Birth Control Methods: From Antiquity to the Future

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1.1 The Past: Unimaginable Suffering

For most of human history people have desperately but unsuccessfully tried to limit natural fertility of 12–15 pregnancies in a woman's lifetime to the individually desired number of children.

Nature had planned an average of 12–15 pregnancies over the 35 years of a woman's fertile years, resulting in about ten deliveries and eight surviving children, with each breastfed for 2 years [1]. If still alive, a woman then entered menopause. In other words, the fertile life of women consisted of a succession of pregnancies and lengthy breastfeeding, interrupted by short periods of menstrual cycles. Women only had about 150 ovulations/menstruations over their lifetimes. Today, women experience almost three times as many menstrual periods compared to the past—an average of about 450 [2–5] (Fig. 1.1).

Uncontrolled fertility drove women and their partners into a despair that is hard to imagine today. Marie Stopes called it "slavery" and "torture" in her famous 1918 brochure *Married Love* [6]. The fate of women due to unmanageable fertility was also portrayed in heartbreaking artwork by women of the time, such as by Kaethe Kollwitz from Germany (Fig. 1.2) and in Margaret Sanger's *Birth Control Review* in the USA (Fig. 1.3).

Throughout history, women have desperately tried everything imaginable to change the natural course of fertility and limit their families to the desired number of children. They used a wide variety of means, but most were ineffective, dangerous, or both, such as the withdrawal method, taking herbs, inserting twigs in the vagina, or jumping off roofs [7]. Countless women have died by ingesting poisonous substances or using other unsafe means to prevent pregnancy or end it once it started [8]. In addition ancient methods were quite ineffective, even though

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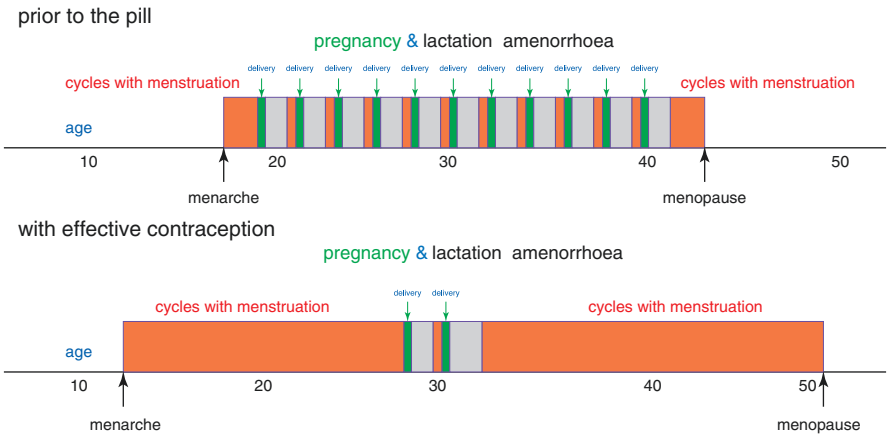

Fig. 1.1 Fertile periods over a woman's lifetime (based on [3, 4])

Fig. 1.2 Charcoal drawing by Kaethe Kollwitz, from "Liebe ohne unerwünschte Kinder" (Love without unwanted children), Vienna, 1913

historical documents indicate that abortion has been practiced occasionally or at least attempted. But there has been a lack or total absence of medical knowledge, pregnancy tests, dedicated instruments, and any way to determine the safe and effective concentration of uterotonic ingredients in plants. In other words, most women throughout history would only realize they are pregnant when they felt "quickening," the first fetal movements around 15 weeks of pregnancy. If they wanted to terminate the pregnancy, they only had highly dangerous and rather ineffective methods available to do what we call today a late abortion. But without any

Fig. 1.3 Illustration from Margaret Sanger's *Birth Control Review*, November 1923

effective contraceptive methods to use after an abortion, it did not make much sense to shorten an unwanted pregnancy, just to get pregnant immediately again. The fact that abortion is forbidden in ancient laws and the Hippocratic Oath therefore rather indicates the fantasy and intention of those in power than real facts.

When contraception was unavailable and abortion was not possible, ineffective, or dangerous, infanticide or abandonment was often the only "solution" for the very frequent unwanted pregnancies. The exposure of newborns was widely practiced in ancient Greece and Rome and throughout the Middle Ages. Even until around 1900, women in Europe would often continue an unwanted pregnancy to term and give away the child to be "cared for." These children were neglected and frequently let to die, which led to the very term of "angel maker," a euphemism attributed in many countries to women who "made an angel" of children by letting it die. This "practice" partially explains the high infant mortality in the past. In the early twentieth century "angel makers" performed more and more (illegal) abortions, which explains that most people today wrongly associate the term with illegal abortion. However the increasing number of abortions performed in the early twentieth century led to a reduced child mortality, although child neglect continued to some extent until the introduction of the pill and legal abortion [9].

> Citation: It would be one of the greatest triumphs of humanity … if the act responsible for procreation could be raised to the level of a voluntary and intentional behaviour in order to separate it from the imperative to satisfy a natural urge. Sigmund Freud, 1898 [10]

Based on real-life past experiences, it is easy to understand Freud's vision of a human triumph as the ability to separate fertility and sexuality. But that dream only became reality a few decades ago.

The discovery of the fertile days by the Austrian Hermann Knaus and the Japanese Kyūsaku Ogino in the 1920s provided the first scientific basis to develop effective contraception [11]. The turning point came with the introduction of the pill and intrauterine devices (IUDs) in the early 1960s. For the first time in human history, women could actually separate their sexuality from their fertility, making it possible for children to be planned and wanted, and for sexuality to express love, happiness, and intimacy as the Swedish activist Elise Ottesen-Jensen worded the human goal [12]. It was a revolution that inevitably led to huge social changes, including the western sexual revolution of 1968.

1.2 The Beginning

A number of dedicated personalities contributed to the development of effective contraception. First the medical and scientific facts had to be developed on which effective methods could later be based on. The Austrian doctor Ludwig Haberlandt has been the first to show that hormonal contraception is possible. In 1921 he demonstrated a temporary hormonal contraception by transplanting ovaries from a pregnant rabbit to a non-pregnant animal [13]. In 1937 Russell Earl Marker discovered the first practical synthesis of progesterone from chemical constituents found in Mexican yams. Carl Djerassi refined the method of synthetic progesterone manufacturing and developed better substances.

In 1951 the biochemist Gregory Pincus received a small grant from the Planned Parenthood Federation of America to begin research into hormonal contraception. Based on his confirmation that progestins induced anovulation, women's right activist Margaret Sanger facilitated a much larger grant in 1952 from her rich friend Katherine McCormick. In total Katherine McCormick granted two million dollars towards the development of the oral contraceptive pill, an enormous amount of money at that time.

In 1953 and 1954 trials were performed with different progestins on infertile patients as contraception was illegal at the time. The physician in charge of the trials was John Rock, a catholic gynecologist who performed the trials at his clinic. Eventually Puerto Rico was therefore chosen for the first clinical trials into the contraceptive effects. Results were mind-blowing. The combination of a progestin and an estrogen gave close to 100% protection from pregnancy. Studies were expanded to Mexico and included thousands of women. One of the main effects of the pill was a reduction in menstrual flow and menstrual pain. In 1957 "the pill" was registered in the USA for these indications. The pill Enovid 10 mg® manufactured by Searle contained 0.15 mg of the synthetic estrogen mestranol and 9.85 mg of a progestin very closely related to the first patented progestin developed by Carl Djerassi. The contraceptive effect was a "side effect." In less than 2 years, close to half a million women were taken the pill, presumably quite often because of the desired "side

effect." In 1957 the pill was approved for contraception in the USA and thereby the first contraceptive pill had been approved.

Around the same time a similar development took place concerning intrauterine contraception. The German gynecologist Ernst Gräfenberg developed the first intrauterine device (IUD) in 1928, which was known as the Gräfenberg ring [14]. But the main challenge in the following decades was to find a material and form that would be highly effective, stay inside the uterus, and not cause too many side effects, especially pain and bleeding. The materials available for early IUDs – silk, silver, gold, or steel – had too many disadvantages for a broader use.

IUD development intensified with the discovery of moldable plastic in the 1960s because it allowed flexible frames. A variety of these new IUDs made it to the market in the 1960s [15, 16], which led the Population Council to organize the first conference on IUDs in 1962 [17].

However, the only mode of action for these inert plastic IUDs was to prevent implantation in the uterine cavity by means of a reaction to a foreign body. This changed with the discovery that a thin copper thread wrapped around the plastic frame increased efficacy by inhibiting sperm from fertilizing an ovum [18]. Since then, all IUDs have consisted of a plastic frame loaded with different active substances, hence the name of the IUD 'Multiload' [19]. Based on this concept, new IUDs were developed with a hormone reservoir that contains a gestagen [20]. These hormonal IUDs are more effective than copper IUDs, have fewer side effects, and are better tolerated.

1.3 Present: The Contraceptive Paradox

Sixty years after the discovery of the pill, an unexpected shift has occurred. Most people have forgotten the brutality of uncontrolled natural fertility. In developed countries, we no longer see families with eight to ten children. Most women have zero to two children and rarely more. Younger generations see this and wrongly assume it is "natural." Twenty percent of women in a recent survey said that zero to three children in a woman's lifetime would be a natural expectation without contraception (Fig. 1.4).

This illusion may be leading many women to avoid artificial/exogenous hormones for contraception and instead search for "natural contraception" without realizing the inherent contradiction of "natural" and "contraception." In fact, letting nature take its course produces an average of 12–15 pregnancies, while contraception subverts nature by imposing one's own will to limit fertility to the desired number of children. It is frequently forgotten today that we must decide whether to control our fertility or let our fertility control our lives.

This distorted perception of natural fertility explains the "pill scare" that occurred in several countries and is documented from the UK and France between 1995 and 2015 [21–24]. Exaggerated and unfounded fears about health risks led to a reduction in effective hormonal contraceptive use, which was not counterbalanced by an increase in effective nonhormonal contraceptive methods [25].

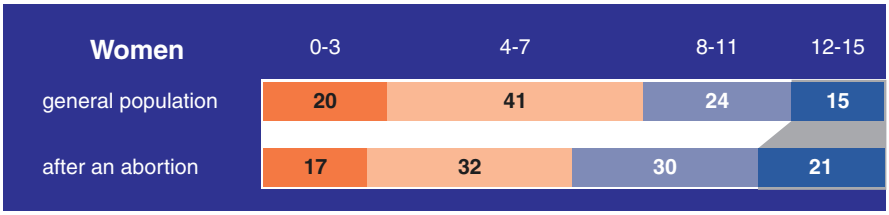

Fig. 1.4 Perception of natural fertility: "How many pregnancies do you think a woman would have in her lifetime if she didn't use effective contraception?". Austrian national contraceptive survey 2019, women n = 881, www.verhuetungsreport.at Survey among abortion patients, Gynmed Clinic Vienna, 2017–2018, n = 300

The "pill scares" led to a reduction in effective contraception, an increase in non-use of contraception, and a subsequent increase in unwanted pregnancies and abortion. This explains the "Contraceptive Paradox" of today: despite an unprecedented number of highly effective contraceptive methods, unplanned pregnancy and abortion rates have stopped decreasing and now remain stable in most Western European countries—but actually increased during media campaigns against the pill.

1.4 The Future

As stated in the Cairo Declaration 25 years ago [26], safe, acceptable, and effective methods for contraception and abortion are fundamental to sexual and reproductive health and rights (SRHR). The leading cause of maternal mortality continues to be lack of access to SRHR [27]. Unrestricted access to effective contraception is also a prerequisite for gender equality and the empowerment of women, especially as long as most methods are to be used by women.

New contraceptive methods are also needed, including improved emergency contraception, new mechanisms of action, and modes of delivery. Additional health benefits of contraceptive methods such as protection against various cancers and a wide range of other benefits should be better recognized.

Until recently, contraceptive development with a few exceptions has focused on the progestogen component of the pill or the dose of ethinylestradiol (EE). New options include exploring other estrogens like E2 and even E4. New delivery systems may not only reduce the risk for complications and side effects but may also offer long-acting reversible and self-controlled methods for women and men, as well as new possibilities for dual protection from unwanted pregnancies and STDs.

Based on mechanisms of action, progesterone receptor modulators (PRMs) might offer notable advantages for many women. PRMs can be used for emergency contraception as well as for regular contraception by various modes of delivery including intrauterine [28]. PRMs have been shown to be effective when used orally as daily pills, once weekly, or monthly and are a well-established method for medical first-trimester abortion as well as throughout pregnancy [29].

The use of PRMs for contraception and their positive health benefits, such as possible protection against breast cancer and prevention of uterine leiomyomas and endometriosis, deserves to be further explored [30]. Progesterone receptor modulators have also been studied for "late emergency contraception" and for menstrual induction [31]. Very early medical abortion (VEMA)—before an intrauterine pregnancy can be visualized by ultrasound—has been shown to be acceptable, safe, and effective [32]. Thus, PRMs provide a model for a woman-centered contraceptive continuum with added health benefits.

1.5 What About Men?

A high number of effective reversible contraceptive methods are available for women, but choices are very limited for men: condoms are only medium-effective (typical Pearl Index 15), and vasectomy is irreversible and thus not an alternative for many men.

As a result, most men depend on their partner's contraceptive use or non-use, which means a lack of control for men. But most men would be willing to use an effective, safe, and reversible method if available, as several studies have shown (with some variation between countries/cultures) [22, 33]. Unfortunately, the biological hurdle is high. It is significantly more difficult to suppress the production of 100 million sperm every day than one ovulation a month. Further, sperm remain viable for up to 3 months in a man's testes, while a woman's ovum can only be fertilized 12–24 h after ovulation. It took humanity thousands of years until 1960 to achieve effective fertility control in women. However, intensive research is underway to develop an effective and reversible method for men as well (International Consortium dedicated to Male Contraception, www.ic-mc.info), so it may just be a matter of time until men have an equal choice of effective contraceptive methods, enabling them to control their own fertility just as women can already do today.

Could an effective and reversible method for men lead to a revolution similar to the introduction of the pill for women? If men can control their fertility, women will find themselves in a new situation: can they trust their partner, or will they prefer to keep fertility control in their own hands? After all, it will always be the woman who gets pregnant. A study has indicated that the majority of women would continue using their own contraception, even if their partner uses an effective method [25].

Nevertheless, improved contraceptive choices for all, including more use of highly effective methods, will bring us a step closer to the vision of Elise Ottesen-Jensen:

> I dream of the day when all children are wanted, when men and women are equal and when sexuality is considered to be the expression of love, happiness and closeness. Elise Ottesen-Jensen, Sweden, 1896–1973.

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