South Australian Perinatal Practice Guideline

Stillbirth Investigations

Note:

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

Note: The words woman/women/mother/she/her have been used throughout this guideline as most pregnant and birthing people identify with their birth sex. However, for the purpose of this guideline, these terms include people who do not identify as women or mothers, including those with a non-binary identity. All clinicians should ask the pregnant person what their preferred term is and ensure this is communicated to the healthcare team.

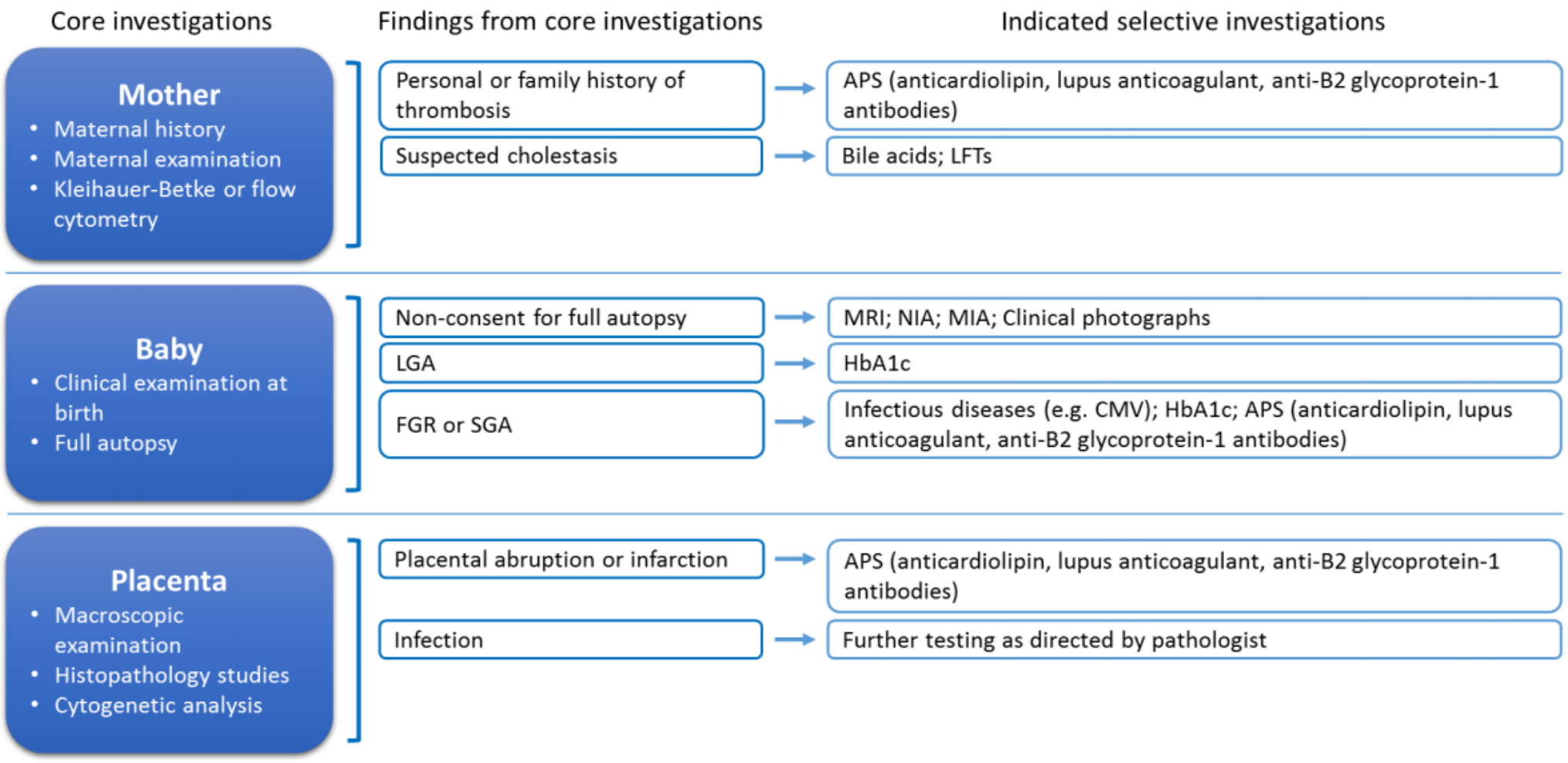
Explanation of the Aboriginal artwork:
The Aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the Aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant woman. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.

Australian Aboriginal Culture is the oldest living culture in the world yet Aboriginal people continue to experience the poorest health outcomes when compared to non-Aboriginal Australians. In South Australia, Aboriginal women are 2-5 times more likely to die in childbirth and their babies are 2-3 times more likely to be of low birth weight. The accumulative effects of stress, low socio economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Despite these unacceptable statistics the birth of an Aboriginal baby is a celebration of life and an important cultural event bringing family together in celebration, obligation and responsibility. The diversity between Aboriginal cultures, language and practices differ greatly and so it is imperative that perinatal services prepare to respectfully manage Aboriginal protocol and provide a culturally positive health care experience for Aboriginal people to ensure the best maternal, neonatal and child health outcomes.

Purpose and Scope of Perinatal Practice Guideline (PPG)

The purpose of this guideline is to describe core investigations that should be undertaken for all stillbirths and additional selective investigations recommended based on core investigations.

Flowchart: Stillbirths Investigation Algorithm (reproduced with permission from PSANZ[1])



APS: Antiphospholipid syndrome; CMA: Chromosomal microarray; CMV: Cytomegalovirus; FGR: Fetal growth restriction; LFTs: Liver Function Tests; LGA: Large-for gestational-age; HbA1c: Haemoglobin A1c; MIA: Minimally-invasive autopsy; MRI: Magnetic Resonance Imaging; NIA: Non-invasive autopsy; SGA: Small for gestational age.

Figure 1: Stillbirth investigations algorithm

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Summary of Practice Recommendations

Core investigations should be considered routine for all stillbirths.

Additional selective investigations should be considered based on core investigations including maternal history.

Clinicians should discuss the value of a full autopsy with parents unless the cause of death is already known.

Some pregnancy investigations clearly negate the need for certain tests but should be assessed on an individual basis.

Depending on individual circumstances and preferences it may not be possible to undertake certain investigations. Consideration of limited testing (including autopsy options) should be discussed with parents.

Clinicians should use their judgement so that all investigations are undertaken around the time of the birth wherever possible.

All investigations should be discussed with a senior clinician to assist with decision-making prior to ordering selective investigations.

Abbreviations

CMA	Chromosomal microarray
CMV	Cytomegalovirus
FACS	Fluorescence-Activated Cell Sorting
FGR	Fetal growth restriction
g	Gram(s)
IUGR	Intrauterine growth restriction
LGA	Large for gestational age
MIA	Minimally invasive autopsy
NIA	Non-invasive autopsy
PPG	Perinatal Practice Guideline
PSANZ	Perinatal Society of Australia and New Zealand
SGA	Small for gestational age

Definitions

Stillbirth	A stillborn baby is at least 20 weeks gestation or, if it cannot be reliably established whether the period of gestation is more or less than 20 weeks, with a body mass of at least 400 grams at birth, that exhibits no sign of respiration or heartbeat, or other sign of life, after birth but does not include the product of a procedure for the termination of a pregnancy.

Introduction

This guideline is adapted with permission from the *PSANZ Clinical Practice Guideline for Care Around Stillbirth and Neonatal Death, Chapter 5 – Investigations for Stillbirth*.[1]

Approximately 75% of the overall perinatal mortality in South Australia is related to stillbirths. Over the past several years approximately 11% of stillbirths had no cause identified, possibly, in part due to the lack of a systematic and up-to-date approach to the investigation of stillbirths for which there is no immediate obvious cause.

Previously several investigations were recommended for all cases of stillbirth, however a number of these are now recommended as selective investigations only. The 'Stillbirth investigations algorithm' summarises the recommended core investigations for all stillbirths, and further selective investigations to be undertaken based on the findings from the core investigations. All women, but in particular,

Aboriginal women should be consulted about any decisions in the first instance.

Aboriginal people experience very high levels of Grief and Loss in their communities. Stillbirth demands ceremonial acknowledgement. Discuss with the Aboriginal Health Professional

Core Investigations to be performed in All Cases of Stillbirth

The following outlines the current investigations recommended routinely for the majority of stillbirths (core investigations) in South Australia (unless the cause of death has been unequivocally determined in pregnancy).

Maternal History

- Medical
- Pregnancy
- Family
- Social

Maternal blood

Kleihauer-Betke test at SA Pathology (preferably prior to birth). If positive, Fluorescence-Activated Cell Sorting (FACS, a type of flow cytometry) to quantify the fetomaternal haemorrhage should also be undertaken.

External examination of the baby

External examination of the baby by the attending clinician should be undertaken as soon as possible after birth and documented in the medical record.

Appendix D – Clinical Examination of Baby Checklist of the *PSANZ Clinical Practice Guideline for Care Around Stillbirth and Neonatal Death*[1] available at URL https://sanda.psanz.com.au/clinical-practice/clinical-guidelines/ is a useful guide that can be printed and used by clinicians.

Where consent for autopsy has been given, the information gained along with maternal history should be forwarded to the State Perinatal Autopsy Service.

Autopsy

Clinicians should discuss the value of a full autopsy with parents unless the cause of death is already known. With parental consent, autopsy should be conducted by the State Perinatal Autopsy Service.

Please refer to the *Perinatal Loss* PPG available at www.sahealth.sa.gov.au/perinatal for further details relating to autopsy, including purpose of autopsy, gaining consent, forms to complete and transport requirements.

The booklet, *When a person dies: The Hospital Autopsy Process. Information for family and friends* should be given to the parents to read before any request for autopsy consent from the medical officer.

Appendix N – Information for Health Professionals Seeking Consent of the *PSANZ Clinical Practice Guideline for Care Around Stillbirth and Neonatal Death*[1] available at URL https://sanda.psanz.com.au/clinical-practice/clinical-guidelines/ provides useful information on how to approach obtaining consent for autopsy.

If the parents decline a full autopsy:

- A non-invasive autopsy (NIA) or minimally-invasive autopsy (MIA) should be offered:
  - Please contact the SA Perinatal Autopsy Service for detail of available options to discuss with parents
- Parents should be asked for their consent to have a detailed external examination by a perinatal pathologist. If this is not possible, a neonatologist, paediatrician or clinical geneticist should conduct the examination and take clinical photographs.[1]
- Clinical photographs (in addition to mementos) should also be undertaken with consent. *Appendix H – Instructions on Taking Clinical Photographs* of the *PSANZ Clinical Practice Guideline for Care Around Stillbirth and Neonatal Death*[1] available at URL https://sanda.psanz.com.au/clinical-practice/clinical-guidelines/ provides further guidance.
- X-ray if skeletal dysplasia suspected
- Magnetic resonance imaging (MRI) where available

Placental and Cord Investigations

Examination of the placenta and cord by the attending clinician should be undertaken and documented in the medical record. Intramembranous placental swabs should be undertaken for microbiology testing.

Whether or not parents' consent to autopsy, the placenta, membranes and cord should be forwarded to the State Perinatal Autopsy Service following maternal consent. They should be placed in a dry sterile container (no formalin or saline) with the container surrounded in ice for transport.

See *Histopathology Management of the Placenta* PPG available at www.sahealth.sa.gov.au/perinatal for details of gross placental examination, placental swabbing and standardised clinical information to include.

If consent for histopathology of the placenta is declined, sampling of placental and cord tissue for karyotyping should be undertaken by the attending clinician following maternal consent, regardless of whether a prenatal karyotype was obtained.[1]

Cytogenetic Investigations

Chromosome microarray (CMA) is superior to standard culture karyotyping and should be undertaken for all stillbirths where the cause is unknown, even if standard karyotyping was undertaken prenatally.

Both fetal and placental tissue should undergo CMA.

Where a specific phenotype is suspected based on family history or examination of the fetus, women should be referred to a clinical geneticist with consideration for additional targeted / extended genetic testing.

Storage of samples

Storage of placental and fetal DNA, blood and amniotic fluid allows for future testing for other potential factors that are not currently identified.[1(p12)]

Consent is required for storage of human samples. Consideration should also be given to an agreed and documented timeframe for storage (e.g. until end of woman's anticipated reproductive age where future testing results may affect pregnancy management).

Selective Investigations based on findings of Core Investigations

The need for additional selective investigations may only become apparent following initial assessment of the stillborn baby and/or at autopsy. Clinicians should use their judgement so that all investigations are undertaken around the time of the birth wherever possible, to avoid the need for multiple follow-up appointments.

Congenital Infections

Routine testing of all stillbirths for infection is no longer recommended. Specific testing to be performed as indicated below:

Cytomegalovirus (CMV)

Consider maternal CMV serology in the presence of the following:

- Placental histopathology shows evidence of infection
- Baby is small for gestational age (SGA)
- Ultrasound shows features suggestive of CMV

Toxoplasmosis

Consider maternal toxoplasmosis serology for women who experienced symptoms of acute toxoplasmosis infection (malaise, fever, lymphadenopathy) during pregnancy.

Parvovirus

Maternal parvovirus serology is recommended when antenatal ultrasound or autopsy finds:

- Severe fetal anaemia
- Non-immune hydrops fetalis
- Fetal cardiomyopathy

Rubella

Testing is usually undertaken as part of routine antenatal screening. Only undertake maternal serology for rubella in the following circumstances:

- Antenatal screening indicated the woman is non-immune or was not undertaken AND the woman experienced clinical features of rubella infection during pregnancy (e.g. fever, transient erythematous rash, lymphadenopathy, arthralgia)
- Autopsy finds features consistent with rubella infection (e.g. IUGR, short stature, cardiac anomalies, inflammatory lesions of the brain, lungs, liver and/or bone marrow)

Syphilis

Testing is usually undertaken as part of routine antenatal screening, with additional screening for women in high risk communities. Only undertake maternal serology for syphilis if there was inadequate antenatal screening. See *Syphilis in Pregnancy* PPG for screening requirements (available at www.sahealth.sa.gov.au/perinatal).

Maternal Blood – Other Investigations

Blood group and antibody screen

If baby is:

- Anaemic
- Jaundiced
- Hydropic

Thrombophilia testing

- Antiphospholipid Syndrome (anticardiolipin, lupus anticoagulant and anti-B2 glycoprotein-1 antibodies) if one or more of the following:
  - Family history of thrombosis
  - Personal history of venous thrombosis
  - Fetal growth restriction
  - Placental abruption
  - Placental infarction
- Prothrombin G20210A mutation and Factor V Leiden mutation if:
  - There are multiple factors from the list above or other clinical suspicion that thrombophilia may have been a factor in the stillbirth

Haemoglobin A1c (HbA1c)

If baby is:

- Small for gestational age (< 10th centile)
- Intrauterine growth restricted
- Large for gestational age (> 90th centile)
- Polyhydramnios is an unexplained feature of the pregnancy

Thyroid function test

Is not recommended in clinically euthyroid women.

Liver function tests and non-fasting bile acids

Recommended if there is a clinical suspicion of intrahepatic cholestasis of pregnancy and/or history of maternal pruritus.

Drug screen

Recommended if there is a suspicion of or known maternal drug use.

Termination of pregnancy for fetal abnormalities

In cases where a termination of pregnancy has been carried out for fetal malformation, an autopsy may still be desirable to confirm the diagnosis or discover unexpected associated anomalies.

Reference

1. Flenady V, Oats J, Gardener G, Masson Vicki, McCowan Lesley, Kent A, Tudehope David, Middleton P, Donnolley N, Boyle F, Horey D, Ellwood D, Gordon A, Sinclair L, Humphrey M, Zuccollo J, Dahlstrom J,Mahomed K,Henry S, Khong Y for the PSANZ Care around the time of stillbirth and neonatal death guidelines group. Clinical Practice Guideline for Care Around Stillbirth and Neonatal Death. Version 3.2, Section 5 – Investigations for Stillbirth. NHMRC Centre of Research Excellence in Stillbirth. Brisbane, Australia, December 2019. Available at https://sanda.psanz.com.au/clinical-practice/clinical-guidelines/

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