



Guidelines on autopsy practice:

Sudden unexpected deaths in infancy and childhood

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NICE has accredited the process used by the Royal College of Pathologists to produce its autopsy guidelines. Accreditation is valid for 5 years from 25 July 2017. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

For full details on our accreditation visit: www.nice.org.uk/accreditation.

Foreword

The autopsy guidelines published by the Royal College of Pathologists (RCPATH) are guidelines which enable pathologists to deal with non-forensic consent and coroner's/procurator fiscal's post-mortem examinations in a consistent manner and to a high standard.

The guidelines are systematically developed statements to assist the decisions of practitioners and are based on the best available evidence at the time the document was prepared. Given that much autopsy work is single observer and one-time only in reality, it has to be recognised that there is no reviewable standard that is mandated beyond that of the FRCPath Part 2 exam or the Certificate of Higher Autopsy Training (CHAT).

Nevertheless, much of this can be reviewed against ante-mortem imaging and other data. This guideline has been developed to cover most common circumstances. However, we recognise that guidelines cannot anticipate every pathological specimen type and clinical scenario. Occasional variation from the practice recommended in this guideline may therefore be required to report a specimen in a way that that maximises benefit to the pathologists, coroners/procurator fiscals and the deceased's family. Pathologists should be prepared to justify any departure from the guidelines.

There is a general requirement from the General Medical Council (GMC) to have continuing professional development (CPD) in all practice areas and this will naturally encompass autopsy practice. Those wishing to develop expertise/specialise in pathology are encouraged to seek appropriate educational opportunities and participate in the relevant external quality assurance (EQA) scheme.

The guidelines themselves constitute the tools for implementation and dissemination of good practice.

The following stakeholders will be consulted for this document:

- the Human Tissue Authority
- the British and Irish Paediatric Pathology Association (BRIPPA)
- Lullaby Trust
- National Child Mortality Database
- SUDC UK
- Royal College of Paediatrics and Child Health.

The information used to develop this autopsy guideline was obtained by undertaking a systematic search of PubMed. Key terms searched are listed in Appendix A. Dates searched were between January 2000 and September 2022. Published evidence was evaluated using modified SIGN guidance (see Appendix B). Consensus of evidence in the guideline was achieved by expert review. Gaps in the evidence were identified by College members via feedback received during consultation.

No major organisational changes or cost implications have been identified that would hinder the implementation of the guidelines.

A formal revision cycle for all guidelines takes place on a 5-yearly cycle. The College will ask the authors of the guideline, to consider whether or not the guideline needs to be revised. A full consultation process will be undertaken if major revisions are required. If minor revisions or changes are required, whereby a short note of the proposed changes will be placed on the College website for 2 weeks for members' attention. If members do not object to the changes, the short notice of change will be incorporated into the guideline and the full revised version (incorporating the changes) will replace the existing version on the College website.

The guideline has been reviewed by the Professional Guidelines team, Death Investigation Committee, Human Tissue Authority, Specialty Advisory Committee and Lay Advisory Group. It will be placed on the College website for consultation with the membership from 11 July 2023 to 8 August 2023. All comments received from the membership will be addressed by the author to the satisfaction of the Clinical Lead for Guideline Review.

This guideline was developed without external funding to the writing group. The authors have declared no conflicts of interest.

1 Introduction

Post-mortem examination of sudden unexpected death in infancy and childhood (SUDIC) is one of the most challenging tasks for paediatric pathologists. The cause of death remains unknown following full investigation in 2/3 SUDIC cases.^{1,2} Half of these can be classified as sudden infant death syndrome (SIDS) or sudden unexplained death in childhood (SUDC), terminologies based on exclusion of other diagnostic entities. In the case of newborns, the cases may also fall within the spectrum of a sudden unexpected neonatal death. Therefore, the scope of SUDIC post-mortem examinations is much wider than just a conventional post-mortem.

In this context, paediatric pathologists are part of a multidisciplinary team (MDT) where communication and sharing information are vital to achieve success.

As the cause of death is often not evident even after the post-mortem examination, thorough documentation of pathological findings and risk factors and comprehensive post-mortem sampling and archiving should enable future ethically approved research (if next of kin consent was granted).

The following sections summarise the aspects that are specific for investigating SUDIC.

1.1 Age group of investigation

This autopsy protocol addresses SUDIC and sudden unexpected neonatal death, adopting the age reference used in the 2016 Kennedy report of up to 24 months.³ Many elements of this protocol are also applicable to deaths in SUDC up to the age of 18 years.³

1.2 Aim of the post-mortem investigation in SUDIC

1.2.1 Legal requirement

The coroner/procurator fiscal is legally required to identify the cause of death. The 2016 Kennedy report states:

'post-mortem examinations in the setting of SUDI are performed on behalf of the coroner, therefore their role is to establish the cause of death and to address the issues related to the circumstances of death, in particular:

- whether the death is attributable to a natural disease process
- the possibility of accidental death
- the possibility of asphyxia/airway obstruction
- the possibility of inflicted injury
- to document the presence or absence of pathological processes and to determine how the death came about.'³

1.2.2 Identify the recognisable SUDIC risk factors

This assists the child death review meeting and addresses questions related to public health issues.

1.2.3 Identify the medical cause of death

The post-mortem report supports the family and contributes to the NHS through a diagnosis. Cases are often complex. The post-mortem findings contribute to patient care, shed light on the clinical picture and provide feedback to improve clinical practice. With the recent advances in molecular genetics, the post-mortem procedure is an opportunity to collect and store samples for further genetic/metabolic diagnostic testing.

1.3 Multiagency approach and 2016 Kennedy report

It has to be emphasised that, in these complex cases, only a multiagency (joint agency response) approach can yield results. In the post-mortem conclusion, the pathologist synthesises the information from the police, coroner's/procurator fiscal's service, lead health professional and clinical team, as appropriate.

The coroner's/procurator fiscal's permission needs to be sought to consult over complex cases with a specialist and/or discuss the case with the clinicians.

Interaction between multiple agencies has been addressed by the Kennedy 2016 report, with regard to hospital samples, ancillary tests, post-mortem skeletal survey and/or post-mortem computed tomography (CT) reported by a paediatric radiologist.

A lead health professional report is also essential, including a home visit and accurate description of the scene of death and the sleeping arrangements (possibly including doll re-enactment), preferably with photographic or video documentation.

It is recommended that the post-mortem report and final wording of the cause of death is discussed at the child death review meeting prior to its submission to the coroner/procurator fiscal to facilitate the coroner's/procurator fiscal's inquiry and final decision regarding the cause of death.

1.3.1 2016 Kennedy report³

Under the auspices of the Royal College of Pathologists and the Royal College of Paediatrics and Child Health, a Working Party was established to produce the 2016 Kennedy report. The Working Party included a very experienced group of people with wide expertise (among them paediatric pathologists). The report created a protocol for the handling of sudden infant death, which was intended to operate nationwide.

The Kennedy report describes the desired multiagency response in child death:

- chapter 7 (page 41) addresses the post-mortem examination

- appendix 6 (page 93) gives guidance on the practice of the post-mortem examination.

The requirements of the post-mortem examination have not changed significantly since the publication of the report, therefore this autopsy guideline is mostly based on their recommendation.

1.4 Non-invasive/less invasive post-mortem examination

Less invasive post-mortem examination using magnetic resonance imaging (MRI), CT or other methods provide some information regarding the likely causes of death in childhood, but their role in SUDIC investigation is still being explored. In some cases, post-mortem imaging may indicate a clear focus of pathology that can be confirmed by limited tissue biopsy and, in such cases, no further examination may be required. However, this depends on the circumstances of the case and should be at the discretion of the pathologist and the coroner on a case-by-case basis.

The data from an NIHR Health Technology Assessment demonstrate that, in 5–10% of SUDC and SUDI cases, the final cause of death is determined by routine histological sampling of macroscopically normal organs, predominantly the heart and lungs, with a few cases contributed by brain, liver and kidney examination. Routine histological sampling, therefore, remains an important aspect of investigation even if post-mortem imaging appears normal.⁴ We emphasise that conventional post-mortem examination is still the gold standard at this time and the range of ancillary tests should not be compromised.

Imaging based post-mortem examination should never be undertaken without an expert external examination of the body having first been performed by an appropriately trained and experienced individual.

Imaging techniques should always include effective imaging of the whole skeleton using an appropriate technique agreed with the radiology team at a local level. In some cases, a CT and/or MRI may provide additional useful information.

Chest CT provides greater accuracy than conventional chest radiography for post-mortem rib fracture detection, with a large study demonstrating 3x improved sensitivity over conventional radiography.⁵ These techniques should be reported, ideally by a paediatric radiologist. CT scan is superior in certain aspects, some places already include it in the post-mortem protocol.

1.5 Organ donation

The option of organ donation is part of the standard end-of-life care that families should be offered to consider, if appropriate. This can help the family with the grieving process and save or transform the life of patients on the transplant waiting list. Absence of regulation on organ donation from SUDIC cases may lead to missed opportunities to save the lives of patients.

This section aims to provide a framework for the consideration of organ donation in SUDIC cases, based on the relevant guidance from the Chief Coroner Guidance 26,⁶ and the Procurator Fiscal Service.⁷

1.5.1 Decision about whether to object to donation

Only the sitting coroner/procurator fiscal (be that the senior coroner for the area in which the deceased lies, an area coroner or an assistant coroners for that area) can make this judicial decision.

Paediatric and neonatal organ donation in Scotland is regulated by the Procurator Fiscal Service (see paragraph 2.14 and 2.15 of the *Agreement between Crown Office and Procurator Fiscal Service and The Scottish Donation and Transplant Group in regard to Organ and Tissue Donation*⁷).

1.5.2 Timing of approach to the coroner/procurator fiscal

If there is a question of organ or tissue donation, the first contact made with the coroner/procurator fiscal is likely to be before death to allow time for assembling and preparing the retrieval and transplant teams. The coroner/procurator fiscal should be fully engaged with those treating the child and the family. Once death has occurred, the pathologist will be notified by the coroner.

1.5.3 Involvement of the paediatric pathologist

The paediatric pathologist has an advisory role in the relevant decision-making team. Formal discussion with involved key professionals is desirable to share relevant information.

A full SUDIC investigation should be carried out in potential organ donation in an orchestrated team effort.

The clinical team remains responsible for the diagnostic work-up and for helping the family to reach an informed decision. The team may involve (but is not restricted to):

- admitting consultant
- SUDIC consultant and/or general paediatrician leading the child safeguarding investigation
- paediatric intensive care unit consultant leading the discussion with the family about end-of-life management
- specialist nurse for organ donation advising on suitability and process of organ donation, as well as supporting and approaching the family if the coroner/procurator fiscal does not raise an objection.

1.5.4 Minimum information required by the paediatric pathologist

The minimum set of information required to enable the paediatric pathologist to form an opinion includes:

- full information as laid out by the SUDIC Protocol
- background, circumstances of death, non-natural causes and non-accidental injury excluded, SUDIC medical investigations to ensure all possible causes of collapse are addressed
- physical examination by a senior paediatrician to exclude injuries, genetic conditions (dysmorphism) and to establish the growth and development
- MRI/CT to exclude injuries, subdural haemorrhage and anatomical abnormalities. These investigations are also essential to give insight into potential pathology of the internal organs. A detailed report is required to describe the anatomy and statement about internal organs and lack of injuries.
- detailed medical history is required
- summary of SUDIC investigations available at the time.

Once organ donation has been consented and agreed, depending on the circumstances, the paediatric pathologist may attend the retrieval operation to assess the patient and any organs retrieved. The retrieving surgeon has to provide detailed documentation on the list and on the condition of the retrieved organs.

1.5.5 Summary

In summary, the role of the paediatric pathologist in the process of organ donation following SUDI is advisory.

If the coroner's/procurator fiscal's decision is in favour of organ donation, with the family's consent, all the information relevant to the SUDIC investigation process needs to be documented and submitted to the pathologist as it will be needed for the pathologist to be able to complete the post-mortem report.

[Level of evidence – Good Practice Point (GPP). Recommended best practice based on the clinical experience of the authors of the writing group.]

1.6 Target users and health benefits of this guideline

The primary target users of this guideline are consultant paediatric pathologists carrying out paediatric post-mortem examinations. The recommendations will also be of value to the coroner's/procurator fiscal's services, consultant paediatricians at A&E departments and local child review panels as guidance on the post-mortem investigation process.

1.7 Glossary

It is important to recapitulate the recommended terminologies of the Kennedy report, quoted here, aiming to use a unified language as outlined by the Working Party.

1.7.1 SUDI/SUDC (sudden unexpected death in infancy/childhood)

This encompasses all cases in which there is death (or collapse leading to death) of an infant or a child, which would not have been reasonably expected to occur 24 hours previously and in whom no pre-existing medical cause of death is apparent. This is a descriptive term used at the point of presentation and will include those deaths for which a cause is ultimately found ('explained SUDI/SUDC') and those that remain unexplained following investigation. While many of these guidelines may be applied if required, they are not necessarily intended to be applied to cases with a previously diagnosed medical condition in which a medical certificate of cause of death can be provided.^{8,9}

1.7.2 Undetermined (or unascertained) pending further investigation

This is a term that may be used by pathologists providing a preliminary report to the coroner/procurator fiscal following the initial post-mortem examination, if no cause of death can be initially identified and there are no features to suggest unnatural death.

1.7.3 Sudden unexpected death in infancy (SUDI)

In this context, this term is used for infants up to 24 months of age in order to facilitate use with other agency investigations.

1.7.4 Sudden infant death syndrome (SIDS)

This refers to the sudden and unexpected death of an infant under 12 months of age, with onset of the lethal episode apparently occurring during normal sleep, which remains unexplained after a thorough investigation including performance of a complete post-mortem examination and review of the circumstances of death and the clinical history.¹⁰

1.7.5 Sudden unexplained death in childhood (SUDC)

The sudden and unexpected death of a child, between 1 and 18 years of age, which remains unexplained after a thorough case investigation is conducted. This must include: examination of the scene of death, performance of a complete post-mortem and a review of the child and family's medical history.¹¹

1.7.6 SUDI, unexplained

This is the preferred term for use in cases in which there is no clear cause of death and there are no features to suggest unnatural death or inflicted injury, but in which the circumstances do not fit the criteria for SIDS (for example, deaths in which the history, scene or circumstances suggest a high likelihood of asphyxia but in which positive evidence of accidental asphyxia is lacking).

1.7.7 Unascertained

This is a legal term often used by coroners/procurator fiscals, pathologists and others involved with death investigation, where the medical cause of death has not been determined to the appropriate legal standard, which is usually the balance of probabilities.

1.7.8 Sudden unexplained neonatal death (SUEND)

SUEND refers to the occurrence of a sudden death in an apparently healthy or near-term infants within the first postnatal week.

1.7.9 Sudden unexpected death in epilepsy (SUDEP)

SUDEP is the sudden, unexpected, witnessed or unwitnessed, non-traumatic and non-drowning death in patients with epilepsy with or without evidence for a seizure and excluding documented status epilepticus, in which post-mortem examination does not reveal a structural or toxicological cause for death.

2 Pathology encountered at autopsy

To give a comprehensive list of possible diagnosis is beyond the scope of the guideline as the subject is so complex. For guidance, please see the relevant handbooks (this list is not complete and is intended to suggest guidance):

- Byard RW, Collins KA. *Forensic Pathology of Infancy and Childhood*. New York, USA: Springer, 2014.
- Husain AN, Stocker JT, Dehner LP. *Stocker and Dehner's Pediatric Pathology (5th edition)*. Netherlands: Wolters Kluwer, 2021.
- Khong TY, Malcomson RDG. *Keeling's Fetal and Neonatal Pathology*. New York, USA: Springer, 2022.
- Cohen MC, Scheimberg IB. *Investigation of Sudden Infant Death Syndrome (Diagnostic Pediatric Pathology)*. Cambridge, UK: Cambridge Medicine, 2019.

3 Specific health and safety aspects

General health and safety guidelines need to be adhered to in paediatric post-mortems. Adaptations to autopsy practice during pandemic or similar situations should follow local, national and international guidance at the time.

[Level of evidence D – Evidence from case series and expert opinion.]

4 Clinical information relevant to the autopsy

Comprehensive clinical information is required before the start of the post-mortem examination. This is best served by a report from the lead health professional, as described by the Kennedy Report 2016.³

This report should include:

- detailed history, including details of pregnancy, delivery, post-natal history, ante-mortem history and precise circumstances of death including family history (previous sibling deaths, consanguinity, drug use, co-sleeping, maternal mental health issues)
- details of the joint home visit by police and lead health professional
- relevant safeguarding information from social care

- relevant family history, including information from general practitioner records
- details of any resuscitation undertaken by bystanders, ambulance or in hospital
- details and results of any investigations, including septic screen, undertaken in hospital
- findings of top to toe examination carried out immediately after death (or soon after hospital admission), which should include body maps and photographs, if relevant.

In addition, information should be obtained from:

- police death scene investigation report with photograph or video recording, where relevant
- report of the coroner's officer/police officer acting for the coroner/procurator fiscal.

[Level of evidence D – Evidence from case series and expert opinion.]

5 The autopsy procedure

- The post mortem examination has to take place on an HTA-licenced premises.
- The SUDIC post-mortem examinations are initiated by written instruction of the coroner/procurator fiscal.
- Following review of the history and discussion with the coroner/procurator fiscal, consider requesting forensic input.
- A full skeletal survey or other appropriate imaging reported by a paediatric radiologist is mandatory in all community deaths below the age of 2 and in elder children at the discretion of the investigating team, based on the circumstances. Many centres have a preference of CT scan of the body, sometimes in combination with the skeletal survey. If there is evidence of any injury, discussion with the coroner/procurator fiscal is warranted and forensic post mortem has to be considered.
- If concerns arise before or during the post-mortem examination about the possibility of neglect or non-accidental injury, the post-mortem should be paused and the case discussed with the coroner/procurator fiscal as it may merit escalation to a forensic post mortem. Social care, the lead health professional and police should be notified so that multi-agency safeguarding procedures can be commenced to safeguard any other children in the family/ wider family or community.

- Consider close adherence to the rules of evidence from the outset of involvement (e.g. identification and corroboration of evidence).
- Full autopsy has to be carried out, with attention to growth parameters, weights, measurements (body, organs and organ ratios if appropriate), referring to standard/local charts and tables. Presence/absence of secretions or blood around nose and mouth and petechial haemorrhages on face, conjunctivae or oral mucosa and possible dysmorphic features have to be described, photo-documented for diagnostic and evidentiary purposes.
- In cases of suspicion of intracranial injury, no needles should be placed within the skull or the eye until the scalp, skull and intracranial contents have been examined and injury excluded.

[Level of evidence D – Evidence from case series and expert opinion.]

6 Specific organ systems to be considered

All organs have to be examined systematically as specified in the paediatric post-mortem protocol guidelines.¹² With regard to the samples to be taken during autopsy, see sections 8 and 9.

7 Organ retention

If trauma to the brain, spinal cord, eye and/or bones is suspected, retaining these organs for specialist referral is recommended.

If the clinical history and/or pathological findings require any particular organ to be retained for further assessment, this should be discussed with the coroner/procurator fiscal's office.

The post-mortem organ retention has to comply with the requirements of the Human Tissue Act 2004.¹³

The Kennedy report gives clear guidance on organ retention for diagnostic and research purposes:

'In general, if the clinical history and pathological findings require any particular organ to be retained by either the paediatric pathologist or specialist colleagues for further assessment to determine the cause of death, this should be discussed with the coroner's office or the procurator fiscal, as appropriate.'

If organ retention is required, the family (meaning in this paragraph: the highest person ranking in a qualifying relationship) should be kept informed and their wishes obtained regarding the fate of such material. As mentioned earlier, where their wish is that the organ be kept for future use, it should be clear what that future use might be and which of the family has given their consent.

If the highest person ranking in a qualifying relationship has given consent for organs or tissues to be retained for research purposes, these may be retained (once the coroner has concluded with the Coronial investigation process).⁷ [Human Tissue Act]

After the jurisdiction of the coroner/procurator fiscal ends (i.e. after the inquest or investigation), consent of the family (the highest person ranking in a qualifying relationship) needs to be sought for retention of histological blocks and slides, frozen tissue and for any other relevant material (nail, bile, blood, bones/skeletons, non-fetal products of conception, i.e. the amniotic fluid, umbilical cord, placenta and membranes), cerebrospinal fluid, faeces, stomach contents and urine. A more detailed list can be found on the HTA website.¹⁴ Considering the complexities in SUDIC diagnosis, not only for the purposes of potential research, but also for further diagnosis.'

The NCMD/SUDC UK have a video resource on tissue retention for families, [available here](#).

[Level of evidence D – Evidence from case series and expert opinion.]

8 Histological examination

Histological examination is the basis of all post-mortem examination in SUDIC. Weber et al. addressed the issue of histological samples in SUDI.¹⁵ They concluded that a non-neuropathological cause of death in explained SUDI can be established from histological examination of lungs, heart, liver and kidneys. Significant histological abnormalities may be detected in selected organs with macroscopically normal appearances. Routine histological sampling of other organs in the absence of specific clinical history or macroscopic abnormalities has a low yield for establishing cause of death.¹⁵ This also indicates that, in these complex cases, a routine set of histological samples needs to be taken as generally accepted by the paediatric pathologists' community.

Histology is mandatory in all SUDIC cases with a recommended minimum blocks for histological examination. The list is based on the paper by Weber et al.¹⁵

Organs:

- brain (A recommendation of blocks is listed here, however, local protocol needs to be developed in conjunction with the neuropathology service. The representative blocks include cerebral hemisphere [frontal, occipital], hippocampi, basal ganglia, pons and medulla, cerebellum, meninges and spinal cord; dura if there is haemorrhage)¹⁶
- epiglottis and larynx
- trachea (including thyroid)
- each lobe of lung (H&E, and Perls' method for iron)
- heart (free wall of left and right ventricle, interventricular septum)
- thymus
- duodenum (including head of pancreas)
- liver (left and right lobe)
- spleen
- mesentery with lymph node
- adrenal glands
- kidneys
- costo-chondral junction of 1 rib (traditionally the right 6th rib)
- muscle (diaphragm and pectoralis major or psoas)
- blocks of any lesion, including representative sample of fractured ribs
- other as specifically indicated.

In cases with no clinical evidence or macroscopic autopsy findings explaining death, it is strongly recommended that the brain is examined only after adequate fixation.

In every case, frozen tissue should be stored to be available for future molecular studies (consider: kidney, liver, heart, and muscle. Due to advancing knowledge on the role of the medulla in the pathophysiology of SIDS, some centres are also freezing a sample from the brain stem).¹⁷

[Level of evidence D – Evidence from case series and expert opinion.]

In some cases, a second opinion from subspecialist expert(s) may be necessary, particularly in paediatric neuropathology, bone pathology, ophthalmic pathology or muscle pathology. The coroner's/procurator fiscal's permission has to be requested before sending histological slides for second look examination.

9 Ancillary investigations

9.1 Toxicology

Unless the deceased had been an inpatient, toxicology should always be conducted. The minimum set of samples where sufficient material is present includes blood, whole preserved and unpreserved in a fluoride bottle and urine. Vitreous humour is desirable if enough material is available. Stomach or bowel contents should be considered if poisoning is suspected. An illicit drug/alcohol screen should be requested and other drugs specified as indicated from the history.

Toxicology centres provide routine analysis and results on illicit and licit drugs and carbon monoxide poisoning in SUDIC toxicology cases. Samples taken during a forensic post mortem or investigation of a suspicious death should be sent to a forensic accredited laboratory. See Table 1 for investigations and sample requirements.^{18–37}

[Level of evidence D – Evidence from case series and expert opinion.]

9.2 Microbiology

The recommended set of samples to be taken for bacteriology and virology analysis is shown in Table 2. Any additional samples should be guided by the clinical history and post-mortem findings. Local protocols should be established based on analytical methods available and sample requirements. Discussion with a virologist or microbiologist is recommended for advice on tests to perform in individual cases.^{38–48}

[Level of evidence D – Evidence from case series and expert opinion.]

9.3 Inherited metabolic diseases

If a genetic or metabolic disorder is considered to have contributed to the cause of death, it is essential to collect samples for analysis to provide genetic counselling of parents and determine reliable risk assessment for future children. A guide to sample requirements is

found in Table 1, including serum, dried blood spot, tissue sample for fibroblast culture, urine and cerebrospinal fluid.

Frozen section, stained with Oil Red O for fat on liver, muscle, heart and kidney, is mandatory in all SUDIC cases.^{49–60}

If mitochondrial disease is suspected, fibroblast culture tests for fatty oxidation flux can be considered. This test is available at [Sheffield Children's NHSFT's newborn screening lab](#) and they can undertake the assay in fibroblasts cultured elsewhere. In this case, further mitochondrial analysis to search for mitochondrial depletion should be conducted in fibroblasts.⁶¹

9.4 Genetic tests

The genetic background of sudden infant and child death has to be investigated. In view of the pathological and genetic results, relevant cases have to be discussed with the clinical geneticists, ideally at regular MDT meetings, with permission from the coroner/procurator fiscal. Results and interpretation of the genetic tests, MDT outcome and recommendation for referral to genetic counselling should be included in the final post-mortem report.

Samples to be sent for genetic investigation (Table 1) include a skin sample or pericardium for fibroblast culture; liaison with the local genetics laboratory is advised. Microarray studies and further DNA extraction can be performed, if recommended by the geneticist, and whole exome sequencing is available in selected cases. Storage of the remaining DNA, if consented, by the local genetic laboratory provides the opportunity for future testing.^{62–77}

In 2023, NHS England included whole genome sequencing in SUDI/SUDC (R441.1), in the rare and inherited disease National Genomic Test Directory.⁷⁸ Cases with a natural cause of death but no apparent medical cause, such as SIDS, are eligible for this investigation. Local patient pathways need to be established to identify eligible cases.

In Scotland review and follow up, including any indicated further investigations, are co-ordinated by the SUDI paediatrician.

9.5 Other investigations

The list of analytic samples is growing and follows the demand based on new research-based evidence. Some examples such as vitamin D and HbA1c are listed in Table 1.

It is helpful to collect samples for storage to be analysed following results of initial investigations.

[Level of evidence D – Evidence from case series and expert opinion.]

Table 1: Mandatory and recommended sample requirements in the investigation of SUDIC.

Indication	Mandatory (M)/ Recommended (R)	Sample	Processing and storage	Investigation
Toxicology	M	Blood preserved in fluoride oxalate tube (1 ml) and unpreserved (5–10 ml)	Send whole blood sample to toxicology lab without processing	Full drug/alcohol screen Carbon monoxide State specific drug analysis if required
Toxicology	M	Urine in plain universal container (1 ml)	Send to toxicology lab without opening bottle	Full drug/alcohol screen. State specific drug analysis if required
Toxicology or biochemistry	R	Vitreous humour in plain universal container (0.2 ml)	Refrigerate, freeze if delayed transport	May reflect serum concentration of some analytes at the time of death (e.g. sodium) Sample for storage
Toxicology	R	Stomach contents in plain universal container	Freeze a sample	Drug screen Note total stomach volume with request
Biochemistry	R	Blood in plain tube (1 ml)	Centrifuge, freeze serum or plasma	As indicated, e.g.: Insulin Vitamin D Tryptase or other enzyme Sample for storage
Biochemistry	R	EDTA whole blood (0.5 ml)	No centrifugation, store refrigerated	HbA1c. May also be analysed on

				fluoride oxalate blood sample
Genetic	M	Skin sample in culture medium	Send to the laboratory, store refrigerated	Genetic testing (e.g. microarray, exome sequencing, panels) Storage for genetics
Inborn metabolic disease	R	Serum or plasma (2–10 ml)	Centrifuge, freeze serum or plasma	Amino acids Sample for storage
Inborn metabolic disease	M	Dried blood spots	Filter paper card provided by laboratory, dry at ambient temperature, store 4–8 °C	Acylcarnitines Other metabolic tests as available
Inborn metabolic disease	M	Urine (2–5 ml)	Freeze at –20 °C	Organic acids Sample for storage
Inborn metabolic disease	M	Skin biopsy	Ideally less than 24 hours post mortem (may be viable for longer). Place in culture medium or sterile NaCl 0.9%, may be stored 1–2 days. Do not freeze.	Enzymatic studies Genetic studies For storage
Inborn metabolic disease	R	Cerebrospinal fluid (0.5 ml)	Freeze immediately, ideally –80 °C.	Cerebrospinal fluid amino acids Other metabolic studies Sample for storage

This information is a guide to investigations. Local protocols should be established following discussion with the laboratories providing sample analysis as there may be variation in analytical methods and sample requirements. It is helpful to provide clinical information to assist the laboratory in selection of tests in the situation where sample volume is limited. Request for specific genetic analysis should be discussed with the clinical genetic team.

Table 2: Samples to be taken in the investigation of infectious disease in SUDIC.

Laboratory	Sample	Type of analysis
Bacteriology	Blood culture – anaerobic and aerobic Cerebrospinal fluid Nasopharyngeal swab Swabs from any identifiable lesion Lung Spleen Intestinal content	Direct bacterial culture (including antibiotic resistance studies)
Virology	Nasopharyngeal swab Lung tissue Intestinal content Cerebrospinal fluid Blood	Molecular analysis If necessary, viral cultures
Samples frozen at –80°C (if possible) for further analysis	0.5 cm ³ heart, muscle, liver, brainstem and kidney Other tissues if relevant Serum	Further molecular analysis (viral or bacterial) as guided by histology Further serology if needed

Samples should be stored up to 2 hours at room temperature or for up to 48 hours refrigerated in suitable transport media. This is a guide to investigation – local protocols should be established. Necessary investigations in individual cases should be guided by the relevant clinicopathological scenarios.

[Level of evidence D – Evidence from case series and expert opinion.]

10 Clinicopathological summary

Clinicopathological summary is an essential and formally separate part of the structured report. It is recommended that addressing the clinicopathological relevance of post-mortem findings, separate issues and thoughts are listed under numbered bullet points in a clear format.

In joint post mortems (with a forensic pathologist), the contents of the report and conclusion always have to be discussed and cross checked with the forensic pathologist. Consideration should be given to whether there are features sufficient enough to suggest inflicted injury or neglect.

The clinicopathological summary should contain the following:

- a statement about the circumstances and whether these are suspicious or not
- a statement about the nourishment and general hygiene
- a statement about growth and development, possible dysmorphic features/developmental abnormalities
- a list of the recognised SUDI risk factors (risk factors for SUDC are not as well established as in SIDS. Evidence of associations with cardiac arrhythmias, hippocampal abnormalities and febrile seizures is emerging and any related investigations or referrals should be considered and highlighted in the summary^{76,79-81}):
 - intrinsic to the infant (e.g. prematurity, failure to thrive, genetic conditions, fetal growth restriction, mild upper respiratory infection)
 - parenting capacity (e.g. drug or alcohol use, mental health, tiredness, single parent, young parental age)
 - environmental (e.g. co-sleeping, evidence of airway obstruction, parental smoking, sleeping circumstances, room temperature, cold weather etc.)
- a summary of the main pathological findings in the context of the clinical history
- a consideration of whether, based on the submitted information and post-mortem findings, the cause of death is natural or non-natural
- a decision regarding whether the pathology satisfactorily explains the clinical circumstances of the death
- a reflection on the result of SUDIC samples (tests taken in hospital at the time of collapse)
- a consideration of whether there are features indicating a familial/genetic disease requiring screening and counselling, further referral of the family.

If no satisfactory cause of death is identified in an infant with typical epidemiological characteristics, a complete medical history has been obtained and the scene of death has been examined, SIDS or SUDC should be considered as a cause of death (preferably following multidisciplinary case review at the child death review meeting).

11 Examples of cause of death opinions/statements

When forming the opinion of death, the recommendation is based on the guidance of the Kennedy 2016 protocol and of the Chief Coroner.

It is our recommendation that:

- professionals working together in responding to unexpected child deaths use the terms SUDI/SUDC at the point of presentation to include all unexpected infant/child deaths
- deaths for which a clear medical or external cause is found should be referred to as such as soon as the cause is identified
- infant deaths under 12 months of age that meet the criteria for a diagnosis of SIDS are labelled as such
- deaths between 1 and 18 years who meet the criteria for a diagnosis of SUDC are labelled as such (if above 18 years the sudden adult death syndrome can be used).

All other unexplained deaths are referred to as 'SUDI, unexplained', 'SUDC, unexplained' or 'Unascertained' until such time that the coroner/procurator fiscal issues a legal cause of death following an inquest that has taken full account of information from the rapid response multi-agency investigation and the local case review meeting.

At the recent 3rd International Congress on SIDS, it was proposed to use the term 'Unexplained Sudden Death in Infancy or SIDS' in the death certificate.⁷⁷

[Level of evidence D – Evidence from case series and expert opinion.]

12 Criteria for audit

The following standards are suggested criteria that might be used in periodic reviews to ensure a post-mortem report for coronial/procurator fiscal autopsies conducted at an institution complies with the national recommendations provided by the [2006 NCEPOD study](#):

- supporting documentations:
 - standards: 95% of supporting documentation was available at the time of the autopsy
 - standards: 95% of autopsy reports documented are satisfactory, good or excellent

- reporting internal examination:
 - standards: 100% of the autopsy report must explain the description of internal appearance
 - standards: 100% of autopsy reports documented are satisfactory, good or excellent
- reporting external examination:
 - standards: 100% of the autopsy report must explain the description of external appearance
 - standards: 100% of autopsy reports documented are satisfactory, good or excellent.

A [template for coronial autopsy audit](#) can be found on The Royal College of Pathologists' website.

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Appendix A Systematic review of evidence

Search strategy

Date

Published literature from 2000 to September 2022.

Literature sources

PubMed.

References cited within papers included in this synthesis and not captured in the PubMed search (e.g. papers pre-2000) were also sourced for further information.

Search term(s)

Sudden infant death and toxicology = 73.

Sudden infant death and microbiology = 183.

Searches for sudden infant death and genetics used the following keywords:

- disease genetics
- cardiovascular diseases
- genetic heart diseases
- molecular autopsy
- whole exome sequencing
- inherited metabolic diseases.

In the context of metabolic conditions, the following keywords were used:

- autopsy
- carbohydrate disorders
- congenital lactic acidosis
- fatty acid oxidation defect
- glutaric aciduria type I
- inborn error of metabolism
- metabolism

- mitochondrial respiratory defects
- organic aciduria
- post-mortem samples
- sudden infant death syndrome
- sudden unexpected death in childhood
- sudden unexpected death in infancy
- urea cycle disorders
- tandem mass spectrometry.

The following search terms were used in the context of toxicology and SUDIC:

- autopsy
- drug
- child forensic medicine
- pathology
- paediatric
- SIDS
- toxicology.

Inclusion and exclusion criteria

Inclusion criteria:

- case series
- post-mortem genetic studies and other non-histological investigations
- post-mortem audit and review
- review papers.

Exclusion criteria:

- case studies
- experimental models.

Appendix B Summary table – Explanation of grades of evidence

(modified from Palmer K *et al. BMJ* 2008; 337:1832)

Grade (level) of evidence	Nature of evidence
Grade A	<p>At least 1 high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target population</p> <p>or</p> <p>A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type.</p>
Grade B	<p>A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target population</p> <p>or</p> <p>Extrapolation evidence from studies described in A.</p>
Grade C	<p>A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high-quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target population</p> <p>or</p> <p>Extrapolation evidence from studies described in B.</p>
Grade D	<p>Non-analytic studies such as case reports, case series or expert opinion</p> <p>or</p> <p>Extrapolation evidence from studies described in C.</p>
Good practice point (GPP)	<p>Recommended best practice based on the clinical experience of the authors of the writing group.</p>

Appendix C AGREE II guideline monitoring sheet

The autopsy guidelines of The Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines. The sections of this autopsy guideline that indicate compliance with each of the AGREE II standards are indicated in the table.

AGREE standard	Section of guideline
Scope and purpose	
1 The overall objective(s) of the guideline is (are) specifically described	Introduction
2 The health question(s) covered by the guideline is (are) specifically described	Introduction
3 The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	Foreword
Stakeholder involvement	
4 The guideline development group includes individuals from all the relevant professional groups	Foreword
5 The views and preferences of the target population (patients, public, etc.) have been sought	Foreword
6 The target users of the guideline are clearly defined	Introduction
Rigour of development	
7 Systematic methods were used to search for evidence	Foreword
8 The criteria for selecting the evidence are clearly described	Foreword
9 The strengths and limitations of the body of evidence are clearly described	Foreword
10 The methods for formulating the recommendations are clearly described	Foreword
11 The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword and Introduction
12 There is an explicit link between the recommendations and the supporting evidence	1–11
13 The guideline has been externally reviewed by experts prior to its publication	Foreword
14 A procedure for updating the guideline is provided	Foreword
Clarity of presentation	
15 The recommendations are specific and unambiguous	1–11
16 The different options for management of the condition or health issue are clearly presented	1–11
17 Key recommendations are easily identifiable	1–11
Applicability	
18 The guideline describes facilitators and barriers to its application	Foreword
19 The guideline provides advice and/or tools on how the recommendations can be put into practice	1–12
20 The potential resource implications of applying the recommendations have been considered	Foreword
21 The guideline presents monitoring and/or auditing criteria	12
Editorial independence	
22 The views of the funding body have not influenced the content of the guideline	Foreword
23 Competing interest of guideline development group members have been recorded and addressed	Foreword