



Guidelines on autopsy practice

Third trimester antepartum and intrapartum stillbirth

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Foreword

The autopsy guidelines published by The Royal College of Pathologists (RCPATH) are guidelines that enable pathologists to deal with non-forensic consent and Coroners' post-mortem examinations in a consistent manner and to a high standard. They are intended primarily for the profession; some technical content may be distressing for the lay audience.

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 cannot realistically be repeated, it has to be recognised that there is no reviewable standard that is mandated beyond that of the FRCPath Part 2 examination. Nevertheless, much of this can be reviewed against ante-mortem imaging and other data. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. The medico-legal risk of departing from the guidelines should be assessed by the autopsy pathologist; just as adherence to the guidelines may not constitute defence against a claim of negligence, so a decision to deviate from them should not necessarily be deemed negligent.

There is a general requirement from the General Medical Council 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 EQA scheme.

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

The stakeholders consulted for this document were:

- British and Irish Paediatric Pathology Association (BRIPPA)
- Sands, the stillbirth and neonatal death charity The Royal College of Obstetrics and Gynaecology (RCOG)
- Human Tissue Authority (HTA) and its Histopathology Working Group, which includes representatives from the Association of Anatomical Pathology Technology, Institute of Biomedical Science, The Coroners Society of England and Wales, the Home Office Forensic Science Regulation Unit and Forensic Pathology Unit and the British Medical Association.

The information used to develop this document was derived from current medical literature and a previous version of this guideline. Much of the content of the document represents custom and practice, and is based on the substantial clinical experience of the authors. All evidence included in this guideline has been graded using modified SIGN guidance. See Appendix B.

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

A formal revision cycle for all guidelines takes place on a five-year 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, a short note of the proposed changes will be placed on the College website for two 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.

This guideline has been reviewed by the College's Death Investigation Group, Lay Governance Group and Clinical Effectiveness Department and was placed on the College website for consultation with the membership from 13 March to 10 April 2017. All comments received from the

membership were addressed by the author to the satisfaction of the Director of Publishing and Engagement.

This guideline was developed without external funding to the writing group. The College requires the authors of guidelines to provide a list of potential conflicts of interest; these are monitored by the Clinical Effectiveness Department and are available on request. The authors have declared no conflicts of interest.

1 Introduction

Post-mortem examination of a baby following an antepartum or intrapartum fetal death may provide a cause of death or at the least provide a partial explanation of the loss and information relevant to the management of subsequent pregnancies.¹⁻⁴ Autopsy is the single most useful investigation and provides information that changes or significantly adds to the clinical information in nearly half of cases.^{5,6} The autopsy is also a valuable audit of clinical care and may facilitate learning from adverse events.

This guideline has been created to assist the pathologist undertaking autopsies in cases of antepartum and intrapartum intrauterine death (stillbirth) of babies in the third trimester (i.e. >24 weeks gestation). It provides practical technical advice on performing the autopsy, guidance on the use of additional investigations and minimum standards for the content of the autopsy report. It is intended as a guide to reasonable practice, rather than a policy statement. If followed, the output from the autopsy should be sufficient to provide useful feedback to the family, to the clinicians involved in the case and for local and national audit. Where possible, references are provided, but it is inevitable that many of the suggestions are based on common UK practice rather than on published evidence, as the latter is often non-existent or sparse. Many pathologists have adopted approaches based on their own experience, evidence and resources, which may differ from these guidelines but which achieve the same outcome. This document does not aim to change such approaches. In addition, the document is not intended as a replacement for standard textbooks, but highlights the principles of undertaking and reporting perinatal autopsies. For detailed guidance on undertaking the autopsy in specific circumstances, the reader is referred to the Further reading list below.

In England, Wales and Northern Ireland, autopsy facilities and procedures must be covered by appropriate licences (issued by the Human Tissue Authority) and consent procedures must be compliant with the relevant Human Tissue Authority *Code of Practice*.⁷ Separate legislation applies in Scotland that does not impose a system of licensing.

1.1 Target users of this guideline

The target primary users of this guideline are UK consultant and trainee perinatal/paediatric pathologists and general histopathologists with an interest in perinatal pathology. The recommendations will also be of value to pathologists working outside the UK, obstetricians, neonatal paediatricians, anatomical pathology technologists (APTs) and bereavement midwives.

2 The role of the autopsy

The role of the autopsy is to:

- provide information regarding the baby to the bereaved family
 - establish the immediate cause and timing of intrauterine death, and where this is not possible, to identify relevant factors in the death

- . identify concomitant diseases, particularly those with implications for subsequent pregnancies (e.g. growth restriction, malformation, maternal diabetes)
- . identify evidence of genetic disease and to allow determination of the likely recurrence risk
- establish whether trauma was (or could be) a cause of intrapartum death provide pathology input for local perinatal mortality review meetings
- provide information for audit purposes (e.g. antenatal diagnosis, pregnancy and intrapartum care)
- provide information for national clinical outcome review programmes.

3 Pathology commonly encountered at autopsy

- Hypoxia
- Growth restriction: symmetric, asymmetric (nutritional)
- Infection
- Congenital malformation
- Trauma: cranial, extracranial
- Blood loss
- Hydrops fetalis
- Fetal conditions secondary to maternal disease e.g. diabetes, hypertension and pre-eclampsia
- Placental and umbilical cord disease
- Changes in the baby and placenta secondary to intrauterine death.

The above is not an exhaustive list and users are referred to the relevant textbooks.

4 Specific health and safety aspects

The pathologist needs to know the results of the antenatal infection screens.

Autopsy practice using universal precautions will significantly protect against accidental transmission of infection, including HIV and other blood-borne viruses.

5 Consent

- Autopsy examination may only be performed with the informed consent of the parents or, in the unlikely event of their absence, by a person in a qualifying relationship as defined by the HTA's *Code of Practice* (Code 1 Consent).⁷
- The consent process should be compliant with the requirements of the HTA's *Code of Practice: Code A: Guiding Principles and the Fundamental Principle of Consent*.⁷
- The autopsy consent form should be compliant with the model Consent form for perinatal post mortem developed by Sands, the stillbirth and neonatal death charity, in conjunction with HTA.⁸

- The pathologist performing the autopsy must see the completed consent form, either as a physical copy or electronically, before commencing the autopsy. Any limitations on the scope of the autopsy must be complied with.
- Any concerns regarding the validity of the consent should be resolved before commencing the autopsy.

[Level of evidence D.]

6 Clinical information relevant to the autopsy

(Best obtained using structured request form, see Appendix A.)

- Patient identification details
- Maternal age/date of birth
- Maternal height, weight and BMI
- Relevant medical and family history, including consanguinity
- Obstetric history, previous pregnancies/deliveries, including previous fetal and neonatal losses (if post-mortem examination had been carried out), malformation and growth restriction and other complications
- History of current pregnancy, including:
 - . estimated delivery date
 - . antenatal infection screen, including HIV
 - . abnormal findings from ultrasound or other antenatal investigations
 - . hypertension/bleeding/pyrexia/membrane rupture
 - . events leading up to intrauterine death and/or delivery
 - . delivery: mode, complications and use of instrumentation
 - . attempted resuscitation.

[Level of evidence GPP.]

7 The autopsy procedure⁹

- Requires availability of appropriately sized instruments; balances for weighing body (i.e. up to approximately 6 kg) and organs (to at least nearest 0.1 g); charts of normal values (baby and placenta)
- Whole body X-ray for gestational assessment, malformation, etc. Recommended in all cases; mandatory for suspected skeletal dysplasia. If available, this may be replaced by other imaging modalities e.g. CT, MRI.
- Photography recommended in all cases, essential to document external and internal abnormalities. Digital photography and secure storage preferred.
- Routine external body measurements (body weight, crown-rump length, crown-heel length, foot length, occipito-frontal circumference)
- Detailed external examination, including: nutritional status/soft tissue and muscle bulk, maceration, local/generalised oedema, pallor, meconium staining, dysmorphic features, evidence of trauma (intrapartum death) and other iatrogenic lesions, assessment of

patency of orifices (including choanae) and palatal fusion, limbs, hands and feet and genitalia

- Longitudinal skin incision on front of body (typically T- or Y-shaped); measurement of fat thickness over sternum (if appropriate)
- Central nervous system (CNS) examination:
 - . median posterior or transverse scalp incision
 - . skull incisions to allow assessment of falx and venous sinuses
 - . assessment of falcine and tentorial injury and meningeal haemorrhage (intrapartum death)
 - . examination for skull fracture or occipital osteodiastasis (intrapartum death)
 - . exclusion of spinal injury by posterior approach (intrapartum death)
 - . if suspected CNS malformation (including ventriculomegaly), examination of posterior fossa structures by posterior approach
 - . observation of gyral pattern to assist gestational assessment
 - . consider removal under water and perhaps in dura especially with marked autolysis: will permit weighing and assessment of gyral pattern
 - . Consider referring the whole central nervous system for neuropathological examination in appropriate cases. This may include sampling peripheral nervous tissue (nerve root, peripheral nerve, muscle etc). Consulting the neuropathology team may be helpful if there is doubt about sampling.

[Level of evidence GPP.]

- Detailed systematic examination of other internal organs, including:
 - . umbilical arteries and vein, ductus venosus
 - . *in situ* examination of the heart and great vessels with sequential segmental analysis of malformations
 - . *in situ* examination of thoracic and abdominal organs; consider removing in continuity to assess abnormal structures crossing diaphragm
 - . weights of internal organs (minimum: brain, heart, lungs, liver, kidneys, thymus, adrenals, spleen)
 - . apply special dissection techniques where appropriate.

[Level of evidence GPP.]

- Detailed examination of placenta and umbilical cord, including:
 - . trimmed weight (after extraplacental membranes and cord detached)
 - . dimensions of placenta, width in two planes and thickness)
 - . umbilical cord: length, diameter, insertion into placental disc, number of vessels, coiling, lesions
 - . membranes: appearance
 - . fetal surface/chorionic vessels: appearance, thrombosis
 - . maternal surface: completeness, craters

- slicing at approximately 1 cm intervals to evaluate parenchyma for colour and focal abnormalities.

[Level of evidence C.]

8 Limited autopsy

Where consent for a full autopsy is not given, limited examination may be of value.¹⁰

Forms of limited examination include:

- autopsy limited to one or more body cavities
- open or needle biopsy of specific internal organs (if feasible)
- external examination of the body with X-ray, photography and genetics (if indicated)
- placental examination only (with genetic testing if indicated)¹¹
- imaging (CT, MRI . if available) alone or with targeted biopsies.¹²

[Level of evidence C and D].

9 Specific significant organ systems

None. All are of significance.

10 Organ retention

- Short-term retention of organs to allow fixation does not require specific consent, provided they are reunited with the body before release for burial/cremation.
- Specific consent should be sought for long-term retention beyond the release of the body, for the purpose of examining the organs. Consider for extra-cranial organs with congenital malformations (particularly heart) if input not available on site at the time from a perinatal pathologist or cardiac morphologist, and the abnormality cannot be satisfactorily recorded by photography.
- Brain for macroscopic and histological assessment. In practice, submersion for a minimum of 2. 3 days in 20% formalin ($\pm 5\%$ acetic acid) will usually produce sufficient fixation to allow adequate sectioning and block sampling to allow the brain to be returned to the body before release for funeral. Longer fixation may be necessary in some complex neuropathology cases. If there is doubt, consult the local neuropathology team.
- The consent form must be carefully checked for consistency with respect to tissue retention and achieving the aims of the autopsy. Consent for permanent archiving of tissues blocks and slides should be included on the post-mortem consent form and should be encouraged as the norm.

[Level of evidence GPP.]

11 Histological examination

Recommended blocks required at full autopsy:⁸

- thymus
- heart (septum and free walls)
- lungs (right and left . each lobe)
- liver (both major lobes)
- pancreas
- spleen
- adrenal glands
- kidneys
- muscle and diaphragm
- stomach, small and large bowels
- larynx/trachea and thyroid
- bone: rib including growth plate in stillbirth; long bone (including growth plate), vertebral body and skull mandatory for suspected skeletal dysplasia
- brain: if preservation allows include cerebral cortex and periventricular white matter (frontal, parietal, temporal and occipital), deep grey matter (caudate, striatum, thalamus), hippocampus, midbrain (inferior colliculi), pons, medulla (inferior olives), cerebellum with dentate nucleus. Sampling may by necessity be more restricted if there is advanced autolysis
- other organ lesions as appropriate
- placenta (at least three full-thickness blocks, plus focal lesions)
- membrane roll
- umbilical cord (at least two).

[Level of evidence D.]

A record of the samples taken should be kept and tissue blocks and slides should be traceable within the laboratory, in line with the requirements of HTA and the UK Accreditation Service.

12 Toxicology

Rarely required, e.g. suspected poisoning of mother, illegal abortion or medical malpractice.

13 Other samples (as indicated by history and macroscopic findings)

- Bacteriology (may still be helpful when there is maceration):
 - . lung (swab/tissue)
 - . blood (swab/formal culture)
 - . other, as dictated by clinical history or macroscopic findings.
- Genetics (DNA microarray preferred if available):
 - . skin/muscle/cardiac blood
 - . placenta

- . samples recommended by local genetics department
- . advise retention of frozen tissue sample (liver/lung/other) as future DNA resource.
- Samples for virology, biochemistry, haematology, electron microscopy, fibroblast culture and/or snap frozen liver/muscle for metabolic biochemistry.

[Level of evidence D.]

14 Imaging

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 modalities, in addition to X-ray, which may be of value include MRI¹² and micro-CT.¹³

The role of MRI imaging in perinatal autopsies has been investigated.¹² MRI imaging can give useful information, particularly on structural malformations in the situation of stillbirth, however, it is poor in detecting infection and hypoxic-ischaemic brain injury, two of the major pathologies frequently encountered. Targeted biopsies may overcome this, but both MRI imaging and the equipment and skills needed to take endoscopic biopsies at post-mortem examination are currently not widely available.

15 Autopsy report⁹

Units may choose, if resources allow, to issue a provisional report giving details of the macroscopic findings shortly after the examination of the body, followed by a final report when all histology and other tests have been completed. Alternatively, only a single, final report may be produced.

The report should include the following sections:

- demographic and identification data
- details of autopsy consent and limitations
- body weight and centile (crude or customised)
- body measurements
- list of main findings
- clinicopathological summary (final report)
- summary of clinical history
- systematic description of external and internal findings and placental examination
- organ weights with relevant reference values and ratios
- details of ancillary tests taken (and results in final report)
- histology (final report)
- list of histology tissue blocks (final report).

[Level of evidence GPP.]

15.1 Clinicopathological summary

The summary should include:

- an assessment of gestational age at death
- in antepartum stillbirth, the degree of maceration and likely timing of death
- explicit statements regarding the presence/absence of growth restriction, malformation, infection and (where appropriate) trauma (negative findings are helpful and may be crucial)
- a discussion of the likely mechanism of death
- concordance or discordance of findings with the clinical history and prenatal testing (if appropriate)
- identification of those cases with an increased risk of recurrence (including growth restriction, maternal diabetes, genetic disease) and requirement/possibility of additional testing.

[Level of evidence GPP.]

16 Criteria for audit

The following standards are suggested criteria that might be used in periodic reviews to ensure a post-mortem examination reports meet national standards.

- Supporting documentation:
 - . standards: supporting documentation was submitted with the body in 95% of cases (NB It is recommended that an autopsy should not be commenced in the absence of clinical information)
 - . standards: 95% of submitted information is satisfactory, good or excellent
 - . standards: a correctly completed autopsy consent form, meeting national requirements is submitted with 95% of cases. (NB an autopsy must not be commenced unless the pathologist has seen a physical copy of the consent form and it is correctly completed).
- Autopsy report:
 - . standards: 100% of autopsy reports must include all of the sections detailed in section 15 (above).
 - . standards: in 100% of autopsy reports the information documented is satisfactory, good or excellent.
 - . standards: in 100% of autopsy reports the clinicopathological summary is clear and concise and, when appropriate, contains the information detailed above.

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Further reading

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2. Khong TY. The perinatal necropsy. In: Khong TY, Malcomson RDG (eds). *Keeling's Fetal and Neonatal Pathology (5th edition)*. London: Springer, 2015.
3. Bove KE. Practice guidelines for autopsy pathology . the perinatal and pediatric autopsy. *Arch Pathol Lab Med* 1997;121:368. 376.
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5. Baergen RN. *Manual of Pathology of the Human Placenta (2nd edition)*. New York: Springer, 2011.

Appendix A Specimen autopsy request form

Clinical information for fetal/perinatal post-mortem examination

Please attach **mother's** sticker here
 Family name
 First name
 DOB / /
 Reg no.....
 Consultant

Please attach **baby's** sticker here
 Family name
 First name
 DOB / /
 Reg no
 Consultant

Ethnic origin _____ Father's ethnic origin (if known) _____ Baby's sex: M/F
 Referring hospital _____ Ward _____
 Hospital of birth (if different) _____

RELEVANT HISTORY:

Maternal height: _____ cm
 Booking weight: _____ kg
 Consanguinity Y/N

Previous pregnancies: G _____ P: _____

Date	Gestation	Delivery	Sex	Outcome
1. _____				
2. _____				
3. _____				
4. _____				
5. _____				

THIS PREGNANCY: booked / unbooked LMP _____ EDD _____ BMI _____
 Gestation: by dates: _____/40 by scan : _____/40 weeks Blood group : _____, Rh D pos / neg
 HBsAg pos / neg Red cell antibodies _____
 Trisomy screening results _____ Medications _____
 Abnormal USS findings _____

Antenatal diagnostic procedures / results: _____

 _____ Karyotype: _____

Threatened abortion: no / yes When _____	Severe anaemia: no / yes
Antepartum haemorrhage: no / yes When _____	Infection risk: low / high Reason _____
Hypertension: no/yes Max b.p. _____	Maternal pyrexia: no / yes When _____
Pre-eclampsia: no/ yes When _____	Other problem _____

LABOUR: onset: spont. / medical/ none IOL for: IUD / TOP / other _____ Fetocide: y / n date _____
Presentation: vertex / breech / other _____ Liquor volume: normal / reduced / increased; colour _____
Rupture of membranes: date _____ time _____ Augmentation (Syntocinon): yes / no
1st stage: __h __min 2nd stage: __h __min Fetal heart last heard (S/B): date _____ time _____
Fetal distress: yes / no specify _____

Delivery: spontaneous / assisted (forceps/ventouse) / CS (elective/emergency) date _____ time _____
Death: date _____ time _____

Baby: Birth weight _____g Apgars: 1st min _____ 5th min _____ 10th min _____
ABNORMALITIES NOTED: nil / _____

For live born infants:
RESUSCITATION: nil / mucus extraction / oxygen / mask / intubation / other _____
_____ Surfactant: yes / no

NEONATAL PROBLEMS:	PROCEDURES:
1. _____	1. _____
2. _____	2. _____
3. _____	3. _____
4. _____	4. _____
5. _____	5. _____

BRIEF SUMMARY OF LATER SYMPTOMS / TREATMENTS AND MAJOR INVESTIGATIONS (including CPAP/ventilation, IV therapy, fits, episodes of collapse, pneumonia, pneumothorax, bleeding problems, type of feeding etc. If complex course, please send photocopy of relevant pages of notes):

SUSPECTED CAUSE(S) OF DEATH:

DEATH REGISTERED AS: livebirth / stillbirth / not registered (miscarriage)

BRIEF SUMMARY OF MAIN HISTORY / SPECIAL POINTS TO BE NOTED AT POST-MORTEM:

Referring doctor / midwife: _____ **Contact no. / bleep no.** _____

ALL BABIES AND PLACENTAS SHOULD BE SENT FRESH IN LEAKPROOF, OPAQUE CONTAINERS UNLESS THERE IS AN INFECTIOUS HAZARD
(In this case, phone to discuss whether the specimen should be fixed in 10% formalin before transportation)
It is essential to send the placenta with a fetus/infant.
ALL SPECIMENS MUST BE CLEARLY LABELLED AND ACCOMPANIED BY A COMPLETED REQUEST AND CONSENT FORM

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 one 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 population.</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 compliance monitoring sheet

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

AGREE II standard	Section of guideline
Scope and purpose	
1 The overall objective(s) of the guideline is (are) specifically described	Foreword, 1
2 The health question(s) covered by the guideline is (are) specifically described	Foreword, 1
3 The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	Foreword, 1
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	1
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	n/a
12 There is an explicit link between the recommendations and the supporting evidence	Throughout
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	Throughout
16 The different options for management of the condition or health issue are clearly presented	Foreword, 7, 8, 14
17 Key recommendations are easily identifiable	Throughout
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	Appendix A
20 The potential resource implications of applying the recommendations have been considered	Foreword
21 The guideline presents monitoring and/or auditing criteria	16
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