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## The Quest for a Magic Bullet

By Malcolm Potts and Robert Wheeler

The standard definition of a perfect contraceptive is one that is highly effective, reversible, free from side effects and completely safe. The goal of contraceptive research has frequently and repetitiously been identified as the development of this perfect one-shot method—a "magic bullet" that will solve the problem of pregnancy prevention as Paul Ehrlich's discovery of Salvarsan in 1909 was expected to solve the problem of syphilis.

Over the past 20 years, however, the hopes and prophecies of those engaged in contraceptive research and development have often gone unfulfilled. No new chemical entity has been introduced into general program use since 1968. In the 1960s, and again in the 1970s, scientists assured us that a male pill would be devised within 10 years. In the 1980s, this prospect is still distant. Work on implants and other forms of female contraception has not moved beyond large-scale field trials. Research on a vaccine to control reproduction is partly stalled.

Undoubtedly, insufficient money has been invested in reproductive and contraceptive research. Since the early 1970s, worldwide expenditures on reproductive research have plateaued, or even declined, when measured in noninflationary dollars. Currently, annual worldwide expenditures for contraceptive research and development amount to U.S. \$154.8 million, or 0.03 cents per capita; in the United States, \$111.6 million, or 49 cents per capita, are invested annually by government, private industry and philanthropists.<sup>1</sup> Put another way, the world spends as much on contraceptive research and development in one year as it spends in 20 minutes on the arms race. Additionally, it has proved difficult to establish a responsible and practical

balance between the obvious need to reduce dangers to potential consumers to a minimum, and the inescapable risks that must accompany the introduction of new drugs and devices.

We suggest that there is also a less visible explanation of the gap that exists between the continuing expressions of need for new contraceptives and expectations concerning them, and the continuing frustration of those expectations. One of the least explored problems involved in contraceptive research is a philosophical rather than a technological one. It may be useful to consider whether contraceptive research is being asked to do something that is impossible, namely, to produce a reversible, highly effective contraceptive free from side effects.

### The One-Shot Solution

That goal has been defined mainly by those who provide family planning services. Possibly, the emphasis of providers is somewhat different from that of the individuals who seek services, and may be influenced by socially defined expectations that are in conflict with the biological parameters of human reproduction. In the West, if one in 1,000 surgical sterilizations is associated with accidental pregnancy, then it makes newspaper headlines and perhaps a medicolegal case for the surgeon involved. Conversely, if there is not an instant return of fertility after the discontinuation of a steroidal contraceptive then that is regarded as a serious side effect. In a sense, the providers of contraceptive services have too often set particularly difficult goals for themselves, emphasizing the all-or-nothing, black-or-white approach to contraceptive technology. Perhaps contraceptive development has been hoist with its own petard.

Currently, efforts are under way to give contraceptive implants a five-year life. From a demographer's point of view, this appears to be a useful target. But from the point of view of potential users, it may be less attrac-

tive. Few women wish to have their children as many as five years apart, and many couples who have had all the children they want would probably prefer sterilization to a hormonal implant.

The prevention of pregnancy, moreover, is not comparable to the treatment of a disease, and there are a number of biological reasons why it may be expected that most one-shot solutions will bring a number of serious problems with them.

The issue is well illustrated by the history of IUDs and oral contraceptives. There is a strong correlation between the size of an intrauterine device, the pregnancy rate and the number of side effects: The larger the device, the lower the pregnancy rate and the greater the number of side effects.<sup>2</sup> The addition of active chemicals to a device is an effort to partially escape from this trap, but the inverse association between pregnancy rate and incidence of side effects tends to recur in one form or another. In the case of oral contraceptives, the higher the dose and the more extensive the systemic effects, the greater the effectiveness and also the greater the probability of problems among users.<sup>3</sup> Again, surgical methods of voluntary sterilization that damage the fallopian tubes the least are the most readily reversed, but in some instances they have higher failure rates than more radical procedures.<sup>4</sup>

The reversible methods of contraception, unlike water taps that turn on and off, reduce the probability of pregnancy by extending the average length of time that it takes to get pregnant.<sup>5</sup> The different methods achieve this biologically reasonable goal with varying degrees of success. Few have a theoretical effectiveness of more than 95-97 percent, and none, with the exception of combined oral contraceptives, provide close to 100 percent protection. (Use-effectiveness is considerably lower.) Once it is recognized that a tradeoff between acceptable side effects and level of protection is reasonable, and once that tradeoff is quantified, it is both more

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interesting and easier to develop contraceptive methods that will fill the bill. Simple methods, such as spermicides or even withdrawal, become significant and worthy of investigation, in view of their ease of use and lack of side effects.

### Shared Methods for Two Individuals

Combinations of fertility-regulation methods have been explored very little, but are intrinsically interesting. They have a common-sense appeal, and observational data suggest that they are already common in practice. If, for example, both partners use a less effective method of contraception, then the probability of pregnancy is decreased dramatically from what it would be if only one partner uses such a method. Shared contraception is particularly effective for methods with a high theoretical effectiveness and low use-effectiveness—for example, the condom. In a situation where a woman uses foam on two-thirds of the occasions on which she has intercourse, while her partner uses a condom on three-quarters of those occasions, then (given the slightly artificial assumption that the two patterns of use are random) both methods would be used together six of every 12 months of use. One partner would be using a method when the other was not five months of the year, and neither would be using a method one month of the year. Or consider the more realistic, but more difficult-to-quantitate, situation in which a couple combine the rhythm method with the use of a barrier method during the most fertile days of the woman's cycle. Shared contraceptive practice could also be used to reduce side effects resulting from long-term use of a method by allowing each partner to assume contraceptive responsibility in sequence.

### Combined Methods for One Individual

A simple method, such as a spermicide, used during an interval of breastfeeding creates an analogous situation in which two factors, both reducing fertility, act together, this time in the same individual.

A more complex combination involves nonsurgical sterilization in women and the use of a medical method to empty the uterus in cases of early menstrual delay when pregnancy is suspected. Voluntary sterilization has proved remarkably popular around the world, indeed, in many developing countries, the demand exceeds the ability of the health-care system to provide currently available surgical technologies.<sup>6</sup> The potential usefulness of a menses-inducer is attested to by the existence of herbal and traditional remedies to induce late menstruation in every known society, and by the cultural,

clinical and ethical advantages of early abortion over late.<sup>7</sup>

Both chemical sterilization and the induction of menstruation are achievable with current technologies. Chemical closure of the fallopian tubes through intrauterine placement of quinacrine has given promising results,<sup>8</sup> and present prostaglandin analogs, both as vaginal suppositories and as intramuscular injections, will induce a delayed period.<sup>9</sup> However, neither method offers 100 percent or perhaps even 95 percent reliability; not all the tubes can be closed and not all the uteri can be emptied every time.

It seems likely that to push effectiveness from the current 90–95 percent level into the 95–100 percent bracket, it may be necessary, in the case of prostaglandins, to choose more active analogs or raise the dosage. In the case of chemical sterilization, it may be necessary to use increasingly complex, expensive instruments or multiply the treatments. A chemical method of sterilization may have a low probability of success when administered only once, but the chances of success can be improved by repeated application. As predictable results are pushed over the 95 or 97 percent effectiveness level, however, users will very likely be exposed to greater risks of unpleasant side effects and, possibly, of danger to their lives. The equation is similar to that already observed in relation to oral contraceptives and IUDs: A high degree of effectiveness is associated with troublesome and sometimes dangerous side effects.

### Contraception and Abortion

The most common combination of fertility-regulation methods is that of contraceptive use backed up by abortion in the event of unintended pregnancy.<sup>10</sup> This pattern exists de facto in most nations that have low birthrates. Policies to recognize or alter the existing balance are of significance to the health of women, and are also the subject of ethical debate. It is instructive—and in some ways surprising—to compare a method that has a high failure rate but few side effects and a good continuation rate, with a method that is highly effective but has many side effects and a poor rate of continuation.

We have used a computer simulation model to show the distribution of births and abortions at the end of two years for 1,000 women who initiate use of a traditional method (e.g., withdrawal) or simple method (e.g., spermicide) or modern method (e.g., the IUD) following a birth. The model assumes, among other things, that fecund women using traditional or simple methods of contraception have a pregnancy rate of about 12 percent per year and a continuation rate of 90 percent at the end of one year; the rates for

fecund women using modern methods are assumed to be about three percent and 50 percent, respectively. Identical and reasonable gestation-specific rates of spontaneous and induced abortion have been assumed for both traditional/simple and modern methods of contraception.

As in any model, some simplifications have been made. For example, the possibility of a woman's adopting contraception after several months of risk-taking but not conceiving has been excluded; and only the first possible birth or abortion following the initial birth has been considered.

The result of the computation is that if 1,000 women begin use of a traditional or simple method with a good continuation rate after a birth, then at the end of two years they will have had 312 conceptions, whereas those using a more effective contraceptive with a lower continuation rate will have had, at the end of two years, 369 conceptions. Some of these conceptions will end in induced abortion. It seems reasonable to conclude that a program combining a supposedly less effective method with the option of early abortion would involve no more fetal wastage than would the use of a more effective method—and it might involve less.

### Implications

Perhaps contraceptive research and development should attempt to introduce modern methods of contraception optimized for good continuation, if necessary at the expense of effectiveness.

The positive health implications for users who combine a simple reversible method, such as the condom or a vaginal barrier, with early legal abortion have been pointed out previously. In both developed and developing countries, such a combination presents markedly fewer risks than dependence on either oral contraceptives or abortion alone.<sup>11</sup> In countries where abortion is illegal and commonly associated with considerable danger, it is possible that a less effective method with a good continuation rate may entail less overall risk for a woman than a highly effective method that is more likely to be abandoned after a shorter interval, thus leaving the woman exposed to the risk of an unwanted pregnancy, which may end in illegally induced abortion.

Another series of interesting implications follows from the possibility of combining an established fertility-regulation method (e.g., induction of menstruation) with a more advanced technology (nonsurgical sterilization) in an effort to accelerate the introduction of a new and sought-after method. In some cases, many years of research and development are spent not on testing the safety of an idea, but

on seeking a high level of effectiveness. In the case of chemical sterilization, however, current technology is on the brink of producing a method that paramedical workers could offer and that is over 90 percent, although not nearly 100 percent, effective. Because of the costs involved and the shortage of facilities and physicians in the developing world, established surgical methods of female sterilization are difficult to make available in poor countries and are sometimes associated with much higher mortality than occurs in developed nations.<sup>12</sup> A chemical method of sterilization not only would be more convenient for the women in such adverse circumstances, but might prove less hazardous as well. However, would a procedure that is only 90–95 percent effective be acceptable to users?

If chemical sterilization is to enter program use, then perhaps it should be offered as an irreversible contraceptive method with a moderate failure rate, in the same way that family planning programs now offer the condom, a reversible method of contraception with a moderate failure rate. From the user's point of view—providing that she has been fully informed of the consequences of adopting a particular method—an unexpected pregnancy following sterilization is basically no different from one following the use of a condom; it only becomes different if the definition and philosophy of contraceptive technology make forceful distinctions between these two family planning choices. In a sense, sterilization, like condom usage, also extends the time it takes to get pregnant, although in the case of sterilization, the average greatly exceeds the biological duration of fertility in most couples. Should a pregnancy occur after nonsurgical sterilization, those who provide contraceptive services could either offer an early abortion or leave the couple to deal with the consequences in exactly the same way—harsh as this may sound—that couples are now left to deal with failures of reversible methods of contraception.

For service providers, the consequences of offering a menses-inducer with an efficacy rate of 90–95 percent would be somewhat different from the consequences of making available a chemical method of sterilization with a 90–95 percent efficacy rate. Although there is no evidence, for example, that prostaglandins can damage a fetus, there might be reasons for concern. And, in the case of those chemicals that might act directly on the fetus or placenta, it would be obligatory to fully and carefully follow up any method failures to ensure that surgical forms of abortion were made very readily available to all those concerned.

### Conclusions

By and large, it is the philosophical definition of our expectations that controls the way in which methods are used. And it is the providers of contraceptive services—not the consumers—who formulate the definitions and determine contraceptive policy. Because the terms *sterilization* and *contraception* carry certain connotations, there are some who find it intrinsically reasonable to provide an abortion to a woman who has been sterilized or even to one who has used an IUD, but balk at providing an abortion for a couple faced with an unwanted pregnancy as a result of failure of a spermicide or some other simple method of contraception. Yet, there are no clinical or sociological data to suggest that the consequences of an unwanted pregnancy are any less serious when the couple have been using a condom than when they have been using an IUD or have undergone voluntary sterilization; only the relationship with the provider of the service is different.

Current reversible methods of contraception are inadequate to meet current goals of family size over a fertile lifetime. The most promising new methods are still in the early stages of development; some may not become available for another 10–15 years.<sup>13</sup> Major improvements in contraceptive continuation rates might be more readily achieved if modest failure rates were tolerated and if comprehensive fertility-control services were made available.

The combination of contraception, sterilization and abortion should enable communities to effectively control their fertility, but service providers continue to perceive this approach as clumsy and unsatisfactory. Although we do not have to content ourselves with present technologies, it is useful to point out that what is currently available offers a wider range of exciting and immediate opportunities than is sometimes realized. Some of the policy implications seem at first glance to be controversial, but in the case of the combination of contraception and abortion, realistic policies linking the two choices could lead not only to fewer unwanted births and fewer individuals suffering serious side effects from contraceptive use and illegal abortion, but also, in the final analysis, to fewer unwanted pregnancies and, therefore, fewer legal and illegal induced abortions.

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