Hormone Releasing Intrauterine Devices [1]

By: Higginbotham, Victoria Keywords: Intrauterine Contraceptives [2]

Hormone releasing intrauterine devices or hormonal IUDs are contraceptive devices placed in a woman's uterus [3] to prevent pregnancy [4] by continuously releasing a low dose of certain hormones [5]. Jouri Valter Tapani Luukkainen, a medical researcher at the University of Helsinki, introduced the first hormonal IUD in 1976. Luukkainen's IUD was a plastic device shaped like a capital T. The horizontal shafts of the IUD held a reservoir of the hormone [6] Levonorgestrel that the IUD slowly released at a constant rate over the IUD's lifetime, allowing the hormonal IUD to remain effective for five to seven years. Women can use hormonal IUDs for long term contraception [7] that requires no maintenance on the part of the user. The hormonal IUD provides women an option for reliable long-term birth control [8] that does not require maintenance to remain effective.

IUDs prevent pregnancy [4] by preventing conception [9]. Conception occurs after a woman ovulates, or releases an egg [10], which normally happens once every twenty-eight days. Once the ovary [11] releases an egg [10], the egg [10] travels through the woman's fallopian tubes [12] towards the uterus [3]. After ovulation [13], a woman's body begins releasing the hormone [6] progesterone [14] to prepare the lining of her uterus [3] for a fertilized egg [15]. If a woman has sex during the period after ovulation [13], sperm [16] may fertilize her egg [10]. If a fertilized egg [15] reaches the uterus [3], the egg [10] can implant on the wall of the uterus [3] and begin developing into an embryo. If a woman does not become pregnant at that point, her body slows the secretion of progesterone [14]. The lowered levels of progesterone [14] cause the lining of the uterus [3] to shed in a process called menstruation [17].

Hormonal IUDs release a synthetic form of the hormone [6] progesterone [14]. During pregnancy [4], progesterone [14] is released by both the woman's body and the placenta [18], which halts the menstrual cycle and ovulation [13] while the fetus [19] develops. IUDs release of the hormone [6] progesterone [14] slowly over a long period of time. The slow release of progesterone [14] allows the IUD to remain effective for several years.

The hormonal IUD has several mechanisms of action that contribute to preventing pregnancy [4]. All IUDs cause the uterus [3] to become inflamed because the woman's immune system responds to the IUD as a foreign body. That response makes the uterus [3] inhospitable to both sperm [16] and potential embryos because the woman's immune system responds to inflammation by actively targeting foreign cells. The inflammatory response prevents pregnancy [4] on two fronts, by preventing sperm [16] from reaching and fertilizing an egg [10] and by preventing any fertilized eggs from implanting in the uterus [3] and developing into a pregnancy [4].

Along with the inflammatory response, there are specific mechanisms of contraceptive action unique to the hormonal IUD. Those effects are attributed to the constant release of a low dose of a synthetic form of the hormone [6] progesterone [14]. To fertilize an egg [10] and form an embryo, sperm [16] must travel through a layer of mucus that covers the woman's cervix [20], the opening at the base of the uterus [3]. In women who use a hormonal IUD, the hormone [6] release causes the cervical mucus to thicken, which makes it difficult for sperm [16] to fertilize an egg [10]. Hormonal IUDs also prevent ovulation [13] in some women because high levels of the hormone [6] progesterone [14] suppress ovulation [13]. If no egg [10] is released from an ovary [11], there is no opportunity for an egg [10] to be fertilized by sperm [16] and result in a pregnancy [4]. Because hormonal IUDs mainly work by releasing a hormone [6] that controls fertility, the device does not need to fit perfectly within the uterus [3] to be effective. That quality makes hormonal IUDs a viable [21] option for most women, even those who have abnormally shaped uteri.

The hormonal IUD developed in the late 1970s was an improvement on earlier IUD technology that had existed since the early part of the twentieth century. Before modern IUDs that release hormones [5], or copper ions in the case of copper IUDs, IUDS were inert devices that prevented pregnancies by provoking an inflammatory response in the uterus [3]. That inflammatory response made the uterus [3] a hostile environment for sperm [16] or potential embryos and therefore prevented pregnancy [4]. In 1909, medical doctor Richard Richter developed the first intrauterine device in Germany. That early IUD was a woven circle of course silkworm [22] gut covered in a layer of celluloid plastic. Richter's IUD was not widely used at the time of its development because of laws in Germany that prohibited birth control [8].

In 1929, Ernst Gräfenberg, also a physician in Germany, developed an IUD named the Gräfenberg ring, which was a ring made of coiled silver wire. Gräfenberg researched the efficacy of his IUD and reported that 1.6 percent of women using the IUD became pregnant. Although Gräfenberg's IUD was effective, it soon became associated with cases of pelvic inflammatory disease [23], a type of pelvic infection. Gräfenberg's peers denounced Gräfenberg and the Gräfenberg ring, and the ring's popularity in Germany declined. The early types of IUDs that were made of metal often caused problems when they were inserted, including pain or lacerations that could later become infected.

In 1958, the introduction of the plastic IUD mitigated some of the problems women had faced with the earlier metal IUDs. In

1960, Lazar Margulies developed the first plastic IUD at Mount Sinai Hospital in New York City, New York. Margulies developed a new type of IUD using thermoplastics. Thermoplastics can be heated to give them a memory of a certain shape. After they are given that memory, thermoplastics can be bent or twisted and still return to their original shape. Margulies used those thermoplastics to create a spiral shaped IUD that could be unwound and inserted into the uterus [3] via a small hollow tube. Once the IUD was expelled from the tube into the uterus [3], the IUD regained its original shape. The use of thermoplastics enabled physicians to insert IUDs with novel shapes comfortably. IUDs in various shapes began to enter the market, including rings and trapezoidal loops. Most of those IUD shapes fell out of favor for reasons including increased side effects. As of 2018, most IUDs are T shaped because the T shape aligns most closely with the shape of the uterine cavity, which reduces side effects and increases effectiveness.

Howard Tatum conceived of the T-shaped IUD, which women still use as of 2018. Tatum noted that the side effect menorrhagia, or abnormally heavy menstrual bleeding, associated with IUDs was caused by the shape of IUDs being incompatible with the shape of a woman's uterine cavity. Tatum claimed that an IUD shaped like a capital T would fit more naturally within the uterus [3], reduce side effects, and be less likely to fall out. Tatum's T shaped IUD reduced bleeding and pain, as well as incidences of expulsion. However, in clinical research, Tatum's IUD did not prevent pregnancy [4] at a high enough rate to be an acceptable birth control [8] device. To remedy that fault, Tatum worked with a colleague, Jaime Zipper, who had found that copper had antifertility effects in rabbits. Together, they added copper wire to the shaft of the T shaped IUD. In 1974, the US Food and Drug Administration [24] or FDA approved the first copper IUD and women in the US began using copper IUDs. The copper IUD is still used as an effective form of birth control [8] as of 2018.

The copper IUD did not completely resolve the issue of menorrhagia. Two years after the introduction of copper IUDs to the market in 1976 Luukkainen released his study on a new hormone [6] releasing IUD. Like Tatum's IUD, Luukkainen's IUD was T shaped, but instead of using copper, Luukkainen replaced the horizontal arms of the T with reservoirs of the hormone [6] d-norgestrel, an artificial progesterone [14]. Luukkainen's study showed that the hormonal IUD was an effective form ofbirth control [8] that also reduced cramping, menorrhagia, and bleeding from normalmenstruation [17] in the women studied. The hormonal IUD has remained mostly the same since Luukkainen developed it. As of 2018, there are several types of hormonal IUD available and they vary in the dose of hormone [6] released and how long they remain effective.

Hormonal IUDs are considered long-term reversible birth control [8] because they can remain effective for three to five years. IUDs are easily removed, and once removed, fertility returns within months. A medical study conducted in 2012 showed that IUDs and other forms of long-lasting birth control [8] such as subdermal implants have low failure rates because they do not require action on the part of the user, unlike the contraceptive pill, which is most effective if taken every day at the same time.

Although IUDs are effective forms of birth control [8], their popularity sharply declined during the 1980s and they have only recently begun to regain popularity in the US as of 2018. In the 1970s, nearly 10 percent of women using birth control [8] chose an IUD, but by 2002, that number had dropped to 1 percent. According to David Hubacher, an epidemiologist who writes for the Guttmacher Institute, the IUD's decline in popularity was due to several factors, including misinformation about the risks of IUDs and the Dalkon Shield.

The Dalkon Shield was an IUD introduced in the US in 1971. The design of the Dalkon Shield exacerbated the usual side effects of IUDs and contributed to effects like infertility [25] and pelvic inflammatory disease [23]. According to the Centers for Disease Control and Prevention in the US, or the CDC, IUDs have been regaining their popularity in the US since the early 2000s due to their high efficacy of preventing pregnancy [4]. According to data the CDC collected in 2013, IUD use has increased by 83 percent in the US since 2002. In 2013, 6.4 percent of women who used contraception [7] in the US used an IUD. IUDs are a popular form of contraception [7] globally, as well. In 2014, 14.3 percent of women who were of reproductive age chose an IUD for contraception [7], though in some countries more than 40 percent of women chose IUDs.

In 2018, women in the US who want to use a hormonal IUD have several options. There are four types of hormonal IUDs approved for use in the US. All four release the same hormone [6], Levonorgestrel, a synthetic version of progesterone [14], but they differ by size, amount of hormone [6] released, and how long they remain effective. The four hormonal IUDs approved for use in the US are marketed under the brand names Mirena, Skyla, Liletta, and Kyleena. Mirena is effective for five years and releases 20 micrograms of Levonorgestrel daily. Mirena is also approved for the treatment of menorrhagia or heavy menstrual bleeding because its relatively high dose of Levonorgestrel may make menstrual bleeding in some women lighter or prevent it completely. According to a study published in *The New England Journal of Medicine* in 2013, hormonal IUDs are more effective than other methods of treatment for controlling heavy menstrual bleeding. Skyla is effective for three years and releases 14 micrograms of Levonorgestrel daily. Liletta is effective for three years and releases 18.6 micrograms of Levonorgestrel daily. Kyleena is approved for five years and releases 17.5 micrograms of Levonorgestrel daily.

All the hormonal IUDs have similar side effects and health risks associated with their use. Women face an increased risk of life-threating infection immediately after a physician places an IUD in them because the placement procedure may introduce bacteria into the woman's body. IUDs also increase the risk of pelvic inflammatory disease [23]. IUDs may perforate or become embedded in a woman's uterus [3] and require surgery to remove. Some women who use hormonal IUDs develop a cyst on their ovary [11]. According to the manufacturers of Mirena, Skyla, and Kyleena, those cysts usually go away on their own and do not require surgery. Women who become pregnant while using an IUD are at risk of having an ectopic pregnancy [26], or a

pregnancy [4] that occurs outside the uterus [3]. Ectopic pregnancy [4] poses potential risks to both the pregnant woman and the fetus [19].

Hormonal IUDs are an effective form of long-term reversible birth control [8] that allows women to have greater control over their fertility. Hormonal IUDs are a popular form of contraception [7] that is over 99 percent effective at preventing pregnancy [4]. IUDs can be used long term, a factor that, when combined with the high effectiveness, makes IUDs a viable [21] alternative to sterilization [27] procedures. Women can also use hormonal IUDs to treat heavy menstrual bleeding and alleviate the symptoms of menorrhagia.

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