.01	1.34
13	0.16	0.31	0.46	0.72	0.99	1.25	0.70	1.02	1.35
14	0.16	0.31	0.46	0.73	1.00	1.26	0.71	1.03	1.36
15	0.16	0.31	0.46	0.74	1.01	1.27	0.72	1.04	1.37
16	0.17	0.31	0.46	0.75	1.02	1.28	0.73	1.05	1.37
17	0.17	0.32	0.46	0.76	1.03	1.29	0.74	1.06	1.38
18	0.17	0.32	0.47	0.77	1.04	1.30	0.75	1.07	1.39
19	0.17	0.32	0.47	0.78	1.04	1.31	0.75	1.08	1.40

*P = predicted normal ventricular wall thickness; L95 = lower 95% confidence limit; U95 = upper 95% confidence limit.

Table 4: Predicted normal ventricular wall thickness (cm) as a function of age in 100 male subjects younger than 20 years old*.

Age (yr)	Right ventricle			Left ventricle			Ventricular septum		
	L95	P	U95	L95	P	U95	L95	P	U95
0	0.01	0.16	0.31	0.11	0.41	0.71	0.16	0.50	0.83
1	0.04	0.21	0.37	0.31	0.61	0.91	0.36	0.70	1.03
2	0.07	0.24	0.40	0.42	0.72	1.01	0.47	0.81	1.14
3	0.09	0.26	0.43	0.49	0.79	1.09	0.54	0.88	1.22
4	0.11	0.28	0.44	0.55	0.84	1.14	0.60	0.94	1.27
5	0.12	0.29	0.46	0.59	0.89	1.19	0.64	0.98	1.32
6	0.13	0.30	0.47	0.63	0.93	1.22	0.68	1.02	1.35
7	0.14	0.31	0.48	0.66	0.96	1.26	0.72	1.05	1.39
8	0.15	0.32	0.49	0.69	0.99	1.28	0.74	1.08	1.42
9	0.16	0.33	0.49	0.71	1.01	1.31	0.77	1.11	1.44
10	0.17	0.33	0.50	0.74	1.03	1.33	0.79	1.13	1.47
11	0.17	0.34	0.51	0.74	1.05	1.35	0.81	1.15	1.49
12	0.18	0.35	0.51	0.78	1.07	1.37	0.83	1.17	1.51
13	0.19	0.35	0.52	0.79	1.09	1.39	0.85	1.19	1.52
14	0.19	0.36	0.52	0.81	1.11	1.41	0.87	1.20	1.54
15	0.20	0.36	0.53	0.83	1.12	1.42	0.88	1.22	1.56
16	0.20	0.37	0.53	0.84	1.14	1.44	0.90	1.23	1.57
17	0.20	0.37	0.54	0.85	1.15	1.45	0.91	1.25	1.58
18	0.21	0.37	0.54	0.87	1.16	1.46	0.93	1.26	1.60
19	0.21	0.38	0.55	0.88	1.18	1.47	0.94	1.27	1.61

*P = predicted normal ventricular wall thickness; L95 = lower 95% confidence limit; U95 = upper 95% confidence limit.

Sudden Death in the Young

Investigators History sheet – Pg1

Decedent Name	
Decedent Date of Birth	
Decedent Gender	□ **Male** □ **Female**
Decedent Next of Kin ***(Name & Ph number)***	
Date of Death	
Time of Death	
Location of Death	
Time Decedent Last Seen Well	
Witnessed Event	□ **Yes** □ **No**

Description: **Circumstances of Death** ***(if appropriate sketch a diagram on page 3)***

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Activity at time of death

Activity?:*(sleep/ rest/ light activity/during or after exercise/swimming/other)*	
Trigger?:*(emotional stress/ fright/auditory stimulus/other)*	
Recent Pregnancy?	□ **Yes** □ **No**

Additional Information/notes

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Investigators History sheet – Pg2

Medical history of the Decedent

Significant illness diagnosed in life?	
Previous faints/collapse?	
Previous seizures/epilepsy?	
Previous palpitations/chest pain/shortness of breath?	
Any medical investigations *(ECG, heart ultrasound, brain scans)*?	
Was the decedent a smoker?	
Problems with cholesterol, diabetes or blood pressure?	
Previous medications	
Current medications *(incl. herbal supplements/vitamin/"over the counter medications")*?	
Recent use of illicit drugs *(cannabis/speed/heroin/ecstasy/party pills/solvents)*?	
Recent surgery or anaesthesia?	
Occupation?	
Congenital deafness?	□ **Yes** □ **No**

Family History

Sudden death in a Family member *(esp. age <40 years)*?	
Close family members under age 40 years with a diagnosed medical/cardiac condition *(e.g. long QT syndrome or hypertrophic cardiomyopathy?)*?	
Sudden Infant Death Syndrome (Cot Deaths)/ Still Births?	
Drowning or Near Drowning?	
Seizures/Epilepsy?	
Any Family members with blood clotting problems or treated with blood thinners *(warfarin)*?	
Motor Vehicle accidents?	
Congenital Deafness?	
Other Cardiac History?	

Any other relevant details or comments about the incident or history:

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Investigators History sheet – Pg3

(Use this page for additional notes/diagram of scene/family tree etc.)

Investigators - History sheet - Pg4

Explanatory Notes

This form applies to deaths occurring suddenly, in a young person (usually under the age of 40 years) in whom death was unexpected and no obvious cause (such as violent trauma) is apparent. This also includes a sudden death occurring in the presence of an illness which would not usually be expected to cause death, such as asthma or epilepsy. Note that some illnesses may have been diagnosed incorrectly in life e.g. some people diagnosed with epilepsy may have had an unrecognized heart condition.

Special notes

The **personal history** and **family history** are very important for the pathologist in a young sudden death. Many conditions causing such deaths may run in the family. Other deaths in the family may be prevented by finding the underlying cause in the deceased. The pathologist may find nothing at autopsy, but a diagnosis may be suspected from the history. Further tests on family members, or genetic tests on the deceased, may ultimately reveal the cause.

Activity at time of death and potential triggers

Certain activities can trigger underlying conditions e.g. swimming can cause sudden death in people with long QT syndrome. It is important to note any activity undertaken prior to or at the time of death.

Medical history of the deceased

Previous sudden collapses, the nature of these and what triggered them, may give important clues. Some medical conditions have an increased likelihood of sudden death-through heart rhythm disturbance, e.g. hypertrophic cardiomyopathy or long QT syndrome.

Any previous medical tests- especially an ECG may clinch a diagnosis in retrospect.
Many medications and drugs can be a trigger for a cardiac arrest.
Congenital deafness is sometimes linked to a severe form of long QT syndrome.

Family History

A family history of young sudden death or cot death makes a familial heart condition more likely. Unexpected drowning- e.g. in a strong swimmer, may well have been due to a loss of consciousness due to a heart rhythm disturbance. The same applies to some road traffic accidents e.g. where no brakes were applied or a car drifted off the road.

Algorithm to guide tissue preservation

Sudden unexpected death in a young person

Age <2 years ⟶ please follow regional SUDI/SIDS protocol to guide metabolic/infectious study

ESSENTIAL IN EVERY CASE

- Histology of the myocardium
- Some tissue or blood suitable for DNA extraction e.g.:
  - ⇒ Blood, (Whole blood frozen to -20ºC in a standard freezer, or blood in an EDTA tube in a standard refrigerator), and/or Myocardium or Spleen (Either deep frozen (-70ºC) or in "RNA later"[23])

STRONGLY ADVISED

- **Cases with normal histology/myocarditis/dilated cardiomyopathy.** Save myocardial tissue and blood for viral PCR
  - ⇒ Fresh EDTA blood is preferable if it can be delivered promptly (2 days max) to the lab.
  - ⇒ Otherwise, frozen whole blood and/or frozen EDTA blood OK (label which is which).
  - ⇒ Myocardium in either "RNA later"[23] or deep frozen.

- **In cases with nocturnal death, a prodromal illness or a period of starvation, especially in young children (< 5 years)**
  - ⇒ Samples for metabolic study (as per SIDS protocols-whole blood, as a Guthrie card, urine, skin for fibroblast culture (tissue culture medium initially at room temperature or 4ºC))

- **In children with unexplained cardiac hypertrophy or unexplained cardiac dilation.**
  - ⇒ Samples for metabolic/mitochondrial study [blood, liver, heart, skeletal muscles] (deep frozen -70ºC). Wrap the small tissue sample in foil and place in a small tube and put immediately into dry ice and store indefinitely at -70ºC. Record the time between death and the time of sampling.