

Intrauterine fetal death: What is the right follow-up?

Besides being emotionally challenging, fetal demise raises a host of questions and increases an obstetrician's medicolegal risk. An expert recommends strategies for determining etiology, counseling the patient, and protecting against litigation.

Very few circumstances in obstetrics evoke feelings as strong as those brought on by third-trimester fetal demise. These events demand that we provide not only emotional support, but also a thorough, objective evaluation of the cause of the death. But because such losses differ significantly from those that occur early in pregnancy, their assessment is unique. The patient and her family will ask "why," seeking answers ranging from the theological to the medical. Our goals should include:

- providing the family with information about the cause of death, as well as emotional guidance;
- determining whether a loss is likely to recur

KEY POINTS

- Fetal chromosomal abnormalities are associated with 5% to 10% of late fetal losses.
- Since amniocytes can survive for several weeks following a fetal demise, amniocentesis can be used to obtain material for karyotyping.
- Once the patient delivers, a careful gross examination of the fetus, cord, membranes, and placenta should be documented in the chart, even if an autopsy is planned.
- Perinatal autopsy continues to play an important role in determining the cause of death, yielding new information in more than 25% of cases.

and suggest possible ways to decrease the risks; and

- minimizing the care provider's liability exposure.

To ensure all these goals are met, a systematic protocol, such as the one described in this article, is vital.

The history and other clues

Once the diagnosis of fetal death is confirmed, and the woman and her family are prepared to move forward, it is critical to obtain a thorough history. Suggested questions include: "Has the patient felt normal over the preceding 24 to 48 hours?" "Has she experienced any recent gastrointestinal (GI) or febrile illnesses?" If either answer is yes, the cause of death may be related to listeriosis, chorioamnionitis, or other infectious processes. See **TABLE 1** for a complete list of questions and their rationales.

Fetal chromosomal abnormalities are associated with 5% to 10% of late fetal losses.¹ With fetal tissue, there is a relatively high rate of post-delivery cell culture failure due to autolysis or contamination. Since amniocytes

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PHYSICIAN CUTOUT

**Documentation recommendations:
checklist for reducing medicolegal risk**

HISTORY

Patient's recent condition, especially 24 to 48 hours prior to fetal demise:

- GI or febrile illness? Yes___ No___
- Blurred vision? Yes___ No___
- Headaches? Yes___ No___
- RUQ pain? Yes___ No___
- Abnormal swelling of face
or hands? Yes___ No___
- Trauma? Yes___ No___
- Domestic violence? Yes___ No___ Ongoing?___
- Bleeding or fluid leakage? Yes___ No___
- Decreased fetal movement? Yes___ No___

LABORATORY STUDIES

- ___ Betke-Kleihauer or flow cytometry
- ___ Urine drug screen
- ___ VDRL
- ___ Rapid plasmin reagin
- ___ Parvovirus antibody
- ___ Cytomegalovirus
- ___ Immunoglobulin M and G
- ___ Antinuclear antibody
- ___ Anticardiolipin antibodies
- ___ Lupus anticoagulant screen
- ___ Factor V Leiden
- ___ Antithrombin III
- ___ Factor C, Factor S
- ___ Hemoglobin A1C
- ___ Creatinine
- ___ Complete blood count with platelets
- ___ Liver function tests
- ___ Uric acid
- ___ Type and screen
- ___ Coombs' test

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IMAGING STUDIES

- ___ Ultrasound
- ___ MRI (if autopsy declined)

GROSS EXAMINATION OF PRODUCTS OF CONCEPTION

- ___ Gross description of anatomic evaluation, including presence or absence of facial abnormalities, number of digits on all extremities, ventral wall defect, number of cord vessels, spinal defects, genitalia, patent anus, and cleft palate:

- ___ Foot length _____

- ___ Obvious trauma? _____

- ___ Weight and assessment of appropriateness of growth _____

- ___ Degree of maceration _____

- ___ Condition of placenta: Intact? Adherent clot? Infarcts? Eccentric cord insertion?
Three vessels? Unusual in any way?

- ___ Did placenta come easily or with difficulty? Evidence of abruption? If D&C performed or placenta manually removed, was uterine cavity normal?

- ___ Cord accident noted? _____

- ___ Amount, color, and odor of amniotic fluid? _____

- ___ How much did mother bleed at delivery? _____

D&C = dilatation and curettage; GI = gastrointestinal; MRI = magnetic resonance imaging; RUQ = right upper quadrant; VDRL = Venereal Disease Research Laboratory [test]



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TABLE 1

Potential screening questions and their rationales

QUESTION	POSSIBLE INDICATION
1. Has the patient felt normal over the preceding 24–48 hours? Has she had any GI or febrile illnesses recently?	Listeriosis, chorioamnionitis, or other infectious processes
2. Has she had blurred vision, headaches, right upper quadrant pain, or abnormal facial or hand swelling?	Preeclampsia with uteroplacental insufficiency
3. Has she been hit, kicked, slapped, or fallen? Has she been in even a minor automobile accident?	Domestic violence or other trauma
4. Has she had any vaginal bleeding or leakage of fluid?	Abruption, amnionitis, or cord prolapse
5. When did she notice decreased fetal movement, if at all?	A clue to timing of the event
6. Has her pregnancy been uncomplicated until now?	Clues to placental problems: elevated maternal serum alpha-fetoprotein, growth problems, smoking, diabetes, hypertension

can survive for several weeks following a fetal demise, consider amniocentesis for karyotyping prior to induction of labor.² If amniocentesis is unacceptable to the patient, pass an intrauterine pressure catheter after amniotomy to obtain an amniotic fluid sample as a backup in case the fetal biopsy specimen fails to grow.

If invasive testing is not feasible or acceptable, other tissue may be used, although it likely will have a lower rate of successful cell culture. If the fetal demise occurs within 24 hours of delivery, obtain for karyotyping a heparinized sample of the fetal cord blood or a blood sample by fetal cardiac puncture. Other acceptable tissue samples include 1 cm² of fetal skin, Achilles tendon, or retro-patellar cartilage. Fetal tissue should be sent, refrigerated, in isotonic saline to the cytogenetic laboratory.

Fetuses with structural abnormalities face a higher risk of intrauterine death than normal fetuses. If the patient will allow it, a complete sonographic evaluation of the fetus for anatomic evaluation is important, especially if one was not done earlier in the pregnancy. Ultrasound also may help determine the approximate time of the demise. For instance,

a recent demise would not yet demonstrate overlapping cranial sutures or postmortem skin edema.

Look closely for evidence of fetal growth restriction, which may provide clues to the cause of death. Long bone measurements may be more reliable measures of fetal size than head and abdominal measurements, due to postmortem soft tissue changes.

Laboratory and autopsy studies

An often overlooked cause of fetal death is fetal-maternal hemorrhage. To evaluate for this, obtain a Betke-Kleihauer test or flow cytometry study prior to amniocentesis or induction of labor. Other laboratory analyses useful in determining the etiology of fetal demise include a urine drug screen and creatinine and hemoglobin A1C levels. For a complete list of potential tests and their rationales, see TABLE 2.

Once the patient delivers, a careful gross examination of the fetus, cord, membranes, and placenta should be documented in the chart, even if an autopsy permit is obtained. Your notes should detail anatomic evaluation of the fetus, with a description of any facial abnor-

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TABLE 2

Laboratory studies

STUDY	POINTS TO
Betke-Kleihauer or flow cytometry*	Fetal-maternal hemorrhage
Urine drug screen*	Cocaine or other drug use
VDRL or RPR, Parvovirus antibody, CMV, IgM and IgG	TORCH infection
Antinuclear antibody	Lupus, other autoimmune disorders
Anticardiolipin antibodies (IgG, IgM), lupus anticoagulant screen, factor V Leiden, antithrombin III, factor C, factor S	Thrombophilia
Hemoglobin A1C	Diabetes
Creatinine	Renal disease
Complete blood count with platelets	Need baseline in case of bleeding; abnormalities point to preeclampsia, disseminated intravascular coagulation screen
Liver function tests, uric acid	Preeclampsia
Type and screen and Coombs' test	Isoimmunization; patient may need to go to the operating room for significant bleeding or failure to deliver

CMV = cytomegalovirus; IgG = immunoglobulin G; IgM = immunoglobulin M; RPR = rapid plasmin reagin; TORCH = toxoplasmosis, other infections, rubella, cytomegalovirus infection, and herpes simplex; VDRL = Venereal Disease Research Laboratory [test]
 * Obtain prior to any other procedure.

malities, the number of digits on all extremities, any spinal or ventral wall defects, genitalia, the number of cord vessels, and, if present, a patent anus and cleft palate. Other important charting suggestions are listed in “Documentation recommendations: checklist for reducing medicolegal risk” on page 65.

Perinatal autopsy continues to play an important role in determining the etiology of late fetal demise, despite the excellence of ultrasound and other imaging modalities. In a study of 400 consecutive instances of perinatal and infant deaths (20 weeks through 1 year) in Wales, an autopsy substantially altered the pre-autopsy assessment of the cause of death in 12% of still-born fetuses and provided new information in 26% of cases.³

If possible, obtain a formal autopsy by a pathologist with experience in perinatal pathology. Request subspecialist perinatal pathologic evaluation at a different laboratory than your own if the local pathologist is

inexperienced or uncomfortable performing perinatal pathology.¹ Discuss with the pathologist any additional information you would like, and confirm that a tissue block can be preserved for potential genetic studies. As the Human Genome Project elucidates the genetic basis for an increasing number of disorders, it is likely that the genetic basis for some fetal deaths will be identified. Having tissue available for future analysis may be helpful. The College of American Pathologists (CAP) publishes practice guidelines for performing and reporting perinatal necropsy.⁴

Request neuropathologic evaluation. If liquefaction does not preclude examination, central nervous system (CNS) changes such as white-matter gliosis, macrophage infiltration, karyorrhexis, and vascular proliferation can provide evidence of earlier hypoxic episodes.

Also request a pathologic examination of the placenta, even if the request for

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autopsy is declined. Placental abnormalities such as circumvallate placenta or infarcts involving more than 20% of the placental surface may cause or be associated with fetal demise. Histologic evidence of infection can be present even when there are no clinical signs of chorioamnionitis; this may be a clue to the diagnosis. The pathologist can best describe any other significant placental pathology, such as floor infarction, fibrosis, and amnion nodosum.

The CAP guidelines emphasize the importance of the pathologist obtaining adequate information about the case, noting: "It is especially true in fetal and perinatal autopsies that the quality and usefulness of autopsy and placental data depend on the effort of the pathologist to obtain the medical history of the mother and integrate the outcome of the pregnancy."⁴ Provide enough history to the pathologist so that she or he can target the evaluation appropriately.

If the mother declines autopsy, consider requesting total-body magnetic resonance imaging (MRI). In one investigation, 3 radiologists interpreted MRI studies performed on 26 postmortem, delivered fetuses; their interpretations were compared to autopsy findings.⁵ All 3 radiologists correctly detected 79% of the autopsy-proven major malformations; at least 1 radiologist identified 91%. Although it is not considered the "gold standard," MRI may provide valuable information for families who decline autopsy.

Counseling the patient

The results of postmortem evaluation may not be known for several weeks. Once the evaluation is completed, schedule an appointment for the patient and her family to return to review all of the findings (if they desire to do so). Spend at least part of this visit assessing the patient's grief response to diagnose possible depression.

Even if the studies fail to pinpoint a specific reason for the fetal death, it can be reas-

suring when many things are "ruled out." If a specific diagnosis has been reached, explain it and any possible recurrence risks. (It may be helpful to have a genetic counselor participate in the discussion.) Identify specific behaviors, such as folic acid supplementation, cessation of tobacco use, or controlling blood sugar levels, that may decrease the patient's risks of poor pregnancy outcomes in the future. It also is important to detail your thorough investigation—and counseling—in the patient's chart, in the event of subsequent litigation. The patient should leave your office with a thorough understanding of what is known and unknown about the death of her fetus. ■

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