

APPENDIX 8

South Australian Protocol for investigation of stillbirths

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Introduction

The perinatal mortality rate for South Australia in 2005 of 3.7 deaths per 1,000 births for infants of at least 1,000g birthweight or 28 weeks gestation is low by international standards. The rate for infants of at least 400g birthweight or 20 weeks gestation was 10.6 deaths per 1,000 births that year. Sixty-seven percent of these perinatal deaths were stillbirths. The Perinatal Subcommittee of the South Australian Maternal, Perinatal and Infant Mortality Committee seeks, amongst other roles, to identify patterns and avoidable factors in perinatal deaths within the state. In 2005, 12% 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 vasculopathies.

A working party was set up in 1997 by the Perinatal Subcommittee to address this issue. It is hoped that the result will facilitate a more systematic and uniform approach to the investigation of stillbirths, resulting not only in a greater understanding of the demographics and underlying pathology, but the possibility of more accurate diagnosis and counselling, and potentially a reduction in recurrences.

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 pre-eclampsia, 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.
- **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.
- **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 drawn for a Kleihauer test and sent along with a sample of maternal serum with the placenta with or without the baby. A slide for Kleihauer will be prepared but only examined if required.
- **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.

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, Herpes 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, calcification of brain or placenta).

- Maternal antibody screen - serum forwarded with baby for later investigation if hydrops is evident at autopsy.

Vasculopathies

Pre-eclampsia/hypertension, placental abruption and intrauterine growth restriction.

All should have a thrombophilia screen comprising -

1. At time of delivery:
 - Anti-cardiolipin antibody.
 - Lupus anticoagulant.
 - Activated Protein C Resistance.
2. At three months post-partum:
 - Activated Protein C Resistance if previous result low or borderline (<2.5).
 - Homocysteine - may be done earlier if follow-up uncertain.
 - Protein S.

Pre-eclampsia or non-proteinuric hypertension

Attention is drawn to those investigations for monitoring maternal welfare published by the Australasian Society for the Study of Hypertension in Pregnancy.¹⁶

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

- Anti-nuclear antibody
- Fetal karyotype (see "Congenital anomaly")

In cases of **placental abruption** a history of trauma, including domestic or other violence, should be sought. The Kleihauer slide (see "Core investigations") should be examined if the diagnosis is in doubt and in all Rhesus negative women to determine the required dose of anti-D.

¹⁶ Brown MA, Hague WM, Higgins J, Lowe S, McGowan L, Oats J, Peek MJ, Rowan JA, Walters BNJ. Consensus Statement. The detection, investigation and management of hypertension in pregnancy. Aust NZ J Obstet Gynaecol 2000;40:133-138.

Where **intrauterine growth restriction** is evident without further evidence of a vasculopathy (hypertension, abruption), 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 deaths which are associated with hypertension, abruption or intrauterine growth restriction should be investigated as such, but in the absence of these and when the fetus is over 1,000g: -

- Kleihauer slide examined (See "Core investigations")
- Cord (or heart) blood (haemoglobin, platelets, 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 "Vasculopathies").
- 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 Rhesus negative).
- Maternal antibody screen.
- Kleihauer slide examined.