# In West Africa, Single-Dose Antibiotic Treats Vaginal Discharge as Effectively as Multiple-Dose Treatment

Among West African women visiting primary care clinics for treatment of vaginal discharge, those given a new single-dose antibiotic treatment are as likely as their counterparts given a standard multiple-dose antibiotic treatment to report relief of their symptoms, even if they are infected with HIV.[1] In a randomized controlled trial, two-thirds of women reported complete resolution of their symptoms by two weeks and about one-third reported partial resolution—regardless of whether they had been treated with a single dose of tinidazole and fluconazole or with multiple doses of metronidazole and vaginal clotrimazole over seven days. The findings were similar among HIV-positive women and among women with different genital infections.

The study population consisted of women visiting primary care clinics in Ghana, Guinea, Mali and Togo during 2004–2005 because of vaginal discharge. At their initial visit, women completed a questionnaire asking about demographic and behavioral factors, symptoms and antibiotic use; underwent a gynecologic examination during which cervical and vaginal samples were collected for pathogen testing; and gave a blood sample for HIV testing. They were then assigned in roughly equal numbers to either a single-dose regimen (tinidazole and fluconazole) or a standard multiple-dose regimen (seven days of oral metronidazole and three days of vaginal clotrimazole). Those with signs of cervicitis or genital ulcers were given additional antibiotics. During a visit two weeks later, the women again completed questionnaires about their symptoms and underwent a gynecologic examination. All women who still reported having discharge were given the multiple-dose regimen as a second treatment.

A total of 1,570 women were enrolled in the trial. Three-fourths were aged 21 years or older. Thirty-seven percent were sex workers; among women who were not sex workers, 81% had had only one sexual partner in the past three months. In the majority of women (63%), the discharge had been present for two weeks or less. Substantial proportions of women with discharge also had vulvar itching (83%), low abdominal pain (35%) and pain during intercourse (31%) or urination (17%). About a third had already been treated for the discharge. Some 52% had signs of cervicitis and 5% had genital ulcers.

Tests for three vaginal infections showed that 46% of both sex workers and non–sex workers had bacterial vaginosis; 24% and 35%, respectively, had candidiasis; and 16% and 6%, respectively, had trichomoniasis. Tests for three cervical infections—chlamydia, gonorrhea and Mycoplasma genitalium—showed that 21% of sex workers and 5% of non–sex workers had at least one of these infections. In addition, 26% of sex workers and 8% of non–sex workers were HIV-positive.

In all, 1,242 women returned for the two-week follow-up visit. Among these women, the proportion who reported that their symptoms had completely resolved did not differ between those given the single-dose regimen (66%) and those given the multiple-dose regimen (64%). Similarly, there was no difference between the single-dose group and the multiple-dose group in the proportion reporting that their symptoms had partially resolved (33% and 34%).

In stratified analyses based on women's reports, the two regimens were equally effective, whether women initially had candidiasis, bacterial vaginosis or trichomoniasis, or a cervical infection. Moreover, among HIV-positive women, the single-dose and multiple-dose regimens yielded similar levels of complete resolution (71% vs. 72%) and partial resolution (28% vs. 25%); these were comparable to levels of complete resolution (68% vs. 65%) and partial resolution (32% vs. 33%) among HIV-negative women. Within each study country, women reported similar responses to the two regimens.

The presence of visible vaginal discharge at the two-week visit was associated with women's perceived response to treatment: In all, 93% of those reporting no resolution and 86% of those reporting a partial resolution in symptoms had visible discharge, compared with only 15% of those reporting complete resolution. Furthermore, the proportion with visible discharge did not differ by treatment regimen, in the study population overall or in the stratified subgroups.

Among women who initially had bacterial vaginosis, the proportion who still had it at the two-week visit did not differ between those who reported complete resolution of symptoms and those who did not (28% vs. 33%) or between those who did and did not have visible discharge (31% vs. 29%). In contrast, among women who initially had candidiasis, the proportion who still had it at the two-week visit was significantly higher among women who reported partial or no resolution of symptoms than among their counterparts who reported complete resolution (49% vs. 25%), and significantly higher among women who still had visible discharge than among those who did not (47% vs. 24%).

In the subset of women who had persistent symptoms and received the multiple-dose regimen as a second treatment, nearly all had complete resolution (81%) or partial resolution (18%) of their symptoms after an additional two weeks. These proportions were identical for women initially given the single-dose treatment and women initially given the multiple-dose treatment. Moreover, they did not differ between women who did and did not have bacterial vaginosis at two weeks, or between women who did and did not have candidiasis at two weeks. In addition, HIV-positive women were as likely as their HIV-negative counterparts to report relief of symptoms after the second treatment.

In a final analysis done to assess possible indicators of cervical infection, none of five signs of cervicitis found on initial examinations (cervical discharge, pus on a cervical swab, cervical bleeding after sampling, cervical inflammation or tenderness with motion of the cervix) was associated with the presence of one or more cervical infections (gonorrhea, chlamydia or *M. genitalium*). However, among women who were sex workers, the greater the number of white blood cells in cervical secretions, the more likely it was that a woman had a cervical infection; among women who were not

sex workers, those who had spermatozoa in vaginal secretions were significantly more likely to have a cervical infection.

Commenting on the findings, the researchers argue that single-dose tinidazole-fluconazole is as effective as multiple-dose metronidazole-clotrimazole for relieving symptoms of vaginal discharge, regardless of underlying infections or HIV status. The single-dose regimen is inexpensive, easily adhered to and well tolerated, they point out; therefore, it "should be considered as a first-line treatment for vaginal discharge syndrome." They add that among women who are sex workers, the visit during which this treatment is dispensed should also be used to promote condom use and screen for cervical infections.–*S. London*

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## In Developing Countries, Most Early Neonatal Deaths Are Caused by Prematurity

In developing countries, stillbirths occur at a rate of about 13 per 1,000 births and early infant deaths at a rate of nine per 1,000 live births—even when women receive antenatal care and deliver in hospitals prepared to handle obstetrical and newborn complications.[1] According to a multinational study among women giving birth for the first time, the leading causes of fetal and early infant deaths combined are spontaneous preterm delivery (accounting for 29% of the deaths) and hypertensive disorders (accounting for 26%). Prematurity is responsible for fully 61% of early infant deaths and is the leading cause of death even in pregnancies near term.

Study data came from a randomized trial of calcium supplementation to prevent preeclampsia, conducted among women who were at elevated risk because they had a low calcium intake and had not previously given birth. Pregnant women visiting general antenatal clinics in six countries—Argentina, Egypt, India, Peru, South Africa and Vietnam—during 2001–2003 were eligible if they had a pregnancy of less than 20 weeks' gestation, had never given birth and did not have hypertension or a history of the condition. Participating women took calcium or a placebo daily until delivery and were examined monthly at the clinics, which were located in hospitals that had neonatal intensive care units or could refer women to such hospitals. The rates of stillbirth (fetal deaths among all births) and early neonatal death (newborn deaths during the first seven days of life among all live births) were determined for pregnancies of at least 28 weeks' gestation. A single cause of each fetal or newborn death was determined from data-collection forms and hospital records.

Analyses were based on 7,993 pregnancies among 8,325 women; the women were nearly equally divided between the calcium and placebo groups. About 1% of the pregnancies were multiple pregnancies.

Overall, 100 pregnancies ended in death of the fetus, corresponding to a rate of about 13 stillbirths per 1,000 births. An additional 71 pregnancies ended in death of the newborn within seven days, corresponding to a rate of nine early neonatal deaths per 1,000 live births. Fully 63% of the pregnancies with an outcome of stillbirth or early neonatal death ended before term; of these pregnancies, four-fifths ended by spontaneous preterm delivery, while one-fifth ended by preterm delivery induced because of medical complications.

As pregnancy advanced, the rates of stillbirth and early neonatal death decreased. Each outcome occurred at a rate of about 400 per 1,000 births at 28 weeks of gestation, but fell sharply to a rate of roughly 20 per 1,000 births at 40 weeks of gestation. In contrast, the risks of these outcomes, as determined by Kaplan-Meier analyses, declined initially but rose later in pregnancy, peaking at 39 weeks of gestation. At that gestational age, the risk of stillbirth was about 350 per 100,000 undelivered fetuses and the risk of early neonatal death was about 400 per 100,000 live births.

On the basis of an obstetric classification system, the leading cause of stillbirths and early neonatal deaths combined was spontaneous preterm labor (labor starting before 37 weeks of gestation), which was the cause in 29% of pregnancies with these outcomes, followed by hypertensive disorders, the cause in 26%. Less common causes were fetal abnormalities (13%), intrapartum-related causes (9%) and unexplained intrauterine fetal death (8%), among others. Compared with women in the placebo group, women in the calcium group had a significantly lower risk of their pregnancy ending in stillbirth or early neonatal death because of hypertensive disorders.

On the basis of an international disease classification system, 61% of the early neonatal deaths were due to prematurity, 23% to asphyxia and birth trauma, 13% to congenital anomalies, 1% to infection and the rest to unknown causes. When these deaths were stratified by the gestational age of the infant at delivery, prematurity was the most common cause of death among infants born before 37 weeks of gestational age; thereafter, asphyxia was the most common cause. The pattern was similar in the calcium group and in the placebo group individually.

An important finding of the study, the researchers point out, was that even though the women and infants received care in secondary and tertiary hospitals, the observed rates of perinatal death still exceed those in developed countries. Another important finding, with implications for the future, was the pattern of causes of deaths; specifically, they assert, the study's results suggest that as obstetric and newborn care becomes more accessible in developing countries, preterm delivery and hypertensive disorders may increase in relative importance as causes of fetal and newborn death, while intrapartum complications may decrease in relative importance. They therefore advocate research into the causes of preterm delivery and hypertensive disorders, with the aim of translating the findings into life-saving interventions. "Advancements in the care of premature infants and prevention of spontaneous preterm labour and hypertensive disorders of pregnancy could lead to a substantial decrease in perinatal mortality in hospital settings in developing countries," they conclude.–*S. London*

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## In India, Men's Sexual Behavior Puts Their Wives' Reproductive Health at Risk

More than one in four women aged 18–45 in Goa, India, had a reproductive tract infection at the time of a 2001–2003 study of the prevalence and determinants of such infections.[1] Although STIs were present in relatively few women (4%), endogenous infections, such as bacterial vaginosis and candidiasis, were common (25%). Being older than 25 at marriage

and using condoms or oral contraceptives had a protective effect against bacterial vaginosis, while having a verbally, physically or sexually abusive husband and being concerned about one's husband's habits (such as alcohol consumption) were associated with an increased risk. A low level of social integration, concern about a husband's extramarital relationships (an indicator of sexual risk), never having been pregnant and having been sterilized were associated with having an STI.

The data come from a population-based sample of women aged 18–50, who were randomly selected from a database of health department records and who resided in the north Goa district, spoke one of the study languages, did not have cognitive impairment and were not pregnant. Of the 3,000 eligible women contacted, 2,494 (83%) consented to participate. The majority of the respondents (75%) were Hindu, 14% were unable to read or write, 68% were homemakers and 36% lived in homes with no toilet facility. Some 33% of women's households were in debt, and 5% of women reported having gone hungry in the three months prior to the study. Data collection involved two stages: a semistructured interview to obtain information regarding participants' social and demographic characteristics, experiences with gender disadvantage, and sexual and reproductive health risk factors; and a gynecological examination to determine the presence of endogenous infections (bacterial vaginosis and candidiasis) and STIs (trichomoniasis and gonorrheal or chlamydial infections).

Overall, 28% of women had a reproductive tract infection; 4% of women had at least one STI, and 25% had an endogenous infection. Bacterial vaginosis, found among 18% of participants, was the most common reproductive tract infection.

The univariate analysis indicated that risk factors for STIs and bacterial vaginosis included being older, being married, having less education, having a small household, lacking a toilet in the home and being in debt ($p<0.1$). Having candidiasis was associated with being younger, being non-Muslim, having fewer than three children and not having tap water in the house.

In a multivariate analysis, having an STI was associated with being married (odds ratio, 2.3), being illiterate (1.8), having fewer than three children in the household (2.2), having no tap water in the home (1.5) and being in debt (1.4). The risk of having bacterial vaginosis increased with age and was associated being married (1.5), being a migrant (1.4) and living in a house with fewer rooms. The risk of having candidiasis increased with women's age and was associated with being non-Muslim (5.3), being unmarried (2.9), not having running water in the house (1.3) and having fewer than three children (1.7).

In further analyses that adjusted for socioeconomic factors, the researchers examined the relationship between reproductive tract infections and risk factors related to gender disadvantage and reproductive health. STI was associated with a low level of social integration—a composite measure based on the degree to which women were able to socialize with friends and relatives and participate in activities outside the home. The odds of having bacterial vaginosis were negatively related to age at marriage. Risk factors for bacterial vaginosis included verbal, physical and sexual abuse by the husband (odds ratios, 1.4, 1.7 and 1.9, respectively), and concern about the husband's extramarital affairs (1.4).

Sexual and reproductive health factors associated with having an STI included never having been pregnant (2.7), having been sterilized (1.7), having a husband with white genital discharge (6.9) and being concerned about the husband's extramarital affairs (4.0). Women who had ever had an abortion were about half as likely as those who had not to receive an STI diagnosis (0.5). Women who reported using the pill or condoms as their main contraceptive method had a significantly lower risk of having bacterial vaginosis (0.2 and 0.6, respectively).

The researchers point out that the association between bacterial vaginosis and gender disadvantage "may reflect the lack of control women have over their hygiene and possible effects of stress on vaginal flora." The link between STIs and women's social isolation, reports of their husbands' genital discharge and concerns about their husbands' affairs further indicate that many women's reproductive health is contingent on their husbands' behaviors. Thus, the researchers suggest that increased focus on treating and preventing STIs in men "may prove to be an effective strategy in controlling the spread of STIs and reducing the burden in women."—*H. Ball*


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## Risk of Death or HIV Infection Similar for Two Infant Feeding Regimens

Among babies born to HIV-infected mothers, those who are fed breast milk and given zidovudine for the first six months of life have a risk of dying or contracting HIV similar to infants who are fed formula and given zidovudine for the first month, according to a randomized study in Botswana.[1] By the age of seven months, the breast-fed infants had a higher rate of HIV infection (9% vs. 6%), but the formula-fed infants had a higher rate of death (9% vs. 5%). At the age of 18 months, the proportion of infants who had died or contracted HIV was essentially the same (14–15%) in the two groups.

The study was part of a larger trial of interventions to reduce mother-to-child HIV transmission, which tested both a peripartum intervention (a single dose of nevirapine vs. placebo, given to both mothers and infants) and the postpartum intervention (breast-feeding plus zidovudine vs. formula feeding plus zidovudine). Pregnant women visiting antenatal clinics in southern Botswana during 2001–2003 were eligible for the study if they were HIV-positive but in fairly good health, at 33–35 weeks of gestation and aged 18 years or older. All women were given zidovudine from 34 weeks of gestation until delivery. After delivery, mothers in one group were advised to feed their infants only formula, and their infants were given zidovudine for one month; mothers in the other group were advised to exclusively breast-feed their infants for six months and then wean them, and their infants were given zidovudine for those six months. Infants were examined and tested periodically though age 18 months. Their rates of HIV infection, death, and the two combined were estimated by the Kaplan-Meier method.

Analyses were based on 1,179 live first-born infants. Their mothers had a median age of about 27 years; one-fourth had a primary education, and two-thirds had a secondary education. Sixty-one percent of mothers did not have any monthly personal income. The majority obtained their drinking water from a tap in the yard (55%) and had a private latrine for their household (74%). The infants had a median birth weight of 3.1 kg. About 8% weighed less than 2.5 kg at birth, and 5% were born prematurely.

By the age of seven months, infants fed

breast milk and given zidovudine had a higher cumulative rate of HIV infection than their counterparts fed formula and given zidovudine (9% vs. 6%). The difference remained significant at 18 months of age (10% vs. 6%). When the peripartum intervention was also considered, the higher rate of HIV infection associated with breast-feeding relative to formula feeding was more pronounced when infants and mothers had been given nevirapine than when they had been given a placebo.

Seven months after birth, infants fed formula and given zidovudine had a higher cumulative rate of death than their counterparts who had been breast-fed and given zidovudine (9% vs 5%). However, the difference was no longer significant at 18 months of age. Diarrhea and pneumonia were the leading causes of death. When the peripartum intervention was also considered, formula feeding was associated with a higher rate of death than breastfeeding when infants and mothers had been given a placebo; in contrast, breast-feeding was associated with a higher rate of death than formula feeding when they had been given nevirapine.

Eighteen months after birth, breast-fed infants given zidovudine and formula-fed infants given zidovudine had essentially the same cumulative rate of death or HIV infection (15% and 14%, respectively). When the peripartum intervention was also considered, breast-feeding was associated with a higher rate of this outcome than formula feeding when infants and mothers had been given nevirapine; in contrast, formula feeding was associated with a higher rate of this outcome than breast-feeding when they had been given a placebo.

In safety analyses, formula-fed infants given zidovudine had higher rates than their breastfed counterparts given zidovudine of severe or worse signs or symptoms (18% vs. 13%) and hospitalization (20% vs. 16%) by the age of seven months. However, the breast-fed infants had a higher rate of abnormal blood tests overall (25% vs. 15%), as well as a higher rate of abnormal tests leading to discontinuation of the zidovudine (9% vs. 2%).

The study's results, according to the researchers, do not definitively support prolonged use of zidovudine in infants to prevent mother-to-child transmission of HIV by breast-feeding. At the same time, they note, the findings underscore the need to assess local patterns of childhood illnesses, particularly infectious ones, before implementing formula feeding as an alternative strategy. The researchers conclude that "further study is warranted to determine the efficacy and safety of other interventions to prevent mother-to-child transmission related to breastfeeding, such as the use of maternal HAART [highly active antiretroviral therapy] during the breastfeeding period."*—S. London*

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## In Honduras, Knowledge Of Emergency Contraception Increases, but Use Does Not

Following public outreach activities promoting emergency contraception, awareness of the method among Honduran adults visiting family planning clinics in two cities quadrupled and concerns about it decreased, but willingness to use the method declined.[1] The proportion of clients who had heard of emergency contraception rose from 5% to 20% between the 2001 preintervention survey and the 2003 postintervention survey, and the proportion who expressed concerns about the method fell from 26% to 20%; over the same period, however, willingness to use the method dropped from 80% to 71%.

This study examined knowledge about, attitudes toward and use of emergency contraception among urban family planning clients following the addition of the method to the National Family Planning Norms in 1999 and countrywide outreach activities that began in 2001. The surveys were conducted at a clinic in Tegucigalpa and another in San Pedro Sula; the clinics are run by a nongovernmental organization, and serve primarily lower-middle-class residents. More than 1,400 respondents were interviewed for the baseline survey and nearly 1,300 at follow-up. Respondents were asked about their demographic characteristics, pregnancy history, sexual behavior and contraceptive use, as well as their knowledge and attitudes about and use of emergency contraception. Chi-square tests determined significant differences between the surveys, and multivariate logistic regression models assessed associations between various characteristics and the emergency contraception measures.

The age distribution of respondents in the two surveys was similar: About 8% were aged 15–19, 43% were in their 20s, 31% were in their 30s and 19% were 40 or older. The proportion of respondents who were female was significantly higher at baseline than at follow-up (85% vs. 81%), as was the proportion of all respondents who had less than a high school education (56% vs. 50%). In each survey, more than eight in 10 respondents were sexually active, and the same proportion had been pregnant or had impregnated a partner; however, the proportion who were currently using a contraceptive declined between surveys (84% vs. 72%). Three-fourths of follow-up clients were married or in common-law unions. There were significant differences between surveys regarding emergency contraception: The level of awareness of the method rose from 5% to 20% of respondents, and the proportion with concerns about the method declined from 26% to 20%, but the proportion willing to use it fell from 80% to 71%. Only 6–8% of respondents in either survey had used the method in the past year.

Awareness of the method increased among all demographic groups, and did not vary by sexual experience, pregnancy history or contraceptive use. Nevertheless, there were differences among various groups. For example, levels of awareness at follow-up were much lower in San Pedro Sula than in Tegucigalpa (9% vs. 28%), and were higher among those aged 15–19 or 20–24 than among those 40 or older (28–30% vs. 12%). Furthermore, awareness levels in the postintervention survey were dramatically different depending on respondents' education: 11% among those with less than a high school education, 17% among those who had finished high school and 42% among those with higher education. Willingness to use emergency contraception fell from 90% to 68% among respondents in San Pedro Sula, and remained steady at 72–73% in Tegucigalpa. Notably, willingness declined for most of the other categories, although not among the youngest age-group or those with the most education. When asked whether the availability of a dedicated product would increase Honduran women's willingness to use the method, 90–93% of respondents in both surveys said that it would.

Multivariate regression analysis found that the likelihood of being aware of emergency contraception was higher among follow-up clients than among baseline clients (odds ratio, 4.9), among those with a high school or higher education compared with those having less

education (1.7 and 5.1, respectively) and among those currently using a contraceptive than among nonusers (1.5). Respondents living in San Pedro Sula were less likely than those in Tegucigalpa to be aware of the method (0.4), and respondents aged 40 or older were less likely than those who were younger to be aware of it (0.5). The odds of being willing to use the method were lower among those aged 30 or older than among those aged 15–29 (0.2–0.5), among females than among males (0.8) and among those assessed at follow-up than among those assessed at baseline (0.5).

The multivariate analysis also found that respondents in San Pedro Sula were less likely to report concerns than were those in Tegucigalpa (odds ratio, 0.8), and that respondents at follow-up were less likely to do so than those at baseline (0.6). However, clients with at least a high school education were more likely to have concerns than those with less education (2.1–3.1), and those who were using a contraceptive were more likely to have concerns than were nonusers (1.5). The most common concerns were that the method caused side effects, acted as an abortifacient, failed often or was ineffective, might harm the fetus if it did fail or might cause future fertility problems.

According to the researchers, the study has several limitations. First, a media campaign by the Catholic Church and Honduran antiabortion groups coincided with the follow-up surveys and may have countered any effect the intervention had on levels of concerns and willingness to use emergency contraception. Second, clients were asked only whether they had used the method in the past year, and the question on willingness may not have differentiated between those who approved of the method and those who felt they would not need to use it. Finally, clients' marital status was not determined at baseline, and so its effect on awareness and use could not be determined.

The researchers suggest that outreach efforts should target young people, both because respondents younger than 25 showed the highest awareness of and willingness to use the method, and because they are at high risk of unwanted pregnancy. They also recommend that efforts be directed at Hondurans with less than a high school education. In addition, they say family planning counseling should be promoted and strengthened among clinic workers, physicians and pharmacists, as these workers could be a valuable source of accurate information. The researchers emphasize that "future educational efforts should be aimed at increasing specific knowledge about emergency contraception, its proper use, and its effectiveness" to counter misinformation, and that proponents of emergency contraception "must develop timely and strategic counter-responses" in this often contested arena of reproductive health.*—J. Thomas*

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