

# OUTCOME OF SUBSEQUENT PREGNANCIES FOLLOWING ANTIBIOTIC THERAPY AFTER PRIMARY OR MULTIPLE SPONTANEOUS ABORTIONS

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*The course of the subsequent pregnancy and the maternal and fetal complications were evaluated in 254 couples who were seen in an infertility clinic after primary or multiple spontaneous abortions. The 100 couples who were treated with antibiotics after pregnancy loss showed a significantly better chance of achieving a subsequent pregnancy. The outcome of pregnancy was significantly better in the antibiotic treated group and the rate of spontaneous abortion recurrence was significantly lower (10 versus 38 per cent). The number of maternal complications was significantly less in the treated group—premature rupture of membranes, three (4 per cent) versus 30 (46 per cent), and postpartum fever, three (4 per cent) versus 23 (35 per cent), respectively. The untreated group experienced a significantly lower percentage of vaginal delivery (56 versus 69 per cent) ( $p < 0.001$ ). In the antibiotic treated group, there were significantly lower rates of fetal complications, including fetal distress, meconium, respiratory distress syndrome, neonatal infection and hyperbilirubinemia. The mean birth weight of infants in the antibiotic treated group was significantly higher (3,529 versus 3,090 grams;  $p < 0.001$ ). Prematurity and postdatism were significantly less frequent in the antibiotic treated group, and the corresponding Apgar scores were significantly better. We, thus, postulate that certain spontaneous abortions may be caused by bacteria present in the genital tract at the time of conception. These bacteria may have an adverse effect on the course of pregnancy and result in increased maternal and fetal complications.*

THE FACTORS which determine the implantation of an intrauterine pregnancy, the course of the pregnancy, events surrounding the delivery and maternal and fetal complications during or after delivery are largely unknown. There is, however, growing evidence that bacterial colonization of the genital tract may be a relevant factor in cer-

tain instances of pregnancy loss and premature rupture of the membranes followed by premature delivery with maternal and fetal infections (1-4). Since early 1977, we have recommended systemic, broad spectrum antibiotic therapy for infertile couples with a past history of spontaneous abortions or premature delivery with maternal or fetal infections. To cover chlamydia and mycoplasma, a four week course of a tetracycline was routinely prescribed to husband and wife. If the results of aerobic and anaerobic bacteria studies of the seminal fluid revealed other organisms, not considered by us to be normal flora of the male genital tract (5), this basic treatment regimen was complemented with specific antibiotics until cultures with negative results were obtained.

This retrospective study was undertaken to compare the pregnancy rate, the courses of pregnancy, the perinatal maternal and fetal morbidity and the outcome of the newborn in those patients to whom antibiotics were administered after primary or multiple spontaneous abortions as compared with a group who did not receive antibiotics prior to the conception of the next pregnancy.

## MATERIALS AND METHODS

*Patient material.* Couples involved in the study were drawn from the patient material of The MacLeod Laboratory for Infertility. Patients were either referred to us from practicing gynecologists for evaluation of the male partner or were among the private patients we studied who were treated during the same time period.

Between January 1979 and 1 July 1981, the medical team at The MacLeod Laboratory has consulted or directly treated 306 infertile couples from the greater metropolitan area in which the wife had experienced one or more prior miscarriages. The seminal fluid of the husband was routinely cultured for mycoplasma, *Chlamydia trachomatis* and aerobic and anaerobic orga-

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TABLE I.—FREQUENCY OF ANTIBIOTIC USAGE

	On antibiotics				p Value
	No		Yes		
	No.	Per cent	No.	Per cent	
Prior miscarriages					<0.008
1 .....	90	70	39	30	
2 .....	42	54	36	46	
3 or more .....	22	47	25	53	
Years trying for pregnancy					<0.001
Less than 0.5 years .....	42	45	51	55	
More than 0.5, less than one year .....	24	56	19	44	
More than one year .....	88	75	30	25	
Positive culture .....	60	42	84	58	<0.001
Empirical .....	94	85	16	15	
Laparoscopy/HSG					<0.001
No .....	54	48	59	52	
Yes .....	100	71	41	29	
Fertility drugs					<0.002
No .....	79	53	71	47	
Yes .....	75	72	29	28	

HSG, Hysterosalpingography.

nisms. All of the couples were advised to begin a four week therapy course of Vibramycin® (doxycycline). If cultures were positive for mycoplasma or for aerobic and anaerobic organisms after the four week doxycycline therapy course, additional antibiotics were ordered according to the sensitivity report.

Of the 100 couples who elected to take antibiotics, 96 used 100 milligrams twice daily of doxycycline for four weeks and four used 500 milligrams four times one daily of tetracycline for four weeks. In addition, 49 used 500 milligrams four times one daily for two weeks, four patients took 500 milligrams four times one daily of erythromycin for two weeks and four patients received other nontetracycline type antibiotics, such as ampicillin or Keflex® (cephalexin). Sixty-one per cent of the couples who accepted the recommended antibiotic treatment regimen received two or more different types of drugs with the maximum length of total antibiotic therapy of 12 weeks. All of the antibiotics were ordered for both husband and wife, and when they were ordered for specific bacteria treatment, a follow-up culture was requested approximately two or three weeks after the conclusion of the course of therapy.

Of the 306 couples who were referred to us during this period, detailed follow-up studies, including direct telephone conversations with the patients and referring physicians, were available for 254 (83 per cent) of these women, after excluding those couples who reported that they had stopped trying for a pregnancy or divorce or separation had occurred. For this reason, only those

patients who took more than two weeks of antibiotics were considered to be adequately treated.

*Microbiologic studies.* For culturing mycoplasma, a sample of 0.2 milliliter of seminal fluid and a cervical swab specimen were inoculated into a 5 milliliter U9 broth and on to an A7 differential agar as described elsewhere (6). For cultivation and identification of *Chlamydia trachomatis*, McCoy cells, purchased from Microbiological Associates (M. A. Bioproducts) were used. These were inoculated after centrifugation of the specimens on to the cells treated with cycloheximide after the procedure of Schachter and Dawson (7). Inoculated cells were incubated at 35 degrees C. for 65 hours. Inclusions were identified using iodine stain or by direct immunofluorescence staining using fluorescein isothiocyanate labeled rabbit anti-*Chlamydia trachomatis* gamma globulin. For the aerobic and anaerobic cultures, Port-A-Cul reduced media (BBL Microbiology Systems Becton Dickinson and Co.) were used for transporting specimens to The Diagnostic Microbiology Laboratory of The New York Hospital where standard procedures or gas chromatography was used to aid in the identification.

Among the 100 couples who accepted the antibiotic therapy, bacteria were isolated from the seminal fluid of the husband. These were: mycoplasma only, 29; aerobic and anaerobic bacteria only, nine; chlamydia only, 13; mycoplasma and aerobic and anaerobic bacteria, eight; mycoplasma and chlamydia, 12; aerobic and anaerobic bacteria and chlamydia, five; mycoplasma, aerobic and anaerobic bacteria and chlamydia, eight, and no isolate, 16.

For those with aerobic and anaerobic bacteria, additional antibiotic therapy was prescribed. These were: Peptococcus species, 12 couples; Group B streptococcus, four couples; Bacteroides species, three couples, Fusobacterium, two couples; Veilonella, two couples; Klebsiella, one couple, and *Escherichia coli*, one couple. The most common reason for erythromycin therapy was a tetracycline resistant mycoplasma infection (27 couples).

*Maternal and fetal complications.* Pre-eclampsia was defined as hypertension developing during the pregnancy in excess of 140 systolic over 90 millimeters of mercury diastolic pressure with proteinuria or edema, or both. The diagnosis of chorioamnionitis was made on the basis of temperature elevation, physical examination and laboratory findings (foul smelling amniotic fluid; uterine tenderness, fetal tachycardia, changes in

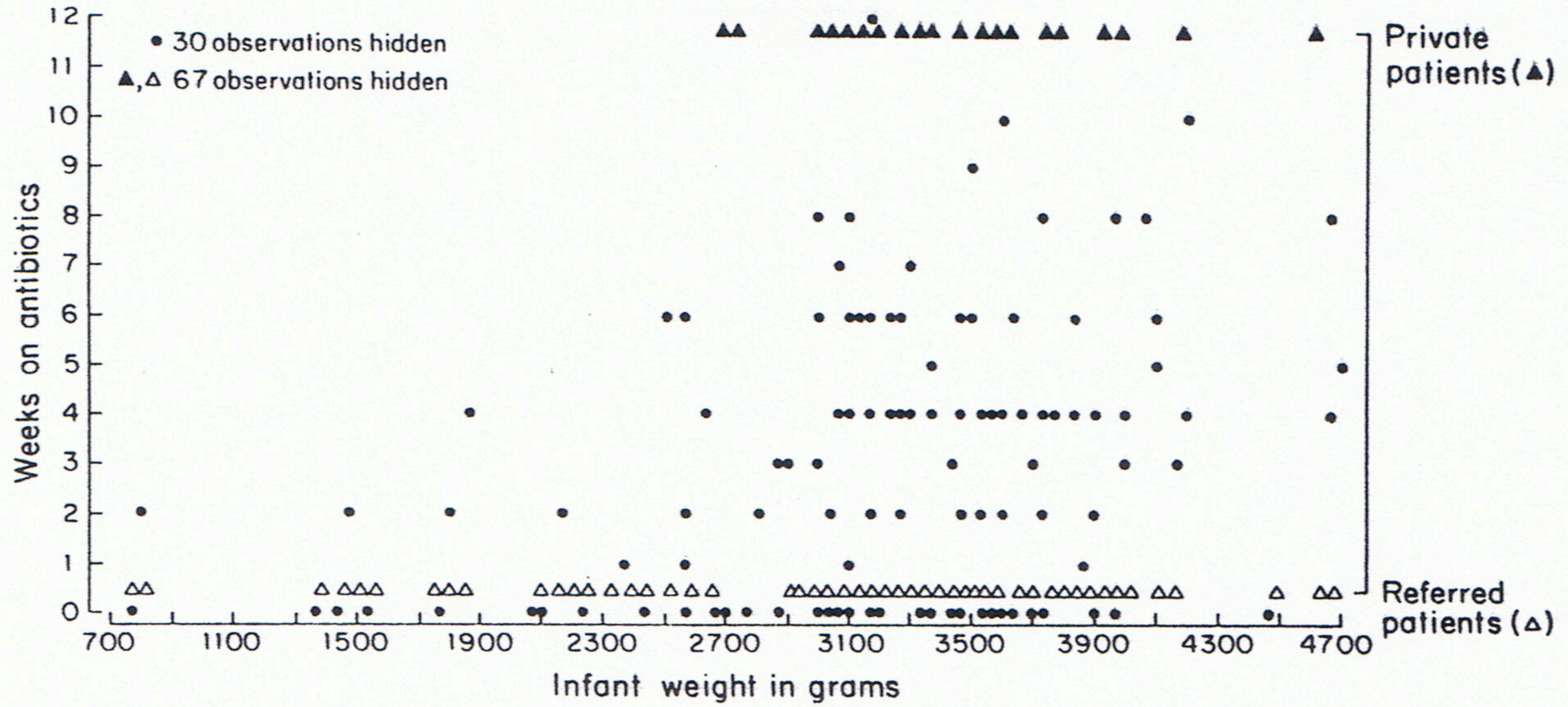


FIG. 1. Dose response relationship between birth weights of newborns and length of antibiotic therapy (closed circles). Comparisons of birthweights of newborns in the private patient group (closed triangles) and among the referred patients (open triangles).

complete blood count and gram stain obtained from the amniotic fluid through amniocentesis). From asymptomatic bacteriuria (more than 100,000 colonies per milliliter) to symptomatic involvement of any part of the urinary tract, patients were registered to have an infection of the urinary tract. Abruptio placenta and placenta previa (partial or complete) were recorded when the classical physical and clinical signs of the condition existed. Incompetent cervix uteri was registered when painless dilation of the cervix uteri was recorded during the second trimester. When the membranes ruptured prior to 38 weeks of completed gestation irrespective of the presence of uterine contractions, premature rupture of the membranes was recorded. Postpartum fever was defined as any temperature elevation that occurred 24 hours after delivery and was recorded at least on two separate occasions and was in excess of 38 degrees C. Postpartum hemorrhage was recorded when blood loss within the first 24 hours post partum exceeded 500 milliliters according to the subjective estimation of the delivering physician. Neither the color nor the consistency of the meconium but rather the presence or absence of it was recorded.

Maternal and fetal indications for cesarean sections were derived from the notes of the delivering physician entered on the patient chart. The most commonly given maternal reasons for cesarean section were cephalopelvic disproportion, lack of progress during labor or previous cesarean section. The most commonly observed fetal indication for cesarean section was fetal dis-

tress, changes observed in fetal heart rate patterns as registered by fetal heart rate monitoring. Since several patients were delivered in hospitals where heart rate tracings were not available for review, the diagnosis of fetal distress was accepted according to the judgement of the delivering physician.

The fetal complications listed herein are registered from the history of the newborn. The respiratory distress syndrome was recorded when characteristic difficulty with breathing was encountered with clinically obvious chest retractions, expiratory grunting, cyanosis with or without typical roentgenographic findings of widespread atelectasis of the lungs and subsequent hyaline membrane formation. The infections recorded during the neonatal period were: conjunctivitis, septic skin infection, gastrointestinal tract infection, omphalitis and urinary tract infection. Congenital malformations and intra-

TABLE II.—LENGTH OF ANTIBIOTIC THERAPY AND FERTILITY OUTCOME

Weeks on antibiotics	No pregnancy,		Mis-carriage,		Viable delivery,		Total,	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
None . . . . .	41	36	29	25	45	39	115	45
2 Weeks or less.	12	31	7	18	20	51	39	15
4 Weeks . . . . .	12	21	5	9	39	70	56	22
More than 4 weeks, less or equal 6 weeks	7	23	2	7	21	70	30	12
More than 6 weeks . . . . .	2	14	0	0	12	86	14	6
Total . . . . .	74	29	43	17	137	54	254	100

p<0.001.

TABLE III.—MATERNAL AND FETAL COMPLICATIONS

	Antibiotics				p Value
	No		Yes		
	No.	Per cent	No.	Per cent	
MATERNAL					
Premature rupture of membranes					
No	35	54	69	96	<0.001
Yes	30	46	3	4	
Mode of delivery					
Vaginal	36	56	50	69	<0.001
Cesarean section for maternal indications	6	9	19	26	
Cesarean section for fetal indications	22	34	3	4	
Postpartum fever					
No	42	65	69	96	<0.001
Yes	23	35	3	4	
FETAL					
Fetal distress					
No	40	62	67	93	<0.001
Yes	25	38	5	7	
Meconium					
No	52	80	69	96	<0.001
Yes	13	20	3	4	
Respiratory distress syndrome					
No	52	81	70	99	<0.001
Yes	12	19	1	1	
Neonatal infection					
No	61	94	72	100	<0.05
Yes	4	6	—	—	
Hyperbilirubinemia					
No	46	71	67	93	<0.001
Yes	19	29	5	7	
Congenital malformation					
No	59	91	71	99	NS
Yes	6	9	1	1	
Intracranial hemorrhage					
No	63	97	72	100	NS
Yes	2	3	—	—	
Intrauterine growth retardation					
No	56	86	68	96	NS
Yes	9	14	3	4	

One patient with mode of delivery unknown; two patients with respiratory distress syndrome unknown; one patient with intrauterine growth retardation unknown.

cranial hemorrhage of the infants were recorded on the basis of clinical signs and gross morphologic appearances. Infants were classified as growth retarded if the birth weight fell below the tenth percentile for the particular gestational age. Diagnosis of neonatal hyperbilirubinemia was based upon the judgement of the pediatrician whether or not the serum bilirubin concentration exceeded usual normal limits for weight or gestational age of the infant. Deviation from ideal gestational age of 275 to 285 days was also recorded.

*Statistical analysis.* Gross classified categorical data were analyzed using chi-square test for Fisher exact test, as appropriate. To investigate the effect of antibiotic therapy in other potentially influencing factors, a multivariate analysis was done using multiple logistic regression (8).

In the context of this investigation, logistic regression was used to determine which factors were associated with an outcome even in the presence of other significantly associated variables. The predictor variables used in the logistic regression were: use of antibiotics (yes or no); reason for antibiotic prescription (positive cultures or empirical); age; race (white, black or other); occupation (blue or white collar); order of marriage (first or second); previous live births in this marriage (yes or no); number of previous miscarriages (one, two, three or more); number of years trying to achieve pregnancy (less than 0.5,  $0.5 \leq 1$ ,  $>1$  year); usage of fertility drugs (yes or no); previous dilation and curettage; myomectomy; tuboplasty; laparoscopy; Shirodkar procedure; use of tocolytic agents and whether the patient was a referred or a private patient (one of ours).

Results of all regression analyses are presented by listing the significant variables (including intercept) and their associated regression coefficients and p values. Analysis was performed only on outcome variables when there were 10 per cent or more outcome events. Results of all statistical analyses were declared significant if  $p < 0.05$ .

## RESULTS

*Comparability of the groups.* Comparisons of couples were made with respect to demographic factors, fertility history, gynecologic procedures and medical history. When analyzing the entire group, 100 of the 254 couples (39 per cent) used more than two weeks of antibiotics. However, when contrasting the private patients ( $n=49$ ) to the referred patients, a significantly higher number of the former group received antibiotics (76 versus 31 per cent,  $p < 0.001$ ). When analyzing the entire group or the private patients separately, there was no association between the decision of the patient to follow the antibiotic treatment plan and race, age, occupation, order of marriage (that is, first marriage, second marriage and so on), occurrence of previous live births, past history of dilation and curettage, myomectomy, tuboplasty, Shirodkar procedure or use of tocolytic agents. The number of patients with a history of diabetes, hypertension, disease of the thyroid gland, smoking, alcoholism or drug abuse was too small to make any meaningful intergroup comparisons.

For all patients, significant associations were found for five factors. The frequency of antibiotic usage increased with the increasing number of prior spontaneous abortions ( $p < 0.008$ ) and de-

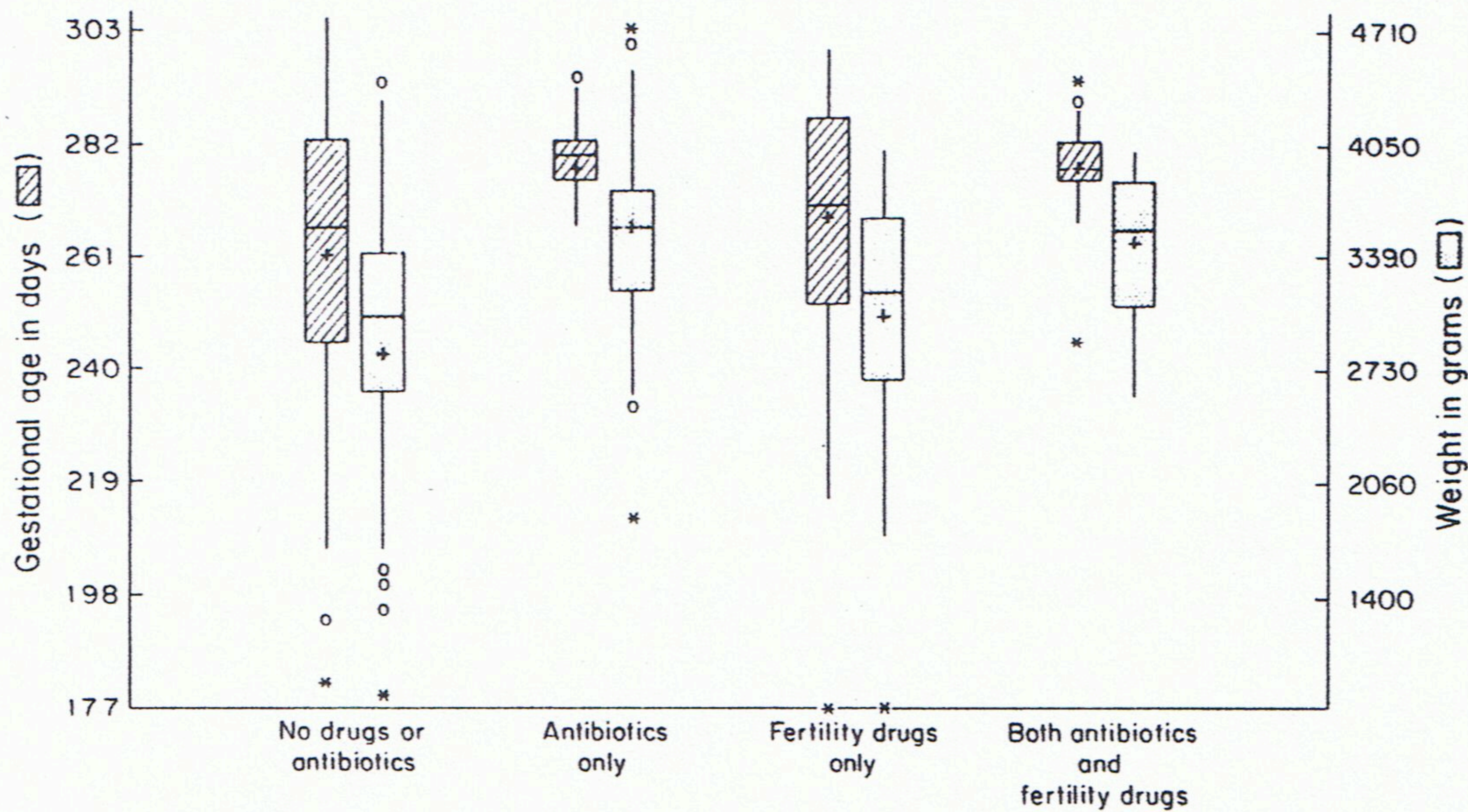


FIG. 2. Comparisons of birthweights and gestational ages in the four groups studied.

creased with increasing length of time trying for a successful pregnancy ( $p < 0.001$ ). Patients with a positive finding at culture (especially with the presence of chlamydia) were more likely to use antibiotics than those patients with a negative culture ( $p < 0.001$ ). Twenty-nine per cent of the women who had had a laparoscopy in the past took antibiotics as compared with 52 per cent of the women who had not had a prior laparoscopy ( $p < 0.001$ ). Women who had taken fertility drugs were less likely to have taken antibiotics (28 per cent) than those who had not taken fertility drugs (47 per cent) ( $p < 0.02$ ). In Table I, the details of these findings are given.

**Fertility outcome.** Couples who used antibiotics were more likely to achieve a pregnancy (70 per cent) than those who did not (66 per cent) ( $p < 0.03$ ). When contrasting the material for the private patients we studied with those for the referred patients, our 63 per cent pregnancy rate did not differ significantly from the 52 per cent pregnancy rate observed in the latter group. Of the 254 women observed, 180 eventually became pregnant. One hundred and thirty-seven (76 per cent) delivered a viable infant. Antibiotic users had a reduced likelihood of subsequent abortion (10 versus 38 per cent) ( $p < 0.01$ ). Of the 43 women who aborted, the trimester of abortion was unrelated to the use of the antibiotics. When examining length of antibiotic therapy and chance to abort the following pregnancy, there was a significant correlation ( $p < 0.001$ ) between length of antibiotic therapy and reduced number of subsequent abortions (Table II).

**Maternal and fetal complications.** When examining pregnancy related complications in the mother, there were no significant antibiotic related differences found in the incidence of pre-eclampsia, urinary tract infection, chorioamnionitis, abruptio placentae, incompetent cervix and postpartum hemorrhage. It has to be mentioned, however, that, except for pre-eclampsia and urinary tract infection, all other mentioned pregnancy related complications occurred only among patients who did not receive antibiotics. The incidence of premature rupture of membranes and postpartum fever was significantly less frequent in the treated group, three (4 per cent) versus 30 (46 per cent) and three (4 per cent) versus 23 (35 per cent), respectively.

In the untreated group, there was a significantly lower percentage of normal vaginal delivery (56 versus 69 per cent) ( $p < 0.01$ ). When cesarean section was indicated, however, in the untreated group, a significantly higher percentage was indicated for fetal reasons while the majority of patients in the antibiotic treated group were cesarean sections for maternal reasons. The incidence rates of meconium during labor and fetal distress developing during the labor process were significantly lower among those women who were treated with antibiotics prior to conception.

In examining neonatal fetal complications, there was a significantly higher occurrence of respiratory distress syndrome, infection and hyperbilirubinemia among those infants who were born to mothers without antibiotic therapy. Congenital malformation, intracranial hemor-

TABLE IV.—FIRST MINUTE APGAR SCORE

Score	—Not treated—		—Antibiotic treated—	
	No.	Per cent	No.	Per cent
1	1	2		
2	2	3		
3	1	2		
4	4	6		
5	4	6		
6	1	2		
7	10	15	3	4
8	8	12	3	4
9	34	52	66	92

rhage and intrauterine growth retardation did not show a significant difference, although most of the affected infants were born to mothers who did not receive antibiotic therapy (Table III).

When comparing the Apgar scores, it is evident again that those patients who received antibiotics tended to deliver babies with seven or more one minute Apgar scores, while there was a wide spread of Apgar scores assigned to babies who were born to mothers who had not received antibiotic therapy (Table IV). There was a significant dose response relationship between the length of antibiotic therapy in weeks and the one minute Apgar score. None of the babies whose mothers received antibiotics for six weeks or more had less than a 9 one minute Apgar score while only 80 per cent of the babies delivered by mothers without antibiotic therapy had a 7 or more one minute Apgar score.

When comparing fetal weight between the antibiotic treated and nontreated group, there was a highly significant dose response relationship between larger babies and the length of antibiotic therapy (Fig. 1, closed circles). The mean weight of infants delivered to mothers without antibiotics was 3,090 grams, significantly contrasting the mean body weight 3,529 grams of infants who were born to mothers with antibiotic therapy ( $p < 0.001$ ). The time of delivery was also significantly affected by the administration of antibiotics. In Figure 2, the delivery dates and the size of the infants in four subdivisions of the group who finally delivered a viable infant are compared. Those who did not receive any treatment, 41 (30 per cent); those who received antibiotic therapy only, 61 (45 per cent); patients who conceived after fertility drugs only, 24 (18 per cent), and finally, the fourth group shows the birth weight and time of delivery of patients who conceived after both fertility drugs and antibiotic combination therapy, 11 (8 per cent).

The results of separate analysis of the patients we studied in contrast with the referred group revealed several significant differences. Among the private patient material, there was a signifi-

cantly higher number of blacks and blue collar workers ( $p < 0.001$ ). In the material from the patients we studied, when cesarean section was indicated in 88 per cent, it was for maternal reasons and in 12 per cent for fetal reasons. This significantly contrasted with the indications among the referred group where 43 per cent was indicated for maternal reasons and 57 per cent for fetal reasons ( $p < 0.001$ ). Seventy-four per cent of the patients we studied delivered vaginally while only 60 per cent of the referred patients experienced vaginal delivery ( $p < 0.001$ ). Similarly, a significant difference was observed in the rate of postpartum fever. The patients we studied had a 6 per cent postpartum fever rate contrasting significantly with the 23 per cent postpartum fever rate of the referred group ( $p < 0.05$ ).

Similar significant differences were observed in the frequency of meconium (zero versus 14 per cent), and fetal distress (6 versus 26 per cent) ( $p < 0.03$  and  $p < 0.04$ ). The private patients also delivered significantly larger infants (Fig. 1, triangles). For infants delivered in our group ( $n = 31$ ), all assigned Apgar scores were above 7. Among the referred patients, 13 of 106 babies were assigned less than a 7 one minute Apgar score (15 per cent). When analyzing fetal complications, in every single category, the patients we studied experienced significantly fewer complications ( $p < 0.02$ ).

*Multivariate analysis.* The logistic regression model was used to investigate possible predictive factors for three types of outcomes: 1, subsequent pregnancy in all 254 patients who had experienced a miscarriage; 2, delivery of a viable infant (that is, absence of miscarriage) among the 180 patients who did become pregnant, and 3, various maternal and fetal complications among the 137 patients who delivered a viable infant. Details of the results are listed in Table V.

The number of years trying to become pregnant was the only variable which was significantly associated with achieving a subsequent pregnancy ( $p < 0.001$ ). The longer a couple had been trying to conceive, the less likely it was that a pregnancy would occur.

In the group of 180 patients who became pregnant, three factors were significantly associated with a subsequent abortion: lack of antibiotic usage ( $p < 0.001$ ), several prior miscarriages ( $p < 0.001$ ) and increased length of time trying to conceive ( $p < 0.01$ ). The odds of abortion among nonusers of antibiotics was 7.3 times more than for users.

Of the 137 patients who delivered a viable in-

fant, the use of antibiotics was associated with a decreased risk of meconium ( $p < 0.007$ ), fetal distress ( $p < 0.001$ ), premature rupture of membranes ( $p < 0.001$ ), postpartum fever ( $p < 0.001$ ), respiratory distress syndrome ( $p < 0.009$ ), hyperbilirubinemia ( $p < 0.004$ ), birthweight below 3,000 grams ( $p < 0.001$ ) and deviation from the ideal delivery date of 280 days ( $p < 0.001$ ). Fetal distress, hyperbilirubinemia and deviation from the ideal gestational age were also significantly associated with increased number of years trying to become pregnant ( $p < 0.03$ , 0.004 and 0.05, respectively). Also, patients in whom the recommendation for antibiotic treatment was based upon empirical grounds had a lower risk of hyperbilirubinemia ( $p < 0.04$ ). The odds of having these complications ranged from 5.0 to 18.7 times higher for nonusers of antibiotics as compared with users.

DISCUSSION

The results of this study suggest that, after a spontaneous abortion, an infertile couple treated with antibiotics has a significantly better chance of experiencing an uncomplicated full-term pregnancy with significantly reduced maternal and fetal morbidity than a couple who is allowed to conceive the subsequent pregnancy without administration of antibiotics. Since the study was a nonrandomized, retrospective analysis, despite the attempt to compare the treated and nontreated groups, we recognize the possibility of chance occurrence of some of these observations.

All of the antibiotics or antibiotic combinations were broad spectrum, with coverage for mycoplasma, chlamydia and a wide range of aerobic and anaerobic organisms. All treatments were continued until negative cultures were obtained. We, therefore, suspect that the elimination of one or several of these micro-organisms was the reason behind the more favorable outcome. The significant difference between the outcome of the pregnancies in the patient material we studied when contrasted with the referred group further suggests an antimicrobial effect. We tend to use antibiotics much more liberally and a higher percentage of the patients we studied received longer or multiple drug coverage. The patients in our study had a significantly higher percentage of lower socioeconomic class patients and a higher number of blacks when compared with the referred patients. Disadvantageous socio-economic background has been invoked as a cause behind unfavorable pregnancy outcome (9). In addition, we suspect, however, that a higher number of

TABLE V.—LOGISTICS REGRESSION ANALYSIS OF CERTAIN PREDICTORS ON SELECTED OUTCOME VARIABLES

Outcome variable	Significant predictor	Regression coefficient	p Value
Occurrence of pregnancy*	Intercept	7.63	<0.001
	Years trying	-2.67	<0.001
Miscarriage after achieving pregnancy†	Intercept	-3.93	<0.001
	Antibiotics	-1.99	<0.001
	Number of previous miscarriages	1.07	<0.001
	Years trying	0.76	<0.01
Meconium‡	Intercept	-1.37	<0.001
	Antibiotics	-2.87	<0.007
Fetal distress‡	Intercept	-1.67	0.007
	Antibiotics	-2.03	0.001
	Years trying	0.59	0.03
Premature rupture of membranes‡	Intercept	-0.19	NS
	Antibiotics	-2.93	<0.001
Postpartum fever‡	Intercept	-0.65	<0.01
	Antibiotics	-2.47	<0.001
Respiratory distress syndrome‡	Intercept	-1.45	<0.001
	Antibiotics	-2.79	<0.009
Hyperbilirubinemia‡	Intercept	-1.99	<0.005
	Years trying	0.91	<0.004
	Antibiotics	-1.87	<0.004
	Empirical	-1.31	<0.04
Newborn weight, <3,000 grams‡	Intercept	-0.44	NS
	Antibiotics	-1.94	0.001
Gestational age, <275 or >285 days	Intercept	0.20	NS
	Antibiotics	-1.60	0.001
	Years trying	0.62	0.05

\*Based on all patients, N=254.

†Based on all pregnancies, N=180.

‡Based on all viable deliveries, N=137.

NS, Not significant.

bacteria colonizing the genital tracts of certain high risk groups may also be a cause behind the increased incidence of pregnancy related complications (10). It has been postulated repeatedly that symptomatic or asymptomatic bacteria present in the genital tract may influence the outcome of the pregnancy resulting in premature rupture of the membrane and premature delivery of smaller infants. Currently, the number one cause of perinatal fetal wastage is prematurity, and among these infants, infectious morbidity is much higher than among full-term infants (11). In our study, both fetal morbidity and serious complications with labor and delivery were less frequent with the use of antibiotic therapy. The results of the study suggest that antibiotic therapy may reduce the number of premature births, the incidence of chorioamnionitis, meconium, fetal distress during labor and, thus, the frequency of cesarean section indicated for fetal reasons. We recognize the possibility, however, that cesarean