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Review Article

Intrauterine Drug Delivery System

D. Reshma Banu*, Kuruva Akhila, E. Anusha, G. Padma, S. Fasiya

Dr. K. V. Subha Reddy Institute of Pharmacy Kurnool.

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ABSTRACT

Writing this overview of intrauterine drug delivery systems was done with the intention of gathering the most recent research, paying particular attention to the many intrauterine techniques that have emerged as the most effective methods for site-specific oral controlled release drug delivery. To end the pregnancy, the medication releases in the uterus. Details about the benefits and drawbacks of IUDDS are provided. IUDs, or intrauterine devices, are used in intrauterine medication delivery systems. They come in a variety of forms and, depending on the type, can be effective for three to 10 years. An effective, reversible form of long-term contraception is the IUD. A unique device that fits into the uterus is called an intra-uterine device. A tiny device called an intrauterine device (IUD) is put within the uterus through the cervix in order to prevent conception. From the IUD, a tiny string extends into the vagina's upper region. During sexual activity, the IUD is undetectable. IUDs may endure one to ten years. In order to stop fertilization, they interfere with the motions of sperm and eggs. They also hinder implantation and alter the uterine lining. The effectiveness of IUDs as birth control is 99.2-99.9%. They offer no defense against HIV/AIDS or other sexually transmitted illnesses. An IUD can be inserted in as little as five to ten minutes. IUD insertion requires a clinician. Usually, you do it during your menstrual cycle. The medical professional will examine your pelvis and determine the exact location of your uterus. After seeing your cervix with a speculum inserted into your vagina, they will clean it with an antiseptic solution. By preventing sperm from accessing an egg that your ovaries have released, an IUD prevents conception.

INTRODUCTION

An intrauterine device, commonly known as an IUD, is a small contraceptive device inserted into the uterus through the cervix to prevent pregnancy.

A thin string attached to the IUD extends into the upper vaginal region, facilitating easy removal using forceps. The contraceptive effectiveness of IUDs is estimated to be between 99.2% and

***Corresponding Author:** D. Reshma Banu

Address: Department of Pharmaceutics, Gourishankar Institute of Pharmaceutical Education and Research, limb, Satara, Maharashtra, India. Pin: 415015.

Email ✉: parameshwarudukuruva9@gmail.com

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99.9%. However, it is important to note that IUDs do not provide protection against sexually transmitted diseases, including HIV/AIDS. While the precise mechanism of action of IUDs remains uncertain, it is believed to induce general biochemical and histological changes in the endometrium. Ionized copper in IUDs is thought to contribute to spermolytic and gametotoxic effects, reducing the viability of gametes and thus lowering the chances of fertilization (not implantation). Copper ions impede sperm motility, capacitation, and survival. Additionally, hormone-releasing IUDs increase the viscosity of cervical

mucus, preventing sperm entry into the cervix. The combination of elevated progesterone and reduced estrogen levels created by hormone-releasing IUDs establishes an environment unfavorable for implantation. It is advisable to replace the IUD every three years for optimal contraceptive efficacy.

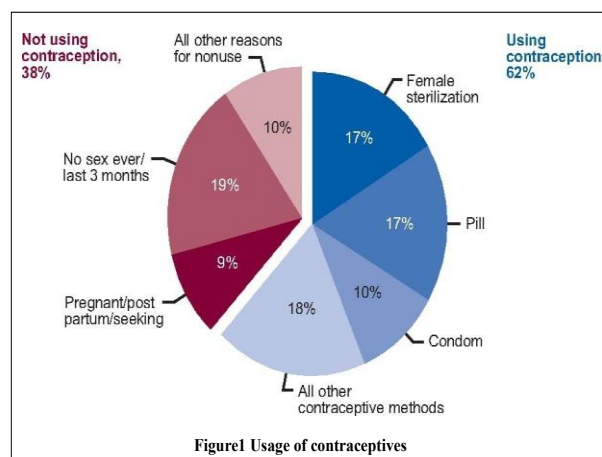
Need Of Contraceptives:

1975-United state

□ From approximately 27 million couples of child baring age 76.3% expressed desire to prevent conception either temporarily or Permanently.

Table 1: Need Of Contraceptives

Method Of Contraception	% Of Those Served
Oral contraceptive pills	26.3
Condom or diaphragm	10.0
Intrauterine devices	6.4
Foam	2.6
Rhythm	2.2
Others	28.8



Three most popular methods of contraception:

- Oral contraceptive pills
- Condoms or diaphragms

- Intrauterine devices (IUDs)- Popular contraceptive methods, especially for long-term reversible contraception, as it can be easily fitted and removed.

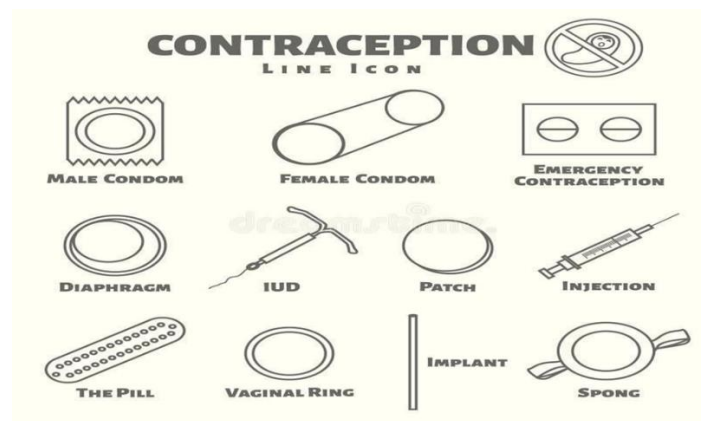
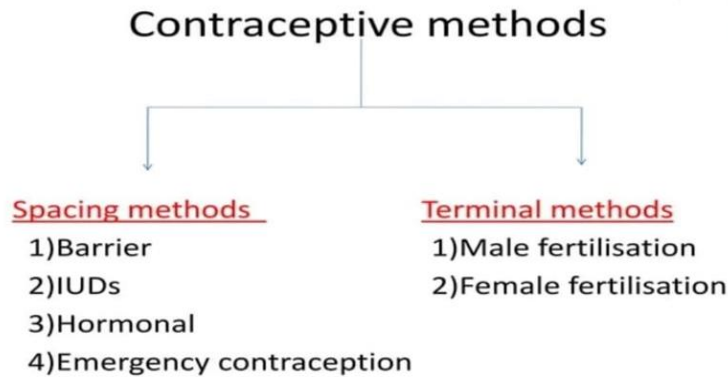


Figure 2 - Types of contraceptives

Effectiveness	Contraceptive Method	How to make your method more effective
Most effective Generally 1 or fewer pregnancies per 100 women in one year	Implants, Female sterilisation, Vasectomy, IUD	One-time procedures; nothing to do or remember
	Injectables	Need repeat injections every 1, 2 or 3 months
Less effective	Pills, Patch, Vaginal Ring	Must take a pill or wear a patch or ring every day
	Lactational amenorrhea method (LAM)	Must follow LAM instructions
	Male condoms	Must use every time you have sex; requires partner's cooperation
Least effective About 30 pregnancies per 100 women in one year	Diaphragm	Must use every time you have sex
	Cervical cap, Sponges, Female condoms	Must use every time you have sex
	Withdrawal, Fertility awareness-based methods (selected), Spermicides	Require partner's cooperation; must abstain or use condoms on fertile day
		Must use every time you have sex

Table 2 -Statistical Data

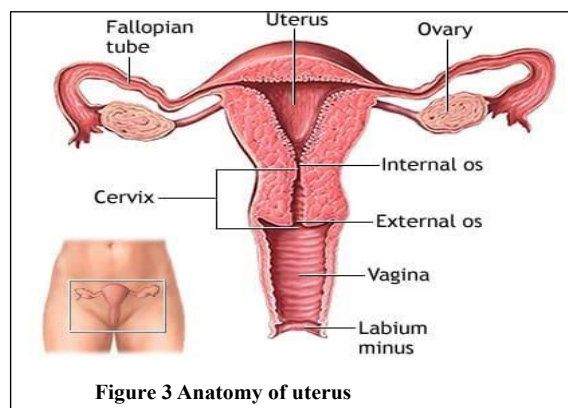
Anatomy Of Uterus:

A pear shaped, thick-walled muscular organ suspended in the anterior wall of pelvic cavity. Shape is triangular and flattened antero-posteriorly.

In normal state, dimensions are 3 inches in length and 2 inches in width. Consists of parts namely: Fundus, Body (Uterine Cavity, Isthmus)

Cervix (Cervical canal, Internal Os, External Os)
Have two openings:
Superior- fallopian tubes

Inferior: Vagina (mouth of Uterus)
Cavity of body
Uterine wall.



Walls of Uterus:

Endometrium is the innermost lining layer of the uterus made up of simple columnar epithelium, areolar connective tissue & endometrial glands. Subdivided into.

- ✓ Stratum Functionalis: Innermost layer, sloughed off during menstruation & grows a new during each cycle
- ✓ Stratum Basalis: It consists of permanent stromal tissue and deep ends of the uterine glands.
- ✓ Myometrium is a thick, muscular middle layer, made up of 3 smooth muscle layers (Middle thick circular & other two longitudinal).

Peritoneum is an external surface of uterus which joins uterus to pelvic cavity through ligaments.

Menstruation cycle:

Refers to the regular changes in the activity of the ovaries and the endometrium (uterus) that make reproduction possible.

Menstrual flow might occur every 21 to 35 days and last two to seven days.

Divided into 4 phases:

1. Menstrual Phase (5 days)

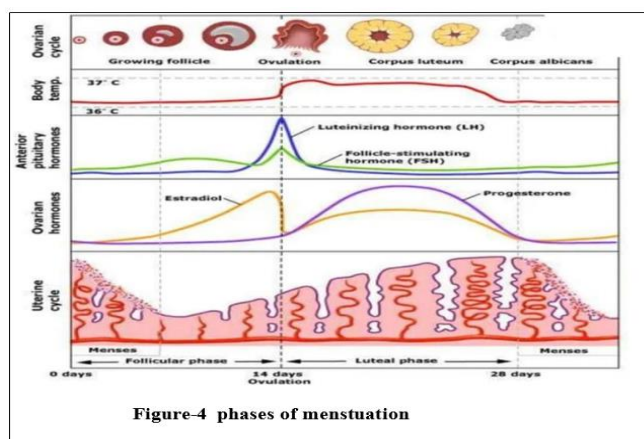
2. Pre-ovulatory phase /Follicular phase (6-13 days)
3. Ovulatory phase (on 14th day)
4. Post-ovulatory phase / Leutial phase (14-28 days)

1.Menstrual phase- (5 days)

- Decrease in levels of estrogen & progesterone
- Stimulates release of prostaglandins
- Produce arteriole constriction, decrease blood supply to s. functionalis
- Cells starts to die & s. functionalis sloughed off.
- Bleeding takes place for about 5 days.

2.Follicular phase- (up to 13th day)

- Estradiole is secreted from ovaries by secondary follicle
- Secondary follicle is converted in graffian follicle.
- Estrogen restores blood supply to endometrium & stimulates formation of s. functionalis from s. basalis.
- S. functionalis starts to grow and become 3-4 mm thick. Endometrial glands increase in length & tortuosity.



Ovulation-(on 14th day):

Release of oocyte outside of ovaries into fallopian tube.

Takes place at the day of 14 of M.C. under the influence of Leutinizing hormone (LH) & Gonadotropin releasing hormone (GnRH) Released oocyte remain viable for 2 days.

Leutial phase-(15-28 day)

In ovary graffian follicle collapse to form corpus luteum. It release progesterone & estrogen.

In uterus, these hormones promote growth, thickning & coiling of endometrium. Glycogen is secreted by glands.

Fertilization- changes remain constant

No fertilization- corpus luteum disappear, decrease in level of estrogen & progesterone.

Menstruation occurs.

Advantages Of Iudds:

- * Highly effective in preventing pregnancy.
- * Inexpensive
- * Does not interrupt sex.
- * Does not require partner's involvement.
- * Can be used for a long period of time.
- * Can be used as an emergency method of birth control.
- * An IUD provides long-term contraception for 3 to 5 years and is cost-effective.
- * It is convenient. You do not need to remember daily pills.
- * It does not interfere with sexual life.

- * Upon its insertion, the user has no botherance to remember about it.
- * The user has nothing to do with it, therefore user related errors are reduced.
- * It does not disturb the hormonal cycle.
- * It is a better option for women avoiding pill.
- * A hormone-releasing IUD (Mirena) is suitable for heavy menstrual bleeding.
- * Copper IUD may reduce the risk of endometrial cancer as does the levonorgestrel IUD

Disadvantages of IUDDS:

- * Does not protect against sexually transmitted infections (STIs).
- * If you get a sexually transmitted infection, the IUD could increase the likelihood of developing pelvic inflammatory disease (infection of the reproductive organs).
- * May increase the likelihood of ectopic pregnancy (pregnancy outside the uterus).
- * Can cause heavier and more painful periods.
- * Cramping and discomfort during and 24-48 hours after insertion.
- * There are risks during insertion and removal that your clinician should discuss with you before inserting an IUD.

Intrauterine Devices:

IUD's are medicated devices intended to release a small quantity of drug into uterus in a sustained manner over prolonged period of time.

3 most popular methods of contraception:

- Oral contraceptive pills
- Condoms or diaphragms
- Intrauterine devices

Table- 3 : Methods of contraception

Methods of contraception	Pregnancies	Births	Deaths				MBR[Mortality Benefit Ratio]
			P	M	Total		
None	60,000	50,000	12	0.0	12.0		—
Condom or diaphragm	13,000	10,833	2.5	0.0	2.5		0.664
Oral pills	100	83	0.0	3.0	3.0		0.060
IUDs	2190	1825	0.44	0.3	0.74		0.015

MBR-Deaths per 1000 births averted as related to pregnancy [p] or method [M] 1,00,000 fertile women data with each method .

History of IUD's

- First generation IUD's were developed in 1920.
- It was constructed from silkworm gut & flexible metal wire.

Eg. Grafenberg star & Ota ring

- Reduce popularity due to:
- Need for frequent removal due to pain & bleeding
- Difficulty in insertion
- Other serious complications

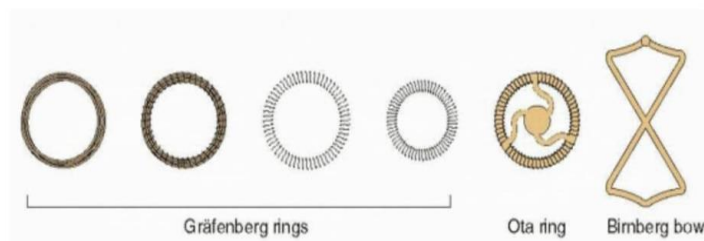


Figure-5 :Grafenberg rings,ota ring,bimberg bow

Controlled Delivery with IUD's

Reports says that use of IUD's has increased within US from 0.8% in 1995 to 7.2% from the period of 2006 to 2014.

Controlled release of intra-uterine systems are used for the delivery of contraceptive steroid hormones. Efficacy of these IUD's is proportional to their surface area that i.e. in direct contact with endometrium (uterus).

- The advantage of this route includes:
- Avoids first pass metabolism.
- Better bioavailability
- Lesser dose needed, compared to oral dose.

➤ Larger IUD's considered to be more effective but expulsion rate is high as these causing:

- Endometrial Compression
- Myocardial Distention
- Uterine cramps

Several Plastic based IUD's (vary shape & size) have been designed with inert biocompatible polymers such as:

- Polyethylene
- Polypropylene
- Ethylene-vinyl acetate co-polymers Silicon Elastomer, etc.

Types Of IUDs:

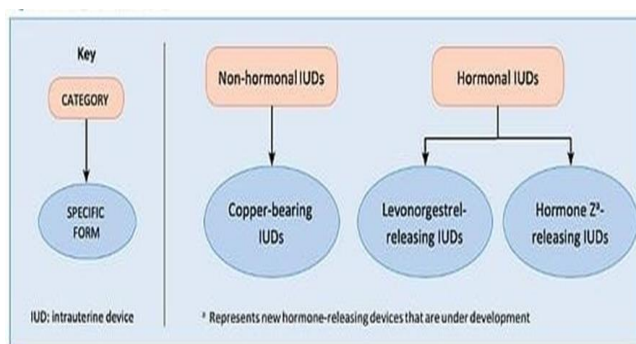


Figure 6 : Intrauterine device

Intrauterine devices (IUDs) are contraceptive devices inserted into the uterus. The main types include:

Copper IUDs:

These release copper ions, which are toxic to sperm and prevent fertilization. They can last up to 10-12 years (e.g., Paragard).

Hormonal IUDs:

These release progestin, which thickens cervical mucus and thin the uterine lining, preventing pregnancy. They typically last 3-7 years (e.g., Mirena, Skyla, Liletta).

A) Non-Hormonal IUDs/Copper-Medicated IUDs:

The intrauterine devices (IUDs) are constructed with a support made of either polypropylene or polyethylene plastic, designated as number 7 or letter T. This design incorporates a fixed quantity of copper wire wound around the device. The T-shaped IUD is widely utilized due to its resemblance to the uterine cavity, preventing displacement, rotation, and expulsion from the cavity. The device features two pliable arms that facilitate insertion by folding during the process and subsequently expanding into a T-shape within the uterus. When fully open, the device measures 36mm in height and 32mm in width. Additionally, the device includes a vertical stem encased with fine copper wire and two horizontal arms covered with copper. Copper medicated IUDs (intrauterine devices) are a form of long-acting reversible contraception. They work by releasing copper

ions, which create an environment that is toxic to sperm, preventing fertilization.

Key points about copper IUDs include:

- Effectiveness: They are over 99% effective at preventing pregnancy.
- Duration: They can remain effective for 5 to 10 years, depending on the specific device.
- Non-hormonal: Unlike hormonal IUDs, copper IUDs do not contain hormones, making them suitable for those who prefer or need to avoid hormonal contraception.
- Menstrual Changes: Some users may experience heavier periods and increased cramping, especially in the first few months after insertion.
- Insertion and Removal: A healthcare provider inserts and removes the IUD during a simple office procedure.

Mechanism Of Action

Non-medicated: Involves foreign body reaction and Medicated develops sterile inflammatory response exerting spermicidal action.

Sides effect of ParaGard (Second generation)

- Anemia
- Backaches
- Spotting between periods
- Vaginal discharge
- Pain during sex
- Copper toxicity
- IUD expulsion

First generation IUD = non medicated/inert IUD

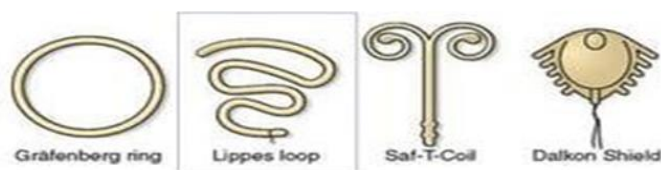


Figure no 7: First generation IUD'S

Antifertility Action: Copper

- Cytotoxic, Spermaticidal & spermato-depressive action.
- It is a competitive inhibitor of steroid-receptor interaction sites.
- Copper is a potent inhibitor of steroid-receptor binding site and acts through direct interference resulting in the increased contraceptive effect of the copper IUD.
- Copper is taken up by endometrial epithelium & stromata.
- Copper inhibits progesterational proliferation and estrogenic activity.
- It has little effect on sperm mobility.

Mechanism Of Antifertility Action Of Copper

- Copper is known to be cytotoxic in high concentration it enhances the spermaticidal and spermato depressive action of an IUD.
- The copper concentration in endometrial epithelium and superficial stromata inhibits the binding of steroids of their receptors.
- Cupric ion inhibits the binding of 17-B-estradiol to human endometrial cytosol.
- Cupric ions shows only little effect on sperm motility
- Copper wire was also blastocystocidal.

Copper-T IUD's

The copper-bearing intrauterine device (IUD) is a small, flexible plastic frame with copper sleeves or wire around it. The device is T shaped made up of polyethylene plastic. The copper wire is coiled around the stem of T. Different grades are available as per the surface area of wire used:

- Cu-T-200
- Cu-T-220C
- Cu-T-380A

Cu-T-200

- US approval -1976.
- Seven copper copper Copper on both arms.
- Retain physical integrity for 15-20 yrs.
- Long acting- beneficial to population in which medical care not readily available.
- The copper wire of surface area 200 mm² exhibits maximum contraceptive activity.

Cu-T-220C

- A new long-acting copper-T IUD. Has 5 solid copper sleeves on the vertical arm of the T and 2 sleeves on the horizontal arm, thereby providing an effective surface area of 220 sq. mm of copper.

- Estimated period of effectiveness of IUD is 20 years.

- Rate of pregnancy, expulsion, and removal for bleeding/pain are less as compared to Cu-T300. **cu-T-380A**

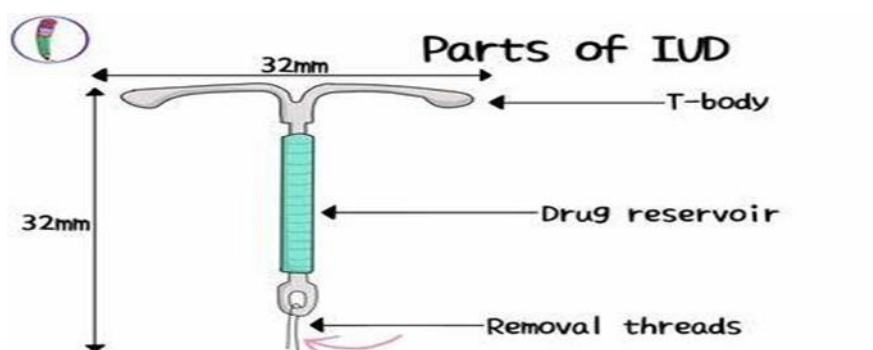
- US approval -1984.

- Two collars of Cu on transverse arm

- Each collar provides additional surface are of 30 sq. mm.

- It is made up of polyethylene frame that holds 380mm² of copper and barium sulphate which makes it radio opaque.

T-shaped polyethylene device wound with 30 mm² copper wire. Efficacy improved when copper wire is located on the transverse arm as in close contact with upper portion of uterine cavity.



Cu-7 IUD

- Mfg by G.D. Searle & Co.
- First device approved by USFDA for 3 yrs of use. 89 mg copper around vertical limb with surface area of 200 sq. mm
- Smaller volume (0.09 cm³) than Cu-T (0.16 cm³) and easily inserted in nulliparous women. Polypropylene plastic device shaped like number 7.
- Release 9.87µg/day for 40 months.
- Cervical dilation not needed.
- Removal is painless.

Release Kinetics: Cu-IUD's:

- It shows continuous release by ionization & chelation process. Cu-wire generally reduces with time due to corrosion & flaking of metal.
- Cu-7-284 deliver Copper at a rate of following expression.

Dosage (mg)=0.3 month :Release rate is 9.87 µg/day and shows linear relationship between cumulative copper release with the duration.

- Reduction in copper release due to formation of
- Corrosion layer- of protein
- Encrustation layer- of calcium (impermeable)

Hormonal IUDs-

The T-shaped contraceptive device is constructed with a polyethylene frame, measuring 32mm both vertically and horizontally. Incorporated within the device is a silicon reservoir containing either levonorgestrel or progesterone, dispersed along the vertical stem. Encasing this stem is a membrane made of

ethylene-vinyl acetate co-polymer, as depicted in. This contraceptive mechanism functions by continuously releasing progestogen directly into the uterus, providing effective prevention of pregnancy for a duration of up to 5 years.

These are two types

- Copper bearing IUDs
- Hormonal bearing IUDs

1. Copper bearing IUDs

- This device uses copper wire wound to the stem. This device is made of T shaped polyethylene plastic.
- There are various grades as per the surface area of Cu-wire such as Cu-T-30, Cu-T-200, Cu-T-380.

Mechanism Of Action:

At a high concentration copper is cytotoxic and enhances spermicidal and spermato depressive action of an IUD.

- Cupric ion (Cu⁺) is a competitive inhibitor of progesterone.
- Evoke sterile inflammatory response in the endometrium.

1. Multi-load Copper IUD's

- Combination of Cu-T & Dalkon Shield without central plastic membrane.

Blunt apex of device fits in to vault of uterine cavity without penetrating endometrial walls. Two teeth-studded side arms adapt to the contours of the uterine cavity.

During uterine contraction Fundus presses against upper edge of IUD, results in bending of arms.

Pregnancy rate-0.3% and Expulsion- 1% only

a. MLCu-250

- Introduced in 1974.
- It comes in short length.
- Provide 3 years of contraceptive protection.

b. MLCu-375

- It has a thicker copper wire, with a surface of 375 square mm.
- It comes in a standard and short length, to suit the size of womb.
- It provides 5 years of contraceptive protection.

Side effects of Copper bearing IUD

Expulsion:

About 2-10% of IUDs are expelled from the uterus. This usually happens in the first few months of use. It is more likely when the IUD is inserted right after childbirth or in a nulliparous woman.

Menstrual Problems:

About 12% of women have Copper T 380-A IUD removed because of increased menstrual bleeding or cramping

Perforation:

- In 1 out of 1000 women, the IUD will get stuck in or puncture the uterus.
- Although its rare it almost always occurs during insertion.

Hormone Releasing IUD's

- Hormone based IUDs contain small amounts of levonorgestrel which is a progestin much like the hormone progesterone ovaries produce.
- Levonorgestrel release causes thinning of uterus lining and also thickens the cervical mucus which makes it difficult for sperm to fertilize an egg.
- Moreover, it prevent ovulation in some women as high levels of progesterone suppress ovulation.
- Available hormone based IUDs such as Mirena (5 yrs), Kyleena (5 yrs) & Jaydess (3 yrs). The amount of hormone released daily varies on the type.

These are two types

- Progesterone releasing IUD
- Levonorgestrel IUD

1. Progesterone releasing IUD:

- This device has a solid poly Ethylene-vinyl acetate side arms and a hollow core .The microcrystalline progesterone in the core in the silicone oil with barium sulphate.
- It is 0.25 mm thick, release via diffusion through rate limiting membrane.
- It is loaded with 38 mg of progesterone releasing rate 65mcg/day.
- It does not inhibit ovulation but interfere with implantation in endometrium, thickening of cervical mucus.

ADVANTAGE

Increased effectiveness, lower menstrual blood flow, decreased dysmenorrhea.

DISADVANTAGE:

Need to be replaced yearly, intermenstrual bleeding, ectopic bleeding.

Anti-fertility Action Progesterone

- Optimum amount of estrogen & progesterone required for proper development.
- Decidual reaction involves enlargement of stromal cells & grow as polyhedral cells rich in glycogen & lipids. These changes takes place in presence of implanted blastocysts on secretory endometrium.
- Endometrial hyper-maturation is unfavorable for implantation and is associated with decidual formation which is induced by Progesterone.
- Once decidual reaction occurred, implantation of blastocyst cannot takes place again.

MOA of Progesterone releasing IUDs:

- They diminish sperm transport through the cervix to the oviduct by increasing the thickness of the cervical mucus
- Steroid releasing devices induces progestational changes that results in



endometrial gland atrophy and inhibit further development of the ova.

Contraceptive efficacy was related with daily dose of progesterone release from device.

Clinical effectiveness

Table-4: Clinical effectiveness of progesterone IUD

Dose [mcg/day]	% Pregnancy
10	5.2
25	2.7
65	1.1
120	0.6

B. Levonorgestrel IUD - Mirena:

- The levonorgestrel-releasing intrauterine device LNg IUD is a new contraceptive method that combines the advantages of both hormonal and intrauterine contraception.
- It is an intrauterine system that has sleeves of levonorgestrel 52mg around its stem
- It is composed of a polyethylene stem covered by matrix Silastin:LNg (2:1) and side arms
- Releases 20 mcg/day lasting for 5 years. Initial release is fast then after 60%
- drug release rate reduces to 16 mcg/day □ Suppresses endometrium and ovulation
- Prevents endometrial proliferation.
- Thickens cervical mucus.

- It also keeps endometrium from growing very thick, making lining poor place for a fertilized egg to implant the grow.
- It may relieve irregular menstrual bleeding and cramping
- Comparative clinical trials with the LNg IUD cover more than 10,000 women-years of follow-up during use over five to seven years. The Pearl pregnancy rate in studies has been 0.0-0.2 per 100 women-years. The overall ectopic Pearl pregnancy rate is 0.02 per 100 woman-years. The LNg IUD is marketed in Denmark, Finland, Norway, Sweden and in the United Kingdom.

DISADVANTAGE

Mechanism Of Action Of Levonorgestrel IUD:

- Prevents fertilization by damaging or killing sperm and making mucus thick and sticky, so sperm can't get through mucus.

- It may cause non cancerous growth called ovarian cyst, which gradually go away on their own.

It can cause hormonal side effects such as breast tenderness, mood swings, headaches.

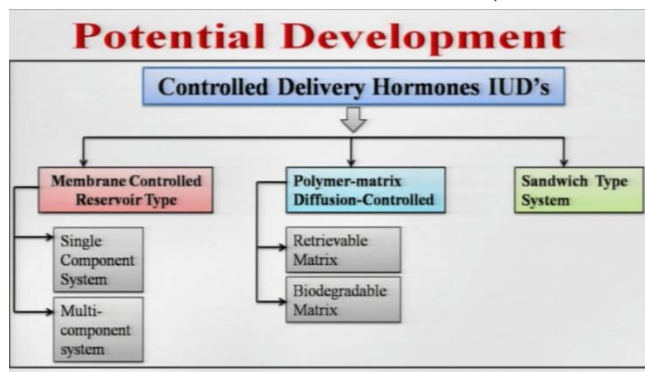


Figure no:9: Potential development

Contraindications of IUDs:

An IUD might not be a good option for you if you have:

- a uterus that is not the usual Shape
- a current pelvic infection.

The hormonal IUD might not be a good option for you if you have :

- been treated for breast cancer
- severe liver disease.

The copper IUD might not be a good option for you if you have:

- heavy periods
- low iron levels endometriosis.

Applications:

Intrauterine drug delivery system has the following applications:

➤ **Emergency Contraception:**

The copper IUD (marketed as Paragard) can be inserted within 5 days after unprotected intercourse.

➤ **Treatment for Heavy Menstrual Bleeding:**

The progesterone intrauterine device (IUD), commonly known as Mirena, is employed to alleviate excessive menstrual bleeding. Comparative studies indicate its superior efficacy when compared to oral progesterone medications. The clinician should recommend the insertion of the IUD only after addressing and resolving other underlying causes of significant bleeding. This method stands as a viable alternative to hysterectomy in the management of such conditions.

➤ **Menopausal Hormone Therapy:**

Mirena offers an alternative approach to administering progesterone as part of combined menopausal hormone replacement therapy. It is particularly beneficial for women who may face challenges with oral progesterone pills. Similar reductions in hot flashes and night sweats are observed in women using Mirena, akin to those utilizing conventional hormone replacement

methods involving estrogen and progesterone in pill and patch forms.

➤ **Treatment for Pelvic Pain:**

Some studies reveal that Mirena IUD reduces pelvic pain associated to endometriosis.

IV. Development Of Intrauterine Devices (IUDS):

The history of IUDs is uncertain, with no clear evidence supporting the insertion of foreign objects into the human uterus for contraception prior to the 20th century. Nonetheless, historical reports suggest that centuries ago, Middle East traders employed a method to prevent pregnancy in camels by inserting pebbles into their uteri before embarking on long treks across the desert. In 1909, Dr. Richard Richter proposed the idea of inserting a ring made of silkworm gut into the uterus. The ring had two ends outside of the cervix for easy checking and removal. In the mid 1920s, Karl Prust and Ernest Graefenberg presented similar theories. Prust advocated for silkworm insertion with a stiff cervical extension of a tightly wound thread and a glass button covering the cervix. Graefenberg proposed a similar model but removed the extensions of the silkworm ring to prevent infections. Detection of the ring's position in the uterus involved the use of X-rays, with a silver wire attached to the ring. This particular device demonstrated a pregnancy rate of approximately 3%. Dr. Graefenberg later modified the ring by wrapping pure silver around it, resulting in gingival argyrosis, where the user's gums turned bluish-black due to silver absorption. Subsequently, he switched to a wire made of German silver, an alloy composed of various metals like copper, which reduced the pregnancy rate to around 1.6%. While this ring gained widespread acceptance in England and other British Empire countries, its sales did not fare well in continental Europe or the United States. During World War II, research and development in the field of contraception were limited. Both Germany



and Japan ceased the use of contraception during this period. A significant breakthrough occurred in 1949 when a method involving silkworm gut was demonstrated. The innovator wrapped the material around her finger, placed it inside a gelatin capsule, and then inserted the capsule into the uterus. As the gelatin liquefied, the thread spread out, resulting in a remarkable drop in the pregnancy rate to a mere 1.1%. Doctors globally celebrated success with various versions of intrauterine devices (IUDs) for several years. Initially, concerns arose regarding the "tails" on IUDs causing pelvic infections, leading to modifications in device designs. In 1960, Dr. Lazar Margulies introduced a breakthrough device made of polyethylene, addressing concerns by allowing the device's end to protrude through the cervix. The first patient to receive this new device was Dr. Margulies' wife. Dr. Alan Guttmacher, Dr. Aquiles Sobrero, and Dr. Christopher Tietze reviewed the inserter tube, coil, and a copy of the hystero-gram. Dr. Jack Lippes played a pivotal role in 1962 by developing and inserting the first plastic IUD, known as the Lippes Loop. Available in various sizes based on a woman's pregnancy history, this inexpensive device featured a string for easy detection and removal. Its simplicity and cost-effectiveness led to widespread adoption worldwide. Subsequently, various IUDs were introduced, with differing levels of success and complications. A significant development occurred in 1969 when some women reported increased cramps and bleeding associated with IUD usage. In response, Dr. Howard Tatum attempted to address these issues by reducing the size of the IUD, resulting in the creation of the plastic T. Although tolerable, this version had a higher pregnancy rate of 18%. Concurrently, Dr. Jaime Zipper made a groundbreaking discovery involving a copper wire in one horn of a rabbit's uterus, establishing the contraceptive effect of intrauterine copper and broadening the

effectiveness of IUDs. In 1970, Dr. Antonio Scommegna introduced a novel T-shaped contraceptive device containing progesterone encased in a semi-permeable capsule in the lower section. The FDA granted approval for its safe usage for a year, and it remained on the market until the early 2000s. The A.H. Robins Company launched the Dalkon Shield IUD in 1971, aggressively marketing it as a highly effective and affordable pregnancy prevention device. Unfortunately, after just three years, it was recalled due to a poorly designed removal string. The unsealed string permitted the entry of bacteria into the uterus, leading to pelvic inflammatory disease, sepsis, and ultimately infertility. A.H. Robins faced around 300,000 lawsuits, resulting in demands for the company's bankruptcy. Subsequently, during the late 1970s and early 1980s, the use of IUDs declined, with several being withdrawn from the market. Only the progesterone-T variant remained available in the U.S. market. In 1988, the Copper-T 380A (Para Gard) was introduced, initially approved for four years and later extended to 10 years based on supporting effectiveness data. In 2001, the levonorgestrel-releasing IUD (Mirena) was introduced in the U.S. On January 9, 2013, the FDA approved a low-dose hormone IUD known as Skyla by Bayer – the first new IUD in 12 years. This device provides protection against pregnancy for three years and is suitable for women without children. It was launched in February 2013. At present, IUDs are considered safe, effective, and a low-risk form of contraception. According to a 2012 study by the Guttmacher Institute, the percentage of women using long-acting, reversible contraceptive methods, such as IUDs, increased from 2.0% in 2002 to 7.7% in 2009. This upward trend continues as more women become aware of contraceptive options and have increased access to the best birth control methods for their needs.

VI. CONCLUSION OF IUD:



The intrauterine device (IUD) stands out as a highly effective contraceptive option, especially for individuals not at risk of contracting sexually transmitted diseases. It is particularly suitable for women who have previously given birth and are in stable, monogamous relationships. Health care providers often recommend the progestin IUD for women experiencing extremely heavy, prolonged, or painful menstruation, as it tends to alleviate or even suppress such conditions. By reducing menstrual blood loss, women using this IUD are less prone to developing iron deficiency anemia, a condition associated with fatigue and other symptoms. Studies have suggested that women with copper IUDs may have a lower risk of endometrial cancer, and some experts speculate a similar effect for the progestin IUD, akin to progestin-only contraceptives like the minipill and the shot. An IUD functions by preventing the meeting of egg and sperm, thereby preventing pregnancy. It may also inhibit the development of a fertilized egg in the uterus. The Nova T or Flexi T 300 IUD boasts about 98.7% efficacy in preventing pregnancy, while the Irena IUD is approximately 99% effective. Although the risk of pregnancy after IUD insertion is minimal, there is always a slight chance. In the event of pregnancy, the IUD should be promptly removed, and a healthcare provider consulted to rule out an ectopic pregnancy. If the pregnancy is not ectopic and the decision is made to continue it, the caregiver can easily remove the IUD if the strings are visible. While there is a slight risk that removing the IUD might lead to pregnancy loss, retaining it poses a greater risk of infection and jeopardizes the woman's health. In rare cases where the IUD cannot be easily removed, the woman may need to decide on the appropriate course of action

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