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SEMINARS IN PERINATOLOGY

Antepartum Testing for Women with Previous Stillbirth

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Women with past histories of stillbirth have been referred for antepartum surveillance since the inception of electronic fetal monitoring. However, this approach was originally based on mid-twentieth century perinatal studies that noted an increase in adverse outcomes in pregnancies subsequent to stillbirth. When these landmark studies were done, Rh immune globulin, ultrasonography, and other important medical advances had not yet occurred. This article discusses whether women who have suffered a past stillbirth remain at increased risk for perinatal mortality and morbidity in future pregnancies and whether antepartum fetal surveillance can reduce the risk of recurrent stillbirth.
Semin Perinatol 32:301-306

KEYWORDS stillbirth, fetal testing, antepartum surveillance, fetal death, intrauterine fetal demise

A history of stillbirth is an accepted indication for antepartum surveillance.[1,2] The purpose of this article was to review the data supporting stillbirth as an indication for fetal testing and to evaluate the reported experience with antepartum surveillance in women who have suffered a previous stillbirth. We also address the question of whether antepartum surveillance is effective at preventing recurrent stillbirth.

Evidence for Stillbirth as a Risk Factor for Poor Future Pregnancy Outcome

Women who have suffered one stillbirth are at increased risk for perinatal mortality in subsequent pregnancies. This was proven in large British and U.S. population studies conducted in the mid-twentieth century. The U.S. study, conducted by the National Institute of Neurological Diseases and Stroke, determined that patients with previous stillbirths had a perinatal mortality rate of 73 per 1000 in subsequent pregnancies and nearly 2% of their surviving children were neurologically abnormal at 1 year of age.[3] The British study reported that the risk of poor outcomes in subsequent pregnancies was more than doubled among women with previous stillbirths.[4] These historic studies predated the era of electronic fetal monitoring, but the reported experiences served as justification for inclusion of stillbirth as an indication for fetal surveillance once the technology became available.

Based on the aforementioned U.S. and British perinatal studies, utilization of antepartum surveillance in women with a past history of stillbirth seems prudent. However, those studies were conducted before the development and wide implementation of several valuable medical breakthroughs such as Rh immune globulin, ultrasonography, serum screening for aneuploidy, and use of home glucose monitoring devices. Several population-based studies on future pregnancy outcomes in women who have experienced a previous stillbirth have recently been published.[5-7] These newer studies have also revealed excess perinatal mortality among women with previous stillbirths.

In 1993, Samueloff and coworkers published a study of recurrent stillbirths at an academic center in San Antonio. The overall stillbirth rate in the 13-year cohort was 8.3 per 1000 births. Of the 403 women who had pregnancies subsequent to stillbirths, 34 experienced recurrent stillbirths for a rate of 84.3 per 1000 births. Thus, risk was 10-fold higher than that of multiparous women who had no previous history of stillbirth. When compared with women with past histories of stillbirth and a live-born infant in subsequent pregnancies, the women who had recurrent stillbirths were more likely to

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From "Antenatal Testing: A Reevaluation," a workshop cosponsored by the Pregnancy and Perinatology Branch (PPB) at the National Institute of Child Health and Human Development, the Office of Rare Diseases, National Institutes of Health, the American College of Obstetricians and Gynecologists, and the American Academy of Pediatrics.

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0146-0005/08/$-see front matter
doi:10.1053/j.semperi.2008.04.014

Table 1 Stillbirth Rates by Race and Past History of Stillbirth

	History of SB	No History of SB
Black	35.9	7.6
White	19.1	4.2
Overall	22.7	4.7

SB rate = SB per 1000 births (live births plus stillbirths).
Modified from Sharma and coworkers.[6]

have diabetes or hypertension. However, half of women with recurrent stillbirth had no chronic medical conditions.[7]

Sharma and coworkers studied a large cohort of Missouri women who gave birth between 1978 and 1997.[5] Future pregnancy outcomes in women who experienced a stillbirth in their first pregnancy were compared with those of women who delivered a live birth in their first pregnancy. The study included 404,201 women: 99.5% had a live birth in the first pregnancy and 0.5% (1979) had a stillbirth, which was defined as an intrauterine death at 20 weeks gestation or more. Compared with women without a history of stillbirth, women with a history of stillbirth in their first pregnancy had a 57% increase in complications in the second pregnancy, including diabetes, chronic hypertension, preeclampsia, eclampsia, and abruptio placenta.

There were 1929 stillbirth cases in the second pregnancy: 45 (2.3% of all cases) occurred in women with a history of stillbirth and 1884 (97.7% of all cases) among those without a stillbirth history. Hence, the stillbirth rate in women with a previous history of fetal death at 20 weeks or more was 22.7 per 1000 as compared with 4.7 per 1000 for those who did not have a stillbirth with their first pregnancies. Table 1 shows the stillbirth rates stratified by race and history of stillbirth in the first pregnancy. Sharma's data revealed a nearly twofold increase in stillbirth rates among black women overall. In pregnancies subsequent to a stillbirth, black women had a stillbirth risk that was sevenfold greater than the national average.

Sharma and coworkers also calculated adjusted estimates for the relationship between prior stillbirth and subsequent stillbirth recurrence. Several models for relative risk were presented in which the reference group comprised women with a live birth in the first pregnancy, live births excluding small for gestational age (SGA), live births excluding preterm births, or live births excluding preterm or SGA. In all models the relative risk of stillbirth among the total population of women with a previous stillbirth was increased over fourfold.

Most studies on stillbirth recurrence comprised patients from the general population, which include women with medical complications and risk factors. This could cause an overestimation of risk in low-risk patients. Sharma and coworkers have also conducted a population study on stillbirth recurrence in a group of relatively low-risk women.[5] The data were again derived from a Missouri database. The relatively low-risk population was defined as nonsmoking women, less than 35 years of age, who were carrying singleton, nonanomalous fetuses. The study group (n = 1050) had experienced a stillbirth in the previous pregnancy, while the control group had live births (n = 261,384). Nine hundred forty-seven stillbirths occurred in the second pregnancies; 20 were in women with past stillbirths (stillbirth rate, 19.0 per 1000 births), and 927 were in the control group (stillbirth rate, 3.6 per 1000 births; $P < 0.001$).

Although the population studies mentioned above are limited by their reliance on birth certificate data and the lack of quantitative assessment of the frequency and severity of maternal conditions, the evidence for stillbirth as a predictor of poor future pregnancy outcome and recurrent stillbirth is compelling. Even in a relatively low-risk population, the adjusted risk of stillbirth is nearly sixfold higher among those with a past history of stillbirth.[5]

Experience with Antepartum Testing for Prevention of Recurrent Stillbirth

Having proven stillbirth as a harbinger of future perinatal mortality and morbidity in studies, conducted before and after the development of important laboratory, imaging, and medical interventions, the next logical step is to consider methods to mitigate future risk. In the hopes of improving pregnancy outcomes in women with a history of stillbirth, clinicians have used antenatal testing since its inception. Prospective randomized trials to test whether fetal monitoring actually reduces recurrent stillbirth have never been done. Early in the history of electronic fetal monitoring, there was a great deal of enthusiasm for the technology and high expectations of efficacy. The apparent lack of risk associated with the use of antepartum fetal surveillance also contributed to its wide adoption for patients with histories of stillbirth. However, the real deterrent to randomized trials was, and still is, the low numbers of affected women (stillbirths occur in <1% of pregnancies) and the need to control for a large number of confounding variables. In fact, these challenges have led to a dearth of retrospective study on the performance of fetal testing to prevent recurrent stillbirth.

Freeman and coworkers reported on 337 women with histories of stillbirth who were followed with antenatal testing.[8] These pregnancies were a subset of a total of 7052 high-risk pregnancies undergoing antenatal testing. Although it was a multi-institutional retrospective study of women seen between 1976 and 1982, the data on antenatal testing indications and results were collected prospectively.

Table 2 Indications for Fetal Testing Among Stillbirth Patients

Indication for Testing	No. of Patients	Percent
Total stillbirth patients	337	—
Previous stillbirth only	163	48.3
Previous stillbirth and hypertension	83	24.6
Previous stillbirth and diabetes	71	21
Previous stillbirth and IUGR	29	8.6
Previous stillbirth and postdates	21	6.2

Note. Multiple diagnoses in some patients.
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Table 3 Antenatal Fetal Testing Indications and Incidence of Positive Contraction Stress Test Results

	No. Tested	No. + CST	%
All tested patients	7052	208	3.0
No previous hx SB	6744	194	2.9
All previous SB	337	19	5.6*
SB + HTN	83	10	12.0*
SB + diabetes	71	4	5.6
SB + IUGR	29	5	17.2*
SB + postdates	21	0	—
SB only indication	163	6	3.7

*$P < 0.05$ when compared to patients without previous stillbirth. Reprinted with permission.[8]

Approximately half of the 337 patients with a previous history of stillbirth had no other reason for testing (Table 2). Acknowledging that perinatal death was too rare an outcome for meaningful statistical comparisons, the authors focused on antenatal test results, morbidity, and need for intervention in the various subgroups.

During the study interval, there were 396 women who were excluded from the study cohort due to noncompliance or "inadequate testing." Three of these women had recurrent stillbirths. All were diabetics who were noncompliant with follow-up testing; two had only one test at 35 to 36 weeks followed by a gap in testing of more than 2 weeks. One had a stillborn infant with multiple anomalies delivered 7 days after an "unsatisfactory test," owing to massive obesity.

No recurrent stillbirths occurred in the group of patients who were properly tested. Nineteen of the 337 patients with a previous stillbirth had positive contraction stress test (CST) results (5.6%), which was nearly double the rate seen in patients without previous stillbirth (Table 3). However, the average number of fetal heart rate tests per patient with a history of stillbirth was 5.0 compared with 2.5 tests per patient for the total population tested. The increased risk of positive CST results among women with stillbirth histories was attributable to pregnancies with past stillbirth and hypertension and past stillbirth plus intrauterine growth restriction as the indications for testing (incidence of positive tests 12 and 17%, respectively). Among the patients with past stillbirth as the only indication for testing (ie, no maternal medical problems, or intrauterine growth restriction), the likelihood of positive CST was not significantly higher than those who had indications for testing, but without a previous stillbirth history (3.7% versus 2.9%). In this study, there was no evaluation of outcomes according to the presence or absence of positive tests results. Therefore, while the study clearly shows that mothers who have experienced a previous stillbirth and who have medical or obstetrical complications in future pregnancies are at greater risk for positive contraction stress test results, there is no way to determine if the outcomes in the patients with positive CST results were poorer.

Freeman and coworkers did make perinatal outcome comparisons in patients with and without histories of stillbirth (Table 4). Patients with a history of stillbirth did not have higher incidences of intrauterine growth restriction, low 5-minutes Apgar scores, late decelerations in labor, or perinatal deaths than the population of patients whose indications for testing did not include stillbirth. However, a significantly higher incidence of respiratory distress syndrome did occur in patients with a history of stillbirth than in all other tested patients (3.9% versus 1.7%; $P < 0.05$). The authors reported that the increase in respiratory distress syndrome was probably due to a greater number of induced labors and primary cesareans (without labor) in women who had histories of stillbirth plus hypertensive disorders, diabetes, or intrauterine growth restriction as their indications for testing. When induction of labor or cesarean section was undertaken in women with a stillbirth history and hypertension, diabetes, or intrauterine growth restriction, approximately half of the interventions were for abnormal fetal heart rate testing results and half were for maternal indications. While respiratory distress syndrome was increased in neonates delivered by mothers with a history of stillbirth, the neonatal death (0.3%) rate was not significantly different than the group of tested pregnancies without a past history of stillbirth (Table 4).

The important findings of Freeman and coworkers can be summarized as follows:

1. A history of previous stillbirth is associated with a greater number of tests per patient than is seen in other patients with high-risk conditions. However, 44% of patients without stillbirth had postdates as an indication for testing, which would significantly limit the

Table 4 Perinatal Outcome for Patients with and Without a Previous Stillbirth

	Hx SB (n = 337)		No Hx SB (n = 6744)		
Outcome	No.	%	No.	%	*P*
BW <10th centile	17	5.0	368	5.5	NS
5 min Apgar <7	13	3.9	178	2.6	NS
Late decels in labor	29	8.6	664	9.8	NS
Fetal death	0	—	25	0.4	NS
Neonatal death	1	0.3	52	0.8	NS
Neonatal RDS	13	3.9	112	1.7	< 0.05

Hx = history; SB = stillbirth; BW = birth weight.
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number of CSTs that would have been done in that group.

2. Patients who have a history of previous stillbirth and a chronic maternal condition or intrauterine growth restriction are at greater risk for having positive contraction stress test results than patients whose indications for testing did not include stillbirth.
3. When a past history of stillbirth was the only indication for testing, there was no increased risk of positive contraction stress test results even though the stillbirth only group probably had more tests per patient than the general antepartum surveillance population. However, patients were high risk (eg, hypertension, diabetes, postdates). Without a group of low-risk controls, we cannot conclude that patients with a prior stillbirth as their only risk factor do not deserve monitoring.
4. Antenatal testing has the potential to increase the risk of premature delivery. Mothers with medical or obstetrical problems and past stillbirths were more likely to have labor inductions and cesarean sections and their neonates were more likely to have respiratory distress syndrome. Presumably, some of these interventions were the result of false-positive contraction stress test results.
5. Antenatal testing is likely to reduce recurrent stillbirth. Extrapolating from the perinatal collaborative data of the mid-twentieth century, in which perinatal mortality in pregnancies following at stillbirth was 7.3%, there should have been 25 perinatal deaths among the 337 women with prior stillbirths. Considering that there was only one neonatal death and no stillbirths in the 337 women who were compliant, antenatal fetal testing probably confers some protection against recurrent stillbirth. The degree to which the low perinatal mortality can be directly attributable to fetal testing as opposed to advances in medical care in the 25 years after the perinatal collaborative studies cannot be quantified.

In 1991, Weeks and coworkers reported on a cohort of 300 women whose sole indication for antepartum testing was a past history of stillbirth.[9] Whereas Freeman and coworkers sought to determine if a past history of stillbirth remained an important risk factor in the modern obstetrics era, Weeks and coworkers sought to determine if the timing of fetal testing in future pregnancies is important and whether the gestational age of the previous stillbirth influenced future pregnancy outcomes. As with the Freeman study, the rarity of recurrent stillbirth meant that outcome data were limited to measures of morbidity. The study group comprised patients seen at two institutions in southern California between 1979 and 1991. For all but the final 2 years, weekly contraction stress testing was used. In the final 2 years, semiweekly modified biophysical profiles (nonstress test plus amniotic fluid index) were used. CST or biophysical profiles were performed as needed to follow-up abnormal modified biophysical profile results. The study goal was to determine when to initiate testing in such women since a variety of approaches were being employed by the referring obstetricians (eg, begin testing 2 to 4 weeks before the gestational age of the previous stillbirth, at 32 weeks for all patients, at 36 weeks for all patients).

To assess the relationship between the gestational age of the previous stillbirth and subsequent pregnancy outcome, Weeks and coworkers compared groups who had early (≤32 weeks) versus late (≥36 weeks) stillbirths in the past. Predictably, the early stillbirth group had significantly more fetal tests per patient. They also had significantly more abnormal test results; however, interventions for abnormal tests and evidence of fetal compromise did not differ between the groups (Table 5).

There was one recurrent stillbirth and no neonatal deaths reported. The one stillbirth occurred in a women who had no live births and two previous stillbirths at 37 to 38 weeks gestation. The autopsy results for these stillbirths was normal. The mother's screening for hypertension, diabetes, thyroid disease, sexually transmitted disease, and collagen vascular disease was negative. Parental karyotypes were also normal. Three days after having a normal CST, that patient presented with a complaint of decreased fetal movement. She was released after having a reactive nonstress test; no decelerations were noted. Despite this, she returned 16 hours later stating that she was totally devoid of fetal movements for 5 hours. Intrauterine death was confirmed and the 35-week stillborn proved to be appropriately grown and structurally normal.

Fifty-three of the 300 study patients delivered at less than 38 weeks (18%). In half of those instances the deliveries

Table 5 Pregnancy Outcome by Gestational Age of Previous Stillbirth

	SB ≤ 32 Weeks (n = 115)	SB ≥ 36 Weeks (n = 148)	P
EGA delivery	38.9 (2.0)	39.1 (2.0)	NS
Birth weight	3270 (560)	3421 (567)	0.03
EGA first test	32.1 (4.0)	34.2 (3.0)	<0.01
Total tests	13.9 (10.7)	8.7 (5.2)	<0.01
Abnormal tests	61.70%	41.90%	<0.01
Delivery for abnormal test	20%	20.90%	NS
C/S for fetal indications	3.50%	6.80%	NS
IUGR	5.20%	2.70%	NS

SD = parenthesis; IUGR = intrauterine growth restriction; C/S = cesarean section; EGA = estimated gestational age; SB = stillbirth. Reprinted with permission.[9]

Table 6 Delivery Indications by Gestational Age

Reason for Delivery	Gestational Age at Delivery	
	<38 Weeks (n = 53)	≥38 Weeks (n = 247)
Positive CST	4 (7.5%)	10 (4.05%)
Equivocal fetal test	8 (15.1%)	19 (7.69%)
Spontaneous labor	27 (50.9%)	156 (63.2%)
Elective induction	0	58 (23.5%)
Abruption	3 (5.7%)	1 (0.40%)
PIH	4 (7.5%)	3 (0.12%)
Other*	7 (13.2%)	0

*Placenta previa, anxiety, classical scar.
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followed spontaneous labor. Approximately one-quarter of deliveries at less than 38 weeks were due to abnormal or equivocal fetal testing results (Table 6). Figure 1 shows the cumulative percentage of patients with positive fetal test results and the cumulative percentage of all women delivered for positive test results (defined as positive CST or biophysical profile (BPP) score of 4/10 or less).

Of the 300 patients tested, 19 had one or more positive antenatal test results (6.4%). There were six patients with positive test results at <36 weeks, three with positive tests at <32 weeks, and three with positive tests at 32 to 35 weeks. All three of the patients with positive results at <32 weeks ultimately delivered at term; none of those pregnancies had abnormal fetal heart rate tracings, intrauterine growth restriction, cesarean for fetal distress, or low 5-minute Apgar scores. Of the three patients who were delivered for positive tests at 32 to 35 weeks, only one had unequivocal evidence of fetal compromise (decreased fetal movement, BPP 2/10, cesarean section for abnormal fetal heart rate tracing). The two remaining patients were induced for abnormal tests at 32 and 35 weeks gestation. They were appropriately grown, premature neonates without apparent intrapartum or neonatal compromise.

Thirteen of the 19 patients with positive fetal test results had their positive results at >36 weeks. The authors did not report the proportion of that group with unequivocal evidence of uteroplacental or fetal compromise.

The important findings from the study of Weeks and coworkers can be summarized as follows:

1. When otherwise healthy women with histories of previous stillbirth are followed with antepartum fetal testing, the stillbirth recurrence risk is low (1 in 300). This stillbirth rate of 3.3 per 1000 is well below the national rate of 7 to 9 per 1000, suggesting that fetal testing can avert recurrent stillbirths.
2. It is not clear that an earlier gestational age at the time of the previous stillbirth correlates with increased risk in future pregnancies when the mothers do not have chronic medical conditions or concomitant obstetrical problems. However, clinicians test earlier in patients whose previous stillbirths occurred early in gestation. This practice is associated with an increase in total tests and in the likelihood of having a positive result (at least when CST is the predominant testing method).
3. In most instances, otherwise healthy women with a history of stillbirth should have fetal testing initiated beyond 32 weeks gestation. This study provides unequivocal evidence of an averted stillbirth in one of six patients with positive CST results at <36 weeks. However, there is also the potential for positive tests results which could result in increased risk of neonatal morbidity owing to prematurity. In this particular study, careful follow-up testing and sound clinical judgment appears to have minimized this risk. However, it is not clear that this can be widely reproduced.
4. Given that the recurrent stillbirth occurred within 3 days of normal CST results in a patient who was compliant, it is apparent that antepartum fetal surveillance cannot prevent all stillbirth recurrences, even in otherwise healthy mothers.

Clinician, Where Do We Go from Here?

As discussed elsewhere in this issue of the journal, a circumspect approach to the evaluation of stillbirth is paramount if we are to identify and understand a patient's particular pathophysiology and reduce the incidence of stillbirth in the United States. The American College of Obstetricians and Gynecologists has recently published a document that outlines the essential components of the maternal, fetal, and placental evaluation and the approach to counseling the family.[10] Especially important is the clinician's understanding of the value of perinatal autopsy and her ability to communicate this to the bereaved family. It is often helpful to delay discussions of autopsy until the day after delivery and to emphasize that the evaluation can be done in ways that will allow mourners to view the baby at memorial ceremonies.

There is compelling evidence that even in the modern obstetrical era, a history of previous stillbirth portends an increased risk in future pregnancies. Although the data on antepartum testing of patients with stillbirth as their only risk factor are limited, we can be reasonably confident that fetal testing confers some protection. CST is no longer used as a

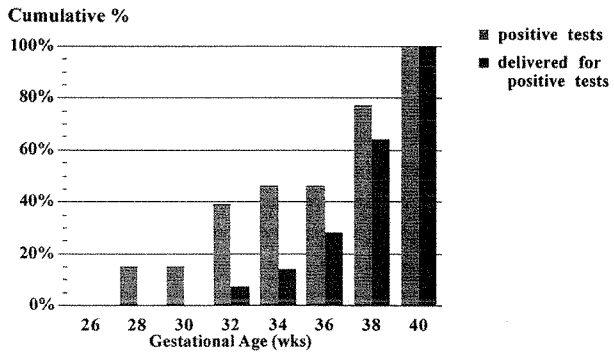

Figure 1 Cumulative percentage of abnormal fetal test results and delivery for abnormal fetal testing with advancing gestational age.

primary surveillance technique. As long as the fetal testing scheme includes weekly evaluation of acute and chronic markers of fetal well-being, as with a modified BPP or biophysical profiles, outcomes should be similar to those reported by Freeman and Weeks. In the absence of chronic medical conditions or concomitant obstetrical complications, healthy mothers with past stillbirths should start their antepartum testing at 32 to 36 weeks gestation.

Investigator, Where Do We Go from Here?

Antepartum surveillance for patients with a previous stillbirth is a longstanding standard of care. Hence, a prospective randomized trial of testing versus no testing is very unlikely to be done. Modified BPP and BPP have completely supplanted CST. Perhaps retrospective studies similar to those of Freeman and Weeks should be repeated. However, against a background stillbirth rate of <1%, over 3000 study patients would be needed to evaluate the risk of recurrent stillbirth. Without a very large multicenter study which includes databases to track confounding variables, fetal test results, and pregnancy outcomes, such a large retrospective study of healthy women with a history of stillbirth is not feasible.

Perhaps the most interesting and feasible area for study is the utility of fetal movement for assessment of fetal well-being. The study by Weeks and coworkers suggests that, in some cases, a mother's perception of decreased fetal movement may be more sensitive than fetal testing. After implementing universal fetal movement assessment in a group of women in San Diego, Moore and Piacquadio[11] noted a reduced stillbirth rate when compared with historical controls. More recently, J. Frederick Froen has championed the concept of assessing changes in maternal perception of fetal movement as opposed to relying on a specified "alarm limit."[12,13] Approximately half of all stillbirths occur at less than 28 weeks gestation.[14,15] Whether these early stillbirths can be averted with fetal movement assessment or modified antepartum surveillance programs is yet to be determined.

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