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ONLINE EXCLUSIVE

# Intrauterine fetal demise: Care in the aftermath, and beyond

The death of a fetus late in pregnancy can be devastating. Your role: Help the mother through the physical process, conduct a postdelivery evaluation, and provide support to the grieving family.

**Richard Temple, MD; Stephanie Smith, MD**
Naval Hospital Camp Lejeune Family Medicine Residency, Camp Lejeune, NC

richard.temple@med.navy.mil

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## PRACTICE RECOMMENDATIONS

› *Consider vaginal misoprostol for achieving delivery following intrauterine fetal demise (IUFD); it is as effective as other vaginal prostaglandin preparations and more effective than oral misoprostol.* (A)

› *Include in your postdelivery evaluation of IUFD autopsy, placental gross and histologic examination, fetal karyotype, and exam for fetomaternal hemorrhage.* (B)

› *Offer grieving parents early emotional support and counseling; research indicates it shortens the bereavement process.* (C)

**Strength of recommendation (SOR)**

(A) Good-quality patient-oriented evidence

(B) Inconsistent or limited-quality patient-oriented evidence

(C) Consensus, usual practice, opinion, disease-oriented evidence, case series

**CASE ►** Louise T, age 26, is pregnant with her first child. She attends all prenatal care visits with her health care team and appears to be doing well. However, at Ms. T's 28-week visit, her physician is unable to detect a fetal heartbeat, or any movement of the fetus. He orders an ultrasound, which confirms his suspicions. Ms. T opts for immediate induction of labor. In his postdelivery evaluation, Ms. T's physician does not determine a definitive cause for the intrauterine fetal demise.

Intrauterine fetal demise (IUFD) is fetal death that occurs after 20 weeks gestation but before birth.[1] If the gestational age is unknown at the time of death, a fetus that weighs ≥350 g is considered an IUFD. In 2005, IUFD occurred at a rate of 6.22 per 1000 pregnancies, which amounted to 25,894 deaths.[1]

Family physicians who provide obstetric care are likely to care for women who have experienced an IUFD. This article describes what that care should include.

## Keep these risk factors in mind

IUFD has been attributed to an extensive range of risk factors and possible causes, including various maternal medical conditions, obstetric complications, and pathologic fetal or placental conditions (**TABLE 1**).[2-8] The 2 most common risk factors—obesity (body mass index [BMI] >30) and smoking—are modifiable and increase the odds of IUFD approximately three-fold.[2] Though less common, 2 other notable risk factors are lupus and chronic renal disease; their impact on IUFD risk varies depending on the severity of the disease.[2] However, keep in mind that these factors may not be causal and that most pregnant women with these conditions will deliver healthy infants.

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**Up to 40% of unexplained cases of IUFD may actually be the result of an incomplete evaluation.**

**TABLE 1**

## Risk factors and potential causes of IUFD[2-8]

| |
|---|
| **Maternal medical conditions** |
| Asthma |
| Diabetes mellitus |
| Hypertension |
| Intrahepatic cholestasis of pregnancy |
| Obesity |
| Renal disease |
| Seizure disorder |
| Smoking |
| Substance abuse |
| Systemic lupus erythematosus |
| Thyroid disease |
| **Obstetric complications** |
| Cervical insufficiency |
| Fetomaternal hemorrhage |
| Multiple gestation |
| Placental abruption |
| Placental insufficiency |
| Preterm labor |
| Preterm premature rupture of membranes |
| Uterine rupture |
| **Maternal or fetal hematologic complications** (eg, antiphospholipid syndrome, heritable thrombophilia, red cell isoimmunization) |
| **Fetal genetic, structural, and karyotypic abnormalities** (eg, autosomal recessive disorders, chromosomal anomalies, fetal metabolic disorders) |
| **Placental and/or fetal infections** (eg, toxoplasmosis, rubella, cytomegalovirus, HSV) |
| **Pathologic placental conditions** (eg, previa, accreta, circumvallate, umbilical cord entrapment) |

HSV, herpes simplex virus; IUFD, intrauterine fetal demise.

## Induce labor, or wait?

A woman experiencing an IUFD is likely to seek care when she notices that the fetus isn't moving or when she experiences contractions, loss of fluid, or vaginal bleeding. Alternatively, she could be asymptomatic, and it may be the physician who suspects IUFD when he/she is unable to hear fetal heart tones. The diagnosis is confirmed by the absence of fetal cardiac activity on ultrasound; physicians may wish to obtain a second ultrasound for confirmation of the diagnosis.

Once IUFD is confirmed, most women choose to immediately undergo induction of labor. However, some elect to wait for spontaneous labor. Approximately 84% to 90% of women will go into spontaneous labor within 2 weeks of fetal death.[9] Unless there is a compelling indication for immediate delivery (eg, coagulopathy, evidence of intrauterine infection, preeclampsia), expectant management may be permitted.

If a mother chooses expectant management, she should undergo periodic follow-up exams to assess for abdominal pain, fever, bleeding, bruising, labor, and emotional lability.[10] Tell patients to seek immediate care if they develop a fever, abdominal pain, foul-smelling or purulent vaginal discharge, moderate bleeding, or bruising, or if they go into labor.

## Vaginal prostaglandin effectively induces labor

Options for labor induction include oral or vaginal prostaglandins, continuous oxytocin infusion, or mechanical dilation (cervical placement of laminaria or a Foley bulb). Factors that affect which method to use include concomitant maternal illness, gestational age, Bishop score, or the presence of a uterine scar from a previous Cesarean section or other surgery. A Cochrane review found vaginal misoprostol was as effective as other vaginal prostaglandin preparations (E2 and F2-alpha) and more effective than oral misoprostol in achieving delivery for second- and third-trimester terminations and fetal deaths.[11] Due to the risk of uterine rupture, most experts advise against use of misoprostol for a woman with a previously scarred uterus at >24 to 26 weeks gestation.[10,12] In this circumstance, consider mechanical dilation followed by oxytocin infusion.

Beyond 28 weeks gestation, misoprostol can be used to induce labor by following the

standard protocols utilized for term pregnancies (**TABLE 2**).[10,12] Some patients may require additional doses of misoprostol to complete the third stage of labor. Pain can be managed via narcotic patient controlled analgesia, periodic use of intravenous narcotics, or continuous epidural.

**TABLE 2**
## Misoprostol protocols for inducing labor[10,12]

| Dose | Route | Frequency |
|---|---|---|
| **< 28 weeks** | | |
| 200 mg | Vaginal | Every 4 hours |
| 200-400 mg | Oral | Every 2-4 hours |
| **>28 weeks** | | |
| 25 mg | Vaginal | Every 4 hours |
| 25 mg | Oral | Every 4 hours |

## A systematic approach to postdelivery evaluation

Although 25% to 60% of IUFDs are classified as "unexplained," in up to 40% of cases the lack of explanation may be due to an incomplete evaluation.[2-4] When performing an evaluation, it is important to be systematic and not confuse association with causality. Kortweg et al[13] analyzed laboratory studies obtained in the evaluation of 1025 fetal deaths in the Netherlands from 2002 to 2008. The most useful tests were placental examination, fetal autopsy, and fetal karyotype, which aided in assigning the cause of death in 96%, 73%, and 29% of cases, respectively. Compared to fetal karyotyping from postpartum tissue sampling, samples obtained via amniocentesis or chorionic villus sampling before inducing labor are much more successful in identifying the cause of death (85% vs 28%).[14]

Testing for fetomaternal hemorrhage, which is the cause of IUFD about 12% of the time, needs to be performed when IUFD is diagnosed.[13] Additional laboratory testing may be helpful depending on the mother's history or symptoms at the time of IUFD. For example, a maternal history of drug use, thyroid disease, diabetes mellitus, hypertension, venous thromboembolism, or febrile illness should prompt further studies (**TABLE 3**).[10,12-15]

## How to help grieving parents

Mothers may feel tremendous guilt upon suffering an IUFD. When addressing grief, mourning, and bereavement after an IUFD, the goal is to support the parents through the grieving process and properly identify when grief becomes pathologic. Grief is pathologic when there is a prolonged response—usually longer than 6 months—and when it interferes with daily activities.[16] In a prospective study, patient characteristics that affected the intensity of grief were advanced gestational age at loss, lack of children in the home, relatively older age, pre-loss neurotic personality, and pre-loss psychiatric symptoms.[17]

Unlike the grief experienced by parents who lose an infant or child, the grief experienced by parents who experience an IUFD may not be socially validated. Therefore, it is important for physicians to acknowledge that patients' feelings of loss are legitimate. Additionally, reassure mothers that there was very likely nothing that she could have done to change the outcome, unless there is compelling evidence to the contrary (eg, drug abuse causing abruption and fetal demise). Avoid using phrases such as "you can always try again."

In a study of 769 women who experienced an IUFD, many reported receiving "support" or "great support" from family members (91.7%), nurses (90%), and physicians (53.4%).[18] Adequate health care support is associated with lower levels of depression and anxiety, but family support appears to be the most important.[18] Women who are single, divorced, or widowed experience higher levels of depression after IUFD than those who are married or cohabitating.[18]

In a different study of support for women who experienced IUFD or death of their child shortly after birth, mothers did not blame doctors or feel that the doctors should make them feel better.[19] However, they did want an explanation in simple language of what had gone wrong and for physicians to listen and accept their distress.[19] This study also found

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**TABLE 3**

## Post-IUFD evaluation: Recommended tests[10,12-15]

| |
|---|
| **All patients** |
| Fetal autopsy |
| Placental gross and histological examination |
| Fetal karyotype |
| Kleihauer-Betke test* |
| **Selective testing** |
| Parvovirus B-19† |
| TORCH titers |
| Fetal and placental swabs‡ |
| Lupus anticoagulant§ |
| Anticardiolipin antibodies§ |
| Thrombophilia testing§: |
| • Factor V Leiden |
| • Prothrombin gene mutation (G20210A) |
| • Antithrombin III |
| • Fasting homocysteine |
| • Protein C and S activity |
| Screen for syphilis¶ |
| Screen for diabetes¶ |
| Indirect Coombs' test¶ |
| Toxicology screen# |
| Thyroid-stimulating hormone** |
| Uterine imaging†† |

IUFD, intrauterine fetal demise; TORCH, toxoplasmosis, rubella, cytomegalovirus, herpes simplex virus.

* Or alternate screen for fetomaternal hemorrhage.

† Consider if fetal hydrops.

‡ Consider if evidence of chorioamnionitis.

§ Consider in cases with severe placental pathology and/or growth restriction or for patients with a personal or family history of thromboembolic disease.

¶ If not performed early in pregnancy or if suspected.

# If abruption, or if drug abuse is suspected.

** If thyroid disease is suspected.

†† If there is recurrent loss, preterm premature rupture of membranes, or preterm labor.

that early support and counseling shortened the bereavement process.[19] Half of women had symptoms of depression and anxiety 6 months after the death of their fetus or child and 20% had these symptoms at 14 months. Fathers, however, recovered more quickly—14% were symptomatic at 6 months.[19]

## Managing a subsequent pregnancy

A retrospective cohort study found that for women who had experienced an IUFD, the odds ratio of having a recurrent IUFD was 1.94 (99% confidence interval, 1.29-2.92) compared to women who had a previous live birth.[20] The risk of recurrent IUFD in a specific patient is related to the underlying pathophysiologic cause of the initial IUFD, and how that cause was addressed. For example, a patient who experienced an IUFD believed to be the result of uncontrolled diabetes can expect to have an improved outcome if her diabetes is brought under control before conceiving and she maintains control throughout the pregnancy. On the contrary, a patient who experienced an IUFD that was believed to be secondary to a nonmodifiable risk factor, such as lupus-induced chronic kidney disease, will continue to have a significant risk of recurrence of IUFD in the subsequent pregnancy.

When managing a subsequent pregnancy of a woman who has experienced an IUFD, review all data from the prior pregnancy as well as the mother's medical conditions. Order any studies in **TABLE 3** that were not previously obtained and are clinically indicated. If applicable, encourage the woman to quite smoking and achieve a healthy BMI (<25).

In addition to routine obstetric care measures, these women should be offered antepartum fetal surveillance starting at 32 weeks gestation, or one to 2 weeks before the gestational age of the fetus at the time of the previous IUFD (whichever is earlier), as well as serial ultrasonography starting at 28 weeks to assess for fetal growth restriction.[12,21] Most experts advise delivery at 39 weeks unless indicated earlier.[12]

**Psychological risks.** IUFD is associated with posttraumatic stress disorder (PTSD) and anxiety in a subsequent pregnancy.[22,23] Approximately 21% of women in one study met criteria for PTSD in the third trimester of the first subsequent pregnancy; this decreased to 4% at one year postpar-

tum.[22] Risk factors for PTSD and anxiety were conceiving within one year of IUFD and a perceived lack of support at time of loss.[22,23] Additionally, women who said they had poor partner support at the time of IUFD were more likely to have more severe PTSD symptoms, such as recurring, involuntary distressing memories of the IUFD, 6 to 8 years later.[24] Because women who become pregnant after having an IUFD are likely to be anxious, physicians should be aware that there may be "false alarms" during the course of these pregnancies.

**CASE ▶** Two years after experiencing an IUFD, Ms. T becomes pregnant. Her physician carefully reviews her medical records and begins fetal surveillance at 26 weeks gestation, including serial ultrasounds. Ms. T's pregnancy and labor proceed without complications, and at 38 weeks, she delivers a healthy 6.3-lb. boy. JFP

**CORRESPONDENCE**
Richard Temple, MD, Naval Hospital Camp Lejeune Family Medicine Residency, 100 Brewster Blvd., Camp Lejeune, NC 28547; richard.temple@med.navy.mil

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**There may be "false alarms" during the course of a woman's pregnancy if she's already experienced an IUFD.**

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