Stillbirth and perinatal death

After stillbirth, what next?

Management of the subsequent pregnancy after an unexplained stillbirth.

Stillbirth is, sadly, a common outcome of pregnancy and across the world more than two-and-a-half million babies are stillborn in the third trimester every year.1 Although record keeping is limited in many parts of the world, it is likely that about 98 per cent of these deaths occur in low- and middle-income countries. However, the rate of stillbirth in Australia is 7.4 per 1000 births and 2206 stillbirths were recorded in 2010.2 In Australia, the risk of stillbirth is highest in women under 20 years of age and women 40 years or more; for Indigenous women it is more than twice as likely than for non-Indigenous women.3

Careful investigation to determine the causes of a stillbirth is important, since knowledge of the aetiology of fetal death may allow informed counselling about risks women and their babies may face in subsequent pregnancy and planning of management strategies.4,5 Unfortunately, no cause for a stillbirth can be found in as many as one-third of cases where the fetal death has occurred antenatally.2 This distressing situation is usually referred to as ‘unexplained stillbirth’ or, in the PSANZ classification, ‘unexplained antepartum death’. In the strict sense, stillbirth should only be classified as ‘unexplained’ if a thorough investigation has failed to yield a likely cause. However, for various reasons, investigation of antepartum fetal death is incomplete in many cases, and the term ‘unexplored’ stillbirth is probably more appropriate.6

When perinatal deaths are classified using the PSANZ perinatal death classification (PDC), unexplained stillbirth accounts for almost 16 per cent of all perinatal deaths and is the largest single diagnostic category after congenital abnormalities and early preterm births are excluded.2 Unexplained stillbirth remains an enigma. A number of large studies have identified risk factors for this condition (see Box 1), yet extensive efforts over many years have not been associated with reductions in the rate of unexplained stillbirth. Many of the risk factors for unexplained stillbirth are difficult to modify: lower socioeconomic status, increased maternal age and Indigenous status, for example. Risk factors such as maternal obesity, smoking and diabetes are routinely addressed during antenatal care and have been for many years. Since the rate of stillbirth does not seem to be falling, a common issue facing providers of maternity care in this setting is how to manage the next and subsequent pregnancies after a woman and her family experience an unexplained fetal death.

Overall, the odds ratio for recurrence of stillbirths from all causes is almost five’, but studies of pregnancy outcomes subsequent to truly unexplained stillbirth have not reported any significant increase in the adjusted risk of perinatal death compared to women who have not suffered a stillbirth.6,7 These statistics should provide reassurance for women and their families. However, those studies did find that pregnancy after stillbirth is characterised by increased rates of induced labour; elective and emergency caesarean section; and adverse pregnancy outcomes such as preterm birth and low birthweight. Changes in the timing and mode of delivery may be an example of a phenomenon known as the Hawthorne effect: when a severe adverse outcome (such as stillbirth) occurs, clinicians will be exceptionally cautious in the next pregnancy, usually maintaining intense surveillance and demonstrating a low threshold to intervene. The management of subsequent pregnancies is often very different and it can be difficult to compare this with management of the first pregnancy.

An Australian study of women who have suffered an unexplained stillbirth found that they want high levels of surveillance and early delivery in their next pregnancy.13 Although early delivery would be expected to reduce the rate of stillbirth at a population level, it increases the potential for iatrogenic complications such as prematurity, failed induction, instrumental delivery, emergency caesarean section and postpartum haemorrhage. While these are preferable to intrauterine death, they are still adverse.

Pre-pregnancy care

It is common for women and their partners to try for another pregnancy soon after stillbirth and older studies have found that almost half of such couples are pregnant within six months.14 It is important to recognise that the grief associated with a stillbirth, especially when no explanation for the loss can be provided, is almost unique. The extensive excitement, preparation and

Box 1. Risk factors for unexplained stillbirth

- Increasing maternal age
- Smoking
- Obesity
- Indigenous status
- Socioeconomic disadvantage and lack of access to healthcare resources
- Increasing parity
- Previous growth restriction
- Diabetes, either pre-existing or gestational
- Maternal anaemia
- Fetal long QT-associated mutations
the interest of family and friends, all make the devastation of stillbirth so much worse. For these reasons, timely consultation with the couple before attempting pregnancy again is very important. Pathological grief responses can be difficult to pick and, if there are any concerns, formal assessment of the couple using instruments such as the Spielberger State-Trait Anxiety Inventory might identify those who could benefit from more formal psychological assessment and support.

Many stillbirths that are thought to be ‘unexplained’ are actually incompletely investigated, sometimes because couples found decision-making difficult and did not consent to investigations such as perinatal autopsy. If possible, a careful review of any investigations performed at the time should be undertaken and the couple informed about knowledge gaps and areas of uncertainty. In some cases, enough investigation was done to exclude aetiologies with a risk of recurrence. However, in many cases, the level of investigation makes it impossible to provide an accurate prognosis.

Whatever the previous results have shown, maternal conditions that increase the risk of stillbirth should be identified. These include hypertension, diabetes, thyroid disease, thrombophilia, lupus, blood group antibodies and hyperhomocysteinemia. If any such conditions are identified, they obviously should be stabilised before attempting pregnancy. Very rarely, chronic infectious conditions associated with stillbirth are diagnosed, the commonest being toxoplasmosis, syphilis and, possibly, chlamydia. There is some evidence that periodontal anaerobes might be associated with adverse pregnancy outcomes, including stillbirth, so dental review is advisable. Women in adverse social circumstances can be adverse pregnancy outcomes, including stillbirth, so dental review is advisable. Women in adverse social circumstances can be offered additional social supports, although strict evidence of the effectiveness such interventions is lacking. Obesity and smoking are important modifiable risk factors for adverse outcome in the next pregnancy.

The inter-pregnancy interval may have an effect on prognosis and it is recognised that conception within 12 months of a perinatal loss is associated with increased levels of depression and anxiety. These emotional states have the potential to influence pregnancy outcome, since management of maternal anxiety and depression may reduce the risk of preterm birth and possibly other adverse pregnancy outcomes.

Early pregnancy management

There is little evidence to guide management in early pregnancy after an unexplained stillbirth. However, early ultrasound can be used to establish the gestational age accurately: the most effective intervention for reducing the rate of stillbirth is likely to be timely delivery, once the fetus is mature, probably no later than 39 weeks gestation, especially for older mothers. Induction of labour is often given in many of these pregnancies and adverse outcomes (emergency caesarean section, instrumental delivery and postpartum haemorrhage) are related to either attempted induction at an early gestation or in older age groups. Accurate determination of gestational age with ultrasound as early as possible reduces the risk of inadvertent premature delivery and failed induction.

Abnormal fetal karyotype may have remained undiagnosed even with careful work-up at the time of a stillbirth and failure of cell culture is common when there has been a delay between death and delivery. Fortunately, this situation is becoming less common with the use of DNA microarrays. The commonest conditions associated with fetal death are trisomies 21, 18 and 13, and these may impart an empirical recurrence risk between five and 15 per cent, depending on the age of the woman. Invasive fetal karyotyping increases the risk of pregnancy loss, so careful counselling is required for younger women. Fortunately, the advent of non-invasive prenatal screening (NIPS) using cell-free fetal DNA obtained from a maternal blood specimen, although expensive, may provide a low-risk method of screening where the recurrence risks are higher.

Management in late pregnancy

Many women who have suffered an unexplained stillbirth request ‘increased fetal surveillance’ and ‘early delivery’ in subsequent pregnancy. Such a management plan is commonly made by obstetricians as well. The methods of surveillance commonly undertaken are regular ultrasound for fetal wellbeing, cardiotocography (CTG) and fetal movement surveillance.

Growth restriction is a factor in many stillbirths with failure to identify growth restriction a common factor. Antenatal measurement of symphysis-fundal height, though almost universal, is of limited value in screening for growth restriction. For these reasons, regular ultrasound might be offered, since growth restriction is a final common pathway for many pathological processes. Uterine artery flow measurement by Doppler has been shown to be a useful predictor of stillbirth related to growth restriction up to 32 weeks gestation, but such testing is of limited value in later pregnancy.

Ultrasound estimates of fetal weight may be falsely reassuring. The use of customised centile charts has been found to be a better predictor of fetal growth restriction and stillbirth, but there is no evidence yet that prospective use of such charts reduces the rate of perinatal death in screened populations. Screening of high-risk populations using Doppler cord flow studies is the only strategy associated with a trend toward improvement in perinatal mortality. However, the optimal frequency of such ultrasounds remains uncertain.

Regular CTG testing to establish ‘fetal wellbeing’ is very commonly practised, yet there is scant evidence to support the practice: the only study of CTG surveillance in pregnancy after stillbirth showed no effect on perinatal mortality. On the basis of current evidence, routine CTG testing undertaken as a screening strategy, in the absence of specific clinical concerns such as reduced fetal movement, is unlikely to benefit the woman.

A time-honoured method of fetal surveillance is formal fetal movement charting, commonly aided by ‘kick charts’. This should be no surprise, since many cases of intrauterine fetal deaths are preceded by a decrease in fetal movements, often for up to 24 hours beforehand, and a wide variety of adverse pregnancy outcomes seem to be associated with reduced fetal movements. Unfortunately, the use of ‘kick charts’ in prospective studies has failed to demonstrate any effect on the rate of perinatal mortality. Reduction in fetal movements is a very common symptom, with as many as 15 per cent of pregnant women presenting with it. Guidelines for management of reported changes in frequency of fetal movements are provided by the Australia and New Zealand Stillbirth Alliance.

Delivery

Women will very commonly request early delivery in their next pregnancy after a stillbirth and such management is very commonly undertaken. The risk of stillbirth, using undelivered fetuses as a denominator, increases almost exponentially after 39
weeks gestation. Management and timing of delivery in these circumstances must be individualised. Fortunately, the majority of pregnancies after an unexplained stillbirth will be uncomplicated. Many authors report that the single most important aspect of management of uncomplicated pregnancies after an unexplained stillbirth may be early delivery, usually by 39 weeks, but sometimes earlier. When delivery is delayed beyond this gestation, careful surveillance should be maintained.

The few studies that guide management in pregnancies after unexplained stillbirth leave many questions unanswered and there is thus an urgent need for a large prospective study in this setting. Because unexplained stillbirth is a relatively uncommon outcome, with only about 2000 such losses each year in Australia, and because stillbirth death is so traumatic it is unlikely that controlled trials of antenatal management will ever be undertaken.

Conclusion
Those involved in the care of a couple who have had an unexplained late fetal death commonly find it distressing and challenging. Many couples will try to become pregnant again and will seek guidance on the risks they face and whether anything can be done differently the next time. Careful surveillance and early delivery play an important role in optimising the outcome. Women and their families must be provided with reassurance and support.

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References
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