67 Assessment of fetal well-being: Fetal heart rate monitoring and the fetal biophysical profile

Yinka Oyelese, Martin Chavez, and Anthony M. Vintzileos

INTRODUCTION

The primary objective of antepartum fetal surveillance is the prevention of stillbirth. A second objective is the timely detection of fetal asphyxia that may result in long-term neurodevelopmental handicap. Antepartum fetal surveillance, for the most part, became possible only in the second half of the 20th century, mainly due to the advent of ultrasound and external continuous electronic fetal heart rate (FHR) monitoring (EFM). These technologies are now widely available and have become accepted as the mainstays of the evaluation of fetal well-being.

The use of any monitoring method to detect fetal compromise has, as a prerequisite, the clear understanding of the pathophysiology by which the particular condition results in adverse perinatal outcome. A test that is reliable for one condition may not be so valuable for predicting outcomes with another condition. Kontopoulos and Vintzileos (1) recently discussed how the efficacy of any antepartum screening test depends on the underlying pathophysiology of the condition and recommended condition-specific antenatal testing. Table 1A lists all the known pathophysiologic processes that can place the fetus at risk for in utero death or neurologic damage, whereas Table 1B lists some of the more common indications for antepartum fetal surveillance. Importantly, no single list of indications could ever cover all the reasons for fetal surveillance. Essentially, any condition that puts the fetus at risk for antepartum death may be considered as an indication for fetal surveillance.

Until late in the 20th century, the main methods of antepartum fetal monitoring were the measurement of fundal height and maternal kick counts. The introduction of the FHR monitor by Hon around 1960 (2) ushered in a new era in fetal well-being assessment. EFM was initially designed for intrapartum assessment of fetal well-being, but it eventually became a tool for antepartum fetal monitoring too. However, it soon became obvious that monitoring of the FHR alone had limitations, especially a high false-positive rate. In 1980, Manning and colleagues introduced the fetal biophysical profile (BPP) (3), which utilizes real-time ultrasound examination of the fetus. While there are numerous other forms of fetal monitoring, such as Doppler for hemodynamic fetal evaluation, this chapter will discuss the role of antepartum FHR monitoring and the BPP in fetal assessment, including the limitations of each technique.

EFM

About 1960, Hon introduced the EFM originally for the purpose of intrapartum assessment of the fetus (4,5). It was observed that certain FHR patterns were strongly predictive of

a non-asphyxiated fetus, while other patterns suggested intrapartum fetal oxygen deprivation (5). Fetuses suffering from intrapartum hypoxia frequently exhibited a slowing of the FHR following a contraction, termed late deceleration. Following the routine introduction of the EFM during labor, there was a remarkable reduction in intrapartum fetal deaths. Subsequently, it was suggested that EFM might play a role in assessing fetal well-being way before the onset of labor. Since the presence of intrapartum late decelerations indicated fetal hypoxia, it was believed that stimulating uterine contractions in patients who were not in labor might help identify fetuses that were at risk of hypoxia in the antepartum period. This led to the “oxytocin challenge test” (OCT), the original antepartum continuous electronic FHR assessment of the fetus, introduced in the early 1970s by Ray and colleagues (6). Using oxytocin, uterine contractions were stimulated, and the presence of FHR late decelerations were considered a positive test and predictive of fetal compromise (7).

The OCT was considered positive if greater than 50% of contractions were followed by late decelerations, and negative if there were no late or significant variable decelerations. An OCT was described as “suspicious” if there were intermittent late or variable decelerations, while the test was deemed “unsatisfactory” if there were fewer than three contractions over a 10-minute period, or if the fetal heart tracing quality was uninterpretable. In cases where there were prolonged contractions that led to decelerations, the term “hyperstimulation” was used. Later, it became apparent that these decelerations could also result from spontaneous uterine contractions, and therefore the test was renamed the “contraction stress test” (CST). Others used nipple stimulation instead of oxytocin to provoke uterine contractions and found similar results (8–13). A positive CST (or OCT) was indicative of uteroplacental insufficiency. During contractions, blood flow to the intervillous space is impeded. A bradycardic response develops due to a chemoreceptor response that is provoked by fetal hypoxia. These late decelerations in the antepartum period were shown to predict subsequent adverse outcomes before, during, and after labor. Several studies demonstrated that though the OCT had a high false-positive rate, the false-negative rate was low, about 1% or less (14). In other words, the risk of fetal death within 1 week after a negative test is negligible. However, the false-positive rate of the OCT is at least 20% to 45% (15,16). Importantly, conditions associated with fetal demise after a negative CST are often umbilical cord accidents and placental abruption, conditions that occur suddenly, and may not necessarily be expected to be predicted by any antepartum surveillance modality (14).

Table 1A Antepartum Maternal/Fetal Pathophysiologic Processes That Can Place the Fetus at Risk for In Utero Death or Neurologic Damage

Pathophysiologic process	Maternal/fetal condition
Decreased uteroplacental blood flow	Chronic hypertension Pre-eclampsia Collagen/renal/vascular disease Most cases of fetal growth restriction (i.e., <32–34 wk)
Decreased gas exchange	Postdate pregnancy, some fetal growth–restricted cases (i.e., >32–34 wk)
Metabolic aberrations	Fetal hyperglycemia Fetal hyperinsulinemia
Fetal sepsis	PROM Intra-amniotic infection Maternal fever, primary subclinical Intra-amniotic infection
Fetal anemia	Fetomaternal hemorrhage Erythroblastosis fetalis Parvovirus B19 infection
Fetal heart failure	Cardiac arrhythmia Nonimmune hydrops Placental chorioangioma Aneurysm of the vein of Galen
Umbilical cord accident	Umbilical cord entanglement (monoamniotic twins) Velamentous cord insertion/Funic presentation Noncoiled umbilical cord Oligohydramnios

Abbreviation: PROM, premature rupture of the membranes.

Table 1B Some Common Indications for Antepartum Fetal Surveillance

Intrauterine growth restriction
Prior stillbirth
Diabetes
Hypertension
Pre-eclampsia
Postdate pregnancies
Preterm premature rupture of the membranes
Oligohydramnios
Decreased fetal movements
Prior stillbirth
Maternal lupus
Multifetal pregnancies, particularly those with growth disturbances or discordance
Cholestasis of pregnancy

Needless to say, the OCT was cumbersome and difficult to perform. In the process of performing OCTs, it was often observed that the presence of FHR accelerations had good predictive value for a non-asphyxiated fetus (17). Consequently, the concept of the nonstress test (NST) was proposed. Since monitoring of fetal movements (including maternal kick counts) had previously been used to assess fetal well-being, the NST was considered an objective method of fetal monitoring. A “reactive” NST was initially defined as one with two to five or more accelerations in 20 minutes. An acceleration is defined

as a transient increase in FHR over the baseline of at least 15 beats/minute (bpm), lasting at least 15 seconds. For pregnancies less than 32 weeks of gestation, an acceleration is a transient increase over the baseline of at least 10bpm, lasting at least 10 seconds.

There are other variables in the heart rate pattern that may suggest fetal well-being or compromise. The normal fetal baseline heart rate is 110 to 160. The baseline heart rate decreases with gestational age, mainly as a consequence of vagal maturation. Fetal tachycardia (defined as a baseline FHR >160bpm) may occur in association with maternal fever, maternal ingestion of stimulants including beta-adrenergic agents. Uncomplicated fetal tachycardias (with accelerations and good variability) are generally associated with a good outcome. However, these require close and thorough evaluation. When there is a persistent complicated tachycardia (including a heart rate greater than 200bpm, where there is minimal or no variability, or where there are decelerations), delivery should be considered, especially at term or near term. Obviously, one must take the entire clinical picture into consideration. For instance, treating maternal fever or stopping stimulant medications may be enough to resolve the tachycardia.

Bradycardia is defined as a baseline FHR <110bpm. Again, this is generally benign if there are accelerations and good variability. However, FHRs of <100bpm may be associated with fetal heart block and require further evaluation. The absence of accelerations or reduced variability may be due to periodicity. However, if this persists for >45 minutes, further evaluation should be undertaken. A sinusoidal FHR pattern (Fig. 1) is considered an ominous pattern (18) and is often associated with fetal anemia or hypovolemia, including that resulting from such causes as isoimmunization, parvovirus infection, placental abruption, twin–twin transfusion syndrome (19–21), and ruptured vasa previa (22). Generally, prompt delivery is indicated, unless the cause of the sinusoidal FHR (such as fetal anemia) can be treated in utero (18,22).

The NST has several advantages over the CST—it is easy to perform and interpret, does not require oxytocin administration, and can be performed in shorter time than the CST. Furthermore, the CST has several absolute and relative contraindications, such as in patients with premature rupture of the membranes, prior classical cesarean delivery, multiple gestations, incompetent cervix, preterm labor, or vaginal bleeding. These important characteristics as well as the predictive reliability of the test made the NST the primary modality of fetal evaluation. Several studies have validated the role of the NST as a predictor of perinatal outcome (23,24). The presence of accelerations is associated with a low risk of fetal hypoxia, while the absence of accelerations carries a significantly higher rate of fetal hypoxia and acidosis. The FHR reactivity is controlled by the autonomic nervous system and the percentage of reactive NSTs increases with fetal maturation. By term, over 90% of fetuses demonstrate reactive NSTs. FHR accelerations are associated with fetal movements. An FHR tracing may be nonreactive due to fetal immaturity, fetal sleep state, maternally administered sedatives, fetal neurologic and cardiac anomalies, fetal hypoxia/acidosis, utero-placental insufficiency, or fetal infection. Unfortunately, the NST also has a high false-positive rate of about 50%, while the

Figure 1 Fetal heart rate tracing demonstrating a sinusoidal fetal heart rate pattern.

false-negative rate is only about 0.3%. Translated differently, a reactive NST carries a very low risk of fetal hypoxia, while a nonreactive NST is only associated with adverse outcomes in less than one-half of cases. Phelan and colleagues reviewed 2226 patients who had undergone 4000 NSTs. Of these, 1564 women with a reactive NST were delivered within 1 week of the test. There were four fetal deaths giving a false-negative rate of 0.026%—these resulted from placental abruption and cord accidents, events that may not be necessarily expected to be predicted by an NST (25).

In the late 1980s, it was observed that fetal auditory stimulation would often lead to FHR accelerations in a fetus that had previously lacked accelerations (26–30). This reduced testing time and also reduced the nonreactive NST rate. An artificial larynx was developed that produced a vibroacoustic signal (VAS). A rapidly occurring acceleration following the stimulation is considered a positive response. A positive VAS was shown to have similar accuracy in predicting good perinatal outcomes as a spontaneously reactive NST, with the advantage of a reduced testing time.

The OCT/CST and NST are performed using an external FHR monitor and a tocodynamometer strapped to the maternal abdomen. The FHR monitor derives its signals ultrasonically or via phonocardiography. Ultrasound is the most widely used technique and provides an accurate tracing in the majority of cases. Perhaps obesity is the major factor that may be associated with an inability to obtain a satisfactory fetal heart tracing. Uterine contractions are monitored via the tocodynamometer. The tocodynamometer monitors the frequency and duration of the contractions, but cannot assess the strength of the contractions. The tocodynamometer may not adequately detect contractions in obese patients.

Antepartum FHR testing has undergone considerable evaluation in several studies. It has been shown to have good prediction of fetal well-being when accelerations are present

Figure 2 Relationship between the fetal biophysical score and umbilical cord arterial pH. Source: From Ref. 33. The American College of Obstetricians and Gynecologists.

Figure 3 Relationship between cord artery pH and absent fetal biophysical activities. The pH tends to be lower in the absence of movements and/or tone compared with nonreactive nonstress test or absent fetal breathing. Results are expressed in means (95% error bars). Abbreviations: No FM, absent fetal movements; No FT, absent fetal tone; No FBM, no fetal breathing movements; NR-NST, nonreactive nonstress test. Source: From Ref. 31.

Figure 4 Relationship between cord artery oxygen partial pressure (pO₂) and absent fetal biophysical activities. The pO₂ tends to be lower in the absence of movements and/or tone compared with nonreactive nonstress test or absent fetal breathing. Results are means expressed in millimeters of mercury (95% error bars). Abbreviations: No FM, absent fetal movements; No FT, absent fetal tone; No FBM, no fetal breathing movements; NR-NST, nonreactive nonstress test. Source: From Ref. 31.

Figure 5 Relationship between cord artery carbon dioxide partial pressure (pCO₂) and absent fetal biophysical activities. The pCO₂ tends to be higher in the absence of movements or tone compared with nonreactive nonstress test or absent fetal breathing. Results are means expressed in millimeters of mercury (95% error bars). Abbreviations: No FM, absent fetal movements; No FT, absent fetal tone; No FBM, no fetal breathing movements; NR-NST, nonreactive nonstress test. Source: From Ref. 31.

and decelerations are absent. However, the converse is not true; the absence of accelerations is not necessarily indicative of a compromised fetus. Thus, EFM was found to be associated with an exceedingly high false-positive rate, resulting in excessive unnecessary interventions such as inductions and cesarean deliveries. It became obvious that there was a need for some other form of surveillance that could reduce this false-positive rate.

THE FETAL BPP

In 1980, Manning and colleagues introduced the BPP (Table 2) (3). This test was based on a more thorough evaluation of the fetus; the main advantage of the BPP over EFM is that the BPP evaluates several different biophysical markers. The FHR allowed the assessment of only a single biophysical marker. Just as a heart rate alone in an adult cannot distinguish between sleep and coma, the FHR, when used alone, has significant limitations, especially in the absence of accelerations. The BPP is analogous to an intrauterine Apgar score with its dynamic variables (acute markers) reflecting fetal CNS function. In addition to FHR reactivity, other acute fetal markers such as fetal movements, fetal breathing movements and tone, as well as assessment of the intrauterine environment, that is, estimation of amniotic fluid volume and placental grading could be objectively evaluated. The fetal BPP was developed to decrease the false-positive results associated with FHR monitoring. The most important element of this testing method is the combination of acute and chronic markers of the fetal condition. The acute markers include FHR reactivity, fetal breathing, fetal movements, and fetal tone, while fetal amniotic fluid volume is a chronic marker of fetal well-being. The BPP avoids the high false-positive rates of the NST and the CST and therefore helps reduce unnecessary interventions.

The Physiologic Basis for the BPP

Acute Markers

The acute fetal biophysical markers—FHR reactivity, fetal movements, fetal breathing movements, and fetal tone—are not random events, but are initiated and regulated by the fetal central nervous system (CNS) (Table 3). The presence of any one of these markers implies that, at the time of testing, the CNS center that controls the particular activity is

Table 2 Fetal Biophysical Profile Scoring (Manning and Coworkers)		
	Score 2	Score 0
Movements	Three or more gross body movements in a 30-min period. Simultaneous trunk and limb movements count as a single movement	Less than three gross body movements in a 30-min period
Tone	At least one movement of a limb from a position of flexion to one of extension, with a rapid return to flexion	Fetal limb in extension with no return to flexion with movement
Breathing	At least 30 sec of sustained fetal breathing movements observed over a 30-min period	Less than 30 sec of sustained fetal breathing movements observed over a 30-min period
Amniotic fluid	At least a single amniotic fluid pocket measuring 2cm × 2cm in two perpendicular planes	No amniotic fluid pocket that measures at least 2cm × 2cm in two perpendicular planes
Fetal heart rate	At least two accelerations (of >15 beats per minute, lasting at least 15 sec) in a 40-min period	Less than two accelerations in 40 min
Source: From Ref. 3.		

Table 3 Fetal Central Nervous System Centers Governing Biophysical Activities and Therefore Tested by the Biophysical Profile

Test	Center
Fetal tone	Cortex–subcortical area
Fetal movements	Cortex nuclei
Fetal breathing movements	Ventral surface of the fourth ventricle
Nonstress test	Posterior hypothalamus, medulla

intact, functional, and therefore non-hypoxic. The converse, however, is not necessarily true; the absence of a single fetal biophysical activity is not always due to hypoxia and acidosis. Fetal biophysical activities such as fetal breathing movements, fetal body movements, and FHR variability all undergo periodic changes. Thus, the absence of biophysical activities is more frequently the result of periodicity rather than a pathologic condition and needs to be interpreted with caution. The periodicity of these biophysical activities may be short term (20–40 minutes) or long term, similar to those diurnal rhythms of extrauterine life. Maternal administration of CNS depressants and sedatives, such as opiates, barbiturates, and benzodiazepines, may inhibit fetal biophysical activities, while factors that cause stimulation of the maternal CNS, for example, hyperglycemia or catecholamines, may result in increased biophysical activities. The effect of fetal hypoxia and acidosis, or fetal infection, on the fetal BPP depends on the severity, duration, chronicity, and frequency of the hypoxic insult(s). Fetal hypoxia may be transient without acidosis, or prolonged with associated metabolic or mixed acidosis, affecting multiple organs. Acute fetal hypoxia (or fetal infection) produces a definite decrease in FHR reactivity (nonreactive NST) and fetal breathing movements, and when severe hypoxia (or infection) abolishes fetal movements and tone (31–33).

The biophysical activities appear progressively in normal fetuses as gestation advances. The first biophysical activity to appear is tone; the fetal tone center begins functioning at 7½–8½ weeks of gestation. This is followed shortly thereafter by the fetal movement center, which begins functioning at approximately 9 weeks of gestation. The fetal breathing movement center starts operating at about 20 to 21 weeks of gestation, and finally the FHR reactivity center becomes functional by the end of the second trimester or early third trimester. These centers vary in their sensitivity to hypoxia and acidosis (31–33). It was first observed by Vintzileos and colleagues that the biophysical activities that become active first in fetal neurodevelopment are the last to become compromised in fetuses exposed to intrauterine asphyxia or intra-amniotic infection (31–33). Thus, the FHR reactivity and breathing centers, controlling the biophysical activities that appear latest in gestation, are the most sensitive and the first to become affected when the fetus is exposed to hypoxia or intra-amniotic infection (31). Data from our prior studies indicate that FHR reactivity and fetal breathing are abolished when the fetal pH is <7.20, whereas fetal movement and tone are abolished at pH values <7.10. Thus, according to the “gradual hypoxia concept,” the earliest biophysical manifestations of fetal compromise (fetal hypoxia or infection) are a loss of

variability in the NST and absence of fetal breathing. As fetal condition deteriorates, fetal movements and then tone become abolished. In our experience, poor fetal tone is associated with the highest perinatal death rate (42.8%) (32). An understanding of this progressive sensitivity of the biophysical activities to fetal hypoxia or infection of the fetal CNS centers is a prerequisite for the correct interpretation of the information derived from the biophysical assessment and allows for accurate assessment of the degree of fetal compromise in high-risk patients with intact as well as ruptured membranes.

Chronic Markers

The most important chronic marker of the BPP is the amniotic fluid volume, although placental grading was also included in the original studies by Vintzileos et al. (3,32). Chronic uteroplacental insufficiency that results in fetal hypoxia is frequently associated with redistribution of cardiac output away from non-vital to vital fetal organs. Thus, there is typically a reduction in renal perfusion, with consequent decreased urine production and, therefore, oligohydramnios. Oligohydramnios places the fetus at high risk for cord compression and in utero death. Several studies have demonstrated a strong correlation between oligohydramnios and increased incidence of adverse perinatal outcome. Chamberlain and colleagues demonstrated, in a study of 7582 referred high-risk patients, that in structurally normal fetuses, the perinatal mortality rates were 1.97 in 1000 in the presence of normal qualitative amniotic fluid volume (largest pocket >2cm and <8cm), whereas rates in fetuses with marginal (largest pocket 1–2cm) and decreased amniotic fluid (largest pocket <1cm) were 37.7 in 1000 and 109.4 in 1000, respectively (34). Another study of 147 pregnancies complicated by oligohydramnios in pregnancies at gestational ages >34 weeks found an increased risk of labor induction, non-reassuring FHR patterns, cesarean delivery, neonatal intensive care unit admission, meconium aspiration, stillbirth, and neonatal death (35). Amniotic fluid volume is not influenced by acute changes in fetal CNS function. Most investigators consider the finding of oligohydramnios, even when it occurs on its own, as an abnormal biophysical assessment even if when all the remaining biophysical parameters are normal and the presence of oligohydramnios is generally regarded as an indication for intensive surveillance (in preterm gestations) or delivery (term or near-term gestations) (3,33,36,37). When spontaneous severe FHR decelerations and oligohydramnios coexist, delivery may be indicated, regardless of gestational age. Vintzileos and colleagues had initially included placental grading in the fetal BPP (32). These investigators observed that patients with grade 3 placentas had an increased incidence of abnormal intrapartum FHR patterns (44.4%) and placental abruption (14.8%) (32). Thus, inclusion of grade 3 placentas in the BPP alerts the obstetrician to the significant risk of intrapartum complications.

Since the early 1980s, attempts have been made to give a score to each biophysical variable to produce a “fetal BPP score.” There are currently two types of scoring systems: one proposed by Manning and coworkers (Table 2) (3) and the other by Vintzileos and coworkers (Table 4) (32). In both scoring systems, a score of >8 is considered reassuring of fetal

Table 4 Criteria for Scoring Biophysical Variables According to Vintzileos and Coworkers

<i>Nonstress test</i>
Score 2 (NST 2): five or more FHR accelerations of at least 15bpm in amplitude and at least 15-sec duration associated with fetal movements in a 20-min period
Score 1 (NST 1): two to four accelerations of at least 15bpm in amplitude and at least 15-sec duration associated with fetal movements in a 20-min period
Score 0 (NST 0): one or fewer accelerations in a 20-min period
<i>Fetal movements</i>
Score 2 (FM 2): at least three gross (trunk and limbs) episodes of fetal movements within 30 min. Simultaneous limb and trunk movements were counted as a single movement
Score 1 (FM 1): one or two fetal movements within 30 min
Score 0 (FM 0): absence of fetal movements within 30 min
<i>Fetal breathing movements</i>
Score 2 (FBM 2): at least one episode of fetal breathing of at least 60-sec duration within a 30-min observation period
Score 1 (FBM 1): at least one episode of fetal breathing lasting 30–60 sec within 30 min
Score 0 (FBM 0): absence of fetal breathing or breathing lasting <30 sec within 30 min
<i>Fetal tone</i>
Score 2 (FT 2): at least one episode of extension of extremities with return to position of flexion, and also one episode of extension of spine with return to position of flexion
Score 1 (FT 1): at least one episode of extension of extremities with return to position of flexion or one episode of extension of spine with return to flexion
Score 0 (FT 0): extremities in extension. Fetal movements not followed by return to flexion. Open hand
<i>Amniotic fluid volume</i>
Score 2 (AF 2): fluid evident throughout the uterine cavity. A pocket that measures >2 cm in vertical diameter
Score 1 (AF 1): a pocket that measures <2 cm but more than vertical diameter
Score 0 (AF 0): crowding of fetal small parts. Largest pocket <1 cm in vertical diameter
<i>Placental grading</i>
Score 2 (PL 2): placental grading 0, 1, or 2
Score 1 (PL 1): placenta posterior difficult to evaluate
Score 0 (PL 0): placental grading 3

Abbreviations: NST, nonstress test; FHR, fetal heart rate; bpm, beats per minute; FM, fetal movements; FBM, fetal breathing movements; FT, fetal tone; AF, amniotic fluid; PL, placental grading. Maximal score 12; minimal score 0. Source: From Ref. 32.

well-being. A score of <8 is non-reassuring and repeat testing or delivery is suggested. A limitation of the original BPP scoring system of Manning et al. is that biophysical activities are given an “all or none” score (3). For instance, if there are movements detected that are insufficient to meet to score of 2, the fetus is assigned a “0” for that biophysical activity. However, most would agree that a fetus that demonstrates two movements over 30 minutes may be different from one that exhibits no movements at all. Thus, the initial assignment of intermediate scores, as proposed by Vintzileos et al. (32), had as its main purpose to identify the minimum requirements for each biophysical component to meet normalcy criteria.

The Fetal BPP and Fetal Acid–Base

The BPP aims at assessing fetal acid–base status at the time of testing. However, in order to assess the accuracy of the fetal BPP in assessing antepartum fetal acid–base status, it is crucial that the acid–base status be assessed shortly after the BPP is performed. Furthermore, labor has a profound effect on acid–base status measured at birth. A major disadvantage of several studies has been the long interval between performing the biophysical assessment and the birth of the infant, as well as the effects of labor and drugs on the fetus. In order to overcome these limitations, Vintzileos and coworkers studied 124 consecutive patients with singleton pregnancies at gestational ages between 26 and 43 weeks, limiting their study to patients undergoing cesarean section prior to the onset of labor (33,38). All patients had a BPP performed within 6 hours of the cesarean section. This BPP was correlated with fetal acid–base status as determined by umbilical cord blood pH measurements. Figure 2 illustrates the relationship between the fetal biophysical score and cord arterial pH. Importantly, all nine fetuses with scores of <4 were acidemic with umbilical cord arterial pH values of 6.99 ± 0.10 (mean $\pm$ SD). Thirteen fetuses with scores of 5 to 7 had a cord artery pH of 7.19 ± 0.06 (mean $\pm$ SD); 9/13 of fetuses (69%) were acidemic. One hundred and two fetuses had a score of >8; in this group of fetuses, the cord artery pH was 7.28 ± 0.04 (mean $\pm$ SD); only two of these (2%) were acidemic. The three groups had statistically different cord arterial pH values. The relationship between the biophysical score and cord venous pH was similar.

As expected, based on the gradual hypoxia hypothesis, there was a relationship between the individual biophysical activities and the umbilical cord blood artery pH values (Fig. 3). When combined biophysical activities were considered, of the 96 fetuses with reactive NSTs and/or fetal breathing present (lasting >30s), none was acidemic. All the remaining fetuses had nonreactive NSTs and absent fetal breathing. However, 17 fetuses had normal (three or more) body movements and tone; the mean pH of this group was 7.20 and 10 (59%) of these fetuses were acidemic. Four fetuses had compromised movements (one to two body movements) or tone; the mean cord blood artery pH was 7.16, and three fetuses (75%) were acidemic. In the seven fetuses with all biophysical activities absent, the mean cord blood artery pH was 6.95, with 100% of them having cord blood artery pH values <7.20. Careful observation of the results suggests that there are different levels of sensitivity to hypoxia and acidosis at which the fetal biophysical activities become compromised. The FHR reactivity and fetal breathing seem to be compromised when the pH is lower than 7.20. At pH values of 7.10 to 7.20, fetal movements and tone are still present but not normal and at pH values <7.10, movements and tone are totally absent. The ability of the individual biophysical components alone and in combination to predict fetal acidemia is shown in Table 5. Of the individual biophysical components, FHR reactivity and fetal breathing had 100% sensitivities and negative predictive values, an observation that suggests that either test is a reasonable choice for primary fetal surveillance. The combination of nonreactive NST and absent fetal breathing movements (the “abnormal test”) improved the specificity and positive predictive values to 92%

Table 5 Efficacy of the Fetal Biophysical Variables to Predict Fetal acidemia

Biophysical variable(s)	Definition of the abnormal test	Sensitivity (%) (n)	Specificity (%) (n)	Positive predictive value (%) (n)	Negative predictive value (%) (n)
Biophysical score	<7	90% (18/20)	96% (100/104)	82% (18/22)	98% (100/102)
Nonstress test, fetal breathing movements	Nonreactive NST and no breathing	100% (20/20)	92% (96/104)	71% (20/28)	100% (96/96)
Nonstress test	Less than one acceleration in 20 min	100% (20/20)	76% (79/104)	44% (20/45)	100% (79/79)
Fetal breathing movements	<30 sec	100% (20/20)	64% (67/104)	35% (20/57)	100% (67/67)
Fetal movements	Less than three	50% (10/20)	96% (100/104)	71% (10/14)	91% (100/110)
Fetal tone	Compromised or absent	45% (9/20)	100% (104/104)	100% (9/9)	90% (104/115)
Amniotic fluid	<1 cm	35% (7/20)	93% (97/104)	50% (7/14)	88% (97/100)
Amniotic fluid	<2 cm	45% (9/20)	86% (89/104)	38% (9/24)	89% (89/100)
Placental grading n, number of fetuses	Grade 3	5% (1/20)	94% (98/104)	14% (1/7)	84% (98/117)

and 71%, respectively. Fetal tone has the highest positive predictive value (100%) for fetal acidemia, but low sensitivity (45%), an observation that suggests that fetal tone alone should not be used for primary fetal surveillance.

Cordocentesis is a technique that allows accurate assessment of relationship between the fetal BPP and fetal umbilical cord blood gas values. Ribbert and colleagues studied 14 severely growth-retarded fetuses, performing a BPP assessment prior to fetal blood sampling by cordocentesis (39). The fetal BPP was correlated with fetal blood pO_2 , pH, oxygen saturation, and oxygen content. It was found that the fetal BPP was a good indicator of the degree of fetal acidemia. Of the individual fetal biophysical activities, FHR reactivity was compromised for ΔpH (observed pH subtracted from the appropriate mean for gestation) below -2 standard deviations (SD)s; fetal breathing movements were compromised for ΔpH values below -3 SDs; fetal body movements and fetal tone were compromised for ΔpH values below -4 SDs. These preliminary data using fetal blood gas values obtained at cordocentesis confirmed the observations of Vintzileos and coworkers in that the fetal BPP can predict the degree of fetal acidemia and that the FHR reactivity and fetal breathing movements are the first, whereas fetal gross body movements and tone are the last, biophysical activities to be compromised during acidemia. In another study of 62 patients undergoing cesarean section prior to the onset of labor, the relationship between fetal biophysical assessment performed within 3 hours of delivery and cord blood gases was investigated (31). It was observed that nonreactive NSTs and absent fetal breathing movements were both associated with lower pH, pO_2 , bicarbonate, base excess and higher pCO_2 than that when the NST was reactive or fetal breathing was present. The absence of fetal movements and/or tone was associated with lower pH, pO_2 , bicarbonate and base excess, and a higher pCO_2 than when fetal body movements and tone were present (Figs. 3–7). These blood gas differences were noted in both cord arterial and venous blood. Thus, the first manifestations of fetal hypoxemia and acidemia are

Figure 6 Relationship between cord artery bicarbonate level and absent fetal biophysical activities. The bicarbonate level tends to be lower in the absence of movements or tone compared with nonreactive nonstress test and absent fetal breathing. Results are means expressed in millimoles per liter (95% error bars). Abbreviations: No FM, absent fetal movements; No FT, absent fetal tone; No FBM, no fetal breathing movements; NR-NST, nonreactive nonstress test; Source: From Ref. 31.

Figure 7 Relationship between cord artery base excess and absent fetal biophysical activities. The base excess tends to be lower in the absence of movements or tone compared with nonreactive nonstress test and absent fetal breathing. Results are means expressed in millimoles per liter (95% error bars). Abbreviations: No FM, absent fetal movements; No FT, absent fetal tone; No FBM, no fetal breathing movements; NR-NST, nonreactive nonstress test. Source: From Ref. 31.

nonreactive NST and the absence of fetal breathing. As hypoxemia becomes more advanced, and hypercapnia and acidemia develop, fetal movements and tone become absent. A similar sequence of events in the deteriorating fetus also occurs in the presence of fetal infection (40).

The BPP: Impact on Perinatal Outcomes

In their initial study of the use of the BPP in clinical practice, Manning et al. (3) measured five biophysical activities (fetal movement, fetal tone, fetal breathing, amniotic fluid volume, and fetal NST) in 216 patients, all of whom delivered within a week of the last BPP. The patients were managed based on their NSTs, not based on the results of the BPPs. These investigators found that each of the five individual biophysical markers had a low false-negative rate, but that all five had a high false-positive rate. However, this false-positive rate varied widely among the different markers. The authors found that combining the markers led to a significant improvement in the false-positive and false-negative rates. There was a significant correlation between abnormal BPP scores and low 5-minute Apgar scores, fetal distress in labor, and perinatal death rate. These authors found a perinatal mortality rate of 0/1000 when all biophysical markers were normal (score 10), but that this rose to 600/1000 when all biophysical activities were abnormal (score 0). The fetal death rate with a score of 0 was 400/1000.

Based on the results of this initial study, Manning and colleagues suggested a management protocol based on BPP scoring that is outlined in Table 6. These investigators used this protocol for patient management in a subsequent prospective study involving 1184 consecutive referred high-risk patients who had 2238 fetal biophysical scores performed (40). The purpose of the study was to assess the impact of using the biophysical score on perinatal death rate in high-risk patients. There were six perinatal deaths, in the study group, giving a perinatal mortality of 5.06 per 1000. This was significantly lower than the predicted rate for a similar high-risk population (65 per 1000). Importantly, this perinatal death rate was also less than half of that in the general population in Manitoba (14.3 per 1000). Only one fetus died after a reassuring biophysical score, thus giving a true false-negative rate of 0.8 per 1000. As an added potential benefit, 13 of 19 (68.4%) fetuses with previously undiagnosed major congenital anomalies,

including 8 with lethal anomalies, were prenatally diagnosed as a result of real-time ultrasound. In two cases, the antepartum detection of the anomaly helped neonatal survival.

In 1983, Vintzileos and coworkers reported their initial experience using a BPP consisting of six variables in 150 patients with high-risk pregnancies during a 30-minute observation period (32). A total of 342 BPPs were performed. The patients were not managed based on the BPP results, but rather based on their nonstress or CSTs. There was a good correlation between the biophysical scores and adverse perinatal outcomes, including intrapartum fetal heart-rate pattern abnormalities, meconium during labor, fetal distress, and the perinatal mortality rate. Fetal biophysical scores (>8) were associated with good pregnancy outcome in all cases. Very abnormal scores (≤4) were almost always associated with fetal distress. The absence of fetal movements was the best predictor of abnormal intrapartum heart-rate patterns (80%), while a nonreactive NST was the best predictor of meconium-stained fluid (33.3%). Oligohydramnios was the best predictor of fetal distress (37.5%) and absent fetal tone was the best predictor of fetal death (42.8%). The 11 fetuses that were acidemic at birth (cord blood artery pH <7.20) all had nonreactive NSTs and absent fetal breathing. There were two fetuses with normal fetal movement and both survived. Of five fetuses with movement present but compromised (one or two body movements in 30 minutes), only one died. Three out of the four fetuses with absent fetal movement died; all three also had absent fetal tone. These observations suggested that the biophysical components do not contribute to the predictive accuracy in an equally proportionate manner.

Baskett et al., using the Manning scoring criteria, reported on 5618 BPP scores performed on 2400 high-risk pregnancies (41). The perinatal mortality in the study population was only 9.2 per 1000, compared with the overall perinatal mortality in the investigators' hospital over the study period of 14.5 per 1000. Structurally normal fetuses with a normal biophysical score had a perinatal mortality of only 1 per 1000. Fetuses with scores of 4 or less had a perinatal mortality rate of 292 per 1000. In this study, the positive predictive value of an abnormal biophysical score for abnormal perinatal outcome (defined as intrapartum fetal distress, 5-minute Apgar score <7, intrauterine growth restriction, or perinatal death) was 79.2%. This predictive power was significantly better than that of the NST, fetal breathing movements, and fetal tone; however, it did not reach statistical significance when compared with fetal movement and amniotic fluid volume.

In the first prospective randomized blinded study of the BPP, Manning et al. randomized 735 women with high-risk pregnancies to BPPs or NSTs for fetal assessment (42). The results of the tests were used for management, but the physicians were not informed of which test had been used. The BPP was shown to have an improved predictive value over the NST for low Apgar scores. The negative predictive values were similar for both forms of fetal assessment. Sensitivity, specificity, and accuracy were not statistically different between the two methods of fetal assessment. In 1985, Platt and colleagues reported their results from a randomized prospective trial comparing the BPP with NST for the assessment of high-risk pregnancies, examining the ability of the tests to predict adverse perinatal outcomes (43).

Table 6 Management Scheme Based on Biophysical Profile Scoring	
Score	Recommended management
8–10	Repeat in 1 week. In diabetic (insulin-dependent) and postdate patients, repeat twice weekly. No indication for active intervention
4–6	If fetal pulmonary maturity assured and cervix favorable, delivery, otherwise repeat in 24 hours. If there is persistent score of 4–6, deliver if fetal pulmonary maturity certain. Otherwise treat with steroids and deliver in 48 hours
0–2	Evaluate for immediate delivery. In cases of certain pulmonary immaturity, give steroids and deliver in 48 hours

A number of 1628 tests were performed on 652 women. The authors found that the diagnostic values for all outcome parameters (apart from the negative predictive value for low 5-minute Apgar scores) were consistently higher with the BPP than the NST. However, only the positive prediction of overall abnormal outcome and negative prediction of small-for-gestational-age infants achieved statistical significance.

Johnson and colleagues reviewed 307 consecutive post-term pregnancies assessed using twice-weekly BPPs and found that the BPP accurately differentiated fetuses with a normal outcome from those at risk for perinatal asphyxia (44). They proposed that conservative management of post-term pregnancies was made possible using the BPP for surveillance and that this had the potential to lead to a reduction in unnecessary inductions and cesarean deliveries. Meanwhile, Benacerraf and colleagues reported their observation on performing BPPs on 1000 women with high-risk pregnancies and found that four of five fetuses with oligohydramnios and absent or poor fetal tone and movements had evidence of fetal compromise at birth (45). Their finding reinforces the fact that oligohydramnios should be considered an ominous sign, regardless of the other variables, and generally should lead to intensive surveillance or delivery.

Vintzileos and coinvestigators described their experience using the BPP in 73 women with healthy pregnancies who had presented with preterm premature rupture of the membranes (PPROM) and were not in labor (46). They observed that PPROM did not affect the BPP. However, a low BPP (<7) predicted impending fetal infection. Subsequently, these investigators performed a retrospective study of 1151 pregnancies complicated by PPROM (47). They found that PPROM was associated with a higher rate of reactive NSTs, absent fetal breathing, and reduced amniotic fluid compared with those pregnancies without PPROM. However, they observed that the overall BPP score was not affected by PPROM in otherwise healthy pregnancies. In a further study, Vintzileos and colleagues compared the BPP with amniocentesis for the diagnosis of chorioamnionitis in patients with PPROM (48). They found that daily BPP assessment was superior to amniocentesis in predicting infection outcome in these women. The role of the BPP in the evaluation of patients with PPROM will be discussed further later in this chapter.

In another study, Manning and coworkers reported on 12,620 high-risk patients who had 26,257 BPP scores (37). There were 93 perinatal deaths of which 24 occurred in structurally normal, non-immunized fetuses (corrected perinatal mortality rate of 1.9 per 1000). Eight of these structurally normal fetuses died within one week of a normal BPP (corrected false-negative rate of 0.634 per 1000). The uncorrected stillbirth rate was 3.64 per 1000 and the uncorrected neonatal death rate was 3.72 per 1000. When the perinatal mortality was correlated with the biophysical score results, it was found that the overall mortality ranged from 0.652 per 1000 tests in pregnancies with a BPP score >8 to 187 per 1000 tests for pregnancies with a BPP score of 0. The overwhelming majority of the BPPs (97.5%) were normal and only 0.76% had a score of <4 . The same authors subsequently reported their experience with 44,828 BPPs (49) performed in 19,221 high-risk pregnancies. The frequency of intrauterine

death among structurally normal fetuses after a reassuring BPP was 0.726 per 1000 (14 deaths). Four of those deaths resulted from cord prolapse, an outcome not likely to be predicted by a normal BPP score. Thus, the false-negative rate of a normal test, excluding cases that the BPP would not have been expected to predict, could have been as low as 0.518 per 1000 (10 deaths). Almost half of the antepartum fetal deaths occurred 5 to 7 days after a normal BPP. Therefore, it is possible that increasing the frequency of testing to twice a week may have prevented some of these deaths. The usefulness of the fetal BPP in predicting perinatal death has also been investigated by Baskett and coworkers (50) in 4184 fetuses. The overall perinatal mortality in the study population was 7.6 per 1000. Fetuses with a normal biophysical score (8–10) had a perinatal mortality rate of 1 per 1000, while fetuses with an equivocal score of 6 had a perinatal mortality rate of 31.3/1000. Finally, fetuses with a BPP score of 0 to 4 had a perinatal mortality of 200 per 1000. The false-negative rate of 0.7 per 1000 was very similar to the false-negative rate previously reported by Manning and coworkers.

Platt and coworkers (51) studied 283 patients who had a total of 1112 BPPs. Patients were managed on the basis of their NST results and not on their BPPs. The perinatal mortality rate for all patients delivered in their institution during the study period was 22.6 per 1000 as opposed to 14 per 1000 (corrected 7 per 1000) for the study population and 7.4 per 1000 for fetuses with a biophysical score of >8 . The authors questioned the predictive accuracy of the biophysical score as compared with the NST alone.

Outcomes with Very Low BPP Scores

Manning and coworkers (52) reported on outcomes of pregnancies with BPP scores of zero. Twenty-nine of 28,655 fetuses (0.092%) had a last BPP score of 0 prior to delivery. The perinatal death rate in this group of 29 fetuses was 48.3% (14 of 29) and the majority (11 of 14) were stillborn. Death occurred as early as 30 minutes and as long as 11 days after the last test. Three asphyxia-related neonatal deaths occurred despite immediate and aggressive intervention. The positive predictive value of a BPP score of 0 for perinatal mortality or morbid perinatal outcome (defined as fetal distress in labor, 5-minute Apgar score <7 , umbilical vein pH <7.20 , or admission to a neonatal intensive care unit for over 24 hours for reasons unrelated to prematurity) was 100%. Thus, these authors argued that the very abnormal fetal BPP (score = 0) should be considered a perinatal emergency. Importantly, some fetuses will survive despite this extremely low biophysical score; thus, procrastination, when the BPP score is 0, based upon the belief that the outcome will be dismal, should be discouraged.

In another study of 26,780 fetuses, Manning and coworkers (53) studied the relationship between the last BPP score and various perinatal outcomes including mortality and morbidity. A highly significant inverse linear correlation was observed between the BPP score and fetal distress, admission to the neonatal intensive care unit, intrauterine growth restriction, low 5-minute Apgar score (<7), and umbilical cord pH <7.20 . No correlation was found between the fetal BPP score and the incidence of meconium or major anomaly.

A highly significant inverse exponential relationship was observed between biophysical score and perinatal mortality. The authors interpreted the data as suggesting that the BPP scoring provides insight into the extent and degree of fetal compromise.

Several other investigators have subsequently found that the BPP, when used appropriately, leads to a reduction in perinatal mortality and adverse pregnancy outcomes in high-risk pregnancies. Furthermore, it has been useful in predicting those pregnancies at risk for an adverse outcome. The BPP was found to be an effective method of antepartum fetal surveillance in patients with diabetes mellitus, hypertension, multiple pregnancies, and other high-risk conditions. However, few years after its introduction into clinical practice, it became apparent that it was often used with inappropriate expectations or interpretation.

Factors Affecting the BPP

While the BPP is now widely used for fetal assessment, questions are often asked about how the BPP may be affected by several factors commonly encountered in obstetrics.

Gestational Age

Because the biophysical activities are gestational age dependent, it has been suggested that the BPP score would vary across gestation. Hence, Vintzileos and coworkers (47) performed 951 serial examinations from 25 to 44 weeks of gestation in 210 patients with intact membranes and normal pregnancy outcome. These investigators observed a significant increase in reactive NSTs after 32 weeks while both fetal breathing movements and amniotic fluid volume were decreased after 40 weeks. Fetal movements and fetal tone remained stable across these gestational ages. The incidence of grade 3 placentas increased significantly after 32 weeks. These variations in the frequencies of the fetal biophysical components from 25 to 44 weeks of gestation agree with the findings of several other investigators (54–57). It should be noted, however, that the frequency of reassuring biophysical scores (>8) did not change significantly from 25 to 44 weeks of gestation. Using the scoring criteria of Manning and coworkers, Baskett (58) had similar findings regarding the changes of the biophysical components throughout gestation. Their study involved pregnancies with normal perinatal outcome (5582 fetuses/11,012 BPPs). There were an increased number of reactive NSTs and fetal breathing movements at 34 to 41 weeks as compared with earlier gestations. The NST, fetal breathing movements, fetal tone, and amniotic fluid volume were more likely to be abnormal in prolonged gestations (42–44 weeks) as compared with term gestations (37–41 weeks). Although changes in the individual biophysical components were noted, the frequency of normal biophysical scores (>8) did not change significantly throughout gestation. The understanding of the gestational age-dependent changes of the biophysical components is mandatory for the proper clinical application of the BPP, especially when one manages very preterm gestations.

Magnesium sulfate is probably the most commonly used tocolytic in the United States. It is also used for seizure prophylaxis in pre-eclampsia. Peaceman and colleagues performed BPPs on 16 women who were treated with

magnesium sulfate tocolysis for preterm labor at gestational ages of 26 to 34 weeks of gestation (59). They found that magnesium sulfate did not affect fetal tone, gross body movements, or amniotic fluid volume. However, they found a reduction in fetal breathing movements and a higher proportion of nonreactive NSTs in fetuses exposed to magnesium sulfate. In another study, Carlan and colleagues (60) found that administration of magnesium sulfate for tocolysis was associated with a lowered score due to reduced fetal breathing movements. These investigators did not find that magnesium sulfate affected any other components of the BPP. Gray and colleagues evaluated the effect of magnesium sulfate on the BPP and failed to demonstrate any effect of magnesium sulfate on the BPP (61).

The corticosteroids betamethasone and dexamethasone are widely used to induce fetal lung maturation in fetuses at risk of preterm delivery. Rotmensch and colleagues found a transient but reversible suppression of fetal breathing movements, body movements, and FHR accelerations in pregnancies exposed to steroids for lung maturation (62). Jackson and colleagues similarly found a reduction in fetal breathing movements and gross body movements in fetuses in pregnancies where betamethasone was administered (63,64). These authors also observed a reduction in amniotic fluid volume. Deren and coworkers observed that fetuses exposed to betamethasone had reduced fetal movements, breathing movements, and a higher number of nonreactive NSTs (64). In a study of 84 pregnancies in whom betamethasone was administered, Kelly and colleagues found a reduction in BPP scores, mainly caused by a reduction in fetal movements, fetal breathing movements, and a greater proportion of nonreactive NSTs (65). In summary, most investigators have found that steroids affect the BPP mainly through a reduction in reactive NSTs, fetal body movements, and fetal breathing movements. However, this reduction in BPP scores is transient (48–72 hours) and has not been associated with worse perinatal outcomes. This transient reduction in FHR reactivity and fetal breathing movements should be taken into consideration in evaluating preterm fetuses, when the mother has been administered corticosteroids, so iatrogenic prematurity can be avoided.

Inappropriate Use of the BPP

Vintzileos and colleagues pointed out several of the reasons that the BPP may be used inappropriately (36). First, these investigators emphasized that the most frequent error among clinicians is to base the management of the patient on the biophysical score alone. They argued that it is crucial that the clinician should utilize the individual components of the score rather than the total score in making management decisions. For instance, a fetus with a reactive NST and a normal amount of amniotic fluid, but demonstrating no tone or movements during the examination is assigned a score of 4. However, both the acute marker, the most sensitive one (reactive NST), and the chronic marker (amniotic fluid volume) have indicated that this fetus is not hypoxemic. Unfortunately, such patients are often said to have failed their BPP and end up being delivered inappropriately and often prematurely. More than likely, the absence of fetal movements, tone, and/or breathing in such a case may be the result of periodicity. Conversely, a fetus with a BPP score of 8, but with severe

oligohydramnios, should be delivered if the gestational age is term or near term, despite the “favorable” BPP score of 8 because this fetus is a candidate for a cord accident and death in utero despite normal biophysical activities at the time of testing.

A second error that is often encountered, when using BPP to guide management, is failing to consider the overall clinical picture of the individual case. For instance, a fetus at term with severe growth restriction should be delivered, despite the presence of a reassuring BPP score.

Third, one should not use the same interval of testing (i.e., weekly) for all cases. Generally, a BPP score is considered reliable for 1 week. However, certain high-risk conditions, such as insulin-dependent diabetes, growth restriction, or postdate pregnancies may require more frequent testing. Manning and colleagues in evaluating 12,620 pregnancies with BPPs found that half of the fetal deaths after reassuring BPP results occur between 5 and 7 days after testing, suggesting that twice-weekly testing may reduce mortality. The interval between testing, therefore, should be individualized based on the circumstances of each particular case. When a test is non-reassuring, rather than repeat the test in 24 hours, as is widely advocated, it is appropriate to extend the period of testing beyond 30 minutes. Extending the testing duration will help differentiate between a compromised fetus and one where biophysical activities are absent due to periodicity, whereas just retesting in 24 hours, as is the usual advice, may result in fetal demise.

Next, some investigators advocate the use of BPP without performing an NST. However, the NST may detect FHR variable decelerations that may detect the fetuses at risk for cord accident. These fetuses may have a normal BPP score, and false reassurance may be provided if an NST is not performed.

Physicians may often delay delivery even with non-reassuring BPP testing due to such concerns as an unfavorable cervix or preterm gestation. This attitude may carry a significant risk of an adverse perinatal outcome. Clinicians should act based on the information derived from the biophysical assessment.

Finally, operator inexperience and faulty technique may lead to incorrect assessment of biophysical activities and inappropriate management decisions. Amniotic fluid measurements should occur in umbilical cord-free pockets. In addition, fetal breathing movements should be considered present only if they are continuous, lasting for more than 30 seconds. Fetal body movements should be considered present only if there are three or more rolling trunk movements observed in a 30-minute period.

Selective Use of the NST

The selective use of the NST was reported by Manning and coworkers (66), who omitted the NST from the initial biophysical evaluation and included only the other four biophysical components (fetal breathing movements, fetal movements, fetal tone, and amniotic fluid volume). The authors studied 2712 patients who had a total number of 7851 tests and showed that the test accuracy was not compromised. In addition, the need for NST was reduced to only 2.7% of the cases. The selective use of the NST improved the efficiency of the authors' testing unit, shortened the duration of the test,

and increased the number of patients who could be tested daily. Another study by Eden and coworkers, however (67), questioned the wisdom of omitting the NST from the initial biophysical evaluation, as fetuses with all normal biophysical components but variable decelerations during NST testing had an increased frequency of abnormal perinatal outcome. Mills and coworkers (68) proposed a two-tier approach to biophysical assessment of the fetus. They performed a retrospective review of 2038 biophysical assessments in 500 high-risk pregnancies. The authors compared the efficacy of the NST and BPP in predicting fetal asphyxia in fetuses with normal and abnormal growth. The sensitivity, specificity, positive predictive value, and negative predictive value of the NST to predict lethal fetal asphyxia were 100%, 77.5%, 0.4%, and 100%, whereas that of the fetal BPP were 100%, 99.7%, 33.3%, and 100%, respectively. The authors suggested that the appropriate biophysical evaluation of the fetus could be determined based on the clinical problem and the fetal growth. According to the authors, when fetal growth is normal, by ultrasound evaluations at every 4 weeks, no biophysical assessment is necessary. If the growth is abnormal, biweekly NSTs and fetal growth checks by ultrasound at every 2 weeks are indicated. The authors concluded that the fetal BPP should be reserved for those cases where the NST is non-reassuring or equivocal. By using this testing method, the authors speculated that they could theoretically reduce their workload of NSTs by >60% and BPPs by >75%.

The BPP in Diabetes and Postdate Pregnancies

Johnson and coworkers (44) managed 307 consecutive post-term pregnancies with twice-weekly BPPs and suggested that if the biophysical score was reassuring, waiting for spontaneous onset of labor was advisable, resulting in good perinatal outcomes with a much lower cesarean section rate (15% vs. 42% for induction patients). The same authors also reported on the use of the fetal BPP in managing 238 diabetic pregnancies who had a total number of 1028 profiles performed (69). In patients with an abnormal score, there was a high rate of intensive care nursery admissions and cesarean section rate (50%). Of the fetuses with normal BPP scores, 57.4% entered spontaneous labor, 31.3% were induced, and the remaining 11.3% were delivered by elective repeat or primary cesarean section. Stillbirths were prevented and 87% of the patients delivered at or near term with minimal maternal or neonatal morbidity. Abnormal BPP scoring was associated with a significantly higher rate of operative intervention and neonatal morbidity. According to the authors, the fetal BPP allows for a safe expectant management in the diabetic pregnancy.

The usefulness of the fetal BPP in twin gestations has been studied by Lodeiro and coworkers (70). Forty-nine twin gestations with additional high-risk factors such as suspected growth retardation of one or both twins, maternal chronic hypertension, or pregnancy-induced hypertension were followed with weekly BPPs. The sensitivity, specificity, positive predictive value, and negative predictive value of the biophysical assessment in predicting fetal distress were 83.3%, 100%, 100%, and 97.7%, respectively. The false-negative rate was 2.2%. However, the only false-negative death resulted from extreme prematurity in a set of twins delivered at

26 weeks of gestation. Four twin gestations had fetal distress in only one of the twins and all eight fetuses (four pairs) had nonreactive NSTs. The BPP accurately predicted the distressed twin of each of the four pairs, and it also correctly identified well-being for its counterpart twin. The authors concluded that the BPP is a safe and effective tool in the antepartum fetal surveillance of twin gestations.

The wisdom of arbitrary assignment of equal score weights for the various biophysical components was questioned by Manning and coworkers (71). In a study of 525 fetuses, they studied the relationship between the last abnormal BPP score, in total and by variable composition, and a variety of abnormal perinatal outcomes such as fetal distress in labor, low 5-minute Apgar score (<7), intrauterine growth restriction, and admission to the neonatal intensive care unit for >24 hours. It was found that all variable combinations for the same score subsets (scores 6, 4, and 2) are not equal in predictive accuracy. For a biophysical score of 6, the probability of fetal distress or death was significantly higher with either nonreactive NST/fetal tone absent or nonreactive NST/absent fetal breathing movements, whereas the probability of fetal distress was significantly lower when fetal breathing movements were absent in the presence of oligohydramnios. Significant variations in positive predictive accuracy also occurred within subsets of variable combinations yielding a BPP score of 4; these variations, however, disappeared with a BPP score of 2. Overall, the NST, amniotic fluid volume, and fetal breathing movements emerged as the most powerful variables for all perinatal outcome measures. Fetal tone seemed to play a lesser role, and fetal movement was found to be important only for predicting fetal distress.

A Rational Approach to Antepartum Fetal Biophysical Assessment

Considering the “gradual hypoxia concept,” and also the 100% sensitivity of the combination of the nonreactive NST and absence of fetal breathing movements for predicting the acidemic fetus, Vintzileos and coworkers recommended a modified fetal evaluation scheme for patients with intact membranes (Fig. 8). This scheme is based on the individual biophysical components rather than the score (32,36). It should be noted that this scheme is also supported by the data of Manning and coworkers (71), which suggest that the NST, amniotic fluid volume, and breathing movements are the most powerful predictors of fetal compromise.

This protocol includes assessment of an acute (NST or fetal breathing) and a chronic marker (amniotic fluid volume). A reactive NST or fetal breathing lasting >30 sec (even in the presence of a nonreactive NST) makes fetal acidemia at the time of testing highly unlikely. However, there is a caveat in patients with uncontrolled diabetes. Hyperglycemia may cause fetuses in diabetic pregnancies to exhibit fetal breathing even in the presence of (lactic) acidemia. Thus, the blood glucose should be checked in diabetic women at the time of the BPP assessment.

When the NST is nonreactive, it becomes crucial to make the differentiation between fetal sleep and fetal acidemia. If fetal breathing lasting greater than 30 seconds is detected, the examination is terminated and further management is based on the amniotic fluid volume assessment. If all biophysical activities (nonreactive NST, fetal breathing, fetal movements, and fetal tone) are absent after 30 minutes of continuous observation, the fetus should be delivered promptly. If the

Figure 8 An algorithm for the use of the modified fetal biophysical profile in antepartum fetal surveillance. Abbreviations: AFV, amniotic fluid volume; FBM, fetal breathing movements; FM, fetal movements; FBP, fetal biophysical profile; FT, fetal tone; FHR, fetal heart rate; NST, nonstress test. Source: From Ref. 74.

fetus has a nonreactive NST and breathing is absent, while movements and tone are normal, testing duration should be extended to differentiate fetal sleep from fetal compromise. The NST is continued until a reactive pattern is observed or until 120 minutes have elapsed. If the NST is still nonreactive, the real-time ultrasound examination should be repeated. If no fetal breathing is observed, and the gestational age is >32 weeks, additional evaluation (i.e., Doppler velocimetry) or delivery may be considered. In very preterm gestations (<32 weeks) in the absence of FHR cyclicity, if there is a nonreactive NST and absent fetal breathing, additional evaluation or delivery should also be considered (72,73). If FHR cyclicity and body movements are both present and normal, then expectant management is indicated. The presence of oligohydramnios and/or variable decelerations during NST suggests that the fetus is at risk for umbilical cord accident, and the fetus should be delivered if the gestation is at or near term. The presence of a normal amount of amniotic fluid and the absence of variable decelerations is reassuring, and expectant management may be reasonable. In the presence of oligohydramnios in a term or a near-term gestation with intact membranes, delivery is indicated regardless of how reassuring the other biophysical components are. In our view, a largest amniotic fluid pocket less than 2 cm (or amniotic fluid index <5cm) defines oligohydramnios. The combination of oligohydramnios and variable decelerations during the NST may indicate the need for delivery in viable, structurally normal fetuses with intact membranes, regardless of gestational age. In very preterm gestations (<32 weeks) in the presence of oligohydramnios and no identifiable fetal anomalies, pregnancies should be managed on a case-by-case basis taking into consideration the results of Doppler velocimetry (if the underlying pathophysiology is reduced uteroplacental blood flow). However, it is crucial to recognize that these fetuses are at increased risk of stillbirth and that while it may be necessary to attempt to prolong gestation to improve maturity at birth, these fetuses may die while being managed conservatively. If delivery is not undertaken, frequent testing (every 24 hours) is an alternative logical plan of management. In this group of fetuses, Doppler studies may assist in deciding management.

Computer-Assisted BPP

The biophysical methods currently used in clinical practice are arbitrary since they do not provide exact quantification of the biophysical activities over a long period, nor do they account for the occasionally long intervals of fetal inactivity, which are frequently observed in normal fetuses. To circumvent these drawbacks, an extended period of concurrent observation of the biophysical activities has been attempted by using computer-assisted systems or phonographic transducers (74,75). Devoe and coworkers (76) have reported their experience by using a computerized system that allowed analysis of the simultaneously acquired biophysical activities in 200 term high-risk fetuses. The biophysical activities obtained for each high-risk fetus were compared with previously established nomograms. The results correlated with the presence or absence of perinatal mortality, fetal distress, a low 5-minute Apgar score (<7), and intrauterine growth retardation. A test was considered abnormal if two or more

biophysical activities quantitatively fell >2 SD below the population mean. A decreased frequency of fetal body movements, decreased amniotic fluid volume, and decreased frequency of FHR accelerations were the most common abnormalities. When fetuses with normal or abnormal perinatal outcomes were classified by the last computerized biophysical test, the sensitivity was 86%, specificity 89%, positive predictive value 75%, negative predictive value 93%, and overall diagnostic accuracy 86.2%. This diagnostic accuracy was significantly better as compared with the arbitrary scoring system of Manning and coworkers. However, this comparison was not based on a randomized trial; in addition, it was not clear whether or not the computer-assisted BPP results influenced patient management.

THE FETAL BPP IN PATIENTS WITH PROM

The effect of PROM on the BPP has been studied extensively. Vintzileos and colleagues performed a retrospective analysis of 1151 fetal BPPs performed between 25 and 44 weeks of gestation in pregnancies with good outcomes (defined as those with no congenital anomalies, infection, fetal distress, or perinatal mortality/morbidity) (47). These investigators compared the fetal BPPs and scores of patients with intact membranes with those who had PPROM, but had good pregnancy outcomes. The frequency of reactive NSTs, fetal breathing, fetal movements, and fetal tone did not change across gestation from 25 to 44 weeks in patients with PROM. However, when compared with patients with intact membranes, those pregnancies with PROM had a higher frequency of reactive NSTs, absent fetal breathing, and reduced amniotic fluid volume. The frequency of nonreactive NST at less than 32 weeks of gestation was only 13.5% in the presence of ruptured membranes. The overall biophysical scoring was not altered by the presence of PROM. The changes in the fetal BPP caused by PROM are summarized in Table 7.

In a prospective study, Vintzileos et al. (46) performed frequent fetal biophysical assessments on 73 patients with PROM with no clinical signs of labor or infection and demonstrated that an abnormal BPP was an early indicator of intra-amniotic infection. A fetal BPP was performed on admission and was repeated every 24 to 48 hours. The last biophysical assessment before delivery was correlated with the development of clinical amnionitis, possible neonatal sepsis, and neonatal sepsis. The diagnosis of possible neonatal sepsis was made when there was strong clinical and laboratory evidence of neonatal infection but the cultures were negative. The diagnosis of neonatal sepsis was made in the presence of positive cultures of blood, urine, or cerebrospinal fluid. There

Table 7 Summary of Changes in the Fetal Biophysical Profile Associated with Premature Rupture of the Membranes

- Increase in fetal heart rate reactivity
- Decrease in fetal breathing movements
- No change in fetal movements
- No change in fetal tone
- No change in the overall biophysical score

was no correlation between the fetal biophysical assessment and intra-amniotic infection in the 20 of the 73 patients who delivered at greater than 24 hours following the last biophysical assessment. Fifty-three patients delivered within 24 hours of the last biophysical examination; in these patients, a biophysical score of >8 was associated with an infection rate of 2.7%, while an abnormal biophysical score (<8) was associated with an overall infection rate of 93.7% (46). The first manifestations of fetal intra-amniotic infection were nonreactive NST and absent fetal breathing. Loss of fetal movement and absent fetal tone occurred only in advanced infections. The best predictor of infection was the overall biophysical score. The fetal biophysical score range was <8 in all the 14 cases with possible neonatal sepsis or neonatal sepsis. No difference in the mean umbilical cord blood pH between the infected and non-infected cases was found, an observation that suggests that the low scores of the infected group were not mediated by hypoxia, but rather by infection. In patients with PROM, the degree of oligohydramnios, one of the components of the BPP, is strongly correlated with pregnancy prolongation, abnormal antepartum and intrapartum FHR patterns, cesarean section rates, fetal distress, infection, and perinatal mortality. Vintzileos and colleagues correlated the degree of oligohydramnios with pregnancy outcome in 90 patients with PROM and no signs of infection or labor (77). Patients with severe oligohydramnios (largest amniotic fluid pocket <1 cm) had the highest frequency of amnionitis (47.3%), possible neonatal sepsis (26.3%), and neonatal sepsis (31.5%), compared with 9.2%, 3.7%, and 1.8%, respectively, in patients with a largest amniotic fluid pocket >2 cm. Based on this finding, these investigators concluded that patients with PROM and severe oligohydramnios should have daily fetal BPPs performed. A retrospective analysis of 127 consecutive patients with PROM who had NSTs performed every 24 to 48 hours as part of the fetal BPP demonstrated that those who initially had a reactive NST and subsequently converted to a nonreactive NST developed clinical intra-amniotic infection in almost 90% of the cases (78). The last NST prior to delivery had sensitivity, specificity, positive, and negative predictive values to predict infection outcome of 78.1%, 86.3%, 67.7%, and 92.1%, respectively. Fetal breathing movements (lasting >30 s) have also been shown to predict intra-amniotic infection. In a study of 130 patients with PROM who were followed with BPP assessments every 24–48 hours, the sensitivity, specificity, positive, and negative predictive values of fetal breathing to predict intra-amniotic infection were 91.6%, 64.8%, 50%, and 95.3%, respectively (79). Of the individual biophysical components, the presence of fetal breathing has been the most reliable in ruling out fetal infection, if observed within 24 hours prior to delivery. Vintzileos and coworkers compared daily fetal BPPs with amniocentesis (for Gram stain and culture) in 58 patients who presented with preterm PROM and no apparent infection or labor (48). In addition to the usual indications for delivery, a positive Gram stain or culture of the amniotic fluid, obtained by amniocentesis, or a persistently abnormal biophysical score (<8) on two examinations, 2 hours apart, in the presence of a nonreactive NST and absent fetal breathing were also considered as the indications for delivery. The last BPP prior to delivery and amniocentesis results on admission were correlated with

infection outcome. All but one of the 13 cases with neonatal infection were associated with an abnormal biophysical assessment. There were two cases with amnionitis without neonatal infection; both cases had normal BPPs. The sensitivity, specificity, positive predictive value, and negative predictive value of the BPP for infection were 80%, 97.6%, 92.3%, and 93.3%, respectively. The sensitivity, specificity, positive predictive value, and negative predictive value of the Gram stain were 60%, 81.3%, 52.9%, and 85.3%, respectively, whereas those of the amniotic fluid cultures were 60%, 86%, 60%, and 86%, respectively. The authors concluded that in preterm PROM daily BPPs are more efficacious than amniocentesis on admission in selecting those patients who either have or will develop intra-amniotic infection and therefore require prompt delivery. Importantly, the fetal BPP is simple, noninvasive, can be repeated daily, or even more frequently and is applicable to all patients. Vintzileos and coworkers (80) managed 73 consecutive patients with PROM with daily BPPs in an attempt to determine whether daily BPPs improved pregnancy outcomes. The pregnancy outcome of this group was compared with the outcomes of two other historic groups: 73 consecutive patients with PROM in the first control group were managed conservatively while the 73 consecutive patients with PROM in the second control group were managed with amniocentesis on admission. Maternal and neonatal infection rates, as well as low 5-minute Apgar scores were significantly less in the study group than among controls. The percentage of mother–infant pairs who developed infection in the study group (10.9%) was significantly less than that in the control group (30.1%). Clinical amnionitis was reduced from 20.5% to 5.4%. The frequencies of possible neonatal sepsis and neonatal sepsis were also lower in the study group compared with the control group (5.4% vs. 13.6% and 1.3% vs. 9.5%, respectively). The study group also had significantly less neonatal sepsis (1.3% vs. 12.3%). The authors concluded that the use of amniocentesis may decrease the incidence of clinical amnionitis, but it does not improve the neonatal infection outcome. The neonatal infection outcome was, however, reduced by using daily biophysical assessment.

In order to investigate the role of fetal acidemia in causing diminished biophysical activities in the setting of subclinical infection and PROM, Vintzileos and coworkers (81) performed a prospective evaluation of 53 consecutive patients with preterm PROM who were delivered solely on the basis of an abnormal fetal biophysical assessment. Fetal acidemia at birth was defined as cord artery pH <7.20 . Of the 53 fetuses, 19 developed no maternal or neonatal infection and none was acidemic at birth. Seventeen fetuses developed possible neonatal sepsis and none was acidemic at birth. Fifteen fetuses developed neonatal sepsis and only five were acidemic at birth. Two fetuses developed clinical amnionitis and only one was acidemic at birth. While fetal acidemia could explain the diminished fetal biophysical activities in 5 of the 15 fetuses who developed neonatal sepsis and in 1 with clinical amnionitis, this mechanism could not explain the compromised biophysical activities in the remaining 10 fetuses with neonatal sepsis and in all 17 fetuses who developed possible neonatal sepsis. A possible explanation for the diminished biophysical activities of the infected non-acidemic fetus may be an increased production of prostaglandins, particularly interleukin-1. Interleukin-1, the main fever

mediator, induces changes in the electroencephalogram that may be responsible for the decreased motor activity during fever in both animals and humans (82). Since interleukin-1 is capable of stimulating prostaglandin production from macrophages and other cell types, it has been suggested that this may be responsible for the decrease in fetal breathing observed not only prior to labor but also in the setting of subclinical infection. This increased prostaglandin secretion may directly inhibit the fetal CNS centers or may indirectly lead to increased peripheral vascular resistance through vasoconstriction of the umbilical and chorionic vessels (83,84). Since there are experimental data to suggest that prostaglandins increase placental vascular resistance through vasoconstriction of umbilical and chorionic vessels, the relationships among umbilical artery velocimetry, the fetal BPP, and placental inflammation in patients with PROM have also been investigated (85). The study population involved 28 consecutive patients with preterm PROM who were followed with daily fetal BPPs and umbilical artery velocimetry. After delivery, placental pathologic examination for evidence of inflammation was performed in all cases. When only the last examination, within 24 hours of delivery, was considered, patients with placental inflammation (choriodecidualitis, umbilical and/or chorionic vasculitis) had higher mean umbilical artery Doppler systolic/diastolic (S:D) ratios (2.92 ± 0.62 vs. 2.29 ± 0.25) and lower biophysical scores (6.2 ± 2.3 vs. 9.1 ± 2.1) compared with those without evidence of placental inflammation. It should be noted that the mean S:D ratio value 24 hours prior to delivery in cases with placental inflammation was 2.92, which is not necessarily higher than the normal range. Fetuses with placental infection increased their S:D ratio during the last 24 hours prior to delivery approximately 30% (which was statistically significant) over the mean value of the preceding days. These data suggest that larger studies are needed to more accurately determine the value of the longitudinal trend in Doppler velocimetry indices in regard to being additional noninvasive means of identifying subclinical intra-amniotic infection. The increase in umbilical vascular resistance supports a role for vasoactive substances, such as prostaglandins, as mediators of infection causing vasoconstriction of umbilical and chorionic vessels. This increase in vascular resistance may compromise uteroplacental circulation and diminish biophysical activities prior to the development of fetal acidemia.

CONCLUSIONS

Antepartum fetal surveillance has led to a reduction in perinatal mortality. The techniques described in this chapter are now widely accepted and almost universally used. A clear understanding of the physiologic basis for these tests and of the pathophysiology of the conditions that can cause fetal death or intrauterine hypoxia is crucial to appropriate application of these surveillance methods. Unfortunately, there will still be some causes of death that cannot be predicted or prevented using these methods.

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