South Australian Perinatal Practice Guidelines

Investigation of stillbirths (SA Protocol)

Introduction

- About 75% of the overall perinatal mortality in South Australia is related to stillbirths. In 2009, 11.1% 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. Currently protocols for investigating such cases vary markedly between hospitals and generally have not kept pace with advances in obstetric knowledge, particularly in the area of vasculopathy.
- It is important that clinicians initiate a comprehensive approach to all cases of stillbirth; however, as in all aspects of clinical medicine **common sense should prevail**. In order to adequately assess causative and contributing factors in cases of stillbirth, certain investigations will be required in all cases, while others can be directed to discovering underlying factors for an obvious cause of death. Lastly, some investigations are best suited to those cases in which no cause of death is apparent. The following protocol attempts to provide a logical approach to each of these areas.

Core investigations

(To be performed in all cases of stillbirth):

- **A detailed history and examination of the mother** along with a careful review of the antenatal record can often provide clues to intercurrent infection, previously undiagnosed preeclampsia, drug use or intra-hepatic cholestasis of pregnancy.
- **Autopsy of the stillbirth.** With parental consent, autopsy should be conducted by the State Perinatal Autopsy Service. In those cases where parents give full consent with regard to autopsy, the perinatal pathologists will take appropriate samples for karyotyping. In those cases there is therefore no need for the obstetrician to take separate fetal samples.
- **Guthrie card.** Where permission for an autopsy has been declined, parents should be asked if blood can be taken for the Newborn Screening Guthrie Card that is requested for all babies in Australia. This blood could be drawn from a heel prick or from the cut end of the umbilical cord of the placenta in case of a fresh stillbirth (< 7 days between intrauterine death and birth).
- **Histopathology of placenta.** Whether or not an autopsy is performed the placenta should be placed in a dry sterile container (no formalin or saline), the container surrounded in ice and forwarded to the State Perinatal Autopsy Service. Histopathological examination combined with other investigations can provide a diagnosis for a current pregnancy and information that can be helpful in planning another pregnancy.
- **Maternal blood** should be tested for fetomaternal haemorrhage with a Kleihauer test at SA Pathology and, if positive Fluorescence-Activated Cell Sorting (FACS, a type of flow cytometry) to quantify the fetomaternal haemorrhage.
- **External examination of the baby.** In cases where parental consent for autopsy cannot be obtained, external examination of the baby by a pathologist experienced in this area, where possible, should be sought. If this is not possible an **X-ray of the baby** and / or a **clinical photograph** should be taken and sent to a major centre for review.

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Contact: South Australian Perinatal Practice Guidelines workgroup at:
cywhs.perinatalprotocol@health.sa.gov.au

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Genetic termination of pregnancy

- 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 malformations.

Congenital anomaly

Investigations to be performed when an intrauterine fetal death occurs in conjunction with a known fetal abnormality:

- Karyotype - preferably on amniotic fluid obtained by amniocentesis since this provides the least contaminated sample, but if maternal consent for this cannot be obtained then on cord blood (if obtainable) or fetal skin. The sample should be obtained, but karyotyping should only proceed if an anomaly which is indicative of a chromosomal abnormality is found at birth or autopsy.
- Maternal serology for syphilis, CMV, Toxoplasma and Parvovirus. Serum should be taken and forwarded with the baby. Investigation for congenital infection should be pursued if anomalies indicative of infection are found (for example, hydrocephalus, hepatomegaly, cataracts, foetal hydrops, calcification of brain or placenta).
- Maternal screen for Blood Group antibodies - serum forwarded with baby for later investigation if hydrops is evident at autopsy.

Placental vasculopathies

Preeclampsia, placental abruption and intrauterine growth restriction.

All should have a thrombophilia screen comprising –

1. At time of delivery:
   - Anti-cardiolipin antibody] *diagnosis of antiphopholipids requires*
   - Lupus anticoagulant] *at least 2 positive tests*
   - Factor V Leiden, prothrombin gene
   - MTHFR 677 CT, 1298 AC

2. At three months post-partum:
   - Homocysteine - may be done earlier if follow-up uncertain.
   - Protein S (A formal diagnosis of protein S deficiency requires 2 abnormal results)

Pre-eclampsia

Those with early onset pre-eclampsia (< 28 weeks) should also have

- Anti-nuclear antibody
- Fetal karyotype (see “Congenital anomaly”)

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Placental abruption:

- In cases of **placental abruption** a history of trauma, including domestic or other violence, should be sought.
- Testing for fetomaternal haemorrhage and D-dimer's is indicated if the diagnosis is in doubt

Intrauterine growth restriction (IUGR):

Where **intrauterine growth restriction** is evident without further evidence of a vasculopathy, the following should be performed in addition to the thrombophilia screen:

- Maternal serology for CMV, Toxoplasma and Rubella (if not immune) on held maternal serum (see "Core investigations ")
- Fetal karyotype (see "Congenital anomaly")
- Maternal urinary drug screen as well as a drug related history

Intrapartum stillbirths

- If associated with preeclampsia, IUGR, and/or abruption – placental vasculopathy protocol
- In the absence of obvious causes; test for fetomaternal haemorrhage and cord (or heart) blood for Hb, platelets and nucleated red blood cells

Unexplained stillbirths

In the absence of discernible factors pertaining to fetal demise, or any obvious congenital anomaly, in addition to the "Core investigations": -

- Maternal serum bile acids - cord blood bile acids if possible
- Maternal serum glucose
- Thrombophilia screen (see above)
- Maternal thyroid stimulating hormone
- Maternal serology - syphilis, CMV, Toxoplasma, Herpes, Parvovirus
- Microbiology - fetal throat swab, placental intermembranous swab
- Drug history and urine drug screen
- Cord or heart blood - haemoglobin, platelets, nucleated red blood cells, blood group (for anti-D if mother is Rhesus negative).
- Maternal antibody screen.
- Fetal-maternal haemorrhage testing
- Check mother's history for possibility of tropic infectious disorders – in case of recent visit to tropical areas contact infectious disease specialist with regard to required samples

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Abbreviations

g	Gram/s
CMV	Cytomegalovirus
FACS	Fluorescence-Activated Cell Sorting
IUGR	Intrauterine growth restriction

Version control and change history

PDS reference: OCE use only

Version	Date from	Date to	Amendment
1.0	18 Sept 12	current	Original version

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