The Confidential Enquiry
Into Maternal Deaths:
The Role Of The Pathologist

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Maternal mortality is an internationally accepted index by which we measure maternal health.
Maternal death is defined in the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) (WHO 1992) as:
The death of a woman while pregnant or within 42 days of the termination of pregnancy, irrespective of the duration and the site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes.
This definition includes deaths of women from pregnancy, terminations of pregnancy, miscarriage and ectopic pregnancy.
AUTOPSY INVESTIGATION

Autopsy, or postmortem examination, is a medical examination of a dead body, including the internal organs, to determine the cause of death.

Violent deaths or deaths occurring under suspicious circumstances, according to law, must be investigated.
In such cases, an autopsy may be performed to determine the cause and manner of death, as well as to collect evidence for legal proceedings.
The Confidential Enquiries into Maternal Deaths in Malaysia (CEMD) was established in 1991. Maternal mortality remains a critical and sensitive indicator of the state of our health delivery system and as such maternal deaths review have become an essential component of any maternity service.
With our multiracial and multicultural society the need to increase the awareness and acceptance of post-mortem examination cannot be over emphasised.
Surprisingly very few pathologists are aware of the existence of the confidential enquiry into maternal deaths.
Maternal autopsies are required for accurate death certification, determination of underlying causes of death, as well as maternal mortality rates.
There is a real need for routine post mortem examinations in all cases of maternal deaths but various legal, social and religious factors stand in the way.
Autopsy is an important investigation tool despite the introduction of new diagnostic techniques.

A meticulous attitude and patience are the keys to a comprehensive examination.
Since the viability and success of an enquiry will depend on a complete autopsy, histopathological and other laboratory examinations, the preferred standard for the investigation of maternal deaths is to have a post-mortem examination conducted by an experienced pathologist who in turn will have consultations with other relevant specialists before performing the autopsy.
Training of adequate specialists in this field is essential if we want a high standard of autopsies to improve the health care delivery system in the future.
In situations where a pathologist is not available, autopsies can be carried out by trained medical officers, who should consult the forensic pathologist or the general pathologist in the area before conducting the autopsy.
Photographs should be taken during the autopsy for further review, assessment and diagnosis.
The role of the autopsy is 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 Confidential Enquiry into Maternal Death Committee.
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.
In many cases, deaths are multifactorial and all clinical information on past pregnancy medical history and present pregnancy is required.

Also whether the delivery took place at home or in hospital and whether patient transfer was involved.

Pre-mortem laboratory data, e.g. blood cultures, blood indices, liver and renal function tests etc. should be made available.
The Autopsy Procedure

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.

Once consent for the autopsy has been received, and it should then be done as soon as possible.
Full autopsy with the pathologist present at the evisceration

If trauma to the utero-cervix and pelvic area is a factor,

consider retaining all the pelvic viscera.
Alternatively, digital photography could replace such retention.

Take digital photographs of other relevant organ lesions for the mortality review meetings that are usual with these deaths.
Placenta - standard examination,

with measurements and weight

and histopathology for inflammation,

infection and placental bed arterial lesions
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.
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.
• **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
• 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.
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.
The Clinico-Pathological Summary continued

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

References


Pathology encountered at the autopsy

Deaths related to pregnancy are categorised into:

1. **Direct**
   the disease is caused by being pregnant and / or delivering a baby

2. **Indirect**
   a disease unrelated to pregnancy directly, but exacerbated by the physical aspects of pregnancy and / or delivery

3. **Fortuitous (Coincidental)**
   a disease physically unrelated to pregnancy
DIRECT CAUSES:

1) Hypertensive disease of pregnancy
   [ eclampsia, pre-eclampsia ]

2) Thrombosis and pulmonary thrombo embolism

3) Haemorrhage

4) HELLP syndrome [ haemolysis, elevated liver enzymes, low platelets ]
5) Amniotic fluid embolism

6) Early pregnancy deaths:
   a. Ectopic
   b. Spontaneous miscarriage
   c. Legal termination
   d. Other [ e.g. termination induced by non-medical personnel. ]

7) Genital tract sepsis
• Abnormally adherent placenta
• Placenta accreta, increta, percreta
• Retained placenta
• Tear or rupture of genital tract
• Spontaneous ii. Iatrogenic
• Autopsy of the foetus 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 foetal skin or lung samples can indicate severity and timing of ascending infection;

• It is recommended to examine the placenta properly, if available, to gain insight into the maternal pathologies.
INDIRECT

Cardiac

a. Congenital heart lesion with pulmonary hypertension

b. Inheritable cardiomyopathy, e.g. hypertrophic cardiomyopathy (HOCM), arrhythmogenic right ventricular cardiomyopathy (ARVCM)

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

**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

e. Dengue Hepatitis
Fortuitous (Coincidental)

• Suicide - some cases are unrelated to pregnancy, reflecting underlying mental health issues;
• Other malignant disease
• Road Traffic accident
• Homicide
• Toxic / illicit drug overdose
• Any other significant clinico-pathological condition
• TRALI (transfusion - associated lung injury)
  b. Fluid overload

• Peripartum dilated cardiomyopathy

• 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

• Choriocarcinoma and hydatidiform mole

• Ovarian hyperstimulation syndrome (OHSS)

• Acute fatty liver of pregnancy 2.2

• Stroke
  a. Subarachnoid haemorrhage
  b. Cerebral infarction
  c. Cerebral venous sinus thrombosis
• Influenza (e.g. epidemic type A – H1N1)
• Pre-existing thrombophilia states, including antiphospholipid syndrome
• Thrombotic thrombocytopenic purpura (TTP) f. Cirrhosis
The other increasingly causes of death seen are:

Dengue

Leptospirosis
Deaths associated with abortion

Legal termination of pregnancy

Death from illegal abortion
Deaths associated with abortion

**Legal termination of pregnancy**

a. When carried out with proper facilities, legal abortion has extremely low mortality rate.

b. Usual method are vacuum aspiration, dilatation and curettage, or hysterotomy in later pregnancy

**Death from illegal abortion**

Risks vary according to the skill, experience and facilities of the abortionist.
DEATHS ASSOCIATED WITH ABORTION

Legal termination of pregnancy

a) Pulmonary embolism from leg vein thrombosis

b) Mishaps associated with anaesthesia

c) DIC and cerebral damage

d) Air embolism following vacuum aspiration

e) Bleeding or infection, which failed to respond to treatment
DEATHS ASSOCIATED WITH ABORTION

Death from illegal abortion

a) Instrumental interference
b) Insufflation of air
c) Dilatation of the cervix
d) Physical violence
e) Syringe aspiration
f) Intrauterine Infection
g) The use of drugs and chemicals
FIGURE 19.4  *Dangers of a criminal abortion.*
THE AUTOPSY IN ABORTION DEATHS
Full possible history is required

Careful examination required:

- Abnormal discoloration of skin such as bronzing of clostridia septicemia and the jaundice in liver damage
- Signs and duration of pregnancy such as abdominal swelling and breast changes
- Burns on the abdomen or inner sides of the upper thighs may indicate efforts at resuscitation by hot-water bottles when a woman has suddenly collapsed during an illegal abortion.
Careful examination required:

- Signs of injury, including bruising or abrasion of the vulva from instrumentation and vaginal bleeding.

- The vagina should be examined for signs of recent or current pregnancy, and attempted or successful recent abortion. Any fluid should be removed by pipette to be examined for soap and chemicals, such as antiseptics.
Careful examination required:

Where any possibility of air embolism is considered, pre-autopsy radiology of chest and abdomen must be performed.

It is the best method of detecting air embolism by visualizing air bubbles in the heart, great veins in the thorax, inferior vena cava, peritoneal cavity and possibly pelvic veins.

MRI/CT Scan may increase the chance of detecting air in the vessels.
Careful examination required:

• The thorax and upper abdomen examined as usual, with particular attention to signs of infection.

• Pelvic organs removed *en bloc*

**Vagina**

a) abrasions, bruises, lacerations, any foreign materials

b) samples kept for chemical and microbiological testing

**Cervix**

a) abnormality notes eg. Instrument marks such as forceps

b) state of dilatation is noted
Pelvic organs removed *en bloc*

**Uterus**

– the colour, and size is noted

– state of interior eg. chorionic sac is still present, its integrity and attachment to deciduae notes

*If fetus present :*
examined for maturity and damage

*If no fetus present :*
POC are sought and the state of placental bed noted.

– Infection, bleeding, air crepitancy noted.
Careful examination required:

Pelvic organs removed *en bloc* –

**Fallopian tubes**

a) The tubes are open and any foreign fluid collected

a) Ovaries are examined
Blood cultures, and peritoneal and other swabs should be taken as indicated by the circumstances.

Extensive histological specimens are taken from all organs and special stains employed where necessary, such as those seeking amniotic squames in lungs and other organs.

Blood, urine, liver and stomach contents are retained for analysis, should this be indicated.
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When pulmonary artery thromboemboli are suspected, it is advantageous to eviscerate the thoracic organs to adequately identify large thromboemboli as they fall out of the transected hilar blood vessels.

Once pulmonary artery thromboemboli are detected, their origin can be verified by dissecting the legs and identifying thrombi in the deep veins.

On occasion, deep venous thrombi will not be identified in the legs, but instead may have arisen in the pelvic/uterine veins.
AMNIOTIC FLUID EMBOLISM

Clinical

– Dyspnoea, hypotension, seizures, followed by cardiovascular arrest
– If death doesn’t occur immediately, consumptive coagulopathy
– Lab – decreased fibrinogen, raised fDP, PTT, PT and low platelets
AMNIOTIC FLUID EMBOLISM

Etiology

2 school of thoughts:

i. Acute embolization of amniotic fluid and debris of fetal origin into maternal circulation with resultant pulmonary microvascular obstruction.

On reaching the lung, these material produces severe transient vasospasm of the pulmonary vasculature, pulmonary hypertension, RHF and hypoxia.
AMNIOTIC FLUID EMBOLISM

Etiology

2 school of thoughts:

ii) Simple exposure of maternal circulation to amniotic fluid triggers a pathophysiologic cascade similar to anaphylactic or septic shock generating physiologic derangements characterising these syndromes.

This explains why fetal debris is not seen in all cases of clinically diagnosed amniotic fluid emboli.
AMNIOTIC FLUID EMBOLISM

Autopsy findings

- Diagnosis made by a combination of clinical signs and symptoms and the findings of mucin derived meconium, fetal squamous cells, lanugo hair, vernix fat globules in the pulmonary vasculature.

- H+E – demonstrates these elements but special stain might better demonstrate individual elements

- Mucin is virtually always present, with cellular elements seen less frequently
AMNIOTIC FLUID EMBOLISM

Autopsy findings

- In substantial number of cases, no fetal elements is seen. This is especially true in deaths during early pregnancy caused by less abundant nature of these element in amniotic fluid at this stage.

- Squamous cells are also identified in non-pregnant women, though the difference in cell count was significant

- Trophoblastic cells can be seen in lung and blood of women who do not have amniotic fluid emboli.
Examination of the lung showed scattered pulmonary arterioles packed with squamous cells and some inflammatory debris.

Note the absence of nuclei in these cells, characteristic of desquamated fetal squamous cells.
4. PREECLAMPSIA / ECLAMPSIA / HELLP SYNDROME / LIVER RUPTURE
4. **Preeclampsia / eclampsia / HELLP syndrome / liver rupture**

*Preeclampsia* is defined as a multisystem complication of pregnancy characterized by hypertension, proteinuria, and edema occurring after 20 weeks gestation in a woman with no previous history of hypertension.

Eclampsia is recognized as preeclampsia complicated by seizure or coma.
Life-threatening complications include seizures and hepatic hemorrhage, which may present as a ruptured subcapsular hematoma.

Other serious complications include pulmonary edema, renal failure and disseminated intravascular coagulation.
• In preeclampsia or eclampsia, hepatic dysfunction may present as elevated liver enzymes, which is a feature of the HELLP syndrome (hemolysis, elevated liver enzymes, low platelets), which is usually limited to the latter half of pregnancy (usually the third trimester).

• In approximately 1% of cases, liver involvement is severe, with spontaneous rupture of the liver, may lead to shock and death.
• Although the pathogenesis of hepatic rupture is not convincingly known, in preeclampsia / eclampsia, it is believed that inflammatory infiltrates and blood flow obstruction lead to hepatic edema and swelling, which can then lead to parenchymal hemorrhage extending to, and through, the hepatic capsule.

• This may present as intrahepatic hemorrhage, subcapsular hematoma, or massive hemoperitoneum from a ruptured hepatic capsule, usually involving the right lobe of the liver.
The liver had a large ruptured subcapsular Hematoma on the right lobe.
Beneath the capsule, the liver parenchyma was soft and had tears extending to a parenchymal hematoma.
5. UTERINE RUPTURE

Uterine rupture is a full thickness tear through the wall of the uterus.
UTERINE RUPTURE

Risk factors

– Prior cesarean section delivery
– Increased gestational age
– Multiparity
– Use of uterotonic drugs such as oxytocin and prostaglandin
– Also occur in cases of prolonged labor with cephalopelvic disproportion
– Also occur during obstetric intervention such as a mid-forceps delivery or during a breech extraction
• The uterus may be predisposed to rupture because of pre existing injury or anomaly, pre existing surgical manipulation, or it may rupture without any predisposing scar.

• A previously scarred uterus is more prone to rupture than an unscarred uterus.
Uterine rupture

At autopsy, there was a large hemoperitoneum, and both fetuses were displaced into the abdominal cavity.
The uterus was ruptured and had a horizontal tear in the region of a prior cesarean section scar.
6. **Hemoperitoneum**

If hemoperitoneum is encountered in a pregnant woman:

- Consider a ruptured ectopic pregnancy, which will likely present in the first trimester of pregnancy.

Should consider a uterine rupture, a ruptured hepatic subcapsular hematoma, or a ruptured splenic artery aneurysm.
Hemoperitoneum

Ectopic pregnancy.
The fetus was found in the fallopian tube.
Hemoperitoneum

Chorionic villi and blood are found inside the fallopian tube.
In pregnancy, DIC may complicate a host of pregnancy-related illnesses/conditions, but most commonly develops in women with placental abruption.

DIC may also develop in women with intrauterine fetal demise, amniotic fluid embolism and in those with massive blood transfusion, preeclampsia and in sepsis.
MATERNAL DEATH
(Deaths Associated with Pregnancy)

- Pulmonary Artery Thromboemboli
- Amniotic Fluid Emboli
- Venous Air Emboli
- Peripartum Cardiomyopathy
- Pregnancy and the Long QT Syndrome
- Coronary Artery Dissection & Aortic Dissection
- Intracerebral Hemorrhage
MATERNAL DEATH
(DEATHS ASSOCIATED WITH PREGNANCY)

- HEMOPERITONEUM
- SPLENIC ARTERY ANEURYSM RUPTURE
- UTERINE RUPTURE
- PREECLAMPSIA/ECLAMPSIA/HELLP SYNDROME/LIVER RUPTURE
- HEPATIC INFARCTION
- ACUTE FATTY LIVER OF PREGNANCY
- THROMBOTIC MICROANGLIOPATHY
- DISSEMINATED INTRAVASCULAR COAGULATION
AMNIOTIC FLUIDS EMBOLISM

Special stain method:

- **Lendrum’s stain** (phloxine - tartazine)
  keratin of amniotic squames is stained red;
  nuclei blue and cytoplasm yellow

- **Fibrin stain**
  Fibrin deposition in many organs as a result of DIC
5. **UTERINE RUPTURE**

- Uterine rupture is a full thickness tear through the wall of the uterus that must be distinguished from uterine dehiscence.

- Uterine dehiscence is an asymptomatic bloodless partial thickness tissue separation through an area of scar tissue - most likely associated with prior cesarean section.
5. **UTERINE RUPTURE**

- Uterine dehiscence may occur in a woman with a prior cesarean section during subsequent vaginal delivery.
- It may also occur at repeat cesarean section delivery in women who have not labored.
Reasons for not wanting a postmortem exam.

- God’s will
- Against the religion
- We are not going to claim insurance
- We are not going to sue the hospital
Recommended tissues for histological examination:

- Brain
- Heart
- Lungs - both
- Liver
- Kidneys
- Spleen
- Uterus
- Placenta
Other samples that may be required:

a) Blood culture
b) Genital tract microbiology
c) Fresh tissues for genetic studies

After the autopsy examination and relevant histo-pathological, microbiological and biochemical results, a comprehensive report should be formulated, to assist the clinical team to come to a diagnosis whether death was direct, indirect or coincidental.
ALTERNATIVES IN MATERNAL MORTALITY

Post Mortem CT Scan:
An Alternative Method In Forensic Medicine
Postmortem CT:

MCT scan allows a relatively quick diagnosis of causes for death.

It also serves for quality assurance in trauma and trauma research.

This method does not substitute formal necropsy.
Cultural differences among the nations of the world may warrant different techniques in forensic medicine, pathology and trauma research.

PMCT might be considered as one of the alternative postmortem diagnostic techniques when autopsies cannot be performed.
Invasive “body-opening” autopsy represents the traditional means of postmortem investigation in humans.

However, modern cross-sectional imaging techniques can supplement and may even partially replace traditional autopsy.
Even though this is a costly examination (for quality assurance in trauma research as well as in accident investigations) the method was found to be of value for **two** main reasons:

1. Results are immediate.
2. When permission to conduct autopsy is very difficult to get.
The documentation and analysis of postmortem findings with CT and MR imaging is investigator independent, objective and noninvasive and will lead to qualitative improvements in forensic pathologic investigation.
References:

• Guidelines on Autopsy Practice – Maternal deaths.

The Royal College of Pathologists

The internet Journal of Rescue and Disaster Medicine 2000 Vol.2 No.1
Guidelines on Autopsy Practice Scenario 5: Maternal death (this document forms part of Guidelines on Autopsy Practice 40)

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