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Intrauterine Fetal Death & Stillbirth:

Guidelines for Investigation

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This is a clinical guideline only, intended for use by perinatal health professionals. Practices may differ across facilities, depending on available resources and prescriber preference. All policies and procedures must be approved by the appropriate processes within each facility/Nova Scotia Health (i.e.: Maternal/Child or Perinatal Committee, Medical Advisory Committee, etc.).

This guideline is written using gendered language, but is meant to be inclusive of all individuals regardless of gender identification. The RCP encourages healthcare professionals to engage in respectful conversation with patients regarding their gender identity and their preferred pronouns, and to apply RCP guidelines as appropriate to meet each person's needs.

INTRODUCTION

Purpose: To present care and investigative options for childbearing persons (and their relatives) who experience intrauterine fetal demise (IUFD) or stillbirth. Discussing options for investigating fetal demise is one of the most challenging conversations perinatal health professionals will initiate. Parents and families may need additional time to carefully consider their options, and follow-up discussion before final decisions can be made and consent given.

- Definition: There is variation in the thresholds for reporting stillbirth, both internationally and across some Canadian provinces; however, the Public Health Agency of Canada provides a Canadian definition for fetal mortality that aligns with definitions used by the Reproductive Care Program (RCP), and the Vital Statistics Division of Service Nova Scotia. This is essential for consistency of data collection and reporting. These three entities define 'stillbirth' accordingly: 'Stillbirth' means the complete expulsion or extraction from its mother after at least twenty weeks pregnancy, or after attaining a weight of five hundred grams or more, of a fetus in which, after such expulsion or extraction, there is no breathing, beating of the heart, pulsation of the umbilical cord, or unmistakable movement of voluntary muscle.
- 'Intrauterine fetal demise' refers to babies with no signs of life in utero.

Prevalence: According to the Nova Scotia Atlee Perinatal Database (2020), the annual provincial stillbirth rate has remained virtually unchanged since 1988. This has ranged from 3.5 to 8.5 per 1000 births, with a mean annual rate of 5.4 per 1000 births.

INFORMED DECISION-MAKING

The childbearing person and family must be provided with information about available investigative options that will assist in determining factors that may have contributed to the fetal death. For many, determining a cause of death will also help determine the risk of recurrence in subsequent pregnancies, and is beneficial for discussions that would likely occur at a later time.

According to the Society of Obstetricians and Gynaecologists of Canada, "The most common causes of antenatal death are placental insufficiency, fetal genetic and structural abnormalities, infection, umbilical cord abnormalities (excluding nuchal loop), hypertensive disorders, and pre-existing diabetes." As such, investigations may involve the mother, fetus, or placenta in accordance with the medical situation. Nonetheless, "a significant proportion of stillbirths remains unexplained even after a thorough evaluation" (ACOG 2020). Informed consent must be obtained and documented.

The following elements are to be included in the consent form for post-mortem examination:

- Purpose and extent of the examination
- Possibility of organ or tissue retention and the purpose (i.e. clinical investigation, research, and/or teaching)
- What should happen to tissues/organ after post-mortem
- Research and education (i.e. in compliance with applicable law, or as approved by the applicable research ethics board)

The process of obtaining informed consent is outlined in the IWK's Policy #580: *Consent for Autopsy*; an example of a consent form is provided in Appendix A.

STANDARD INVESTIGATIONS

The following investigations are indicated for <u>ALL</u> intrauterine fetal deaths; these may be modified in accordance with the parent's preferences.

More specific details are provided in the text following this table

Timing	Category	Investigation
All IUFDs (Antepartum)	Basic	Previous OBS history Current pregnancy Review of antenatal investigations including u/s Maternal/paternal family and personal history
	Counseling parents	Include value of autopsy, placental examination, and genetic analysis
	Maternal	Ultrasound (see details below) Kleihauer-Betke CBC including platelets
All IUFDs (Postpartum)	Infant	External examination Offer autopsy (complete, imaging, or selective) and obtain consent Obtain with consent: cord blood or other fetal tissue for genetic analysis (if no consent for antepartum collection, or unable to obtain; consult genetics for guidance)
	Placenta	Meticulous examination by perinatal pathologist, including: • Cord: thrombosis and true knot • Placenta: infarcts, calcifications, thrombosis, hematoma, abruption (clot), and vascular malformation • Signs of subclinical infection, funisitis, and amnionitis: Histology is warranted, as are bacterial cultures of the chorion and fetal surface of the placenta.

When results are available for all investigations	Health Care Team: Multidisciplinary review using site-specific Quality Assurance process to evaluate factors contributing to fetal demise. Follow-up: Investigation findings should be reviewed with the mother's Primary Care Provider, who will review these in turn with the mother and appropriate family members.

Maternal Investigations:

- **Ultrasound (for IUFD)**
  - When fetal death is suspected, an ultrasound (u/s) examination should be undertaken to confirm the diagnosis and to determine fetal presentation. Further management will depend on these findings. Additional u/s assessment may be difficult, based on length of fetal demise and resources available locally.
- **Thorough history includes:**
  - Obstetric history of
    - recurrent miscarriages;
    - previous child with anomaly, hereditary condition, or growth restriction;
    - previous gestational hypertension or preeclampsia;
    - previous gestational diabetes mellitus (GDM);
    - previous placental abruption; or
    - previous fetal demise.
  - Current pregnancy:
    - maternal age;
    - gestational age at fetal death;
    - co-morbidities: i.e. hypertension, GDM, cholestasis;
    - pre-pregnancy BMI and gestational weight gain;
    - complications of multifetal gestation (i.e. twin-twin transfusion syndrome, twin reversed arterial perfusion syndrome, and discordant growth);
    - placental abruption;
    - maternal-fetal haemorrhage;
    - abdominal trauma;
    - preterm labour or rupture of membranes;
    - gestational age at onset of prenatal care;
    - congenital malformations; or
    - infections including chorioamnionitis.
  - Family history of
    - recurrent spontaneous abortions;
    - venous thromboembolism (VTE) or pulmonary embolism (PE);
    - congenital anomaly or abnormal karyotype;
    - hereditary condition or syndrome;
    - developmental delay;
    - child with dysmorphic features; or
    - consanguinity.

- Maternal medical history of
  - VTE or PE;
  - diabetes mellitus;
  - chronic hypertension;
  - antiphospholipid syndrome;
  - thrombophilia;
  - Systemic Lupus Erythematosus (SLE) or other autoimmune diseases;
  - epilepsy;
  - severe anaemia;
  - consanguinity;
  - heart disease or other chronic medical conditions (e.g. renal disease) ; or
  - tobacco, alcohol, drug or medication use/misuse.

- **Laboratory testing**
  - Complete Blood Count (CBC) including platelets (if not drawn recently)
  - Kleihauer-Betke test (regardless of Rh status)

Infant Investigations:

- **External Examination**
  - Document complete examination including morphologic abnormalities on maternal health record
  - Document birth weight and placenta weight on maternal health record
  - Obtain consent to take photographs (+/- imaging autopsy – see specifics below)
- **Autopsy**

  An autopsy is one of the most useful steps in determining the cause of fetal death; when performed by experienced perinatal pathologists, it is useful in identifying potential causes of death in 42.4% of cases (SOGC 2020).
  - Obtain informed consent for complete, imaging, or selective autopsy
  - Neuropathologic exam should be requested if indicated by history or prenatal ultrasound findings. In this case, ensure parents understand that complete examination requires the brain to be kept for a few weeks or months, after which it is cremated.
  - If complete autopsy is declined → discuss imaging or selective autopsy
  - If all autopsy options are declined → obtain consent to take photographs (digital images/photos - taken by pathology) and Diagnostic Imaging (X-ray, computed tomography scan, or magnetic resonance imaging, if available).
- **Sex Determination**

  If the genital sex is not clear and the parents do not wish for post-mortem testing in any form, they might wish to judge the sex themselves for registration purposes, perhaps based on an earlier scan, or ask the midwife or doctor to make a judgment. Other parents might choose to not determine a sex for the baby and give a neutral name. Stillborn babies can be registered as having indeterminate sex.

Placental Investigation:

- **Examination of Placenta**
  - For all IUFDs, the placenta and umbilical cord should be examined manually then routinely sent to perinatal pathology for clinical examination.

SELECTIVE INVESTIGATIONS

This suggested list may be modified when a specific cause of IUFD or stillbirth is obvious, or in accordance with the parent's preferences.

Condition present (known or suspected)	Category	Investigation
Congenital anomalies	Cerebral anomalies	MRI or neuropathologic exam (consent required)
	Other congenital anomalies	Radiography or MRI as indicated (consent required) Fetal/cord genetic testing (karyotype, QF-PCR, or microarray – consult with Maritime Medical Genetics)
Maternal Disease	Hypertension	CBC + reticulocyte count AST ALT LDH Uric Acid Urine protein CRPs Bile salts
	Thyroid disease	TSH Free T4
	Diabetes (known or suspected due to family history, maternal obesity, glucosuria, polyhydramnios, or fetal macrosomia)	Hb A1C Fasting glucose Random glucose OGTT 75 grams
	Suspected substance use	Toxicology screen (consent required)
Maternal and/or Fetal Infection	Swabs for culture (as appropriate)	Maternal vaginal-rectal swabs Fetal swabs Placental swabs
	Maternal serology (as appropriate)	Toxoplasmosis Rubella Cytomegalovirus (CMV) Syphilis Parvovirus B19

Condition present (known or suspected)	Category	Investigation
Maternal and/or Fetal Infection (continued)	Fetal blood	Cord or cardiac blood for C&S
Inherited Thrombophilia • family history of hereditary thrombophilia, or • maternal history of DVT, or • evidence of fetal growth restriction or placental disease	Tests which may be completed based on clinical presentation	Factor V Leiden mutation Prothrombin Gene mutation MTHFR mutation
	Tests to be ordered 6-8 weeks postpartum (Prearrange prior to discharge)	FVIII Antithrombin Protein C Protein S Thrombin Time Plasma homocysteine Serum homocysteine (fasting)
Acquired Thrombophilia • fetal growth restriction, or • autoimmune disease	Antiphospholipid Syndrome	Lupus anticoagulant Anticardiolipin antibody Anti-beta2 glycoprotein 1 antibody
	Autoimmune disease	Anti-nuclear antibodies
Fetal Hydrops	Consider consult to Maritime Medical Genetics for non-immune hydrops	
	Maternal blood	Blood type & antibody screen Haemoglobin electrophoresis Parvovirus B19IgM Toxoplasmosis IgM Rubella IgM (*if mother non-immune)
	Amniotic fluid	Metabolic disease testing
	Fetal or Cord Blood	Blood type Haemoglobin electrophoresis CBC, differential, reticulocyte count
Neonatal Allo-Immune Thrombocytopenia (NAIT)	Fetal	CBC, differential, reticulocyte count
	Maternal, Paternal, & cord/fetal blood	NAIT Investigation ***consult with IWK Blood transfusion service for collection instructions**

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APPENDIX A: EXAMPLE - AUTOPSY CONSENT FORM

Consent for Autopsy

Appendix E:
Consent for Autopsy

Consent for Autopsy

I, _____, being allowed by law to consent, hereby allow the pathologists of the IWK Health Centre to perform an autopsy upon:

_____ _____ _____
(Last name of patient) (First name) (Middle name)

The autopsy procedure has been explained to me by _____ in terms that I fully understand. I have been given an opportunity to read the **Autopsy Information Sheet** and have received answers to any questions I asked. I may withdraw or change this consent before the autopsy has taken place.

Having considered the following options for autopsy, I authorize one of the following with a checkmark (✔)
***Each option may require diagnostic imaging and digital images, and may include tissue sampling for genetic testing.**

❑ **Complete Autopsy (Includes a Neuropathologic Exam)**	❑ **General Autopsy (Excludes a Neuropathologic Exam)**	❑ **Directed Autopsy (Organ Specific)**
A complete autopsy includes a Neuropathologic Exam providing detailed information about the brain and spinal cord. I understand this would require the tissues of the brain/spinal cord be kept until the exam is completed.	A general autopsy does not include a Neuropathologic Exam but does include detailed examination of the rest of the body.	Which I understand will give detailed information about the specific organ(s) being examined. **Please list organs:** _____ _____

Other Instructions_____
_____
_____
_____ *(Initials)* _____

After the autopsy process is complete: (Please Circle)

1. Return all organs examined with the body (excluding brain and/or spinal cord in the case of Complete Autopsy. **If no, see below**) Yes No

   - Keep organ(s)/tissue samples until examination(s) are complete for:
     (a) future diagnosis or determination of risk to my family Yes No
     (b) medical education (sample(s) will be non-identifiable) Yes No
     (c) research purposes (sample(s) will be non-identifiable) Yes No

2. Use digital images for medical education. The remains will not be identifiable. Yes No

For any organ(s)/tissues that are kept, the IWK will provide common cremation and burial at the IWK Memorial Site.

Please send final autopsy report to: Dr(s)/NP(s): _____

_____

_____ _____ _____ _____
(Time) (Day/month/year) (Signature of person allowed to consent) (Print name & relationship of person allowed to consent)

_____ _____ _____ _____
(Time) (Day/month/year) (Signature, print name and designation of person getting consent)

_____ _____ _____ _____
(Time) (Day/month/year) (Signature, print name & designation of witness to telephone consent)

_____ _____ _____ _____
(Time) (Day/month/year) (Signature, print name of pathologist reviewing the terms of the consent)

This is a CONTROLLED document for internal use only. Any documents appearing in paper form are not controlled and should be checked against the server file version prior to use.