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Perinatal Correlates of *Ureaplasma urealyticum* in Placenta Parenchyma of Singleton Pregnancies That End Before 28 weeks of Gestation

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Abstract

Objectives—The purpose of this work was to examine the relationship between *Ureaplasma urealyticum* in the placenta and perinatal outcomes in extreme pre-term deliveries and to explore the influence of bacteria co-infection on perinatal outcomes in *U urealyticum*-positive placentas.

Methods—Under sterile conditions, a piece of chorion from 866 singleton deliveries before 28 weeks' gestation was obtained and flash frozen. The tissue was later homogenized and cultured for *Ureaplasma* and bacteria. Placentas were also examined histologically. Maternal and neonatal data were obtained prospectively. Each infant had three sets of cranial ultrasound scans between days 1 to 4, 5 to 14, and between day 15 and 40th week post conceptional age. CUS findings were by consensus of 2 or 2 of 3 sonologists.

Results—*U urealyticum* was recovered from 6% and bacteria from 47%; 47% of placentas had no bacteria detectable. Sixty-seven percent of *U urealyticum*-positive placentas also harbored bacteria. Placentas that harbored *U urealyticum* only were more likely than sterile placentas to be associated

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What's Known on This Subject: Intrauterine infection with *Ureaplasma urealyticum* is associated with increased risk of adverse perinatal outcomes, including chorioamnionitis, preterm labor and delivery, and neonatal morbidities. Trials of antibiotics against *U urealyticum* have not consistently reduced the risk of these adverse consequences.

What This Study Adds: *U urealyticum*-positive placentas frequently harbor bacteria. Placental coinfection with *U urealyticum* and bacteria did not enhance the adverse effects associated with *U urealyticum*. Study of *U urealyticum* and pregnancy outcomes must control for confounding by other intrauterine organisms.

with a higher prevalence of preterm labor and preterm premature rupture of membranes, as well as umbilical cord, fetal vessel, membrane and parenchymal inflammation and to predict intraventricular hemorrhage and echolucent brain lesions. Placentas that harbored *U urealyticum* only were similar to placentas that harbored bacteria only. The recovery of *U urealyticum* and bacteria from the same placenta did not enhance the differences between placentas with *U urealyticum* alone and sterile placentas. Recovery of *U urealyticum* only was not associated with a higher risk of death before day 7 of life.

Conclusions—The presence of *U urealyticum* in placental parenchyma before 28 weeks is associated with increased risk of preterm labor and delivery, higher risk of fetal and maternal inflammation, and increased risk of intraventricular hemorrhage and echolucent brain lesions but not of early neonatal death.

Keywords

Ureaplasma; placenta; inflammation; preterm delivery; brain injury

Introduction

Ureaplasma Urealyticum is detected frequently in the uterine cavity following preterm labor and delivery (1-4). Recovery of *U urealyticum* from the amniotic fluid and placenta is associated with chorioamnionitis (1,5), elevated amniotic fluid concentrations of proinflammatory cytokines (6,7), matrix metalloproteinases (8), increased risk of preterm premature rupture of membranes (pPROM) and preterm delivery (2,9). However, a review of studies of *U urealyticum* and preterm delivery reveals gaps in 3 important areas. First, none of the studies evaluated the significance of *U urealyticum* in the placenta in pregnancies that end before 28 weeks; rather, they focused mostly on pregnancies that end before 32 to 36 weeks (2-4,10). Second, most studies of intrauterine *U urealyticum* in preterm deliveries cultured amniotic fluid (9), the chorioamnionic surface (3,11), or combinations of amniotic fluid, amniotic membrane and placenta (2,12,13), making comparisons among studies difficult. Third, few studies have evaluated intrauterine *U urealyticum* in the context of bacteria recovered simultaneously from the uterine cavity (2,6). We addressed these gaps in the Extremely Low Gestational Age Newborn (ELGAN) Study.

In an effort to test the hypothesis that isolation of *U urealyticum* from placental parenchyma is associated with increased prevalence of moderate-to-severe placental inflammation, we evaluated placental parenchyma for the presence of *U urealyticum* and inflammation in a prospective study designed to identify factors associated with neurologic injury in infants delivered before 28 weeks of gestation. We also tested the hypothesis that recovery of *U urealyticum* from the placenta increases the risk of early perinatal complications including brain lesions on cranial ultrasound (CUS) and early neonatal death in 866 extremely preterm newborn singletons.

Materials and Methods

The ELGAN Study

The ELGAN study was designed to identify characteristics and exposures that increase the risk of structural and functional neurologic disorders in ELGANs. From March 2002 to August 2004, women delivering between gestational ages 23 to 27^{6/7} weeks at 1 of 14 participating institutions were asked to enroll in the study. The individual institutional review boards approved the enrollment and consent processes. Details of maternal and infant enrollment have been described (14). A total of 1249 mothers of 1506 infants consented to participate in the study; 260 women were either missed or did not consent to participate. We limited this analysis

to placentas from singleton pregnancies because placental assignment was not always clear or feasible in multi-fetal gestations, and more than half of the placentas from multi-fetal gestations were fused. Exclusion of multi-fetal placentas and placentas not evaluated histologically and microbiologically resulted in a sample of 866 placentas.

After delivery, a trained research nurse interviewed each mother in her native language, and prospectively reviewed the maternal and neonatal charts to obtain demographic, pregnancy, delivery and neonatal variables as described in detail elsewhere (14). We used structured data collection forms and procedure manuals with a priori defined variables and outcomes. The birth weight *z* score, defined as the number of SDs above or below the median weight of infants at the same gestational age in a standard data set (15) was noted.

We obtained protocol CUS scans with digitized 7.5- and 10.0-MHz high-frequency transducers, using the anterior fontanel as the sonographic window (16). Details of CUS protocol and interpretation in the ELGAN cohort have been reported elsewhere (17). We performed 3 sets of protocol scans: first scans were obtained between days 1 and 4, second scans between days 5 and 14, and third scans between the day 15 and week 40. In our sample of 866 singletons with both placental histology and microbiology, 506 had all 3 sets of CUS studies.

Two independent readers who were not provided clinical information read all ultrasound scans. Each set was first read by a study sonologist at the institution of the infant's birth and then sent as electronic images to a sonologist at another ELGAN Study institution for a second reading. When the 2 readers differed in their recognition of intraventricular hemorrhage (IVH), moderate-to-severe ventriculomegaly, echodense lesions, and echolucent lesions, the films were sent to a "tie-breaking" reader who was blinded to what the previous readers reported. Interobserver variability in interpretation of the CUS findings was acceptably low, except for echodense lesions (17).

Details of placental handling and processing in the ELGAN cohort have been reported (18, 19). We transported delivered placentas to the sampling room in sterile basins to ensure that contamination did not occur. More importantly, we obtained placenta tissue after separating the amnionic membrane from the chorion with sterile forceps and scissors to expose a sterile field. Thereafter, we used a new set of sterile instruments to obtain a 1-cm³ piece of chorion and underlying tissue from the placenta as described earlier (19). Eighty-two percent of the samples were obtained within 1 hour of delivery. The specimen was flash frozen in a sterile 2 ml cryovial in liquid nitrogen and stored frozen at -80°C until it was shipped on dry ice to a central microbiology laboratory in Boston. Thereafter, specimens were stored frozen at -80°C until analyzed.

For microbiologic evaluation a portion was obtained from each placenta specimen after thawing and was weighed and homogenized in sterile phosphate buffered saline to achieve a 10-fold weight/volume dilution, as described elsewhere (19). Serial 10-fold dilutions of the homogenates were made in phosphate buffered saline and aliquots of samples and dilutions plated onto selective and nonselective media and incubated in appropriate conditions for aerobic, anaerobic, mycoplasmal and ureaplasma isolation and identification (19,20). In an effort to improve the sensitivity of bacteria detection in placenta, we applied polymerase chain reaction (PCR) techniques to homogenized placental specimens using universal bacterial primers and primers specific to *U. urealyticum*. Although the primer sets and PCR methods were able to detect low copy levels of DNA in vaginal swabs, PCR did not detect any bacterial DNA even in specimens known to contain high numbers of bacteria by culture (19). Onderdonk et al (19) speculated that placental tissues before freezing contain active ingredients that either degrade or block the detection of bacterial DNA in homogenized chorion-decidual specimens.

After sterile removal of the specimen for microbiologic assessment, and collection of specimens for other studies, study site pathologists examined the whole placenta within 24 hrs of delivery, as described elsewhere (18). Representative sections were taken from all abnormal areas, as well as routine sections of umbilical cord, membrane roll, and full thickness sections from the center and a paracentral zone of the placental disk, as per the College of American Pathologists Conference guidelines (21). Study pathologists examined the slides for histologic evidence of abruption, inflammation of the chorionic plate, chorion/deciduas, and fetal vasculitis, as described in detail elsewhere(18).

Data Analysis—Information collected on standardized data forms was entered into a central database and analyzed by using Stata Release 10.0 (Stata Corp LP, College Station, TX) statistical software. The generalized form of null hypothesis tested is that recovery of *U urealyticum* is not associated with any maternal, pregnancy or newborn characteristic. We used Fisher's exact test for pairwise comparisons of discrete variables and present data as column percentages. *P* values < 0.05 were considered statistically significant.

Results

A total of 866 placentas from 1006 singleton deliveries before 28 weeks of gestation were subjected to histologic and microbiologic evaluations. *U. urealyticum* was recovered from 52 (6%) and bacteria from 407 (47%; bacteria only), and 407 placentas (47%, no bacteria) had no bacteria detected by culture. Overall, microorganisms were recovered from 459 (53%) of 866 of our cohort.

Thirty-five (67%) of the 52 *U urealyticum*-positive placentas harbored bacteria (Uu⁺ bacteria); 27% had 1, whereas 40% had ≥ 2 other organisms isolated along with *U urealyticum* (Table 1). Aerobic and anaerobic organisms were recovered from similar proportions of *U urealyticum*-positive placentas (data not shown). Vaginal organisms were recovered from 33%, *Mycoplasma sp* from 19%, but *Chlamydia sp* was not isolated from *U urealyticum*-positive placentas in this sample. In the analysis, we contrast infants with “*U urealyticum* only” and “Uu⁺ bacteria” to infants with “bacteria only” and “no bacteria”.

Maternal Demographic, Pregnancy, Labor and Delivery Characteristics

Mothers whose placentas harbored *U urealyticum* only were more likely to be single compared to mothers with sterile placentas (Tables 2 and 3). However, age, years of education, or primigravidity did not vary appreciably among the 4 groups. Compared to women whose placenta harbored no bacteria, women whose placenta harbored *U urealyticum* only were approximately twice as likely to present with preterm labor or pPROM. They were also more likely to have rupture of membranes > 24 hours but less likely to have been delivered by cesarean section. Isolation of Uu⁺ bacteria did not enhance the differences between the *U urealyticum* only and no bacteria groups.

Neonatal Characteristics and CUS Findings

Infants with *U urealyticum* only did not differ from infants with no bacteria in gestational age, birth weight, or risk of death before 7 days; however, they were less likely to be born at the lower gestational ages and to die before day 7 compared to infants with bacteria only (Table 4). Compared to infants with no bacteria, infants with *U urealyticum* only had a modestly higher incidence of IVH, an appreciably lower incidence of moderate-to-severe ventriculomegaly and approximately twice the incidence of echolucent white matter brain lesions. The Score for Neonatal Acute Physiology II is an illness severity indicator based on physiologic information gathered within the first postnatal hours. The prevalence of Score for Neonatal Acute Physiology II ≥ 30 was similar in all 4 groups (Table 5).

Placental Characteristics

Placentas with *U urealyticum* only had increased frequencies of neutrophilic infiltration of fetal vessels in the chorionic plate, umbilical cord vasculitis, and moderate-to-severe inflammation in the chorion and decidua compared with placentas with no bacteria (Table 6). This difference was not enhanced by the simultaneous isolation of bacteria from *U urealyticum*-positive placentas, and placentas with bacteria only were not appreciably different from placentas with *U urealyticum* only. Placental vasculopathy, indicated by thrombosis of fetal stem vessels, placental infarction and increased syncytial knots was less likely in placentas with *U urealyticum* only than in placentas with no bacteria.

Discussion

Because we cultured placenta parenchyma for *U urealyticum* as well as bacteria, we were able to show that placentas that harbored *U urealyticum* and sterile placentas differed in their tendency to be inflamed, to come from pregnancies with different disorders leading to preterm delivery, to predict brain ultrasound lesions in extreme low gestational age newborns. We were also able to show that placentas that harbored *U urealyticum* alone were similar to placentas that harbored bacteria only and that the isolation of bacteria from *U urealyticum*-positive placentas did not accentuate the difference between *U urealyticum*-positive and sterile placentas.

U urealyticum in Placental Parenchyma and Placental Inflammation

In agreement with reports by others (11,22), recovery of *U urealyticum* from the placenta was associated in this sample with an increased risk of fetal vasculitis. Fetal vasculitis has been associated with neonatal sepsis (23), IVH (24), and white matter damage (25). Consequently, our finding that *U urealyticum* was not associated with a measure of illness severity supports the possibility that relatively benign and not-so-benign forms of umbilical cord vasculitis exist (22). Alternatively, *U urealyticum* may result in a different pattern of cord inflammation. Umbilical vasculitis that includes arteritis has been associated with a higher rate of neonatal complications than either the absence of cord inflammation or the presence of cord inflammation without arteritis (23). A study of the pattern of umbilical vessel involvement in fetal vasculitis in *U urealyticum*-positive compared to bacteria-only positive placentas may help explain the observed differences in outcomes.

U urealyticum in the Placenta, Preterm Labor, pPROM and Neonatal Outcomes

Intrauterine infection seems to be a major cause of pPROM, spontaneous preterm labor and preterm delivery (4,26); the lower the gestational age at delivery, the higher the frequency of intrauterine infection. Our finding that pregnancies with placental *U urealyticum* had an increased risk of pPROM and preterm labor corroborates these previous findings. This might be expected, because *U urealyticum* in the amniotic fluid and choriodecidual tissue activates the decidua and fetal membranes to produce a number of cytokines (6,7) and other bacterial products that stimulate prostaglandin synthesis and release (27) and initiate neutrophil chemotaxis and activation, synthesis and release of metalloproteases (8) and other bioactive substances. Prostaglandins stimulate uterine contractions, whereas metalloproteases attack and remodel collagen in the cervix and chorioamniotic membranes, leading to cervical ripening, pPROM and preterm labor (26). However, the precise role of *U urealyticum* in the pathogenesis of these adverse pregnancy outcomes remains unclear. In one study, isolation of bacteria from the chorioamniotic space, not *U urealyticum*, was associated with a higher risk of preterm delivery (3) and $\leq 75\%$ of pregnancies with *U urealyticum* in the amniotic fluid during midtrimester amniocentesis get to term (28,29). Furthermore, trials of antimicrobial agents active against *U urealyticum* in colonized women at risk for preterm delivery (30) and in colonized women in preterm labor (31) have shown neither a consistent reduction in rate of

preterm labor nor prolongation of pregnancy. In the present report, placentas that harbored bacteria only were associated with earlier gestational age at delivery and higher risk of IVH and death in the first 7 days of life. Previous studies that demonstrated association between intrauterine *U urealyticum* and adverse pregnancy outcomes did not take into account the possible role of other intrauterine bacteria (2,4,9). In our sample, >60% *U urealyticum*-positive placentas also harbored bacteria. This is comparable to studies that reported the recovery of bacterial pathogens from the uterine cavity in 40 – 90% of women with intrauterine *U urealyticum* infection (2,32). In a recent study, *U urealyticum* was recovered from the cord blood in 17% of preterm infants delivered between 23 and 32 weeks of gestation (10). The study also showed that placentas from 90% of infants with positive cord blood culture for *U urealyticum* and/or *Mycoplasma hominis* were positive for other organisms. Failure to control for potential confounding by other intrauterine organisms probably contributes to the weak and variable association between *U urealyticum* and pregnancy outcomes.

Placental *U urealyticum* and Abnormal CUS Findings

Compared to sterile placentas, recovery of *U urealyticum* only from placenta parenchyma in this report is associated with an increased frequency of fetal vasculitis and CUS evidence of echolucent cerebral lesions. Others have shown that recovery of *U urealyticum* from cultures of chorionic surface is associated with an increased risk of fetal vasculitis but not of echolucent brain lesions in VLBW infants (11). On the other hand, VLBW infants with fetal vasculitis and intact membranes have been shown to have substantially increased risk of white matter echolucency (25). It has been postulated that the fetal inflammatory response in the later situation is probably less intense and of longer duration, resulting from intrauterine infection with less virulent organisms like *U. urealyticum* (25,33). Our finding of an increased frequency of fetal vasculitis and a modestly increased risk of IVH in infants whose placentas harbored *U urealyticum* lends support to the association between fetal vasculitis and IVH. However, recovery of *U urealyticum* from the amniotic fluid (9,34), amnion and placental tissue (35) has not been consistently associated with increased frequency of IVH in VLBW infants. However, none of the studies evaluating the association between intrauterine *U. urealyticum* and IVH examined placenta or umbilical cord for fetal vasculitis.

Limitations and Strengths of Study

The small number of infants with *U urealyticum* detected in the placental parenchyma is a limitation to the study. The low rate may reflect effectiveness of our efforts to limit sample contamination. A second limitation is our inability to use PCR. We attribute this to interfering substances in the placenta parenchyma (18,19). However, the culture methods employed appear to be as sensitive as PCR for detecting *U urealyticum* associated with preterm delivery, based on the results of other investigators (9).

A third limitation is that both our study and comparison groups include cases with different clinical presentation, including spontaneous preterm labor, pPROM and deliveries undertaken for maternal and fetal indications.

The strengths of our study include the large number of infants enrolled and the prospective nature of the study. The gestational-age-defined sample of infants born between 23 and 27^{6/7} weeks of gestation enabled us to evaluate a fairly homogenous high-risk population compared to studies that utilized birth-weight-defined samples, which can have an over-representation of growth restricted newborns (4,25). Furthermore, the ELGAN study sample afforded us a unique opportunity to compare perinatal outcomes associated with recovery of *U urealyticum*, alone or with bacteria, with outcomes when the placenta is sterile.

Conclusions

Among placentas delivered before 28 weeks' gestation, the presence of *U urealyticum* alone was associated with an increased prevalence of pPROM, preterm labor, preterm delivery, and histologic indicators of fetal and maternal inflammation when compared to cases with sterile placentas. The recovery of bacteria from *U urealyticum*-positive placentas did not enhance these differences with sterile placentas. The precise role *U urealyticum* in the pathogenesis of intrauterine inflammation and associated adverse pregnancy outcomes remains unclear. Infants whose placentas were positive for *U urealyticum* had an appreciably increased risk of echolucent white matter lesions and a modest increase in risk of IVH but not increased neonatal illness severity or risk of early neonatal death. Because >60% of *U urealyticum*-positive placentas also harbored bacteria, future studies of the impact of intrauterine *U urealyticum* on pregnancy outcomes must include methods to identify and control for the confounding effects of intrauterine bacteria.

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Abbreviations

CUS	cranial ultrasound
IVH	intraventricular hemorrhage
VM	ventriculomegaly
EL	echolucent lesions
ED	echodense lesions
pPROM	preterm premature rupture of membranes
PCR	polymerase chain reaction
ELGAN	extremely low gestational age newborn
Uu+ bacteria	U ureaplasma-positive placentas harboring bacteria

TABLE 1
Bacteria Isolated Along With *U urealyticum* From Placentas in 52 Singleton ELGANS

	No. (N=52)	Percentage
No. of organisms isolated:		
0	17	33
1	14	27
≥2	21	40
<i>Actinomyces sp</i>	5	10
<i>Prevotella bivia</i>	6	11
<i>Corynebacterium sp</i>	8	15
<i>Escherichia coli</i>	3	6
<i>Lactobacillus sp</i>	5	10
<i>Peptostrep magnus</i>	6	11
<i>Propionibacterium sp</i>	3	6
<i>Staphylococcus sp</i>	15	29
Group B Strep	1	2
Group D Strep	3	6
A hemolytic Strep	3	6
Anaerobic Strep	4	8
<i>Gardnerella vaginalis</i>	4	8
<i>Mycoplasma sp</i> ^a	10	19
Skin organisms ^b	19	37
Vaginal organisms ^c	17	33
Total number placentas	52	100

^aThese were not *U urealyticum*

^bData include *Corynebacterium sp*, *Propionibacterium sp*, *Staphylococcus sp*

^cData include *Prevotella bivia*, *Lactobacillus sp*, *Peptostrep magnus*, *Gardnerella vaginalis*

TABLE 2
Selected Demographic and Pregnancy Characteristics of Mothers of Singleton ELGANS Classified According to Results of Infant Placental Cultures

Maternal Characteristics	<i>U urealyticum</i> Only, %	Uu ⁺ Bacteria, %	Bacteria Only, %	No Bacteria, %	Row Totals, N	p ^a
Race						
White	47	35	50	52	430	.33
Black	35	35	36	33	292	-
Other	18	29	15	15	133	-
Age (years)						
< 21	6	35	18	19	155	.09
21-35	81	56	63	67	537	-
> 35	13	9	19	15	138	-
Years of education						
< 12	6	22	23	19	165	.30
12 to <16	69	63	53	53	432	-
≥16	25	16	24	28	205	-
Marital status						
Single	65	74	53	46	440	.004
Gravidity						
Primigravida	38	45	34	38	301	.47
This pregnancy^b						
Fever	0	9	8	6	57	.52
Vaginal/cervical Infection	13	21	16	11	110	.07
Medication						
Antibiotic ^b	50	47	33	30	262	.11
Maximum No. of women	17	35	407	407	866	-

-, indicates no data.

^aBy Fisher's exact test

^bData may be in > 1 category

TABLE 3
Selected Labor and Delivery Characteristics of Mothers and ELGANs Classified by Results of Infant Placental Cultures

Labor and Delivery Characteristics	<i>U ureaplasma</i> Only, %	Uu ⁺ Bacteria, %	Bacteria Only, %	No Bacteria, %	Row Totals, N	p ^a
Maternal fever,						
> 100.4°F	6	9	9	4	55	.009
Initiator of delivery						
PTL	59	51	41	35	338	≤.001
pPROM	35	34	28	15	195	-
PE	0	0	10	29	160	-
Abruption	6	14	12	11	101	-
Cerv insuf	0	0	6	4	44	-
Fetal indic	0	0	2	5	28	-
Antenatal steroids						
Any	88	89	85	91	762	.02
Complete	82	71	63	58	530	.08
Cesarean delivery						
Yes	47	37	47	71	501	≤.001
5-min Apgar score ≤ 6	18	14	21	18	168	.75
Duration of ROM, h						
< 1	41	46	49	66	494	≤.001
1-24	21	9	20	11	132	-
> 24	35	46	32	23	240	-
Duration of Labor, h						
0	12	11	20	42	258	≤.001
≤ 12	6	26	27	18	192	-
> 12	82	63	53	40	416	-
Maximum No. of women	17	35	407	407	866	- ^a

PTL indicates preterm labor; PE, preeclampsia; Cerv insuf, cervical insufficiency; Fetal indic, fetal indication; ROM, rupture of membranes; - no data.

^aFisher's exact test

TABLE 4
Selected Newborn Characteristics Classified by Results of Placental Cultures

Newborn's Characteristics	<i>U. urealyticum</i> Only, %	Uu ⁺ Bacteria, %	Bacteria Only, %	No Bacteria, %	Row Totals, N	p ^a
Gestational age, completed weeks						
23	6	9	12	5	74	<.001
24	18	17	25	14	167	-
25	18	20	19	22	179	-
26	24	26	20	28	211	-
27	35	29	23	30	235	-
Birth weight, g						
< 750	35	37	47	44	390	.62
751 - 1000	35	46	36	39	328	-
> 1000	29	17	17	16	148	-
Birth weight z score						
Less than -1	6	6	17	30	194	≤.001
-1 or more to < 0	47	51	35	33	305	-
≥ 0	47	43	48	37	367	-
Ultrasound lesions						
IVH	25	21	28	17	194	.002
VM	0	12	16	8	100	.001
ED	13	18	20	12	137	.02
EL	12	9	11	5	70	.03
Died ≤ 7 days, Yes	6	3	9	4	54	.03
Maximum No. of infants	17	35	407	407	866	-

VM indicates moderate-to-severe ventriculomegaly; ED, echodense lesions; EL, echolucent lesions; -, no data.

^aBy Fisher's exact test

TABLE 5
Percentage of Children Identified by Both the Column and Row Characteristics Who had a Score of Neonatal Acute Physiology II (SNAP-II) $\geq 30^{\dagger}$

Gestational Age, Completed Weeks	<i>U. urealyticum</i> Only, %	Uu ⁺ Bacteria, %	Bacteria Only, %	No Bacteria, %	Row Totals, N	p ^a
23-24	25	33	53	46	234	.41
25-26	29	6	23	22	388	.44
27	0	20	12	11	227	.73
Maximum No. of infants	17	35	407	407	866	-

^aBy Fisher's exact test

TABLE 6
Distribution of Characteristic Histologic Lesions of the Placentas Classified According to Culture Results

Placental Histologic Characteristic	U u Only, %	Un ⁺ Bacteria, %	Bacteria Only, %	No Bacteria, %	Row Totals, N	P ^a
Inflammation of the chorionic plate (stage 3 and grade 3)	18	38	32	15	205	≤0.001
Neutrophils in fetal vessels of the chorionic plate	35	41	43	16	252	≤0.001
Umbilical cord inflammation	47	39	45	21	276	≤0.001
Moderate-to-severe inflammation in chorion/decidua	65	51	58	28	370	≤0.001
Thrombosis of fetal stem vessels	0	3	7	5	50	0.552
Infarct	6	14	18	24	175	0.04
Increased syncytial knots	6	17	13	27	167	≤0.001
Decidual hemorrhage/fibrin deposition	12	23	23	19	180	0.34
Maximum No. of placentas	17	35	407	407	866	

^aBy Fisher's exact test