

orally, 6% administered it intravaginally, and 29% used both routes. Reported doses ranged from 200 mcg to 16,800 mcg; the median was 800 mcg. Most women took the entire dose at once, but many who took a massive dose did so over several days.

Overall, 52% of the women who used misoprostol began bleeding within 12 hours of taking the drug, and 13% began bleeding at 12-24 hours. Some 19% had to wait 2-10 days for bleeding to begin, however, and 16% waited even longer. The proportion reporting that bleeding started within 12 hours rose with gestation, and was higher among women who used the drug both orally and vaginally than among those who took it only orally.

Among the 454 women for whom hospital records included an admission diagnosis, 72% had an incomplete abortion and only 4% had a complete abortion; nearly 20% were classified as having a threatened or inevitable abortion, 3% were judged to have premature labor and 2% had a missed abortion. In all, 85% of the women required surgical intervention; this proportion decreased with gestation, from 89% of those who used misoprostol before 12 weeks' gestation to 50% who used it at 20 weeks' gestation or later.

Morbidity was substantial among women who used misoprostol, but the proportions who had signs of infection (17%), who required blood transfusion (1%) or who had physical injuries (1%) were significantly lower than, for example, the comparable proportions among women who used an invasive method such as insertion of a catheter (50%, 11% and 9%, respectively, $p < .0005$). Three women who used misoprostol died—one after suffering a ruptured uterus and two from sepsis.

In the matched group of 803 women who delivered at term, 35% said they had wanted to terminate their pregnancy, and 18% had attempted to do so; 6% of the women who delivered said they had taken misoprostol. Another 5% had taken a drug they could not identify, so the rate of exposure to misoprostol may have approached 11% in this group.

The number of Brazilian women who have used misoprostol to induce abortion is unknown; so, too, are the proportions of these women who require medical care. From the data on women delivering at term, however, the researchers argue that it is clear that many women have used the drug unsuccessfully. These women, some have suggested, may be exposing their fetus to a risk of **malformation**,² but this possibility requires further scientific re-

search. Nonetheless, the investigators note alternatives to unsafe abortion are urgently needed in Brazil.

The Fortaleza Study

In a second study analyzing the extent of misoprostol use for abortion induction in Brazil, researchers reviewed data for women undergoing uterine evacuation after attempted induced abortion at the main obstetric hospital in Fortaleza, the capital of Ceara State, between January 1990 and July 1992.³ Misoprostol was freely available in Ceara in 1990, but debate about the availability of misoprostol and its link to uterine evacuation and other complications led to a ban on sales of the drug in Ceara in July 1991.

According to a cross-sectional study of medical records at the obstetric hospital of the Federal University of Ceara, 593 women needed uterine evacuation after an illegal induced abortion during 1991. Of these abortions, 75% were attributed to the use of misoprostol, and 16% to other drugs. The monthly number of uterine evacuations related to clandestine abortion at this hospital climbed through the first several months of 1990 and peaked at 89 in August of that year. By July 1991, when misoprostol sales were suspended statewide, the monthly number of evacuations had fallen to 62. With the drug available only clandestinely, the decline continued until December 1991, when the number of uterine evacuations leveled off at about 20 per month.

The experience with misoprostol, according to the researchers, is "an interesting example of how social problems can be bypassed by perverse strategies and false solutions in countries where people are not adequately informed about contraception." They argue that inadequate access to contraceptive services is the primary reason for the large numbers of unplanned pregnancies in Brazil, and is a major public health issue for women; the "poor control" of drug marketing exacerbates the problem, they add, by encouraging the misuse of drugs. "The availability of a weak abortifacient," the investigators conclude, "cannot compensate for the lack of access to family planning and health care." -D. Hollander

References

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Quinacrine Sterilization Method Found Effective Among Women in Vietnam

Quinacrine hydrochloride pellets, which, when inserted in the uterus, cause inflammation and scarring that permanently block the fallopian tubes, may be a safe and effective method of nonsurgical sterilization. In field trials involving 31,781 Vietnamese women who were sterilized with quinacrine, no deaths occurred, very few women reported serious complications and only 3% subsequently became pregnant.' According to the investigators, the use of quinacrine as a nonsurgical sterilization method, developed in the 1970s, could lead to fewer deaths and complications than the number associated with surgical sterilization and could provide a high level of contraceptive protection at a very low cost.

To evaluate the safety, effectiveness, acceptance and delivery of quinacrine as a sterilization method, researchers conducted trials of the drug at rural health centers in 24 provinces in Vietnam from 1989 to 1992. Participation in the study was voluntary. Women who were at least aged 30 and who had at least two living children aged three or older were eligible to use the method. All participants in the study were sexually active, were not using another contraceptive method and were at least six weeks beyond pregnancy termination.

The women were examined before insertion of the quinacrine pellets. Those who had cervical inflammation were treated before receiving quinacrine. A doctor or midwife inserted seven 252 mg quinacrine pellets into the uterus through a cold-sterilized Copper-T IUD inserter. The majority of participants received two doses: The first was inserted during days 5-12 of the menstrual cycle and the second was inserted one month later. Some groups of women received only one dose. The researchers compared failure rates of the groups to determine the method's effectiveness according to dose.

Patients were asked to return for follow-up one, three, six and 12 months after insertion of the last pellet, and every six months thereafter. All were monitored for serious complications, side effects, pregnancy (including ectopic pregnancy) and birth defects among infants conceived after their mother received quinacrine.

Among 31,781 women who received one or two doses of quinacrine, 818 became pregnant; 19 of the pregnancies were ectopic, six ended in spontaneous abortions, 684 ended by induced abortion, 79 were live births, one was stillborn and 29

pregnancies were continuing at the end of the study. No deaths or uterine perforations occurred as a result of quinacrine insertion. Eight participants experienced serious complications possibly related to quinacrine sterilization: Two had severe bleeding, two had fusion of their cervical canal, and one each had severe pain and amenorrhea, premenstrual pain and dysmenorrhea, suspected pelvic inflammatory disease, and severe allergic reaction.

All conceptions that occurred within one month of quinacrine insertion were aborted by menstrual regulation. Among 80 pregnancies that were carried to term, one preterm infant died and one was stillborn. One infant who was conceived 2.5 months after quinacrine insertion was anencephalic; however, the researchers suspect that this defect may have resulted from exposure to agricultural chemicals, as another woman from the same commune who had not received quinacrine also gave birth to an anencephalic infant. All other infants were normal.

Among 508 women who were studied for menstrual changes and side effects, the most commonly occurring side effects after the first insertion of quinacrine were vaginal itching (23%), headache (20%) and lower abdominal pain (15%). The side effects lasted from a few hours to a few days and tended to be milder after the second insertion. Although most women (77%) had no change in menstrual flow, 19% experienced a decrease and 4% reported an increase.

Health centers with a minimum of 50 patients at the 12-month follow-up were included in an analysis of efficacy. When the researchers compared the effectiveness of quinacrine by number of doses, they found that the women who had been given only one dose had twice as great a failure rate as those who had received two doses: Cumulative pregnancy rates one year after insertion were 2.6% among 9,461 women with two insertions, compared with 5.2% among 2,225 women with only one insertion.

To determine if the skill and experience of those who performed the insertion affected the efficacy of the method, the investigators examined the incidence of failure with increasing experience among 88 health workers who performed insertions on 4,010 women in one province. Among 88 health workers, 32 had had at least one failure, and these failures had resulted in 165 pregnancies (4% of the 4,010 sterilizations). The experience levels of clinicians who had had failures varied from more than 100 insertions to fewer than 10. Fail-

ure rates among eight health workers who had completed more than 100 insertions ranged from 3% to 9%.

Among clinicians who had experienced failures, those who had performed 10 or fewer insertions had the highest failure rates (17%), while those who had performed 100 or more had the lowest rates (5%). However, when all 88 clinicians were included in the analysis, experience did not have an important effect on failure rates. The researchers concluded that in terms of method efficacy, the skill of the clinician was more important than the amount of insertion experience.

Before conducting these trials, the investigators assumed that the concentration of quinacrine would be evenly distributed throughout the uterus; thus, the pellets could be placed anywhere in the uterus to achieve tubal occlusion. However, their findings regarding insertion and efficacy lead them to suspect that placement of the pellet may be related to effectiveness. They advise further research to examine the effect of insertion technique and other skills on the method's efficacy.

The authors of the study assert that quinacrine is a much safer method of sterilization than surgical sterilization: They estimate that surgical sterilization of the same number of women probably would have resulted in 30 deaths and 540-1,812 cases of serious complications, compared with no deaths and only eight cases of serious complications related to quinacrine.

The investigators advise that quinacrine sterilization, which appears to be safe, effective and easy to deliver, could increase contraceptive prevalence in developing countries among women who do not want more children. They also view it as a way to reduce maternal mortality, which is at a level of 380 deaths per 100,000 live births in Vietnam. The researchers estimate that 242 maternal deaths were prevented as a result of these 31,781 sterilizations. Considering the cost of two insertions of quinacrine, which is less than US \$1.00, they conclude that "this procedure represents our most cost-effective way of lowering maternal mortality."

A critique of the study issued by the Association for Voluntary Surgical Contraception (AVSC) noted several problems.² For example, some women did not meet the inclusion criteria: In one province, 473 study participants were younger than 30, and 17 women were breastfeeding at the time of treatment, implying that their children were younger than three. Failure rates are based on a subsample of 11,686 women, and side effects are based on a subsample

of only 508 women from one province, but the investigators extrapolate these findings to the entire sample of 31,781.

In addition, the investigators state that their study supports the results of previous research on monkeys indicating no risk of mutagenicity, but base this conclusion on only 80 cases. AVSC advises that "further carefully designed studies that specifically address short- and long-term safety are needed," and that "quinacrine pellets for female sterilization should continue to be considered an experimental procedure."—S. Edwards

References

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Pill-Associated Strokes Found Less for Low-Dose Than for Higher Dose Pill

Although use of low-dose oral contraceptives is associated with an increased risk of cerebral thromboembolic attack, this risk is significantly lower than that associated with the higher dose pills used in the 1960s and 1970s, according to a recent Danish study.¹ This decrease in risk appears to be the result of reductions in the dosage of estrogen. The researcher estimates that if no reproductive-age women had ever used the pill, their risk of stroke would be reduced by about 15%.

Studies conducted in the 1960s and 1970s showed that oral contraceptive users had a risk of cerebral thromboembolic attack 4-25 times that of nonusers. However, because the hormone concentrations in oral contraceptives have been reduced over the past 10-20 years, a Danish researcher reexamined the risk of stroke among women likely to have used the oral contraceptive formulations available in the 1990s.

The retrospective case-control study evaluated the association between oral contraceptive use and stroke in 794 Danish women aged 15-44 who had suffered a cerebral thromboembolic attack. Stroke patients were located using the National Patient Register, which keeps track of individuals seen in any of Denmark's medical, neurological, neurosurgical or gynecologic departments. Using Denmark's National Person Register, he randomly selected 1,588 age-matched controls (two for each stroke patient). (Age matching in-