Maternal Fever During Labor — What Does It Mean?

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Background: **Several studies have shown maternal fever to be associated with chorioamnionitis and neonatal sepsis if at least two of the following five criteria are also present: maternal tachycardia, purulent or foul-smelling amniotic fluid, fetal tachycardia, uterine tenderness, or maternal leukocytosis. Less is known about the risk of neonatal sepsis when the presence of maternal fever in labor is the only criterion.**

Methods: **A retrospective medical record review searching for women who had a fever greater than 100.4°F while in the active phase of labor during a 1-year period at the University of Michigan was undertaken to investigate the relation between isolated maternal fever in labor and neonatal sepsis. Eighty-two cases of maternal fever were found.**

Results: **Forty-six women met the clinical criteria for chorioamnionitis, and 6 of the 7 neonates with sepsis diagnosed were born to these mothers. There were no significant differences found in admission or intrapartum factors between women who did and did not meet clinical criteria for chorioamnionitis, and there was no association between these factors and neonatal sepsis. Epidural anesthesia was administered to 91 percent of these women and might be associated with maternal fever during labor. Using maternal clinical criteria for chorioamnionitis and a neonatal band cell-total neutrophil ratio of 0.2 or greater instead of the current system to determine the need for newborn antibiotic administration would improve the positive predictive value (12.5 percent versus 9.3 percent) and specificity (34.6 percent versus 16 percent) without compromising sensitivity (100 percent). All septic and probably septic newborns would be treated, and neonatal antibiotic administration would be reduced by 17 percent.**

Conclusions: **The addition of the maternal clinical criteria for chorioamnionitis to the criteria already used for diagnosing and treating neonatal sepsis could prove useful in decisions regarding the selective administration of intrapartum antibiotics and prediction of risk of neonatal sepsis. (J Am Board Fam Pract 1994; 7:14-24.)**

Maternal fever during labor presents a diagnostic dilemma for clinicians, because an elevated temperature can be caused by a variety of conditions ranging from the innocuous upper respiratory tract infection to the potentially serious chorioamnionitis. It is hypothesized that maternal temperature elevations might be secondary to an extrauterine infection of the urinary or respiratory tract,[1] increased metabolic rate during the anxiety and stress of labor,[2,3] failure to maintain adequate maternal hydration,[1] exposure to poorly ventilated and overheated delivery rooms,[4] epidural anesthesia,[4-6] or the transient bacteremia that occurs with a vaginal delivery.[7] Studies of maternal fever during labor have focused on fever as an indicator of chorioamnionitis and have excluded fevers not associated with infection. As a result the various causes of fever during labor remain undocumented. Several studies have shown that a maternal fever greater than 100 to 100.4°F with at least two of the following criteria — maternal tachycardia, purulent or foul-smelling amniotic fluid, fetal tachycardia, uterine tenderness, or maternal leukocytosis — is highly associated with the probability of maternal chorioamnionitis and the resultant risk of neonatal sepsis.[1,8-11]

Studies using the above criteria for probable chorioamnionitis have been done to examine the possible benefits of intrapartum maternal antibiotic administration in an effort to reduce the incidence of neonatal sepsis. It has been proposed that intrapartum maternal antibiotic administration results in fewer positive neonatal blood cultures and thus fewer cases of neonatal sepsis.[12-14] Because neonatal sepsis has a high morbidity and mortality rate, some clinicians believe that maternal fever alone is enough to indicate a high probability of chorioamnionitis and that intrapartum

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antibiotics should be administered as early as possible to prevent possible neonatal infection. In addition, because of concern that maternal antibiotic administration will cause the newborn's cultures to be falsely sterile, some clinicians advocate treating all neonates with a 7-day course of intravenous antibiotics for possible meningitis if there is a history of intrapartum antibiotic administration. As a result, in care centers where intrapartum antibiotic administration is advocated solely based on the presence of maternal fever, many neonates could receive a mandatory 7-day course of intravenous antibiotics without any demonstrable benefit.

This retrospective study was designed to investigate maternal fever during labor and its correlation with chorioamnionitis and possible neonatal sepsis. We reviewed past cases of maternal fever during labor at the University of Michigan Medical Center to (1) determine the percentage of cases in which maternal fevers are indicative of chorioamnionitis by clinical criteria; (2) evaluate how accurate clinicians are in diagnosing chorioamnionitis intrapartum; (3) record the circumstances of each febrile episode so that the various causes of maternal fever might be considered; (4) determine which clinical factors, such as laboratory values and physical examination signs, are associated with septic neonates; (5) determine whether placental cultures are being routinely obtained in cases of maternal fever and whether they are useful predictors of neonatal sepsis;[15-19] (6) determine whether there is a correlation between placental cultures and chorioamnionitis despite intrapartum antibiotic use; and (7) evaluate the outcomes of maternal fever in terms of neonatal and maternal sequelae.

Methods

We conducted a retrospective medical record review of all women who were at least 34 weeks' gestation, who gave birth at the University of Michigan Medical Center between November 1988 and January 1990, and who developed a temperature greater than 100.4°F during the active phase of stage I or stage II labor. We excluded women who were less than 34 weeks' gestation because of the disproportionately high risk of chorioamnionitis and neonatal sepsis and because we were interested in investigating a patient population more representative of women cared for by the family physician who practices obstetrics.[20] We did not study the months of May and November 1989 as the data were not available for collection. We searched the delivery records for 2270 mothers and 2325 neonates for documentation of maternal fever, chorioamnionitis, or maternal antibiotic administration for which the cause was unclear (e.g., not for subacute bacterial endocarditis or Cesarean section prophylaxis). If the delivery record had any of the above findings, the complete hospital records for both mother and neonate were obtained for data collection.

To measure the accuracy of this method of case identification, we compared the delivery records from the 206 births that occurred in October of 1989 with the individual hospital records, including the nursing and anesthesiology flow sheets on which temperature values were recorded and physician inpatient notes, to ensure that no maternal fevers were missed. Of 206 deliveries, four maternal fevers were not recorded on the delivery records. One fever occurred during a pregnancy termination with prostaglandin gel at 23 weeks' gestation and one had been present for the week before the delivery of a dead fetus. The other two fevers occurred as a single temperature elevation just before delivery and were not addressed by the physicians caring for the mother or neonate. Because two of the fevers occurred in patients who did not fit our study criteria, the failure rate for record identification was 0.98 percent. Because the other two fevers did not result in a change in maternal or neonatal care, this method of record identification was deemed acceptable.

Of the study population of 2270 mothers, 82 mothers met the criteria for maternal fever during labor (3.6 percent), and we reviewed their complete hospital maternal and neonatal records for maternal sequelae including chorioamnionitis and endometritis and for neonatal sequelae including sepsis. The sequelae were determined by the results of laboratory tests obtained, reasons given for maternal and neonatal antibiotic administration, and recorded maternal and neonatal discharge diagnoses. We defined the active phase of stage I labor as cervical dilatation of at least 4 cm with a strong, regular contraction pattern until full dilatation was reached. We defined stage II labor as the time from full cervical dilatation to delivery of the infant. Using previously well-studied clinical criteria, we defined chorioamnio-

nitis as a maternal temperature greater than 100.4°F plus two of the following criteria: maternal tachycardia (heart rate more than 100 beats per minute for at least 5 minutes), uterine tenderness, fetal tachycardia (heart rate more than 160 beats per minute for at least 5 minutes), foul-smelling or purulent amniotic fluid, or maternal leukocytosis (white cell count greater than 2 standard deviations above the mean, which was greater than 16,000/mm^3).[1,8-11] Epidural anesthesia was initiated with a blockade of a 3-mL solution of 1.5 percent lidocaine with epinephrine (1:2,000). A test dose of 6 mL to 10 mL of 0.125 percent bupivacaine with 5 μg/mL of fentanyl citrate was then administered, and if the test dose was tolerated, an infusion into the epidural space was begun with a solution of 0.125 percent bupivacaine with 2 μg/mL of fentanyl citrate at approximately 8–12 mL/h.

In many of the neonatal records, a diagnosis of rule out sepsis or no diagnosis at all was recorded. We therefore assigned cases a diagnosis according to the following criteria: we used the diagnosis "sepsis ruled out" if the neonate received antibiotics for 72 hours or less and all cultures had no growth. We used "possible sepsis" if it was stated in the record that the neonate received 7 days of antibiotic therapy because the cultures were considered to be inaccurate as a result of maternal pretreatment with antibiotics, if the neonate received 7 days of antibiotics for positive maternal cultures, if the neonate received more than 72 hours of antibiotic therapy with no reason given, or if the neonate had positive maternal cultures and was treated for 72 or fewer hours. We used "probable sepsis" if the neonate showed septic findings on physical examination, such as cyanotic episodes, lethargy, poor feeding, or temperature instability, and improved with 7 days of antibiotics or if the pediatricians noted that the neonate had other abnormal laboratory values, such as elevated cerebrospinal fluid protein or white cell count, and indicated that these abnormalities affected the duration of antibiotic therapy. We defined "neonatal sepsis" as a positive culture (blood, cerebrospinal fluid, or urine), a positive cerebrospinal fluid or urine group B β-hemolytic streptococcus latex agglutination test, or infection documented by chest radiograph. Although sepsis is traditionally defined as a positive blood culture, we expanded the definition to include serious bacterial infection, because in neonates these infections often lead to sepsis despite the inability to document this finding on blood culture.[21,22] We used "normal newborn" if no neonatal antibiotics were given.

Once the data collection was completed, we performed statistical analyses to measure the association between maternal fever and (1) maternal and newborn sequelae, (2) chorioamnionitis, and (3) placental cultures. We analyzed the categorical variables with a chi-square test or the Fisher exact test and used a two-tailed Student t-test and analysis of variance for the continuous variables with 95 percent confidence intervals. We also examined the differences between continuous variables having a nonnormal distribution using the Mann-Whitney U test. A $P < 0.05$ was considered statistically significant. We compared the group of patients with chorioamnionitis (n = 46) with both the group of patients who definitely did not meet the criteria for chorioamnionitis (n = 26) and the group formed when the 10 patients for whom there were insufficient data available were added to the latter group (n = 36). Because we found no statistically significant differences, we present the combined group (n = 36) in the tables for statistical comparison.

Results

The mean maternal age for the study population was 25.2 years (range 14 to 40 years), and the mean estimated gestational age was 40 weeks. Sixty-five percent of the women were white, 22 percent were African-American, and 11 percent were Asian. Sixty-one percent of the women had at least one prenatal complication, including 33 percent who smoked cigarettes during pregnancy, 10 percent who had preterm labor, and 8 percent who had pregnancy-induced hypertension. Forty-six women (56 percent) had symptoms that met the clinical criteria for chorioamnionitis, for an incidence of 2.0 percent. Maternal and fetal tachycardia was the most common combination of clinical features (70 percent), followed by maternal and fetal tachycardia plus uterine tenderness in 4 (8.7 percent), increased maternal white cell count and fetal tachycardia in 4 (8.7 percent), uterine tenderness and fetal tachycardia in 2 (4.3 percent), increased maternal white cell count plus fetal and maternal tachycardia in 1 (2.2 percent), foul-smelling amniotic fluid plus maternal and

Table 1. Admission and Intrapartum Data of Women with and without Chorioamnionitis.

Parameters	Women with Clinical Chorioamnionitis* (n = 46)	Women without Clinical Chorioamnionitis* (n = 36)
Admission		
Type of labor onset (%)		
Spontaneous	76	64
Augmented	17	17
Induced	7	19
Reason for induction (%)		
Postdates	67 (2)	43 (3)
Spontaneous rupture of membranes without labor	33 (1)	43 (3)
Macrosomia	0	14 (1)
Membrane status (%)		
Ruptured	59	69
Intact	41	31
Intrapartum		
Type of fetal monitoring (%)		
Continuous external	9	8
Intermittent external	2	0
Continuous internal and external	89	92
Epidural anesthesia (%)	96	86
Duration of epidural anesthesia (hours)	9 ± 5†	9 ± 5†
Completely dilated cervix (%)	65	53
Risk factors for chorioamnionitis		
Duration of labor (hours)	18 ± 9	16 ± 7
Duration of ruptured membranes (hours)	17 ± 10	23 ± 21
Duration of internal monitors (hours)	10 ± 5	11 ± 7
Number of cervical checks (mean)	8 ± 3	8 ± 3
Clinical indicators for chorioamnionitis		
Duration of fever during labor (hours)	4 ± 2	3 ± 2
Maximum temperature in labor (°F)	101.3 ± 0.9	101.3 ± 0.9
Maternal tachycardia (%)	85	25
Uterine tenderness (%)	13	0
Foul-smelling amniotic fluic (%)	7	0
Maternal antibiotics given during labor (%)	87	81

*No significant differences were found between groups.
†± SD from the mean.

fetal tachycardia in 1 (2.2 percent), foul-smelling amniotic fluid and fetal tachycardia in 1 (2.2 percent), and maternal tachycardia and foul-smelling amniotic fluid in 1 (2.2 percent). Twenty-six women (31.7 percent) definitely did not have chorioamnionitis by these criteria. The clinical diagnosis of chorioamnionitis could not be established for 10 cases because a maternal white cell count was not obtained.

Of the 46 patients whose symptoms met the clinical criteria for chorioamnionitis, 21 (43.5 percent) had chorioamnionitis diagnosed by their clinicians. Of the 26 patients whose symptoms definitely did not fit the criteria for chorioamnionitis, 16 (61.5 percent) had chorioamnionitis diagnosed by their physicians. One of these 26 women had a urinary tract infection, 1 had a herpes infection, 2 had placenta cultures positive for group B β-hemolytic streptococcus, and 22 had no defined cause for the fever by such objective criteria as laboratory cultures or by such subjective criteria as a history of recent infection, symptoms of respiratory or urinary tract infection, or such observations as elevated external environmental temperature. Of the 10 women who were of indeterminate status with regard to the clinical diagnosis of chorioamnionitis, 6 had chorioamnionitis diagnosed by their clinicians. One of these 10 women had a cervical culture positive for *Ureaplasma urealyticum* and a blood culture

Table 2. Percentage of Fetal Intrapartum Complications Experienced by Women with and without Chorioamnionitis.

Complications	Women with Clinical Chorioamnionitis* (n = 46)	Women without Clinical Chorioamnionitis* (n =36)
Meconium	37	42
Scalp pH taken	33	22
Abnormal (pH < 7.25)	13	12
Reason for scalp pH		
Fetal distress	7	0
Late decelerations	29	25
Variable decelerations	43	12
Poor beat-to-beat variability	14	63
Other	7	0
Fetal tachycardia	98	47

*No significant differences were found between groups.

positive for *Propionibacterium*, 1 had a cervical culture positive for group B β-hemolytic streptococcus, 1 had a placenta culture positive for *Bacteroides uniformis*, and 1 had a placenta culture positive for group B β-hemolytic streptococcus. The remaining 6 women had no known cause for the fever.

Epidural anesthesia was administered to 75 of the 82 study patients (91 percent). Of the 46 patients meeting the clinical criteria for chorioamnionitis, 44 received an epidural anesthetic, whereas 23 of the 26 patients who did not have clinical chorioamnionitis received epidural anesthesia. Six of the 10 patients with indeterminate data had fevers of unknown origin, and 5 received epidural anesthesia.

The maternal admission and intrapartum data are summarized in Table 1. The majority of women (60 percent) reached complete cervical dilatation, had both external and internal monitors placed, received an epidural anesthetic, and were given antibiotics during labor. There were no significant differences noted for admission or intrapartum parameters between women with or without clinical chorioamnionitis. No admission or intrapartum parameters were associated with neonatal sepsis. Reasons listed in the medical records for antibiotic administration included maternal fever in 36 cases (52.2 percent), suspected chorioamnionitis in 29 (42 percent), urinary tract infection in 2 (2.9 percent), and cervical infection in 2 (2.9 percent). No other potential sources of maternal fever were indicated.

Table 2 presents fetal intrapartum complications. We noted no significant differences in fetal complications between women with and without chorioamnionitis. Table 3 contains the delivery outcomes comparing women with and without clinical chorioamnionitis. There were no maternal or neonatal deaths. The association between chorioamnionitis and female sex of the neonate almost reached significance ($\chi^2 = 3.60, P = 0.057$). No associations were found between intrapartum fetal complications and neonatal sepsis.

Table 4 summarizes the neonatal data. Antibiotics were administered to 70 of the 82 neonates. The primary reasons listed in the medical records for initiating antibiotics were maternal fever, maternal antibiotics administered in labor, maternal chorioamnionitis, and maternal infection. Three neonates showed clinical signs of sepsis on physical examination, and 1 additional neonate was probably septic based on laboratory data. These factors resulted in a decision to begin antibiotics. Seven of the neonates (8.5 percent) met the study criteria for sepsis and all received antibiotics.

The maternal culture results are summarized in Table 5. The majority of the cervical, urine, and placenta cultures were negative. Of the 22 positive placenta cultures, 21 samples were obtained from women who were exposed to intrapartum antibiotics. There was no association between a positive placenta culture and the clinical diagnosis of chorioamnionitis. Of the 7 septic neonates, 4 had placenta cultures taken. Two placenta cultures were positive for group B β-hemolytic streptococcus as were the corresponding neonatal cultures. The most common organism isolated from the placental cultures was group B β-hemolytic streptococcus. There was no association between positive maternal cultures (cervical, vaginal, urine, or blood) and the criteria for diagnosing clinical chorioamnionitis or neonatal sepsis.

Six neonates of mothers with clinical chorioamnionitis had symptoms that fit the criteria for neonatal sepsis, and all received antibiotics. The remaining septic neonate had a mother for whom we had insufficient information available to determine the presence of chorioamnionitis, and he received antibiotics as well. This infant had a positive urine group B β-hemolytic streptococcus latex agglutination test and a ratio of band cells to total neutrophils of greater than or equal to 0.2. Therefore, the 7 neonates had either a positive chest radiograph, blood, cerebrospinal fluid, or

Table 3. Delivery Outcomes of Women with and without Chorioamnionitis.

Outcomes	Women with Clinical Chorioamnionitis* (n = 46)	Women without Clinical Chorioamnionitis* (n = 36)
Maternal		
Type of delivery (%)		
Spontaneous vaginal	50	28
Cesarean section	37	58
Forceps or vacuum extraction	13	14
Reason for operative delivery (%)		
Second-stage arrest	87 (20)	61 (16)
Fetal distress	4 (1)	11 (3)
Cephalopelvic disproportion	0	8 (2)
Maternal fatigue	4 (1)	4 (1)
Elective	0	4 (1)
Life-threatening fever	0	4 (1)
Herpes infection	0	4 (1)
Failed induction	0	4 (1)
Transverse lie	4 (1)	0
Maximum temperature postpartum (°F)	100.5 ± 1.0†	100.1 ± 1.1†
Duration of antibiotics (hours)	17 ± 33† (40)	27 ± 41† (29)
Final diagnosis (%)		
Chorioamnionitis	44 (20)	58 (21)
Increased maternal temperature	52 (24)	30 (11)
Chorioamnionitis plus increased maternal temperature	2 (1)	0
Urinary tract infection (UTI)	2 (1)	0
UTI plus increased maternal temperature	0	3 (1)
Increased external temperature	0	3 (1)
Herpes infection	0	6 (2)
Neonatal		
Birth weight (gram)	3411 ± 541†	3500 ± 573†
Sex (%)		
Male	46	67
Female	54	33
Apgar 1 minute (mean)	6.3	6.8
Apgar 5 minutes (mean)	8.4	8.6

*No significant differences were found between groups.
†± SD from the mean.

urine culture or cerebrospinal fluid or urine group B β-hemolytic streptococcus latex agglutination test, resulting in an incidence of sepsis of 8.5 percent if maternal fever was present. Laboratory information on the 7 septic neonates is summarized in Table 6. Two additional neonates had positive blood cultures, one with nongroup D enterococcus and the other with rare diphtheroids and lactobacillus organisms. These cultures were thought by their clinicians to be contaminants, and thus these infants did not have sepsis diagnosed and did not receive full antibiotic treatment. All 4 of the neonates with probable sepsis diagnosed received antibiotics and had mothers whose symptoms met the clinical criteria for chorioamnionitis.

There was a significant association between a clinical diagnosis of chorioamnionitis and the first neonatal band cell-total neutrophil ratio obtained (0.25 versus 0.16, $P < 0.04$). In addition, there was an association demonstrated between a diagnosis of neonatal sepsis and the first neonatal white cell count value obtained (12,785/mm^3 versus 18,298/mm^3, $P < 0.017$), the number of neonatal segmented cells in the first white cell count (27.8 percent versus 47.6 percent, $P < 0.0026$), the first neonatal white cell count band cell-total neutrophil ratio (0.46 versus 0.19, $P < 0.0009$), and duration of antibiotics in the neonate (216.8 hours versus 81.4, $P < 0.0000$). Compared with the system currently used by clinicians at the University of Michigan Medical Center to deter-

Table 4. Outcome of Neonates (n = 82) Born to Women with and without Chorioamnionitis.

Outcomes	No. (%)
Antibiotics given	70 (85)
Timing of postnatal administration (mean hours)	3.1 Range 0.5–11.0
Reasons for antibiotics*	
Maternal fever	68 (97)
Maternal antibiotics given	60 (86)
Maternal chorioamnionitis	28 (40)
Maternal infection	14 (20)
Poor feeding	2 (3)
Hypoglycemia	2 (3)
Positive neonatal cultures	2 (3)
Increased respiratory rate	1 (1)
Poor color (blue-gray)	1 (1)
Irritability	1 (1)
Foul-smelling baby	1 (1)
Increased neonatal temperature	1 (1)
Duration of antibiotics (mean hours)	126 Range 48–336
Discharge diagnosis	
Normal newborn	12 (15)
Sepsis ruled-out	33 (40)
Possible sepsis	26 (32)
Probable sepsis	4 (5)
Sepsis	7 (8)

*More than one reason could be given.

mine the need for administration of antibiotics to potentially septic newborns, the use of both the maternal clinical criteria for chorioamnionitis and a neonatal band cell-total neutrophil ratio of 0.2 or more in predicting neonatal sepsis improved the positive predictive value (12.5 percent versus 9.3 percent) and specificity (34.6 percent versus 16 percent) without compromising sensitivity (100 percent) or the negative predictive value (100 percent). This strategy would decrease neonatal antibiotic administration by 17 percent.

If the sixth neonate's mother had recorded symptoms that met the criteria for chorioamnionitis instead of having indeterminate status (a limitation of the retrospective study format), the use of maternal clinical criteria for chorioamnionitis alone in predicting neonatal sepsis would improve the positive predictive value (14.8 percent versus 9.3 percent) and specificity (46.6 percent versus 16 percent) without compromising sensitivity (100 percent) or the negative predictive value (100 percent). Neonatal antibiotic administration would be decreased by 33 percent.

Discussion

Clinical Criteria for Chorioamnionitis

Forty-six patients (56 percent) had symptoms that met the clinical criteria for chorioamnionitis in this study population of 82 women with a temperature greater than 100.4°F in labor. The incidence of chorioamnionitis was unexpectedly high at 2.0 percent, which is double the expected incidence of 0.7 to 1.3 percent noted in previous studies.[9,23] The high incidence of chorioamnionitis in this sample could be attributed to the greater likelihood of high-risk patients being treated at a tertiary referral center

Table 5. Culture Results of Women with and without Chorioamnionitis.

Culture Type	Percent Obtained	Percent Positive	Results	Number of Cultures
Cervix	28	48	Chlamydia	1
			GBS* and *Ureaplasma urealyticum*	1
			GBS	2
			Yeast	1
			U. urealyticum	1
			Herpesvirus	1
			Unknown	4
			Negative	12
Vagina	4	66	*Gardnerella*	1
			Herpesvirus	1
			Negative	1
Urine	21	24	*Escherichia coli*	2
			Klebsiella pneumoniae	2
			Negative	13
Blood	5	25	*Propionibacterium*	1
Placenta	46	58		
Swab 3			GBS	8
Unknown 35			*E. coli*	3
			Coagulase-negative staphylococcus	2
			Gram-positive cocci	2
			Bacteroides fragilis	1
			Diptheroid and *Lactobacillus*	1
			B. uniformis	1
			Serratia marcescens	1
			GBS and group D enterococcus	1
			Gram-negative rod and gram-positive rod	1
			Gram-positive rod	1
			Negative	16

*GBS = Group B β-hemolytic streptococcus.

Table 6. Septic Neonatal Laboratory Data.

Diagnostic Study	Infant 1	Infant 2	Infant 3	Infant 4	Infant 5	Infant 6	Infant 7
Chest radiograph results	Infiltrate	Infiltrate	Normal	Normal	N/A	N/A	Normal
White cell count							
Initial							
Value (per mm^3)	5400	1300	22400	16000	5900	4900	21600
Band cell-neutrophil ratio	0.80	0.0	0.0	0.50	0.70	0.13	0.18
Ratio ≥ 0.2	Yes	No	No	Yes	Yes	No	No
Second							
Ratio ≥ 0.2	No	N/A	No	N/A	Yes	Yes	N/A
Cultures							
Blood	*E. coli*	NG	NG	NG	NG	NG	NG
Cerebrospinal fluid (CSF)	NG	N/A	Gram-positive cocci	Rare diptheroid and *Lactobacillus*	NG	NG	NG
CSF GBS LA	N/A	N/A	Negative	N/A	Negative	Negative	Negative
Urine	NG	NG	NG	N/A	N/A	N/A	N/A
Urine GBS LA	Negative	Negative	Negative	N/A	Positive	Positive	Positive
Placenta	NG	NG	GBS	N/A	N/A	N/A	GBS
Duration of antibiotics (days)	14	7	7	14	7	7	7

N/A = not obtained, NG = no growth, GBS = group B β-hemolytic streptococcus, LA = latex agglutination.

or to the definition of chorioamnionitis used in this study.

Attempts to improve both the sensitivity and timing of the diagnosis of chorioamnionitis have resulted in controversy. Newton, et al.[24] found parity, duration of rupture of membranes, and duration of internal monitors to be risk factors that had separate contributions to the probability of clinical chorioamnionitis. Soper, et al.[9] found that the duration of labor, number of vaginal examinations, duration of ruptured membranes, and use of internal monitors were independently associated with chorioamnionitis. The studies by Yoder, et al.[8] and Sperling, et al.,[12] as well as this study, did not confirm these associations. These discrepancies might reflect population differences, slight differences in the clinical criteria used for diagnosing chorioamnionitis, failure to account for expected temperature changes that normally occur with labor progression, or failure to account for different temperature responses based on parity and type of anesthesia.

Causes of Maternal Fever in Labor

To avoid misclassifying women to the group at risk of chorioamnionitis, a more thorough understanding of maternal temperature control in labor is needed. Only five studies could be found; Marx and Loew[2] (11 cases) found that temperatures increased temporarily with contractions (0.03°–0.2°C) and progressively during labor (cumulative mean 1.46°C in primaparas and 0.51°C in multiparas), and Goodlin and Chapin[3] (50 cases) found lower maternal temperatures associated with poor pain relief, significant hyperventilation, and perspiration. Goodlin and Chapin[3] found no association between the administration of epidural anesthesia and increases in maternal temperature, as did Kapusta, et al.,[25] (n = 33) who showed 50 percent of patients with epidural anesthesia had increased leg and chest temperatures but no changes in core temperature. In the present study, of the 22 patients for whom a diagnosis of clinical chorioamnionitis was not substantiated and a possible source for the fever could not be determined retrospectively, 20 had received an epidural anesthetic. Fusi, et al.[4] (40 cases) noted that patients who receive epidural anesthesia during labor are at increased risk of developing a fever with at least a 1°C elevation in vaginal temperature noted every 7 hours. The temperature of women receiving meperidine in the study remained constant ($P < 0.001$). Vinson, et al.[5] (n = 28) found that maternal temperature during labor increased 0.07°C per hour of epidural anesthetic exposure ($P = 0.002$), while Camann, et al.[6] (53 cases) found maternal temperature during labor increased 0.1°C per hour of exposure to epidural anesthesia. In our study patients with and without the clinical symptoms meeting the criteria for chorioamnionitis developed a fever on average 6.5 hours after epidural administration. If the observations of Fusi, et al. are

correct, the epidural anesthetic alone would be expected to result in elevation of the maternal temperature from 98.6°F to 100.4°F during this time.

It is unclear why the maternal temperature rises with epidural analgesia. The results from the previously cited studies might have differed because of different medications used for the epidural anesthesia, different methods of maternal temperature measurement, and varying durations of time used for maternal temperature measurements. Hypotheses to explain rises in maternal temperature with epidural anesthesia include decreased heat loss through evaporation as a result of decreased maternal hyperventilation once pain relief is achieved, reduced sweating produced by the epidural anesthetic-induced sympathetic blockade and reactive upper body vasoconstriction, the local anesthetic effect in the epidural space, and a dissociation between the regional anesthesia blockade of warm and cold sensations.[4] Seven of the 20 patients did not have a cervical, vaginal, urine, blood, or placenta culture taken, so an infectious process could have caused the fever instead of, or in addition to, the epidural anesthetic.[4] Prospective investigation of maternal temperature elevation with the administration of epidural anesthesia is needed to confirm this association and to determine its clinical significance. Because of the likely association between elevated maternal temperature and epidural anesthesia, however, clinicians are encouraged to consider using the clinical criteria for chorioamnionitis instead of attributing an isolated maternal fever to chorioamnionitis in patients who receive an epidural anesthetic.

Value of Placental Cultures in Predicting Neonatal Sepsis

Placenta cultures and amniotic fluid Gram stain have been suggested as means of improving decision making regarding antibiotic administration and duration for women suspected of having chorioamnionitis. The usefulness of placenta cultures has been questioned as the 24- to 48-hour delay in obtaining results does not aid intrapartum management. Deep section samples of the placenta, however, appear to be relatively unaffected by previous antibiotic administration[15] and could be helpful in deciding which neonates are at risk for sepsis. Of the 38 placenta samples for culture taken in our study, three were designated as collected by swabs and the rest were unrecorded (the majority, if not all, of the clinicians at the University of Michigan Medical Center submit placenta samples collected by swabs). There was no association of positive placental cultures with the clinical diagnosis of chorioamnionitis, neonatal sepsis, or with previous antibiotic use.

Diagnosing Neonatal Sepsis

Our study showed a significant association between neonatal sepsis and the first neonatal segmented cell value obtained and the first neonatal band cell-total neutrophil ratio. Other criteria used to predict sepsis, such as an erythrocyte sedimentation rate, latex haptoglobin, and latex C-reactive protein,[26,27] are not routinely obtained at the University of Michigan Medical Center. Combining the maternal clinical criteria for chorioamnionitis and a neonatal band cell-total neutrophil ratio of 0.2 or greater in predicting neonatal sepsis resulted in an improved positive predictive value and specificity without compromising sensitivity. As neonatal sepsis results in high morbidity and mortality, screening instruments must maintain high sensitivity with respect to the diagnosis while attempting to limit the numbers of well infants misclassified as ill.

It is important to note that the seventh septic neonate (with indeterminate maternal criteria) had an elevated second band cell-total neutrophil ratio obtained within 24 hours of birth. Rozycki, et al.[28] showed that 21 percent (13 of 61) of septic neonates had a falsely normal white cell count at birth. Eight of the 13 patients in their study had an abnormal white cell count when the count was repeated within 24 hours.[28] It is our opinion that obtaining an initial neonatal white cell count with differential and a follow-up white cell count with differential within 24 hours based on the infant's clinical status is useful when deciding upon antibiotic administration.

Antibiotic Treatment for Newborns

Controversy continues regarding the value of using intrapartum antibiotics to reduce the incidence of neonatal sepsis. Sperling, et al.[12] and Gibbs, et al.[14] found an increased incidence of neonatal sepsis in women who received postpartum instead of intrapartum antibiotics, whereas Gilstrap, et al.[13] found no difference. In all three studies, it is unclear whether intrapartum antibiotics improved neonatal outcome by preventing bacteremia by means of transplacental passage of

antibiotics or whether the antibiotics rendered some of the neonatal cultures falsely sterile.

Using a nonsystematic approach to the diagnosis of chorioamnionitis, physicians in this study treated 69 (84.1 percent) of the women with fever with intrapartum antibiotics. Seventy neonates (85.4 percent) received antibiotics shortly after birth, and 60 of these received antibiotics in part because of maternal intrapartum antibiotic administration. Neonatal antibiotic administration, however, is not without morbidity. In addition to the concern of encouraging the growth of resistant organisms, there are many factors to consider before initiating antibiotics. Obtaining the initial cultures at birth involves an increased risk of bleeding, infection, and injury to the spinal cord, whereas the use of intravenous catheters for antibiotic administration is associated with an increased risk of infection as well. Ototoxicity and nephrotoxicity can result from aminoglycoside use, and ampicillin and cephalosporins are associated with anaphylaxis and other adverse reactions.

Altered parent-child interactions can occur, as some parents find bonding difficult with intravenous lines and monitors in place. These altered interactions might persist as the child grows and is regarded as the sick or special child of the family. Efforts are usually made to encourage breast-feeding while the neonate is hospitalized, but a mother might find the restrictions too inconvenient and switch to bottle feeding instead. Increased financial cost must also be considered, because the neonate must spend extra days in the hospital receiving specialized nursing care and antibiotics. Selective intrapartum maternal antibiotic administration might be a reasonable option if maternal selection criteria with a high specificity for chorioamnionitis can be established in prospective studies and if neonatal culture media can compensate for intrapartum exposure to antibiotics.

Conclusions from this study are limited by the retrospective data collection resulting in missing data and by the large proportion of women and newborns receiving antibiotics. It is possible that the neonates born to mothers who did not meet the clinical criteria for chorioamnionitis but were treated with antibiotics did well as a result; in effect, they did not display any signs of neonatal sepsis. In addition, we have no long-term follow-up data on newborns and cannot comment on the incidence of possible sequelae, such as late-onset group B β-hemolytic streptococcus disease. We believe that our method of case identification was accurate and that this study therefore reflects the experience in a tertiary care center with women who develop fever in active labor. Prospective and perhaps multicenter studies are needed to try to define further causes of maternal fever and predictive criteria of chorioamnionitis and resultant neonatal sepsis, particularly in primary care settings.

Summary

The use of clinical criteria for chorioamnionitis in our study population predicted at least 6 of the 7 neonates with sepsis. The use of maternal clinical criteria for chorioamnionitis in predicting neonatal sepsis might have been even more accurate had our retrospective study not been limited by missing maternal data for the seventh septic neonate. In addition, the neonatal cultures did not appear to be rendered falsely sterile by intrapartum antibiotic administration. The findings of this study suggest that it could be possible to administer intrapartum antibiotics selectively to mothers who meet the clinical criteria for chorioamnionitis and give antibiotics to their neonates postpartum after cultures have been obtained. Additional neonates of women with isolated intrapartum fever who have a white cell band cell-total neutrophil ratio of 0.2 or greater, develop a positive blood culture, or have clinical signs of sepsis could be given antibiotics after urine and cerebrospinal fluid cultures are obtained. This method would have resulted in treatment of all neonates with sepsis and probable sepsis detected in this study and reduced neonatal antibiotic administration by 17 percent. Clinicians are encouraged to study the application of clinical criteria for chorioamnionitis and screening laboratory studies (that include a deep-section placenta culture and such neonatal tests as a band cell-total neutrophil ratio 0.2 or more) to establish better those mothers at risk for chorioamnionitis and neonates at risk for sepsis and to consider more selective use of intrapartum and postpartum antibiotic administration.

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