

ACOG PRACTICE BULLETIN



CLINICAL MANAGEMENT GUIDELINES FOR OBSTETRICIAN–GYNECOLOGISTS

NUMBER 102, MARCH 2009

(Replaces Committee Opinion Number 383, October 2007)

Management of Stillbirth

This Practice Bulletin was developed by the ACOG Committee on Practice Bulletins—Obstetrics with the assistance of Ruth C. Fretts, MD. The information is designed to aid practitioners in making decisions about appropriate obstetric and gynecologic care. These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

Stillbirth is one of the most common adverse pregnancy outcomes, complicating 1 in 160 deliveries in the United States. Approximately 25,000 stillbirths at 20 weeks or greater of gestation are reported annually (1). The purpose of this bulletin is to review the current information on stillbirth, including definitions and management, the evaluation of a stillbirth, and strategies for prevention.

Background

Definition

The United States National Center for Health Statistics defines *fetal death* as the delivery of a fetus showing no signs of life as indicated by the absence of breathing, heart beats, pulsation of the umbilical cord, or definite movements of voluntary muscles (2). There is not complete uniformity among states with regard to birth weight and gestational age criteria for reporting fetal deaths. However, the suggested requirement is to report fetal deaths at 20 weeks or greater of gestation (if the gestational age is known), or a weight greater than or equal to 350 grams if the gestational age is not known (3). The cutoff of 350 grams is the 50th percentile for weight at 20 weeks of gestation.

The term stillbirth is preferred among parent groups, and more recent research efforts have begun using this term in place of fetal death. Therefore, in this document, the term stillbirth is used. It must be emphasized that the criteria for stillbirth do not imply a point of viability and were chosen to facilitate uniform data collection.

In the United States, fetal losses related to terminations of pregnancy for lethal fetal anomalies and inductions of labor for previable premature rupture of membranes are specifically excluded from the stillbirth statistics and are classified as terminations of pregnancy.

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Frequency of Occurrence

In 2004, the stillbirth rate in the United States was 6.2 per 1,000 births, down from 6.4 per 1,000 births in 2002 (1). Since 1990, the rate of early stillbirth (20–27 weeks) has remained stable at approximately 3.2 per 1,000 births, while the rate of late stillbirth (28 weeks or greater) has decreased from 4.3 to 3.1 per 1,000 births.

Risk Factors

In developed countries, the most prevalent risk factors associated with stillbirth are non-Hispanic black race, nulliparity, advanced maternal age, and obesity (see Table 1 for additional risk factors). From a public health perspective, obesity, smoking, and drug and alcohol use are common potentially modifiable risk factors for adverse pregnancy outcome.

Racial Factors

In the United States, Hispanic, Asian, and Native American women, and non-Hispanic white women all have stillbirth rates of less than 6 per 1,000. In contrast, stillbirth rates have been consistently and significantly higher in non-Hispanic black women at a rate of 11.25 per 1,000 (1). The reason for this health care disparity is multifactorial and the subject of ongoing research. Higher rates of stillbirth persist among non-Hispanic black women with adequate prenatal care; this has been attributed to higher rates of diabetes mellitus, hypertension, placental abruption, and premature rupture of membranes (4, 5).

Comorbidities

Hypertension and diabetes are two of the most common medical comorbid pregnancy conditions (6). Population-based studies demonstrated a twofold to fivefold increase in the risk of stillbirth among women with

pregestational diabetes (7, 8). However, with preconception care and optimal glycemic control, the risk of perinatal death may be reduced (9, 10). Patients with a personal history or family history of thromboembolism or multiple inherited or acquired thrombophilias appear to have an increased risk of stillbirth, but there is no evidence that screening an unselected population is either clinically effective or cost-effective (11). Other reported medical risk factors for stillbirth in the United States are described in Table 2.

Obesity

Obesity is defined as a prepregnancy body mass index (BMI) (defined as weight in kilograms divided by height in meters squared) of 30 or greater and is the fastest growing health problem in the United States (12). Obesity in pregnancy is associated with an increased risk of both early fetal loss and stillbirth (13). In a national database, the risk of stillbirth was 5.5/1,000 for nonobese mothers, 8/1,000 for those with a BMI of 30–39.9 and 11/1,000 for women with a BMI greater than 40.0 (14). There is some evidence that the obesity-related stillbirth risk increases with gestational age. In one study, the hazard ratio for stillbirth increased from 2.1 at 28–36 weeks to 4.6 at 40 weeks of gestation (15). The reason for this association is likely multifactorial, but obesity is associated with a fivefold increase in stillbirth associated with placental dysfunction. Obesity remains an independent risk factor for stillbirth even after controlling for smoking, gestational diabetes, and preeclampsia. (16–18).

Multiple Gestations

The stillbirth rate among multiple gestations is four times higher than among singletons (19.6 per 1,000) (19). Higher rates are due both to complications specific to multiple gestation (such as twin–twin transfusion syndrome), as well as

Table 1. Commonly Reported Maternal Risk Factors and Causes for Stillbirth

| Developed Countries | Developing Countries |
|---|---|
| Congenital and karyotypic anomalies | Obstructed and prolonged labor and associated asphyxia, infection, and birth injury |
| Growth restriction and placental abnormalities | Infection especially syphilis and gram-negative infections |
| Medical diseases such as diabetes, systemic lupus erythematosus, renal disease, thyroid disorders, and cholestasis of pregnancy | Hypertensive disease and complications of preeclampsia and eclampsia |
| Hypertensive disease and preeclampsia | Congenital anomalies |
| Infection such as human parvovirus B19, syphilis, streptococcal infection, and listeria | Poor nutritional status |
| Smoking | Malaria |
| Multiple gestation | Sickle cell disease |

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Table 2. Estimates of Maternal Risk Factors and Risk of Stillbirth

| Condition | Prevalence | Estimated rate of stillbirth | OR* |
|--|------------|------------------------------|---------|
| All pregnancies | | 6.4/1000 | 1.0 |
| Low-risk pregnancies | 80% | 4.0–5.5/1000 | 0.86 |
| Hypertensive disorders | | | |
| Chronic hypertension | 6%–10% | 6–25/1000 | 1.5–2.7 |
| Pregnancy-induced hypertension | | | |
| Mild | 5.8%–7.7% | 9–51/1000 | 1.2–4.0 |
| Severe | 1.3%–3.3% | 12–29/1000 | 1.8–4.4 |
| Diabetes | | | |
| Treated with diet | 2.5%–5% | 6–10/1000 | 1.2–2.2 |
| Treated with insulin | 2.4% | 6–35/1000 | 1.7–7.0 |
| SLE | <1% | 40–150/1000 | 6–20 |
| Renal disease | <1% | 15–200/1000 | 2.2–30 |
| Thyroid disorders | 0.2%–2% | 12–20/1000 | 2.2–3.0 |
| Thrombophilia | 1%–5% | 18–40/1000 | 2.8–5.0 |
| Cholestasis of pregnancy | <0.1% | 12–30/1000 | 1.8–4.4 |
| Smoking >10 cigarettes | 10%–20% | 10–15/1000 | 1.7–3.0 |
| Obesity (prepregnancy) | | | |
| BMI 25–29.9 kg/m ² | 21% | 12–15/1000 | 1.9–2.7 |
| BMI >30 | 20% | 13–18/1000 | 2.1–2.8 |
| Low educational attainment (<12 y vs. 12 y+) | 30% | 10–13/1000 | 1.6–2.0 |
| Previous growth-restricted infant (<10%) | 6.7% | 12–30/1000 | 2–4.6 |
| Previous stillbirth | 0.5%–1.0% | 9–20/1000 | 1.4–3.2 |
| Multiple gestation | | | |
| Twins | 2.7% | 12/1000 | 1.0–2.8 |
| Triplets | 0.14% | 34/1000 | 2.8–3.7 |
| Advanced maternal age (reference <35 y) | | | |
| 35–39 y | 15%–18% | 11–14/1000 | 1.8–2.2 |
| 40 y+ | 2% | 11–21/1000 | 1.8–3.3 |
| Black women compared with white women | 15% | 12–14/1000 | 2.0–2.2 |

*OR of the factor present compared to the risk factor absent.

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to increased risks of common complications such as advanced maternal age, fetal abnormalities, and growth restriction.

Maternal Age Older Than 35 years

Older maternal age is associated with an increased risk of stillbirth in both nulliparous and multiparous women (9, 20). A significant proportion of perinatal deaths seen in older women are related to lethal congenital and chromosomal anomalies. The introduction of population-based screening for chromosomal abnormalities has contributed

to lower rates of this type of perinatal demise (21). Large-scale studies suggest that an increased risk of unexplained stillbirth late in pregnancy persists in older women, even after controlling for risk factors such as hypertension, diabetes, placenta previa, and multiple gestation (20, 22, 23). In addition, there appears to be an interaction between first birth and advanced maternal age that places primiparous older women at an increased risk (20). Based on one study, the estimated risk of stillbirth is 1 in 116 in a 40-year-old nulliparous woman after 37 weeks of gestation, compared with 1 in 304 in a multiparous woman of the same age (20).

Past Obstetric History

Women with previous pregnancy complications, such as preterm delivery, growth restriction, or preeclampsia, are at increased risk of stillbirth in subsequent pregnancies (24). The relationship is strongest for explained stillbirth and there also is a persistent 1.7-fold to 2-fold increase in unexplained stillbirth associated with these pregnancy complications. In addition, the risk of subsequent stillbirth is twice as high for women with a prior live born, growth restricted infant delivered before 32 weeks of gestation than for women with a prior stillbirth (25). The relationship between prior cesarean delivery and subsequent stillbirth remains controversial. This association has not been confirmed in three large studies from the United States (26–28). In the largest of these studies, the unexplained fetal death rates at term for women with and without a previous cesarean delivery were 0.8 and 0.7 per 1,000 births, respectively (27). In contrast, in two large studies from the United Kingdom, previous cesarean delivery was associated with an increased rate of explained (29) and unexplained stillbirth (24) with an increased odds ratio of 1.5 for all causes of subsequent stillbirth.

Potential Causes of Stillbirth

The study of specific causes of stillbirth has been hampered by the lack of uniform protocols for evaluating and classifying stillbirths and by decreasing autopsy rates. In most cases, fetal death certificates are filled out before a full postnatal investigation, and amended death certificates are rarely filed when additional information from the stillbirth evaluation emerges. In any specific case, it may be difficult to assign a definite cause to a stillbirth. A significant proportion of stillbirths remain unexplained even after a thorough evaluation (22, 23).

Fetal Growth Restriction

Fetal growth restriction is associated with a significant increase in the risk of stillbirth with the most severely affected fetuses (weight less than the 2.5th percentile) being at the greatest risk (30). The cumulative risk of fetal death is approximately 1.5% at fetal weights less than the 10th percentile, increasing to a risk of 2.5% at less than the 5th percentile for gestational age (31, 32). Fetal growth restriction is associated with some fetal aneuploidies, fetal infection, maternal smoking, hypertension, autoimmune disease, obesity, and diabetes.

Placental Abruption

Placental abruption is another common cause of stillbirth. If abruption occurs in the preterm fetus, it is more likely to cause stillbirth. The rates of abruption appear to be increasing (33). Maternal cocaine and other illicit

drug use, smoking, hypertension, and preeclampsia are all significant contributors to abruption and stillbirth (34–37). Fetomaternal hemorrhage in the absence of placental abruption is a rare cause of stillbirth and occurs mainly in unusual scenarios, such as chorioangioma or choriocarcinoma.

Chromosomal and Genetic Abnormalities

An abnormal karyotype can be found in approximately 8–13% of stillbirths (38–40). The rate of karyotypic abnormalities exceeds 20% in fetuses with anatomic abnormalities or in those with growth restriction, but the rate of chromosomal anomalies found in normally formed fetuses was found to be 4.6% in one large series (40). If an abnormal karyotype is found in association with stillbirth, the most common abnormalities are monosomy X (23%), trisomy 21 (23%), trisomy 18 (21%), and trisomy 13 (8%). Confined placental mosaicism also has been associated with an increased risk of stillbirth, but currently is not part of standard testing (41). Karyotypic analysis underestimates the contribution of genetic abnormalities to stillbirth because in up to 50% of karyotype attempts cell culture is unsuccessful (39). One strategy to increase the yield of cell culture is to perform an amniocentesis before the delivery. This is typically performed after the woman has had an opportunity to process the death of her baby and after an epidural is placed. In a large Dutch study, invasive testing had a much greater tissue culture rate (85%) than fetal tissue sampling after birth (28%) (40). In addition, routine assessments for single gene defects and microdeletions currently are not recommended because of uncertainty of the role of these genetic anomalies. However, it is likely that no single-gene defect is likely to be responsible for a significant proportion of stillbirth. Genetic evaluation for specific abnormalities should be guided by the clinical history and detected fetal abnormalities. Approximately 20% of stillborn fetuses have dysmorphic features or skeletal abnormalities and 15–20% have a major malformation (38, 42).

Infection

In developed countries, most stillbirths related to infection occur in the premature fetus. It has been estimated that infection is implicated in up to 19% of stillbirths at less than 28 weeks of gestation, but only 2% of stillbirths at term (43). There is considerable variation in the reported proportion of stillbirths related to infection due in part to differences in classification methods. Pathogens that are causally associated with stillbirth, include parvovirus, cytomegalovirus, *Listeria monocytogenes*, and syphilis. In the developing world, malaria is a significant preventable cause of stillbirth.

Cord Events

Although many stillbirths are attributed to a cord accident, this diagnosis should be made with caution. Cord abnormalities, including a nuchal cord, are found in approximately 30% of normal births and may be an incidental finding (44). In order to attribute a stillbirth to a cord accident there should be evidence of obstruction or circulatory compromise on umbilical cord examination. In addition, other causes of stillbirth should be excluded.

Management

Sensitivity is needed when discussing evaluation of a stillborn fetus with the family. In discussing options, clinicians should refer to the fetus by name, if one was given. Grief-stricken parents may be reluctant to consent to evaluation or autopsy examination, and some may have religious or cultural objections. Parents should be informed about the reasons for autopsy, procedures (eg, the face usually is not disfigured) and potential costs. Even though the bereaved parents may not want the information initially, health care providers should emphasize that results of the evaluation may be useful to the patient and her family in planning future pregnancies. If the family objects to a standard autopsy, they should be informed of the potential value of less invasive methods of evaluation, including the use of photographs, X-ray imaging, ultrasonography, magnetic resonance imaging, and tissue sampling (blood or skin). These methods may help to identify a syndrome or chromosomal abnormality even without full autopsy data. Syndrome identification may delineate etiologic and pathogenetic factors that could have predictive significance for recurrence risk and the risk of other associated anomalies (45).

After a stillbirth or neonatal death, proper management includes obtaining a complete perinatal and family history, performing a physical examination of the fetus (with documentation by description and photography, if possible), and obtaining laboratory studies (see Fig. 1). To ascertain the etiology and provide appropriate counseling to the family, clinical–pathologic correlation is best accomplished by a team comprising obstetricians, pediatricians or neonatologists, pathologists, and geneticists. Initial evaluation by a geneticist or pathologist may help the team coordinate the evaluation and the needed follow-up.

Clinical Considerations

► What are the essential components of an evaluation of a fetal death?

The most important tests in the evaluation of a stillbirth are fetal autopsy; examination of the placenta, cord, and membranes; and karyotype evaluation. An algorithm for

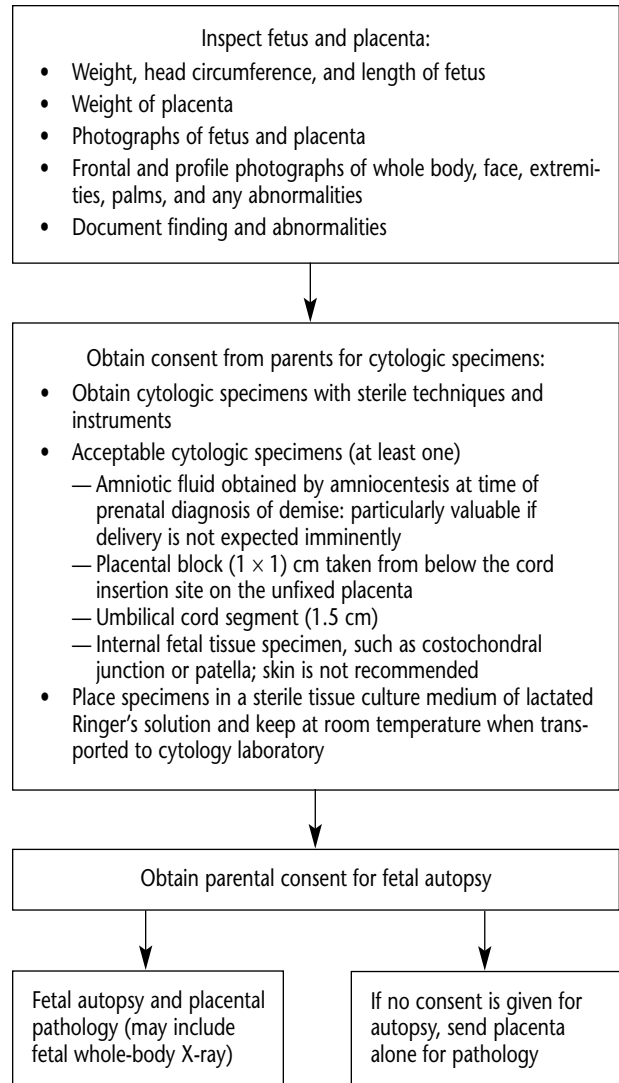


Figure 1. Flow chart for fetal and placental evaluation

evaluation is given in Figure 1. Specific aspects of the evaluation are outlined as follows and in Table 3.

Examination of the Stillborn Fetus

The general examination of the stillborn fetus should be done promptly, noting any dysmorphic features and obtaining measurements of weight, length, and head circumference (46–48). Foot length may be especially useful before 23 weeks of gestation to ascertain gestational age. Photographs of the whole body (unclothed); frontal and profile views of the face, extremities, and palms; and close-up photographs of specific abnormalities are vital for subsequent review and consultation with a specialist, particularly if no geneticist is available at the institution. Even if parents have declined an autopsy, a description of any obvious abnormalities of the stillborn fetus should be

Table 3. Alternatives to a Complete Autopsy

| Examination | Strengths and Limitations |
|---|--|
| Placental examination and external examination by a perinatal pathologist (generally includes measurements of the baby, X-rays, and photographs) | Will be more likely to identify syndromes, congenital abnormality, and timing of death as well as growth abnormalities. Will be able to detect placental and cord infections Will miss fetal infections and internal congenital and CNS anomalies |
| Placental examination and external examination by a perinatal pathologist, and selected biopsies (this generally includes measurements of the baby, X-rays, and photographs) | Same as above but will be more likely to identify fetal infections |
| Gross and microscopic placental examination and external and internal examination of the fetus by a perinatal pathologist, organs are left with the body, and the brain is not examined (this generally includes measurements of the baby, X-rays, and photographs) | Allows the baby to be returned to the family with all of the organs. Will miss central nervous system pathology, but will detect internal congenital abnormalities and be able to assess the role of infection |
| Head sparing autopsy | Benefits of full autopsy, may miss some CNS pathology |
| MRI (plus or minus directed needle biopsy) | May be very useful when the family requires burial intact in a timely manner. MRI is good in the identification of CNS pathology, but other abnormalities such as cardiac abnormalities are more likely to be missed. Infections will not be diagnosed unless additional needle biopsies are considered. This strategy has not been compared with traditional autopsy |
| Ultrasound | Best done while in utero, but can be done after birth. The head, kidney, or abdomen can be evaluated, but only static images of the heart can be seen. Not as good as MRI for the brain, but may be able to provide some useful information if a previous fetal radiologic survey was not performed. Limited by the degree of maceration, and does not assess role of infection in the fetal death |

Abbreviations: CNS, central nervous system; MRI, magnetic resonance imaging

included in the medical record. Measurements may be accomplished by the obstetrician, pathologist, or other specialist, such as a neonatologist, depending on the institutional protocol.

Autopsy as well as examination of the placenta should be offered. This is especially true when dysmorphic features, inconsistent growth measurements, anomalies, hydrops, or growth restriction are present. Parents should be given the opportunity to hold the baby and perform cultural or religious activities, such as baptism, before the autopsy. Whole-body X-ray with anterior–posterior and lateral views may reveal an unrecognized skeletal abnormality or further define a grossly apparent deformity.

When a full autopsy is performed, it should follow published guidelines for perinatal autopsy (49, 50). The pathologist should be aware of the clinical history and suspected genetic diagnoses, as well as any necessary tissue collection that needs to be performed for additional analyses.

Examination of the Placenta

Gross and microscopic examination of the placenta is an essential component of the evaluation of any stillbirth and should include an examination of the membranes and umbilical cord that may corroborate autopsy find-

ings. Even if the family declines fetal autopsy, histologic study of the placenta usually is acceptable and can be valuable in identifying underlying etiologies (51, 52).

Fetal Laboratory Studies

Karyotypic analyses are of sufficient yield that it should be performed in all cases of stillbirth after appropriate parental permission is obtained (40). If chromosomal culture is not successful, *in situ* hybridization can be used to detect common chromosomal abnormalities. Chromosomal information is particularly valuable if the fetus displays dysmorphic features, inconsistent growth measurements, anomalies, hydrops, or growth restriction. Fetal karyotype also is important if a parent carries a balanced chromosomal rearrangement (eg, translocation or inversion) or has a mosaic karyotype. Samples of amniotic fluid, umbilical cord, fetal tissue, or placenta may be obtained for chromosomal and any other relevant tests. Amniocentesis for fetal karyotyping has the highest yield and is particularly valuable if delivery is not expected imminently (40).

After delivery, the most viable tissue generally is the placenta or segment of umbilical cord closest to the placenta, followed by fetal cartilage obtained from the costochondral junction or patella (see Fig. 1) (53–55).

Appropriate history and physical findings should be sent to the laboratory for the laboratory personnel to choose any appropriate cytogenetic tests.

The Wisconsin Stillbirth Service program estimated that the real cost of a stillbirth assessment was approximately \$1,450 in 2001 (56). The most significant information gained was a change in the estimated risk of recurrent stillbirth (42% of cases). Other consequences were a change in the recommendations for subsequent pregnancies with respect to prenatal diagnosis (in 22%) and preconception management (in 1%).

Maternal Evaluation

A thorough maternal history should be taken looking for known conditions or symptoms suggestive of those that have been associated with stillbirth (Table 4). In addition to obstetric history, including exposures (eg, medications and viral infections), a family history with a three-generation pedigree, if possible, should be reviewed. Any pertinent information in the maternal or paternal pedigree should be documented and investigated further. Relevant original medical records and documentation should be obtained whenever possible. The gestational age by last menstrual period, maternal examinations, laboratory data, and ultrasound examination should be recorded for correlation with the physical examination of the neonate. Possible nongenetic causes, such as infection, placental abruption, and umbilical cord abnormality also should be considered.

Investigation for fetal–maternal hemorrhage should be conducted shortly after the diagnosis of the demise (57). Maternal testing for lupus anticoagulant, anticardiolipin antibodies, human parvovirus B19 immunoglobulin G and immunoglobulin M antibodies and thyroid stimulating hormone may provide information that could affect future pregnancy management (58–60). In cases with severe placental pathology, significant growth restriction, or in the setting of a family or personal history of thrombosis, factor V Leiden mutation, prothrombin mutation, antithrombin III level, MTHFR gene mutation, protein C activity, and protein S activity may provide information that could affect future pregnancy management (58–60). However, routine testing for thrombophilias is controversial and may lead to unnecessary interventions.

- ▶ ***What are the options for management of the current pregnancy after confirmation of a diagnosis of fetal death?***

Methods of Delivery

The method and timing of delivery after a fetal death depends on the gestational age at which the death occur-

red, on the maternal history of a previous uterine scar, and maternal preference. Although most patients will desire prompt delivery, the timing of delivery is not critical; coagulopathies are associated with prolonged fetal retention and are uncommon. In the second trimester, dilation and evacuation can be offered if an experienced provider is available, although patients should be counseled that dilation and evacuation may limit efficacy of autopsy for the detection of macroscopic fetal abnormalities.

Labor induction is appropriate at later gestational ages, if second trimester dilation and evacuation is unavailable, or based on patient preference. Much of the data for management of fetal demise has been extrapolated from randomized trials of management of second trimester pregnancy termination. Before 28 weeks of gestation, vaginal misoprostol appears to be the most efficient method of induction, regardless of cervical Bishop score (61, 62), although high-dose oxytocin infusion also is an acceptable choice (63, 64). Typical dosages for misoprostol use are 200–400 mcg vaginally every 4–12 hours. After 28 weeks of gestation, induction of labor should be managed according to usual obstetric protocols. Cesarean delivery for fetal demise should be reserved for unusual circumstances because it is associated with potential maternal morbidity without any fetal benefit.

Several studies have evaluated the use of misoprostol at a dosage of 400 mcg every 6 hours in women with a stillbirth between 24 and 28 weeks of gestation and a prior uterine scar (65, 66). Available evidence from randomized trials supports the use of vaginal misoprostol as a medical treatment to terminate nonviable pregnancies before 24 weeks of gestation (67). Further research is required to assess effectiveness and safety, optimal route of administration, and dose.

In patients after 28 weeks of gestation, cervical ripening with a transcervical Foley catheter has been associated with uterine rupture rates comparable to spontaneous labor (68) and this may be a helpful adjunct in patients with an unfavorable cervical examination. Therefore, based on limited data in patients with a prior low transverse cesarean delivery, trial of labor remains a favorable option. There are limited data to guide clinical practice in a patient with a prior classical cesarean delivery, and the delivery plan should be individualized.

- ▶ ***What support services and clinical counseling should be offered to the patient with a fetal death?***

Patient support should include emotional support and clear communication of test results. Referral to a bereavement counselor, religious leader, peer support group, or

Table 4. Elements of the Stillbirth Evaluation

| Key Components | Details | Comments |
|-----------------|---|----------|
| Patient history | <p>Family history</p> <ul style="list-style-type: none">• Recurrent spontaneous abortions• Venous thromboembolism or pulmonary embolism• Congenital anomaly or abnormal karyotype• Hereditary condition or syndrome• Developmental delay• Consanguinity <p>Maternal history</p> <ul style="list-style-type: none">• Prior venous thromboembolism or pulmonary embolism• Diabetes mellitus• Chronic hypertension• Thrombophilia• Systemic lupus erythematosus• Autoimmune disease• Epilepsy• Severe anemia• Heart disease• Tobacco, alcohol, drug or medication abuse <p>Obstetric history</p> <ul style="list-style-type: none">• Recurrent miscarriages• Previous child with anomaly, hereditary condition, or growth restriction• Previous gestational hypertension or preeclampsia• Previous gestational diabetes mellitus• Previous placental abruption• Previous fetal demise <p>Current pregnancy</p> <ul style="list-style-type: none">• Maternal age• Gestational age at fetal death• Medical conditions complicating pregnancy<ul style="list-style-type: none">—Hypertension—Gestational diabetes mellitus—Systemic lupus erythematosus—Cholestasis• Pregnancy weight gain and body mass index• Complications of multifetal gestation, such as twin–twin transfusion syndrome, twin reversed arterial perfusion syndrome, and discordant growth• Placental abruption• Abdominal trauma• Preterm labor or rupture of membranes• Gestational age at onset of prenatal care• Abnormalities seen on an ultrasound image• Infections or chorioamnionitis | |

(continued)

Table 4. Elements of the Stillbirth Evaluation (continued)

| Key Components | Details | Comments |
|---------------------------------------|--|--|
| Fetal autopsy | If patient declines, external evaluation by a trained perinatal pathologist. Other options include photographs, X-ray imaging, ultrasonography, magnetic resonance imaging, and sampling of tissues, such as blood or skin. | Provides important information in approximately 30% of cases |
| Fetal karyotype | Amniocentesis before delivery provides the greatest yield (84%). Umbilical cord proximal to placenta if amniocentesis declined (30%). Fluorescence in situ hybridization may be useful if fetal cells cannot be cultured. | Abnormalities found approximately 8% |
| Placental examination | Includes evaluation for signs of viral or bacterial infection. Discuss available tests with pathologist. | Provides additional information in 30% of cases. Infection is more common in preterm stillbirth (19% versus 2% at term) |
| Maternal evaluation at time of demise | <ul style="list-style-type: none"> • Complete blood count • Fetal–maternal hemorrhage screen: Kleihauer–Betke test or comparable test for fetal cells in maternal circulation • Human parvovirus B-19 immunoglobulin G and immunoglobulin M antibody • Syphilis • Lupus anticoagulant • Anticardiolipin antibodies • Thyroid-stimulating hormone • Thrombophilia (selected cases only) <ul style="list-style-type: none"> —Factor V Leiden —Prothrombin gene mutation —Antithrombin III —Fasting homocysteine | Routine testing for thrombophilias is controversial and may lead to unnecessary interventions. Consider in cases with severe placental pathology and or growth restriction, or in the setting of a personal or family history of thromboembolic disease. |
| Postpartum | Protein S and protein C activity (selected cases) Parental karyotype (if appropriate) | |
| In selected cases | Indirect Coombs test Glucose screening (oral glucose tolerance test, hemoglobin A1c) Toxicology screen | If not performed previously in pregnancy. In the large for gestational age baby In cases of placental abruption or when drug use is suspected |
| Unproven benefit | Antinuclear antibody test Serology for toxoplasmosis, rubella, cytomegalovirus, herpes simplex virus | Many times is an incidental finding and may lead to unnecessary interventions Rarely helpful, infection causing death is made by history and examining the baby, placenta, and cord |
| Developing technology | Comparative genomic hybridization Testing for single-gene mutations Testing for confined placental mosaicism and nucleic acid-based testing for infection | The value of these has not yet been established |

mental health professional may be advisable for management of grief and depression. Feelings of guilt or anger in parents who have experienced a perinatal death are common and may be magnified when there is an abnormal child or a genetic defect. However, some parents may welcome discussion and find relief in autopsy results. The

results of the tests are important even when no specific diagnosis is identified (69). The results of the autopsy, placental examination, laboratory tests, and cytogenetic studies should be communicated to the involved clinicians and to the family of the deceased infant in a timely manner. If there was no growth of the fetal chromosomes

(or these were not obtained), further consultation with a genetics or maternal–fetal medicine subspecialist is advised to discuss the need for parental chromosomal testing. A copy of the results of the tests and a list of diagnoses excluded should be provided to the patients.

- ▶ ***For the patient with a history of an unexplained fetal death in a previous pregnancy, how should clinical management be altered in subsequent pregnancies?***

Recurrence Counseling

Counseling can be hampered by insufficient information regarding the etiology of the prior stillbirth. In many cases, the prior stillbirth may be unexplained despite a thorough evaluation. In patients in whom complete evaluation for previous stillbirth was not done, evaluation should be completed with parental permission. When specific risks are identified, the risk of recurrence may be quantifiable. In low-risk women with unexplained stillbirth, the risk of recurrence stillbirth after 20 weeks is estimated at 7.8–10.5/1,000 with most of this risk occurring before 37 weeks of gestation. The risk of recurrent stillbirth after 37 weeks is very low at 1.8/1,000. In comparison, women with a history of a live birth complicated by preterm fetal growth restriction have a stillbirth rate of 21.8/1,000 in a subsequent pregnancy (25). Rates of recurrent fetal loss are higher in women with medical complications such as diabetes or hypertension or in those with obstetric problems with a significant recurrence risk, such as placental abruption. Despite reassurances, the patient is likely to be anxious and to require ongoing support.

Antepartum Surveillance

There is little evidence-based data to guide the treating clinician in the antepartum surveillance of a patient who had a prior unexplained stillbirth. In patients with a history of stillbirth, antepartum testing may be initiated at 32–34 weeks of gestation. However, this approach is associated with potential morbidity and cost: rates of delivery for abnormal or equivocal testing were 16.3% at or before 39 weeks of gestation and 1% before 36 weeks of gestation. Similarly, the authors of one study estimate that antenatal testing before 37 weeks of gestation results in a 1.5% rate of iatrogenic prematurity for intervention based on false-positive test results (70). The excess risk of infant mortality due to late preterm birth is 8.8/1,000 at 32–33 weeks of gestation and 3/1,000 at 34–36 weeks of gestation (71), and this must be considered in any strategy that may lead to iatrogenic late preterm birth.

Fetal Kick Counting

Multiple studies have demonstrated that women who report decreased fetal movement are at increased risk for adverse perinatal outcome (72). Although fetal kick counting is an inexpensive test of fetal well being, the effectiveness in preventing stillbirth is uncertain (73).

Timing of Delivery

The decision to proceed with early delivery to prevent stillbirth must incorporate an understanding of the increased risks of maternal and neonatal complications compared with the potential benefits. Deliveries before 39 weeks of gestation are associated with an increased risk of admission to neonatal special care units for respiratory complications and other neonatal morbidities. Details of pregnancy for women with a prior stillbirth are listed in the box.

Summary of Recommendations and Conclusions

The following recommendations and conclusions are based on good and consistent scientific evidence. (Level A)

- ▶ In low-risk women with unexplained stillbirth the risk of recurrence stillbirth after 20 weeks of gestation is estimated at 7.8–10.5/1,000 with most of this risk occurring before 37 weeks of gestation.
- ▶ The most prevalent risk factors associated with stillbirth are non-Hispanic black race, nulliparity, advanced maternal age, and obesity (Table 1).
- ▶ The risk of subsequent still birth is twice as high for women with a prior live born, growth restricted infant delivered before 32 weeks of gestation than for women with a prior stillbirth.
- ▶ Amniocentesis for fetal karyotyping has the highest yield and is particularly valuable if delivery is not expected imminently.

The following recommendations and conclusions are based primarily on limited or inconsistent scientific evidence (Level B):

- ▶ In the second trimester, dilation and evacuation can be offered. Labor induction also is appropriate at later gestational ages, if second trimester dilation and evacuation is unavailable, or based on patient preference.

Management of Subsequent Pregnancy After Stillbirth

Preconception or initial prenatal visit

Detailed medical and obstetric history
Evaluation and workup of previous stillbirth
Determination of recurrence risk
Smoking cessation
Weight loss in obese women (preconception only)
Genetic counseling if family genetic condition exists
Diabetes screen
Thrombophilia workup: antiphospholipid antibodies (only if specifically indicated)
Support and reassurance

First trimester

Dating ultrasonography
First-trimester screen: pregnancy-associated plasma protein A, human chorionic gonadotropin, and nuchal translucency*
Support and reassurance

Second trimester

Fetal ultrasonographic anatomic survey at 18–20 weeks of gestation
Maternal serum screening (Quadruple) or single marker alpha fetoprotein if first trimester screening*
Support and reassurance

Third trimester

Ultrasonographic screening for fetal growth restriction after 28 weeks of gestation
Kick counts starting at 28 weeks of gestation
Antepartum fetal surveillance starting at 32 weeks of gestation or 1–2 weeks earlier than prior stillbirth
Support and reassurance

Delivery

Elective induction at 39 weeks of gestation
Delivery before 39 weeks of gestation only with documented fetal lung maturity by amniocentesis

*Provides risk modification but does not alter management (Adapted from Reddy UM. Prediction and prevention of recurrent stillbirth. *Obstet Gynecol* 2007;110:1151–64.)

- ▶ Induction of labor with vaginal misoprostol is safe and effective in patients with a prior cesarean delivery with a low transverse uterine scar before 28 weeks of gestation.

The following recommendations and conclusions are based primarily on consensus and expert opinion (Level C):

- ▶ The most important tests in the evaluation of a stillbirth are fetal autopsy; examination of the placenta, cord, and membranes; and karyotype evaluation.
- ▶ Patient support should include emotional support and clear communication of test results. Referral to a bereavement counselor, religious leader, peer support group, or mental health professional may be advisable for management of grief and depression.

Performance Measure

The percentage of stillbirths for which placental evaluation was performed and autopsy was offered

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The MEDLINE database, the Cochrane Library, and ACOG’s own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1985 and April 2008. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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ISSN 1099-3630

**The American College of Obstetricians and Gynecologists
409 12th Street, SW, PO Box 96920, Washington, DC 20090-6920**

Management of stillbirth. *ACOG Practice Bulletin* No. 102. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2009; 113:748–61.