Population Reports

New Contraceptive Choices

Melissa May, Population Council

Highlights

Contents

Published by The INFO Project, Center for Communication Programs, Johns Hopkins Bloomberg School of Public Health, 111 Market Place, Suite 310, Baltimore, Maryland 21202, USA

April 2005

Family planning users and providers have been calling for more choices. They want contraceptive methods that provide highly effective protection and at the same time cause fewer side effects, cost less, and are easier to use. In response, researchers are improving existing contraceptives and developing new ways to deliver hormones.

Offering a wide range of safe, effective, and convenient family planning methods encourages more people to use contraception. Having more choices helps ensure that users are satisfied with their family planning method. Most new methods reaching the market today result from investments made years ago. Virtually all methods undergo a long process of research and rigorous testing for safety and effectiveness and must obtain regulatory approvals before becoming available.

Key Developments

This report focuses on selected innovations in contraceptives that are more effective, have fewer side effects, are less costly to manufacture, and are easier to deliver than many current options. A few of the new contraceptives discussed in this report are already available in some countries, others are on the brink of introduction, and still others are several years away from reaching the market. Among the improved contra-

ceptives that have recently become available or are under development are the following:

Vaginal rings. Vaginal rings are a new way to deliver contraceptive hormones to the bloodstream. They are controlled by the user. Rings are easier to use correctly than oral contraceptives (OCs). Combined estrogen and progestin rings contain lower doses of hormones and cause fewer bleeding disturbances than combined OCs.

Transdermal patches. The contraceptive patch works by slowly releasing a combination of progestin and estrogen through the skin. The patch is safe, highly effective at preventing pregnancy, controlled by the user, and requires attention just once a week.

Implants. New research on implants has focused on different progestins that make it possible to reduce the number of rods or capsules from six to one or two. Also, the new implants produce fewer bleeding disturbances and ensure safety for use while breastfeeding.

Combined injectables. Combined injectables, compared with progestin-only injectables, disturb vaginal bleeding patterns less and allow earlier return to ovulation after women discontinue their use. Most combined injectables are injected once a month compared with once every two or three months for progestin-only injectables.

Condoms. New male condoms are being developed from nonlatex materials, while new female condoms are being developed in latex. Manufacturing condoms in different materials will expand variety, reduce cost, avoid allergic reactions, and so encourage condom use.

Fertility awareness-based methods. Two new fertility awareness-based family planning approaches—the Standard Days Method and the TwoDay Method—simplify older fertility awareness-based methods, making it easier for couples to track the woman's fertile days and know when to avoid unprotected sexual intercourse.

Oral contraceptives. Pharmaceutical companies are introducing new hormonal formulations of OCs designed to reduce side effects, and thus encourage continuation.

IUDs. New IUDs in development contain hormones or are frameless. They may make insertion and removal easier and reduce expulsion, pain, and bleeding—innovations that could lead to greater acceptability and use.

Transcervical sterilization. Transcervical methods for women are nonsurgical. They result in contraceptive protection comparable to surgical sterilization but are safer and easier to provide. They reach the fallopian tubes through the vagina and uterus.

Male hormonal contraceptives. Hormonal contraception for men that could be as effective as OCs for women is in the clinical trial stages of development. Male hormonal contraception would offer men a reversible and convenient method to control their fertility.

This report was prepared by Ushma D. Upadhyay, MPH. Indu Adhikary, MPH, and Catherine Richey provided research assistance. Bryant Robey, Editor. Richard D. Blackburn, Senior Research Analyst. Design by Linda D. Sadler. Production by John R. Fiege, Deborah Hall, Peter Hammerer, and Mónica Jiménez.

Population Reports appreciates the assistance of the following reviewers: Gabriel Bialy, Lee Claypool, Jeanette Cachan, Laneta Dorflinger, Henry Gabelnick, John Guillebaud, David Grimes, S.K. Gupta, Michael Harper, Michelle J. Hindin, Monica Jasis, Elaine Lissner, Christine Mauck, Stephen D. Mumford, Roberto Rivera, Pauline Russell-Brown, Sheldon H. Segal, Susheela Singh, Bulbul Sood, J. Joseph Speidel, Irving Sivin, Jeff Spieler, Regina Sitruk-Ware, David Sokal, Robert Spirtas, Markus Steiner, Anil Suri, G.P. Talwar, Kirsten Vogelsong, Mary Beth Weinberger, Dirk Wildemeersch, and Barry R. Zirkin.

Suggested citation: Upadhyay, U.D. *New Contraceptive Choices.* **Population Reports**, Series M, No. 19. Baltimore, Johns Hopkins Bloomberg School of Public Health, The INFO Project. April 2005. Available online: http://www.populationreports.org/m19/

Volume XXXII, Number 3

The INFO Project
Center for Communication Programs
The Johns Hopkins Bloomberg School of Public Health

Jane T. Bertrand, PhD, MBA, Professor and Director, Center for Communication Programs and Principal Investigator, The INFO Project

Ward Rinehart, Project Director

Stephen M. Goldstein, Chief, Publications Division

Population Reports (USPS 063-150) is published by The INFO Project, Johns Hopkins Center for Communication Programs, at 111 Market Place, Suite 310, Baltimore, Maryland 21202, USA.

Population Reports is designed to provide an accurate and authoritative overview of important developments in family planning and related health issues. The opinions expressed herein are those of the authors and do not necessarily reflect the views of the US Agency for International Development or The Johns Hopkins University.

Published with support from the Agency for International Development (USAID), Global, GH/POP/PEC, under the terms of Grant No. GPH-A-00-02-00003-00.

U.S. Agency for International Development

The Long Road of Contraceptive Development

A new contraceptive travels a long road before reaching the public. Most of today's new contraceptives result from investments started 10 to 20 years ago. Most potential new contraceptives undergo extensive research and rigorous clinical trials as part of their development and must obtain government regulatory approvals before they become available to the public.

Regulatory decisions made by the US Food and Drug Administration (US FDA) and the European Medicines Evaluation Agency (EMEA) play an important role in the introduction of new contraceptive methods in developing countries as well as in the US and Europe (1). The contraceptives distributed by the US Agency for International Development (USAID)—one of the largest suppliers of contraceptives in the developing world—usually need approval from the US FDA before they can be offered to organizations that receive support from USAID (248). Many developing countries have their own approval or registration processes for new health care products, but, because they have limited regulatory infrastructure, they often rely on US or European regulatory approval as a guideline (270).

After receiving regulatory approvals, new contraceptive methods reach people in developing countries primarily through two routes. First, some new methods may be introduced into national family planning programs for distribution through public-sector clinics and nongovernmental organizations (NGOs), often with support from donor agencies such as the United Nations Population Fund (UNFPA) and USAID. Second, private pharmaceutical companies that develop contraceptive methods may contract with manufacturers and distributors that make them available for sale through pharmacies, private clinics, and other retailers.

Not all new methods will reach developing countries, however. For each new method that becomes approved, donors and country programs must weigh the added cost of introducing it against the added benefits for contraceptive users (212, 272). Many factors other than regulatory approval—including logistics infrastructure, service delivery systems, method characteristics, cultural norms, and user preferences—influence how soon a new method is introduced into a country, or whether it is introduced there at all (111).

Testing Can Take Years

Typically, even before clinical trials in humans start, potential new contraceptives face several years of preclinical testing involving test-tube, or "in-vitro" studies, followed by testing in live animals. Preclinical testing evaluates the safety of the drug, device, or materials used to make the proposed method. After completing preclinical testing, a research organization seeking US FDA approval submits to the regulatory agency an Investigational New Drug Application or an Investigational Device Exemption to begin clinical trials. The method then must undergo three or four phases of clinical trials (see Table 1).

Generally, companies prefer to introduce new contraceptives that are modifications of currently available products because they have already proven safe and effective and therefore require fewer clinical trials and less expense and time than developing completely novel approaches to contraception (74, 111). Most recent advances in contraception have been variants of existing methods. Still, it is biologically and technologically feasible to go further—to develop entirely new methods that are more effective, have fewer side effects, and are more acceptable than many methods currently in development (112) (see Web Supplement, "Novel Gene-Based Approaches Promise Dramatic Change in Contraception" at http://www.populationreports.org/m19/supplements/novel.shtml).

Will Advances in Contraception Continue?

Are pharmaceutical companies and other organizations making sufficient investments today to keep up with future contraceptive needs and to take advantage of scientific advances? Contraceptive research and development is funded primarily by the World Health Organization (WHO), the US National Institutes of Health (NIH), USAID, charitable foundations, and small private companies (112). Contraceptive research and development in the pharmaceutical industry in recent years has been done primarily in Europe or by smaller US companies.

Table 1. The Four Phases of US FDA Clinical Trials

Phase	*Typical Length of Study Period*	*Typical Number of Study Participants*	*Purpose*
Phase I	1 to 2 years	20 to 80	Determine safe dosage and identify obvious side effects in humans. Evaluate safety of drugs or devices.
Phase II	1 to 2 years	100 to 300	Evaluate initial effectiveness, decide on dose, and further evaluate safety.
Phase III	2 to 4 years	200 to 3,000	Confirm effectiveness, monitor side effects and safety, compare with other contraceptives, and collect information that will enable methods to be used safely.
Phase IV (not always required)	Ongoing	Unlimited	After US FDA approval, postmarketing studies sometimes are required to evaluate risks, benefits, and optimal use. Also, to identify rare events that might not have been detected in clinical trials, or that occur in specific groups of people.

Source: Adapted from National Institutes of Health, 2002 (169). ***Population Reports***

Most large, for-profit manufacturers will pursue development of a potential contraceptive only if the estimated future profits are substantial enough to make up for the large investment costs (111, 112). Pharmaceutical companies tend to view the US market for contraceptives as saturated and potential markets in developing countries as unprofitable (205). Also, to justify investment in a new contraceptive method, the company must project that it could offer a better financial return than other investments could offer (231).

Companies also worry about lawsuits and liability associated with potential new contraceptives (17, 205). Risk is less tolerated in preventive medical products and approaches for healthy people—such as contraception—than in curative ones for sick people (111, 181, 231). Moreover, products related to reproduction often elicit emotional reactions and cause controversies that other medical products do not (181, 205). Family planning advocates have expressed concern that regulatory agencies hold contraceptives to more restrictive standards than other drugs or devices (35, 81, 181, 231).

To help compensate for diminishing pharmaceutical company investment, manufacturers of contraceptive products are collaborating with academic research centers and nonprofit organizations (111). International networks and public-private partnerships for contraceptive development have been instrumental in attracting and retaining donor and private-sector interest in contraceptive development (80, 112).

Scope of This Report

This report does not attempt to cover all new contraceptive methods that have been recently released or that are in research and development. The report focuses on selected innovations in contraceptives that are more effective, less costly to manufacture, easier to deliver, and that cause fewer side effects than currently available options. The report also covers some existing contraceptive methods that are not yet widely known or generally available, or that have recently been approved by the US FDA. Additional new methods, including innovative gene-based approaches and cervical barriers, are covered in a Web Supplement to this report, available at: http://www.populationreports.org/m19/supplements. ❖❖

NuvaRing (actual size) is the first vaginal ring to be widely available. It releases a combined formula of a progestin and an estrogen. It was approved by the US FDA in 2001.

Organon USA Inc.

Vaginal Rings

Vaginal rings, recently approved by the US FDA and on the market in some countries, offer a new way to deliver hormones into the bloodstream to prevent pregnancy. Combined estrogen and progestin rings offer good cycle control and deliver hormones more steadily than combined oral contraceptives (OCs).

Women can control the use of vaginal rings. To use the vaginal ring, a woman inserts it into the vagina with her fingers, placing it anywhere that feels comfortable. It fits best in the higher part of the vagina. Studies in developed countries have found that women follow rules for correct use at rates higher than those seen in studies of combined OCs (38, 69, 198).

The ring remains in place all day and night and requires no further attention (187). Hormones diffuse continuously from a reservoir within the ring, first into vaginal tissues and then into the bloodstream. If necessary, the ring can be removed for up to three hours for comfort during sexual intercourse, for cleaning, or for any other reason. Rings come both as combined formulations—containing a progestin and an estrogen—and as progestin-only formulations.

Two Combined Vaginal Rings

The combined formula NuvaRing®, developed by the pharmaceutical company Organon, is the first vaginal ring to be widely introduced. It has been approved in nine European countries since the late 1990s—more than 30 years since the first patent was granted for vaginal rings (28). The US FDA approved NuvaRing in 2001 (249).

Brazil and Chile are the only developing countries where NuvaRing is available, and its availability in other developing countries is unlikely because of its high cost. NuvaRing is also available in Europe and the US. Organon plans to introduce NuvaRing in Australia and Canada in 2005 and in the UK no sooner than 2006 (5).

NuvaRing releases 120 µg (micrograms) of the progestin etonogestrel and 15 µg of the estrogen ethinyl estradiol per day. Women use NuvaRing for three weeks, then remove it for one week, during which they have withdrawal bleeding. A new NuvaRing is needed for each four-week cycle. Thus a woman would require 13 rings per year; a single ring can last up to 35 days (167). While large studies have not examined continuous use of the vaginal ring, smaller studies suggest that women may be able to safely use combined vaginal rings consecutively for four weeks at a time, skipping the withdrawal bleeding (63, 166). Studies on continuous use are underway.

Another ring, still in clinical trials, releases a combination of 150 µg of a different progestin, Nestorone®, and 15 µg of the estrogen ethinyl estradiol per day. The Population Council, with USAID support, is developing this ring specifically for use in developing countries. It will be effective for over 12 months, making it more cost-effective than NuvaRing. Users would keep the ring in place for three weeks, then remove it for the fourth week to allow a withdrawal

bleed, and then reinsert the same ring for another three weeks (119). Early clinical trials have been promising (136), and phase III trials are planned to begin in 2005 (214).

Effectiveness. Combined rings release sufficient amounts of estrogen and progestin to prevent ovulation (166). In addition, the progestin thickens cervical mucus and suppresses endometrial growth (235). In a pooled analysis of 2,322 women using NuvaRing in Canada, the US, and Europe, there were 1.2 pregnancies per 100 women in the first year of use. Women used the ring correctly in 86% of cycles (69).

Side effects. In general, bleeding problems are less frequent among users of combined vaginal rings than among users of combined OCs (38, 69, 175) or of progestin-only rings (29). Breakthrough bleeding can occur, but this side effect is not common (198).

Other side effects occur about as often among users of combined rings as with combined OCs (38). In the pooled analysis of 2,322 women, the most commonly reported side effects were headache and vaginitis, each of which occurred among less than 6% of users. Less than 5% reported white vaginal discharge, vaginal discomfort, weight increase, nausea, mood changes, breast tenderness, uterine cramps, or acne (69).

Two Progestin-Only Rings

Two types of progestin-only rings are available or in development—Progering, a ring containing the natural hormone progesterone, and a ring yet to be named containing the synthetic progestin Nestorone. Progestin-only rings function mainly by thickening cervical mucus to prevent sperm penetration. They also have some effect on preventing ovulation and build-up of the endometrium (164).

While progestin-only rings are less effective overall than rings containing both a progestin and an estrogen, they are highly effective among breastfeeding women because breastfeeding itself provides some protection from pregnancy. Also, they may be more appropriate than combined rings for breastfeeding women because they do not contain estrogen, which could reduce milk production (152). The most common reason for discontinuation of progestin-only rings is weaning, as mothers choose more effective contraception after they stop breastfeeding. Bleeding disturbances, a common side effect of all progestin-only methods, is another frequent reason for discontinuation, but it is less likely to be noticed while a woman is breastfeeding (39, 152, 153).

Progesterone rings. Progesterone rings are highly effective at preventing pregnancy among lactating women, studies show—not significantly different from the IUD. Each ring releases 10 mg (milligrams) of progesterone daily and lasts for three months. Women can use these rings continuously for up to one year, after which effectiveness declines (152, 217, 220). Progering was registered and approved in Chile and Peru in 1998 for use by breastfeeding women. The Population Council, CONRAD, and the private company Silesia, funded its research and development.

In clinical trials women using the progesterone ring reported experiencing vaginal problems related to discharge, urinary discomfort, bleeding disturbances, and reproductive tract infection (152, 199). In a Chilean study of breastfeeding women, less than 5% of users experienced any one of these side effects (153).

Nestorone rings. Nestorone rings, which also were developed by the Population Council (215), are similar to progesterone rings but rely on ST-1435, a more potent synthetic progestin that has unique properties. This ring will release 50, 75, or 100 µg of Nestorone per day (214).

The Population Council focused research on Nestorone after discovering that, when taken orally, it is rapidly metabolized and inactivated. This feature makes it particularly appropriate for use by breastfeeding women, because infants who ingest breast milk will not absorb the progestin in the breast milk, not even in the tiny and probably unimportant amounts that are ingested when other progestin-only methods are used (215). (For information on other Nestorone-based methods, see "Nestorone spray gel," p. 7, and "Nestorone implants," p. 8.)

Nestorone-releasing rings provide effective protection from pregnancy for lactating women for up to one year, even if weaning takes place earlier (41, 152, 215). Clinical trials on Nestorone rings have been suspended until the Population Council obtains more funding to continue them (214).

Acceptability

Generally, women like vaginal rings, according to acceptability studies in Australia, Canada, Chile, the Dominican Republic, the US, and 12 European countries. Primary reasons for approval include that rings were effective, easy to insert, use, and remove, and did not require daily action (173, 258).

The studies find that some women dislike the vaginal ring for the same reasons others like it, however. That is, they do not want the responsibility of inserting and removing it (258). A participant in one clinical trial chose an IUD over the ring because, as she said, "I may forget to put [the ring] back in, or I might remove it and then not be able to reinsert it" (199). Additionally, some women did not like the ring because they prefer not to touch their vaginas, and some dislike its tendency to slip out (173). ❖❖

Vaginal Rings

Description: Hormone-releasing ring kept in the vagina and remaining in place day and night for three weeks or one year, depending on the formulation.

Stage of development: Two on the market and several others in clinical trials.

Effectiveness: 1.2 to 1.5 pregnancies per 100 women in the first year as typically used.

How they work: Release progestin alone or progestin with estrogen into the vaginal walls and through to the bloodstream, preventing ovulation, thickening cervical mucus, and suppressing endometrial growth.

What's new? New, user-controlled method of hormone delivery. Combined rings offer better cycle control with more steadily released hormones than combined OCs.

Transdermal Contraception

Description: Patches, sprays, or gels, applied weekly or daily, that transfer hormones through the skin.

QUICK LOOK

Stage of development: One product marketed.

Effectiveness: Patches—0.8 to 1.3 pregnancies per 100 women in the first year as typically used.

How they work: Patches release estrogen and progestin through the skin, preventing ovulation, thickening the cervical mucus, and suppressing endometrial growth.

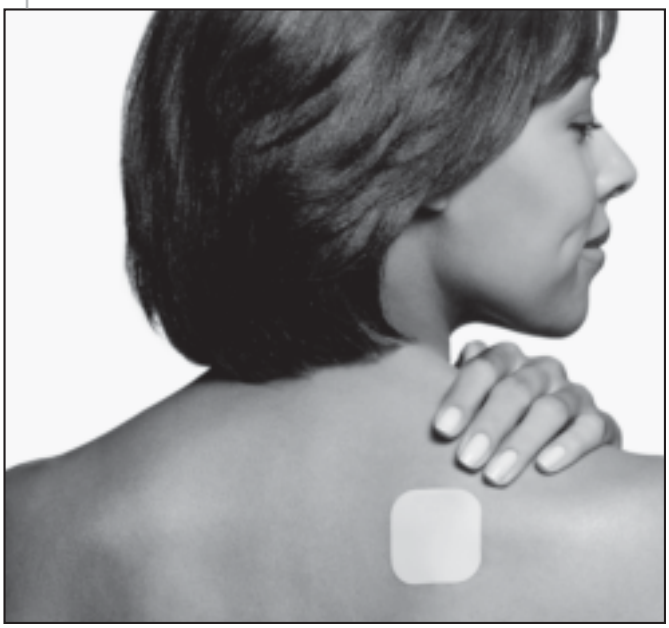
What's new? Patches require attention just once a week. Used correctly at higher rates than combined OCs. Sprays or gels transfer fast-drying progestins onto the skin. They are absorbed immediately and diffuse into the bloodstream.

Transdermal Contraception

A new hormonal contraceptive method, the patch, works transdermally—that is, by slowly releasing a combination of progestin and estrogen through the skin. The new contraceptive patches are user-controlled and require attention just once a week (210, 285). Other transdermal contraception in development includes sprays and gels.

Combined Patches

The only contraceptive patch on the market today is Ortho Evra® (also called Evra outside the US), developed by Ortho-McNeil Pharmaceutical. It was approved by the US FDA in 2002 and is available in Europe and in Canada, Hong Kong, Singapore, South Korea, and the US.



Ortho-McNeil Pharmaceutical

The only contraceptive patch on the market today, Ortho Evra, releases a combined hormonal formula that is as effective as OCs, and many women find it easier to use correctly.

The combined patch delivers 150 µg of the progestin norelgestromin and 20 µg of the estrogen ethinyl estradiol per day. A user wears a patch for one week, after which she must replace that patch with a new one each week for a total of three weeks, followed by one week with no patch. The hormones in the patch protect against pregnancy by preventing ovulation, thickening cervical mucus, and suppressing endometrial growth. More than 70,000 of the patches have been clinically tested worldwide among more than 3,300 women (19).

Ortho Evra is a square patch, each side about 4.45 centimeters (1.75 inches) long, resembling a light brown bandage. The developer is investigating additional colors to match a greater variety of skin tones. The patch contains three layers: an outer protective layer of polyester, a medicated adhesive middle layer, and a clear polyester release liner, which is removed just before application. The adhesive layer continuously delivers hormones through the skin into the bloodstream. The patch can be placed on the buttocks, lower abdomen, upper outer arm, or the upper body (front or back, but not on the breasts).

The patch adheres well to the skin, allowing women to perform regular daily activities such as bathing, swimming, working, and exercising without interruption even in warm, humid climates (280). The patch falls entirely off in about 2% of cases, especially if women place it where they have applied creams, oils, powder, or make-up (22, 225).

Women who like combined OCs but have trouble remembering daily pill-taking may be good candidates for the Ortho Evra patch (44). It provides effectiveness and cycle control similar to OCs' as correctly used. In clinical trials women liked the patch as much as OCs (100, 209).

Another patch is in development. Schering AG in Germany is developing a weekly combined patch that is in phase III clinical trials. This clear patch measures 3.16 centimeters (1.25 inches) on each side (half the size of Ortho Evra) and releases 50 µg per day of the progestin gestodene and 18 µg of the estrogen ethinyl estradiol (101, 202). Because most of the published research is on Ortho-McNeil's patch, the following discussion focuses on Ortho Evra.

Correct use. Correct use entails applying the first patch within five days after menstruation begins and then changing it each week for three weeks. The patch is applied to a new location each week and once in place should not be moved. For the fourth week no patch is worn, to allow for withdrawal bleeding (179, 280). Women may be able to use the patch continuously, using a fourth patch in the fourth week, skipping the withdrawal bleeding period. Studies are in progress to evaluate continuous use (20).

Women report using the patch correctly more often than they use OCs correctly. In a comparative study, for example, women used the patch correctly in 88% of their cycles compared with 78% of cycles among OC users (22). In a clinical trial of the patch alone, women used it correctly in 90% of cycles (225).

Younger women who have trouble following rules for correct use of OCs may find it easier to use the patch correctly. One study comparing correct use among patch users and OC users found that patch users under age 20 reported using it correctly in 89% of cycles while OC

users under age 20 reported taking their pills correctly in only 68% of cycles (14).

Effectiveness. When the Ortho Evra patch is used correctly, 0.6 of every 100 women (6 per 1,000) become pregnant in the first year of use according to pooled data from three clinical studies (285). Even when not used correctly all of the time, the patch is still highly effective; in typical use 0.8 of every 100 women (8 per 1,000) become pregnant in the first year of use (285). Another international multicenter study found a correct-use pregnancy rate of 1.1 per 100 women and a typical-use rate of 1.3 per 100 women, a rate lower than for women in the control group using combined OCs (22).

The same analysis found a lower effectiveness rate among women weighing more than 198 pounds (90 kgs). While the reasons that weight may affect the effectiveness of the Ortho Evra patch are unclear (44, 285), a study that found similar results among OC users hypothesized either that heavier women more rapidly metabolize the hormones, or that extra fat absorbs the steroids so there are reduced levels of circulating steroids in the blood (107).

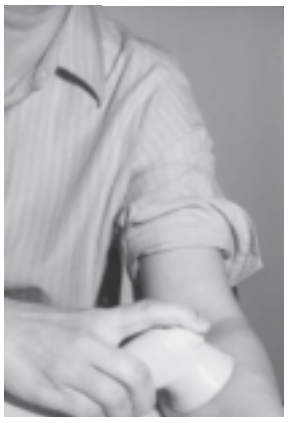
Side effects. The most commonly reported side effects of the Ortho Evra patch are skin irritation or rash at the site of application, affecting about 20% of users in clinical trials (22). Other reported side effects are those also commonly associated with combined OC use.

The incidence of breakthrough bleeding and spotting is low among users of the Ortho Evra patch and decreases the longer they use it (225). One large clinical trial found that during the first month of use 18% of users reported breakthrough bleeding and spotting, significantly more than among combined OC users. After the second month, however, the incidence of bleeding irregularities declined among patch users, and there were no significant differences in bleeding or spotting thereafter (22).

Spray-On Contraceptives

The progestin Nestorone, appropriate for breastfeeding women, can be delivered transdermally not only through a patch but also through a spray or gel. Phase I clinical trials of the Nestorone Metered Dose Transdermal System, a daily progestin-only spray-on contraceptive, began in Australia in 2004. The spray-on approach is a new technique for transferring a preset dose of fast-drying hormones onto the skin. The spray is absorbed almost instantaneously, so there is no risk of washing it off. The hormone collects as a reservoir within the skin, from which it then slowly diffuses into the bloodstream (279). In a clinical trial a Nestorone gel applied to the skin daily for three months suppressed ovulation in 83% of participants applying 1.2 mg per day (215). ❖❖

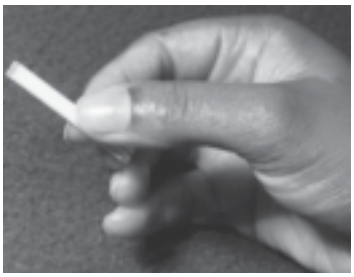
Ortho-McNeil Pharmaceutical



Spray-on contraception is a new way to supply a preset dose of hormones.

Contraceptive Implants

New research on contraceptive implants has focused on reducing the number of rods or capsules by using different progestins, minimizing side effects, particularly bleeding disturbances, and assuring that implants are safe for use while breastfeeding (221). Women around the world use Norplant® implants, the first implant available, approved by the US FDA in 1990. Norplant implants employ six capsules to deliver the progestin levonorgestrel. They provide excellent contraceptive protection but in some countries also have high discontinuation rates due to bleeding disturbances. Such bleeding changes are the most common side effect of implant use and the reason women give most often for discontinuing use (87, 193).



Karen Tweedy-Holmes, Population Council

Jadelle, a new implant, uses only 1 rod and is easier to insert and remove than Norplant implants.

The newer implants are similar to Norplant implants but offer several improvements. The new implants consist of one or two rods or capsules. Like Norplant implants, they are inserted just under the skin of the upper arm to deliver progestins into the bloodstream. Most use rods rather than capsules. Rods differ from capsules in that they are filled with a mixture of steroid crystals and polymer. Capsules, on the other hand, are hollow polymer tubes filled with free steroid crystals (62).

Two of the new implants—Jadelle® and Implanon®—are approved in many countries, while the other new formulation, Nestorone, is not yet on the market. The new implants have been slow to become available. There are several reasons: They are expensive to develop and market, their initial expense is too high for many family planning programs, and they require provider training in techniques of insertion and removal.

Also, for some women the advantages of implants may not be much greater than those of other methods such as the IUD, which is longer lasting and less expensive. Nevertheless, experts and pharmaceutical companies expect that over the next decade, as more countries register the new implants, they will replace Norplant implants and will be offered by some family planning programs that have not provided implants previously (106, 221).

New implant systems with fewer capsules or rods make insertion and removal much easier and produce fewer complications and less discomfort for users compared with Norplant's six capsules (150, 218). The newer implants are inserted using a specially designed preloaded applicator that eliminates the need for a separate incision (216).

Most insertions of Jadelle take less than five minutes (218, 222). Rates of complications and removal are about half

those for Norplant implants (216). For trained providers using a preloaded disposable applicator, Implanon insertion takes less than one minute (254).

New Formulations with Fewer Rods

New implants deliver the progestin levonorgestrel (Jadelle and Chinese No. 2), etonogestrel (Implanon), or ST-1435 (Elcometrine and Nestorone implant). Implants work primarily by thickening cervical mucus so that it is impenetrable to sperm, preventing ovulation in many cycles, and supressing endometrial growth (30, 62, 66).

Levonorgestrel implants. The implant Jadelle (formerly known as Norplant-2) was developed by the Population Council and is manufactured by Schering Oy (formerly Leiras Pharmaceuticals) in Finland. It was first approved in Thailand and Indonesia and later approved in several African countries as well as several Scandinavian and Western European countries and the US. It is available through the private sector in Europe and through national family planning programs in Colombia, Dominican Republic, Ethiopia, Guatemala, Kenya, Mauritius, Panama, Rwanda, Singapore, Yemen, Zambia, and Zimbabwe (106).

Jadelle implants have never been available in the US, however (273). Wyeth, the company that held the distribution license, decided not to market it, and the Population Council is looking for a new US distributor (217).

Jadelle was designed to deliver the same daily dose of levonorgestrel that Norplant delivers, but from two rods instead of six capsules, by releasing the progestin at a higher rate per rod. In a clinical trial of Jadelle involving 1,198 women, none became pregnant in the first four years of use, and 1 per 100 women became pregnant in the fifth year of use (218). Initial effectiveness studies led several countries to label Jadelle as providing three years of protection. Since later studies demonstrated that its contraceptive effect lasts at least five years, many countries, including the US, have now labeled it for five years of use (71, 224). Jadelle's side effects, continuation rates, and contraceptive effectiveness rates are similar to Norplant's (2, 61), but Jadelle is easier to insert and remove (218).

The Chinese No. 2 implant system, also called Sinoplant or Sino-implant, and developed by Dahua Pharmaceutical in China, is nearly identical to Jadelle but contains more levonorgestrel (150 instead of 140 mg) (71).

New Contraceptive Implants

QUICK LOOK

Description: One or two progestin-releasing rods inserted just under the skin.

Stage of development: One entering phase III clinical trials and two being marketed worldwide.

Effectiveness: 0.3 to 1.1 pregnancies per 100 women in the first year of use as typically used.

How they work: Progestin released under the skin thickens the cervical mucus, prevents ovulation in many cycles, and suppresses endometrial growth.

What's new? Fewer rods than Norplant implants and therefore easier and quicker to insert and remove.

Etonogestrel implants. In 1998, after 12 years of research, Organon launched its etonogestrel implant Implanon (178). Indonesia was the first country to approve Implanon, in 1998. Since then more than 40 European and Asian countries have approved it (273). Organon applied for US FDA approval of Implanon in 2004 and expects approval in 2005 (65).

Implanon consists of a single rod labeled to provide three years of protection from pregnancy, although several studies have found that its contraceptive effect may last at least four years (3, 131). While women using Norplant, Jadelle, or Nestorone have incomplete and inconsistent inhibition of ovulation, Implanon users have few if any ovulatory cycles (148). In clinical trials no women became pregnant over the 5,000 woman-years of study (2, 62).

Nestorone implants. The progestin ST-1435 (also known as Nestorone) is found in the Nestorone implant, which is being developed by the Population Council (214). Effective for two years, the Nestorone implant is a single rod made of a silicone rubber membrane that controls the release rate (68). It is designed specifically for breastfeeding women. Infants of breastfeeding mothers who are using the Nestorone implant have no detectable progestin in their blood (56, 67). The Nestorone implant development program began in the early 1980s (134) and has completed phase II clinical trials. The Population Council is looking for partners to continue the development of this implant (214).

Lactating women have found the Nesterone implant acceptable, but nonlactating women have complained of prolonged and irregular bleeding (219). When the implant was compared with the Copper-T 380A IUD for more than 2,000 woman-months of use by 200 breastfeeding women, no pregnancies occurred in either group, but Nestorone implant users had significantly less irregular bleeding (151).

Side Effects

Bleeding disturbances, including amenorrhea, spotting, and irregular or prolonged bleeding, are the greatest drawbacks of all implants (62, 273). In some clinical trials bleeding disturbances account for up to half of all reasons given for discontinuation. These side effects usually diminish with continued use, and many women have more regular bleeding patterns after six to nine months of use (57, 61, 87).

The exact mechanism of progestin-induced bleeding disturbances is not completely understood, but implant users experiencing such disturbances are at no more risk of becoming pregnant than users not experiencing them (62). The bleeding patterns reported for different progestin implants vary, as do women's tolerance of bleeding, and it is not possible to predict bleeding patterns for individuals (62).

A review of studies reported that infection or pain at the implant site occurred in less than 7% of users. In an analysis of reported side effects of implants, the most frequent side effects that are probably related to implant use are headaches and acne, both reported by less than 30% of users. Weight gain, dizziness, and mood changes are mentioned by less than 20% of users. Rates of these problems are similar among users of the different implants (40).

Combined Injectables

Combined injectables—that is, injectable contraceptives that contain both a progestin and an estrogen—are gaining new attention among family planning clients and providers. Combined formulations are generally injected once a month compared with once every two or three months for progestin-only injectables such as norethindrone enanthate (NET-EN) and depot-medroxyprogesterone acetate (DMPA). Compared with progestin-only injectables, combined injectables disturb vaginal bleeding patterns less and allow earlier return to ovulation after women discontinue use (170, 271).

The following discussion focuses on the newer combined injectables: Cyclofem® (also known as Lunelle®, Lunella®, Cyclo-Provera®, Novafem®, and Feminena) and Mesigyna® (also known as Norigynon®) (see Table 2). Combined injectables have been studied since the 1960s, and several formations have been used in some countries for the past two decades. Older combined injectable formulations that are still in use include Chinese Injectable No. 1 (also known as Gravibinon®) and deladroxate (available in Latin America under various trade names, including Perlutal®, Patectro, and Topasel®) (135, 170).

While even the newer combined injectables have been on the market for years, they have become more widely known and used in recent years because new safety and effectiveness data have become available. The US FDA has approved Lunelle, although it is currently not available in the US (250). It delivers 25 mg of MPA and 5 mg estradiol cypionate.

WHO accelerated the development of Cyclofem for use in developing countries in response to requests from India, Mexico, and other countries in the 1970s for a safe and effective monthly injectable (170). Today Cyclofem is available in 18 countries, mostly in Latin America and Asia (114).

Another monthly injectable, Mesigyna, delivers 50 mg NET-EN and 5 mg estradiol valerate. Mesigyna was developed by WHO and first made available by Schering AG at about the same time as Cyclofem. Today it is registered in 36 countries, primarily in Latin America and Asia (96, 114).

Effectiveness

Combined injectables provide contraception mainly by preventing ovulation but also by thickening the cervical mucus and suppressing endometrial growth. In clinical trials 0.1 to 0.4 of every 100 women (1 to 4 women per 1,000) became pregnant in the first year of use (59, 200, 271). Studies of combined injectables in regular use, rather than in clinical trials, have found pregnancy rates just as low (86, 96). Women who stop using combined injectables can become pregnant as soon as six weeks after their last injection, which is much sooner than for women stopping DMPA (191).

Combined Injectables

Description: Monthly injections containing both a progestin and an estrogen.

Stage of development: On the market in many countries.

Effectiveness: 0.1 to 0.4 pregnancies per 100 women per year of use as typically used.

How they work: Injected estrogen and progestin prevent ovulation, thicken the cervical mucus, and suppress endometrial growth.

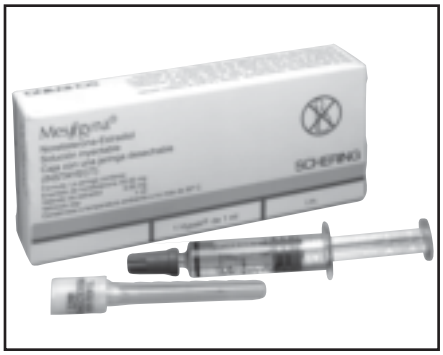
What's new? Gaining new attention among family planning clients and providers due to recent US FDA approval. Provide better cycle control than progestin-only injectables such as DMPA.

Side Effects and Access Problems

Side effects of combined injectables, especially bleeding disturbances, are the primary cause of discontinuation (86, 95). Other reported side effects of combined injectables include headaches, dizziness, and breast tenderness (59, 125, 271)—side effects typical of hormonal contraceptive methods generally.

Another common reason for discontinuation is a lack of access. Many women are unable to return to the clinic or pharmacy every month for another injection (76, 200), while clinics sometimes are unable to resupply at the pace needed (118). Some clinics have drastic shortages and are unable to give women their injection when they return (146).

Still, discontinuation rates for combined monthly injectables are lower than those for progestin-only injectables. A main reason for the difference is that irregular bleeding patterns are less common with combined injectable use, and they tend to decrease with length of use. At the end of



Schering AG

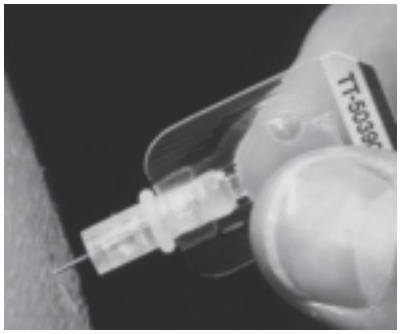
Combined injectables have gained attention after US FDA approval. They offer better cycle control than DMPA.

Table 2. Newer Combined Injectables

Trade name	*Progestin*	*Estrogen*
Cyclofem/Cyclo-Provera	25 mg Medroxyprogesterone acetate	5 mg Estradiol cypionate
Feminena/Lunelle/Lunella		
Mesigyna/Norigynon	50 mg Norethisterone enanthate	5 mg Estradiol valerate

Source: United Nations Development Programme, United Nations Population Fund, World Health Organization, and World Bank (247)

Population Reports



PATH

The subcutaneous DMPA formulation will be available only in Uniject, a single-use syringe that is easier to use than other syringes.

one year of use an average of 70% of combined injectable users experience their regular monthly bleeding compared with about 8% of DMPA users. Amenorrhea is also less common among users of combined monthly injectables than with DMPA. Most women who discontinue use for bleeding-related reasons cite heavy, prolonged, or irregular bleeding (271).

To provide better access to combined injectables, the Program for Approved Technology in Health (PATH) is promoting the use of Uniject, its single-use, prefilled, nonreusable syringe. Uniject would allow community health workers to provide the injections or women to give themselves the injections. In Brazil a study found that about two-thirds of participants agreed to receive training and to use Uniject to self-administer a monthly injectable contraceptive. Of these 56 women, 93% correctly self-administered the injectable, and 57% preferred self-injection at home over going to a clinic each month (26). ❖❖

New DMPA Formulation Approved

Subcutaneous depot-medroxyprogesterone (DMPA-SC)—a new low-dose formulation of the currently available DMPA—received approval from the US FDA in December 2004 under the name depo-subQ provera 104™. It will be launched in the US in 2005 (207). DMPA-SC is injected into the tissues just under the skin with a finer, shorter needle than for conventional DMPA, which is injected deep into the muscle. As a result, providers giving DMPA-SC injections require less training than is needed for conventional DMPA injections.

The new formulation provides slower and more sustained absorption of the progestin than conventional DMPA, while consistently preventing ovulation (49, 115). This formulation allows for a 30% lower dose of progestin (104 mg instead of 150 mg) but with the same duration of effect as conventional DMPA (116). As with currently available DMPA, users of DMPA-SC have their injections every three months. Effectiveness and reported side effects also are similar (116).

DMPA-SC will be available only in a pre-filled Uniject syringe. In a study in Poland women preferred home injections of DMPA-SC with the Uniject syringe over receiving their injections at a doctor's office (117). PATH which developed and patented Uniject, licensed the Uniject technology to Becton Dickenson (BD) in 1996. Pfizer is currently negotiating an agreement with PATH and BD to distribute DMPA-SC in the Uniject syringe to developing countries, with USAID support (207, 232).

Condoms

Increasingly, companies are manufacturing male and female condoms in different materials to expand variety and encourage use. Male condoms are being developed in nonlatex varieties, and female condoms, first made of polyurethane, are now being developed in latex form.

While condoms provide the best protection against HIV infection, other new barrier methods in development also may provide some protection, especially when used along with microbicides, when microbicides become available. (See *INFO Reports*, "Microbicides: New Potential for Protection," January 2005). These new barrier methods include cervical caps, diaphragm-like devices, and sponges that emphasize comfort and ease of use (see Web Supplement, "Vaginal Barriers" at http://www.populationreports.org/m19/supplements/vaginal.shtml).

Male Condoms

Newer forms of male condoms include synthetic nonlatex condoms, which many men prefer. For men who are sensitive or allergic to latex, new condom materials include polyurethane and styrene ethylene butylene styrene (SEBS), a synthetic material known commercially as Tactylon®.

Synthetic nonlatex male condoms. Polyurethane and SEBS condoms have two advantages over latex condoms. They have a longer shelf life and can be used with oil-based lubricants, which can damage latex condoms (84). Some users also say nonlatex condoms have less odor, fit more comfortably and are less constricting, and transfer body heat better than latex condoms (84). Surveys to confirm these impressions have not been conducted, however.

Polyurethane condoms have been available in the US since 1995 (250). SEBS condoms are not yet marketed (70). The availability of nonlatex condoms in developing countries is limited. A Colombian company, Natural Sensation, has been producing polyurethane condoms since 1993, branded as Unique® condoms for men and Unisex® condoms for men and women. These brands are available throughout Latin America (46).

Many studies have examined differences between synthetic nonlatex and latex condoms (45, 54, 84, 190, 234, 245, 255). An analysis of data from 10 comparative studies found that more users preferred synthetic nonlatex condoms and said they would recommend them to others. Several synthetic nonlatex condoms (Durex Avanti, eZ-on, and Tactylon), however, broke or slipped more often during intercourse or withdrawal than latex condoms (84). Despite the greater breakage and slippage rates, most were as effective as latex condoms in preventing pregnancy (84).

Female Condoms

Women in focus-group studies say that they want contraceptive barrier methods whose use they could control (97, 186). The only female condom available, however,

the FC Female Condom® (formerly Reality), is made of polyurethane and is too costly for many family planning programs or clients. Several newer female condoms—the FC2, the VA feminine condom, and the PATH Woman's Condom—are made of less costly materials. They are now in clinical trials.

FC2 Female Condom. The FC2 Female Condom is a second-generation female condom developed by the Female Health Company (FHC). It is based on the polyurethane FC Female Condom but could cost less than half as much. The FC2 Female Condom is made from synthetic latex, which is softer than polyurethane, and is assembled through a dipping process, a less expensive technique than the polyurethane method of welding (137).

The FC2 Female Condom is expected to become available to developing countries in 2005. A phase II clinical trial comparing FC2 with the original FC Female Condom has been completed, and the product is awaiting CE Marking in Europe—a designation indicating that a product meets health and safety standards. The manufacturer also plans to apply for US FDA approval (137).

VA feminine condom. The VA feminine condom, also known as the Reddy female condom and as V-Amour, contains a soft sponge to hold it in place inside the vagina rather than a ring as used in the FC Female Condom. Also, it has a V-shaped external rim. Its manufacturer, Medtech Products Ltd., and Intellx, Inc., introduced it in Germany and Spain on a limited basis in 2002, as the first latex female condom (180).

The VA feminine condom has received CE Marking and will be marketed in Western Europe and in Brazil, India, and South Africa starting in 2005 (155, 180). CONRAD and Family Health International (FHI) are conducting phase III clinical trials on a fifth redesign of the condom to determine effectiveness and acceptability (70, 79, 155). Upon completion of these studies, the manufacturer plans to apply for US FDA approval (180).

Natural Sensation

At a manufacturing plant in Colombia, a technician tests the Unique brand polyurethane condom. Polyurethane condoms have a longer shelf life than latex condoms.

New Condoms

Description: Male condoms—A sheath made of nonlatex materials placed over the penis. Female condoms—a sheath made of latex inserted into the vagina.

Stage of development: Some already on the market and others in clinical trials.

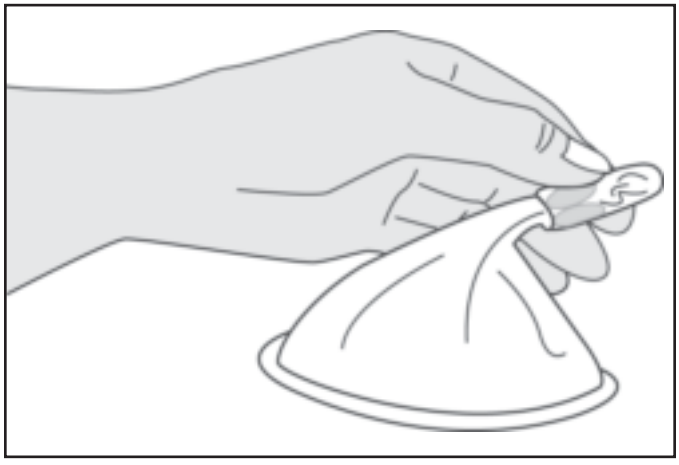
Effectiveness: Probably similar to other condoms—10 to 15 pregnancies per 100 women per year as typically used.

How they work: Cover the cervix or the penis to block sperm from entering the cervical canal.

What's new? Designed to expand variety, encourage use, cause fewer allergies, or cost less than other available barrier methods.

PATH Woman's Condom. Since 1998 PATH has been developing a new female condom. PATH has tested 50 different prototypes for ease of insertion, comfort, stability, design, and cost. The final product consists of a dissolving capsule intended to make insertion easier, a polyurethane condom pouch, and a soft outer ring, allowing for nearly universal fit. Once inserted, sections of urethane foam on the condom pouch allow the condom to cling lightly to the vaginal walls so that it does not move during use (24, 25).

In 2004 PATH completed a study among 60 couples during 180 product uses in Mexico, South Africa, and Thailand. The study found that 98% of women and 99% of their partners were satisfied with the way the condom felt (23). Phase I clinical trials evaluating the safety and acceptability of the PATH Woman's Condom compared with the original FC Female Condom are currently underway in the US, with support from CONRAD, and are expected to finish by mid-2005. PATH expects US FDA approval in 2007 (23, 24). ❖❖



PATH

The PATH woman's condom, currently in development, is designed for easy insertion, near-universal fit, and reasonable cost—features that many women value in a barrier method.

Fertility Awareness-Based Methods

Two new variations on fertility awareness-based approaches—the Standard Days Method™ and the TwoDay Method™—help women track their fertile days. Incorporating these or other fertility awareness-based methods into family planning services can appeal particularly to couples who do not want to use supply or clinical methods because of personal beliefs, financial constraints, lack of access to other contraceptives, or other reasons (161, 233). Both methods have been developed by the Institute for Reproductive Health (IRH) at Georgetown University, with support from USAID.

Family planning methods based on fertility awareness depend on commitment from and cooperation of both partners to avoid unprotected sex during the woman's fertile times. Male involvement is crucial to effective use of these methods (121, 165). Thus they are impractical for couples who cannot communicate about sex. Also, women who lack the power to choose when to have sex are not good candidates for these methods (99).

The Standard Days Method

Couples can use the Standard Days Method to identify their likely fertile days and limit unprotected sex to days on which the woman is not likely to be fertile. To help women keep track of their fertile days, the developers of the method have created a string of color-coded beads called CycleBeads™ that represent a woman's menstrual cycle. To use CycleBeads, a woman moves a rubber ring to the next bead each day to identify where she is in her cycle. The color-coded beads indicate whether she is on a fertile or infertile day. When the rubber ring is on a white bead, it signifies a fertile day, and thus the couple should avoid unprotected sex.

The Standard Days Method is based on the timing of the "fertile window" during the woman's menstrual cycle—several days before ovulation and a few hours after—when she can become pregnant. The timing of ovulation varies among women and across cycles for the same woman. The developers of the Standard Days Method used a computer simulation that took into account this variation to determine how to provide maximum protection from pregnancy, while minimizing the number of days that users must avoid unprotected sex. Their analyses concluded that the fertile period most likely occurs between days 8 and 19 of the menstrual cycle (16, 260).

The Standard Days Method works best for women who usually (in at least 10 of every 12 cycles) have menstrual cycles between 26 and 32 days long (16). The Standard Days Method is not effective for women who have shorter or longer cycles, because they may ovulate outside of days 8 through 19. Some women may think they have regular cycles but do not. Through screening and monitoring, family planning providers can help identify women for whom this method will be most effective (213).

Effectiveness. For women who have regular cycles (between 26 and 32 days long) the Standard Days Method is about as effective as barrier methods. In a clinical trial in Bolivia, Peru, and the Philippines, which included only women who have regular cycles, typical use of the Standard Days Method resulted in 12 pregnancies per 100 women in one year of use. Typical use includes abstaining or using condoms, withdrawal, or no method at all on fertile days. Among those who used the method

Georgetown University, Institute for Reproductive Health

To use the Standard Days Method, a woman avoids unprotected sex on days 8 through 19 of her cycle. Color-coded CycleBeads help track the woman's fertile days. Male involvement is crucial to effective use.

New Fertility Awareness-Based Methods

Description: Tracking one's fertility and avoiding unprotected sex on fertile days.

QUICK LOOK

Stage of development: Included in some programs.

Effectiveness: Standard Days Method—12 pregnancies per 100 women per year as typically used. TwoDay Method—14 pregnancies per 100 women per year as typically used.

How they work: Avoiding unprotected intercourse during days identified as probably fertile.

What's new? Provide simplified ways to track fertile days with the use of colored beads or secretion diary.

correctly (abstaining from sex during the fertile days), 5 of every 100 women became pregnant in one year (16).

The TwoDay Method

The TwoDay Method helps women determine whether they are fertile on any given day based on the presence or absence of cervical secretions. The method is based on the fact that a woman's cervical secretions are key to her fertility. Without cervical secretions, sperm have difficulty traveling to the egg (37, 176).

The TwoDay Method is appropriate for women with cycles of any length, regardless of regularity (15). Couples who can use the TwoDay Method successfully are those who can avoid unprotected sex for about 10–15 days per cycle.

To use the TwoDay Method, a woman asks herself two questions each day: (1) "Did I notice secretions today?" and (2) "Did I notice secretions yesterday?" If she noticed secretions of any type either today or yesterday, she would consider herself fertile and avoid unprotected sex. If she did not notice cervical secretions for two days consecutively, she would be unlikely to get pregnant from sex taking place today (15, 274).

The TwoDay Method was developed to provide a simpler approach to identifying the fertile days than either the Billings Ovulation Method or the Symptothermal Method, which also involve observations of cervical secretions (109). Users of these other two methods must differentiate among multiple characteristics of their cervical secretions (color, texture, and general appearance), correctly interpret changes in secretion patterns, or also observe changes in basal body temperature.

Effectiveness. In a clinical trial of the TwoDay Method in Guatemala, Peru, and the Philippines, typical use of the method resulted in 14 pregnancies per 100 women in one year. Of women using the method correctly (abstaining from sex on fertile days), 4 of every 100 became pregnant in one year (15). After initial counseling, most participants (over 96%) were able to detect the presence or absence of cervical secretions. Continuation rates at the end of one year were only about 53%, however. Of those not completing the study, the largest group, about 16% of participants, was asked to leave the study because they either had cycles that were too long for study requirements, or they could not follow the protocol. Another 10% of participants dropped out because they became pregnant, and the remainder left the study for other reasons (15). ❖❖

Seasonale, a new continuous-use OC, comes in a 3-month supply. Women take 1 active pill per day for 84 days and then take inactive pills for 7 days. Continuous-use OCs reduce the number of bleeding days and related side effects.

Barr Labs

New Oral Contraceptives

Description: Continuous-use products and pills containing new progestins.

Stage of development: Marketed.

Effectiveness: Similar to other combined OCs (6 to 8 pregnancies per 100 women in the first year as typically used). Continuous-use OCs may be more effective.

How they work: Deliver progestin alone or with estrogen, preventing ovulation, thickening cervical mucus, and suppressing endometrial growth.

What's new? Continuous pill use reduces annual number of menstrual cycles to four and reduces side effects. New progestins may reduce side effects.

Oral Contraceptives

Pharmaceutical companies periodically introduce new OC formulations, usually focused on reducing side effects and so increasing continuation, while maintaining high effectiveness. Recently introduced OCs include a dedicated continuous-use formulation, a combined OC containing a new progestin, and a new progestin-only OC.

Continuous-Use Oral Contraceptives

More and more reproductive health experts are questioning the necessity for the monthly withdrawal bleed, which OC users experience while taking the seven inactive pills or seven days without pills in each month's cycle (124, 242). New research has found that women can safely and effectively use many monophasic OCs continuously for a few cycles in a row, skipping the inactive pills (8, 163, 237, 238). ("Monophasic" means that each active pill in the cycle contains the same amount of hormones.)

The monthly regimen of 21 active pills containing estrogen and progestin, followed by 7 inactive pills, was created to promote monthly withdrawal bleeding and to mimic spontaneous menstrual cycles (58). Taking active pills continuously allows women to reduce the number of times they experience monthly bleeding per year and to reduce the number of bleeding days (162). Continuous-use OCs also significantly reduce the side effects associated with hormone withdrawal, including migraines, headaches, premenstrual syndrome, mood changes, and heavy or painful monthly bleeding, which women experience primarily on the days they take the inactive pills (237, 238).

Women taking OCs continuously are about twice as likely as women using the conventional regimen to have breakthrough bleeding between periods, which leads many to discontinue use. Breakthrough bleeding and spotting diminish after about eight or nine months of use, however (8, 162). Researchers have studied a few different OCs for continuous use with different results in controlling breakthrough bleeding and other side effects (50, 163, 211).

One formulation, Seasonale®, is packaged specifically for continuous-use and is US FDA approved. It contains 150 µg of the progestin levonorgestrel and 30 µg of the estrogen ethinyl estradiol. Seasonale users take a pill

every day for 84 days (12 weeks) and then take hormone-free pills for 7 days. Only 10 months after Seasonale became available, more than 260,000 prescriptions for it had been written in the US (73). Its developer, Barr Laboratories plans to apply for approval in other countries (60).

Drospirenone Combined Oral Contraceptive

Drospirenone is the new progestin in the combined OC Yasmin®, developed by Schering AG. Yasmin contains 3 mg of drospirenone and 30 µg of the estrogen ethinyl estradiol (EE). Yasmin received US FDA approval in 2001 and is now available in Australia, the US, and Europe.

Drospirenone/EE pills are about as effective as other combined OCs in the first year of use (108, 182). The unique progestin drospirenone provides several benefits for some women in addition to preventing pregnancy (211, 243). For women who already experience acne and excess hair growth, clinical trials suggest that drospirenone/EE could reduce these conditions. Some clinical trials have found that drospirenone/EE causes less water retention and thus less fluid-related weight gain than other combined OCs (108, 177). Other trials have found that some users have an improved sense of well-being (13, 149, 201).

Side effects of drospirenone/EE are similar to those of other combined OCs and include headache, breast pain, nausea, and abdominal pain (108). Reports of several cases of venous thromboembolism (VTE) in the UK raised concerns about drospirenone increasing the risk of VTE (208). There is no epidemiological evidence, however, to suggest that users of combined OCs containing drospirenone have any greater risk of VTE than users of other combined OCs (103).

Desogestrel Progestin-Only Oral Contraceptive

Desogestrel is the progestin in the new pill Cerazette®, developed by Organon. It is available primarily in Brazil, Ecuador, Hong Kong, Mexico, and some countries of Western Europe (114). Organon has not decided whether to apply for US FDA approval for Cerazette (138).

Users take a daily pill containing 75 µg of desogestrel. Unlike other progestin-only pills that work mainly by making cervical mucus thicker so that sperm cannot reach the egg, desogestrel works primarily by preventing ovulation (78, 132). Also, desogestrel is unique among progestin-only pills in that a woman can take a pill as much as 12 hours late without reducing effectiveness (132). In contrast, the effectiveness of other progestin-only pills may be compromised if pills are taken as few as three hours late (based on hormone levels) (33).

In clinical trials there were about 0.2 pregnancies per 100 women (2 pregnancies per 1,000 women) using desogestrel correctly in the first year of use, a rate similar to that of combined OCs (51). Some researchers, however, question whether there is enough evidence to say that desogestrel is as effective as combined OCs, because sufficient clinical trials directly comparing desogestrel and combined OC have not been completed (72). ❖❖

Intrauterine Devices

New IUDs now on the market make insertion and removal easier and reduce expulsion, pain, and bleeding. These advances could lead to greater acceptance and use of the IUD (53, 268). New IUDs include the intrauterine system (IUS)—a type of IUD that gradually releases a progestin, which makes menstruation lighter and less painful (11)—and the frameless IUD GyneFix®, which is anchored into the uterine wall.

A Progestin-Releasing IUS

The levonorgestrel-releasing intrauterine system—marketed under the name Mirena (or LevoNova® in Scandinavia)—first entered the market in Finland in 1990. It has been approved for use in more than 100 other countries over the last 15 years; the US FDA approved Mirena in 2000 (188). In 2004 the developers—the Population Council and the pharmaceutical company Leiras Oy (now Schering Oy)—established the International Contraceptive Access Foundation, which will provide public-sector organizations with the method free or at low cost in order to increase access to contraception for women in developing countries (189).

The levonorgestrel IUS initially delivers 20 µg of levonorgestrel per day. The US FDA has approved it for five

Berlex

Mirena is a new type of IUD that gradually releases the progestin levonorgestrel. Progestin-releasing IUDs make menstruation lighter and less painful. Mirena has been approved for 5 years of use in more than 100 countries.

years of use (223). It is significantly more effective than copper IUDs with 250 mm^2 of copper or less, such as the Nova-T IUD, but no more effective than IUDs with greater than 250 mm^2 of copper (82). The levonorgestrel IUS is also about as effective as female sterilization but—unlike sterilization—is easily reversible (223). Studies show that 0.1 to 0.2 women per 100 (1 to 2 women per 1,000) using the levonorgestrel IUS when properly inserted become pregnant in the first year of use. After 5 years of use 0.5 to 1.1 women per 100 become pregnant (11, 99).

Side effects are similar to those of other hormonal contraceptive methods. In a randomized, comparative trial users of the levonorgestrel IUS reported significantly higher rates of acne, dizziness, headaches, breast tenderness, nausea and vomiting, weight gain, and ovarian cysts (223).

In the first three months of use, the levonorgestrel IUS also causes bleeding disturbances, including breakthrough bleeding and spotting. Over time, the levonorgestrel IUS causes less bleeding than copper-bearing IUDs (183, 223, 240). Heavy or prolonged bleeding is significantly less common, and amenorrhea is significantly more common among levonorgestrel IUS users than among copper-bearing IUD users (11, 244). Between 20% and 50% of users have amenorrhea by one year (27, 104, 147). Women can also use the levonorgestrel IUS to treat heavy, prolonged bleeding or painful menstrual cramps and it may be a useful alternative to hysterectomy for some women (110).

The Belgian research organization Contrel is developing a T-shaped levonogestrel-releasing IUS, called Femilis™, with a small version for women who have never been pregnant (and so have smaller uteruses), called Femilis Slim. These aim to simplify insertion procedures with a "push-in technique" that does not require a plunger, as with Mirena. Femilis and Femilis Slim could be inserted by trained health care providers who do not often insert IUDs (266).

Frameless IUDs

The frameless IUD—made without the plastic T-shaped frame common to most other types of IUDs—consists of several copper cylinders tied together on a string. It is anchored one centimeter deep into the fundus (top) of the uterus. This design is intended to cause less pain and bleeding than framed devices (154).

GyneFix, the newest frameless IUD, was introduced in Europe in the early 1990s, following 15 years of research to improve ease of insertion and attachment to the uterine wall (64, 264). It is also available in China and through Marie Stopes International programs in Latin America, Asia, and Africa. Its developer plans to apply for US FDA approval (263).

Frameless IUDs, such as GyneFix, do not have the plastic T-shaped frame of conventional IUDs. Instead, they consist of several copper cylinders tied together on a string. The device is anchored 1 centimeter deep into the fundus of the uterus.

Small, non-comparative studies demonstrate promising results for GyneFix in minimizing menstrual blood loss and discontinuation (12, 264). Randomized controlled trials involving GyneFix have not yet provided clear support for the benefits expected, however (174). Expulsion rates have been higher than found in early clinical trials (64,154).

The frameless IUD requires an entirely different insertion technique than the framed IUD, and the level of skill required to insert them is high (154, 232, 262). Providers face difficulty with insertion even with the use of a new inserter mechanism, introduced by the developer to simplify insertion (42). The frameless IUD is less likely to be expelled when inserted by an experienced provider (262).

Another frameless IUD in development, FibroPlant-LNG, releases the progestin levonorgestrel. Based on the design of the GyneFix IUD, it too is anchored into the fundus of the uterus. FibroPlant-LNG delivers 14 µg of levonorgestrel daily and prevents pregnancy for at least three years (268).

Initial studies suggest that FibroPlant-LNG would be highly acceptable and may reduce bleeding (12, 267). For example, a pilot study of 109 women approaching menopause found that few women experienced hormonal side effects, such as irregular bleeding and spotting, even during the first three months after insertion—factors that contributed to a 98% continuation rate after the first year of use among women in the study (265, 267, 268). ❖❖

New Intrauterine Devices

Description: Progestin-releasing IUDs and IUDs without the conventional T-shaped frame.

Stage of Development: On the market.

Effectiveness: 0.1 to 2.5 pregnancies per 100 women in the first year of use as typically used.

How they work: Stimulate a sterile inflammatory response in the uterine cavity that is toxic to sperm. Progestin-releasing IUDs additionally thicken cervical mucus and suppress endometrial growth.

What's new? Progestin-releasing IUDs cause significantly less bleeding than conventional copper IUDs. They can also be used to treat heavy or excessive menstrual flow. New shapes in IUDs may reduce expulsion, pain, and bleeding.

Transcervical Female Sterilization

Researchers are pursuing new methods of permanent contraception for women that provide protection comparable to surgical sterilization but are safer or easier to provide. The new developments focus on transcervical methods—that is, methods that reach the fallopian tubes through the vagina and uterus. They include chemicals, such as quinacrine, and plugs, such as the Adiana procedure. Microcoils, such as Essure®, are already on the market.

Currently, most female sterilization procedures involve tubal ligation, in which a woman's fallopian tubes are surgically cut or blocked by applying clips, rings, or heat. The two most common surgical approaches are minilaparotomy and laparoscopy. These approaches require skilled medical professionals and sterile conditions. Minilaparotomy requires local anesthesia, and laparoscopy requires general anesthesia (168). The newer approaches, because they do not involve surgery, can increase access to sterilization (269).

Essure—A Microcoil

The microcoil Essure (formerly named STOP), developed by the US firm Conceptus, is a spring-like device that a trained clinician using a hysteroscope inserts through the vagina into the uterus and then into each fallopian tube. Over the three months following the procedure, scar tissue grows into the device. The scar tissue permanently plugs the fallopian tubes so that sperm cannot pass through to fertilize an egg (252).

The insertion procedure can be performed with a local anesthetic in an outpatient setting in less than one hour, with rapid return to normal activities for the client (55, 127). Clinicians need to be skilled in hysteroscopy to place the microcoil properly, however.

In clinical trials some women required two attempts for successful insertion but ultimately microcoil insertion was successful in 90% to 95% of women (55, 126, 246). The most common reasons for placement failure are tubal obstruction and stenosis—a narrowing or constriction of the fallopian tube. Placement of Essure must always be confirmed, usually with an x-ray test or ultrasound imaging three months after insertion (126, 241).

Once successfully inserted, Essure appears to be at least as effective as surgical sterilization (52). Women need to use a temporary contraceptive method for three months after insertion to allow time for scar tissue to form. After the scar tissue is formed, Essure is not reversible (252). About three-fourths of women experience some pain after the procedure (127).

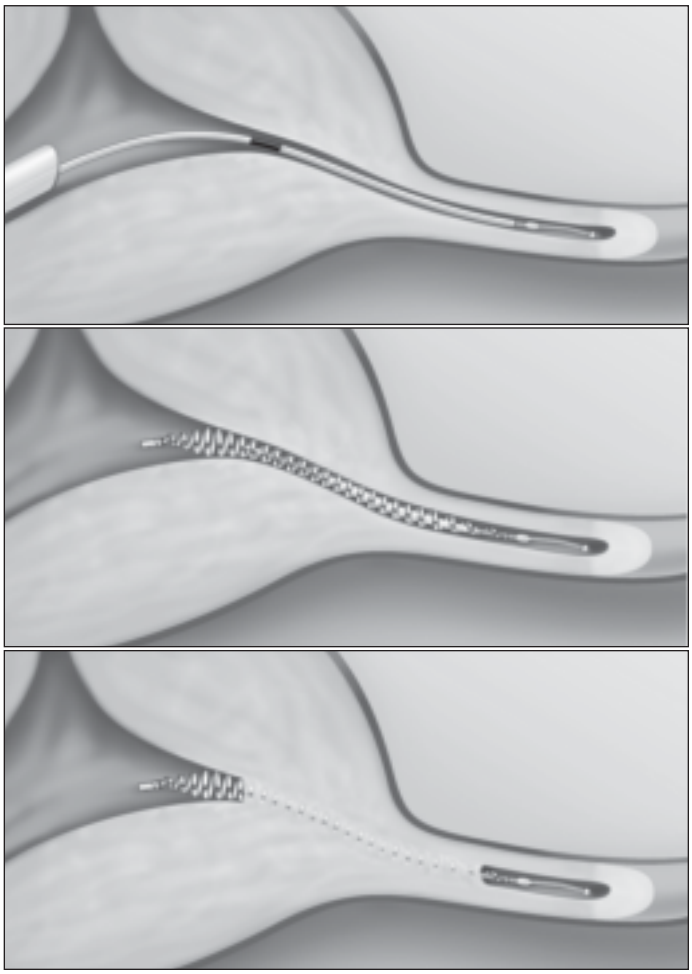
Essure has been approved by regulatory agencies in Europe and in Australia, Canada, Indonesia, Singapore, Turkey, and the US (52, 55, 278). Essure is unlikely to be introduced in developing countries any time soon, however, because of the high cost and complexity of the hysteroscope required for insertion (206).

Quinacrine—A Chemical Compound

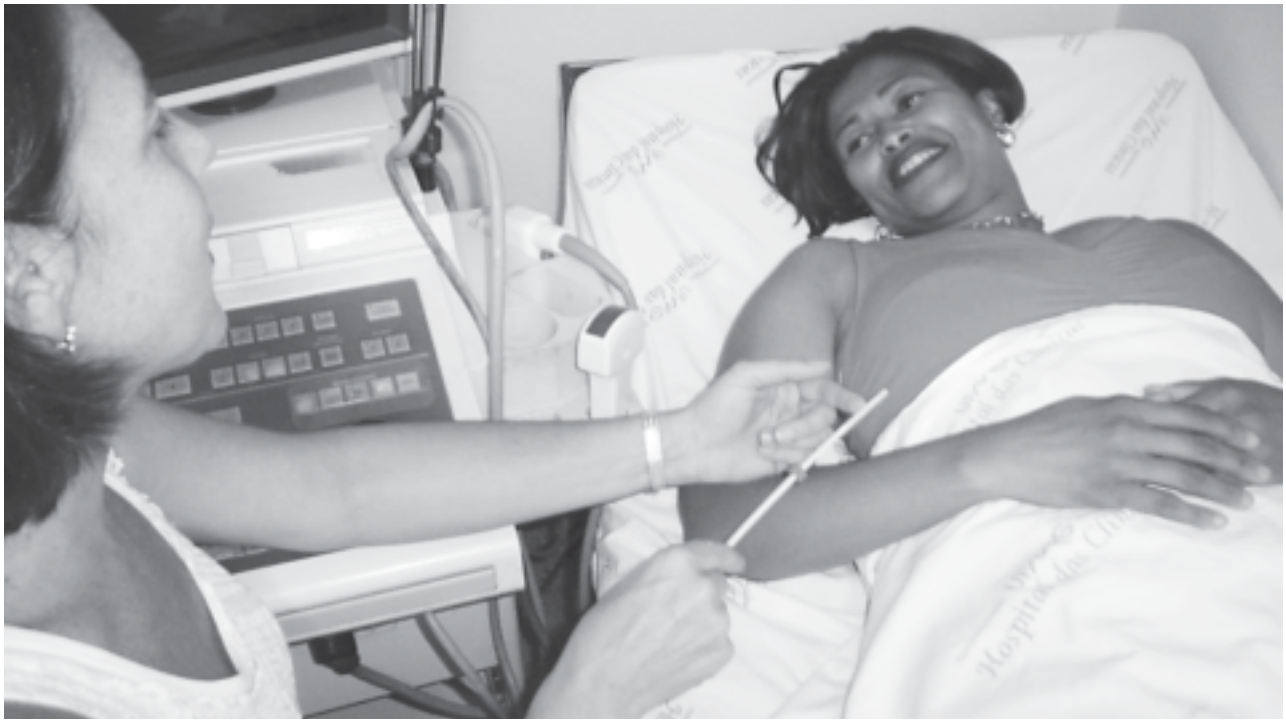
Quinacrine is a chemical compound in the form of pellets that, when inserted into the uterus, results in permanent sterilization by producing scarring to block the fallopian tubes (286). Quinacrine can be provided by most trained health care providers and does not require a physician (105).

Quinacrine is already US FDA-approved for oral antimalarial treatment and is available worldwide. Researchers have been studying quinacrine for sterilization over the last 20 years in many countries, including Chile, Egypt, India, Indonesia, Iran, Malaysia, and Vietnam (4, 18, 36, 75, 77, 105, 230, 286). Its regulatory approval by the US FDA and other agencies for use as a sterilization method, however, will depend on the results of safety evaluations and toxicology studies. These studies are underway, as well as clinical trials approved by the US FDA. A phase I clinical trial ended in 2003 (140), and additional trials are planned (139, 226).

Images courtesy of Conceptus Incorporated



Essure, a new nonsurgical sterilization method, is a spring-like device inserted through the uterus into each fallopian tube. Scar tissue then blocks the passage of eggs down the tubes.



Claudia Ramos de Carvalho Ferreira

A health care provider discusses quinacrine insertion with a client. Quinacrine is a chemical compound in the form of a pellet that, when inserted into the uterus, results in sterilization by producing scarring that blocks the fallopian tubes.

The precise effectiveness rate of quinacrine as a sterilization agent is debated because different insertion procedures result in different rates. A review of studies concluded that the pregnancy rate is one to two pregnancies per 100 women after two years of use (129, 287)—less effective than surgical sterilization. A study that included all types of quinacrine insertion procedures, regardless of how well the provider was trained, found that 9.8 women per 100 become pregnant within five years of use (227).

Reported side effects after insertion are usually brief and mild. They include lower abdominal pain, headache, dizziness, backache, vaginal itching or irritation, vaginal discharge, and fever. Some women report menstrual pattern changes, usually reduced bleeding (75, 229, 230). Serious complications related to quinacrine appear to be fewer than with surgical sterilization (105, 128).

The safety of quinacrine as a sterilization method is still in question (32). FHI is currently conducting research, including toxicology studies, to determine whether intrauterine use of quinacrine poses a risk of cancer. Results from these studies are expected in 2007 (32, 226). Long-term follow-up done in 1995–96 of almost 1,500 Chilean women who had the quinacrine sterilization procedure found no increased risk of cancer up to 19 years later (228).

Some women's rights groups have opposed quinacrine on the grounds that toxicology and animal studies did not precede clinical trials, which is the established research procedure; that large-scale clinical trials began before smaller safety studies were complete; and that in some places women were not informed of its experimental nature or offered other contraceptives (34, 184, 185). If current toxicology and clinical trials show quinacrine to be safe and effective, this evidence could help resolve these objections (226).

The Adiana Procedure

The Adiana procedure is a transervical sterilization procedure in which a clinician delivers a catheter through a hysteroscope into the fallopian tube and uses the catheter to apply low-level radiofrequency energy, creating a superficial lesion. Then the clinician places a porous, plastic implant, called a matrix, into the lesion. The matrix remains in the fallopian tube, and the surrounding tissue grows into it over the next 12 weeks. The ingrown tissue results in total closure of the fallopian tube.

Because it requires use of an expensive hysteroscope, the Adiana procedure is unlikely to be introduced in developing countries in the foreseeable future. Clinical studies are underway, and its developers, Adiana, Inc., expect US FDA approval in 2005 (21, 194). ❖❖

Transcervical Sterilization

Description: Procedures that prevent pregnancy permanently by reaching and blocking the fallopian tubes through the vagina and uterus.

Stage of development: Some methods on the market and others in clinical trials.

QUICK LOOK

Effectiveness: 0.2 to 2 pregnancies per 100 women in the first year of use.

How they work: Blocks the egg from descending a fallopian tube.

What's new? Sterilization procedures for women that do not require surgery.

Male Hormonal Contraception

Hormonal contraception for men has been in clinical stages of development for almost two decades and is now in phase III clinical trials in China (253). This approach works by using testosterone or a combination of testosterone and a progestin to suppress sperm production. When testosterone is added to a man's system, testosterone levels are lowered in the testes, resulting in reduced sperm production (6).

Pills, patches, injections, and implants have been tested to deliver various formulations of testosterone (159). In clinical trials injected formulations appear to be most effective in suppressing sperm production (159, 172, 257).

If clinical trials prove successful, a hormonal contraceptive method for men may be available in China by 2006 and in other countries several years later (171). Once on the market, this new hormonal approach would give men a choice of effective reversible contraception beyond just condoms. Also in development are long-term but potentially reversible male contraceptives, which focus on accessing the vas deferens to block sperm (see box, p. 19).

Landmark Trials Provide Proof

Two large-scale international clinical trials provided the initial evidence that testosterone can sufficiently suppress sperm production to serve as a viable contraceptive. The first study, in seven countries between 1986 and 1990, involved 271 men who received weekly injections of 200 mg of the hormone compound testosterone enanthate (275). The second study, in nine countries in 1994, involved 399 men who received testosterone enanthate on the same schedule (276).

These studies, which were sponsored by WHO in collaboration with CONRAD, established that hormonal methods would work for men and also defined the level to which sperm counts must decline in order to prevent men's partners from becoming pregnant. Also, the second study established that a hormonal contraceptive could be effective—about one pregnancy among the partners of every 100 men per year of use when sperm production is adequately suppressed (276).

Male Hormonal Contraception

Method description: Most likely a monthly or bimonthly injection or implant delivering a combination of testosterone and a progestin.

Stage of development: In phase II and III clinical trials.

Effectiveness: Probably fewer than 1.4 pregnancies among partners of every 100 men per year of use.

How they work: Prevent sperm production.

What's new? Provide men with another reversible, effective method to control fertility.

Testosterone-Only Formulations

If the phase III clinical trials underway in China confirm phase II results (90), China could become the first country to register a hormonal male contraceptive method and to offer it in the national family planning program (253). One thousand Chinese men in 10 centers are receiving an initial dose of 1,000 mg of a testosterone formulation, testosterone undecanoate (TU), followed by 500 mg of it in doses given either every four or every six weeks for two years. Testosterone undecanoate is among the newest and most successful testosterone preparations. It is longer acting than other compounds such as testosterone enanthate, and it allows men to receive injections bimonthly or monthly instead of weekly (284).

Testosterone by itself does not suppress sperm production in non-Asian men as well as it does in Asian men, and therefore in other regions a male hormonal contraceptive would most likely combine a testosterone with another hormonal compound to improve effectiveness (276). Studies have been unable to pinpoint the cause for the difference in effectiveness between Asian men and other men (120, 156, 256).

The two primary challenges remaining for developing other male hormonal contraceptives are the need for frequent injections and the inability to uniformly supress sperm production in all users (89). Researchers are looking into longer-acting formulations of testosterone and combined hormonal formulations to overcome these challenges.

Combined Formulations

Combining testosterone with such compounds as progestins or gonadotropin-releasing hormone (GnRH) analogs speeds and improves suppression of sperm production and allows use of less testosterone, thus reducing testosterone-induced side effects (172, 257). To find the best contraceptive effect, researchers in several countries around the world are conducting small-scale clinical trials of combined formulas. Progestins appear to be the most promising. The studies are testing various delivery systems, separate from the delivery system for testosterone, to deliver the progestin, including a pill, patch, injection, and implant (10, 43, 85, 130, 158).

Major organizations involved in researching these compounds include WHO, CONRAD, the Institute of Reproductive Medicine of the University in Germany, Schering AG, Organon, and the Population Council, which is investigating a more potent synthetic hormone, MENT®, as a substitute for testosterone (192, 203, 239).

Side effects. In small clinical trials combined testosterone and progestin formulas caused no serious side effects or medical complications. Male hormonal contraception is likely to have little impact on men's sex drive or aggressive behavior, study results suggest (122).

Combining progestin with a testosterone appears to reduce, although not eliminate, the side effects of testosterone (7, 9, 31, 157). Side effects of testosterone alone have included pain at the injection site, acne, weight gain, and suppression of high density lipoprotein (HDL)

New Long-Term Male Contraception in Clinical Trials

Two new methods of male contraception under development—RISUG and the Intra Vas Device (IVD)—result in long-term infertility and have the potential advantage of being reversible. They are currently in clinical trials.

RISUG: Injected Gel Blocks Sperm

RISUG (an acronym for "Reversible Inhibition of Sperm Under Guidance") is a clear polymer gel made of styrene maleic anhydride (SMA) mixed with dimethyl sulfoxide (DMSO). It was developed at the Indian Institute of Technology and the All India Institute of Medical Sciences in India. RISUG is injected into the vas deferens, the duct that carries sperm from the epididymis to the ejaculatory duct. Although the mechanism of action is not completely understood, study results suggest that RISUG partially blocks the vas deferens while also causing the membranes of passing sperm to rupture, thereby disabling most sperm that do get through (47, 48, 133, 143, 145).

Results from phase I and phase II clinical trials have suggested that RISUG may be both safe and effective as a contraceptive (92, 93). In clinical trials RISUG caused some temporary side effects such as scrotal swelling in about one-third of participants (92, 93, 94). A toxicity study is being planned to further evaluate RISUG's safety (142). A phase III clinical trial began in India involving 140 men, but it has been postponed until the results of the toxicity studies are complete (48, 142).

The results of animal studies indicate that sperm reappear in the ejaculate when RISUG is flushed out with DMSO or sodium bicarbonate, or noninvasively forced out using massage, vibration, and low-level electrical current. A formal reversal study in humans has not yet been conducted (91, 133, 144).

Phase II clinical trials show that users have no sperm or only sperm incapable of moving for at least one year (93, 94). Long-term follow-up studies of clinical trial participants, as well as larger studies, are essential to provide a greater understanding of RISUG's safety and effectiveness (232).

Although RISUG has been studied for more than two decades, researchers are concerned that preclinical testing has been inadequate, and some are questioning the thoroughness of toxicity testing (232). The Indian government is beginning to address those concerns by providing support for the planned toxicology studies (91, 142).

Intra Vas Device: Two Implanted Plugs Block Sperm

The Intra Vas Device (IVD—originally called the Shug) is a device that is implanted into the vas deferens. It uses two plugs in each vas deferens, so that any sperm passing by one plug will be stopped by the second (141). In animal tests the IVD resulted in no sperm in the ejaculate (282), and after removal of the devices all primates ejaculated normal numbers of sperm again (283).

Placing and removing the IVD does not require special surgical training; it could be provided as a contraceptive choice wherever no-scalpel vasectomy can be provided. Animal tests suggest that implantation and removal can each be accomplished in 20 minutes (282, 283).

Among 30 men in a pilot study, the IVD drastically reduced numbers of sperm in the ejaculate of all participants; 27 men had either no sperm or only sperm incapable of moving (281). Shepherd Medical, the company that owns the rights to IVD, will apply for US FDA approval in 2005 to begin a phase II clinical trial that will follow 90 US men over 18 months. The study will assess the IVD's safety, ability to block the vas deferens, and overall contraceptive effectiveness (236).

cholesterol—the healthy type of cholesterol that has been associated with reduced risk of atherosclerosis (hardening of the arteries). HDL returns to normal levels after discontinuation of testosterone use (160, 277). Large, long-term studies are needed to assess all of the side effects of combined formulas (172).

Effectiveness. The contraceptive effectiveness of any male hormonal formulation of course depends on how well it can suppress sperm production. Researchers are aiming to develop a combined formulation that will reduce sperm counts to fewer than 1 million per milliliter of ejaculate, a level that would result in an effectiveness rate of 1.4 pregnancies per year among partners of 100 men using it (113, 276).

Several combinations of progestins and testosterone have been able to produce either low sperm counts or no sperm in nearly 100% of the study participants in small clinical trials. All progestins tested appear promising in suppressing sperm production, and no one progestin seems superior to the others (89, 257). Larger clinical trials, in which subjects will be treated for longer periods of time, are planned (159).

Acceptability

Advances in male hormonal contraception have lagged behind advances in female hormonal contraception (204). One reason is that contraception has been seen as the woman's responsibility. Also, researchers have been cautious about the potential effects of hormone use on men's emotional and sexual well-being (98, 197).

When developing female contraceptives, potential side effects can appear minor in comparison with the large health benefits of avoiding unintended pregnancy and childbearing. In contrast, when developing contraceptive methods for healthy men who do not face the risks of pregnancy and childbirth, the impacts of side effects can appear relatively large (123, 197).

Studies suggest, however, that many men are willing to take on the side effects and health risks of contraceptive use (102, 195, 196, 259). Many men and women in surveys, focus groups, and interviews say that they want to share the responsibility for contraception. Studies of the potential acceptability of male hormonal contraception also suggest that women would trust their partners to use the method reliably (88).

Bibliography

An asterisk (*) denotes an item that was particularly useful in the preparation of this issue of **Population Reports.**

1. ACCESS WORKING GROUP OF THE MICROBICIDE INITIATIVE. Preparing for microbicide access and use. New York, Rockefeller Foundation Microbicide Initiative, 2002. 38 p. (Available: <http://www.rockfound.org/Documents/488/rep6_preparing.pdf>)

*2. AFFANDI, B. Long-acting progestogens. Best Practice and Research. Clinical Obstetrics and Gynaecology. 16(2): 169-179. Apr. 2002.

3. AFFANDI, B., KORVER, T., GEURTS, T.B., and COELINGH BENNINK, H.J. A pilot efficacy study with a single-rod contraceptive implant (Implanon) in 200 Indonesian women treated for < or = 4 years. Contraception 59(3): 167-174. Mar. 1999.

4. AGOESTINA, T. and KUSUMA, I. Clinical evaluation of quinacrine pellets for chemical female sterilization. Advances in Contraception 8(2): 141-151. Jun. 1992.

5. ALEXANDER, N.J. (Organon Pharmaceuticals USA, Inc.) [Availability of NuvaRing in developing countries] Personal communication, Nov. 4, 2004.

6. AMORY, J.K. and BREMNER, W. Endocrine regulation of testicular function in men: Implications for contraceptive development. Molecular and Cellular Endocrinology 182(2): 175-179. Sep. 2001.

7. ANAWALT, B.D., BEBB, R.A., BREMNER, W.J., and MATSUMOTO, A.M. A lower dosage levonorgestrel and testosterone combination effectively suppresses spermatogenesis and circulating gonadotropin levels with fewer metabolic effects than higher dosage combinations. Journal of Andrology 20(3): 407-414. May-Jun. 1999.

8. ANDERSON, F.D. and HAIT, H. A multicenter, randomized study of an extended cycle oral contraceptive. Contraception 68(2): 89-96. Aug. 2003.

*9. ANDERSON, R.A. and BAIRD, D.T. Male contraception. Endocrine Reviews 23(6): 735-762. Dec. 2002.

10. ANDERSON, R.A., KINNIBURGH, D., and BAIRD, D.T. Suppression of spermatogenesis by etonogestrel implants with depot testosterone: potential for long-acting male contraception. Journal of Clinical Endocrinology and Metabolism 87(8): 3640-3649. Aug. 2002.

11. ANDERSSON, K., ODLIND, V., and RYBO, G. Levonorgestrel-releasing and copper-releasing (Nova T) IUDs during five years of use: A randomized comparative trial. Contraception 49(1): 56-72. Jan. 1994.

12. ANDRADE, A.T., SOUZA, J.P., ANDRADE, G.N., ROWE, P.J., and WILDEMEERSCH, D. Assessment of menstrual blood loss in Brazilian users of the frameless copper-releasing IUD with copper surface area of 330 mm^2 and the frameless levonorgestrel-releasing intrauterine system. Contraception 70(2): 173-177. Aug. 2004.

13. APTER, D., BORSOS, A., BAUMGARTNER, W., MELIS, G.B., VEXIAU-ROBERT, D., COLLIGS-HAKERT, A., PALMER, M., and KELLY, S. Effect of an oral contraceptive containing drospirenone and ethinylestradiol on general well-being and fluid-related symptoms. European Journal of Contraception and Reproductive Health Care 8(1): 37-51. Mar. 2003.

14. ARCHER, D.F., BIGRIGG, A., SMALLWOOD, G.H., SHANGOLD, G.A., CREASY, G.W., and FISHER, A.C. Assessment of compliance with a weekly contraceptive patch (Ortho Evra/Evra) among North American women. Fertility and Sterility 77(2 Suppl 2): S27-31. Feb. 2002.

*15. ARÉVALO, M., JENNINGS, V., NIKULA, M., and SINAI, I. Efficacy of the new TwoDay Method of family planning. Fertility and Sterility 82(4): 885-892. Oct. 2004.

*16. ARÉVALO, M., JENNINGS, V., and SINAI, I. Efficacy of a new method of family planning: The Standard Days Method. Contraception 65(5): 333-338. May 2002.

17. ARKIN, M.M. Products liability and the threat to contraception. Civil Justice Memo, No. 36, Feb. 1999.

18. ARSHAT, H., ANG ENG, S., and KWA SIEW, K. Nonsurgical female sterilization with quinacrine pellets: Malaysian experience. Malaysian Journal of Reproductive Health 5(2): 61-69. Dec. 1987.

19. ASSOCIATION OF REPRODUCTIVE HEALTH PROFESSIONALS (ARHP). Frequently asked questions about the contraceptive patch. Health and Sexuality Magazine, Jan. 2, 2002.

20. ASSOCIATION OF REPRODUCTIVE HEALTH PROFESSIONALS (ARHP). Other Hormonal Methods for Reducing Menstruation. Clinical Proceedings, Sep. 2004. p. 13.

21. ASSOCIATION OF REPRODUCTIVE HEALTH PROFESSIONALS (ARHP). Transcervical methods in the US pipeline. Clinical Proceedings, May 7, 2002. p. 15.

*22. AUDET, M.C., MOREAU, M., KOLTUN, W.D., WALDBAUM, A.S., SHANGOLD, G., FISHER, A.C., and CREASY, G.W. Evaluation of contraceptive efficacy and cycle control of a transdermal contraceptive patch vs an oral contraceptive: A randomized controlled trial. Journal of the American Medical Association 285(18): 2347-2354. May 9, 2001.

23. AUSTIN, G. (Program for Appropriate Technology in Health (PATH)) [PATH Woman's Condom] Personal communication, Jan. 4, 2005. (Available: <http://apha.confex.com/apha/132am/techprogram/paper_76029.htm>)

24. AUSTIN, G., COFFEY, P., COHEN, J., KILBOURNE-BROOK, M., SEAMANS, Y., and PATH WOMAN'S CONDOM TEAM. Evaluating the PATH Woman's Condom. Presented at the APHA 132nd Annual Meeting, Washington DC, Nov. 6-10, 2004.

25. AUSTIN, G., COFFEY, P., COHEN, J., KILBOURNE-BROOK, M., SEAMANS, Y., and PATH WOMAN'S CONDOM TEAM. Including users to develop a refined female condom. Presented at the APHA 132nd Annual Meeting, Washington DC, Nov. 6-10, 2004.

26. BAHAMONDES, L., MARCHI, N.M., NAKAGAVA, H.M., DE MELO, M.L., CRISTOFOLETTI MDE, L., PELLINI, E., SCOZZAFAVE, R.H., and PETTA, C. Self-administration with Uniject of the once-a-month injectable contraceptive Cyclofem. Contraception 56(5): 301-304. Nov. 1997.

27. BALDASZTI, E., WIMMER-PUCHINGER, B., and LOSCHKE, K. Acceptability of the long-term contraceptive levonorgestrel-releasing intrauterine system (Mirena): A 3-year follow-up study. Contraception 67(2): 87-91. Feb. 2003.

28. BALLAGH, S.A. Vaginal ring hormone delivery systems in contraception and menopause. Clinical Obstetrics and Gynecology 44(1): 106-113. Mar. 2001

29. BALLAGH, S.A., MISHELL, D.R., JR., JACKANICZ, T.M., LACARRA, M., and EGGENA, P. Dose-finding study of a contraceptive ring releasing norethindrone acetate/ethinyl estradiol. Contraception 50(6): 535-549. Dec. 1994.

30. BARBOSA, I., COUTINHO, E., HIRSCH, C., LADIPO, O., OLSSON, S.E., and ULMSTEN, U. Effects of a single contraceptive Silastic implant containing nomegestrol acetate on ovarian function and cervical mucus production during 2 years. Fertility and Sterility 65(4): 724-729. Apr. 1996.

31. BEBB, R.A., ANAWALT, B.D., CHRISTENSEN, R.B., PAULSEN, C.A., BREMNER, W.J., and MATSUMOTO, A.M. Combined administration of levonorgestrel and testosterone induces more rapid and effective suppression of spermatogenesis than testosterone alone: A promising male contraceptive approach. Journal of Clinical Endocrinology and Metabolism 81(2): 757-762. Feb. 1996.

32. BENAGIANO, G. Non-surgical female sterilization with quinacrine: An update. Contraception 63(5): 239-245. May 2001.

33. BENAGIANO, G. and PRIMIERO, F.M. Seventy-five microgram desogestrel minipill, a new perspective in estrogen-free contraception. Annals of the New York Academy of Sciences 997: 163-173. Nov. 2003.

34. BERER, M. Quinacrine family-planning method [letter; comment]. Lancet 343(8910): 1426.

35. BERGER, L. After long hiatus, new contraceptives emerge. New York Times. (New York), Dec. 10, 2002. p. F5.

36. BHATT, R. and WASZAK, C.S. Four-year follow-up of insertion of quinacrine hydrochloride pellets as a means of nonsurgical female sterilization. Fertility and Sterility 44(3): 303-306. Sep. 1985.

37. BIGELOW, J.L., DUNSON, D.B., STANFORD, J.B., ECOCHARD, R., GNOTH, C., and COLOMBO, B. Mucus observations in the fertile window: A better predictor of conception than timing of intercourse. Human Reproduction 19(4): 889-892. Apr. 2004.

38. BJARNADOTTIR, R.I., TUPPURAINEN, M., and KILLICK, S.R. Comparison of cycle control with a combined contraceptive vaginal ring and oral levonorgestrel/ethinyl estradiol. American Journal of Obstetrical Gynecology 186(3): 389-395. Mar. 2002.

39. BRACHE, V., ALVAREZ-SANCHEZ, F., FAUNDES, A., JACKANICZ, T., MISHELL, D.R., JR., and LAHTEENMAKI, P. Progestin-only contraceptive rings. Steroids 65(10-11): 687-691. Oct.-Nov. 2000.

*40. BRACHE, V., FAUNDES, A., ALVAREZ, F., and COCHON, L. Nonmenstrual adverse events during use of implantable contraceptives for women: Data from clinical trials. Contraception 65(1): 63-74. Jan. 2002.

41. BRACHE, V., MISHELL, D.R., LAHTEENMAKI, P., ALVAREZ, F., ELOMAA, K., JACKANICZ, T., and FAUNDES, A. Ovarian function during use of vaginal rings delivering three different doses of Nestorone. Contraception 63(5): 257-261. May 2001.

42. BROCKMEYER, A., KISHEN, M., and WEBB, A. New GyneFix introducer. Journal of Family Planning and Reproductive Health Care 30(1): 65. Jan. 2004.

43. BUCHTER, D., VON ECKARDSTEIN, S., VON ECKARDSTEIN, A., KAMISCHKE, A., SIMONI, M., BEHRE, H.M., and NIESCHLAG, E. Clinical trial of transdermal testosterone and oral levonorgestrel for male contraception. Journal of Clinical Endocrinology and Metabolism 84(4): 1244-1249. Apr. 1999.

44. BURKMAN, R.T. The transdermal contraceptive patch: A new approach to hormonal contraception. International Journal of Fertility and Women's Medicine 47(2): 69-76. Mar.-Apr. 2002.

45. CALLAHAN, M., MAUCK, C., TAYLOR, D., FREZIERES, R., WALSH, T., and MARTENS, M. Comparative evaluation of three Tactylon(TM) condoms and a latex condom during vaginal intercourse: Breakage and slippage. Contraception 61(3): 205-215. Mar. 2000.

46. CARTER, E. (Family Health International) [Synthetic condoms] Personal communication, Jan. 24, 2005.

47. CHAKI, S.P., DAS, H.C., and MISRO, M.M. A short-term evaluation of semen and accessory sex gland function in phase III trial subjects receiving intravasal contraceptive RISUG. Contraception 67(1): 73-78. Jan. 2003.

48. CHAUDHURY, K., BHATTACHARYYA, A.K., and GUHA, S.K. Studies on the membrane integrity of human sperm treated with a new injectable male contraceptive. Human Reproduction 19(8): 1826-1830. Aug. 2004.

49. CHENG TOH, Y., JAIN, J., RAHNNY, M.H., BODE, F.R., and ROSS, D. Suppression of ovulation by a new subcutaneous depot medroxyprogesterone acetate (104 mg/0.65 ml) contraceptive formulation in Asian women. Clinical Therapeutics 26(11): 1845-1854. Nov. 2004.

50. CLARKE, A.K. and MILLER, S.J. The debate regarding continuous use of oral contraceptives. Annals of Pharmacotherapy 35(11): 1480-1484. Nov. 2001.

51. COLLABORATIVE STUDY GROUP ON THE DESOGESTREL-CONTAINING PROGESTOGEN-ONLY PILL. A double-blind study comparing the contraceptive efficacy, acceptability and safety of two progestogen-only pills containing desogestrel 75 micrograms/day or levonorgestrel 30 micrograms/day. European Journal of Contraception and Reproductive Health Care 3(4): 169-178. Dec. 1998.

52. CONCEPTUS. Physician clinical data for Essure. <http://www.essure.com/hcp/hcp_clinical_data.aspx> Conceptus, Accessed Nov. 19, 2003.

53. CONTRACEPTION REPORT. Modern IUDs: Part II. Contraception Report, Vol. 9 No. 5, Nov. 1998. (Available: <http://www.contraceptiononline.org/contrareport/pdfs/09_05.pdf>)

54. COOK, L., NANDA, K., and TAYLOR, D. Randomized crossover trial comparing the eZ.on plastic condom and a latex condom. Contraception 63(1): 25-31. Jan. 2001.

55. COOPER, J.M., CARIGNAN, C.S., CHER, D., and KERIN, J.F. Microinsert nonincisional hysteroscopic sterilization. Obstetrics and Gynecology 102(1): 59-67. Jul. 2003.

56. COUTINHO, E.M., ATHAYDE, C., DANTAS, C., HIRSCH, C., and BARBOSA, I. Use of a single implant of elcometrine (ST-1435), a nonorally active progestin, as a long acting contraceptive for postpartum nursing women. Contraception 59(2): 115-122. Feb. 1999.

57. COUTINHO, E.M., DE SOUZA, J.C., ATHAYDE, C., BARBOSA, I.C., ALVAREZ, F., BRACHE, V., GU, Z.P., EMUVEYAN, E.E., ADEKUNLE, A.O., DEVOTO, L., SHAABAN, M.M., SALEM, H.T., AFFANDI, B., DE ACOSTA, O.M., MATI, J., and LADIPO, O.A. Multicenter clinical trial on the efficacy and acceptability of a single contraceptive implant of nomegestrol acetate, Uniplant. Contraception 53(2): 121-125. Feb. 1996.

58. COUTINHO, E.M. and SEGAL, S.J. Is menstruation obsolete? New York, Oxford University Press, 1999. 190 p.

59. COUTINHO, E.M., SPINOLA, P., TOMAZ, G., MORAIS, K., NASSAR DE SOUZA, R., SABINO PINHO NETO, J., DE BARROS LEAL, W., BOMFIM HIPPOLITO, S., and D'AUREA ABRANCHES, A. Efficacy, acceptability, and clinical effects of a low-dose injectable contraceptive combination of dihydroxyprogesterone acetophenide and estradiol enanthate. Contraception 61(4): 277-280. Apr. 2000.

60. COX, C.A. FDA approves Barr's SEASONALE®, an extended-cycle oral contraceptive. Sep. 2003.

61. CRAVIOTO, M.D.C., ALVARADO, G., CANTO-DE-CETINA, T., BASSOL, S., OROPEZA, G., SANTOS-YUNG, R., VALENCIA, J., PALMA, Y., FUZIWARA, J.L., NAVARRETE, T., GARZA-FLORES, J., and PEREZ-PALACIOS, G. A multicenter comparative study on the efficacy, safety, and acceptability of the contraceptive subdermal implants Norplant and Norplant-II. Contraception 55(6): 359-367. Jun. 1997.

*62. CROXATTO, H.B. Progestin implants. Steroids 65(10-11): 681-685. Oct-Nov. 2000.

63. DAVIES, G.C., FENG, L.X., and NEWTON, J.R. The effects of a combined contraceptive vaginal ring releasing ethinyloestradiol and 3-ketodesogestrel on vaginal flora. Contraception 45(5): 511-518. May 1992.

64. DENNIS, J. and HAMPTON, N. IUDs: Which device? Journal of Family Planning and Reproductive Health Care 28(2): 61-68. Apr. 2002.

65. DESENA, F. (Organon) [Implanon approval] Personal communication, Jun. 3, 2004.

66. DEVOTO, L., KOHEN, P., BARNHART, K., ALBA, F., POMMER, R., RETAMALES, I., and COUTINHO, E. Hormonal profile, endometrial histology and ovarian ultrasound assessment during 1 year of nomegestrol acetate implant (Uniplant). Human Reproduction 12(4): 708-713. Apr. 1997.

67. DIAZ, S. Contraceptive implants and lactation. Contraception 65(1): 39-46. Jan. 2002.

68. DIAZ, S., SCHIAPPACASSE, V., PAVEZ, M., ZEPEDA, A., MOO-YOUNG, A.J., BRANDEIS, A., LAHTEENMAKI, P., and CROXATTO, H.B. Clinical trial with Nestorone subdermal contraceptive implants. Contraception 51(1): 33-38. Jan. 1995.

*69. DIEBEN, T.O., ROUMEN, F.J., and APTER, D. Efficacy, cycle control, and user acceptability of a novel combined contraceptive vaginal ring. Obstetrics and Gynecology 100(3): 585-593. Sep. 2002.

70. DORFLINGER, L. (Family Health International) [Contraceptive Development] Personal communication, June 23, 2004.

71. DORFLINGER, L.J. Metabolic effects of implantable steroid contraceptives for women. Contraception 65(1): 47-62. Jan. 2002.

72. DRUG AND THERAPEUTICS BULLETIN. Is Cerazette the minipill of choice? Drug and Therapeutics Bulletin 41(9): 68-69. Sep. 2003.

73. EASTERN VIRGINIA MEDICAL SCHOOL. Seasonale rights bring $20 million. Sep. 17, 2004. (Available: <http://www.evms.edu/about/news/features/2004-09-17-seasonale.html>)

74. EDELMAN, D.A. and VAN OS, W.A. Contraceptive development and testing in the United States of America. International Journal of Fertility 35(4): 206-210. Jul.-Aug. 1990.
75. EL KADY, A.A., NAGIB, H.S., and KESSEL, E. Efficacy and safety of repeated transcervical quinacrine pellet insertions for female sterilization. Fertility and Sterility 59(2): 301-304. 1993.
76. EL NAHAL, N., HASSAN, E.O., and EL HOUSSINIE, M. Acceptability of once-a-month injectable contraceptives Cyclofem and Mesigyna: Focus group discussion. Contraception 59(6): 369-375. Jun. 1999.
77. EL SAHWI, S., KAMEL, M., HAIBA, N., and OSMAN, M. Hysteroscopic and hysterosalpingographic study after intrauterine insertion of quinacrine pellets for non-surgical sterilization. Advances in Contraceptive Delivery Systems 8(1-2): 151-159. 1992.
78. FACULTY OF FAMILY PLANNING AND REPRODUCTIVE HEALTH CARE. CLINICAL EFFECTIVENESS UNIT. Desogestrel-only pill (Cerazette). Journal of Family Planning and Reproductive Health Care 29(3): 162-164. Jul. 2003.
79. FAMILY HEALTH INTERNATIONAL (FHI). The Female Condom: From research to the marketplace. Arlington, VA, AIDSCAP Women's Initiative, FHI, 1997. 43 p.
80. FATHALLA, M.F. Contraception-21. International Journal of Gynecology and Obstetrics 67(2): S5-S12. Dec. 1, 1999.
81. FISHEL, J. Contraceptive technologies: How much choice do we really have? Mar-Apr. 1997. (ZPG REPORTER) 2 p.
*82. FRENCH, R., VAN VLIET, H., COWAN, F., MANSOUR, D., MORRIS, S., HUGHES, D., ROBINSON, A., PROCTOR, T., SUMMERBELL, C., LOGAN, S., HELMERHORST, F., and GUILLEBAUD, J. Hormonally impregnated intrauterine systems (IUSs) versus other forms of reversible contraceptives as effective methods of preventing pregnancy. Cochrane Database of Systematic Reviews (3): CD001776. 2004.
83. GAFFIELD, M.L. Systematic review of the evidence for improving access to quality care in family planning: Medical eligibility criteria for contraceptive use. [Unpublished]. 2004.
*84. GALLO, M.F., GRIMES, D.A., and SCHULZ, K.F. Non-latex versus latex male condoms for contraception. Cochrane Database of Systematic Reviews (2): CD003550. Nov. 2003.
85. GAO, E., LIN, C., GUI, Y., LI, L., and HE, C. Inhibitine effects of sino-implant plus testosterone undecanoate (TU) on spermatogenesis in Chinese men. Reproduction and Contraception 10(2): 98-105. 1999.
86. GARZA-FLORES, J., MORAKS DEL OLMO, A., FUZIWARA, J.L., FIGUEROA, J.G., ALONSO, A., MONROY, J., PEREZ, M., URBINA-FUENTES, M., GUEVARA, S.J., CEDENO, E., BARRIOS, R., FERMAN, J.J., MEDINA, L.M., VELAZQUEZ, E., and PEREZ-PALACIOS, G. Introduction of Cyclofem once-a-month injectable contraceptive in Mexico. Contraception 58(1): 7-12. Jul. 1998.
87. GLASIER, A. Implantable contraceptives for women: Effectiveness, discontinuation rates, return of fertility, and outcome of pregnancies. Contraception 65(1): 29-37. Jan. 2002.
88. GLASIER, A.F., ANAKWE, R., EVERINGTON, D., MARTIN, C.W., VAN DER SPUY, Z., CHENG, L., HO, P.C., and ANDERSON, R.A. Would women trust their partners to use a male pill? Human Reproduction 15(3): 646-649. 2000.
*89. GRIMES, D., GALLO, M., GRIGORIEVA, V., NANDA, K., and SCHULZ, K. Steroid hormones for contraception in men. Cochrane Database of Systematic Reviews (3): CD004316. 2004.
*90. GU, Y.Q., WANG, X.H., XU, D., PENG, L., CHENG, L.F., HUANG, M.K., HUANG, Z.J., and ZHANG, G.Y. A multicenter contraceptive efficacy study of injectable testosterone undecanoate in healthy Chinese men. Journal of Clinical Endocrinology and Metabolism 88(2): 562-568. Feb. 2003.
91. GUHA, S.K. (Indian Institute of Technology) [Risug] Personal communication, July 11, 2004.
92. GUHA, S.K., SINGH, G., ANAND, S., ANSARI, S., KUMAR, S., and KOUL, V. Phase I clinical trial of an injectable contraceptive for the male. Contraception 48(4): 367-375. Oct. 1993.
93. GUHA, S.K., SINGH, G., ANSARI, S., KUMAR, S., SRIVASTAVA, A., KOUL, V., DAS, H.C., MALHOTRA, R.L., and DAS, S.K. Phase II clinical trial of a vas deferens injectable contraceptive for the male. Contraception 56(4): 245-250. Oct. 1997.
94. GUHA, S.K., SINGH, G., SRIVASTAVA, A., DAS, H.C., BHARDWAJ, J.C., MATHUR, V., KOUL, J.C., MALHOTRA, R.L., and DAS, S.K. Two-year clinical efficacy trial with dose variations of a vas deferens injectable contraceptive for the male. Contraception 58: 165-174. Sep. 1998.
*95. HALL, P.E. The introduction of Cyclofem into national family planning programmes: Experience from studies in Indonesia, Jamaica, Mexico, Thailand and Tunisia. Task Force on Research on Introduction and Transfer of Technologies for Fertility Regulation, Special Programme of Research, Development and Research Training in Human Reproduction, World Health Organization, Geneva, Switzerland. Contraception 49(5): 489-507. May 1994.
96. HALL, P.E. New once-a-month injectable contraceptives, with particular reference to Cyclofem/Cyclo-Provera. International Journal of Gynaecology and Obstetrics 62(Suppl 1): S43-56. Aug. 1998.
97. HAMMETT, T.M., MASON, T.H., JOANIS, C.L., FOSTER, S.E., HARMON, P., ROBLES, R.R., FINLINSON, H.A., FEUDO, R., VINING-BETHEA, S., JETER, G., MAYER, K.H., DOHERTY-IDDINGS, P., and SEAGE, G.R., 3rd. Acceptability of formulations and application methods for vaginal microbicides among drug-involved women: Results of product trials in three cities. Sexually Transmitted Diseases 27(2): 119-126. Feb. 2000.
98. HANDELSMAN, D.J. Hormonal male contraception: Lessons from the East when the Western market fails. [Editorial]. Journal of Clinical Endocrinology and Metabolism 88(2): 559-561. Feb. 2003.
99. HATCHER, R.A., TRUSSELL, J., STEWART, F., NELSON, A., CATES, W., GUEST, F., and KOWAL, D. Contraceptive technology: Eighteenth revised edition. New York, Ardent Media, Inc., 2004.
100. HEDON, B., HELMERHOST, F., CRONJE, H., SHANGOLD, G., FISHER, A., and CREASY, G. Comparison of efficacy, cycle control, compliance, and safety in users of a contraceptive patch vs an oral contraceptive. International Journal of Gynaecology and Obstetrics 70 (Suppl 1): 78. 2000.
101. HEGER-MAHN, D., WARLIMONT, C., FAUSTMANN, T., GERLINGER, C., and KLIPPING, C. Combined ethinylestradiol/gestodene contraceptive patch: Two-center, open-label study of ovulation inhibition, acceptability and safety over two cycles in female volunteers. European Journal of Contraception and Reproductive Health Care 9(3). Sep. 2004.
102. HEINEMANN, K., SAAD, F., WIESEMES, M., WHITE, S., and HEINEMANN, L. Attitudes toward male fertility control: Results of a multinational survey on four continents. Human Reproduction 20(2): 549-556. Jan. 2005.
103. HEINEMANN, L.A. and DINGER, J. Safety of a new oral contraceptive containing drospirenone. Drug Safety 27(13): 1001-1018. 2004.
104. HIDALGO, M., BAHAMONDES, L., PERROTTI, M., DIAZ, J., DANTAS-MONTEIRO, C., and PETTA, C. Bleeding patterns and clinical performance of the levonorgestrel-releasing intrauterine system (Mirena) up to two years. Contraception 65(2): 129-132. Feb. 2002.
105. HIEU, D.T., TAN, T.T., TAN, D.N., NGUYET, P.T., THAN, P., and VINH, D.Q. 31,781 cases of non-surgical female sterilisation with quinacrine pellets in Vietnam. Lancet 342(8865): 213-217. Jul. 24, 1993.
106. HOLOPAINEN, J. (Schering Oy) [JADELLE ®] Personal communication, Jan. 11, 2005.
107. HOLT, V.L., CUSHING-HAUGEN, K.L., and DALING, J.R. Body weight and risk of oral contraceptive failure. Obstetrics and Gynecology 99(5 Pt 1): 820-827. May 2002.
108. HUBER, J., FOIDART, J.M., WUTTKE, W., MERKI-FELD, G.S., THE, H.S., GERLINGER, C., SCHELLSCHMIDT, I., and HEITHECKER, R. Efficacy and tolerability of a monophasic oral contraceptive containing ethinylestradiol and drospirenone. European Journal of Contraception and Reproductive Health Care 5(1): 25-34. Mar. 2000.
109. HUME, K. Fertility awareness in the 1990s: The Billings Ovulation Method of natural family planning, its scientific basis, practical application and effectiveness. Advances in Contraception 7(2-3): 301-311. Jun.-Sep. 1991.
110. HURSKAINEN, R. and PAAVONEN, J. Levonorgestrel-releasing intrauterine system in the treatment of heavy menstrual bleeding. Current Opinion in Obstetrics and Gynecology 16(6): 487-490. Dec. 2004.
*111. INSTITUTE OF MEDICINE (IOM). Contraceptive research and development: Looking to the future. Harrison, P.F. and Rosenfield, A., eds. Washington, DC, National Academy Press, 1996.
*112. INSTITUTE OF MEDICINE (IOM). New frontiers in contraceptive research: A blueprint for action. Nass, S.J. and Strauss, J.F., eds. Institute of Medicine (IOM), Jan. 21, 2004. 248 p.
113. INTERNATIONAL JOURNAL OF ANDROLOGY. Sixth summit meeting consensus: Recommendations for regulatory approval for hormonal male contraception. International Journal of Andrology 25(6): 375. Jul. 2002.
114. INTERNATIONAL PLANNED PARENTHOOD FEDERATION. Directory of hormonal contraceptives. <http://contraceptive.ippf.org/(rlyna245m2vhrjfqdj304v45)/Default.aspx> International Planned Parenthood Federation, Accessed Oct. 30, 2003.
115. JAIN, J., DUTTON, C., NICOSIA, A., WAJSZCZUK, C., BODE, F.R., and MISHELL, D.R., JR. Pharmacokinetics, ovulation suppression and return to ovulation following a lower dose subcutaneous formulation of Depo-Provera. Contraception 70(1): 11-18. Jul. 2004.
116. JAIN, J., JAKIMIUK, A.J., BODE, F.R., ROSS, D., and KAUNITZ, A.M. Contraceptive efficacy and safety of DMPA-SC. Contraception 70(4): 269-275. Oct. 2004.
117. JAKIMIUK, A. A new highly effective subcutaneous contraceptive injection. Presented at the 7th European Society of Contraception Congress, Genova, Italy, Department of Surgical Gynecology, University School of Medicine, Lublin, Poland. Apr. 10, 2002.
118. JASIS, M. (Centro Mujeres) [Injectable supply in Latin America] Personal communication, Sep. 7, 2004.
119. JOHANSSON, E.D. and SITRUK-WARE, R. New delivery systems in contraception: Vaginal rings. American Journal of Obstetrical Gynecology 190(Suppl 4): S54-59. Apr. 2004.
120. JOHNSON, L., BARNARD, J.J., RODRIGUEZ, L., SMITH, E.C., SWERDLOFF, R.S., WANG, X.H., and WANG, C. Ethnic differences in testicular structure and spermatogenic potential may predispose testes of Asian men to a heightened sensitivity to steroidal contraceptives. Journal of Andrology 19(3): 348-357. May-Jun. 1998.
121. JOHRI, L. and LUNDGREN, R. Introduction of the standard days method into CARE India's community-based reproductive health programs. [Final report for the Institute for Reproductive Health (IRH)]. Washington, DC, IRH, 2003.
122. KAMISCHKE, A., HEUERMANN, T., KRUGER, K., VON ECKARDSTEIN, S., SCHELLSCHMIDT, I., RUBIG, A., and NIESCHLAG, E. An effective hormonal male contraceptive using testosterone undecanoate with oral or injectable norethisterone preparations. Journal of Clinical Endocrinology and Metabolism 87(2): 530-539. Feb. 2002.
123. KAMMEN, J.V. and OUDSHOORN, N. Gender and risk assessment in contraceptive technologies. Sociology of Health and Illness 24(4): 436-461. Jul. 1, 2002.
124. KAUNITZ, A.M. Menstruation: Choosing whether...and when. Contraception 62(6): 277-284. Dec. 2000.
125. KAUNITZ, A.M., GARCEAU, R.J., and CROMIE, M.A. Comparative safety, efficacy, and cycle control of Lunelle monthly contraceptive injection (medroxyprogesterone acetate and estradiol cypionate injectable suspension) and Ortho-Novum 7/7/7 oral contraceptive (norethindrone/ethinyl estradiol triphasic). Lunelle Study Group. Contraception 60(4): 179-187. Oct. 1999.
126. KERIN, J.F., CARIGNAN, C.S., and CHER, D. The safety and effectiveness of a new hysteroscopic method for permanent birth control: Results of the first Essure pbc clinical study. Australian and New Zealand Journal of Obstetrics and Gynaecology 41(4): 364-370. Nov. 2001.
*127. KERIN, J.F., COOPER, J.M., PRICE, T., HERENDAEL, B.J., CAYUELA-FONT, E., CHER, D., and CARIGNAN, C.S. Hysteroscopic sterilization using a micro-insert device: Results of a multicentre Phase II study. Human Reproduction 18(6): 1223-1230. Jun. 2003.
128. KESSEL, E. 100,000 quinacrine sterilizations. Advances in Contraception 12(2): 69-76. Jun. 1996.
129. KESSEL, E. Quinacrine sterilization: An assessment of risks for ectopic pregnancy, birth defects and cancer. Advances in Contraception 14(2): 81-90. Jun. 1998.
130. KINNIBURGH, D., ZHU, H., CHENG, L., KICMAN, A.T., BAIRD, D.T., and ANDERSON, R.A. Oral desogestrel with testosterone pellets induces consistent suppression of spermatogenesis to azoospermia in both Caucasian and Chinese men. Human Reproduction 17(6): 1490-1501. Jun. 2002.
131. KIRIWAT, O., PATANAYINDEE, A., KOETSAWANG, S., KORVER, T., and BENNINK, H.J. A 4-year pilot study on the efficacy and safety of Implanon, a single-rod hormonal contraceptive implant, in healthy women in Thailand. European Journal of Contraception and Reproductive Health Care 3(2): 85-91. Jun. 1998.
132. KORVER, T., KLIPPING, C., HEGER-MAHN, D., DUIJKERS, I., VAN OSTA, G., and DIEBEN, T. Maintenance of ovulation inhibition with the 75-microg desogestrel-only contraceptive pill (Cerazette®) after scheduled 12-h delays in tablet intake. Contraception 71(1): 8-13. Jan. 2005.
133. KOUL, V., SRIVASTAV, A., and GUHA, S.K. Reversibility with sodium bicarbonate of styrene maleic anhydride, an intravasal injectable contraceptive, in male rats. Contraception 58(4): 227-231. Oct. 1998.
134. KURUNMAKI, H., TOIVONEN, J., LAHTEENMAKI, P., and LUUKKAINEN, T. Contraception with subdermal ST-1435 capsules: Side-effects, endocrine profiles and liver function related to different lengths of capsules. Contraception 31(3): 305-318. Mar. 1985.
135. LANDE, R.E. New era for injectables. Population Reports, Series K, No. 5. Baltimore, Johns Hopkins School of Public Health, Population Information Program, Aug. 1995. 32 p. (Available: <http://www.infoforhealth.org/pr/k5edsum.shtml>)
136. LAURIKKA-ROUTTI, M., HAUKKAMAA, M., and HEIKINHEIMO, O. A contraceptive vaginal ring releasing ethinyl estradiol and the progestin ST-1435: Bleeding control, serum steroid concentrations, serum lipids and serum chemistry. Contraception 42(1): 111-120. Jul. 1990.
137. LEEPER, M.A. (The Female Health Company) [FC2 female condom] Personal communication, Jan. 5, 2005.
138. LEVIS, H. (Organon) [Cerazette and US FDA approval] Personal communication, Jan 21, 2004.
139. LIPPES, J. (School of Medicine, State University of New York at Buffalo) [Quinacrine trials] Personal communication, May 28, 2004.
140. LIPPES, J., BRAR, M., GERBRACHT, K., NEFF, P., and KOKKINAKIS, S. An FDA phase I clinical trial of quinacrine sterilization (QS). International Journal of Gynaecology and Obstetrics 83(Suppl 2): S45-49. Oct. 2003.
141. LISSNER, E. Frontiers in nonhormonal male contraception: A call for research. Male Contraception Information Project, Mar. 8, 1994. (Available: <http://www.gumption.org/mcip/paper.html>)
142. LISSNER, E. (Male Contraception Information Project) [RISUG and IVD] Personal communication, Jan. 6, 2005.
143. LOHIYA, N.K., MANIVANNAN, B., and MISHRA, P.K. Ultrastructural changes in the spermatozoa of langur monkeys Presbytis entellus entellus after vas occlusion with styrene maleic anhydride. Contraception 57(2): 125-132. Feb. 1998.
144. LOHIYA, N.K., MANIVANNAN, B., and MISHRA, P.K. Repeated vas occlusion and non-invasive reversal with styrene maleic anhydride for male contraception in langur monkeys. International Journal of Andrology 23(1): 36-42. Feb. 2000.
145. LOHIYA, N.K., MANIVANNAN, B., MISHRA, P.K., PATHAK, N., and BALASUBRAMANIAN, S.P. Intravasal contraception with styrene maleic anhydride and its noninvasive

reversal in langur monkeys (Presbytis entellus entellus). Contraception 58(2): 119-128. Aug. 1998.
146. LUBIS, F., FAJANS, P., and SIMMONS, R. Maintaining technical quality of care in the introduction of Cyclofem in a national family planning program: Findings from Indonesia. Contraception 49(5): 527-541. May 1994.
147. LUUKKAINEN, T., ALLONEN, H., HAUKKAMAA, M., HOLMA, P., PYORALA, T., TERHO, J., TOIVONEN, J., BATAR, I., LAMPE, L., ANDERSSON, K., ET AL. Effective contraception with the levonorgestrel-releasing intrauterine device: 12-month report of a European multicenter study. Contraception 36(2): 169-179. Aug. 1987.
148. MAKARAINEN, L., VAN BEEK, A., TUOMIVAARA, L., ASPLUND, B., and COELINGH BENNINK, H. Ovarian function during the use of a single contraceptive implant: Implanon compared with Norplant. Fertility and Sterility 69(4): 714-721. Apr. 1998.
149. MANSOUR, D. Experiences with Yasmin: The acceptability of a novel oral contraceptive and its effect on well-being. European Journal of Contraception and Reproductive Health Care 7(Suppl 3) 35-41; discussion 42-43. Dec. 2002.
150. MASCARENHAS, L. Insertion and removal of Implanon. Contraception 58(6 Suppl): 79S-83S. Dec. 1998.
151. MASSAI, M.R., DIAZ, S., QUINTEROS, E., REYES, M.V., HERREROS, C., ZEPEDA, A., CROXATTO, H.B., and MOO-YOUNG, A.J. Contraceptive efficacy and clinical performance of Nestorone implants in postpartum women. Contraception 64(6): 369-376. Dec. 2001.
*152. MASSAI, R., DIAZ, S., JACKANICZ, T., and CROXATTO, H.B. Vaginal rings for contraception in lactating women. Steroids 65(10-11): 703-707. Oct.-Nov. 2000.
153. MASSAI, R., MIRANDA, P., VALDES, P., LAVIN, P., ZEPEDA, A., CASADO, M.E., SILVA, M.A., FETIS, G., BRAVO, C., CHANDIA, O., PERALTA, O., CROXATTO, H.B., and DIAZ, S. Preregistration study on the safety and contraceptive efficacy of a progesterone-releasing vaginal ring in Chilean nursing women. Contraception 60(1): 9-14. Jul. 1999.
154. MASTERS, T. and EVERETT, S. Intrauterine and barrier contraception (a practical review of recent developments). Current Obstetrics and Gynaecology 15(1): 31-37. Feb. 2005.
155. MELDRUM, J. Caution on female latex condom, may need further work for HIV prevention. Dec. 17, 2002. (Available: <http://www.aidsmap.com/news/newsdisplay2.asp?newsId=1808>)
156. MERIGGIOLA, M.C. and BREMNER, W.J. Progestin-androgen combination regimens for male contraception. Journal of Andrology 18(3): 240-244. May-Jun. 1997.
157. MERIGGIOLA, M.C., BREMNER, W.J., PAULSEN, C.A., VALDISERRI, A., INCORVAIA, L., MOTTA, R., PAVANI, A., CAPELLI, M., and FLAMIGNI, C. A combined regimen of cyproterone acetate and testosterone enanthate as a potentially highly effective male contraceptive. Journal of Clinical Endocrinology and Metabolism 81(8): 3018-3023. Aug. 1996.
158. MERIGGIOLA, M.C., COSTANTINO, A., CERPOLINI, S., BREMNER, W.J., HUEBLER, D., MORSELLI-LABATE, A.M., KIRSCH, B., BERTACCINI, A., PELUSI, C., and PELUSI, G. Testosterone undecanoate maintains spermatogenic suppression induced by cyproterone acetate plus testosterone undecanoate in normal men. Journal of Clinical Endocrinology and Metabolism 88(12): 5818-5826. Dec. 2003.
159. MERIGGIOLA, M.C., FARLEY, T.M., and MBIZVO, M.T. A review of androgen-progestin regimens for male contraception. Journal of Andrology 24(4): 466-483. Jul.-Aug. 2003.
160. MERIGGIOLA, M.C., MARCOVINA, S., PAULSEN, C.A., and BREMNER, W.J. Testosterone enanthate at a dose of 200 mg/week decreases HDL-cholesterol levels in healthy men. International Journal of Andrology 18(5): 237-242. Oct. 1995.
161. MIKOLAJCZYK, R.T., STANFORD, J.B., and RAUCH-FUSS, M. Factors influencing the choice to use modern natural family planning. Contraception 67(4): 253-258. Apr. 2003.
*162. MILLER, L. and HUGHES, J.P. Continuous combination oral contraceptive pills to eliminate withdrawal bleeding: A randomized trial. Obstetrics and Gynecology 101(4): 653-661. Apr. 2003.
163. MILLER, L. and NOTTER, K.M. Menstrual reduction with extended use of combination oral contraceptive pills: Randomized controlled trial. Obstetrics and Gynecology 98(5 Pt 1): 771-778. Nov. 2001.
164. MISHELL, D.R., JR. Vaginal contraceptive rings. Annals of Medicine 25(2): 191-197. Apr. 1993.
165. MONROY, M., LUNDGREN, R. Strategies for integrating the standard days method into community programs to expand choice in El Salvador. [Final Technical Report prepared for the Institute for Reproductive Health (IRH)]. Washington, DC, IRH, 2003. 39 p.
166. MULDERS, T.M. and DIEBEN, T.O. Use of the novel combined contraceptive vaginal ring NuvaRing for ovulation inhibition. Fertility and Sterility 75(5): 865-870. May 2001.
167. MULDERS, T.M., DIEBEN, T.O., and BENNINK, H.J. Ovarian function with a novel combined contraceptive vaginal ring. Human Reproduction 17(10): 2594-2599. Oct. 2002.
168. NARDIN, J.M., KULIER, R., and BOULVAIN, M. Techniques for the interruption of tubal patency for female sterilisation. Cochrane Database of Systematic Reviews (1): CD003034. 2003.
169. NATIONAL INSTITUTES OF HEALTH. An introduction to clinical trials. <www.clinicaltrials.gov> National Institutes of Health, Accessed Apr. 14, 2004.
170. NEWTON, J.R., D'ARCANGUES, C., and HALL, P.E. A review of "once-a-month" combined injectable contraceptives. Journal of Obstetrics and Gynecology 4(Suppl 1): S1-34. 1994.
171. NIESCHLAG, E. Progress for men: Development of male hormonal contraception. Karger Gazette 66: 8-9. Apr. 2003. (Available: <http://www.karger.com/gazette/gazett66.pdf>)
172. NIESCHLAG, E., ZITZMANN, M., and KAMISCHKE, A. Use of progestins in male contraception. Steroids 68(10-13): 965-972. Nov. 2003.
173. NOVÁK, A., DE LA LOGE, C., ABETZ, L., and VAN DER MEULEN, E.A. The combined contraceptive vaginal ring, NuvaRing: An international study of user acceptability. Contraception 67(3): 187-194. Mar. 2003.
174. O'BRIEN, P.A. and MARFLEET, C. Frameless versus classical intrauterine device for contraception. Cochrane Database of Systematic Reviews (4): CD003282. 2001.
175. ODDSSON, K., LEIFELS-FISCHER, B., WIEL-MASSON, D., DE MELO, N.R., BENEDETTO, C., VERHOEVEN, C.H., and DIEBEN, T.O. Superior cycle control with a contraceptive vaginal ring (NuvaRing) compared with an oral contraceptive containing 30 {micro}g ethinylestradiol and 150 {micro}g levonorgestrel: A randomized trial. Human Reproduction 20(2): 557-562. Feb. 2005.
176. ODEBLAD, E. Cervical mucus and their functions. Journal of the Irish College of Physicians and Surgeons 26: 27-32. Jan. 1997.
177. OELKERS, W., FOIDART, J.M., DOMBROVICZ, N., WELTER, A., and HEITHECKER, R. Effects of a new oral contraceptive containing an antimineralocorticoid progestogen, drospirenone, on the renin-aldosterone system, body weight, blood pressure, glucose tolerance, and lipid metabolism. The Journal of Clinical Endocrinology and Metabolism 80(6): 1816-1821. Jun. 1995.
178. ORGANON. Implanon® (etonogestrel). <http://www.organon.com/products/contraception/implanon.asp> Accessed Aug. 26, 2003.
179. ORTHO-MCNEIL PHARMACEUTICAL. ORTHO EVRA frequently asked questions. <http://www.orthoevra.com/birth-control-patch/faqs.html>
180. OSTERBERG, B. (Intellx, Inc.) [VA feminine condom] Personal communication, Dec. 19, 2004.
181. OUDSHOORN, N. Drugs for healthy people: The culture of testing hormonal contraceptives for women and men. Clio Medica 66: 123-140. 2002.
182. PARSEY, K.S. and PONG, A. An open-label, multicenter study to evaluate Yasmin, a low-dose combination oral contraceptive containing drospirenone, a new progestogen. Contraception 61(2): 105-111. Feb. 2000.
183. PEDRON, N. Menstrual blood loss in IUD users: Comparative study of eleven different IUDs in Mexican women. Advances in Contraceptive Delivery Systems 11(3-4): 245-253. 1995.
184. PINE, R.N. and POLLACK, A.E. Putting an ear to the ground: Where now with quinacrine? International Journal of Gynaecology and Obstetrics 69(1): 55-65. 2000.
185. POLLACK, A.E. and CARIGNAN, C.S. The use of quinacrine pellets for nonsurgical female sterilisation. Reproductive Health Matters (2): 119-122. Nov. 1993.
186. POOL, R., WHITWORTH, J.A., GREEN, G., MBONYE, A.K., HARRISON, S., WILKINSON, J., and HART, G.J. An acceptability study of female-controlled methods of protection against HIV and STDs in south-western Uganda. International Journal of STD and AIDS 11(3): 162-167. Mar. 2000.
187. POPULATION COUNCIL. Contraceptive rings provide simple protection. Population Briefs 3(2): 4. Jun. 1997.
188. POPULATION COUNCIL. Mirena®-induced drop in menstrual bleeding studied. Population Briefs [Newsletter], Vol. 9 No. 1, Feb. 2003. (Available: <http://www.popcouncil.org/publications/popbriefs/pb9(1)_4.html>)
189. POPULATION COUNCIL. The Population Council joins forces with Schering to establish the International Contraceptive Access Foundation. May 4, 2004. (Available: <http://www.popcouncil.org/mediacenter/newsreleases/ICA.html>)
190. POTTER, W.D. and DE VILLEMEUR, M. Clinical breakage, slippage and acceptability of a new commercial polyurethane condom: A randomized, controlled study. Contraception 68(1): 39-45. Jul. 2003.
191. RAHIMY, M.H. and RYAN, K.K. Lunelle monthly contraceptive injection (medroxyprogesterone acetate and estradiol cypionate injectable suspension): Assessment of return of ovulation after three monthly injections in surgically sterile women. Contraception 60(4): 189-200. Oct. 1999.
192. RAMACHANDRA, S.G., RAMESH, V., KRISHNAMURTHY, H.N., KUMAR, N., SUNDARAM, K., HARDY, M.P., and RAO, A.J. Effect of chronic administration of 7alpha-methyl-19-nortestosterone on serum testosterone, number of spermatozoa and fertility in adult male bonnet monkeys (Macaca radiata). Reproduction 124(2): 301-309. Aug. 2002.
193. REHAN, N., INAYATULLAH, A., and CHAUDHARY, I. Norplant: Reasons for discontinuation and side-effects. European Journal of Contraception and Reproductive Health Care 5(2): 113-118. Jun. 2000.
194. REINBERG, S. Novel transcervical sterilization procedure successful in humans. (Chicago), May 1, 2001. (Available: <http://www.stadtlander.com/reuters/repro/927241011.html>)
195. RINGHEIM, K. Male involvement and contraceptive methods for men: Present and future. Social Change 26(3-4): 88-99. Sep.-Dec. 1996.
196. RINGHEIM, K. Whither methods for men? Emerging gender issues in contraception. Reproductive Health Matters (7): 79-89. May 1996.
197. ROBBINS, A. The effects of hormones on male sexuality. Findings from clinical trials on male contraception. In: Zeidenstein, S. and Moore, K., eds. Learning about Sexuality: A Practical Beginning. New York, Population Council, 1996. p. 278-297.
198. ROUMEN, F.J., APTER, D., MULDERS, T.M., and DIEBEN, T.O. Efficacy, tolerability and acceptability of a novel contraceptive vaginal ring releasing etonogestrel and ethinyl oestradiol. Human Reproduction 16(3): 469-475. Mar. 2001.
199. SANCHEZ, S., ARAYA, C., TIJERO, M., and DIAZ, S. Women's perceptions and experience with the progesterone vaginal ring for contraception during breastfeeding. Reproductive Health Matters: 49-57. 1997. (Available: <http://www.who.int/reproductive-health/publications/beyond_acceptability_users_perspectives_on_contraception/sanchez.en.pdf>)
*200. SANG, G.W., SHAO, Q.X., GE, R.S., GE, J.L., CHEN, J.K., SONG, S., FANG, K.J., HE, M.L., LUO, S.Y., CHEN, S.F., ET AL. A multicentred phase III comparative clinical trial of Mesigyna, Cyclofem and Injectable No. 1 given monthly by intramuscular injection to Chinese women. I. Contraceptive efficacy and side effects. Contraception 51(3): 167-183. Mar. 1995.
201. SANGTHAWAN, M. and TANEEPANICHSKUL, S. A comparative study of monophasic oral contraceptives containing either drospirenone 3 mg or levonorgestrel 150 microg on premenstrual symptoms. Contraception 71(1): 1-7. Jan. 2005.
202. SCHERING AG. Annual report pursuant to section 13 or 15(d) of the securities exchange act of 1934: For the fiscal year ended December 31, 2002. Schering, Mar. 18, 2003. 200 p. (Available: <http://www.schering.de/html/de/50_media/download/_files/2002/fin_rep/20f/0220f_gesamt.pdf>)
203. SCHERING AG. Male fertility control. <http://www.schering.de/scripts/en/30_rd/areas/andro/fertcontr.php> Accessed Jun. 30, 2004.
204. SCHULMAN, A. Too much to swallow? The Boston Phoenix. (Boston), Apr. 13-20, 2000. (Available: <http://www.bostonphoenix.com/archive/features/00/04/13/male%5Fpill.html>)
205. SEGAL, S.J. Liability concerns in contraceptive research and development. International Journal of Gynecology and Obstetrics 67(2): S141-S151. Dec. 1, 1999.
206. SHELTON, J.D. New non-surgical sterilization. Jan. 27, 2003. (Contraceptive Pearls) (Available: <http://www.jhuccp.org/pearls/2003/01-27.shtml>)
207. SHELTON, J.D. FDA approval of SC Depo-Provera. Jan. 26, 2005. (Contraceptive Pearls) (Available: <http://www.jhuccp.org/pearls/pearl.php?id=301>)
208. SHULMAN, L.P. and GOLDZIEHER, J.W. The truth about oral contraceptives and venous thromboembolism. Journal of Reproductive Medicine 48(11 Suppl): 930-938. Nov. 2003.
209. SIBAI, B.M., ODLIND, V., MEADOR, M.L., SHANGOLD, G.A., FISHER, A.C., and CREASY, G.W. A comparative and pooled analysis of the safety and tolerability of the contraceptive patch (Ortho Evra/Evra). Fertility and Sterility 77(2 Suppl 2): S19-26. Feb. 2002.
210. SICAT, B.L. Ortho Evra, a new contraceptive patch. Pharmacotherapy 23(4): 472-480. Apr. 2003.
211. SILLEM, M., SCHNEIDEREIT, R., HEITHECKER, R., and MUECK, A.O. Use of an oral contraceptive containing drospirenone in an extended regimen. European Journal of Contraception and Reproductive Health Care 8(3): 162-169. Sep. 2003.
212. SIMMONS, R., HALL, P., DIAZ, J., DIAZ, M., FAJANS, P., and SATIA, J. The strategic approach to contraceptive introduction. Studies in Family Planning 28(2): 79-94. Jun. 1997.
213. SINAI, I., JENNINGS, V., and ARÉVALO, M. The importance of screening and monitoring: The Standard Days Method and cycle regularity. Contraception 69(3): 201-206. Mar. 2004.
214. SITRUK-WARE, R. (Population Council) [Contraceptive development at the Population Council] Personal communication, Jun. 25, 2004.
*215. SITRUK-WARE, R., SMALL, M., KUMAR, N., TSONG, Y.Y., SUNDARAM, K., and JACKANICZ, T. Nestorone: Clinical applications for contraception and HRT. Steroids 68(10-13): 907-913. Nov. 2003.
216. SIVIN, I. Risks and benefits, advantages and disadvantages of levonorgestrel-releasing contraceptive implants. Drug Safety 26(5): 303-335. 2003.
217. SIVIN, I. (Population Council) [Implanon and progesterone releasing ring in Chile and Peru] Personal communication, Jun. 1, 2004.
*218. SIVIN, I., CAMPODONICO, I., KIRIWAT, O., HOLMA, P., DIAZ, S., WAN, L., BISWAS, A., VIEGAS, O., EL DIN ABDALLA, K., ANANT, M.P., PAVEZ, M., and STERN, J. The performance of levonorgestrel rod and Norplant contraceptive implants: A 5 year randomized study. Human Reproduction 13(12): 3371-3378. Dec. 1998.
219. SIVIN, I., CROXATTO, H., BAHAMONDES, L., BRACHE, V., ALVAREZ, F., MASSAI, R., SCHECHTER, J., RANTA, S., KUMAR, N., WU, E., TEJEDA, A.S., REYES, V., TRAVERS, E., ALLEN, A., and MOO-YOUNG, A. Two-year performance of a Nestorone-releasing contraceptive implant: A three-center study of 300 women. Contraception 69(2): 137-144. Feb. 2004.
220. SIVIN, I., DIAZ, S., CROXATTO, H.B., MIRANDA, P., SHAABAN, M., SAYED, E.H., XIAO, B., WU, S.C., DU, M., ALVAREZ, F., BRACHE, V., BASNAYAKE, S., MCCARTHY, T.,

LACARRA, M., MISHELL, D.R., JR., KOETSAWANG, S., STERN, J., and JACKANICZ, T. Contraceptives for lactating women: A comparative trial of a progesterone-releasing vaginal ring and the copper T 380A IUD. Contraception 55(4): 225-232. Apr. 1997.
221. SIVIN, I. and MOO-YOUNG, A. Recent developments in contraceptive implants at the Population Council. Contraception 65(1): 113-119. Jan. 2002.
222. SIVIN, I., NASH, H., and WALDMAN, S. Jadelle levonorgestrel rod implants: A summary of scientific data and lessons learned from programmatic experience. New York, Population Council, 2002.
223. SIVIN, I. and STERN, J. Health during prolonged use of levonorgestrel 20 micrograms/d and the copper TCu 380Ag intrauterine contraceptive devices: A multicenter study. International Committee for Contraception Research (ICCR). Fertility and Sterility 61(1): 70-77. Jan. 1994.
224. SIVIN, I., WAN, L., RANTA, S., ALVAREZ, F., BRACHE, V., MISHELL, D.R., JR., DARNEY, P., BISWAS, A., DIAZ, S., KIRIWAT, O., ANANT, M.P., KLAISLE, C., PAVEZ, M., and SCHECHTER, J. Levonorgestrel concentrations during 7 years of continuous use of Jadelle contraceptive implants. Contraception 64(1): 43-49. Jul. 2001.
*225. SMALLWOOD, G.H., MEADOR, M.L., LENIHAN, J.P., SHANGOLD, G.A., FISHER, A.C., and CREASY, G.W. Efficacy and safety of a transdermal contraceptive system. Obstetrics and Gynecology 98(5 Pt 1): 799-805. Nov. 2001.
226. SOKAL, D. (Family Health International) [FHI Toxicology Studies on Quinacrine] Personal communication, May 20, 2004.
227. SOKAL, D., HIEU, D.T., WEINER, D.H., VINH, D.Q., HUU VACH, T., and HANENBERG, R. Long-term follow-up after quinacrine sterilization in Vietnam. Part I: Interim efficacy analysis. Fertility and Sterility 74(6): 1084-1091. Dec. 2000.
*228. SOKAL, D.C., DABANCENS, A., GUZMAN-SERANI, R., and ZIPPER, J. Cancer risk among women sterilized with transcervical quinacrine in Chile: An update through 1996. Fertility and Sterility 74(1): 169-171. Jul. 2000.
229. SOKAL, D.C., ZIPPER, J., and KING, T. Transcervical quinacrine sterilization: Clinical experience. International Journal of Gynaecology and Obstetrics 51(Suppl 1): S57-69. Dec. 1995.
230. SOROODI-MOGHADDAM, S. Quinacrine pellet method of nonsurgical female sterilization in Iran: Preliminary report on a clinical trial. International Family Planning Perspectives 22: 122-123, 127. Sep. 1996.
231. SPEIDEL, J. Barriers to Contraceptive Development in the United States. Washington, DC, Population Crisis Committee, May 8, 1992. (Testimony presented to 102nd Congress)
232. SPIELER, J. (USAID) [New contraceptive methods] Personal communication, Aug. 31, 2004.
233. STANFORD, J.B., LEMAIRE, J.C., and THURMAN, P.B. Women's interest in natural family planning. Journal of Family Practice 46(1): 65-71. Jan. 1998.
234. STEINER, M.J., DOMINIK, R., ROUNTREE, R.W., NANDA, K., and DORFLINGER, L.J. Contraceptive effectiveness of a polyurethane condom and a latex condom: A randomized controlled trial. Obstetrics and Gynecology 101(3): 539-547. Mar. 2003.
235. STEWART, F. and BARNHART, K. The vaginal contraceptive ring: Efficacy, caution, and instructions. Contraceptive Technology Reports, Vol. BB507 Feb. 2002. p. 1-4.
236. STICE, J. (Shepherd Medical) [Intra Vas Device] Personal communication, Aug. 9, 2004.
237. SULAK, P.J., KUEHL, T.J., ORTIZ, M., and SHULL, B.L. Acceptance of altering the standard 21-day/7-day oral contraceptive regimen to delay menses and reduce hormone withdrawal symptoms. American Journal of Obstetrical Gynecology 186(6): 1142-1149. Jun. 2002.
238. SULAK, P.J., SCOW, R.D., PREECE, C., RIGGS, M.W., and KUEHL, T.J. Hormone withdrawal symptoms in oral contraceptive users. Obstetrics and Gynecology 95(2): 261-266. Feb. 2000.
239. SUNDARAM, K. and KUMAR, N. 7alpha-methyl-19-nortestosterone (MENT): The optimal androgen for male contraception and replacement therapy. International Journal of Andrology 23(Suppl 2): 13-15. 2000.
240. SUVISAARI, J. and LÄHTEENMÄKI, P. Detailed analysis of menstrual bleeding patterns after postmenstrual and postabortal insertion of a copper IUD or a levonorgestrel-releasing intrauterine system. Contraception 54: 201-208. Oct. 1996.
241. TEO, M., MEAGHER, S., and KOVACS, G. Ultrasound detection of the Essure permanent birth control device: A case series. Australian and New Zealand Journal of Obstetrics and Gynaecology 43(5): 378-380. Oct. 2003.
242. THOMAS, S.L. and ELLERTSON, C. Nuisance or natural and healthy: Should monthly menstruation be optional for women? Lancet 355(9207): 922-924. Mar. 11, 2000.
243. THORNEYCROFT, I.H. Yasmin: The reason why. European Journal of Contraception and Reproductive Health Care 7(Suppl 3): 13-18; discussion 42-43. Dec. 2002.
244. TOIVONEN, J., LUUKKAINEN, T., and ALLONEN, H. Protective effect of intrauterine release of levonorgestrel on pelvic infection: Three years' comparative experience of levonorgestrel and copper-releasing intrauterine devices. Obstetrics and Gynecology 77(2): 261-264. Feb. 1991.
245. TRUSSELL, J., WARNER, D.L., and HATCHER, R. Condom performance during vaginal intercourse: Comparison of Trojan-Enz and Tactylon condoms. Contraception 45(1): 11-19. Jan. 1992.
246. UBEDA, A., LABASTIDA, R., and DEXEUS, S. Essure: A new device for hysteroscopic tubal sterilization in an outpatient setting. Fertility and Sterility 82(1): 196-199. Jul. 2004.
247. UNITED NATIONS DEVELOPMENT PROGRAMME, UNITED NATIONS POPULATION FUND, WORLD HEALTH ORGANIZATION, and WORLD BANK SPECIAL PROGRAMME OF RESEARCH, DEVELOPMENT AND RESEARCH TRAINING IN HUMAN REPRODUCTION, TASK FORCE ON LONG-ACTING SYSTEMIC AGENTS FOR FERTILITY REGULATION. Comparative study of the effects of two once-a-month injectable contraceptives (Cyclofem and Mesigyna) and one oral contraceptive (Ortho-Novum 1/35) on coagulation and fibrinolysis. Contraception 68(3): 159-176. Sep. 2003.
248. UNITED STATES AGENCY FOR INTERNATIONAL DEVELOPMENT (USAID). Acquisition and assistance ADS chapter 312: Eligibility of commodities. Jul. 27, 2004. (Major Functional Series 300) 20 p. (Available: <http://www.usaid.gov/policy/ads/300/312.pdf>)
249. UNITED STATES FOOD AND DRUG ADMINISTRATION (US FDA). FDA approves first hormonal vaginal contraceptive ring. (Washington, DC), Oct. 3, 2001. (Available: <http://www.fda.gov/bbs/topics/ANSWERS/2001/ ANS01107.html>)
250. UNITED STATES FOOD AND DRUG ADMINISTRATION (US FDA). Birth control guide. <http://www.fda.gov/fdac/features/1997/babytabl.html> Accessed Aug. 12, 2003.
251. UPADHYAY, U.D. Informed choice in family planning: Helping people decide. Population Reports, Series J, No. 50. Baltimore, Johns Hopkins School of Public Health, Population Information Program, Spring 2001. 39 p. (Available: <http://www.jhuccp.org/pr/j50edsum.shtml>, Accessed Aug. 3, 2002)
252. VALLE, R.F., CARIGNAN, C.S., and WRIGHT, T.C. Tissue response to the STOP microcoil transcervical permanent contraceptive device: Results from a prehysterectomy study. Fertility and Sterility 76(5): 974-980. Nov. 2001.
253. WAITES, G.M. Development of methods of male contraception: Impact of the World Health Organization Task Force. Fertility and Sterility 80(1): 1-15. Jul. 2003.
254. WALLING, M. Development of contraceptive implants. British Journal of Family Planning 26(1): 12-13. Jan. 2000.
255. WALSH, T.L., FREZIERES, R.G., PEACOCK, K., NELSON, A.L., CLARK, V.A., and BERNSTEIN, L. Evaluation of the efficacy of a nonlatex condom: Results from a randomized, controlled clinical trial. Perspectives on Sexual and Reproductive Health 35(2): 79-86. Mar.-Apr. 2003.
256. WANG, C. and SWERDLOFF, R.S. Male contraception. Best Practice and Research. Clinical Obstetrics and Gynaecology 16(2): 193-203. Apr. 2002.
*257. WANG, C. and SWERDLOFF, R.S. Male hormonal contraception. American Journal of Obstetrical Gynecology 190 (4 Suppl): S60-68. Apr. 2004.
258. WEISBERG, E., FRASER, I.S., MISHELL, D.R., JR., LACARRA, M., and BARDIN, C.W. The acceptability of a combined oestrogen/progestogen contraceptive vaginal ring. Contraception 51(1): 39-44. Jan. 1995.
259. WESTON, G.C., SCHLIPALIUS, M.L., BHUINNEAIN, M.N., and VOLLENHOVEN, B.J. Will Australian men use male hormonal contraception? A survey of a postpartum population. Medical Journal of Australia 176(5): 208-210. Mar. 4, 2002.
260. WILCOX, A.J., DUNSON, D., and BAIRD, D.D. The timing of the "fertile window" in the menstrual cycle: Day specific estimates from a prospective study. British Medical Journal 321(7271): 1259-1262. Nov. 18, 2000.
261. WILCOX, A.J., WEINBERG, C.R., and BAIRD, D.D. Timing of sexual intercourse in relation to ovulation. Effects on the probability of conception, survival of the pregnancy, and sex of the baby. New England Journal of Medicine 333(23): 1517-1521. Dec. 7, 1995.
262. WILDEMEERSCH, D. Further information and recommendations to prevent perforation with the frameless GyneFix IUD. Journal of Family Planning and Reproductive Health Care 27(4): 241. Oct. 2001.
263. WILDEMEERSCH, D. (Contrel Research) [Availability of GyneFix] Personal communication, Jan. 27, 2005.
264. WILDEMEERSCH, D., BATAR, I., AFFANDI, B., ANDRADE, A., SHANGCHUN, W., JING, H., and XIAOMING, C. The 'frameless' intrauterine system for long-term, reversible contraception: A review of 15 years of clinical experience. Journal of Obstetrics and Gynaecology Research 29(3): 164-173. Jun. 2003.
265. WILDEMEERSCH, D., DHONT, M., WEYERS, S., and TEMMERMAN, M. Miniature, low-dose, intrauterine drug-delivery systems. Annals of the New York Academy of Sciences 997: 174-184. Nov. 2003.
266. WILDEMEERSCH, D., JANSSENS, D., VRIJENS, M., and WEYERS, S. Ease of insertion, contraceptive efficacy and safety of new T-shaped levonorgestrel-releasing intrauterine systems. Presented at the 8th Congress of the European Society of Contraception, Edinburgh, Scotland, Jun. 23-36, 2004.
267. WILDEMEERSCH, D., SCHACHT, E., and WILDEMEERSCH, P. Contraception and treatment in the perimenopause with a novel "frameless" intrauterine levonorgestrel-releasing drug delivery system: An extended pilot study. Contraception 66(2): 93-99. Aug. 2002.
*268. WILDEMEERSCH, D., SCHACHT, E., WILDEMEERSCH, P., JANSSENS, D., and THIERY, M. Development of a miniature, low-dose, frameless intrauterine levonorgestrel-releasing system for contraception and treatment: A review of initial clinical experience. Reproductive Biomedicine Online 4(1): 71-82. Jan.-Feb. 2002.
269. WILSON, E.W. The development of new technologies for female sterilization: Conclusions and recommendations for research. International Journal of Gynaecology and Obstetrics 51(Suppl 1): S71-S74. 1995.
270. WONDEMAGEGNEHU, E. Effective drug regulation: What can countries do? Geneva, World Health Organization, Mar. 1999.
*271. WORLD HEALTH ORGANIZATION (WHO). Facts about once-a-month injectable contraceptives: Memorandum from a WHO meeting. Bulletin of the World Health Organization 71(6): 677-689. 1993.
272. WORLD HEALTH ORGANIZATION (WHO). Making decisions about contraceptive introduction: A guide for conducting assessments to broaden contraceptive choice and improve quality of care. Geneva, UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction, 2002.
273. WORLD HEALTH ORGANIZATION (WHO). Contraceptive implants come of age. Progress in Reproductive Health Research (61): 2-5. 2003.
274. WORLD HEALTH ORGANIZATION (WHO). Improving access to quality care in family planning: Medical eligibility criteria for contraceptive use. 3nd ed. Geneva, WHO, 2004.
*275. WORLD HEALTH ORGANIZATION TASK FORCE ON METHODS FOR THE REGULATION OF MALE FERTILITY. Contraceptive efficacy of testosterone-induced azoospermia in normal men. Lancet 336(8721): 955-959. Oct. 20, 1990.
*276. WORLD HEALTH ORGANIZATION TASK FORCE ON METHODS FOR THE REGULATION OF MALE FERTILITY. Contraceptive efficacy of testosterone-induced azoospermia and oligozoospermia in normal men. Fertility and Sterility 65(4): 821-829. Apr. 1996.
277. WU, F.C., FARLEY, T.M., PEREGOUDOV, A., and WAITES, G.M. Effects of testosterone enanthate in normal men: Experience from a multicenter contraceptive efficacy study. World Health Organization Task Force on Methods for the Regulation of Male Fertility. Fertility and Sterility 65(3): 626-636. Mar. 1996.
278. YOSHINAGA, L. (Conceptus) [Effectiveness of Essure] Personal communication, Mar. 11, 2003.
279. YOUNG, E. Spray-on female contraceptive to start trial. New Scientist. (Sydney, Australia), Nov. 27, 2003. (Available: <http://www.newscientist.com/news/news.jsp?id=ns99994431>)
280. ZACUR, H.A., HEDON, B., MANSOUR, D., SHANGOLD, G.A., FISHER, A.C., and CREASY, G.W. Integrated summary of Ortho Evra/Evra contraceptive patch adhesion in varied climates and conditions. Fertility and Sterility 77(2 Suppl 2): S32-35. Feb. 2002.
281. ZANEVELD, L., DE CASTRO, M., FARIA, G., DERRICK, F., and FERRARO, R. The soft hollow plug ("shug"): A potentially reversible vas deferens blocking device. In: Rajalakshmi, M. and Griffin, P., eds. Male Contraception: Present and Future. New Delhi, New Age International Publishers, 1999. p. 293-307.
282. ZANEVELD, L.J., BURNS, J.W., BEYLER, S., DEPEL, W., and SHAPIRO, S. Development of a potentially reversible vas deferens occlusion device and evaluation in primates. Fertility and Sterility 49(3): 527-533. Mar. 1988.
283. ZANEVELD, L.J.D. [The Shug] Personal communication, Jul. 1, 2004.
284. ZHANG, G.Y., GU, Y.Q., WANG, X.H., CUI, Y.G., and BREMNER, W.J. A clinical trial of injectable testosterone undecanoate as a potential male contraceptive in normal Chinese men. Journal of Clinical Endocrinology and Metabolism 84(10): 3642-3647. Oct. 1999.
285. ZIEMAN, M., GUILLEBAUD, J., WEISBERG, E., SHANGOLD, G.A., FISHER, A.C., and CREASY, G.W. Contraceptive efficacy and cycle control with the Ortho Evra/Evra transdermal system: The analysis of pooled data. Fertility and Sterility 77(2 Suppl 2): S13-18. Feb. 2002.
286. ZIPPER, J., COLE, L.P., GOLDSMITH, A., WHEELER, R., and RIVERA, M. Quinacrine hydrochloride pellets: Preliminary data on a nonsurgical method of female sterilization. International Journal of Gynaecology and Obstetrics 18(4): 275-279. 1980.
*287. ZIPPER, J. and KESSEL, E. Quinacrine sterilization: A retrospective. International Journal of Gynaecology and Obstetrics 83 (Suppl 2): S7-11. Oct. 2003.

ISSN 0887-0241

POPULATION REPORTS

Population Reports are free in any quantity to developing countries. In USA and other developed countries, multiple copies are US$2.00 each; full set of reports in print, $35.00; with binder, $40.00. Send payment in US$ with order. **Population Reports** in print in English are listed below. Many are also available in French, Portuguese, and Spanish, as indicated by abbreviations after each title on the order form below.

TO ORDER, please complete the form below. (PRINT or TYPE clearly.)

Mail to: INFO, Johns Hopkins Bloomberg School of Public Health
111 Market Place, Suite 310, Baltimore, MD 21202, USA
Fax: (410) 659-2645 E-mail: Orders@jhuccp.org Website: http://www.infoforhealth.org

Family name _____ **Given name** _____

Organization _____

Address _____

_____

Population Reports in Print

1. ❑ Send ___ copies of each future issue of **Population Reports.**
   ❑ I am already on the **Population Reports** mailing list.
   ❑ Send me a binder (in developed countries, US$7.00).
2. Language: ❑English ❑French ❑Portuguese ❑Spanish.
3. Check (✓) the issues you want:

ORAL CONTRACEPTIVES—Series A
___ A-9 Oral Contraceptives—An Update [2000] *(F,S)*
___ A-10 Helping Women Use the Pill [2000] *(F,S)*

INTRAUTERINE DEVICES—Series B
___ B-6 IUDs—An Update [1995] *(F,P,S)*

BARRIER METHODS—Series H
___ H-9 Closing the Condom Gap [1999] *(F,P,S)*

FAMILY PLANNING PROGRAMS—Series J
___ J-39 Paying for Family Planning [1991] *(F,S)*
___ J-41 *Supplement:* Female Genital Mutilation: A Reproductive Health Concern [1995] *(F)*
___ J-42 Helping the News Media Cover Family Planning [1995] *(F,S)*
___ J-43 Meeting Unmet Need: New Strategies [1996] *(F,S)*
___ J-45 People Who Move: New Reproductive Health Focus [1997] *(F,S)*
___ J-46 Reproductive Health: New Perspectives on Men's Participation [1998] *(F, S)*
___ J-47 Family Planning Programs: Improving Quality [1998] *(F,P,S)*
___ J-49 Why Family Planning Matters [1999] *(F,S)*
___ J-50 Informed Choice in Family Planning: Helping People Decide [2001] *(F,P,S)*
___ J-51 Family Planning Logistics: Strengthening the Supply Chain [2002] *(F,S)*
___ J-52 Performance Improvement [2002] *(F,S)*

INJECTABLES AND IMPLANTS—Series K
___ K-4 *Guide:* Guide to Norplant Counseling [1992] *(F,S)*
___ K-5 New Era for Injectables [1995] *(F,P,S)*
___ K-5 *Guide:* Guide to Counseling on Injectables [1995] *(F,P,S)*
___ K-5 *Fact Sheet:* DMPA at a Glance [1995] *(F,P,S)*

ISSUES IN WORLD HEALTH—Series L
___ L-10 *Wall chart:* Family Planning After Postabortion Treatment [1997] *(F,P,S)*
___ L-11 Ending Violence Against Women [1999] *(F,P,S)*
___ L-12 Youth and HIV/AIDS: Can We Avoid Catastrophe? [2001] *(F,P,S)*
___ L-13 Birth Spacing: Three to Five Saves Lives [2002] *(F,S)*

SPECIAL TOPICS—Series M
___ M-13 Winning the Food Race [1997] *(F,S)*
___ M-14 Solutions for a Water-Short World [1998] *(F,S)*
___ M-15 Population and the Environment: The Global Challenge [2000] *(F,S)*
___ M-16 Meeting the Urban Challenge [2002] *(F,S)*
___ M-17 New Survey Findings: The Reproductive Revolution Continues [2003] *(F,S)*
___ M-18 Men's Surveys: New Findings [2004] *(F,S)*
___ M-19 New Contraceptive Choices [2005]

MAXIMIZING ACCESS AND QUALITY—Series Q
___ Q-1 Improving Client-Provider Interaction [2003] *(F,S)*
___ Q-2 Organizing Work Better [2004] *(F,S)*

❑ The Essentials of Contraceptive Technology Handbook *(F,S)*

❑ The Essentials of Contraceptive Technology Wall Chart *(F,S)*

POPLINE Digital Services

Please send details on the following products/services:

❑ **POPLINE:** the world's larget bibliographic database on population, family planning, and related health issues, is available in CD-ROM (free of charge to developing countries) and on the Internet, at no charge, at: http://www.popline.com

❑ **Document Delivery:** Receive full-text copies of POPLINE documents by mail or by e-mail.

Special topic CD-ROMS:

❑ International Family Planning Perspectives CD-ROM
❑ New Survey Findings CD-ROM

Searches: POPLINE searches can be requested by sending an e-mail to: popline@jhuccp.org or mail or fax to address above.