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### Are we Meeting the Global Challenges of Effective

**Contraception?** 

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### Key-Note Lectures – Monday, September 13<sup>th</sup> Are we Meeting the Global Challenges of Effective Contraception?

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Unintended pregnancies continue to present a major unsolved problem in the landscape of global health care. In order for contraception to be effective, it must also be safe, acceptable and accessible. Whereas contraception is generally considered a problem of developing nations, the reality is that many developed countries continue to have many unwanted pregnancies. To meet the global challenge of effective contraception, technical innovation must therefore be coupled with education, cultural understanding and efficient distribution. **J Reproduktionsmed Endokrinol 2010; 7 (4): 217–9**.

Key words: contraception, contraceptive effectiveness, IUD, post-coital contraception

### Introduction

Contraception is as old as human culture. From the earliest times of written history, we find indications that human beings have actively attempted to control the reproductive process. From the Bible to an ancient Egyptian Papyrus, there is clear indication that human culture was not just interested in enhancing fertility, but in many cases, actually wanted to prevent conception. Cultural evolution and technology have made great strides in contraceptive methodology since then. While not perfect, a number of highly effective methods to prevent conception now exist. In spite of these advances, millions of unplanned, unwanted pregnancies continue to occur in the world each year. This is true not only in developing nations, but also in many so-called "civilized" countries. These unwanted pregnancies are not only associated with significant morbidity and mortality, but also lead to the continued need for abortion services. This review provides an overview of available contraceptive methods in an effort to point out that whereas contraceptive technology has been successful in helping to empower individual women to exercise control over their reproductive choice, the many unwanted pregnancies in the world today clearly demonstrate that there are continued challenges in delivering the available technology to all of those who would benefit.

### What is Effective Contraception?

In order for contraception to be effective, it must effectively prevent pregnancies, not just with ideal usage ("efficacy"), such as occurs during clinical trials, but in actual practice ("effectiveness"). The method must be completely reversible, to allow conception when it is subsequently desired. It must be safe, and free of untoward side effects that may detract from its use. The method must be acceptable to those who wish to use it and cannot be cumbersome or clumsy, as it will inevitably not be used in the "real world". Finally, the contraceptive method must be accessible in that it cannot be expensive, hard to find, or be associated with an excessively high investment of time and effort.

It is interesting to note that, at least to the Western culture, there are a number of contraceptive methods that meet all of these criteria [1]. However, the concept of "acceptable" and "accessible" may not be perceived in the same way by other cultures. And so the final missing piece is one of education, in that the population at risk must be informed of the available methods, and such information must be stripped of its mystery and consequent misconceptions that so often accompany the introduction of all new technologies.

### Current Contraceptive Methods

#### **Natural Methods**

Coitus interruptus, or withdrawal, is probably the oldest and most commonly used method in the world. In this method, the male partner must withdraw the penis during coitus so that none of the ejaculate is deposited in the vagina. In perfect use, the method is quite effective, with an estimated 4 % failures per year of use. Unintended pregnancies occur if the male partner is not able to control the maneuver properly, or in a timely fashion. Although concern has been raised in the past about the risk of pregnancy from sperm in the pre-ejaculate, recent small studies have failed to find any viable sperm in this fluid [2].

As an alternative, couples may use "natural family planning" or may combine withdrawal with natural family planning. In this method, couples abstain from sexual intercourse during the fertile period, which is now recognized as lasting from approximately 5 days prior to ovulation to 1 day after ovulation. Since ovulation does not occur at the same time each month, a reasonable margin of error must be built into the system. Utilizing a combination of methods to determine the time of ovulation, and "perfect use", natural family planning is estimated to have an annual failure rate between 2 and 9 %.

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During the postpartum period, breastfeeding provides very good contraceptive protection as long as breastfeeding is used exclusively and the woman remains amenorrheic. Under these circumstances, lack of ovulation provides a 98 % success rate. A secondary method is recommended when menstruation resumes, the frequency of breastfeeding is reduced, or the baby reaches 6 months of age [4].

**Barrier Methods and Spermicides** It is unclear whether condoms were used in ancient civilizations. The oldest claimed drawing of a condom is in the French cave "Grotte des Comarrelles"; the paintings in this cave are 12 to 15 thousand years old. In the 16th century, Gabriele Falloppio (after whom the Fallopian tube is named) is credited with the development of the modern condom. He described linen sheets soaked in a chemical solution which were then used to cover the penis, specifically for the purpose of avoiding the transmission of syphilis. Subsequent condoms were often made from animal intestines. In 1839, Charles Goodyear developed the rubber vulcanization process, and the first rubber condom was produced in 1855. By the end of the 19th century, "rubber" had become a commonly used term for condoms in countries around the world. The invention of latex in 1920 led to latex condoms. By 1931, condoms were standard issue to members of the United States military with a resulting steep decline in the incidence of sexually transmitted disease among the military. Prior to the development of the combination oral contraceptive pill, condoms remained among the most popular methods of contraception. In perfect use, they are 98 % effective, but in typical use, up to 15 % of couples conceive in one year [3, 5]. An early version of the diaphragm, a large cervical cap, was developed in the late 1800s in Germany. A variety of modifications have taken place since then, including the cervical cap, and female condom. Spermicidal agents are formulated in foams and gels and may be used either by themselves or in combination with female barrier methods (or condoms). Because the vehicle (foam or gel) may be displaced during intercourse, failure rates of spermicides alone are high. Barrier methods are highly dependent on the motivation of the couple using these methods. In perfect use, female barrier methods achieve success rates in excess of 90 %. However, in typical use, 20– 30 % of women will conceive [3, 6, 7].

### **Hormonal Contraception**

Early studies demonstrating that progesterone injections could block ovulation in animals are generally credited to Gregory Pincus, who conducted these studies in the 1950s. In his collaboration with John Rock, progesterone was also used as a potential treatment for infertility. The idea was that progesterone would suppress ovulation, and then, when withdrawn, would induce a "rebound" effect, leading to ovulation and subsequent conception. The first orally active progestin, norethindrone, was synthesized by Carl Djerassi in 1951. Subsequently, Colton developed norethynodrel in 1953. An estrogen component was added to decrease breakthrough bleeding and enhance cycle control. The first combination pill (Enovid) was approved for "menstrual regulation" in 1957. Finally, in 1960 Enovid was approved for contraception.

The initial formulation of Enovid contained a large dose of steroids by today's standards. The estrogen component consisted of 150 mcg of mestranol and progesterone activity was supplied by 9.85 mg of norethynodrel. This high dose of estrogen was associated with an increased risk of thromboembolic phenomena. As data accumulated, the estrogen dose quickly dropped and subsequent formulations contained 100 mcg, 80 mcg or 50 mcg of mestranol. In the 1970s, mestranol was replaced by ethinyl estradiol (a metabolite of mestranol) and its dose was further reduced to 35, 30 and eventually, 20 mcg per pill. In 1989, all formulations containing more than 50 mcg of estrogen were withdrawn from the market. The decreasing estrogen dose substantially lowered the risk of thromoembolic events.

The oral contraceptive pill, when used correctly, is an extremely effective form of contraception, with less than 1 % unintended pregnancies associated with perfect use. In typical use, however, because of the need to remember to take the pill everyday, annual failure rates are between 5 and 10 % [3, 8]. Whereas the basic concept of the oral contraceptive pill as a combination of orally active estrogen and a progestin has not changed since its inception, the actual formulations have undergone considerable modification. The initial formulation consisted of 21 active pills and a 7-day pill-free interval, which allowed for menstrual bleeding. The purpose for menses was primarily to reassure the user that pregnancy had not occurred. As the dose of hormones was gradually diminished, a variety of strategies was developed to diminish the incidence of breakthrough bleeding associated with the lower doses of steroids, including biphasic and triphasic formulations, which varied the dose of hormones throughout the month. In the early 2000s, extended monophasic regimens allowed women to take oral contraceptives for 12 weeks at a time with only one bleeding episode every 3 months. Other regimens reduced the pill-free interval from 7 days to 4 days while others simply suggested that patients take the combination pill everyday without a need for withdraw bleeding. Over the past 50 years, the many non-contraceptive health benefits of low dose oral contraceptives became appreciated [9].

Since it is the progestin component of oral contraceptives that blocks ovulation, it is possible to use progestin alone as the contraceptive agent. The primary problem with progestin-only pills is a high incidence of breakthrough bleeding, which diminishes the acceptability of this form of contraception. The notable advantage of progestin-only contraception is that the progestin may be delivered via monthly injection (such as Depo-Provera) or may be delivered via subcutaneously-placed implants. Whereas the implants are associated with irregular uterine bleeding, their primary appeal (and high success rate) lies in that they last for several years and therefore the user is not required to take a daily pill or actively engage the contraceptive method when it is required. Most recently, a single subdermal implant of ethylene glycol acetate containing 68 mg of etonogestrel (the active metabolite of desogestrel) has been introduced into clinical use. It appears to be effective for 3 years and no pregnancies were reported in more than 28,000 cycles in three studies [10].

## Intrauterine Devices and Systems (IUDs and IUSs)

The modern intrauterine device (IUD) traces its origin to the Grafenberg ring in the 1930s. The ring was a loop of silver wire inserted into the uterus. It required a second instrument for removal, as there was no string. In the 1960s, plastic devices, including the loop, spiral and coil were developed. There are many misperceptions associated with IUDs, including that they cause pelvic inflammatory disease, that they act as abortifacients, and that they predispose to ectopic pregnancies. Since the IUD has to be placed via the cervix, it is reasonable to expect that bacteria may be carried to the cavity. However, contamination of the endometrial cavity appears to occur only during insertion. Long-term users of IUDs have no increase in pelvic inflammatory disease. A notable exception here is the Dalkon shield, which had a poly-filament tail string. The tiny gaps between the filaments provided a pathway for pathogens to ascend from the vaginal canal to the endometrial cavity [11].

The mechanism of action of the IUD appears to be the generation of a sterile inflammatory reaction in the endometrial cavity. The endometrial milieu is hostile to embryo-implantation but also prevents fertilization by preventing sperm ascent to the upper genital tract. Ectopic pregnancies are less frequent in women who use an IUD than in women who do not use any contraception. However, since the IUD is more effective in blocking an intrauterine pregnancy than an extrauterine pregnancy, women who do conceive with an IUD *in situ* should be monitored carefully for ectopic pregnancy.

Modern IUDs and IUSs utilize either copper or levonorgestrel to maximize efficacy and to minimize side effects. The modern systems are so effective, that they compare favorably with tubal sterilization in terms of efficacy, yet they remain completely reversible. Recent studies have confirmed the efficacy of IUD placement in the immediate post-partum period. This method has tremendous potential to increase the accessibility and thus increase the acceptability of the IUD to as many women as possible [12].

#### **Emergency Contraception**

Emergency contraception refers to contraceptive measures that are taken after sex in order to prevent pregnancy. The first regimen consisted of high-dose estrogens (DES) taken for 5 days. This method was pioneered in the 1960s and was thought to be effective. In retrospect, however, its efficacy is unclear. In the 1970s, Yuzpe developed a regimen consisting of four high-dose oral contraceptive pills taken during a 24-hour time period. This regimen was effective if taken within 72 hours after intercourse, probably as a result of its progestin component [8, 13].

Progestin-only post-coital contraception was also investigated in the 1970s. The currently-used Plan B contains 250 mcg of levonorgestrel, and most likely works by inhibiting ovulation; if implantation has taken place, there is no further effect. Other effective forms of post-coital contraception include the insertion of an IUD, which may prevent implantation [14], and the use of selective progesterone receptor modulators (SPERMs), which work for up to 5 days after unprotected intercourse by interfering with implantation. Both mifeprostone and ulipristal ecetate (Ellaone) have been shown by to be effective.

#### Challenges of Effective Contraception

It seems intuitive that the goal of effective contraception is to prevent all unwanted pregnancies. However, in spite of the development of several methods of contraception, many of which are highly effective, unwanted pregnancies continue to be highly prevalent around the world. This is not just true of developing nations, but also of many so-called "civilized" countries, especially the United States. It is clear that in addition to efficacy and safety, contraceptive methods must be associated with acceptability and availability in order to achieve the goal of prevention of unwanted pregnancies.

It is likely that different strategies will have to be employed in different parts of the world to make this goal a reality. In developing nations, where medical care may only be sought at the time of delivery, the post-partum insertion of an intrauterine device may be very helpful to limit fecundability. In highly developed countries, education of the population, especially in schools, has the greatest potential for making sure that contraceptive technology is understood and available to all those to seek it.

It should be pointed out that modern development of contraception has paralleled cultural advances made by women during the past 50 years. Thus, it could be argued that contraception has empowered women to enter the work force, attain personal goals, and that it has helped to level the playing field for women in the professional workplace. Of course, it is not possible to demonstrate that this is a cause and affect relationship, as opposed to simply an association. However, it is possible to state that on an individual basis, the general availability of contraception was an essential first step in bringing about gender equality. The next step, to bring contraception to all corners of the world, and to limit, or even eliminate all unwanted pregnancies, remains a goal and a challenge for the years ahead.

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