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Fetal biophysical profile score

VI. Correlation with antepartum umbilical venous fetal pH

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OBJECTIVE: Our objective was to determine the relationship, if any, between the fetal biophysical profile score and antepartum umbilical venous pH.

STUDY DESIGN: This was a prospective observational study conducted concurrently in two centers and involving two discrete high-risk groups of fetuses. Fetal biophysical profile scores were compared with umbilical venous pH values measured in blood obtained by immediate cordocentesis. A total of 493 paired observations of biophysical profile score and pH were made; 104 observations were of fetuses with intrauterine growth retardation and 389 observations were of fetuses with alloimmune anemia.

RESULTS: In both data sets there was a highly significant linear correlation between biophysical profile score and umbilical venous pH. Poor biophysical profile score performance (a score of 0 of 10) was always associated with a pH <7.20, whereas the pH was always >7.20 when the biophysical profile score was 10 of 10. Sequenced sensitivity of short-term biophysical variables in the detection of acidemia was observed.

CONCLUSION: The fetal biophysical profile score accurately predicts antepartum umbilical venous pH. (AM J OBSTET GYNECOL 1993;169:755-63.)

Key words: Fetal biophysical profile score, intrauterine growth retardation, alloimmune fetuses

The major goals of antepartum fetal assessment are to determine the presence or absence of fetal asphyxia and, when present, to estimate the degree of fetal compromise in order to strike the clinical balance between the risks of continued intrauterine life (conservative management) and the risks attendant with delivery (interventional management). Ideally, fetal asphyxia might best be identified and quantified by direct analysis of fetal blood. Ultrasonographically guided percutaneous umbilical vessel puncture (cordocentesis) is now a recognized technique in modern perinatal medicine, but the procedure does not lend itself to repeated sampling at close intervals and it is not without measurable risk.[1]

In the experimental fetal animal model and in the human fetus, asphyxia has been shown to elicit reproducible changes in the incidence and character of fetal biophysical variables.[2-5] Because high-resolution dynamic ultrasonographic methods may be used to monitor such variables in the human fetus without direct fetal risk, it follows that such observations might give an indirect but accurate insight into the presence and magnitude of fetal asphyxia. Fetal biophysical profile scoring is a method of antenatal surveillance that uses

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dynamic ultrasonographic monitoring of four short-term fetal biophysical variables (fetal breathing movements, gross body movements, tone, and heart rate reactivity (nonstres test [NST]) and one long-term variable (amniotic fluid volume). A highly significant inverse relationship between last biophysical profile score result and perinatal mortality and morbidity, including birth asphyxia, is well documented.[6-8] The purpose of our study was to examine these associations further by determining the relationship, if any, between the fetal biophysical profile score and fetal acidosis as measured antenatally in fetal blood obtained by cordocentesis.

Material and methods

Study population. Paired measures of the fetal biophysical profile score and antenatal fetal umbilical venous pH were made concurrently in two separate centers in two discrete high-risk fetal populations. At the Health Sciences Centre, University of Manitoba, Winnipeg, 389 paired observations were made in 108 fetuses with alloimmune anemia of sufficient severity to require intrauterine transfusion. At King's College Hospital, London, 104 observations were made in 104 structurally normal, karyotypically normal, severely growth-related fetuses. In this population intrauterine growth retardation (IUGR) was defined by an abdominal circumference >2 SD below the mean for known gestational age (range 2 to 10 SD below mean).

Methods. At each center the fetal biophysical profile score was determined by an experienced observer and interpreted according to the standard criteria of Manning et al.[7] In the very immature fetus (<24 weeks) the NST criteria were modified so that a normal test result was defined as the presence of visible long-term variability and the coupling of any fetal heart rate acceleration (≥5 beats/min) with fetal movements. By convention an equivocal score was defined as a biophysical profile score of 6 of 10, an abnormal score was defined as a biophysical profile score of either 4 or 2 of 10, and a very abnormal biophysical profile score was defined as a score of 0 of 10. All biophysical profile scores were based on an assessment of all five variables. The assignment of an equivocal or abnormal biophysical profile score was made only after a minimum of 30 minutes of continuous ultrasonographic observation. In all instances the fetal biophysical profile score was obtained and recorded before cordocentesis in unmedicated mothers. After determination of the biophysical profile score, ultrasonographically guided cordocentesis was performed by an experienced operator. The clinical indications for cordocentesis varied between the two populations. The major indication in the fetuses with IUGR was determination of karyotype, and the sole indication in the Rh group was determination of fetal hemoglobin before intravascular fetal transfusion. All fetal blood samples were taken from the umbilical vein and confirmed by direct needle visualization and observation of a saline solution flush. The volume of blood aspirated varied by indication and gestational age and ranged from 1 ml to 8 ml. An aliquot of umbilical venous blood (250 μl) was analyzed immediately for blood gas and pH values with a standard automated system (Radiometer ABL 330 blood gas analyzer). This report concerns the relationship between biophysical profile score and umbilical venous pH. The relationship between fetal blood gases and biophysical profile score will be reported subsequently.

Statistical analysis. Mean pH values were calculated by initially converting to a hydrogen ion concentration and then reconverting to pH. A battery of parametric and nonparametric statistical tests were used for data analysis. Distribution of variables was studied by χ^2 analysis. Population means were compared by the Student t test. Trend analysis was by simple (linear) regression. Factor analysis by multiple regression, after analysis of variance, was used to assess gestational age and disease-status influences. Test statistics were calculated by standard means; a negative predictive value was used to evaluate normal biophysical profile scores, and a positive predictive value was used to assess abnormal scores. The Fisher exact test was employed for small populations (e.g., a biophysical profile score of 2 and a biophysical profile score of 0). A p value of ≤ 0.05 was used to define statistical significance.

Results

In total, 493 antenatal paired observations of fetal biophysical profile score and umbilical vein pH were made. These data were derived from two discrete high-risk populations. At King's College Hospital, London, 104 paired observations were made in 104 severely growth-retarded fetuses (abdominal circumference 2 to 10 SD below mean for gestational age); the gestational age at testing in this population ranged from 18 to 35 weeks (mean gestational age 28.37 weeks). At Women's Hospital, University of Manitoba, Winnipeg, 389 paired observations were made in 108 fetuses with alloimmune anemia of sufficient severity to warrant intrauterine transfusion. In this population the number of paired observations per fetus ranged from one to nine (mean 3.6 per patient); the interval between repeat paired observations of biophysical profile score and cordocentesis ranged from 1 to 19 days. The gestational age at paired observation ranged from 17.5 to 36 weeks' gestation (mean 26.4 weeks). Twenty-five of these fetuses (23.1%) were grossly hydropic at initial assessment.

The distribution of biophysical profile scores varied significantly between the two high-risk study groups (Table I). Among fetuses with alloimmune anemia the

Table I. Distribution of biophysical profile score, mean umbilical venous pH (±2 SD), and pH range for paired observations in total and according to high-risk category

Biophysical profile score results	High-risk category											
	Alloimmune (n = 389)				IUGR (n = 104)				Total (n = 493)			
	No.	% of total	pH Mean	pH Range	No.	% of total	pH Mean	pH Range	No.	% of total	pH Mean	pH Range
10	338	86.8	7.37 ± 0.07	7.25-7.44	19	18.3*	7.36 ± 0.07	7.29-7.38	357	72.4	7.37 ± 0.06	7.25-7.44
8	13	3.4	7.37 ± 0.01	7.29-7.44	35	33.6*	7.35 ± 0.06	7.27-7.41	48	9.7	7.35 ± 0.06	7.27-7.44
6	13	3.4	7.31 ± 0.12†	7.20-7.44	20	19.2*	7.32 ± 0.09†	7.23-7.35	33	6.7	7.31 ± 0.01†	7.20-7.44
4	7	1.7	7.21 ± 0.19†	7.08-7.33	18	17.4*	7.29 ± 0.09†	7.22-7.36	25	5.2	6.27 ± 0.14†	7.08-7.33
2	13	3.4	7.19 ± 0.26	6.98-7.38	10	9.6	7.19 ± 0.14†	7.11-7.33	23	4.6	7.19 ± 0.002†	6.98-7.38
0	5	1.3	7.05 ± 0.16†	6.90-7.13	2	1.9	7.12	7.08-7.17	7	1.4	7.07 ± 0.15†	6.90-7.17
TOTAL	389	–	7.35 ± 0.136		104	–	7.33 ± 0.137		493	–	7.34 ± 0.135	

*Significantly different than incidence observed for alloimmune fetuses ($p < 0.05$, χ^2 or Fisher exact test).
†Significantly lower than value recorded for immediate higher biophysical profile score ($p < 0.05$ Student t test).

incidence of a normal biophysical profile score (≥8) was significantly higher than in fetuses with IUGR (90.2% vs 52.9%, $p < 0.05$, χ^2) and the incidence of equivocal biophysical profile scores (biophysical profile score ≤6) was significantly lower (3.4% vs 19.2%, respectively; $p < 0.05$), as was the incidence of an abnormal biophysical profile score (5.1% vs 27%, respectively; $p < 0.05$). The incidence of a very abnormal biophysical profile score (biophysical profile score = 0) was similar between fetuses with alloimmune anemia and fetuses with IUGR (1.3% vs 1.9%, respectively; not significant). These differences in distribution of biophysical profile scores persisted when the initial observations (before any treatment) in fetuses with alloimmune anemia ($n = 108$) were compared with the observations in fetuses with IUGR ($n = 104$). A significant difference in the incidence of oligohydramnios between fetuses with alloimmune anemia (3.2%) and fetuses with IUGR (46%) accounted for >90% of the variance in biophysical profile score distribution; hydramnios was present in 31% of the fetuses with alloimmune anemia. The distribution of normal and abnormal test results for the four short-term variables of the composite biophysical profile score (fetal breathing movements, fetal tone, fetal gross body movements, NST) did not vary significantly between the two subpopulations. Irrespective of the observed differences in distribution of biophysical profile scores between these two groups, the mean umbilical venous pH per biophysical profile score was similar (Table I). The mean umbilical venous pH for all samples from growth-retarded fetuses was 7.33 ± 0.137, and for all samples from Rh fetuses it was 7.35 ± 0.136 (not significant).

For the total paired samples ($n = 493$) there was a highly significant inverse linear correlation between biophysical profile score and umbilical vein pH ($R^2 = 0.5173$, $p < 0.0001$) (Fig. 1). Among 104 paired observations in fetuses with IUGR a highly significant inverse linear relationship between biophysical profile score and umbilical venous pH was observed ($r^2 = 0.5175$, $p < 0.001$) (Fig. 2). A similar relationship was observed among 389 paired observations in alloimmune fetuses ($R^2 = 0.5171$, $p < 0.0001$) (Fig. 2). The correlation between biophysical profile score and umbilical vein pH did not vary significantly between subpopulations (Fig. 2). Overall, mean pH showed a highly significant inverse linear relationship with individual biophysical profile score on simple regression ($R^2 = 0.912$, $p < 0.0001$) (Fig. 3). The mean umbilical venous pH was similar for biophysical profile scores of 10 and 8 but was significantly lower for each biophysical profile score ≤6 (Fig. 3). These differences persisted when the data were segregated by gestational age category (<26 weeks, 26 to 31 weeks, >31 weeks).

Varying the threshold value for "normal" in the assessment of umbilical venous pH altered the distribution of subthreshold pH results for biophysical profile score result categories (Fig. 4) and altered test accuracy parameters (Table II). A value of 7.35 used to define the lower limit of normal resulted in a negative predictive accuracy (for biophysical profile score ≥8) of 82.3% (333/405 normal biophysical profile scores) and a specificity of 95.7% (333/348 normal pH values) (Table II). The positive predictive accuracy of an abnormal biophysical profile score that predicted an abnormal pH ranged from 35% for a biophysical profile score of 6 to 100% for a biophysical profile score of 0. Overall, abnormal biophysical profile score results (≤6) yielded a positive predictive accuracy of 83% and a sensitivity of 50%. Use of a pH of 7.25 to define the lower limit of

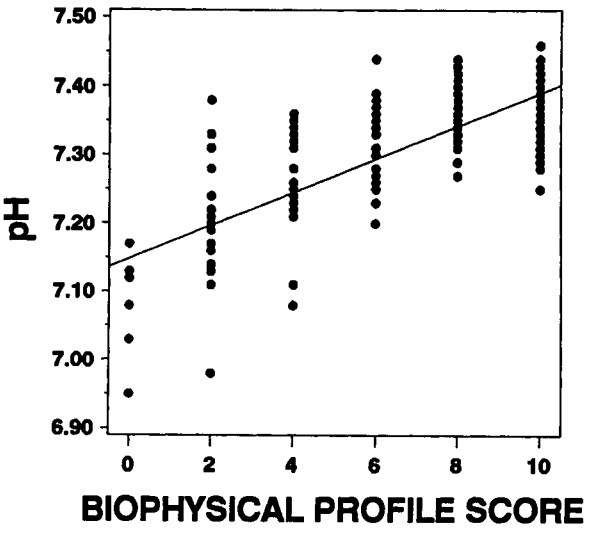

Fig. 1. Biophysical profile score and umbilical venous pH. Highly significant linear relationship is observed between biophysical profile score and pH (N = 493); pH = 7.132 + 0.248 × biophysical profile score. R^2 = 0.5173, $p < 0.001$.

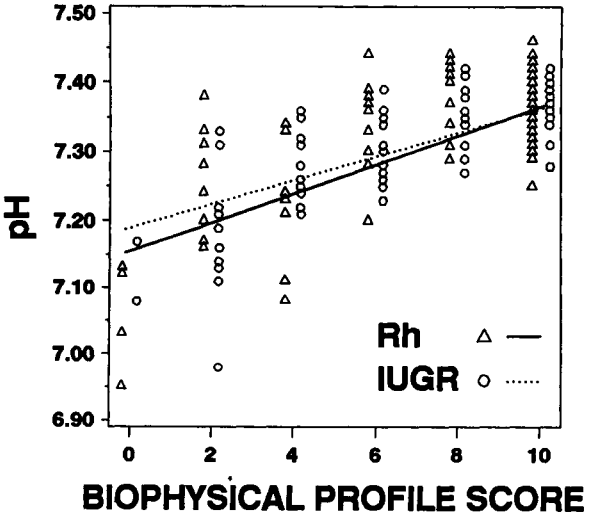

Fig. 2. Biophysical profile and umbilical venous pH for two high-risk categories. For observation in fetuses with IUGR (n = 104) R^2 was 0.5175, and for alloimmune observations (n = 389) R^2 was 0.5171. Both linear correlations are highly significant ($p < 0.0001$). No significant variation between the two regression lines is noted.

normal resulted in a negative predictive accuracy of 100% and a specificity of 88.6% with a normal biophysical profile score. The positive predictive accuracy with an abnormal biophysical profile score ranged from 10% for a biophysical profile score of 6 to 100% for a biophysical profile score of 0. Abnormal biophysical profile scores (<6) yielded a positive predictive accuracy for an umbilical venous pH <7.25 of 41% and a sensitivity of 100% overall.

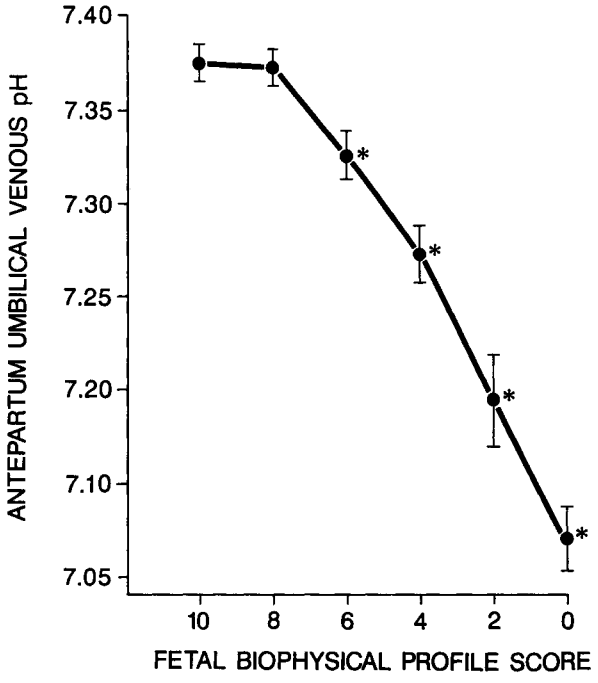

Fig. 3. Mean umbilical vein pH (±2 SD) per fetal biophysical profile score category. Mean pH did not vary significantly between biophysical profile scores of 10 and 8 of 10 but fell significantly and progressively for a biophysical profile score of ≤6 of 10. Significant linear correlation between mean pH per biophysical profile score was observed (R^2 was 0.912, $p < 0.01$). *Asterisk,* Significantly lower than mean pH value for immediately higher biophysical profile score ($p < 0.01$, Student t test).

The distribution of individual variables of the fetal biophysical profile score that were coded normal or abnormal according to fixed criteria was varied (as shown in Table III). The most common abnormal results occurred for the NST (27.4%), and the least common abnormal results occurred with fetal movements (7.4%). For each of the five individual variables of the biophysical profile score, the mean pH with a normal result was significantly higher than the mean observed for an abnormal result. When the four short-term biophysical variables (NST, fetal breathing movements, fetal tone, fetal gross body movements) were determined to be normal, there were no significant differences in mean pH. In contrast, differences were observed between the mean pH associated with abnormal results. The highest mean pH for an abnormal variable result was observed with NST (7.28 ± 0.11), the least for abnormal fetal movements (7.16 ± 0.08) (Fig. 5). The mean pH for normal amniotic fluid volume was significantly lower than the mean pH observed for any of the normal short-term variables. The mean pH for abnormal amniotic fluid volume did not vary significantly from the mean for abnormal fetal movements and tone but was significantly lower than the

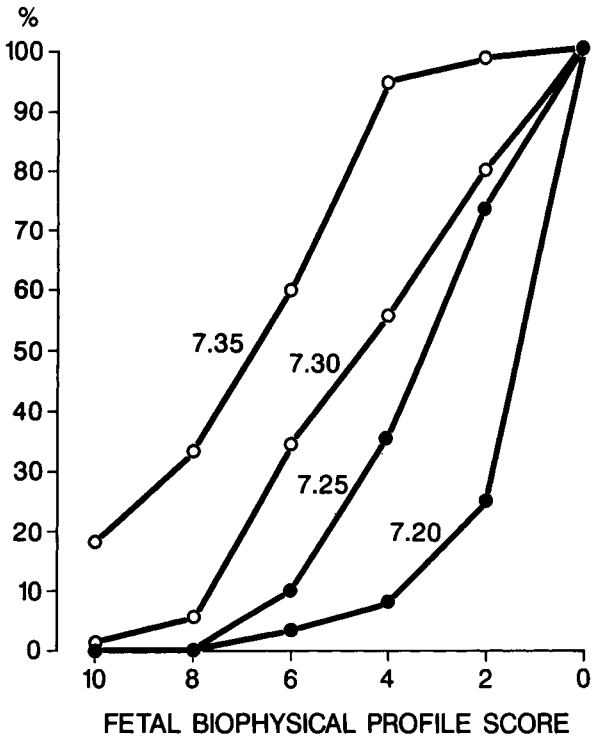

Fig. 4. Percentage of observations for each biophysical profile score that fell below an arbitrary umbilical venous pH.

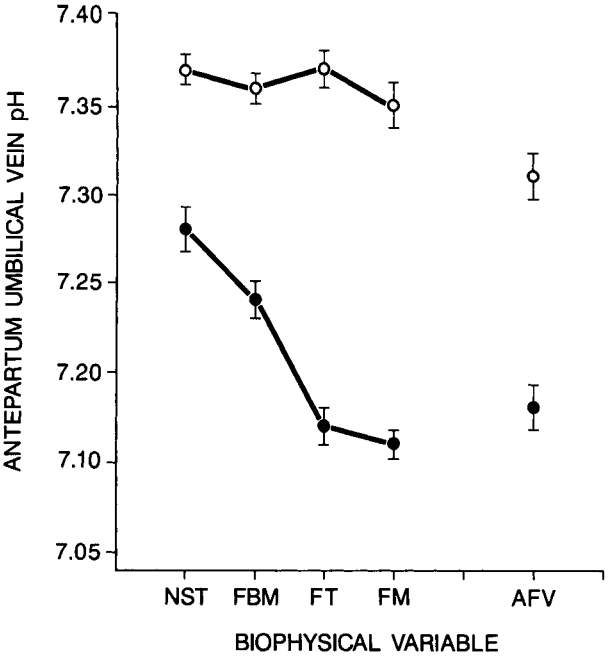

Fig. 5. Mean umbilical venous pH (±2 SD) observed for each individual component of fetal biophysical profile score. For all variables mean pH for an abnormal result (●) was significantly lower than for corresponding normal value (○) ($p < 0.001$, Student t test). Within abnormal variable category, mean pH was significantly lower for absent fetal breathing movements as compared with nonreactive NST and for absent fetal tone as compared with absent fetal breathing movements ($p < 0.01$, Student t test). Mean pH for abnormal amniotic fluid volume was significantly lower than that for abnormal fetal breathing movements. For normal variables *(upper curve)* there was no significant difference in mean pH for short-term variables but a significantly lower pH in normal amniotic fluid volume.

mean for abnormal NST and abnormal fetal breathing movements ($p < 0.05$, Student t test).

Among the 104 growth-retarded fetuses, only one paired pH per biophysical profile score observation was made, which precluded trend analysis. In contrast, in 90 of 108 transfused fetuses with alloimmune anemia (83.3%) serial paired observations were made (range 2 to 9 per patient). In 73 of these 90 fetuses (81%) both the biophysical profile score and the umbilical venous pH were consistently normal (biophysical profile score ≥8, pH 7.30 to 7.44, respectively). In the remaining 17 fetuses (19%), in at least one sequence of paired observations the first biophysical profile score was not normal (≤6). In 14 of these fetuses the biophysical profile score returned to normal by the subsequent observation; in these fetuses the initial umbilical venous pH was normal (≥7.25) in six cases (range 7.26 to 7.33) and abnormal in eight cases (range 7.03 to 7.24). In all these cases the pH reverted to and remained normal in all subsequent observations (range 7.29 to 7.44). The recovery in pH was often dramatic. One fetus began with a biophysical profile score of 0 and a pH of 7.03 and recovered (with transfusion) so that at the next observation, and 4 days later, the biophysical profile score was 10 and the pH was 7.41.

In three sequenced paired observations the biophysical profile score did not improve. In one of these cases the initial biophysical profile score and the subsequent biophysical profile score remained at 6 of 10, whereas the pH increased from 7.36 to 7.39. Hydrops was resolving when this fetus (a twin) was delivered spontaneously at 25 weeks and died. The companion twin, also hydropic, began with a biophysical profile score of 2 and a pH of 7.24 and had a final biophysical profile score of 6 and a pH of 7.30. This twin also died of gross immaturity. A third fetus had a biophysical profile score of 2 and a pH of 7.21. Within 2 days the biophysical profile score deteriorated to 0 and the pH to 7.03; the fetus died despite immediate repeat transfusion. The cause of death was assumed to be posttransfusion traumatic hemorrhage.

In all 389 procedures in the 108 fetuses with alloimmune anemia a repeat biophysical profile score was obtained within 24 hours (whereas repeat pH measurement was deferred until the next scheduled procedure). These observations offer insight into the time course for recovery from an abnormal biophysical profile score. In all successfully transfused fetuses there was improvement in the score; usually the score returned to normal.

Table II. Test accuracy parameters for biophysical profile score result against umbilical venous pH

Biophysical profile score result	*No.*	*< 7.35 (%)*	*< 7.30 (%)*	*< 7.25 (%)*	*7.20 (%)*
Normal (8-10)	405				
Negative predictive accuracy		82.2	97.7	100	100
False-negative		17.8	2.3	0	0
Specificity		95.7	89.5	88.6	84.9
Sensitivity		49.6	85.2	100	100
Equivocal (6)	33				
False-positive		39.4	63.6	89.9	97
Positive predictive accuracy		60.6	36.4	9.1	3
Specificity		95.4	94.9	93	92.3
Sensitivity		21.7	57.1	100	100
Abnormal (2-4)	48				
False-positive		4.4	31.3	45.8	83.3
Positive predictive accuracy		95.6	68.7	54.2	16.7
Specificity		99.4	96	94.8	90.1
Sensitivity		39	78.6	100	100
Very abnormal biophysical profile score	7				
False-positive		0	0	0	0
Positive predictive accuracy		100	100	100	100
Specificity		100	100	100	100
Sensitivity		8.8	43.7	100	100

The time course for recovery of short-term biophysical variables was remarkably short. In nonparalyzed fetuses improvements in score usually occurred shortly after the onset of the transfusion, and the score stabilized by 6 to 12 hours. In the paralyzed fetuses (pancuronium) a similar but delayed response was consistently observed. The return of amniotic fluid volume to normal levels was usual in both oligohydramnios and overt hydramnios, but this was delayed for several days.

Comment

Fetal biophysical profile scoring is based on the theory that an asphyxial insult, regardless of cause, will elicit adaptive protective fetal responses that are manifest in consistent changes in dynamic ultrasonographically monitored fetal biophysical variables. These adaptive responses may be separated according to the time course for the appearance of altered biophysical variables. An immediate fetal response to asphyxia is to suppress some or all of the energy-consuming, central nervous system–generated, short-term biophysical activities (fetal breathing, heart rate acceleration, movement, and tone). Suppression of these activities may reduce fetal oxygen consumption by as much as 17%.[9] Concurrently, asphyxia induces a chemoreceptor (primarily in the aortic arch) reflex redistribution of cardiac output toward essential fetal organs (brain, heart, adrenal glands, and placenta) at the expense of the other organ systems.[10] This compensatory response results in altered perfusion of fetal kidneys and lungs, which, over time, causes a reduction in amniotic fluid volume (oligohydramnios). The observation made between the biophysical profile score and umbilical vein pH fits well within and supports this theoretical framework.

A highly significant linear relationship between paired biophysical profile score and umbilical vein pH was observed for the total population and for each of the two high-risk subgroups. Umbilical venous pH is known to decline slightly with advancing gestational age in normal fetuses (slope −0.002 pH units).[11] Stratifications of these data by gestational age groupings to account for these minor changes did not alter these significant relationships. Therefore the linear relationship of biophysical profile score and pH may be considered constant across the gestational age range of this study (17½ to 35 weeks). The distribution of biophysical profile scores varied by high-risk subgroup category, an effect largely caused by differences in one variable, amniotic fluid volume. These differences are expected and explicable by differences in underlying pathophysiologic events. Sustained and progressive placental hypoperfusion that results in impaired placental function and long-term stimulation of the cardiac output redistribution reflex is a prime pathophysiologic process for IUGR and accounts for both the impaired and often disproportionate growth and the high likelihood of reduced kidney and lung production of amniotic fluid. The high incidence of oligohydramnios observed among IUGR fetuses (46%) is expected and has been reported previously.[12] In contrast, in the fetuses with

Table III. Mean umbilical venous pH for normal and abnormal variables for each of five components of biophysical profile score

Biophysical variable	*Classification*							
	Normal				*Abnormal*			
	No.	*% of total*	*pH ± 2 SD*		*No.*	*% of total*	*pH ± 2 SD*	
			Mean	*Range*			*Mean*	*Range*
NST	358	72.6	7.37 ± 0.07*	7.25-7.44	135	27.4	7.28 ± 0.11	6.90-7.44
Fetal breathing movement	417	84.6	7.36 ± 0.08*	7.20-7.44	76	15.4	7.24 ± 0.09†	6.90-7.44
Fetal tone	450	91.3	7.37 ± 0.09*	7.08-7.44	43	8.7	7.17 ± 0.10†	6.90-7.38
Fetal gross body movement	457	92.6	7.35 ± 0.14*	7.08-7.44	36	7.4	7.16 ± 0.08	6.90-7.37
Amniotic fluid volume	433	87.8	7.31 ± 0.12†	6.98-7.44	60	12.2	7.18 ± 0.11*	7.03-7.31

*Significantly higher than mean value for abnormal variable ($p < 0.01$, Student t test).
†Significantly lower than mean value for above-ranked variable ($p < 0.05$, Student t test).

alloimmune anemia the cardiovascular system is hyperdynamic and organ blood flow is high. Normal or increased amniotic fluid volume is the norm for these affected fetuses. It is notable that among 38 fetuses with abnormal biophysical profile scores, overt hydramnios was present in 19 and was the only "normal" parameter in 9 of the 13 cases in which the biophysical profile score was 2. In more advanced disease placental and tissue edema may impair placental and organ perfusion and diffusion and may become manifest by oligohydramnios. Hence oligohydramnios is a relatively uncommon and late finding among fetuses with alloimmune anemia. In this study the incidence of oligohydramnios in fetuses with alloimmune anemia was 3.6%. Of key importance is the observation that in either group the umbilical venous pH falls significantly as biophysical profile score falls and that this relationship remains consistent and virtually indistinguishable despite the difference in underlying pathophysiologic events. Because these two quite discrete high-risk populations behave in a common fashion with regard to biophysical profile score and pH, it seems likely that a similar relationship could be reasonably extrapolated to other high-risk groups.

The relationship between biophysical profile score and antepartum umbilical venous pH is not unexpected because similar observations have been reported between biophysical profile score and cord blood obtained after either spontaneous delivery[7] or elective cesarean section before labor.[13, 14] The comparison of absolute values may not be exact because the pH of umbilical venous cord blood collected at delivery is known to be significantly lower than antepartum umbilical venous pH.[15] Ribbert et al. studied 14 severely growth-retarded fetuses at between 29 and 35 weeks and noted a significant linear correlation between biophysical profile score and antepartum umbilical venous pH (cordocentesis).[16] By contrast, in a study of 150 fetuses Okamura et al.[13, 17] failed to demonstrate any relationship between a modified biophysical profile score and umbilical venous pH. In this study 41 (27%) fetuses had an abnormal modified biophysical profile score (≤ 7); 39 of these fetuses (95%) had a pH >7.25 (range 7.26 to 7.46), and the two remaining fetuses had a pH of 7.24. The difference between those results and the results of our study is perplexing. Some of the variations may be a result of differences in the study population. In the Okamura study 50% of the fetuses sampled were anomalous, whereas in our study all fetuses were structurally normal. It has been our experience in $>100{,}000$ observations of biophysical profile score that the incidence of abnormal results is sharply increased in anomalous fetuses (Manning FA, Harman CR. Unpublished observations). However, even allowing for these potential sources of variance, there may still remain a major inexplicable discrepancy between the two studies.

Defining normal values for antepartum umbilical venous pH is a difficult problem because cordocentesis in normal uncomplicated pregnancy is not warranted. Nicolaides et al.[11] reported normative data in 208 fetuses of appropriate size for gestational age between 17 and 38 weeks; 104 of these fetuses (50%) had structural anomalies that were visible by ultrasonography.[8] In these fetuses the mean umbilical venous pH was 7.41 and the value for 2 SD below the mean was 7.35. However, the relationship between antepartum umbilical pH and perinatal outcome was not reported in this study. There are not enough studies that describe this relationship or identify the critical pH value that would warrant intervention because of fetal indications. The clinical circumstances are quite different for fetal biophysical profile scoring. The relationship of the biophysical profile score to perinatal outcome, both morbidity and mortality, has been studied extensively

by different clinical investigators,[5-8, 18, 19] and management protocols that are based on the score have been proposed and tested prospectively.[6-8, 18, 19] Predictive accuracy parameters for the biophysical profile score against morbidity and mortality yield consistent results: a normal score is a powerful predictor of normal outcome, an equivocal score is a poor predictor of abnormal outcome, and a decrease from an abnormal to a very abnormal score is a progressively more accurate and powerful predictor of abnormal outcome.[7] Therefore one reasonable approach to defining the clinically relevant normal lower limit of umbilical venous pH would be to determine the pH at which the test accuracy parameters for biophysical profile score were most practice. According to this method, the data from this study suggest that the lower limit of normal for umbilical venous pH is 7.25 (Table II, Fig. 5). The ultimate proof of this theorem would require a prospective randomized trial of biophysical profile score and umbilical venous pH. Such a trial may not be forthcoming in the near future.

The mean pH for the normal and abnormal result of any given short-term biophysical variable may reflect the sensitivity of the central nervous system regulatory center. Vintzileos et al.[20] studied 62 structurally normal fetuses delivered by elective cesarean section at between 25 and 37 weeks and noted a significant difference in mean umbilical arterial pH between normal-abnormal variable dyads, and among abnormal variables they observed a significantly lower mean pH for absent fetal movements and tone. The comparison of acute biophysical variable results with mean umbilical venous pH in our study yielded a similar pattern. In both studies there was a significant difference in fetal pH between the normal and abnormal variable results, but there was no difference in mean fetal pH among normal variable results. Both studies demonstrated a difference in mean pH between some abnormal variables, although the pattern was not identical. In our study the mean pH for absent fetal breathing was significantly lower than for a nonreactive NST, and mean pH for abnormal fetal tone was statistically indistinguishable from the mean for abnormal fetal movement. The explanation and clinical significance of these differences, if any, are obscure.

The data from both studies confirm that some ordering exists in the sensitivity of central nervous system regulatory centers to acidemia. Our data suggest that sensitivity of these centers to acidemia might be established by as early as 17 to 18 weeks' gestation. This supposition is supported by the observation that stratification of the data by gestational age did not affect the relationships between biophysical profile score and umbilical venous pH and by the anecdotal observation of coincident profound acidemia and a very abnormal biophysical profile score as early as 17½ weeks' gestation. These data may also suggest that for at least some of the short-term biophysical variables there may be a relatively short interval between the time the regulatory center begins to function and the time it acquires sensitivity to acidemia. Thus, for example, fetal breathing movements tend to first appear around 14 to 16 weeks, and sensitivity to acidemia is already present by 17 to 18 weeks. These data also confirm that changes in amniotic fluid volume in association with acidemia may occur early in fetal life (in this study as early as 17½ weeks). This new information on the gestational age at which biophysical variables may reflect fetal acidemia may be of some clinical importance as methods are developed for amelioration and treatment of asphyxial conditions in the very immature fetus. Already fetal biophysical profile scoring has proved a useful adjunct in determination of the urgency of intravascular transfusion in the very immature severely affected fetuses with alloimmune anemia (Harman CR, Manning FA, Unpublished observations).

The data from this study offer insight into the recovery time for a suppressed central nervous system regulatory center. In the severely anemic fetus the circulating hemoglobin rises immediately on the onset of intravascular transfusion and likely becomes fully oxygenated in a single pass through the placenta. The effect of increased oxygen delivery to the fetal brain on short-term biophysical activities is quite remarkable. On occasion the short-term variables appear and are normal within minutes of initiation of the transfusion. These anecdotal observations imply that the recovery time of the central nervous system center must be short indeed. Furthermore, the serial paired observations in the fetuses with alloimmune anemia indicate that the fetus can recover from a profound acidemia and that the return of normal biophysical variables is an indication that such recovery is under way. The long-term neurologic sequelae, if any, of intermittent episodes of acidemia are unknown and will obviously require study.

As a final point, the data in this study indicate that the biophysical profile score method may be used reproducibly by different investigators, in different settings, and with different high-risk populations. To this end, the remarkably similar correlation between biophysical profile score and umbilical venous pH between King's College in London and Health Sciences Centre, in Winnipeg are reassuring.

These data confirm the relationship between biophysical profile score and umbilical venous pH. Perhaps more important from the clinical perspective, these data confirm that a normal biophysical profile score virtually excludes the possibility of acidemia and suggest that an asphyxial process will result in both an

abnormal biophysical profile score and acidemia. The value of the biophysical profile score in assessment of the fetus at risk of asphyxia appears substantiated.

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