



## Guidelines on Autopsy Practice

### Scenario 5: Maternal death

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Under review

## 1. The role of the autopsy

To identify the pathologies in the patient and contribute critically to the clinico-pathological evaluation of the death.

*Maternal death autopsies assume greater significance than most other deaths since all the autopsy reports are scrutinised closely in preparation for reports for the UK Confidential Enquiry into Maternal Death (part of CMACE). Since these reports make recommendations for improving national obstetric practice, optimum quality of reports, clearly determining what actually happened to cause the death, are critical. It is important that an autopsy is performed in the great majority of cases.*

These Guidelines are intended to help the pathologist focus on the issues raised by a death related to pregnancy and thus optimise the autopsy procedure; they include nearly all the clinico-pathological scenarios likely to be encountered.

It is evident that experience is required for these cases, as well as good mortuary and laboratory facilities. Pathologists should not be averse to referring maternal autopsies to centres that have seen more cases.

## 2. Pathology encountered at the autopsy

Deaths related to pregnancy are categorised into:

- Direct – the disease is caused by being pregnant and/or delivering a baby
- Indirect – a disease unrelated to pregnancy directly, but exacerbated by the physical aspects of pregnancy and/or delivery
- Coincidental – a disease physically unrelated to pregnancy.

The major entities include the following.

### 2.1 Direct

- Venous thrombosis and pulmonary embolism
- Hypertensive disease of pregnancy [pre-eclampsia (PET), eclampsia]
  - a. Subtype of PET: HELLP syndrome in PET (haemolysis, elevated liver enzymes, low platelets)
- Peripartum haemorrhage
  - a. Uterine atony
  - b. Abruptio of the placenta
  - c. Placenta praevia
  - d. Abnormally adherent placenta
    - i. Placenta accreta, increta, percreta
  - e. Retained placenta
  - f. Tear or rupture of genital tract
    - i. Spontaneous
    - ii. Iatrogenic
- Life support for peripartum haemorrhage
  - a. TRALI (transfusion-associated lung injury)
  - b. Fluid overload
- Peripartum dilated cardiomyopathy (defined as cardiac failure from last month of pregnancy up to 5 months post-partum; other causes excluded)
- Amniotic fluid embolism
- Early pregnancy deaths
  - a. Ectopic pregnancy and haemorrhage
  - b. Spontaneous miscarriage
  - c. Legal termination
- Genital tract sepsis – puerperal sepsis

- Anaesthetic (general and regional anaesthesia)
- Air embolism
- Ogilvie's syndrome (pseudo-obstruction of the large bowel)
- Choriocarcinoma and hydatidiform mole
- Ovarian hyperstimulation syndrome (OHSS)
- Acute fatty liver of pregnancy

## 2.2 Indirect

- Cardiac
  - a. Congenital heart lesion with pulmonary hypertension
  - b. Inheritable cardiomyopathy, e.g. hypertrophic cardiomyopathy (HOCM), arrhythmogenic right ventricular cardiomyopathy (ARVC)
  - c. Acquired cardiac muscle disease, e.g. ischaemic heart disease, endocardial fibroelastosis
  - d. Obesity and sudden cardiac death
  - e. Valvular disease, e.g. in IV drug users, rheumatic mitral stenosis
- Systemic hypertension
- Idiopathic arterial (primary) pulmonary hypertension
- Pre-existing thrombophilia states, including antiphospholipid syndrome
- Thrombotic thrombocytopenic purpura (TTP)
- Stroke
  - a. Subarachnoid haemorrhage
  - b. Cerebral infarction
  - c. Cerebral venous sinus thrombosis
- Other cardiovascular diseases
  - a. Dissection of aorta
  - b. Dissection of coronary artery
  - c. Dissection of splenic artery
- Psychiatric, including suicide related to pregnancy and delivery
- Epilepsy [sudden unexplained death in epilepsy (SUDEP)]
- Malignant disease worsened by pregnancy (breast, cervix)
- Community-acquired sepsis
- Acute anaphylaxis from drug treatment, e.g. antibiotics
- Other diseases:
  - a. HIV/AIDS and tuberculosis
  - b. Sickle cell disease (HbSS and HbSC)
  - c. Connective tissue disease – systemic lupus erythematosus (SLE)
  - d. Diabetes mellitus – gestational and pre-existing diabetes; this includes the hypoglycaemic 'dead in bed' syndrome
  - e. Influenza (e.g. epidemic type A – H1N1)
  - f. Cirrhosis
  - g. Any other clinico-pathological condition that the pregnant state makes worse; these include inherited and acquired conditions, and the patient may have been specifically warned of the hazards of becoming pregnant.

## 2.3 Coincidental

- Death by own hands (suicide – some cases are unrelated to pregnancy, reflecting underlying mental health issues; note that only Coroners/Procurator Fiscals can make the verdict of 'suicide')
- Other malignant disease
- Stroke (early in pregnancy)
- Road accident
- Homicide
- Toxic/illicit drug overdose

- Any other significant clinico-pathological condition

These deaths are further sub-classified into 'Maternal deaths' (up to 42 days following abortion, miscarriage or delivery – the international definition), and 'Late maternal deaths' (more than 42 days to 1 year following abortion, miscarriage or delivery).

In many cases, there may be a combined Direct + Indirect pathogenesis, and the deaths are multifactorial.

### 3. Clinical information relevant to the autopsy

- All clinical information on past pregnancy history and present pregnancy is required. Also whether the delivery took place at home or in hospital, and whether patient transfer was involved. When drafting the final report, care needs to be taken over sensitive issues such as previous terminations and pregnancies if they may not be known to relatives.
- Information on the delivery process, e.g. Caesarian, forceps, transfusions
- Clinical and drug information on pre-existing medical conditions, including pre-eclampsia, renal disease, cardiac disease and haematological conditions such as sickle disease
- Family history of thrombosis and thromboembolism
- The fetal/neonatal information is also relevant, e.g. infected peri-partum, small-for-dates, traumatised
- Ideally, the case should be discussed at the time and place of autopsy with the relevant obstetricians and clinicians, to establish the major issues, or via a phone call
- Pre-mortem laboratory data, e.g. blood cultures, blood clotting and platelet counts, liver and renal function tests

### 4. Specific health and safety aspects

None, but note that the proportion of mothers in the UK who are HIV and/or HCV-infected is increasing.

### 5. The autopsy procedure

1. On admission to the mortuary, take blood cultures (aerobic & anaerobic) from a sterile upper body site on *all* cases, unless another cause of death is already evident. This can only be done once coronial authorisation (or relatives' consent) for the autopsy has been received, and it should then be done as soon as possible.
2. Full autopsy with the pathologist present at the evisceration
3. Reserve autopsy blood – untreated and spun – in case of later need for analysis
4. If trauma to the utero-cervix and pelvic area is a factor, consider retaining all the pelvic viscera for optimal evaluation after fixation, and later inspection by referee pathologists and clinicians. Alternatively, digital photography could replace such retention
5. Take digital photographs (under GMC standards of anonymity) of other relevant organ lesions for the mortality review meetings that are usual with these deaths.

### 6. Specific significant organ systems

- Heart – malformation; acquired disease, including hypertension; air embolism
- Arterial system – aneurysms of aorta, splenic and other arteries
- Lung – amniotic fluid embolism (high MW cytokeratin markers and complementary endothelial cell markers are useful), thromboembolism, fat embolism
- Brain – infarction, subarachnoid haemorrhage (with or without berry aneurysm), sagittal sinus thrombosis and other strokes; eclampsia

- Uterus and genital tract:
  - a. particular attention to possible trauma
  - b. infection
- Fallopian tube and ovary in cases of ectopic pregnancy
- Ovaries if ovarian hyperstimulation syndrome considered
- Placenta – standard examination, with measurements and weight, and histopathology for inflammation, infection, and placental bed arterial lesions
- Bone marrow, femoral long bone, and spleen if sickle cell disease (see Scenario 2: Autopsy for sickle cell disease and sickle trait)

## 7. Specific scenarios and important entities

### 7.1 Pre-eclampsia (PET) and eclampsia (defined as tonic–clonic seizure in a patient with PET)

- a. Intracerebral haemorrhage – major or petechial
- b. Cerebral oedema, hypoxic damage and infarction – vasogenic aetiology
- c. Kidney lesion = glomerular endotheliosis
- d. Liver: periportal necrosis and haemorrhage (HELLP syndrome)
- e. Note: PET/eclampsia deaths may occur in the community between antenatal visits. Thus brain, kidney and liver histopathology can be critical in making the diagnosis at autopsy

### 7.2 Sepsis

This is complicated, and the previous tendency to lump all the scenarios under 'puerperal sepsis' over-simplifies the issues of pathogenesis. A proportion of Group A streptococcal sepsis is community-acquired infection via the respiratory tract, with pregnancy possibly making the infection more virulent. The following are the main clinico-pathological entities:

- a. Pre-term spontaneous rupture of membranes and ascending infection
- b. Direct infection of the genital tract during or shortly after the delivery
- c. Nasopharyngeal tract (community-acquired) infection, transfer of bacterium to vagina, ascending infection and bacteraemia
- d. Necrotising fasciitis following a genital tract tear
- e. MRSA infection acquired in hospital
- f. Sepsis from an organ not related directly to the genital tract, e.g. pneumonia, breast (mastitis), Caesarean section skin wound infection, heart valve endocarditis

### 7.3 Intra-abdominal haemorrhage

- a. Uterine rupture
- b. Ectopic pregnancy
- c. Tear of an abdominal wall artery during or after Caesarean section
- d. Ruptured aortic aneurysm or dissection
- e. Rupture of splenic artery aneurysm
- f. Rupture of liver or spleen capsules
- g. Haemorrhage from liver in HELLP syndrome

### 7.4 Deaths related to anaesthesia

- a. Aspiration pneumonitis
- b. Difficulties in airway patency peri- and post-anaesthesia
- c. Overdose of opiate drugs for pain
- d. Infection introduced by spinal/epidural anaesthesia
- e. Other anaesthetic complications such as anaphylaxis, hyperthermia

## 7.5 Termination of pregnancy

- a. Criminal (unsafe) abortion
  - i. Infection
  - ii. Air embolism
  - iii. Perforation of uterus
- b. Medical or surgical termination
  - i. Uterus rupture from prostaglandin induction
  - ii. Trauma to genital tract and perforation of uterus
  - iii. Infection and air embolism

## 7.6 Sudden unexpected cardiac death

An area of growing concern where detailed depiction of the heart is essential (see also RCPATH Autopsy Guideline 'Sudden death with likely cardiac pathology', 2005)

- a. Sudden arrhythmic cardiac death (SADS) with a morphologically normal heart
- b. SADS in an hypertrophied heart
  - i. Cause of hypertrophy known – e.g. hypertension
  - ii. Cause of hypertrophy undetermined
  - iii. Obesity-associated ('obesity cardiomyopathy')
- c. One of the described cardiomyopathies, e.g. ARVC, HOCM

## 7.7 Pulmonary 'flash' oedema

- a. Cardiomyopathy ± obesity
- b. Hypertensive heart disease
- c. PET and acute lung injury
- d. Fluid overload
- e. TRALI

## 7.8. Disseminated intravascular coagulation (DIC)

A confusing pathology with many causes and differential diagnoses.

- a. Obtain the pre-mortem haematology laboratory results
- b. Differentiate between DIC and thrombotic thrombocytopenic purpura (TTP) from the laboratory results and the histopathology
- c. Consider to prove or exclude as causes of DIC
  - i. Severe sepsis
  - ii. Uterine atony and other causes of peri-partum haemorrhage
  - iii. Amniotic fluid embolism
  - iv. Pre-eclampsia

## 7.9 Fetus

There may be a fetus retained within the mother; or accompanying the mother, following peri-mortem caesarian section or other delivery

- a. If the fetus lived and then died, the coroner has potential jurisdiction
- b. If the fetus never lived, then the coroner has no jurisdiction; an autopsy would need consent from the relatives, unless there are special circumstances
- c. Autopsy of the fetus is usually unnecessary as this will contribute little or nothing to the understanding of the mother's cause of death. Exceptions to this are ?sepsis, when fetal skin or lung samples can indicate severity and timing of ascending infection; and the exceptionally rare event of a fetal malignant tumour that might have spread to the mother
- d. Note: it is always worth examining the placenta properly, if available, to gain insight into the maternal pathologies

## 8. Organ retention guidance – *to consider*

- The genital tract in cases of trauma
- The heart in cases of sudden arrhythmic death syndrome with or without obesity
- The brain in cases of cerebral haemorrhage without specific preceding cause, and if the clinical scenario is unclear but evidently involves brain death

## 9. Recommended minimum blocks for histological examination – best practice

- Lungs, both
- Heart slice with circumferential blocking (see Autopsy Guideline ‘Sudden death with likely cardiac pathology’ 2005)
- Liver
- Kidney
- Brain
- Uterus
- Placenta – if available, with sampling of cord, amnion and placental cake; this is critical for evaluating ascending genital tract infection
- Bone marrow
- Spleen

## 10. Other samples that may be required

- Genital tract microbiology
- Kidney for electron microscopy in cases of suspected pre-eclampsia
- Standard samples for toxicology (blood, urine, vitreous, gastric contents) if illicit drug intake is a possible factor
- Blood samples for assessment of anti-epileptic drug intake
- Blood sample for mast cell tryptase analysis (in suspected anaphylaxis)
- Review of the pathology of any previous surgical resection specimens of relevance to the pregnancy, e.g. a hysterectomy specimen, products of conception. This may require liaison with other laboratories
- Blood sample and transfused blood sample (in the laboratory) if TRALI is suspected.

## 11. The clinico-pathological summary

This must be comprehensive, to assist the clinical team, the Coroner or Procurator Fiscal (if a medico-legal autopsy), CMACE (Centre for Maternal and Child Enquiries) and local audit. The death may be straightforward or complex; it may only be formulated after a multidisciplinary meeting with, for example, the obstetrician, obstetric physician, cardiologist, intensivist, anaesthetist and midwife/nursing team.

Decide whether the death is Direct, Indirect or Coincidental in relation to the pregnancy.

Note that autopsies performed on patients who collapse from an undetermined event, and are then on life support systems in intensive care for weeks or months, are unlikely to identify the nature of that event, if pre-mortem investigations have not done so.

## 12. Specimen cause of death opinions/statements

- 1a. Massive uterine haemorrhage
  - 1b. Uterine atony
  - 1c. Recent vaginal delivery at 40 weeks' gestation
- 
- 1a. Amniotic fluid embolism

- 1b. Third trimester vaginal delivery on xx/xx/xx [date]
- 1a. Cardiorespiratory failure
- 1b. Lupus erythematosus lung disease
- 2. Pregnancy, delivered spontaneously at 28 weeks' gestation
- 1a. Septic shock due to Group A streptococcal infection
- 1b. Genital tract sepsis following delivery at term pregnancy
- 1a. Liver failure
- 1b. Fatty liver due to antiretroviral therapy for HIV disease, and third trimester pregnancy
- 1a. Pulmonary hypertension
- 1b. Congenital ventricular septal defect with reversed shunt
- 2. Caesarian section delivery at 34 weeks' gestation on xx/xx/xx [date]
- 1a. Acute pulmonary hypertension
- 1b. Disseminated carcinoma of the lung
- 1. Recent delivery at term
- 1a. Acute lung injury and organising pneumonia
- 1b. Complications of general anaesthesia
- 1c. Placenta praevia (caesarian section on x/x/xx), third trimester pregnancy

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Note CEMACH changed its title in 2009 to CMACE – Centre for Maternal and Child Enquiries.