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# An epidemiologic investigation of the possible association between maternal diabetes and maternal hypertension and placental infection with Ureaplasma urealyticum.

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# AN EPIDEMIOLOGIC INVESTIGATION OF THE POSSIBLE ASSOCIATION BETWEEN MATERNAL DIABETES AND MATERNAL HYPERTENSION AND PLACENTAL INFECTION WITH *Ureaplasma urealyticum*

by

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A DISSERTATION

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## Abstract of Dissertation

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Title An Epidemiologic Investigation of the Possible Association Between Maternal Diabetes and Maternal Hypertension and Placental Infection with Ureaplasma urealyticum

Ureaplasma urealyticum is a cell wall free bacterium found in the lower urogenital tract of up to 83.1% of all sexually active adult women. Up to 90% of all pregnant women have also been shown to be infected with U. urealyticum through endocervical cultures, whereas only up to 15% of pregnant women have cultural evidence of ureaplasmal infection of the placenta. A cross-sectional study was conducted at the University Hospital of the University of Alabama at Birmingham, which included 645 of 815 (79%) Cesarean section deliveries with intact fetal membranes. The purpose of this study was to evaluate the association between maternal diabetes, maternal hypertension, and placental infection with Ureaplasma urealyticum. Using multivariate logistic regression to control for confounding factors, it was found that in this population, the odds ratio for placental infection, given maternal diabetes, was 1.39 ($CI_{95}$ = 0.48, 4.00), indicating that there was no association between maternal diabetes and placental infection with U. urealyticum. Odds ratios of 0.29 ($CI_{95}$ = 0.12, 0.68) for any diagnosis of hypertension, 0.52 ($CI_{95}$ = 0.13, 1.99) for chronic hypertension, 0.28 ($CI_{95}$ = 0.11, 0.76) for pregnancy-induced (acute) hypertension, 0.23 ($CI_{95}$ = 0.02, 2.77) for acute superimposed on chronic hypertension, and 0.29 ($CI_{95}$ = 0.12, 0.70) for a measured abnormal increase in maternal blood pressure during pregnancy, indicate a negative association between at least some forms of hypertension and placental infection with Ureaplasma urealyticum. Whether this effect is due to a reduction in the prevalence of Ureaplasma infection in the lower genital tract prior to pregnancy or to a suppression of the progression of infection during the pregnancy could not be determined in this study. However, there is evidence,

both pathologic and in the form of quantitative measurements, that there is a reduction of blood flow to the placenta in the presence of hypertension during pregnancy, and this may be one possible explanation for the results found in this study.

Abstract Approved By:

| | |
|---|---|
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# CHAPTER 1

# INTRODUCTION

## Biology/Ecology of the Ureaplasmas

The ureaplasmas are spheroidally to coccobacillary shaped cell-wall-free organisms of the order mycoplasmatales, family mycoplasmataceae. Their size ranges from 100 to 850 nanometers, with an average of 330 nanometers. They are nonmotile and stain gram negatively, but are poorly visualized. The ureaplasmas have a genome of approximately 4-5 x $10^8$ daltons, and G+C content in DNA of 27-30 mol percent. Their growth is optimized when the pH is at 6 and the temperature is 37°C. Ureaplasmas are microaerophilic and, on solid agar, produce colonies 15-60 $\mu$m, although there may not necessarily be growth on the surface of the medium. They all require sterol for growth and have the ability to reduce nicotinamide adenine dinucleotide oxidase in their cytoplasm. These organisms do not ferment carbohydrates and are sensitive to tetracycline, erythromycin, streptomycin, chloramphenicol, gentamicin, and kanamycin. They are differentiated from the genus Mycoplasma by their ability to hydrolyse urea.[125]

Ureaplasmas were first isolated in 1954 from the urethra of men with urethritis and identified as "T-strain" mycoplasmas.[112] It wasn't until 1967 that the observations on urease activity[113] and the requirement of urea for growth of these organisms,[34] which differentiated them from other mycoplasmas, was published. This characteristic was the basis for the eventual designation of Ureaplasma as a separate genus in 1974.[115] Since the time of the first isolations, ureaplasmas have been isolated from a wide variety of host species. These include humans, non-human primates, mammals, and avian species. At this time, there are only two recognized species of ureaplasma: Ureaplasma urealyticum, which is found in humans, and U. diversum, which inhabits cattle. Isolates from other species have not yet been given species designations, pending

acquisition of an adequate number of isolates with which to conduct the necessary analyses and comparisons.

U. urealyticum and U. diversum have been isolated from the upper and lower portions of both the urogenital and respiratory tracts of their respective host species. Isolates have been made from one or more of these sites in other species of animals, but not from all four sites in any one species. This may simply be a reflection of how actively these organisms were sought in a given host. Overall, however, most isolations from all hosts species (18 total) combined have been made from the lower genital tract (14/18), followed by upper respiratory (10/18), lower respiratory (5/18), and upper urogenital (4/18) tracts.[126] U. urealyticum has also been isolated from placental and amniotic fluid cultures from pregnant women, areas viewed as an extension of the upper genital tract.[8, 19, 21, 37, 41, 124]

Isolations from the products of both spontaneous[20, 28, 65, 66, 101, 117] and induced abortions[20, 101, 117] have been well documented. Isolations of U. urealyticum have also been made from the cerebral spinal fluid of infants,[40, 111, 135] as well as synovial fluid,[121, 131, 136] from abscess material in older patients,[10, 121, 131] and from human blood.[37, 42, 82]

There have been a wide variety of tests and typing schemes used to differentiate U. urealyticum isolates serologically. The original classifications were proposed by Black in 1973, and used the growth inhibition (GI) test to separate T-mycoplasmas into eight serogroups.[6] These same typing groups were subsequently used for the basis of typing schemes employing indirect immunofluorescence, indirect hemagglutination, and polyacrylamide-gel electrophoretic (PAGE) tests,[7] as well as an enzyme-linked immunosorbent assay (ELISA),[15, 129] and an indirect immunoperoxidase (IP) test.[94] Subsequently, Lin and Kass expanded the groupings to 11 serotypes, using a complement-dependent mycoplasmacidal test.[73] Lin and Kass' classification retained the original eight serotype designations while adding three new, previously unrecognized groups.[73] Subsequently, Robertson and associates developed a different grouping system, again retaining Black's original eight groups. Robertson and Stempke added a ninth group, which was different from any of Lin et al.'s. new groups.[102] Later, they added a 10th group. Then, by using a modified

etabolic inhibition test along with a colony epifluorescence test, they were able to combine their system with Lin's to produce a 14-group serotyping system.[74,103] The 14-serotype scheme is the system generally used at this time, although some workers have suggested a 16-group system based on the mycoplasmacidal assay.[62,72] Additionally, by using a combination of DNA homology, restriction endonuclease DNA digestion patterns, PAGE patterns, and sensitivity to manganese salts, these serogroups can be further separated into two major genomic clusters and one serogroup, which does not fit into either cluster.[3]

## Association with Various Conditions/Diseases

Ureaplasma urealyticum is routinely isolated from normal, healthy individuals,[32, 43, 54, 112] as well as from patients with a wide variety of medical problems. However, isolation from an individual with a given problem or illness does not necessarily mean that there is a causal association between U. urealyticum and the existence of the condition.

### Ureaplasma Infection in the Upper and Lower Urogenital Tract

Studies consistently find an association between U. urealyticum and nongonoccocal urethritis[9, 16, 25, 33, 112] and Reiter's syndrome, a triad of diseases that includes urethritis, followed by conjunctivitis and arthritis.[33] U. urealyticum has also been isolated from the prostate glands of men suffering from chronic prostatitis;[16, 17, 91] however, its ability to cause the condition has not been established. Likewise, the organisms have been isolated from the bladder of healthy individuals[43] and from the bladder[5, 84] and kidney[5] in cases of upper urinary tract diseases, such as pyelonephritis.[5]

U. urealyticum has been isolated from approximately equal proportions of healthy control patients and women suffering from pelvic inflammatory disease (PID).[32, 75] It is possible that it causes disease in a small subset of women,[51] and it has been suggested that U. urealyticum may act as a secondary or opportunistic invader under certain circumstances.[122, 123]

Although there is no question that U. urealyticum can be isolated from both men and women suffering from involuntary infertility or reproductive failure, there is conflicting evidence as to whether there is a true association, causal or otherwise, between the organism and the disease process.[23, 44, 45, 46, 55, 56, 65, 100, 120] Isolation of U. urealyticum has been found to be associated with a

reduction in sperm cell counts and an increase in sperm cell abnormalities of the male partner of infertile couples.[36] There is also good evidence that the organisms actually colonize specific portions of the sperm cell, and can be found in association with specific cell anomalies.[35]

## Ureaplasma and Pregnancy Outcomes

There have been numerous studies looking at the association between U. urealyticum and various pregnancy outcomes. The majority of studies have shown an association between Ureaplasma and spontaneous abortion,[20, 31, 50, 65, 66, 101, 117, 120] although there are some conflicting data.[49] The association holds up when the spontaneous abortions are compared to therapeutic abortions (Table 1). Studies have also shown an association between chorioamnionitis and infant colonization with Ureaplasma[90] as well as with placental infection.[31, 53, 67, 95, 96]

Table 1. Isolation rates (percent) of Ureaplasma urealyticum from the conceptus of spontaneous and induced abortions

| | TYPE OF ABORTION | | | |
|---|---|---|---|---|
| | Induced | Spontaneous | OR ($CI_{95}$) | p |
| Robertson et al.[a] | 8.0 | 24.0 | 3.4 (2.0, 4.8) | <.001 |
| Somplinsky et al.[b] | 0.0 | 62.0 | ∞ (1.8, ∞ ) | .003 |
| Caspi et al.[c] | 3.7 | 32.1 | 11.8 (6.9, 16.6) | <.001 |

[a] Robertson et al.[101]
[b] Slompinsky et al.[117]
[c] Caspi et al.[20]

## Ureaplasma Infection in Fetuses and Infants

Researchers looking at the relationship between cervical colonization and low birthweight infants have shown conflicting results. Studies in Mexican-American,[49] Navajo,[4] and British women[50] failed to find an increased risk of low birthweight outcome with a positive ureaplasma cervical culture. However, several other studies have found an increased risk of reduced birthweight with cervical,[12, 61] placental,[31, 67] or infant nasal/throat[12, 64] infection with U. urealyticum.

Maternal endocervical infection with ureaplasma has not been found to be associated with intrauterine growth retardation (IUGR).[50, 93] When considering whether or not there is an

association between placental infection and IUGR, there are conflicting results.[31, 67] The difficulty in comparing these results is that the criteria for IUGR differed from study to study.

Evidence of fetal bronchopneumonic infection with Ureaplasma has been documented as early as 19 weeks gestational age.[28, 97, 106] Waites et al.[134] detailed three cases of persistent pulmonary hypertension in newborns in which the infants were infected with Ureaplasma, two of whom subsequently died. Other studies have shown an association between maternal and infant infection with Ureaplasma and the subsequent development of respiratory disease,[98, 107, 118] but not with prolonged oxygen dependence.[107] In a series of 290 perinatal deaths, Ureaplasma was the only organism isolated from the lungs of 24 infant; of these, 22 were stillbirths, and 23 were diagnosed as having congenital pneumonia.[124] It has been shown that, among low birthweight infants infected with Ureaplasma, the lower the weight class, the higher the risk for development of chronic lung disease (Table 2).[22, 109, 133]

Although individual cases of meningitis due to Ureaplasma infection have been verified,[40] prospective studies have given conflicting results as to the association between Ureaplasma and meningitis.[71, 111, 135]

Ureaplasma has also been found to be associated with perinatal death. In a study by Quinn et al., Ureaplasma was isolated from 56.5% of infants with no known morphologic or anatomic cause of death, and only 10% of the normal living controls.[95]

## Serovar Associations with Various Conditions/Diseases

A listing of the serotypes associated with various conditions for which studies have been done is compiled in Table 3. Due to various typing methods and schemes used, it is difficult to compare the results of different studies. Several studies failed to find any difference in the distribution of the different serotypes in normal men,[92] or normal infants and mothers when tested for a serologic response.[99] However, several studies have found an increase in certain serotypes in sexually active men[114, 119, 132] and in women who experienced normal pregnancies.[87]

Although the study by Piot[92] did not find an association between any particular serotype of Ureaplasma and nongonococcal urethritis (NGU), other studies have found an association.[114, 119]

Associations have also been found in cases of chronic prostatitis, and renal stones.[114] Another study found an increase in the proportion of various serotypes in cases of atrophic pyelonephritis, glomerulonephritis, and recurrent urinary tract infection.[52]

Table 2. Development of chronic lung disease (CLD) in low birthweight infants by Ureaplasma status

| Study | Birthweight Criteria | Percent CLD Uu + | Uu - | p |
|---|---|---|---|---|
| Sánchez and Regan[a] | ≤2000 g | 30 | 8 | ≤.05 |
| Wang et al.[b] | ≤1250 g | 72 | 32 | ≤.0001 |
| Cassell et al.[c] | ≤1000 g | 82 | 41 | ≤.02 |

[a] Sánchez and Regan,[109] CLD measured at 30 days of age
[b] Wang et al.,[133] CLD measured at 28 days of age
[c] Cassell et al.,[22] CLD measured at 28 days of age

In studies of infertile women,[24, 25] increases of certain serotypes were found that were different from the pattern found in proven fertile women.[24] In serologic[99] and culture[101] studies of women with a history of pregnancy loss, there were significant increases in reactions against as many as five different serotypes of Ureaplasma. Among infants with respiratory disease, there is evidence for an association between disease with death and two serotypes (serotypes 4 and 8), and a third serotype was associated with disease and survival (serotype 5).[98]

## Risk Factors for Infection

### Infections in Infants

It has been noted that a greater proportion of female infants are infected than males at birth, and that an infant born vaginally is at higher risk of being infected than one born via cesarean section.[78] In a study population with six sets of twins delivered vaginally, 66.6% (4/6) of the sets had an infant infected with either Ureaplasma or Mycoplasma, although the authors did not differentiate between the two in this part of the study. In each case, only the first-born infant was infected.[64] Although the authors did not state why this should be the case, it would seem

Table 3. Serotypes of U. urealyticum found in association with various conditions

| Condition | Serotype |
|---|---|
| Normal | |
| male urethra | 2 3 4 8 9 10 11 13 14 |
| female endocervix | 3 6 |
| placenta | 3 6 11 13 14 |
| conceptus (theraputic abortion) | 3 6 11 13 14 |
| Nongonoccocal urethritis (NGU) | 3 4 11 13 14 |
| Chronic prostatitis | 4 |
| Recurrent urinary tract infection (RUTI) | 1 3 6 |
| Atrophic pyelonephritis | 1 3 6 |
| Glomerulonephritis | 1 6 |
| Renal stones | 1 |
| Infertility | 1 3 4 5 6 8 |
| Spontaneous abortion | 3 4 6 8 11 13 14 |
| Premature rupture of membranes (PROM) | 3 6 |
| Stillbirth | 3 |
| Respiratory disease | |
| all cases | 4 7 8 |
| with death | 4 8 |
| survived | 5 |

reasonable that during the process of the first infant passing through the birth canal, it became infected and reduced the population of the organism in the canal to below infective levels.

Additionally, there is a trend for increased risk of infection with decreased birth weight. If this risk is assessed using as the groups infants <2500 grams and those ≥2500 grams, those in the former group are significantly more likely to be infected at birth.[64] Whether the low birthweight is due to the infection or is indicative of an underlying condition in the pregnancy which, in turn, predisposes the infant to becoming infected has not yet been determined.

**Infections in Children**

Using urinary culture isolation as the indicator of infection status,[38] an age trend in proportion infected was seen in normal children. There was an increase in proportion infected with increasing age, that started earlier in females and exhibited a quicker increase to a higher level. The increasing rate of infection with age may be due to the effect of two separate factors, the sexual activity of the individual and/or the hormonal status of the female.

**Sexual Activity and Infection in Adults**

It has been effectively demonstrated that the degree of sexual activity and particular sexual practices are major factors in determining the risk of infection in both the male[83] and the female (Table 4).[79, 80] It has been shown that even having genital contact without actual intercourse increases the risk of infection for the individual. Additionally, the risk of infection increases with the number of different sexual partners. Not surprisingly, use of barrier contraceptives reduces the risk of infection, but does not eliminate it. When McCormack et al.[79] compared sexually active and inactive women in a predominately white population (98.9%), they found an infection rate of only 5.6% in the inactive group and a rate of 49.1% in the active group. The mean age of the study population was 20.6 years. A subsequent study by McCormack and co-workers, using a more racially diversified group of women, found infection rates of 18.6% and 62.1% in the inactive and active groups, respectively.[80] However, they did not detail the age composition of this study group. Iwasaka et al.[57] also compared sexually inactive and active women in Japan and found infection rates of 22.4% for inactive and 66.7% for active women. However, the active group was almost 11

Table 4. Percent Ureaplasmal infection in men and women as a function of sexual activity and contraceptive practices

| Activity | Male[a] | | | Female[b] | | | |
|---|---|---|---|---|---|---|---|
| | Overall | Barrier | | Overall | Overall | Barrier | |
| | | Yes | No | | | Yes | No |
| No genital contact | 0.0 | - | - | 5.6 | 18.6 | - | - |
| Genital apposition without penetration | 6.7 | - | - | 26.7 | - | - | - |
| Intercourse | | | | | | | |
| Any | 35.9 | 14.3 | 42.9 | 49.1 | 62.1 | 50.0 | 66.6 |
| 1 partner | 18.8 | 10.0 | 22.7 | 37.5 | 38.8 | 38.2 | 39.1 |
| 2 partners | 26.1 | - | 35.3 | 54.5 | 54.4 | 47.4 | 57.1 |
| $\geq 3$ partners | 44.8 | 21.1 | 51.5 | 75.0 | 76.4 | 57.4 | 83.1 |

[a] urinary tract
[b] vaginal tract

years older than the inactive group (32.9 vs. 22.4 years mean age). Among pregnant women, the infection rates ranged from a low of 54% to a high of 90% in different populations (Table 5).[11, 48, 49, 57, 70, 100]

**Hormonal Influence on Infection Rates in Females**

In looking at the influence of hormones on infection rates in women, Iwasaka et al.[57] found a vaginal colonization rate of 48% in newborn females, which dropped to 28.6% at 30 days of age,and to 4.8% at a mean age of 5.8 years. In another study,[47] conducted on a population of predominantly black girls between the ages of 2 months and 15 years, 27% of those between the ages of 2 months and 2 years, 22% of those between 3 and 10 years, and 40% of those between 11 and 15 years of age were positive. Forty percent of the girls in the oldest group were post-menarcheal. Unfortunately, the authors did not evaluate differences in the pre- and post-menarcheal girls in this group nor compare those who were sexually active with those who were not in order to differentiate between the effects of hormonal changes and sexual activity.

Table 5. Endocervical infection rates in pregnant women of various racial groups

| Study group | Country | Rate (%) |
|---|---|---|
| American Indian[a] | US | 81.2 |
| Black[b] | US | 90.0 |
| Caucasian[c] | France | 54.0 |
| Caucasian/Hispanic[a] | US | 72.5 |
| Japanese[d] | Japan | 77.9 |
| Unspecified[e] | US | 60.0 |
| Unspecified[f] | US | 71.1 |

[a] Harrison[49]
[b] Hardy et al.[48]
[c] Liepmann et al.[70]
[d] Iwasaka et al.[57]
[e] Rehewy et al.[100]
[f] Braun et al.[11]

When Iwasaka et. al.[57] evaluated pregnant women, they found an infection rate of 77.9% (mean age of 28.8). They then compared the rates in pregnancies delivering at <35 weeks (mean age 28.4) and >36 weeks (mean age 29.2), and found rates of 70% and 82%, respectively. By 7 days postpartum, the infection rate had dropped to 67.6%, and by 35 days, the rate had dropped still further to 23.9%, approximately the same level found in the sexually inactive group. Rehewy et al.[100] compared rates of infection between sexually active and pregnant women ages 20 to 42, and found that 42.9% of the sexually active women were infected with Ureaplasma, whereas 60% of the pregnant women were positive.

One group of researchers found an increased prevalence of Ureaplasma infections in women who used oral contraceptives, but due to their study design, they could not explore the question as to whether hormonal changes or sexual activity was the contributing factor.[81]

Post-menopausal women were also evaluated. Those with an intact cervix had an infection rate of 35.7%, and those without a cervix had a rate of only 10%. The overall infection rate of this group of women was 25%. The ages of the two groups were comparable (61.9 and 62.0 years); unfortunately, the authors did not determine the sexual activity of these women.[57]

### Other Factors

Savige et al.[110] found that an increased proportion of pre-eclamptic women demonstrated bladder urine infected with Ureaplasma when compared to normal pregnant women (20% vs. 7%, $p = .01$). These researchers also found that the organisms were present in higher numbers in the pre-eclamptic women. On the other hand, Kundsin et al.[67] found a negative association between placental colonization and maternal diabetes or pre-eclampsia. The authors did not state whether the diabetes was pre-existing or gestational, or what level of control was achieved in these women.

## Diabetes

Insulin-dependent diabetes dellitus (IDDM, or Type I) is a metabolic disorder characterized by the inability to oxidize carbohydrates, due primarily to destruction of ß-cells in the pancreas, resulting in the loss of insulin production. Consequences of this loss are hyperglycemia, leading to

glycosuria and polyuria. Additionally, aberrations in the process of breaking down fats may lead to acidosis and ketosis, which may eventually cause coma and death.

The diagnostic criteria for IDDM in non-pregnant adults are any of the following:[89]

A. The presence of the classic symptoms of diabetes, i.e., polyuria, polydipsia, ketonuria, and rapid weight loss in conjunction with a gross and unequivocal elevation of plasma glucose.

B. Elevated fasting glucose concentration on more than one occasion, as measured by:

| | |
|---|---|
| venous plasma | ≥140 mg/dl |
| venous whole blood | ≥120 mg/dl |
| capillary whole blood | ≥120 mg/dl. |

C. If the fasting glucose concentration does not exceed the criteria in section B, but there is a sustained increase in the oral glucose tolerance test (OGTT) concentrations at both 2 hours and at some other 30-minute sampling point between administration of a 75-gram glucose dose and the 2-hour sample, as measured by:

| | |
|---|---|
| venous plasma | ≥200 mg/dl |
| venous whole blood | ≥180 mg/dl |
| capillary whole blood | ≥200 mg/dl.(page 1049) |

The diagnostic criteria for IDDM in children are either one of the following:[89]

A. Presence of the classic symptoms of diabetes, as in section A for adults, along with a random plasma glucose concentration >200 mg/dl.

B. If the child is asymptomatic, then both an elevated fasting plasma glucose concentration and a sustained glucose concentration during the OGTT on more than one occasion using the same criteria as in section C, above, using a modified dose of oral glucose (1.75 g/kg ideal body weight up to 75 g), concentrations measured by:

Fasting value:

| | |
|---|---|
| venous plasma | ≥140 mg/dl |
| venous whole blood | ≥120 mg/dl |
| capillary whole blood | ≥120 mg/dl. |

2 hour OGTT values:

| | |
|---|---|
| venous plasma | ≥200 mg/dl |
| venous whole blood | ≥180 mg/dl |
| capillary whole blood | ≥200 mg/dl.(page 1049) |

Non-insulin-dependent diabetes mellitus (NIDDM, or Type II) is a form of diabetes that usually, but not exclusively, has its onset after the age of 40. Sixty to 90% of all cases of NIDDM are obese. NIDDM diabetics do not require the use of insulin to control their illness, although it

may be used to correct some conditions associated with the disease, and they are not prone to the development of ketosis. The NIDDM diabetic may produce serum levels of insulin that are elevated, normal, or low. In the obese subclass of patients, the control of their weight may be enough to improve their glucose tolerance. NIDDM is diagnosed based on a fasting plasma glucose level $\geq$140 mg/dl, without the other signs and symptoms of diabetes associated with IDDM (ketosis, etc.).[89] The secondary complications associated with IDDM, such as hypertension, retinopathy, and nephropathy, are also seen in individuals with NIDDM.[138]

Gestational diabetes mellitus (GDM) is a carbohydrate intolerance that is first diagnosed, or has its onset, during pregnancy. This intolerance usually resolves after the completion of the pregnancy. It may be controlled either with diet or insulin therapy. The criteria for diagnosis is a 100-gram oral glucose tolerance test during a pregnancy that yields 2 or more glucose concentrations equal to or greater than the following:[89]

A. Venous plasma

| | |
|---|---|
| Fasting: | 105 mg/dl |
| 1 hour post ingestion | 190 mg/dl |
| 2 hour post ingestion | 165 mg/dl |
| 3 hour post ingestion | 145 mg/dl. |

B. Venous or capillary whole blood

| | |
|---|---|
| Fasting: | 90 mg/dl |
| 1 hour post ingestion | 170 mg/dl |
| 2 hour post ingestion | 145 mg/dl |
| 3 hour post ingestion | 125 mg/dl. (page 1050) |

Diabetes during pregnancy is classified based on time or age of onset and secondary complications present.[137] The classifications routinely used are listed in Table 6. The general criteria for the diagnosis and classification of DM are illustrated in Figure 1.

## Hypertension

The diagnosis of chronic hypertension (CHT) in adults is confirmed when the average of two or more diastolic blood pressure readings is 90 mmHg or higher on at least two subsequent visits, or when the average of two or more systolic blood pressure readings is higher than 140 mmHg on two or more subsequent visits.[58]

Table 6. White[137] classification of diabetes in pregnant women

| CLASS | CRITERION |
|---|---|
| Class A | |
| $A_1$ | Glycosuria with a positive OGTT insulinopenia |
| $A_2$ | Abnormal OGTT with hyperinsulinism |
| $A_3$ | Obesity with an abnormal OGTT and insulinopenia |
| Class B | Maturity onset (age over 20), duration < 10 years, no vascular lesions |
| Class C | |
| $C_1$ | Onset age 10-19 years |
| $C_2$ | Duration of 10-19 years |
| Class D | |
| $D_1$ | Onset < 10 years of age |
| $D_2$ | Duration >20 years |
| $D_3$ | Benign retinopathy |
| $D_4$ | Calcified leg vessels |
| $D_5$ | Hypertension |
| Class E | Calcification of pelvic arteries |
| Class F | Nephropathy |
| Class G | Many failures |
| Class H | Cardiopathy |
| Class R | Proliferating retinopathy |
| Class T | Renal transplant |

Gestational, or pregnancy induced hypertension (PIH) is defined as either a single measurement of a diastolic blood pressure $\geq$110 mmHg or two consecutive measurements of diastolic blood pressure of 90 mmHg, 4 or more hours apart.[26] Pre-eclampsia is defined as proteinuria in addition to either CHT or PIH. Proteinuria can be diagnosed either by one 24-hour urine collection, with total protein excretion of $\geq$300 mg per 24 hours, or by two "clean-catch-midstream" or catheter specimens collected $\geq$4 hours apart, with 1 g/l of albumin or 2+ or more on a reagent strip or sulfosalicylic acid "cold" test, or 0.3 g/l of albumin or 1+ on a reagent strip when the specific gravity of the urine is <1.030 and the pH is <8.0.[26] Eclampsia has the same

diagnostic criteria as pre-eclampsia, with the addition of the occurrence of convulsions during pregnancy or labor, or up to 7 days postpartum, which are not caused by epilepsy or any other preexisting convulsive disorder.[26]

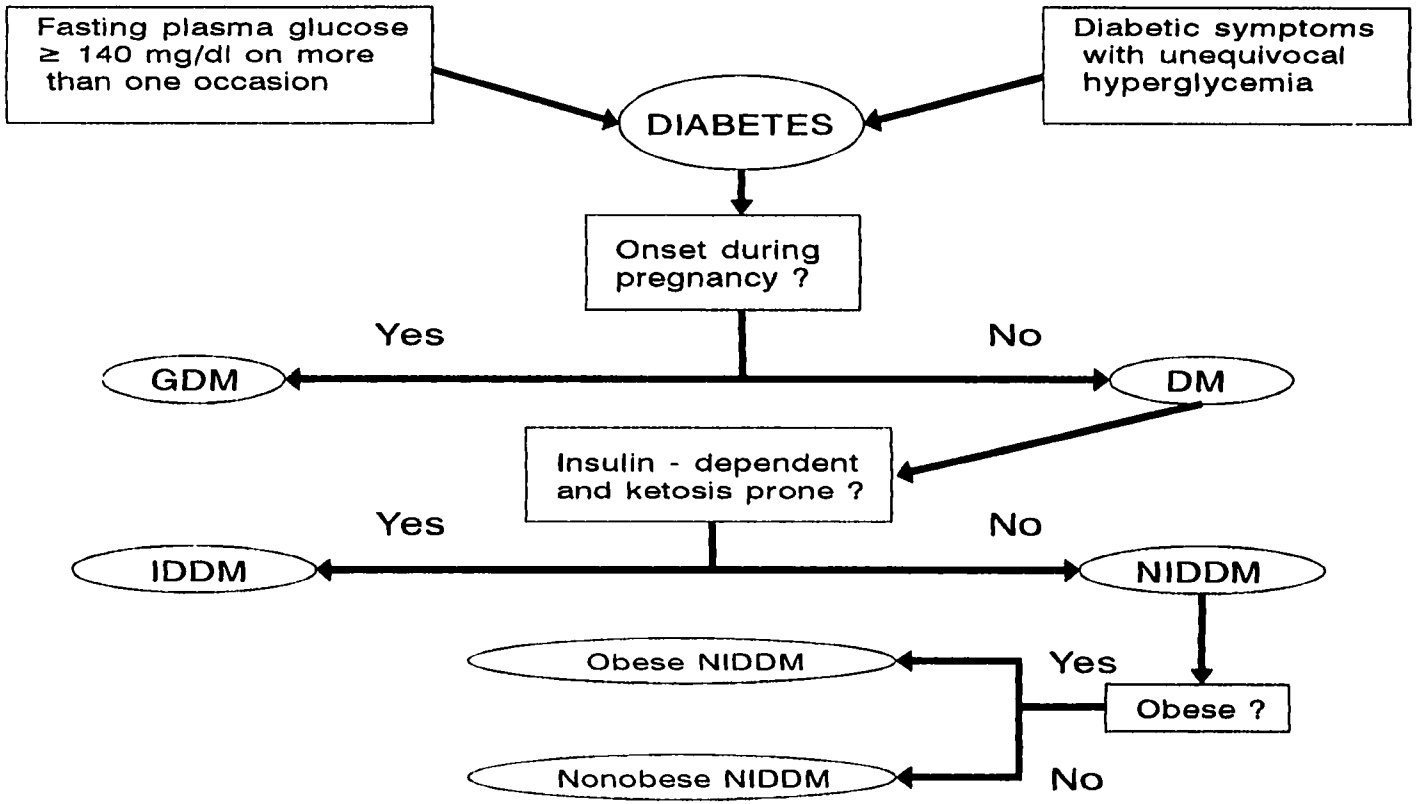


Figure 1. Diagnosis and classification of diabetes mellitus.

## CHAPTER 2

## RATIONALE

### Diabetes

It has been shown in a retrospective study that diabetic women are at increased risk of endometritis and wound infection after a Cesarean section delivery.[27] This increase has been seen in both normal and diabetic pregnancies as the overall risk of subsequent infection after delivery increased (Table 7). High risk was defined as either rupture of membranes or labor prior to

Table 7. Infection rates (percent) of low- and high-risk pregnancies of diabetic and non-diabetic women

| | Low risk | High risk | p |
|---|---|---|---|
| Non-diabetic | 1.8 | 6.0 | NS |
| Diabetic | 9.0 | 25.0 | .067 |
| p | .042 | .032 | <.001[a] |

[a] High-risk diabetic compared against low-risk non-diabetic pregnancy

Cesarean section, and low risk as not having experienced either. Diabetics were at a significantly higher risk of infection in both categories of low and high risk when compared to non-diabetics in the same classifications. Pregnant diabetic patients have also been shown to be at increased risk for infection with Group B Streptococcus [RR 2.04, CI (level not specified) 1.03, 3.79; p <0.05]. The increase in risk was essentially the same whether the diabetes was gestational or pre-existing.[76] Among the general non-pregnant population of individuals infected with Lancefield Group C or G Streptococci, there was an association with DM as a predisposing condition.[108, 130]

Animal studies in rats with chemically induced diabetes have demonstrated changes in protein metabolism in both the placenta and fetus.[18, 104] In the placenta, the rates of protein

synthesis were comparable in both normal and diabetic animals throughout the pregnancy. However, late in the pregnancy, there was a dramatic decrease in the degradative rate of protein in the placentas of the diabetic animals, which, in the face of unaltered synthesis rates, led to the development of enlarged placentas.[104] In the fetus, the rate of protein synthesis was lower in the fetuses of diabetic rats than that of normal animals. Additionally, the rate of protein degradation in the fetuses of the compromised animals was increased, which led to the production of smaller fetuses.[18] A similar mechanism may also play a role in the growth-impaired human fetus. An alteration in the balance between the synthesis and degradation of protein could lead to an excess of urea, one of the byproducts of protein metabolism, providing an increase in availability of a substrate for Ureaplasmal growth.

## Hypertension

It has been shown that, during pregnancy, there is a significant shift to the right of the oxyhemoglobin dissociation curve ($P_{50}$) during each trimester. The shift increases with gestational age, which makes more oxygen available to the fetus as the pregnancy progresses. However, in pre-eclamptic women at term, the $P_{50}$ curve is shifted to the left of that of a normal non-pregnant woman, which would lead to reduced availability of oxygen for both mother and fetus, and significantly so, when compared to the expected value of a normal pregnant woman ($p<.001$).[60] In a subsequent study, it was found that the carboxyhemoglobin levels were significantly increased in pre-eclamptic women as compared to normal pregnant women (2.8% vs 0.7%, $p<0.001$), reducing the availability of oxygen. This study reconfirmed the lower $P_{50}$ values found in the earlier study, and proposed the increased levels of carboxyhemoglobin as the mechanism for the lowered $P_{50}$ curve.[59] Reduction of available oxygen in the maternal and fetal environment may be advantageous for the growth of U. urealyticum, a microaerophilic organism.

A study by Musci and coworkers[86] has demonstrated mitogenic activity in the sera of pre-eclamptic women, indicating endothelial cell injury, and Rogers et al.[105] demonstrated an endothelial cell cytotoxic serum factor in preeclamptic women. This injury can cause the secretion of mitogens and vasoactive factors, due to the production of peptide growth factors by the endothelial cells or

by the release of stored products by activated platelets. These components, or their degradative products, could act as growth promoters or substrates for Ureaplasma. Cellular injury could also compromise the integrity of the endothelial lining of the blood vessels, allowing easier passage of any infectious agent into the blood and through the placental barrier.

## Hypotheses

Two hypotheses were tested in this study. Either maternal diabetes, or maternal hypertension, by virtue of physiologic changes in the maternal-uteroplacental environment due to either of these conditions, expose the placenta to an increased risk of infection with Ureaplasma urealyticum. Secondly, hypertension will be further subdivided into chronic and pregnancy-induced (acute) hypertension, to see if either type has a greater effect on the risk of infection.

# CHAPTER 3

# METHODS

## Study Design

A cross-sectional study of Cesarean section births without rupture of the fetal membrane was conducted. This sampling controlled for the possibility of infection due to contamination by passage through the birth canal, or by migration of the organism back to the placenta after the rupture of the fetal membranes. The study population consisted of all women who had a Cesarean section performed at the University of Alabama at Birmingham Medical Centers between October 26, 1987, and July 31, 1990. Only those women who delivered an infant with an intact fetal membrane during this time were enrolled in the study. If a woman met the criteria for enrollment into the study more than once during the study period, only the first delivery was included in the analysis.

The specific aim of this study was to evaluate if there is an increased prevalence of placental infection with Ureaplasma urealyticum among pregnant women with the predisposing conditions of maternal diabetes or hypertension. The diabetic conditions considered in this study are insulin dependent diabetes dellitus (IDDM), non-insulin independent diabetes mellitus (NIDDM) and gestational diabetes (GDM). These conditions were considered as a single group. Hypertensive conditions included in the study were both chronic (CHT) and acute, also called pregnancy induced (PIH), hypertension. The conditions were considered individually by subgroups of the major hypertensive complications (pre-existing or pregnancy-induced, superimposed), as well as the pooled groups (all diabetes or all hypertension).

## Power Calculations

Prior to closing the data collection period, power estimates were developed, based on the population characteristics (Table 8) and rate of enrollment in December of 1989. If the rate of enrollment per month remained constant, and the proportions of complications and the incidence of infections remained the same, there would have been an estimated 573 births enrolled by the end of July 1990, the originally anticipated ending date for this study. The estimated numbers for the various subgroups of this population are listed in Table 9. Using the formula:

> Power = 1 - $\Phi(A)$, for a binary outcome measurement using a chi-square approximation with non-uniform allocation, where:
>
> $\Phi(A)$ = proportion of area of a N(0,1) distribution that is to the left of a point A, and

$$A = \frac{Z\alpha\sqrt{PQ/n_c + PQ/n_n} - |P_c - P_n|}{\sqrt{P_cQ_c/n_c + P_nQ_n/n_n}}$$

with:
- $Z_\alpha$ = Z value for error level
- P = proportion of population infected
- Q = proportion of population not infected
- $P_n$ = proportion of comparison population infected
- $P_c$ = proportion of population with complication infected ( hypothesized )
- $n_n$ = number in comparison group
- $n_c$ = number in complication group,

the proportions in Table 8, and the n's from Table 9, power estimations for a 1-tailed test were produced with a hypothesized 2-fold increase in infection rate for the complication groups for the estimated population size at the closing date for this study (Table 10). Because the biological changes would be expected to be the same for all types of diabetes, although they would be acting for a shorter duration in gestational diabetes, it seemed both reasonable and appropriate to pool these conditions.

Accepting an error rate of .10, all classes of complications would have a power >.80. If a more conservative error rate of .05 is used, then the power for the chronic hypertension group drops to <.80.

Power estimates were also calculated for several different odds ratios (1.5, 2.0, 2.5, and 3.0), using the one-sided test at two error levels. The curves for the differing ORs for the different

Table 8. Characteristics of the mothers and infants enrolled into the study population through December 31, 1989

| | | Number | Percent | |
|---|---|---|---|---|
| Mother | Total | 433 | | |
| | Infected | 50[a] | 11.5 | |
| | Confirmed diabetes (pre-existing and gestational) | 61 | 14.1 | |
| | Chronic hypertension | 45 | 10.4 | |
| | Pregnancy-induced hypertension | 79 | 18.2 | |
| | Hypertensive illness | 117 | 27.0 | |
| Placentas | Total | 455 | | |
| | Infected | 55 | 12.1 | |
| | Sets of twins | 23 | | |
| | At least one placenta infected | 9 | 39.1 | |
| | Both placentas infected | 5 | 21.7 | 55.5[b] |
| | Only one infant with intact membrane | 1 | 4.4 | |

[a] Number of women yielding at least one infected placenta
[b] Percent of infected sets (5/9)

complication groups are presented in Appendix 1. As can be seen from the curves, should the OR actually be $\geq 2.5$, there would be adequate power to detect this. However, if the true OR for any group should be 1.5, all of the groups would have power $< .80$.

## Data Collection

### Infection status

Placentas were collected aseptically at delivery, and laboratory personnel were notified. The placentas were refrigerated until processing, usually within one hour of birth. Using aseptic

Table 9. Estimated study size and characteristics

| | $n_c$[a] | $n_n$[b] |
|---|---|---|
| All diabetics | 81 | 492 |
| Chronic hypertension (CHT) | 60 | 513 |
| Pregnancy-induced hypertension (PIH) | 137 | 436 |
| CHT or PIH | 155 | 418 |
| Total infected | 67 | 506 |

[a] = Number in population with condition
[b] = Number in population without the condition

Table 10. Power calculations for estimated study population (N=573), with a 2-fold increase in the proportion infected

| Group | Number | | Power | |
|---|---|---|---|---|
| | $n_c$[a] | $n_n$[b] | $\alpha=.10$ | $\alpha=.05$ |
| Diabetes (all classes) | 81 | 492 | .91 | .85 |
| Chronic hypertension | 60 | 513 | .84 | .76 |
| Pregnancy-induced hypertension | 137 | 436 | .97 | .94 |
| Either hypertensive complication | 155 | 418 | .97 | .95 |

[a] = Number with the complication of interest
[b] = Number without the complication of interest

technique, the chorioamniotic membrane was removed from the placenta with a sterile blade, and three to five sets of parallel incisions were made on the fetal side of the placenta. For each set of incisions, the surface layer of the placenta between the two incisions of the set was peeled back, and three swabs were swabbed between the chorion and amnion of one of the incisions. One swab was used to make a slide for gram staining, and the remaining two were used to inoculate 1.5-2.0 ml of

2-sucrose phosphate (2SP). The swabs were expressed and discarded, and the resulting suspension was used to inoculate culture broths and plates for the isolation of Ureaplasma, Mycoplasma, other aerobic and anaerobic bacteria, and fungi. From the second incision of each set, at least 1 $cm^2$ was teased out into a sterile petri dish and thoroughly minced in 1.8 mls of 2SP, and the resulting suspension was used to inoculate the media. For each inoculum, approximately 0.5 ml was drawn up into a 10-cc syringe, and 0.1 ml was inoculated into one tube each of Chopped Meat Carbohydrate Media (CMC), Brain Heart Infusion Broth (BHI), Tricosel, and McCoy cell line cell culture. Dilutions of the original inoculum were made by adding 0.1 ml of the original suspension to 0.9 ml each of 10B[114] with Cefobid and SP4[127, 128] with Cefobid, and then making serial 10-fold dilutions out through the $10^{-5}$ dilution.

Using an 0.01-ml calibrated loop, the following agar plates were inoculated with the original 2SP suspensions and streaked for isolation: two plates of Campylobacter medium (Campys), and one each of chocolate agar, sabaroud dextrose agar (SAB), human blood-tween 80 agar (HBT), and pre-reduced Columbia blood agar (CBA). A plate of A8[128] agar was divided into sections, and 0.02 ml of the original 2SP inoculum and the 10B dilutions were spot-inoculated onto the plate for colony counts. Incubation conditions for the various media and the organisms isolated from them are listed in Table 11.

If growth was observed in the BHI or CMC, a gram stain was made, and those media were inoculated onto appropriate media for isolation and identification of the organisms present. BHI was inoculated onto blood agar (BA) and eosin-methylene blue agar (EMB), which were incubated at 37°C for 2 days under aerobic conditions, and onto chocolate agar, which was handled as shown in Table 11. CMC was inoculated on BA, chocolate agar, and CBA, and incubated as previously noted.

Ureaplasma and Mycoplasma were identified by their growth in the appropriate medium and morphologic characteristics on A8 medium. Aerobic bacteria other than Ureaplasma were identified using the API strip systems for gram positive and gram negative organisms, and the anaerobic organisms were identified using gas liquid chromatography (GLC) and additional sugar

Table 11. Incubation conditions for culture media and organisms

| Medium | Form | Atmosphere | Temperature (°C) | Days held | Organism |
|---|---|---|---|---|---|
| BHI | Broth | Aerobic | 37 | 7 | Aerobic bacteria other than Ureaplasma |
| 10B | Broth | Aerobic | 37 | 14 | Ureaplasma |
| SP4 | Broth | Aerobic | 37 | 60 | Mycoplasma |
| Trichosel | Broth | Aerobic | 37 | 5 | Tricomonas |
| SAB | Agar | Aerobic | 37 | 30 | Fungi |
| A8 | Agar | 5% $CO_2$ | 37 | 14 | Ureaplasma, Mycoplasma |
| HBT | Agar | 5-10% $CO_2$ | 37 | 2 | Gardenerella vaginalis |
| Campys | Agar | 5-10% $CO_2$ | 37, 42 | 2 | Champylobacter |
| Chocholate | Agar | 5-10% $CO_2$ | 37 | 2 | Bacteria other than Ureaplasma |
| Chlamydia | TC* | 4.5% $CO_2$ | 37 | 2 | Chlamydia |
| CMC | Broth | Anaerobic | 37 | 5 | Anaerobic bacteria |
| CBA | Agar | Anaerobic | 37 | 5 | Anaerobic bacteria |

* TC = Tissue culture, cyclohexamide treated McCoy cell mono-layer.

utilization tests, as needed. Chlamydia were identified using fluorescein-conjugated monoclonal antibodies and immunofluorescent microscopy to visualize inclusion bodies in the McCoy cells. Trichomonas was identified by examining a wet prep after 2 and 5 days of incubation, at 450X magnification using bright field illumination.

**Maternal Characteristics**

Maternal characteristics required for analysis were obtained from the Obstetrical Automated Record System (OBAR) and the University Hospital's medical records. OBAR is an integrated, computerized medical record system, which draws on obstetrical patients from the University and Cooper Green Hospitals, and the Jefferson County Health Department Clinics. Information for the OBAR system on the mothers and fetuses was collected during prenatal visits, and maternal and infant information was collected at delivery on standardized forms (Appendix 2). Prenatal clinic records are validated by a monthly medical records audit, whereby a random sample of the previous month's records are reviewed to compare against the data actually entered into the OBAR database. The discharge summary for each birth undergoes a chief resident's review comparing the summary against the actual records.

In this study, pre-existing diabetes was defined as an established history of diabetes, either by abnormal blood glucose levels, as described previously, or a documented history of treatment with either anti-diabetic drugs or diet, in a non-pregnant individual. A history of previous incidence of gestational diabetes that resolved after delivery was not counted as a current diabetic. Gestational diabetes was defined as diagnosis made during the current pregnancy, in a woman with no history of diabetes during non-pregnant periods of life. Diagnostic criteria included either a documented 3-hour oral glucose tolerance test with a minimum of two abnormal readings, multiple fasting blood glucose levels $\geq$140 mg/dl, or documented use of any anti-diabetic treatment initiated during the pregnancy.

For this study, a woman was classified as a chronic hypertensive if she had documented evidence of hypertension during the non-pregnant periods of her life. Evidence consisted of either the appropriate increase in blood pressure, as previously described, or documented treatment with

any antihypertensive agent. An increase during the first trimester was considered to be a case of chronic hypertension. Pregnancy-induced (acute) hypertension was verified by a documented increase of blood pressure occurring after the beginning of the second trimester. The minimum readings required were either two diastolic readings $\geq$90 mmHg or two systolic readings $\geq$140 mmHg, or one of each, separated by at least 6 hours, or a single diastolic reading $\geq$110 mmHg. A woman who experienced acute hypertension during a previous pregnancy that resolved with no further signs or symptoms of hypertension during the intervening time or the current pregnancy was not classified as a hypertensive for purposes of this study.

## Validation of Complication Status

The complication status of the women in this study was validated by a medical record review. All records indicating the presence of one of the complications of interest were requested from the University Hospital Medical Records Division and reviewed, using the previously detailed criteria for determination of complication status. Any record with no indication of a complication but with missing data was also reviewed. Finally, a 20% random sample of the remaining records with all information present and without any indication of complications was also reviewed.

## Data Analysis

The independent variables considered were: 1) any diabetes, 2) pre-existing hypertension, and 3) gestational hypertension. Pre-existing diabetes and gestational diabetes were evaluated as a single group. The hypertensive classes of conditions were evaluated both individually and as a group.

The outcome variable was whether or not the mother experienced a pregnancy in which one or more placentas were infected with Ureaplasma urealyticum. Infection status was ascertained by culturing each placenta. Culture material consisted of both swabs and tissue inoculated on solid agar and in liquid media. A placenta was considered to be positive for Ureaplasma if at least one of these samples produced growth of the organism. The individuals who determined the culture status of the placentas were blinded to the complication status of the women tested.

Confounding variables controlled for in the analysis included the following: maternal age, race, marital status, socioeconomic status (measured by level of education and insurance coverage), smoking status, presence of placental infection with any other organisms, presence or absence of labor and the duration of labor when present, pre-term delivery both during the present and previous deliveries, and primigravida status.

Analysis of the maternal data set consisted of comparing the proportion with the target condition in the women with placentas infected with Ureaplasma against women whose placentas had no evidence of placental infection with Ureaplasma.

Chi-square analysis of the 2 X 2 contingency tables was conducted on both the crude data and the data stratified by the appropriate subclasses of the complications. When appropriate, due to small numbers, Fisher's exact test was used, rather than the chi-square.

Logistic regression analysis was used to determine the odds ratio (OR) and confidence intervals for the risk of a mother producing an infected placenta given the mother's complication status during her pregnancy. Use of this type of analysis allowed for building a model that took into consideration the known risk factors for infection with Ureaplasma. Various models have been used to determine risk factors for infection with Ureaplasma in different populations.[4, 49, 53, 67, 80, 81, 95] Variables that have been associated with infection and were included in the initial model are as follows: race,[67, 80] maternal age,[4, 53, 67] marital status,[67, 81] smoking,[67, 80] concurrent bacterial infection of the placenta[4, 49] duration of labor,[4, 53] and SES as determined by years of education.[53] As we had access to information concerning insurance coverage, we also used this as a measure of SES. For all analyses, a p-value $<0.05$ was considered a significant result, p-values $\geq 0.05$ - 0.10 were given as their actual value, and p-values $>0.10$ were considered not significant and presented as NS. Because the hypothesis was that there would be an increased risk of infection with Ureaplasma in the complication groups, chi-square and Fisher's exact tests were 1-tailed. Multivariate logistic regression probabilities were reported as 2-tailed: any difference from the null expectation of no difference.

# CHAPTER 4

# RESULTS

## Comparison of Study Population Groups

Between October 26, 1987 and December 31, 1990, a total of 8,222 deliveries were recorded in the OBAR system for the University Hospital. The type of delivery was classified as either vaginal (VAG), Cesarean section with ruptured membranes (CRM), or Cesarean section with intact fetal membranes (CIM). Of the 8,222 deliveries, 256 were not classified as to the type of delivery experienced. The characterization of the types of deliveries is shown in Figure 2. Of the 815 Cesarean section deliveries, 646 were enrolled into the study, and 169 were missed due to duty clerks and nurses not informing the study nurse on call that a delivery had taken place so that the specimens could be processed. One woman enrolled who delivered twins was excluded when it was determined that the Cesarean section was for the second infant following a vaginal delivery of the first infant.

Demographic characteristics of the different delivery groups are listed in Table 12. The three delivery groups differed significantly from each other (Table 12). The racial composition of the VAG group was comparable to that of the CRM group, with the proportion of blacks being almost 2-fold greater than whites in both groups (Table 13). However, the proportions of blacks and whites were approximately equal in the CIM group, which was significantly different from either of the other two groups (Tables 14 and 15). The marital status characteristics did not differ significantly between the two Cesarean groups, but each group did differ from the vaginal delivery group. This difference was due entirely to differences between the black women in each group ($p \leq 0.05$ for VAG versus CRM and VAG versus CIM). Mean maternal age at delivery differed significantly among all three groups, with the vaginal delivery group being the youngest,

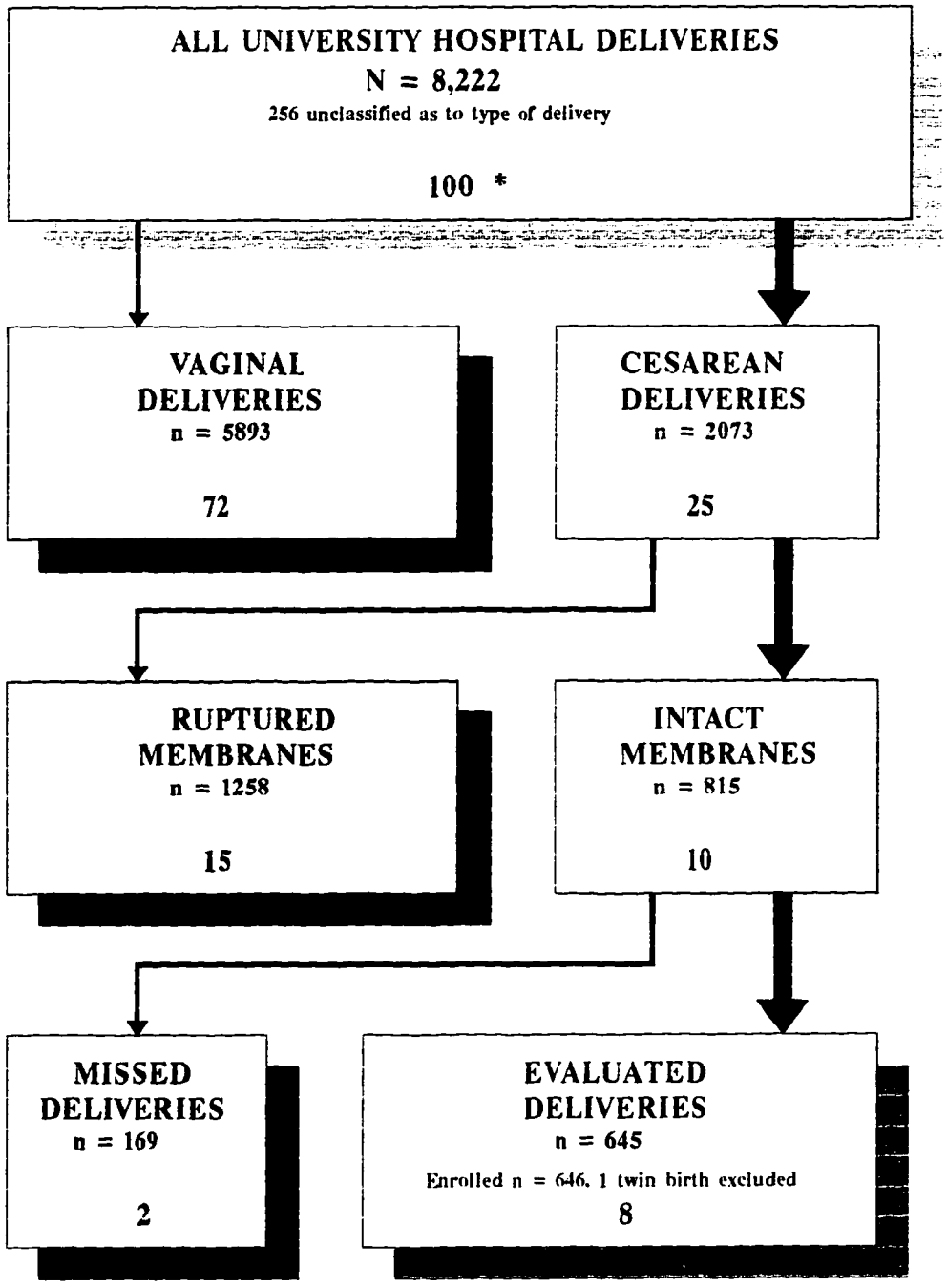


Figure 2. Study admission flow chart.

Table 12. Population characterization for University Hospital deliveries between October 26, 1987 and December 31, 1990

| | | TYPE OF DELIVERY | | | |
|---|---|---|---|---|---|
| | | Vaginal (n = 5,893) | Cesarean ruptured membrane (n=1,258) | Cesarean intact membrane enrolled (n = 645) | |
| % Race | White | 34.6 | 38.1 | 47.4 | |
| | Black | 64.9 | 61.5 | 52.2 | |
| | Other | 0.5 | 0.4 | 0.4 | *** |
| % Marital status | Single | 54.1 | 48.1 | 40.8 | |
| | Married | 37.4 | 44.8 | 50.4 | |
| | Divorced | 4.2 | 3.5 | 4.2 | |
| | Separated | 4.1 | 3.3 | 4.4 | |
| | Widowed | 0.3 | 0.2 | 0.2 | *** |
| Mean maternal age | | 24.3 | 25.6 | 26.3 | *** |
| Mean years of education | | 11.8 | 12.1 | 12.1 | *** |
| % w/ Medical coverage | Insured | 11.9 | 30.5 | 32.0 | |
| | Indigent | 88.1 | 69.5 | 68.0 | *** |
| % Previous C-section | | 2.3 | 6.7 | 12.3 | *** |
| Mean hours of labor | | 15.7 | 20.6 | 11.3 | *** |
| Mean birth weight (gms) | | 3041.9 | 2796.1 | 2662.3 | *** |
| Mean gestational age (weeks) | | 37.7 | 36.5 | 36.1 | *** |
| % Pre-term delivery | | 21.3 | 37.4 | 44.3 | *** |
| % Post-term delivery | | 0.5 | 1.0 | 0.9 | * |
| % Multiple births | | 8.7 | 13.2 | 5.6 | *** |
| % Smoked during pregnancy | | 19.3 | 15.8 | 25.6 | *** |
| % Alcohol use during pregnancy | | 10.9 | 7.7 | 10.1 | * |
| % Any history of drug use | | 8.3 | 6.1 | 3.9 | ** |
| % Anomalies | | 1.8 | 5.1 | 6.7 | *** |
| % History of venerial disease | | 1.2 | 1.4 | 14.8 | *** |
| % Maternal infection during pregnancy | | 8.3 | 7.9 | 6.5 | |

Table 12. - Continued.

| | TYPE OF DELIVERY | | |
|---|---|---|---|
| | Vaginal (n = 5,893) | Cesarean ruptured membrane (n=1,258) | Cesarean intact membrane enrolled (n = 645) |
| % Urinary tract infection during pregnancy | 2.0 | 2.2 | 10.6 *** |
| % Amnionitis | 5.4 | 9.6 | 1.4 *** |
| % History of kidney disease | 8.8 | 12.1 | 13.5 ** |
| % History of heart disease | 3.6 | 4.4 | 6.7 * |
| % Hypertension (delivery history) | 8.2 | 19.4 | 26.9 *** |
| % Diabetes (delivery history) | 2.9 | 8.4 | 14.9 *** |

* $p \leq .05$ comparing all three groups.
** $p \leq .001$ comparing all three groups.
*** $p \leq .0001$ comparing all three groups.

(24.3 years), followed by the group with ruptured membranes (25.6 years), and the intact membranes group (26.3 years). The differences between the VAG and CRM groups were due primarily to differences between the blacks (23.9 versus 25.3 years, $p \leq 0.001$), and entirely from the blacks for the CRM/CIM comparison (23.3 versus 26.1 years, $p \leq 0.05$). Mean years of education were comparable for the VAG and CIM groups, and the two Cesarean section groups were comparable. However, even though the mean years of education were equal for the two Cesarean section groups (12.1 years), when each group was compared against the VAG group, the CRM was found to be significantly different from the VAG group. This finding can be attributed to the differences in sample sizes and that the variances were equal only for the VAG and CRM groups of women.

The women who required a Cesarean section were approximately 3 times as likely to have some type of commercial medical insurance than those who delivered vaginally. Women in the CRM group were about 3 times as likely, and the CIM group 5 times as likely as women in the VAG group to have had a previous Cesarean section. These differences were comparable across

Table 13. Comparison of maternal characteristics of women experiencing either a vaginal deliver or a Cesarean section with ruptured fetal membranes

| | | TYPE OF DELIVERY | | |
|---|---|---|---|---|
| | | Vaginal (n = 5,893) | Cesarean ruptured membrane (n = 1,258) | |
| % Race | White | 34.6 | 38.1 | |
| | Black | 64.9 | 61.5 | |
| | Other | 0.5 | 0.4 | |
| % Marital status | Single | 54.1 | 48.1 | |
| | Married | 37.4 | 44.8 | |
| | Divorced | 4.2 | 3.5 | |
| | Separated | 4.1 | 3.3 | |
| | Widowed | 0.3 | 0.2 | *** |
| Mean maternal age | | 24.3 | 25.6 | *** |
| Mean years of education | | 11.8 | 12.1 | ** |
| % w/ Medical coverage | Insured | 11.9 | 30.5 | |
| | Indigent | 88.1 | 69.5 | *** |
| % Previous C-section | | 2.3 | 6.7 | *** |
| Mean hours of labor | | 15.7 | 20.6 | |
| Mean birth weight (gms) | | 3041.9 | 2796.1 | *** |
| Mean gestational age (weeks) | | 37.7 | 36.5 | *** |
| % Pre-term delivery | | 21.3 | 37.4 | *** |
| % Post-term delivery | | 0.5 | 1.0 | * |
| % Multiple births | | 8.7 | 13.2 | *** |
| % Smoked during pregnancy | | 19.3 | 15.8 | * |
| % Alcohol use during pregnancy | | 10.9 | 7.7 | ** |
| % Any history of drug use | | 8.3 | 6.1 | * |
| % Anomalies | | 1.8 | 5.1 | *** |
| % History of venereal disease | | 1.2 | 1.4 | |
| % Maternal infection during pregnancy | | 8.3 | 7.9 | |

Table 13. - Continued.

| | TYPE OF DELIVERY | |
|---|---|---|
| | Vaginal (n = 5,893) | Cesarean ruptured membrane (n = 1,258) |
| % Urinary tract infection during pregnancy | 2.0 | 2.2 |
| % Amnionitis | 5.4 | 9.6 *** |
| % History of kidney disease | 8.8 | 12.1 * |
| % History of heart disease | 3.6 | 4.4 |
| % Hypertension (delivery history) | 8.2 | 19.4 *** |
| % Diabetes (delivery history) | 2.9 | 8.4 *** |

*p ≤.05
**p ≤.001
***p ≤.0001

the races. The mean length of labor was comparable for the VAG and CRM groups (Table 13), but the time was significantly shorter for the CIM group, regardless of the comparison group (Tables 14, 15).

There was a downward trend in both mean birth weight and gestational age at delivery, with the highest being the vaginal delivery group, followed by Cesarean sections with ruptured membranes, and, finally the study group of Cesarean sections without ruptured membranes. When comparing these groups, however, it must be noted that the averages for the vaginal and Cesarean section with ruptured membranes would reflect the age when the fetus actually was instigating labor and delivery. Many of those in the intact membrane groups had an iatrogenic gestational age, reflective of when the physician decided to deliver the fetus, regardless of whether or not that would have been the actual time at which the fetus would have been delivered naturally, without intervention. This point may also help explain the increasing proportion of preterm births in the groups. Although the proportion of post term (>42 weeks) deliveries was comparable between the two Cesarean section groups, there was an approximately 2-fold increase over that seen in the vaginal deliveries.

Table 14. Comparison of maternal characteristics of women experiencing either a vaginal delivery or a Cesarean section with intact fetal membranes

| | | TYPE OF DELIVERY | | |
|---|---|---|---|---|
| | | Vaginal (n = 5,893) | Cesarean intact membrane enrolled (n = 645) | |
| % Race | White | 34.6 | 47.4 | |
| | Black | 64.9 | 52.2 | |
| | Other | 0.5 | 0.4 | *** |
| % Marital status | Single | 54.1 | 40.8 | |
| | Married | 37.4 | 50.4 | |
| | Divorced | 4.2 | 4.2 | |
| | Separated | 4.1 | 4.4 | |
| | Widowed | 0.3 | 0.2 | *** |
| Mean maternal age | | 24.3 | 26.3 | *** |
| Mean years of education | | 11.8 | 12.1 | |
| % w/ Medical coverage | Insured | 11.9 | 32.0 | |
| | Indigent | 88.1 | 68.0 | *** |
| % Previous C-sec | | 2.3 | 12.3 | *** |
| Mean hours of labor | | 15.7 | 11.3 | * |
| Mean birth weight (gms) | | 3041.9 | 2662.3 | *** |
| Mean gestational age (weeks) | | 37.7 | 36.1 | *** |
| % Pre-term delivery | | 21.3 | 44.3 | *** |
| % Post-term delivery | | 0.5 | 0.9 | |
| % Multiple births | | 8.7 | 5.6 | * |
| % Smoked during pregnancy | | 19.3 | 25.6 | ** |
| % Alcohol use during pregnancy | | 10.9 | 10.1 | |
| % Any history of drug use | | 8.3 | 3.9 | * |
| % Anomalies | | 1.8 | 6.7 | *** |
| % History of venereal disease | | 1.2 | 14.8 | *** |

Table 14. - Continued.

| | TYPE OF DELIVERY | |
|---|---|---|
| | Vaginal (n = 5,893) | Cesarean intact membrane enrolled (n = 645) |
| % Maternal infection during pregnancy | 8.3 | 6.5 |
| % Urinary tract infection during pregnancy | 2.0 | 10.6 *** |
| % Amnionitis | 5.4 | 1.4 *** |
| % History of kidney disease | 8.8 | 13.5 * |
| % History of heart disease | 3.6 | 6.7 * |
| % Hypertension (delivery history) | 8.2 | 26.9 *** |
| % Diabetes (delivery history) | 2.9 | 14.9 *** |

* $p \leq .05$
** $p \leq .001$
*** $p \leq .0001$

There was a higher proportion of multiple births comparing Cesarean sections with ruptured membranes to vaginal deliveries, and a smaller proportion when comparing Cesarean section with intact membranes population to the vaginal delivery population.

There was an increased proportion of women who smoked during their pregnancy in the intact membrane group as opposed to the other two groups, and a slight decrease in a history of drug abuse. The regular use of alcohol during pregnancy varied greatly among the three groups. There was a 2.8- to 3.7-fold increase in fetal anomalies in the Cesarean section groups as compared to the vaginal delivery group. The history of venereal disease was increased in the women with intact membranes (8.9%) as compared to the other two groups (1.2% for vaginal deliveries and 1.4% for Cesarean section with ruptured membranes). The history of urinary tract infections during the pregnancy was increased 5-fold in the intact membrane group when compared to the other two groups. Amnionitis was increased in the group who had a section with rupture of membranes and decreased in the intact membrane group, when compared to the vaginal delivery

Table 15. Comparison of maternal characteristics of women experiencing a Cesarean section delivery with or without intact fetal membranes

| | | TYPE OF DELIVERY | | |
|---|---|---|---|---|
| | | Cesarean ruptured membrane (n = 1,258) | Cesarean intact membrane enrolled (n = 645) | |
| % Race | White | 38.1 | 47.4 | |
| | Black | 61.5 | 52.2 | |
| | Other | 0.4 | 0.4 | *** |
| % Marital status | Single | 48.1 | 40.8 | |
| | Married | 44.8 | 50.4 | |
| | Divorced | 3.5 | 4.2 | |
| | Separated | 3.3 | 4.4 | |
| | Widowed | 0.2 | 0.2 | |
| Mean maternal age | | 25.6 | 26.3 | * |
| Mean years of education | | 12.1 | 12.1 | |
| % w/ Medical coverage | Insured | 30.5 | 32.0 | |
| | Indigent | 69.5 | 68.0 | |
| % Previous C-sec | | 6.7 | 12.3 | ** |
| Mean hours of labor | | 20.6 | 11.3 | ** |
| Mean birth weight (gms) | | 2796.1 | 2662.3 | * |
| Mean gestational age (weeks) | | 36.5 | 36.1 | |
| % Pre-term delivery | | 37.4 | 44.3 | * |
| % Post-term delivery | | 1.0 | 0.9 | |
| % Multiple births | | 13.2 | 5.6 | *** |
| % Smoked during pregnancy | | 15.8 | 25.6 | *** |
| % Alcohol use during pregnancy | | 7.7 | 10.1 | |
| % Any history of drug use | | 6.1 | 3.9 | |
| % Anomalies | | 5.1 | 6.7 | |
| % History of venereal disease | | 1.4 | 14.8 | *** |
| % Maternal infection during pregnancy | | 7.9 | 6.5 | |

Table 15. - Continued.

| | TYPE OF DELIVERY | |
|---|---|---|
| | Cesarean ruptured membrane (n = 1,258) | Cesarean intact membrane enrolled (n = 645) |
| % Urinary tract infection during pregnancy | 2.2 | 10.6 *** |
| % Amnionitis | 9.6 | 1.4 *** |
| % History of kidney disease | 12.1 | 13.5 |
| % History of heart disease | 4.4 | 6.7 |
| % Hypertension (delivery history) | 19.4 | 26.9 *** |
| % Diabetes (delivery history) | 8.4 | 14.9 *** |

* $p \leq .05$
** $p \leq .001$
*** $p \leq .0001$

group. The history of other maternal infections excluding urinary tract infections during the pregnancy, such as respiratory infections, vaginitis, and tuberculosis during the pregnancy, was comparable for all of the groups.

There was a increase in the prevalence of kidney disease in women who experienced a Cesarean section compared to the vaginal delivery group. The women who were delivered with an intact membrane had between 1.5 and 2 times the amount of reported heart disease, as compared to either of the other two groups. Using the vaginal delivery group as a baseline, there was a 2.4-fold increase in the proportion of women with reported hypertension at the time of delivery in the women in the ruptured membrane group, and a 3.3-fold increase in the women in the enrolled intact membrane group. There was a 3- to 4-fold increase in diabetes at delivery for the Cesarean delivery groups compared to the vaginal delivery group.

Of the 169 appropriate deliveries missed, information was available only for those that occurred during the last 2 full years of the study (1989 and 1990, N = 76). The only characteristics

for which the enrolled and missed groups differed were mean gestational age ($p \leq .001$), mean birth weight ($p \leq .05$), percent preterm delivery ($p \leq .05$), and percent multiple births ($p \leq .0001$) (Table 16).

## Validation of Complication Status

A 20% random sample of all records that were marked negative in all of the possible variable fields for each complication was selected for full medical record review to determine if there was any evidence of diabetes or hypertension present. Of the 27 records examined, none showed any evidence of missclassification. All records with either any indication of a complication or a negative status with missing data were reviewed to acertain complication status. Of the 411 women listed as non-diabetic, 1 was positive (0.24%), and of the 313 non-hypertensive cases, 3 actually were hypertensive (0.96%). If we make the assumption that all of the 139 cases that were completly filled out as negative actually were negative, the false nagative rate for diabetes was 0.18%, and for hypertension, the rate was 0.66% There were 2 false positive diabetes cases out of 95 listed cases, for a false positive rate of 2.11%, and 12 cases missclassified out of 193 hypertensives, for a rate of 6.22%. Final analysis was conducted on the corrected diabetic and hypertensive status.

## Risk of Placental Infection with Ureaplasma urealyticum

Chi-square tests were done based on the mother's status for the given variable and whether or not she delivered one or more placenta that tested positive for Ureaplasma urealyticum (Table 17). The Fisher's exact test was used when 20% or more of the expected cell frequencies were <5. Two Asians and 1 Hispanic were deleted from this analysis. Race; socioeconomic status, as measured by either education or insurance status; smoking during pregnancy; and the presence of diabetes were not significantly associated with placental infection. Spontaneous delivery (type of delivery) was defined as a delivery in which spontaneous labor was the reason for performing the Cesarean section. Spontaneous delivery was compared against an indicated delivery, in which the physician made the decision to deliver the fetus, either with or without induction of labor, as in the case of fetal distress or fetopelvic disproportion.

Table 16. Population characterization of women eligible for enrollment in the study between October 26, 1987 and December 31, 1990

| | | Enrolled (n = 646) | Missed (n = 76) |
|---|---|---|---|
| % Race | White | 47.3 | 39.5 |
| | Black | 52.2 | 60.5 |
| % Marital status | Single | 40.8 | 41.9 |
| | Married | 50.4 | 50.0 |
| | Divorced | 4.2 | 4.1 |
| | Separated | 3.5 | 4.1 |
| | Widowed | 0.3 | 0.0 |
| Mean maternal age | | 26.3 | 26.7 |
| Mean years of education | | 12.1 | 11.9 |
| % w/ Medical coverage | Insured | 32.0 | 37.0 |
| | Indigent | 68.0 | 63.0 |
| % Previous C-sec | | 11.7 | 16.1 |
| Mean hrs labor | | 11.3 | 28.6 |
| Mean birth weight | | 2662.3 | 2375.2 * |
| Mean gestational age | | 36.1 | 34.2 ** |
| % Preterm | | 44.5 | 61.8 * |
| % Post maturity | | 0.9 | 1.3 |
| % Multiple births | | 5.6 | 19.7 *** |
| % Smokers | | 25.6 | 26.8 |
| % Alcohol use | | 10.1 | 15.0 |
| % Drug use | | 3.9 | 5.0 |
| % Anomalies | | 6.7 | 4.0 |
| % Venereal disease | | 14.9 | 19.5 |
| % Maternal infection | | 6.5 | 9.2 |
| % Urinary tract infection | | 10.6 | 5.0 |
| % Amnionitis | | 1.4 | 2.7 |

Table 16 - Continued.

| | Enrolled (n = 646) | Missed (n = 76) |
|---|---|---|
| % Kidney disease | 13.5 | 10.0 |
| % Heart disease | 6.7 | 7.5 |
| % Hypertension (delivery history) | 26.2 | 21.6 |
| % Diabetes (delivery history) | 11.3 | 9.2 |

* $p \leq .05$
** $p \leq .001$
*** $p \leq .0001$

Among non-diabetic women, 12.4% had at least one placenta infected with Ureaplasma urealyticum, compared against 7.3% of all diabetic women (p = .151). This comparison did not control for hypertensive status. Normotensive women had a prevalence of 13.8%, women with any type of hypertension had a prevalence of 6.4%, without adjustment for diabetes (p = .007). Among normotensive, non-diabetic women, 14.4% delivered at least one infected placenta, compared to 9.3% of the women with only diabetes, 6.8% of the women with only hypertension, and 4.8% of the women who had both complications (Figure 3). When the individual hypertensive classifications were considered, 8.0% of the women with acute (pregnancy induced) hypertension, 5.6% of those with chronic hypertension, and none of those with acute superimposed on chronic hypertension developed an infected placenta compared against 13.8% of those women who were normotensive (Figure 4).

**Multivariate Analysis for the Prediction of Placental Infection with Ureaplasma**

For the initial analysis using univariate logistic regression (Table 18) to explore the association between placental infection with U. urealyticum and the individual maternal characteristics, the three non-black/non-white individuals were excluded from the analysis of the race variable. Because race was not significantly associated with infection, these three women were re-entered into the group for purposes of multivariate logistic regression model building. A test for trend for hours of labor and gestational age was included as part of the final model. No attempt

Table 17. Odds ratios, chi-square, and Fisher's exact tests for placental infection with Ureaplasma, given selected maternal characteristics

| Variable | | Percent positive (number) | Odds ratio | Confidence interval (95%) | P-value |
|---|---|---|---|---|---|
| Spontaneous delivery | no | 6.06 (28) | | | |
| | yes | 25.68 (47) | 5.36 | 3.23, 8.89 | < <.001 |
| Race | white | 10.49 (32) | | | |
| | black | 12.76 (43) | 1.25 | 0.75, 2.09 | .441 |
| Maternal age (years) | >19 | 10.18 (57) | | | |
| | <20 | 21.18 (18) | 2.37 | 1.32, 4.27 | .003 |
| Hours of labor | none | 5.84 (23) | | | |
| | 1 - 6 | 16.46 (13) | 3.18 | 1.44, 6.95 | <.003 |
| | 7 - 12 | 14.29 ( 7) | 2.68 | 1.08, 6.10 | .036 § |
| | 13 - 24 | 17.39 ( 8) | 3.38 | 1.43, 7.50 | .009 § |
| | >24 | 37.50 (21) | 9.69 | 4.62, 20.33 | < <.001 |
| Hours of labor | <25 | 9.17 (54) | | | |
| | >24 | 37.50 (21) | 5.94 | 3.23, 10.93 | < <.001 |
| Gestational age (weeks) | >36 | 6.69 (24) | | | |
| | 30 - 36 | 16.35 (26) | 2.73 | 1.45, 5.12 | .001 |
| | <30 | 28.21 (22) | 5.48 | 2.75, 10.96 | < <.001 |
| Gestational age (weeks) | >29 | 9.65 (50) | | | |
| | <30 | 28.56 (22) | 3.68 | 2.07, 6.52 | < <.001 |
| Previous pre-term delivery | no | 7.05 (26) | | | |
| | yes | 17.82 (49 | 2.86 | 1.73, 4.74 | < <.001 |
| Primigravida | no | 8.97 (35) | | | |
| | yes | 15.38 (36) | 1.84 | 1.12, 3.03 | .015 |
| Uninsured | no | 11.11 (15) | | | |
| | yes | 12.89 (37) | 1.18 | 0.63, 2.24 | .604 |
| Education (years) | <8 | 9.95 (22) | | | |
| | >7 | 13.33 ( 2) | 1.39 | 0.21, 4.82 | .655 § |
| Smoked during pregnancy | no | 10.11 (37) | | | |
| | yes | 14.29 (18) | 1.48 | 0.81, 2.71 | .199 |
| Marital status | married † | 8.68 (29) | | | |
| | single ‡ | 18.97 (44) | 2.46 | 1.49, 4.07 | < <.001 |
| Multiple birth this delivery | no | 9.85 (60) | | | |
| | yes | 41.67 (15) | 6.30 | 3.33, 15.55 | < <.001 § |

Table 17. - Continued

| Variable | | Percent positive (number) | Odds ratio | Confidence interval (95%) | P-value |
|---|---|---|---|---|---|
| Other bacteria isolated | no | 8.29 (46) | | | |
| | yes | 32.22 (29) | 5.26 | 3.08, 8.98 | < <.001 |
| Diabetes mellitus | no | 12.39 (68) | | | |
| | yes | 7.29 ( 7) | 0.56 | 0.25, 1.25 | .151 |
| Hypertension | no | 13.82 (63) | | | |
| | yes | 6.35 (12) | 0.42 | 0.22, 0.80 | .007 |
| Elevated pressure during pregnancy | no | 13.47 (64) | | | |
| | yes | 6.47 (11) | 0.44 | 0.23, 0.86 | .015 |
| Chronic hypertension | no | 12.68 (72) | | | |
| | yes | 3.90 ( 3) | 0.28 | 0.09, 0.91 | .024 |
| Acute hypertension | no | 12.94 (66) | | | |
| | yes | 6.67 ( 9) | 0.48 | 0.23, 0.99 | .043 |

§ Fisher's exact test
† Married, separated or divorced
‡ Single, widowed, other

was made to control for the degree of control of the complications of interest because this information was both poorly characterized and subjective.

Testing was done using the mother's characteristic and her overall Ureaplasma infection status. Marital status, labor class, gestational age class, type of delivery, and primigravida delivery were no longer significant when entered into the full model. Marital status and primagravida were removed from the model. Type of delivery, labor class, and gestational age class were kept in the final model because these factors have been shown to be associated with infection (unpublished data). Previous preterm delivery was also retained in the final model, because there was an association with preterm delivery; previous preterm deliveries may have been due to placental infection with Ureaplasma.

The final models used are detailed in Table 19. The core group of variables remained the same but the factors of interest (diabetes and hypertension) were changed to give four separate models. Because almost half of the diabetics also had some form of hypertension during their

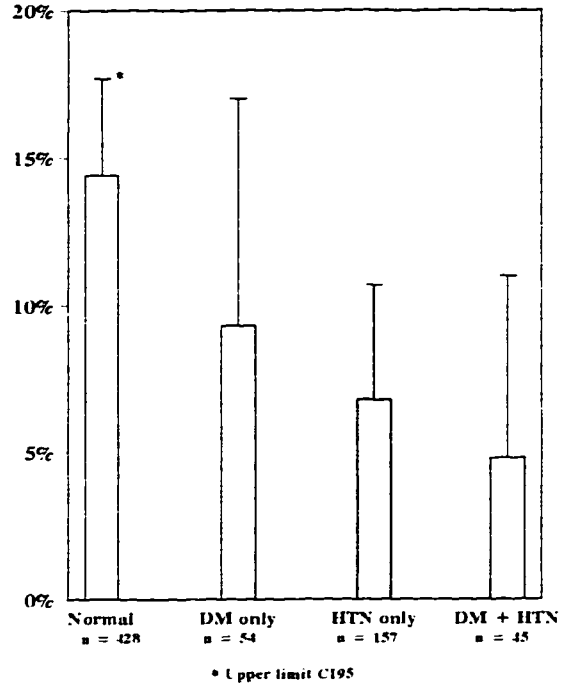


Figure 3. Placental infection status with Ureaplasma urealyticum by complication classification.

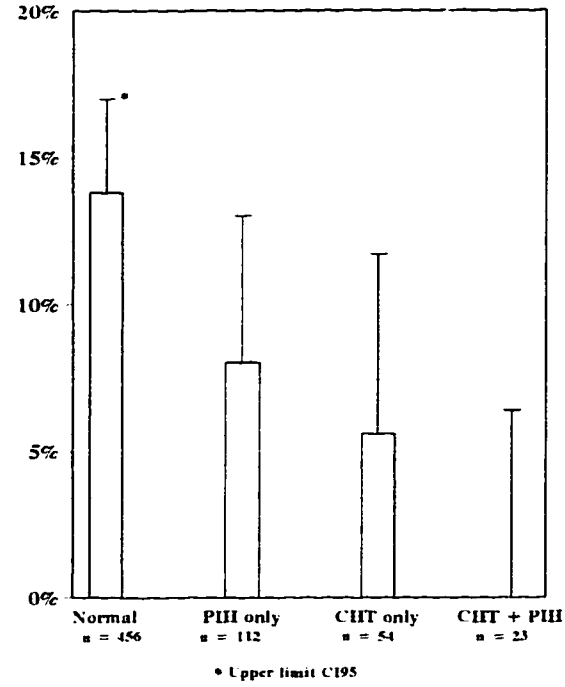


Figure 4. Placental infection status with Ureaplasma urealyticum by hypertensive classification.

pregnancy, the first model separates the factors into either factor alone and both factors together. The second model considered any diagnosis of hypertension, the third model considered only hypertension based on experiencing an elevated blood pressure during the pregnancy, and the final model considered the two classes of hypertension (acute and chronic). From this last model, a risk estimate for experiencing both types of hypertension was calculated. The confidence intervals for this estimate were calculated under the assumption of non-independence.

Table 18. Significant odds ratio estimates for placental infection with Ureaplasma urealyticum by univariate logistic regression

| Variable | Odds ratio | ($CI_{95}$: L,U) | p-value |
|---|---|---|---|
| Spontaneous delivery | 5.36 | (3.23, 8.89) | < <.001 |
| Labor >24 hours | 5.94 | (3.23, 10.89) | < <.001 |
| Gestational age <30 weeks | 3.68 | (2.07, 6.52) | < <.001 |
| Previous pre-term delivery | 2.86 | (1.73, 4.74) | < <.001 |
| Multiple birth this delivery | 6.54 | (3.20, 13.35) | < <.001 |
| Mother's age <20 years | 2.37 | (1.32, 4.27) | .004 |
| Other bacteria isolated from placenta | 9.53 | (5.65, 16.10) | < <.001 |
| Diabetes | 0.56 | (0.25, 1.25) | .156 |
| Hypertension | 0.42 | (0.22, 0.80) | .008 |
| Elevated blood pressure during pregnancy | 0.44 | (0.23, 0.86) | .017 |
| Chronic hypertension | 0.28 | (0.09, 0.91) | .034 |
| Acute hypertension | 0.48 | (0.23, 0.99) | .047 |

The odds ratio for placental infection with Ureaplasma, given a woman had some form of diabetes during her pregnancy, was 1.34 ( $CI_{95}$ = 0.47, 3.80; p = 0.588 ) (Table 20, Figure 5). These results control for the core variables and hypertension in any form, and indicate that there is no association between maternal diabetes and placental infection with Ureaplasma urealyticum. Controlling for diabetes as well as the core variables, the odds ratio for placental infection, given

any type of hypertension, was 0.28 ( $CI_{95}$ = 0.11, .72; p = 0.008 ), indicating that there is a negative association between placental infection with U. urealyticum and maternal hypertension during pregnancy (Table 20, Figure 5).

Table 19. Logistic regression models

| | | |
|---|---|---|
| DEPENDENT VARIABLE = | CODING | |
| Placental infection with Ureaplasma urealyticum | yes | = 1 |
| | no | = 0 |
| INDEPENDENT VARIABLES ( Core ) = | | |
| Type of labor: | indicated | = 0 |
| | spontaneous | = 1 |
| Labor class: | no labor | = 0 |
| | 1 - 6 hours | = 1 |
| | 7 - 12 hours | = 2 |
| | 13 - 24 hours | = 3 |
| | >24 hours | = 4 |
| Gestational age: | >36 weeks | = 0 |
| | 30 - 36 weeks | = 1 |
| | <30 weeks | = 2 |
| Multiple births this delivery | no | = 0 |
| | yes | = 1 |
| Maternal age | >19 years | = 0 |
| | <20 years | = 1 |
| History of previous preterm delivery | no | = 0 |
| | yes | = 1 |
| Any other bacteria isolated from the placenta this delivery | no | = 0 |
| | yes | = 1 |
| INDEPENDENT VARIABLES ( Model ) = | | |
| Model 1. Hypertension only | no | = 0 |
| | yes | = 1 |
| Diabetes only | no | = 0 |
| | yes | = 1 |
| Diabetes with hypertension | no | = 0 |
| | yes | = 1 |
| Model 2. Any diagnosis of hypertension | no | = 0 |
| | yes | = 1 |

Table 19 - Continued.

| | | | |
|---|---|---|---|
| Model 3. | Any elevated blood pressure during current pregnancy | no<br>yes | = 0<br>= 1 |
| | INDEPENDENT VARIABLE = | | CODING |
| Model 4. | Chronic hypertension | no<br>yes | = 0<br>= 1 |
| | Acute (pregnancy induced) hypertension | no<br>yes | = 0<br>= 1 |
| | Acute superimposed on chronic hypertension | no<br>yes | = 0<br>= 1 |

Because no association was found between diabetes and infection, analysis of the relationship between placental infection with Ureaplasma and hypertension was done without controlling for this factor (Table 21). When all hypertensive classifications were considered as a group, the odds ratio for any placental infection with Ureaplasma for a given pregnancy was 0.30 ($CI_{95}$ = 0.13, 0.71; p = 0.006 ). The odds ratio was the same if a woman was classified as hypertensive only if she experienced an elevated blood pressure during her pregnancy ( 0.30, $CI_{95}$ = 0.13, 0.72; p = 0.007 ) (Figure 6). When evaluating pregnancy outcome based on the type of hypertension experienced, the odds ratios were 0.57 ( $CI_{95}$ = 0.15, 2.15; p = 0.410 ) for chronic hypertension, 0.29 ( $CI_{95}$ = 0.11, 0.76; p = 0.012 ) for acute hypertension, and 0.26 ( $CI_{95}$ = 0.03, 2.38; p = 0.248 ) for those with both types of hypertension (Figure 6). Because all of the individuals in this last group were negative for Ureaplasma, one individual was randomly chosen to be assigned as positive for this model only, so that an estimate and confidence interval could be obtained. Without this adjustment, the odds ratio was zero, with an infinite upper limit.

Table 20. Odds ratio estimates for placental infection with Ureaplasma urealyticum by multivariate logistic regression, Model I

| Variable | | Odds ratio | ( $CI_{95}$: L,U ) | p-value |
|---|---|---|---|---|
| Spontaneous delivery | | 1.42 | ( 0.56, 3.60 ) | .455 |
| Labor hours | 1-6 | 1.29 | ( 0.97, 1.71 ) | |
| | 7-12 | 1.66 | ( 0.95, 2.91 ) | |
| | 13-24 | 2.15 | ( 0.93, 4.97 ) | |
| | >24 | 2.77 | ( 0.90, 8.49 ) | .075 † |
| Gestational age (weeks) | 30-36 | 1.69 | ( 0.96 2.98 ) | |
| | <30 | 2.86 | ( 0.92, 8.87 ) | .068 † |
| Previous pre-term delivery | | 1.66 | ( 0.71, 3.90 ) | .243 |
| Multiple birth this delivery | | 5.30 | ( 2.12, 13.29 ) | <.001 |
| Mother <20 years of age | | 2.35 | ( 1.14, 4.81 ) | .021 |
| Other bacteria isolated from placenta | | 4.05 | ( 2.09, 7.84 ) | <<.001 |
| Diabetes only | | 1.34 | ( 0.47, 3.80 ) | .588 |
| Hypertension only | | 0.28 | ( 0.11, 0.72 ) | .008 |
| Diabetes with hypertension | | 0.48 | ( 0.10, 2.30 ) | .360 |

† Test for trend

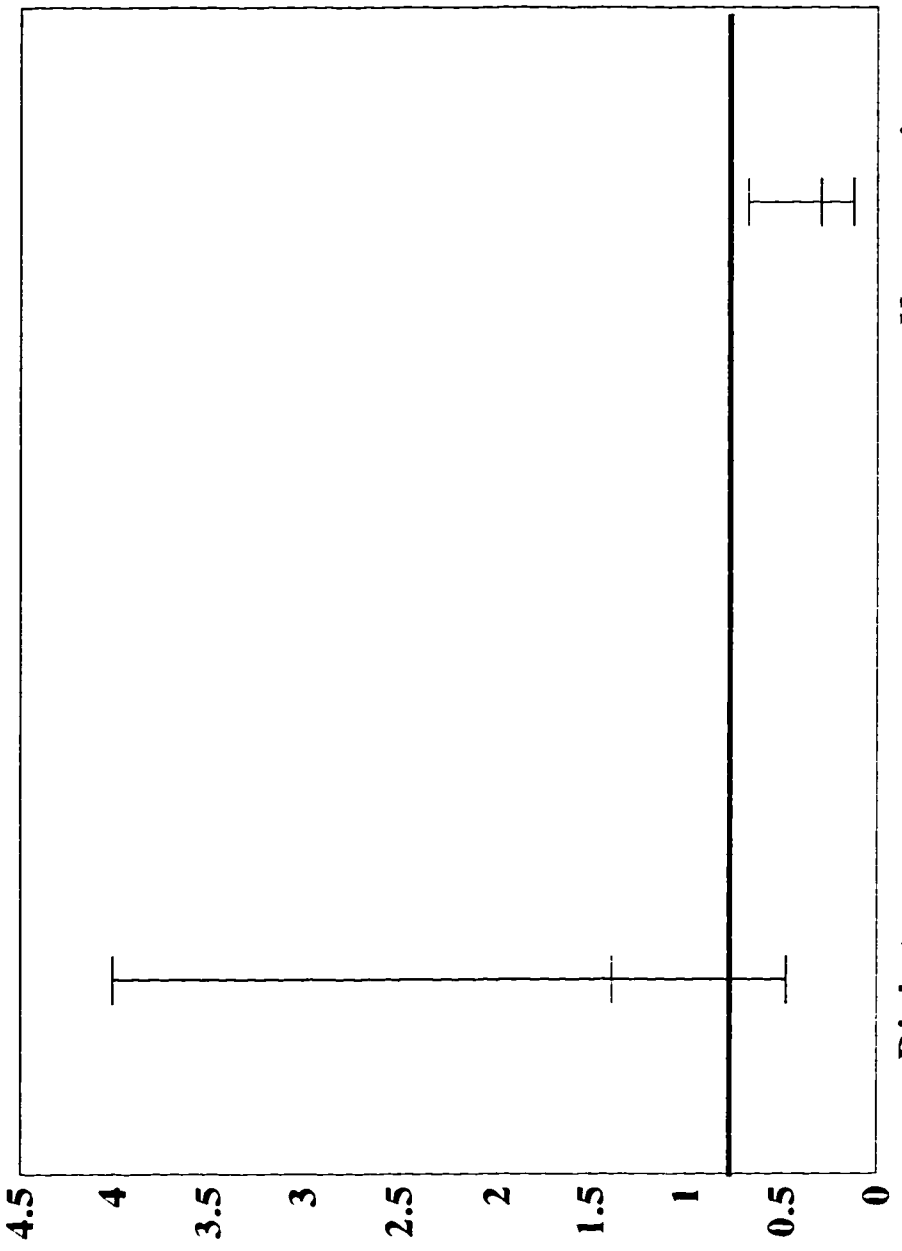


Figure 5. Odds ratios for placental infection with Ureaplasma urealyticum associated with diabetes only or hypertension only.

Table 21. Odds ratio estimates for placental infection with Ureaplasma urealyticum for various hypertension classifications using multivariate logistic regression, Models II - IV

| Variable | | Any diagnosis of hypertension | | | | Elevated blood pressure in pregnancy | | | | By sub-classification of hypertension | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | OR | ($CI_{95}$: L,U) | p-value | | OR | ($CI_{95}$: L,U) | p-value | | OR | ($CI_{95}$: L,U) | p-value | |
| Spontaneous delivery | | 1.37 | ( 0.54, 3.45 ) | .506 | | 1.42 | ( 0.57, 3.56 ) | .456 | | 1.44 | ( 0.55, 3.60 ) | .436 | |
| Labor hours | 1-6 | 1.31 | ( 0.99, 1.73 ) | | | 1.32 | ( 0.99, 1.74 ) | | | 1.28 | ( 0.97, 1.68 ) | | |
| | 7-12 | 1.71 | ( 0.97, 3.00 ) | | | 1.73 | ( 0.98, 3.04 ) | | | 1.63 | ( 0.94, 2.83 ) | | |
| | 13-24 | 2.23 | ( 0.96, 5.18 ) | | | 2.28 | ( 0.98, 5.31 ) | | | 2.08 | ( 0.91, 4.77 ) | | |
| | >24 | 2.91 | ( 0.95, 8.97 ) | .063 | * | 2.99 | ( 0.97, 9.25 ) | .057 | | 2.65 | ( 0.88, 8.03 ) | .084 | |
| Gestational age (weeks) | 30-36 | 1.64 | ( 0.94, 2.87 ) | | | 1.62 | ( 0.93, 2.81 ) | | | 1.66 | ( 0.95, 2.89 ) | | |
| | <30 | 2.70 | ( 0.89, 8.26 ) | .081 | * | 2.61 | ( 0.86, 7.90 ) | .090 | | 2.74 | ( 0.90, 8.33 ) | .075 | |
| Previous preterm delivery | | 1.67 | ( 0.72, 3.92 ) | .235 | | 1.67 | ( 0.71, 3.90 ) | .237 | | 1.73 | ( 0.75, 4.00 ) | .200 | |
| Multiple birth this delivery | | 5.08 | ( 2.47, 10.44 ) | < .001 | | 5.00 | ( 2.03, 12.34 ) | < .001 | | 5.00 | ( 2.03, 12.34 ) | < .001 | |
| Mother <20 years of age | | 2.32 | ( 1.13, 4.77 ) | .022 | | 2.39 | ( 1.16, 4.92 ) | .019 | | 2.34 | ( 1.12, 4.84 ) | .023 | |
| Other bacteria isolated from placenta | | 3.92 | ( 2.04, 7.56 ) | << .001 | | 3.90 | ( 2.03, 7.50 ) | << .001 | | 3.78 | ( 2.22, 6.43 ) | << .001 | |

Table 21. Continued.

| Variable | Any diagnosis of hypertension | | | Elevated blood pressure in pregnancy | | | By sub-classification of hypertension | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | OR | ($CI_{95}$: L,U) | p-value | OR | ($CI_{95}$: L,U) | p-value | OR | ($CI_{95}$: L,U) | p-value | |
| Any hypertension | 0.30 | ( 0.13, 0.71 ) | .006 | | | | | | | |
| Elevated blood pressure during pregnancy | | | | 0.30 | ( 0.13, 0.72) | .007 | | | | |
| Chronic hypertension | | | | | | | 0.57 | ( 0.15, 2.15 ) | .410 | |
| Acute hypertension | | | | | | | 0.29 | ( 0.11, 0.76 ) | .012 | |
| Acute superimposed on chronic hypertension | | | | | | | 0.26 | ( 0.03, 2.38 ) | .248 | ** |

* Test for trend

** Zero cell gives an odds ratio of zero, maximum odds ratio and $CI_{95}$ derived by random assignment of Ureaplasma positive status to one of the women with acute hypertension superimposed on chronic hypertension

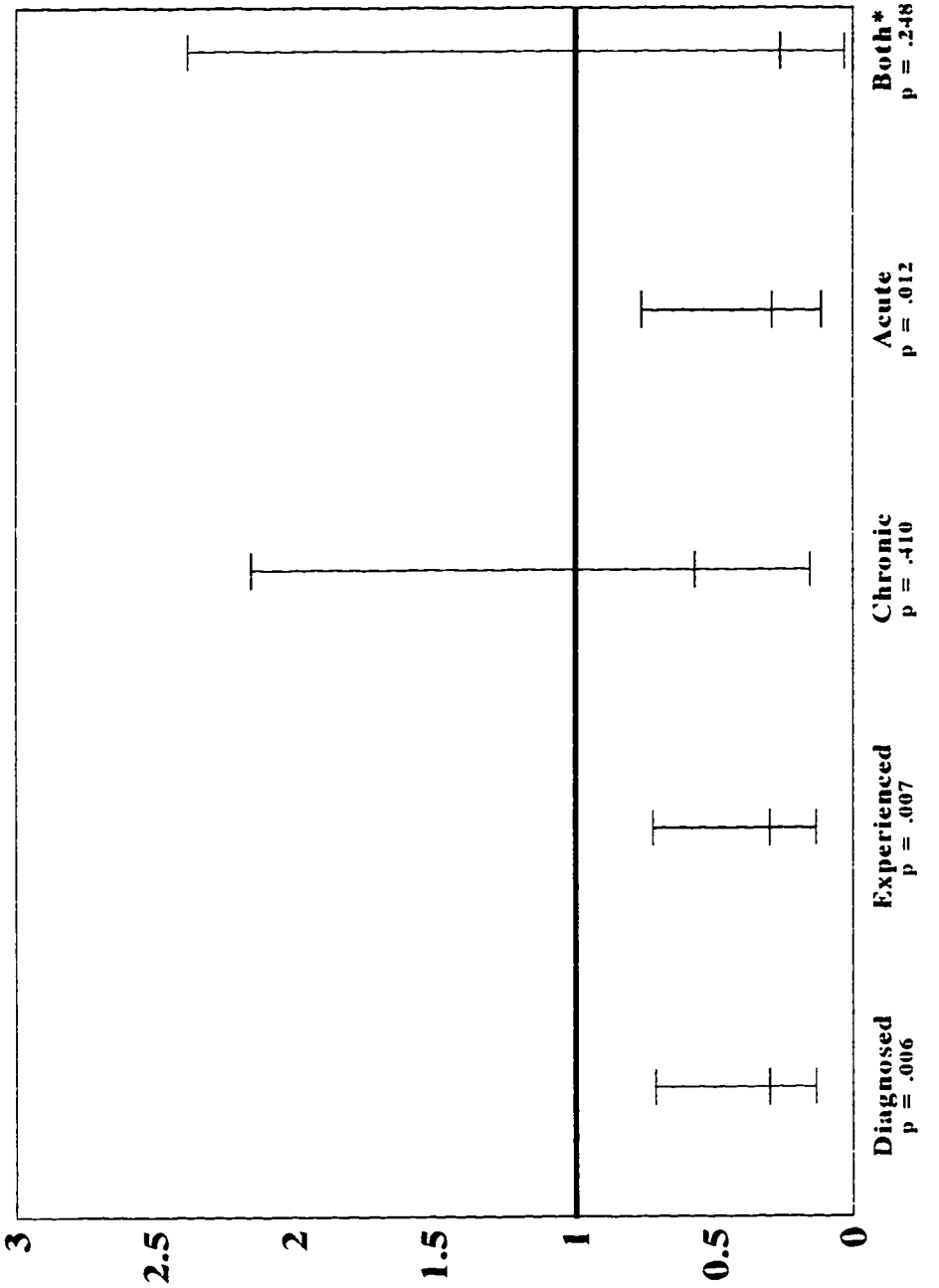


Figure 6. Odds ratios for placental infection with Ureaplasma urealyticum by hypertension classification.

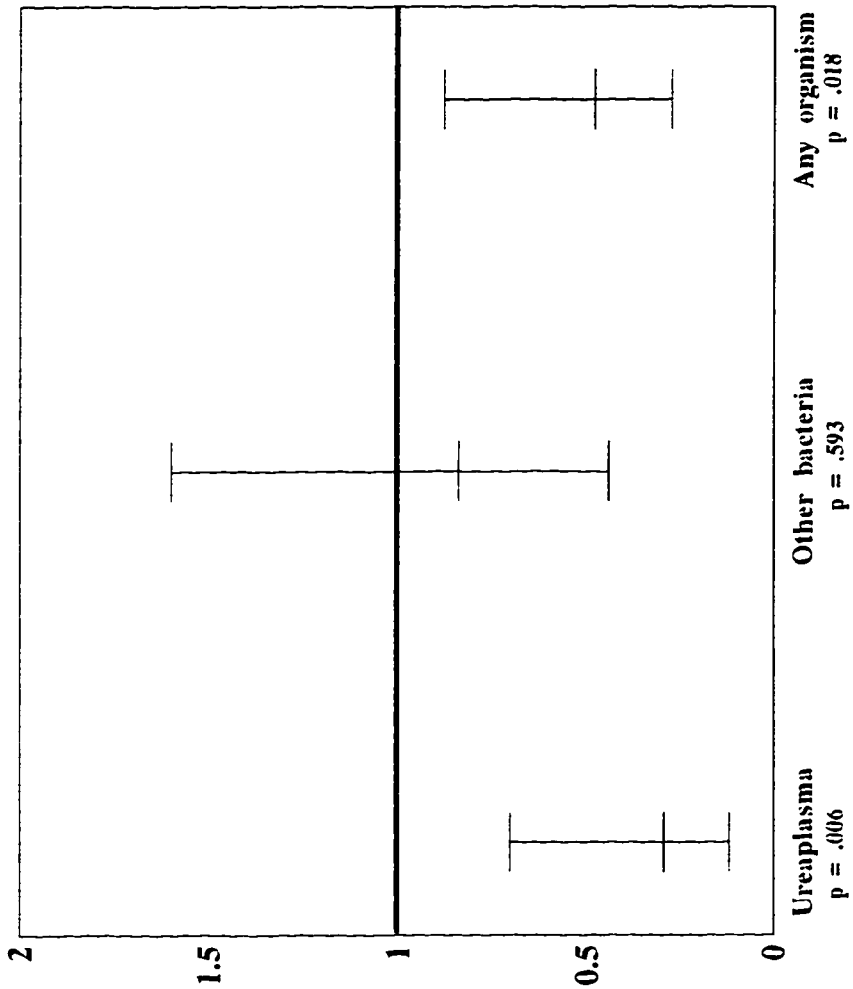


Figure 7. Odds ratios for placental infection with any bacteria associated with elevated blood pressure during pregnancy.

# CHAPTER 5

# DISCUSSION

## Diabetes

The preceding analysis indicates that, in the case of diabetes, there is no evidence to conclude that there is an association, either positive or negative, between diabetes and placental infection with Ureaplasma urealyticum. This is not in agreement with the studies that found an increase in infection rates of other bacteria in diabetic women both during and after a pregnancy.[27, 30, 76] The study involving post-Cesarean section infection[27] did not characterize the types of organisms isolated from the infections, whereas the antepartum studies were concerned specifically with Group B Streptococcus (GBS),[30, 76] an organism of particular concern due to its association with neonatal infections.[29, 30, 69] Studies of Group C and Group G Streptococcal infections found 23%[108] and 14%[130] of cases, respectively, were associated with diabetic patients. It was hypothesized that the increased availability of glucose in these patients favored the fermentative metabolism of these streptococci.[76] This situation may counterbalance any aberration in the rates of protein synthesis and degradation in both the placenta and fetus, removing any advantage to the Ureaplasma. This could be accomplished by giving the streptococci a competitive edge early on in colonization and competition for additional nutrients, or the byproducts of the fermentative process could alter the maternal physiological environment enough to make it unfavorable to the Ureaplasmas.

Analysis of the data in this study would indicate that, if any of these situations existed, they either did not confer an advantage to the Ureaplasma, or that other factors associated with the hypertensive conditions induced a stronger protective effect.

## Hypertension

Both human and animal studies have demonstrated a reduction in placental blood flow during hypertensive pregnancies.[1, 2, 13, 39, 63, 68, 77, 85, 88, 116] This reduction has been determined through both the measurement of uteroplacental blood flow rates[1, 2, 13, 68, 77, 85] and evaluation of placental pathology criteria.[39, 63, 88, 116] Hallmark features of the placental pathology associated with reduced blood flow were inadequate transformation of uteroplacental spiral arteries and acute atherosis. The same features also were found to be associated with preterm delivery[88] and fetal growth retardation.[14, 39, 116] The pathology was seen with these adverse outcomes even in the absence of a measured abnormal increase of blood pressure during the pregnancy.[14, 88, 116] Flow rate reduction attributed to hypertension ranged from 23-60% of normal.[1, 13, 17] When clearance time from the placental bed of radioactive sodium chloride ($^{24}$NaCl) was measured as a surrogate for blood flow, the clearance rates for mildly and severely pre-eclamptic women, compared to normotensive pregnant women was 1.9 and 3.7 times greater, respectively.

The reduction of the flow rate in the uteroplacental complex would naturally lead to a reduction in the amount of nutrients available to the fetus for growth. Although a normal placenta has an excess capacity, compared to need, of up to 50%,[1, 77] the reduction of the nutrient supply could also adversely affect the ability of Ureaplasma to thrive in the placental environment. If this were the case, there should also be a reduction in the proportion of placentas infected with other bacteria. Accordingly, the odds ratios, using placental infection with bacteria other than Ureaplasma and placental infection with either Ureaplasma or other bacteria as the dependent variable, were calculated (Figure 7) for women who experienced an elevated blood pressure during pregnancy. Although the odds ratio for bacteria other than Ureaplasma was $< 1$, it was not significantly reduced compared to women without an abnormal increase in blood pressure (0.84, $CL_{95}$ = 0.44, 1.60; p = 0.593). When any type of bacterial infection was considered, the odds ratio was significantly reduced (0.48, $CL_{95}$ = 0.27, 0.88; p = 0.018).

A total of 21 other species of bacteria were isolated from the placentas of the 645 women in this study. Ureaplasma urealyticum was the single most frequently isolated organism in this study (n = 75), followed by Peptostreptococcus species (n = 24), Mycoplasma hominis (n = 22),

Gardnerella vaginalis (n = 21), Streptococcus species (n = 18), and Propionibacterium species (n = 15). All other species had <10 isolations each. When comparing the distributions of the above mentioned organisms in women with and without an abnormally elevated blood pressure during their pregnancy, M. hominis (1.8 versus 4.0%), G. vaginalis (2.4 versus 3.6%), Streptococcus species (2.9 versus 2.7%), and Propionibacterium species (2.9 versus 2.1%) showed no significant differences. Only Peptostreptococcus species (0.59 versus 4.8%) showed a significant reduction in prevalence. A failure to detect a reduction may be a reflection of having too small a sample size to detect a difference in these other organisms, either individually or pooled.

Neither the age of the mother nor SES impacted on the risk of hypertension in general. Although the logistic regression model controlled for the relationship between age and Ureaplasma infection, the relationship between hypertension and age could have confounded the results. However, when considering any diagnosis of hypertension and age, 32.4% of those under the age of 20 (n = 85) were hypertensive, compared to 28.8% of those over the age of 20 (n = 560, 2-tailed $X^2$, p = 0.429). Chronic hypertension was significantly reduced in the younger women (1.2 vs. 13.6%, 2-tailed $X^2$, p <0.001), whereas the younger women were almost twice as likely to experience pregnancy-induced hypertension (32.9 vs. 19.1%, 2-tailed $X^2$, p <0.01). If a measured abnormal elevation of blood pressure during pregnancy is considered, the younger women were comparable to the older women (32.9 vs. 25.4.1%, 2-tailed $X^2$, p = 0.15). The proportions of women with hypertension in the low and high SES groups were not significantly different, regardless of the classification of hypertension used. Because an actual abnormal elevation of blood pressure during pregnancy seems to be the driving force in the reduced risk of placental infections, it would appear that neither age nor SES have any affect on the risk of measured hypertension during pregnancy in this population.

## Additional Findings

The finding that smoking was not associated with Ureaplasma infection of the placenta in this study population was contradictory to previously published findings.[67, 80] This could have been due to the fact that smoking was a risk factor for having a Cesarean section delivery with intact

membranes, as seen by the significant increase in the proportion of smokers in this group as compared to either of the other delivery groups (Tables 12, 14, and 15).

Primigravida and marital status were no longer significant in the multivariate models because these factors were tied heavily to maternal age, with women <20 years of age more likely to be primigravida for the current delivery (OR, 6.66, $CI_{95}$ 3.94, 11.25), and more likely to be single (OR, 2.78, $CI_{95}$ 1.68, 4.59).

Although spontaneous delivery was no longer significant in the final multivariate models, it was retained because Ureaplasma has been shown to be a risk factor for very early preterm delivery (>30 weeks gestational age) among spontaneous, but not indicated deliveries in this population (data not shown). Ureaplasma may act in some way to initiate early labor and, therefore, spontaneous delivery, as earlier defined, could act as a marker for placental infection, at least among low gestational age deliveries.

The significant association of length of labor and placental infection with Ureaplasma is consistent with other studies and is most probably due to a combination of the dilation of the cervix, allowing freer access of the flora of the lower genital tract to the uterus and placenta, and the wicking of mucus and fluids into the uterus as the contractions of labor continue. The longer the labor, the better the chance the organisms that have been drawn up into the uterus have of colonizing the uteroplacental environment.

The finding of previous preterm delivery being significantly associated with placental infection with Ureaplasma would be consistent with the finding of the association between low gestational age at delivery and Ureaplasma infection. Ureaplasma infection could indicate a chronic infection of the uterine environment. Even if the current delivery was not preterm, or very preterm, the Ureaplasma could be present, but its activity suppressed due to the mother's immune response to a chronic infection.

The association between placental infection with Ureaplasma and maternal age <20 years is consistent with the studies previously cited. Why this should be the case is unclear, in light of the fact that risk of infection increases with the total number of sexual partners, and it would be expected that women <20 years of age would have had fewer partners than women over the age of

20. It may be that the hormonal or immune status of the women, or the composition of the vaginal flora may simply make it easier for the Ureaplasma to colonize the endocervical environment. Another possibility might be that beginning sexual activity at an earlier age may increase the likelihood of having multiple partners. Further studies in this area would be useful.

The finding of an association between multiple gestation and placental infection with U. urealyticum was surprising. It is certainly unclear as to what conditions associated with a multiple delivery would be advantageous for movement of the organism up into the placenta. If, in fact, the reduced risk of infection in the presence of an abnormally increased blood pressure is due to a decrease in the blood flow, then it may be possible that an increased demand for blood in the multiple delivery may increase the risk of infection. Another possible explanation my be that there is an increased pressure on the cervix due to larger than usual contents of the uterus, which over the course of the pregnancy may cause some stretching of the cervical opening, allowing the organism to be wicked up into the uterus. This could also explain the finding that in vaginal deliveries of multiple gestations, only the first born of the sets of twins discussed were infected with either Ureaplasma or Mycoplasma.[64]

The strong association between placental infection with other bacteria and Ureaplasma should not be surprising. Any event that would allow a breach of what is essentially a sterile environment by one bacterium should allow any others that are present in the lower genital tract at that time to also move up into the uteroplacental environment. A general contamination of this environment would be an event marker, and the distribution of the species found could reflect either their distribution in the lower tract, or their varying ability to maintain colonization once they have moved into the new environment.

## Sexual Activity Prior to and During Pregnancy

Information of the mother's sexual activity was not available for analysis in this study. Because Ureaplasma colonization and infection is a result of sexual activity, knowledge of the type and extent of activity would be useful to determine the mothers' initial risk of infection of the lower urogenital tract. The women with and without the complications of interest could possibly differ in such characteristics as age at first intercourse, number of sexual partners, and sexual activity during

pregnancy. The severity of their illness and age of onset may alter their activity in all of these areas, and therefore decrease their overall initial risk of lower tract infection, which would be a prerequisite for the infection to move up into the placenta, the results of which would be to support the null hypothesis or produce a negative association.

## Antibiotic Treatment Prior to or During Pregnancy

Antibiotic treatment prior to or during pregnancy may also differ among the two groups of women. Although an attempt was made to collect data on antibiotic use during the pregnancy and labor (if present), there is no information on antibiotic use prior to conception. Depending on the types of antibiotics used, this may decrease the mothers' risk of being infected with Ureaplasma. If there was an increase in overall infection rates with other organisms among the women with diabetes or hypertension, treatment for those infections with antibiotics active against Ureaplasma might incidentally cure an unrealized infection with Ureaplasma. This, in effect, would reduce the risk of placental infection by reducing the prevalence of lower tract infection with Ureaplasma.

## Control of Medical Condition

The level of control of the patient's complication (i.e., diabetes or hypertension) may have an effect on her risk of infection. If, indeed, the metabolic conditions produced by the uncontrolled complication favor or reduce the risk of either the infection of the lower urogenital tract or the spread of Ureaplasma infection to the placenta, proper control of the condition may mask the true risk of infection due to the condition. Unfortunately, rarely does a record state categorically whether the level of control is good, poor, or nonexistent and, at best, this would be a subjective assessment that would vary from clinician to clinician. However, as previously noted, when the odds ratio was calculated for only those who had experienced an abnormal increase in blood pressure during the pregnancy, which would be a reasonable surrogate for the lack of control of the condition, it was essentially identical to that of the odds ratio for any diagnosis of hypertension.

## Comparability to the General Population

Associations found in this study group may not be generalizable to the larger population of pregnant women. By and large, this is a highly selected group of high-risk pregnancies. The current policy for performance of a Cesarean section at University Hospital requires that there be a

bona fide medical reason for the procedure; elective Cesareans are not supposed to be performed, although occasionally some are performed. Although infection of the placenta implies infection of the lower genital tract, the lack of infection of the placenta by no means implies a lack of organisms in the lower tract. The ureaplasmal infection status of the lower urogenital tract of these women is unknown, and, therefore, it is unknown if the risk of upper urogenital tract infection for the comparison group is the same as for the general population. If the rate is higher in our comparison group than in the general population, it may explain in part the reduction in risk for the hypertensives; whereas, if the rate is lower, the risk in the general population may be underestimated. If the infection rate of the lower genital tract of the women in the complication groups is lower than the general population, the interpretation of the odds ratios could shift from a negative association to either a null or positive association, depending on the magnitude of the difference.

Another possible source of non-comparability could arise if any of the other indications for Cesarean section were capable of enhancing Ureaplasma's ability to infect the placenta. Even if the infection rates in the lower genital tract for both the study and comparison groups were the same as that of the general population, it would be likely that, in this study population, any increase in risk due to the complications of interest may appear to be smaller that they actually are, or masked all together.

## CHAPTER 6

## SUMMARY

A cross-sectional study was conducted at the University Hospital of The University of Alabama at Birmingham, which included 645 of 815 (79%) Cesarean section deliveries with intact fetal membranes. The purpose of this study was to evaluate the association between maternal diabetes, maternal hypertension, and placental infection with Ureaplasma urealyticum. There were 75 women with at least one placenta showing cultural evidence of infection with Ureaplasma urealyticum. U. urealyticum was the single most frequently isolated organism in this population.

Using multivariate logistic regression to control for confounding factors, it was found that, in this population, the odds ratio for placental infection, given maternal diabetes, was 1.39 ($CI_{95}$ = 0.48, 4.00), indicating that there was no association between maternal diabetes and placental infection with U. urealyticum. Odds ratios of 0.30 ($CI_{95}$ = 0.13, 0.71) for any diagnosis of hypertension, 0.57 ($CI_{95}$ = 0.15, 2.15) for chronic hypertension, 0.29 ($CI_{95}$ = 0.11, 0.76) for pregnancy-induced (acute) hypertension, 0.26 ($CI_{95}$ = 0.03, 2.38) for acute superimposed on chronic hypertension, and 0.30 ($CI_{95}$ = 0.13, 0.72) for a measured abnormal increase in maternal blood pressure during pregnancy indicate a negative association between at least some forms of hypertension and placental infection with Ureaplasma urealyticum. Whether this effect was due to a reduction in the prevalence of Ureaplasma infection in the lower genital tract prior to pregnancy, or a suppression of the progression of infection during the pregnancy could not be determined in this study. However, there is evidence, both pathological and in the form of quantitative measurements, that there is a reduction of blood flow to the placenta in the presence of hypertension during pregnancy, and this may be one possible explanation for the results found in this study.

Additionally, placental infection with Ureaplasma urealyticum was found to be possitively associated with increased length of labor, previous preterm delivery, maternal age of <20 years, multiple births, and placental infections with other bacteria. Additional prospective studies that would acertain the infection status of the lower genital tract prior to pregnancy would be needed to clarify the nature of the association, as well as clarify the issue of comparability to the general population of pregnant women.

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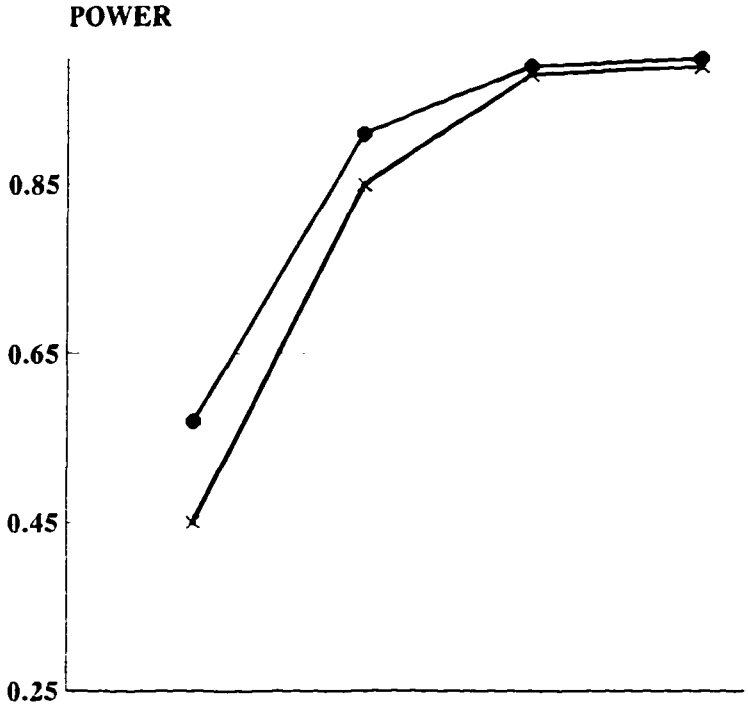
# APPENDIX 1

## POWER CURVES

# Power Calculations
# All Diabetes



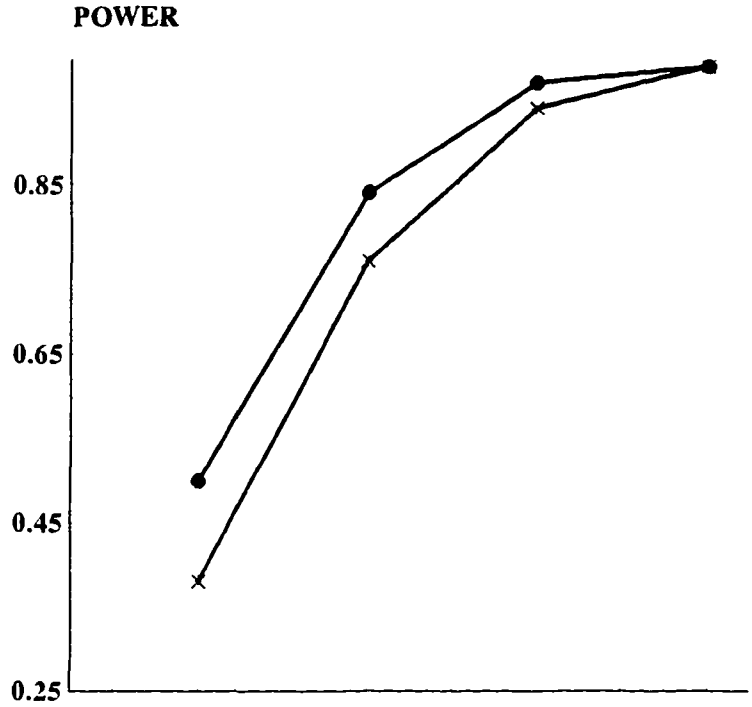

| | | | | |
|---|---|---|---|---|
| alpha = .10 | 0.57 | 0.91 | 0.99 | 1 |
| alpha = .05 | 0.45 | 0.85 | 0.98 | 0.99 |

ODDS RATIO

alpha = .10 alpha = .05

N = 573

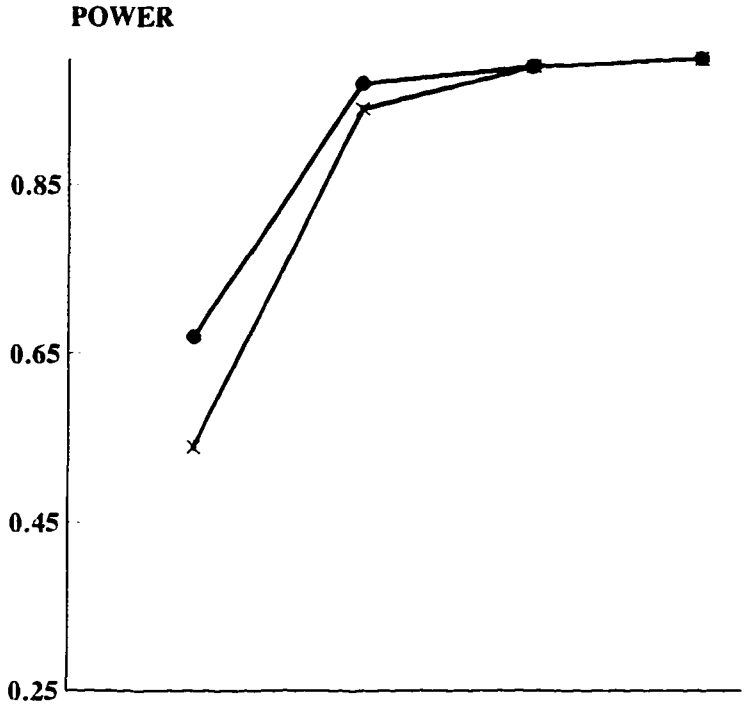
# Power Calculations
# All Chronic Hypertension




| | 1.5 | 2.0 | 2.5 | 3.0 |
|---|---|---|---|---|
| alpha = .10 | 0.5 | 0.84 | 0.97 | 0.99 |
| alpha = .05 | 0.38 | 0.76 | 0.94 | 0.99 |

N = 573

# Power Calculations
# All Pregnancy Induced Hypertension



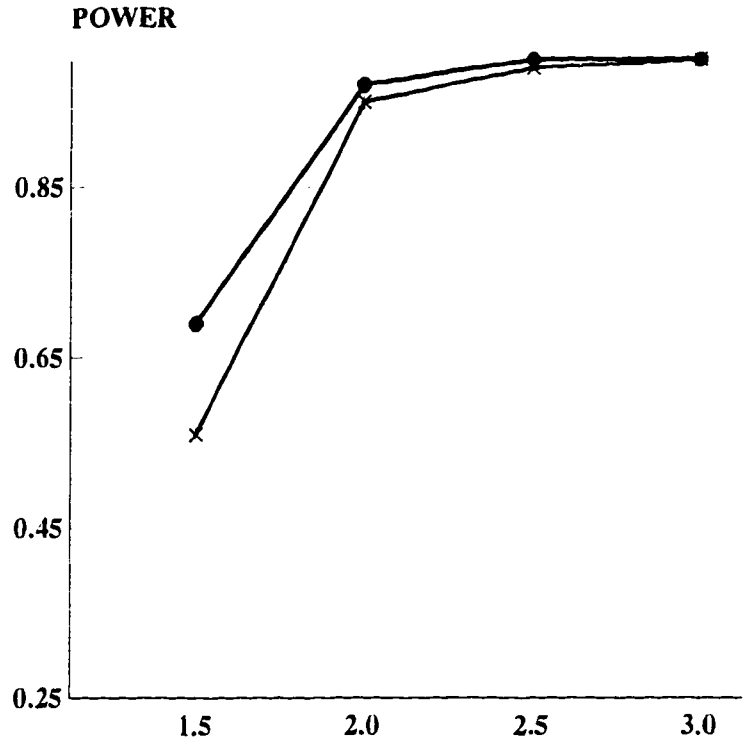

| | | | | |
|---|---|---|---|---|
| alpha = .10 | 0.67 | 0.97 | 0.99 | 1 |
| alpha = .05 | 0.54 | 0.94 | 0.99 | 1 |

ODDS RATIO

alpha = .10 alpha = .05

N = 573

# Power Calculations
# All Hypertension (CHT or PIH)




| | 1.5 | 2.0 | 2.5 | 3.0 |
|---|---|---|---|---|
| alpha = .10 | 0.69 | 0.97 | 1 | 1 |
| alpha = .05 | 0.56 | 0.95 | 0.99 | 1 |

N = 573

## APPENDIX 2

OBAR DATA SHEETS

# PRENATAL HISTORY

OBAR NO. _____ CHART NO _____ INTERVIEWER: _____

NAME. _____ CLINIC: _____ DATE. _____
Last First (M)

| Birthdate Mo Day Yr | Age | Race (circle) W B O | Marital Status (circle) S M W D Sep | Address Zip. Phone: | Medicaid No: |
|---|---|---|---|---|---|

| Plans to Deliver: | Occupation: Homemaker ____ Outside work ____ Student ____ | If outside work type | Last Grade Completed | Emergency Contact: Relationship Phone |
|---|---|---|---|---|

**FAMILY HISTORY**

Code: F—Father M—Mother PGP—Paternal Grandparent MGP—Maternal Grandparent S—Sibling O—Negative

Hypertension ____ TB ____ DES ____
Heart Disease ____ Epilepsy ____ Mult Births ____
Diabetes ____ Allergies-Asthma ____ Comments

| | O-Neg +-Pos | Comments: |
|---|---|---|
| Plans to breast feed? | | |
| Desires T.L.? | | |
| Preg. Planned? | | |

Genetic Screening: Neg Hx ____ Pos Hx ____ If Pos Hx, mark (+) appropriate indications below:

Down's Syndrome (mongolism) ____ Hydrocephalus ____ Cystic Fibrosis ____ Mental Retardation ____
Spinda Bifida ____ Hemophilia ____ A stillborn ____ Other inherited disorders ____
Meningomyelocele ____ Muscular Dystrophy ____ Birth Defect(s) ____ Comments:

**PAST MEDICAL HISTORY**

| History | O-Neg +-Pos | Detail Pos./Remarks Include date & Type of Rx | History | O-Neg +-Pos | Detail Pos./Remarks Include Date & Type of Rx |
|---|---|---|---|---|---|
| Diabetes | | | Drug Sensitivity (Specify & mark chart) | | |
| Hypertension | | | | | |
| Heart Disease | | | | | |
| Kidney Disease | | | Blood Dyscrasia (Anemia) | | |
| Tuberculosis | | | Blood Transfusion | | |
| Rheumatic Fever | | | Rh ABO Sens | | |
| Thyroid Dysfunction | | | Allergies-Asthma | | |
| Epilepsy | | | Operations-Year & Reas | | |
| Varicosities | | | Accidents | | |
| Phlebitis | | | Nervous & Mental | | |
| Herpes | | | GYN Disorder | | |
| Hepatitis B | | | German Measles | | |
| Use of Narcotics | | | Venereal Disease | | |
| Use of Tobacco | | # cigs/day prior to preg ____ | # cigs/day now ____ | | Age onset Smoking ____ Yr |
| Use of Alcohol | | # drinks/wk prior to preg ____ | # drinks/wk now ____ | | Age onset drinking ____ Yr |

**OBSTETRICAL HISTORY—THIS PREGNANCY**

| History | O-Neg +-Pos | Detail Pos./Remarks Include date & Type of Rx | History | O-Neg +-Pos | Detail Pos./Remarks Include date & Type of Rx |
|---|---|---|---|---|---|
| Bleeding | | | Edema | | |
| Vaginal Discharge | | | Abdominal Pain | | |
| Nausea | | | Urinary Complaints | | |
| Vomiting | | | German Measles | | |
| Indigestion | | | Other Viral Illnesses | | |
| Constipation | | | Radiation specify | | |
| Diarrhea | | | Accident | | |
| Headache | | | Medications | | |

Initial Prenatal Visit Site _____

Site Codes:

| | | | |
|---|---|---|---|
| 00-BHC | 05-Faculty | 10-Non Jefco MD Clin | 20 Other |
| 01-CHC | 06-Comp Clin | 11-Non Jefco Pvt MD | |
| 02-EHC | 07-THC | 12-Jefco Pvt MD | |
| 03-NHC | 08-CGH | 13-UAB Family Practice | |
| 04-WHC | 09-UAH | 14-Save a life Campaign | |

Trimester at first prenatal visit _____

0-First 2-Third
1-Second 3-Unknown

Comments

JCDH MR 027 6/85

# PRENATAL PHYSICAL EXAMINATION

OBAR NO _____ CHART NO _____

NAME _____ AGE _____ CLINIC _____

| Full Term | Prem. | Abort. | Live | Mult. Births | Menstrual Periods: Onset / Age - Yrs | LMP: ( ) Known ___/___/___ (LMP / Date) ( ) Approximate (Month known, day uncertain) ( ) Unknown (Month & day unknown) | If day of LMP is uncertain, was it the: ( ) First of the month? ( ) Middle of the month? ( ) End of the month? |
|---|---|---|---|---|---|---|---|

Was the LMP normal in timing, amount, duration? ( ) No ( ) Yes

PAST PREGNANCIES

| Last Ten | Date Mo/Yr | Preg Abort E/S/T | Born A/D | GA Wks. | Weight Lbs/Ozs | Type Del- V/C | Labor (Hours) | Place Deliv | New A/D | Comments / Complications |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | |
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PELVIC EXAM: ( ) Not Examined ( ) Examined DATE OF EXAM: ___/___/___

| Systems | Normal ✓ | ✓ Selected Abnormalities | | | | Other | Detail All Positi |
|---|---|---|---|---|---|---|---|
| 1 Skin | | ( ) Rashes | ( ) Eruptions | ( ) Pallor | ( ) Jaundice | | |
| 2 Eyes | | ( ) Lid Lag | ( ) Unequal Pupils | ( ) Light Reflex | ( ) > Light Reflex | | |
| 3 ENT | | ( ) Abn. Mucosa | ( ) Exudates | ( ) Inflammation | ( ) Hearing Loss | | |
| 4 Mouth/Teeth | | ( ) Caries | ( ) Gingivitis | ( ) Sores | ( ) Dentures | | |
| 5 Neck/Thyroid | | ( ) Asymmetry | ( ) Adenopathy | ( ) Enlarged Thy | ( ) Pulsations | | |
| 6 Chest | | ( ) Asymmetry | ( ) > A-P Diam | ( ) Rub | ( ) | | |
| 7 Lungs | | ( ) < Sounds | ( ) > Sounds | ( ) Rales/Rhonchi | ( ) Wheezing | | |
| 8 Breasts | | ( ) Asymmetry | ( ) Mass/Nodule | ( ) Discharge | ( ) Tenderness | | |
| 9 Heart | | ( ) Abn. Size | ( ) Arrhythmias | ( ) Murmurs | ( ) Sounds | | |
| 10 Abdomen | | ( ) Mass | ( ) Hernia | ( ) Obese | ( ) Scars | | |
| 11 Extremities | | ( ) Varicosities | ( ) Ulcerations | ( ) Edema | ( ) Deformations | | |
| 12 Reflexes | | ( ) Unequal | ( ) Hypoactive | ( ) Hyperactive | ( ) Absent | | |
| Pelvic Exam | | | | | | | |
| 13 Vulva | | ( ) Varicosities | ( ) Vulvitis | ( ) Condyloma | ( ) Lesions | | |
| 14 Perineum | | ( ) Old Lacerations | ( ) Relaxed | ( ) Surgical Scar | ( ) | | |
| 15 Vagina | | ( ) Discharge | ( ) Varicosities | ( ) Cystocele | ( ) Rectocele | | |
| 16 Cervix | | ( ) Open | ( ) Inflamed | ( ) Bleeding | ( ) Lesions | | |
| 17 Adnexa (L) | | ( ) Not Palpable | ( ) Thickened | ( ) Tender | ( ) Masses | | |
| (R) | | ( ) Not Palpable | ( ) Thickened | ( ) Tender | ( ) Masses | | |
| 18 Uterus | | ( ) Sm. for Dates | ( ) Lrg. for Dates | ( ) Fibroids | ( ) | | |
| 19 Rectum | | ( ) Int. Hemorrhoids | ( ) Ext. Hemorrhoids/Mass | ( ) | ( ) | | |

| Pelvimetry | Arch | Coccyx | Sacrum | Ischial Spines | | Adequate | Borderline | Contracted | Prognosis for Delivery |
|---|---|---|---|---|---|---|---|---|---|
| Diagonal Conj ___ cm | o ___ Normal | o ___ Mobile | o ___ Concave | o ___ Average | Inlet | ___ | ___ | ___ | Good ___ Fair ___ |
| Prom. Reached? ___ N/T | ' ___ Wide | ' ___ Forward | ' ___ Straight | ' ___ Prominent | Mid Pelvis | ___ | ___ | ___ | |
| Trans Diam Out ___ cm | ' ___ Narrow | ' ___ Rigid | ' ___ Convex | ' ___ Blunt | Outlet | ___ | ___ | ___ | Signed ___ |

Pelvic Exam and/or Comments

Progress Notes:

## PRENATAL SUBSEQUENT VISITS

OB ARNO _____ CHART NO _____

NAME _____

AGE _____ HGT _____ cm CLINIC _____

Third Trimester Risks
Rh-Negative _____
Previous C/S _____
AS-AC _____
UTI _____
Herpes _____

**FETUS**

- Visit Date (Yr _____ )
- Weeks Gest Best Est
- Ht Fundus (cm)
- Presentation - VTX BR Trans
- FHT Present 1 | 2 / Quadrant 3 | 4 or O - Absent
- Fetal Movement P -present D -decreased A -absent

**OBJECTIVE DATA**

- Sx: +-Present, O-Absent — Edema, Bleeding, Discharge, Dysuria, Other
- Blood Pressure
- Recheck Blood Pressure
- Wt Kg. (Non-Pregnant wt _____ kgs)
- Nutrition Code
- Date WIC Certified ___/___/___
- Routine - Therapeutic R / T
- HGB or HCT
- URINE — Sugar (0/4+), Albumin (0/4+), Testuria CC (0/-), Testuria MC (0/-), Number of Colonies, Ketones
- For Rh neg - Antibody Scr initially & @ 23, 28, 32, 36 wks
- Rhogam Date _____
- Tests — VDRL - Neg / Pos; GC - Neg / Pos; Diabetic Screen - Numeric Value; GTT - Neg / Pos / Eq; Urine Culture - Neg / Pos / Eq

**SONAR**

- Date Sonar Performed
- BPD (wks)
- FL (wks)
- Placental Location Fun/Ant/Post/Prev

- Next Appointment Date
- Site of Next Visit
- RN Name (Initials & Last Name)
- MD Name (Initials & Last Name)

| TEST | Blood/Rh Type | HGB Screen | Ht Titer | UCG | Rubella Screen | Mant. Tine | Pap Smear |
|---|---|---|---|---|---|---|---|
| Date | | | | | | | |
| Results | A B AB O / + - | AA AS SS AC SC Af | | + - | Immune/Not Immune | Neg + | |

**EDC**

EDC Computations From LMP ___/___/___ : ___/___/___ Working EDC ___/___/___

Initial Exam ____ wks on ___/___/___ : ___/___/___

Fetal Heart First Heard on ___/___/___ : ___/___/___ (Revised) ___/___/___

Quickening Noted on ___/___/___ : ___/___/___

NAME: _____

RECORD #: _____

ROUTINE PRENATAL LAB

| | ITEM | DATE | RESULT | NOTED BY | PROBLEM |
|---|---|---|---|---|---|
| Initial Visit | Rh type | | | | |
| | Ab screen | | | | |
| | Pap smear | | | | |
| | VDRL | | | | |
| | GC | | | | |
| | PCV | | | | |
| | Urine C&S | | | | |
| | HI titer | | | | |
| | S-Hgb Screen | | | | |
| | Hepatitis B surf. antigen | | | | |
| 16 weeks | MSAFP | | | | |
| 24-28 weeks | 50gm Glucola screen FBS | | | | |
| | 1 Hr. | | | | |
| | PCV | | | | |
| 28 weeks | RhoGam (if indicated) | | | | |
| 36 weeks | PCV | | | | |
| | Repeat VDRL (if indicated) | | | | |
| | Repeat GC (if indicated) | | | | |

NAME: _____

RECORD #: _____

SPECIAL PRENATAL LAB TESTS

| | DATE: | RESULTS |
|---|---|---|
| Glucose Tolerance Test | _____ | FBS_____ |
| | | 1 hr._____ |
| | | 2 hr._____ |
| | | 3 hr._____ |
| Hemoglobin $A_1C$ | _____ | _____ |
| ANA | _____ | _____ |
| Anticardiolipin | _____ | _____ |
| Lupus Anticoagulant (LAC) | _____ | _____ |
| Thyroid studies: | | |
| $T_3$ Resin Uptake | _____ | _____ |
| Total $T_4$ | _____ | _____ |
| TSH | _____ | _____ |
| Fetal karyotype, AF-AFP | _____ | _____ |

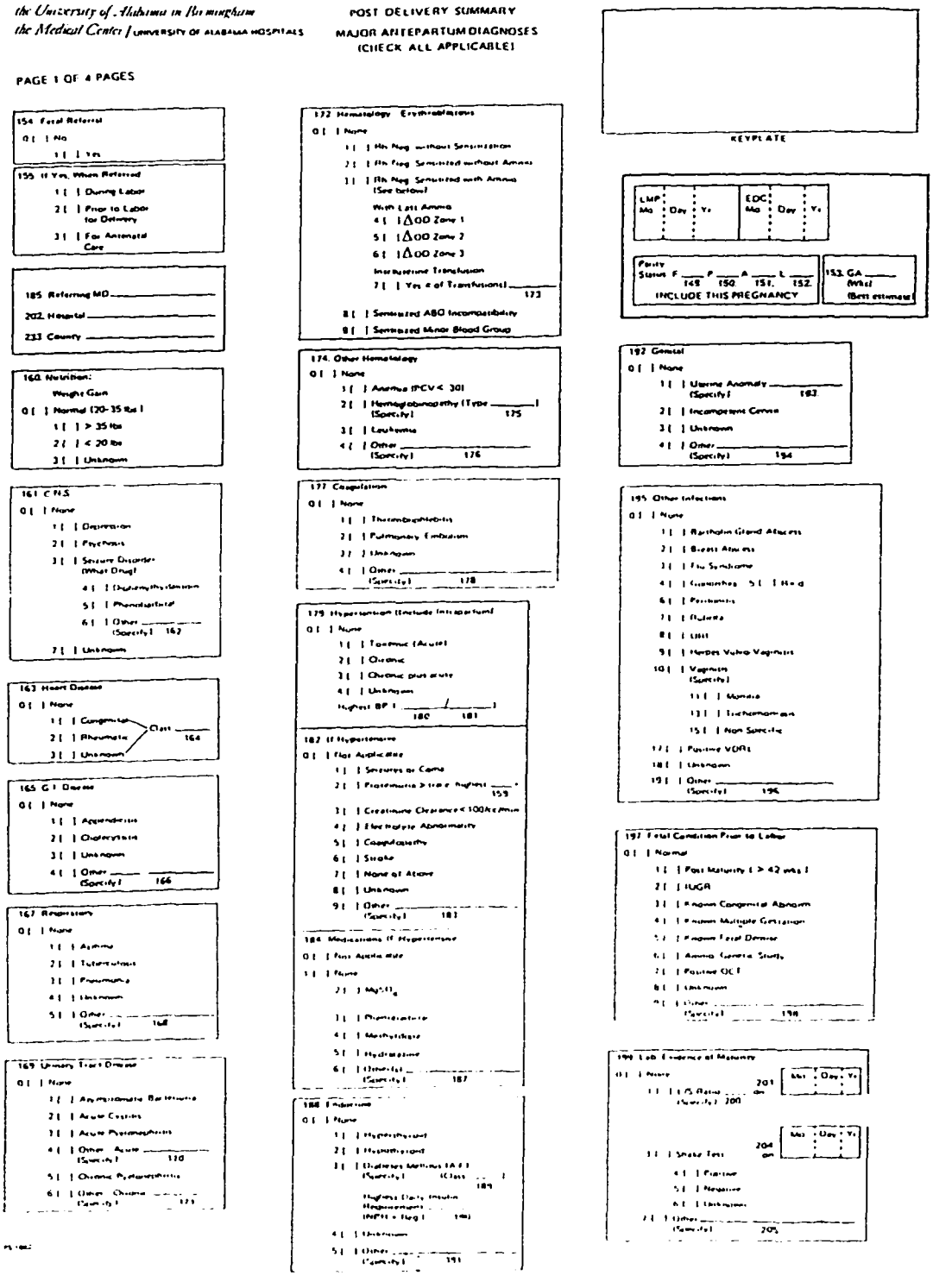
24-hr. Urine

| | Date: __/__/__ | Date: __/__/__ | Date: __/__/__ |
|---|---|---|---|
| Serum creatinine | _____ | _____ | _____ |
| Urine Protein | _____ | _____ | _____ |
| Creatinine clearance | _____ | _____ | _____ |

Other_____

_____

_____



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PAGE 2 OF 4 PAGES

KEYPLATE

206 Cervix (On Admission)
0 [ ] Not Examined 2 [ ] Examined
1 [ ] Unknown

| | 0 | 1 | 2 | 3 |
|---|---|---|---|---|
| 207. Dilatation (Cm) | 0 | 1-2 | 3-4 | 5 |
| 208. Effacement (%) | 0-30 | 40-50 | 60-70 | 80 |
| 209. Station | -3 | -2 | -1-0 | +1 |
| 210. Consistency | firm | med | soft | |
| 211. Position | — | posterior | mid | anterior |

Total Bishop Score _____ 212

213 Premature Labor (< 36 Weeks)
0 [ ] No
1 [ ] Yes, No Attempt to Inhibit
2 [ ] Yes, Attempt to Inhibit (Check Below)
3 [ ] Successful 4 [ ] Failed
5 [ ] Unknown

214 Agent Used to Inhibit Labor
1 [ ] Alcohol
2 [ ] Terbutaline
3 [ ] Other _____ (Specify) 215

216 Labor
0 [ ] No Labor
1 [ ] Spontaneous
2 [ ] Induced
3 [ ] Augmented

If Labor,
218 Date of Onset 249 Date of Delivery
217 Time of Onset 158 Time of Delivery
(Use 24 hr clock) (Use 24 hr clock)

Circle appropriate answer

| | 0 | 1 | 2 | 3 |
|---|---|---|---|---|
| | | hours | | |
| 219 Latent stage (< 1cm/hr) | 0-5 | 5-10 | 10-20 | >20 |
| 221 Active stage (> 1cm/hr) | 0-2 | 2-5 | 5-10 | >10 |
| 157 2nd stage | <1 | 1-2 | 2-3 | >3 |
| 159 3rd stage | <15min | 15 [illegible] | 2 [illegible] | |

223 Labor Curve (Check All Applicable)
0 [ ] No Labor
1 [ ] Normal Labor Pattern
2 [ ] Prolonged Latent Phase (>20 hrs Primigravida; >14 hrs Multigravida)
3 [ ] Protracted Dilatation (>1.0 Cm/Hr Primigravida; >1.5 Cm/Hr Multigravida)
4 [ ] Arrest of Dilatation (Requires C/S)
5 [ ] Protracted Descent (Prolonged 2nd Stage)
6 [ ] Arrest of Descent (Requires C/S or Forceps)
7 [ ] Prolonged 3rd Stage (> 30 Min)
8 [ ] Failed Trial of Labor
9 [ ] Unknown

Indications For Uterine Stimulant (Check All Applicable From Each Column)

| | 224. For Induction | 225. For Augmentation |
|---|---|---|
| 0 [ ] | Not Applicable | |
| 1 [ ] | Elective | 1 [ ] |
| 2 [ ] | Abruptio Placenta | 2 [ ] |
| 3 [ ] | Amnionitis | 3 [ ] |
| 4 [ ] | Chronic Hypertension | 4 [ ] |
| 5 [ ] | Toxemia | 5 [ ] |
| 6 [ ] | Diabetes Mellitus | 6 [ ] |
| 7 [ ] | Erythroblastosis | 7 [ ] |
| 8 [ ] | Positive OCT | 8 [ ] |
| 9 [ ] | PROM | 9 [ ] |
| 10 [ ] | Prolonged Pregnancy | 10 [ ] |
| | Hypotonic Contractions | 11 [ ] |
| | Poor Progress With Adequate Contractions | 12 [ ] |
| 11 [ ] | Other | 13 [ ] |
| | (Specify) | |
| 226 | | 227 |

Primary Indication (Among Those Above)
228 _____

Uterine Stimulant (Not For Placental)

| | 229 For Induction | 230 For Augmentation |
|---|---|---|
| 0 [ ] | None | 0 [ ] None |
| 1 [ ] | AROM | 1 [ ] |
| 2 [ ] | Oxytocin | 2 [ ] |
| 3 [ ] | Prostaglandin | 3 [ ] |
| 4 [ ] | Stripping of Membranes | 4 [ ] |
| 5 [ ] | Other | 5 [ ] |
| | (Specify) | |
| 231 | | 232 |

235 Reaction to Uterine Stimulant
0 [ ] Not Applicable
1 [ ] No Unusual Reaction
2 [ ] No Uterine Response
3 [ ] Sustained Contraction For _____ Min 236
4 [ ] Pressions Increased Uterine Tone
5 [ ] Unknown
6 [ ] Other Unusual Reaction _____ (Specify) 237

238 Diagnosis of CPD (Check All Applicable)
0 [ ] None
1 [ ] By Arrest of Labor
2 [ ] By Physical Exam
3 [ ] By X Ray Pelvimetry

239. X Ray Pelvimetry
0 [ ] None

| | AP | Trans |
|---|---|---|
| 240-241. Inlet | | |
| Mid- 242-243. Pelvis | | |
| 244-245. Outlet | | |

246 Episiotomy
0 [ ] None
1 [ ] Median
2 [ ] Medio Lateral

247 Lacerations (Region)
0 [ ] None
1 [ ] Uterine
2 [ ] Vaginal
3 [ ] Cervical
4 [ ] Perineal - 2°
5 [ ] Perineal - 3°
6 [ ] Perineal - 4°
7 [ ] Other _____ (Specify) 248

250 Cause of Excessive Bleeding
0 [ ] No Excessive Bleeding
1 [ ] Placenta Previa
2 [ ] Placental Abruption
3 [ ] Marginal Sinus Rupture
4 [ ] Uterine Atony
5 [ ] Lacerations
6 [ ] Hematoma
7 [ ] Unknown
8 [ ] Other _____ (Specify) 251

252 Blood Loss at Delivery
0 [ ] Normal
1 [ ] Excessive Amount _____ cc 253

254 Procedures with Delivery
0 [ ] None
1 [ ] Episiotomy
2 [ ] BTL Immediately Postpartum
3 [ ] BTL with C/S
4 [ ] Curettage
5 [ ] Hysterectomy Ligation
6 [ ] Hysterectomy Postpartum
7 [ ] Hysterectomy with C/S
8 [ ] Oophorectomy or Ovarian Cystectomy
9 [ ] Transfusion
10 [ ] Other _____ (Specify) 255

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INFANT SHEET

PAGE 3 OF 4 PAGES (FILL OUT ANOTHER SEPARATE SHEET FOR EACH INFANT)

KEYPLATE

339. Infant's Hosp #

257. This Birth
1 [ ] Singleton
2 [ ] Twin
3 [ ] Triplet

258. If Multiple Birth
1 [ ] Child A (1°)
2 [ ] Child B (2°)
3 [ ] Child C (3°)

Maternal Data

259. *VDRL Results*
0 [ ] Negative
1 [ ] Positive
2 [ ] Unknown

260. Rh Factor
0 [ ] Positive
1 [ ] Negative
2 [ ] Unknown

261. Blood Type
1 [ ] A
2 [ ] B
3 [ ] AB
4 [ ] O
5 [ ] Unknown

328 Placental Wt. _____ gms.

262. Birth weight _____ gms.

263 Sex
1 [ ] Male
2 [ ] Female
3 [ ] Unknown

APGAR SCORES (Specify)
1 Min _____ 264
5 Min _____ 265.

266. Infant Outcome
0 [ ] Alive
1 [ ] Fetal Demise Antepartum
2 [ ] Fetal Demise Intrapartum
3 [ ] Immediate Neonatal Demise

267 If Alive, Infant Condition Prior to Transfer
0 [ ] Satisfactory
1 [ ] Other _____ (Explain) 268

269 Congenital Anomalies
0 [ ] No
1 [ ] Yes _____ (Describe) _____ 270

271 Fetal Monitor
0 [ ] Not Done
1 [ ] External
2 [ ] Internal

272. If Fetal Monitoring (Check All Applicable)
0 [ ] Normal
1 [ ] FHR Baseline < 120 BPM
2 [ ] FHR Baseline > 160 BPM
3 [ ] Decreased Beat-to Beat Variability
Variable Decelerations (Recurrent)
4 [ ] Max. Decelerations < 30 BPM
5 [ ] Max. Decelerations 30-50 BPM
6 [ ] Max. Decelerations > 50 BPM
Late Decelerations (Recurrent)
7 [ ] Max. Decelerations < 10 BPM
8 [ ] Max. Decelerations 10-30 BPM
9 [ ] Max. Decelerations > 30 BPM
Prolonged Decelerations
10 [ ] > 2 Min.
11 [ ] Other _____ (Specify) 273.

274. Fetal Distress Diagnosis By: (Check All Applicable)
0 [ ] None
1 [ ] Fetal Demise PTA
2 [ ] Fetal Demise in Labor
3 [ ] Cord Prolapse
4 [ ] Scalp Ph Lowest _____ 275
5 [ ] Scalp $pO_2$ Lowest _____ 276
6 [ ] Scalp $pCO_2$ Highest _____ 277.
7 [ ] Meconium
8 [ ] Monitor Tracing in Labor
9 [ ] Positive OCT
10 [ ] Shoulder Dystocia
11 [ ] Other _____ (Specify) 278

279. Treatment of Distress (Check All Applicable)
0 [ ] Not Applicable
1 [ ] Untreated
2 [ ] Oxygen by Mask
3 [ ] Change in Position
4 [ ] Immediate Delivery
5 [ ] Other _____

Rupture of Membranes
280 Date of Rupture
Mo : Day : Yr

281. Time of Rupture _____ : _____ (Use 24Hr. Clock)

282. Type of Rupture
0 [ ] Spontaneous
1 [ ] Artificial

Duration of Rupture (To Nearest Hr.)
283. Prior to Onset of Labor _____ (Leave Blank if N.A.)
284. Prior to Delivery _____ (0 Means at Delivery)

285. Reason for Amniotomy
0 [ ] Not Performed
1 [ ] Elective
2 [ ] Terminal in DR or at C/S
3 [ ] Induction of Labor
4 [ ] Augmentation of Labor
5 [ ] Monitor Fetus
6 [ ] Unintentional
7 [ ] Unknown
8 [ ] Other _____ (Specify) 286.

287. Amniotic Fluid
0 [ ] Clear
1 [ ] Meconium
2 [ ] Bloody
3 [ ] Unknown

288 Amniotic Volume
0 [ ] Normal
1 [ ] Oligohydramnios
2 [ ] Polyhydramnios
3 [ ] Unknown

289 Resuscitation (Excluding Bulb Syringe)
0 [ ] None
1 [ ] $O_2$ to Face
2 [ ] $O_2$ with Positive Pressure
3 [ ] Laryngoscopy
4 [ ] Endotracheal
5 [ ] Other _____ (Specify) 290

291. Etiology of Fever in Labor ( > 99.6° )
0 [ ] No Fever
_____ °F Highest Temp with Fever 292.
1 [ ] Amnionitis
2 [ ] UTI
3 [ ] URI
4 [ ] Unknown
5 [ ] Other _____ (Specify) 293.

294. Amnionitis Diagnosis by (Check all Applicable)
0 [ ] Not Applicable
1 [ ] Fever
2 [ ] WBC in AF
3 [ ] Bacteria in AF
4 [ ] Leukocytosis - Based on WBC= _____ 295.
5 [ ] Fetal Tachycardia
6 [ ] Uterine Tenderness
7 [ ] Foul Discharge
8 [ ] Other _____ (Specify) 296

297 Antibiotics in Labor
0 [ ] None
1 [ ] Prophylactic
2 [ ] Indicated (Explain) _____ 298

299 Type (List) _____

300 Cord Pathology
0 [ ] None
1 [ ] Nuchal X1
2 [ ] Nuchal X2
3 [ ] 2 Vessels
4 [ ] True Knot
5 [ ] Hematoma
6 [ ] Vasa Previa
7 [ ] Other _____ (Specify) 301.

306 Other Comments _____

* mm



White copy - chart, yellow copy - nursery, pink copy - computer

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PAGE 4 OF 4 PAGES

## INFANT SHEET

(Fill out another separate sheet for each infant)

KEYPLATE



**302. Site of Delivery**
0 [ ] Delivery Room
1 [ ] Ambulance
2 [ ] Emergency Room
3 [ ] Home
4 [ ] Hospital-Other Rooms, Halls
5 [ ] Hospital - Labor Room
6 [ ] Private Vehicle
7 [ ] Unknown

**303. Labor Analgesia**
0 [ ] None

| | Drug | Total Dosage |
|---|---|---|
| 304.-305. | Demerol | _____ mg |
| 307.-308. | Largon | _____ mg |
| 310.-311. | _____ | _____ mg |

**313. Anesthesia**
0 [ ] None
1 [ ] Local
2 [ ] Paracervical
3 [ ] Pudendal
4 [ ] Conduction
5 [ ] Spinal
6 [ ] $N_2O$ or Penthrane Analgesia
7 [ ] General Endotracheal
8 [ ] Other _____ (Specify) 314

**315. Any Anesthesia Complications**
0 [ ] No
1 [ ] Yes _____ (Explain) 316.

**317. Type of Delivery**
1 [ ] Spontaneous (No manual rotation)
2 [ ] Spontaneous (Manual rotation)
3 [ ] C/S
4 [ ] Elective Low Forceps
5 [ ] Indicated Low Forceps
6 [ ] Indicated Mid Forceps (without Rotation)
7 [ ] Indicated Mid Forceps (with Rotation)
8 [ ] Assisted Breech Extraction
9 [ ] Assisted Breech Extraction with Forceps
10 [ ] Total Breech Extraction
11 [ ] Indicated Vacuum Extraction
12 [ ] Version and Extraction
13 [ ] Destructive Forceps
14 [ ] Other _____

**Presenting Part at Delivery (Check From Each Column)**

| 318 | | 319. | |
|---|---|---|---|
| 1 [ ] | Occiput | 1 [ ] | Anterior |
| 2 [ ] | Mentum | 2 [ ] | Posterior |
| 3 [ ] | Brow | 3 [ ] | Transverse |
| 4 [ ] | Sacrum | 4 [ ] | Unknown |
| 5 [ ] | Shoulder | | |
| 6 [ ] | Unknown | | |

**320. Station Immediately Prior to Forceps or C/S (-4 to +4)**
0 [ ] Not Applicable or _____ Station

**321. If Breech (Before Attempts at Delivery)**
0 [ ] Not Applicable
1 [ ] Frank
2 [ ] Complete
3 [ ] Single Footling
4 [ ] Double Footling
5 [ ] Unknown

**Indications (Check All Applicable)**

| | 322 For Forceps | 323 For Total Breech Extraction |
|---|---|---|
| 0 [ ] | Not Applicable | 0 [ ] |
| 1 [ ] | Elective | 1 [ ] |
| 2 [ ] | Fetal Distress | 2 [ ] |
| 3 [ ] | Maternal Distress | 3 [ ] |
| 4 [ ] | Secondary Arrest of Descent | 4 [ ] |
| 5 [ ] | Aftercoming Head of Breech 2nd Twin | 5 [ ] |

**324. Type of Forceps**
0 [ ] None
1 [ ] Barton
2 [ ] Elliot
3 [ ] Kielland
4 [ ] Piper
5 [ ] Simpson
6 [ ] Tucker McLean
7 [ ] Other _____ (Specify) 325

**326. Placenta**
0 [ ] Normal
1 [ ] Abruption
2 [ ] Accessory Lobe
3 [ ] Acreta
4 [ ] Battledore
5 [ ] Marginal Sinus
6 [ ] Percreta
7 [ ] Previa
8 [ ] Velamentous Insertion
9 [ ] Other _____

**327. Placenta Delivery Method**
0 [ ] Spontaneous Delivery
1 [ ] Expressed
2 [ ] Manual Removal

**329. Cesarean Section**
0 [ ] None
1 [ ] Low Transverse
2 [ ] Low Vertical
3 [ ] Classical
4 [ ] Other _____ (Specify) 330.

**331. Indications for Above (Check all Applicable)**
1 [ ] Abruption
2 [ ] Amnionitis
3 [ ] Breech
4 [ ] Cervical Cerclage
5 [ ] Cord Prolapse
6 [ ] Fetopelvic Disproportion
7 [ ] Diabetes Mellitus
8 [ ] Elderly Primigravida
9 [ ] Erythroblastosis
10 [ ] Elective Repeat
11 [ ] Fetal Distress
12 [ ] Labor Abnormality
13 [ ] Malpresentation other Than Breech
14 [ ] Placenta Previa
15 [ ] Poor OB History
16 [ ] Positive OCT
17 [ ] PROM
18 [ ] Hypertension
19 [ ] Uterine Anomaly
20 [ ] Other _____ (Specify) 332

**Primary Indication (Among Those Above)**
333. _____

**334. Lactation Inhibition**
0 [ ] None with Breast Feeding
1 [ ] None without Breast Feeding
2 [ ] Bromocriptine
3 [ ] Diethylstilbestrol
4 [ ] Stilbestrol
5 [ ] Tace
6 [ ] Other _____ (Specify) 335

Primary _____ Name 336 Code
Secondary _____ Name 337 Code
Attending _____ Name 338 Code
Med Stud _____ Name

PS 1065

KEYPLATE

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Page 5 / MATERIAL DISCHARGE



FILL OUT AT DISCHARGE
(CHECK ALL APPLICABLE)

Discharge B/P ____ / ____
365 366

____ Last PCV Postpartum
393

394 Transfusion
0 [ ] No
1 [ ] Yes

341 Postpartum Hemorrhage
0 [ ] None
1 [ ] Uterine Atony
2 [ ] Retained Placenta
3 [ ] Cervix Laceration
4 [ ] Vaginal Laceration
5 [ ] Uterine Rupture
6 [ ] Hematoma
7 [ ] Other ____ (Specify) 342.

343 Postpartum Infection
0 [ ] No infection
____ °F Highest Temp with infection
344
1 [ ] Episiotomy Infection
2 [ ] Endometritis
3 [ ] Pyelonephritis
4 [ ] Cystitis
5 [ ] Wound Infection
6 [ ] Peritonitis
7 [ ] Septicemia
8 [ ] Fever Unknown Etiology
9 [ ] Atelectasis/Pneumonia
10 [ ] Mastitis
11 [ ] Other ____ (Specify) 345

346 Antibiotics Postpartum
0 [ ] None
1 [ ] Penicillin
2 [ ] Ampicillin
3 [ ] Gentamycin
4 [ ] Clindamycin
5 [ ] Cephalosporin
6 [ ] Chloramphenicol
7 [ ] Other ____ (Specify) 347

348 Miscellaneous Problems
0 [ ] Normal Course
1 [ ] Thrombophlebitis
2 [ ] Pulmonary Embolism
3 [ ] Coagulopathy
4 [ ] Spinal Headache
5 [ ] Stroke
6 [ ] Mechanical Bowel Obstruction
7 [ ] Ileus
8 [ ] Wound Dehiscence
9 [ ] Other ____ (Specify) 349

350 Postpartum Procedures
0 [ ] None
1 [ ] Uterine Packing
2 [ ] BTL Postpartum
3 [ ] Salpingectomy
4 [ ] Hysterectomy
5 [ ] Appendectomy
6 [ ] Hypogastric Ligation
7 [ ] Curettage
8 [ ] Ovarian Cystectomy
9 [ ] Oophorectomy
10 [ ] Wound Resuturing
11 [ ] Other ____ (Specify) 351.

352. Immunization
0 [ ] None indicated
1 [ ] Rhogam
2 [ ] Rubella
3 [ ] Other ____ (Specify) 353

354 Contraceptive Counseling
0 [ ] No
1 [ ] Yes (See below)

355 Method Chosen
0 [ ] None Desired
Tubal Ligation
1 [ ] Done Postpartum
2 [ ] To be scheduled
IUD
3 [ ] Inserted Postpartum
4 [ ] To be done later
Oral Contraceptives
5 [ ] Rx prescribed in Hospital
6 [ ] Ovral
7 [ ] Norinyl 1 50
8 [ ] Norinyl 1 80
9 [ ] Other ____ (Specify) 356
10 [ ] To be prescribed later
11 [ ] Condoms/Foam
12 [ ] Diaphragm
13 [ ] Other ____ (Specify) 357

363 Are Oral Contraceptives contraindicated?
0 [ ] no 1 [ ] yes If yes, why? ____
364

358 Discharge Medications (other than oral contraceptives)

| 0 [ ] None | Name | Dose | Schedule | Duration |
|---|---|---|---|---|
| 359, 360 | Iron Sulfate | ____ | Mg/Day | ____ |
| | ____ | ____ | ____ | ____ |
| | ____ | ____ | ____ | ____ |
| | ____ | ____ | ____ | ____ |

383 Maternal Death
0 [ ] No
1 [ ] Yes (Explain)
____
384.

Followup Needed
375. [ ] 0 Routine
at ____ clinic in ____ wks
380. 381
If not routine, explain problem
376. ____
Place ____ wks ____
377. ____
Place ____ wks: ____
378. ____
Place ____ wks ____
379 ____
Place ____ wks ____
Mo Day Yr
387 Date of Discharge ____ ____ ____

389 Other Comments
____
____
____

Current Information
509 Phone ____
511 St. ____
512 City ____ 514 Zip ____

Primary ____
Name 390
Secondary ____
Name 391
Attending ____
Name 392
Med. Stud. ____
Name

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DISCHARGE FORM

Key Plate

NAME:_____ HOSP. NO.:_____ ROOM:_____

SURG.:_____ ASSIST:_____

DATE OPER. OR E.D. VISIT_____ ADMITTED:_____ DISCHARGED:_____

DOCTOR/SERV.:_____ DICTATED:_____ TRANSCRIBED:_____

1 DIAGNOSIS PROCEDURES
2 1. Mature/Premature/Post-term Birth, Living Child
3 2. Appropriate/Small/Large Size for Gest. Age
4 3.
5 4.
6 5.
7 6.
8 ADMISSION HISTORY: This ____ gm White/Black Female/Male twin #/singleton born at____hrs.,__
9
10 is a product of a ___ y/o F___ P___ A___ L___ following a ___ wk gestation.
11 Apgar 1' ___ Pregnancy:
12 5' ___ Labor
13 Resus- ___ None ___ abn FHT:
14 citation ___ $O_2$ to face ___ meconium:
15 ___ $O_2$ by Pos Pres Delivery:
16 ___ intubated
17 ___ drugs(specify)
18
19 ADMISSION PHYSICAL EXAM: NORMAL ABNORMAL Gestational Age_____Wks.
20 COMMENTS:
21 Congenital Anomalies:
22 1.
23 2.
24 HOSPITAL COURSE: NORMAL ABNORMAL
25
26
27 DISCHARGE PHYSICAL EXAM: NORMAL ABNORMAL DISCHARGE WEIGHT:_____
28 COMMENTS:
29
30
31 LABORATORY DATA: RF_____ IFA TOXO_____ VDRL_____
32 MAXIMUM BILIRUBIN: Indirect_____ Total_____
33 OTHER:
34 Blood Type: ___
35 Rh: ___
36 Coombs': ___
37
38 DISPOSITION: WELL BABY CLINIC:_____; CHILDREN'S CLINIC_____; PRIVATE:_____
39 Followup in _____week(s) Family Practice Center
40
41 OTHER: Breast/Bottle Feeding
42
43 MEDS: 1.
44 2.
45 3
46 _____, M.D.

# School of Public Health
# University of Alabama at Birmingham
# Dissertation Approval Form

Name of Candidate: Richard Sinsky

Major Subject: Public Health (Epidemiology)

Title of Dissertation: An Epidemiologic Investigation of the Possible Association Between Maternal Diabetes and Maternal Hypertension and Placental Infection with Ureaplasma Urealyticum

Dissertation Committee:

Rodney C.L. Ho, Chair

David N. Cassell

Robert Weckerly

Laura Rubenstein

Lynne Wagenknecht

Department Chair — Date

Academic Affairs Dean — Date: 3-7-97

Dean, School of Public Health — Date: 1-10-97