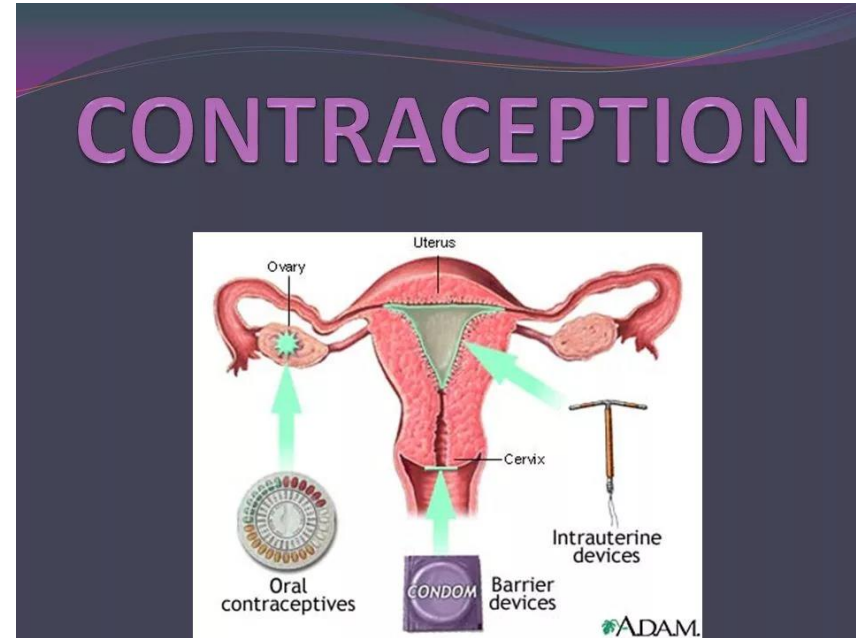


Hormonal therapy in
gynecology
Infertility

Lyzikova Yu.A.

Contraception

- When conception has been prevented by a sexually active individual through the use of various devices, agents, drugs, sexual practices and or surgical procedures it is referred to as contraception.



Contraception and fertility control

- **Fertility control** includes both fertility inhibition (contraception) and fertility stimulation.
- Fertility stimulation is related to the problem of the infertile couples,
- contraception includes all measures, temporary or permanent, designed to prevent pregnancy.

Ideal contraceptive method

- widely acceptable,
- inexpensive,
- simple to use,
- safe,
- highly effective
- requiring minimal motivation, maintenance and supervision.
- **No one single universally acceptable method has yet been discovered**

**Average Cost of Contraception for a Woman in the U.S.
Annualized Costs for One Year of Method Use**

Method	Average Cost Per Unit	# of Units Used in a Year	Total Cost Year 1	Likely # of Years of Use	Average Cost Per Year
CycleBeads®	\$14.00	1	\$14	2	\$7
IUD	\$700.00	1	\$700	10	\$70
Condoms	\$1.25	100	\$125	NA	\$125
Spermicides	\$1.80	100	\$180	NA	\$180
Shot/DepoProvera®	\$50.00	4	\$200	NA	\$200
Oral Contraceptives	\$30.00	13	\$390	NA	\$390
NuvaRing®	\$30.00	13	\$390	NA	\$390
The Patch	\$30.00	13	\$390	NA	\$390

Represents a method which requires a one time purchase.

Represents a method which requires individual units for each act of intercourse.

Represents a method which requires ongoing purchase.

Costs based on information from Planned Parenthood, Consumer Reports, and suggested retailer prices.

Likely # of Years of Use for CycleBeads is based on research that shows the typical length of use by women using this method. The device can potentially be used indefinitely.

Likely # of Years of Use for IUD is based on manufacturer's claim that it is "good for 10 years of use".

Costs can vary based on the source for the methods and individual insurance coverage.

Natural family planning

January						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

Vaginal ring



Female condoms

Contraceptive patch



Male condoms



Injectables



Oral contraceptives



Intrauterine devices



Contraception

- **Temporary**
- **Permanent**

Contraception (temporary)

- **User dependent:**
- Barrier
- Oral contraceptives
- Fertility awareness methods
- **User independent**
- Intrauterine devices
- Implants (progestogen only)
- Progestogen only injectables.

Barrier

Box No : 1

- ◆ **Mechanical**

Male — Condom

Female — Condom, diaphragm, cervical cap

- ◆ **Chemical**

(Vaginal contraceptives)

Creams — Delfen (nonoxynol-9, 12.5 %)

Jelly — Koromex, Volpar paste

Foam tablets—Aerosol foams, Chlorimin T or
Contab, Sponge (Today)

- ◆ **Combination**

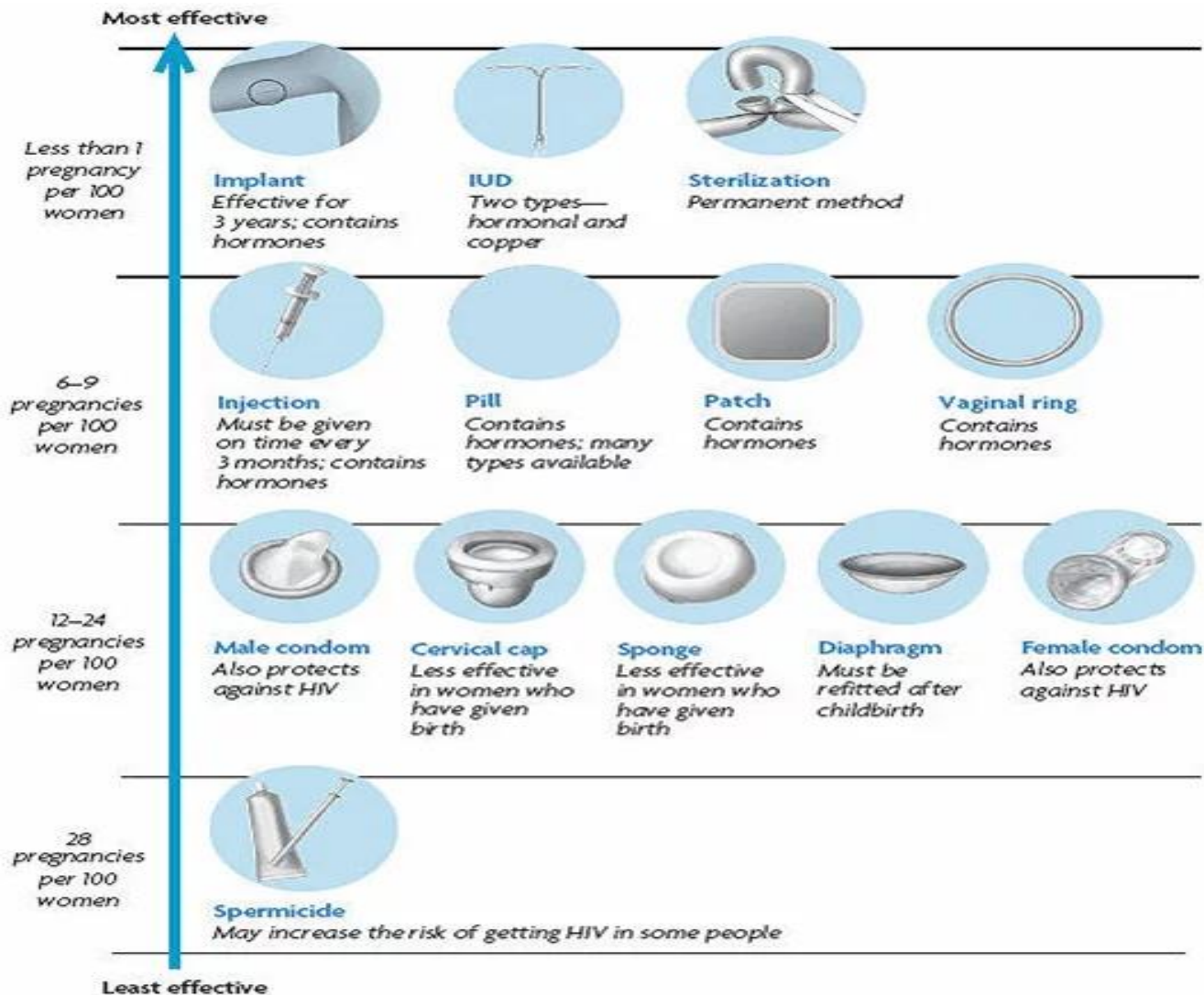
Combined use of mechanical and chemical

Chemical

- Spermicides are available as vaginal foams, gels, creams, tablets and suppositories.
- Usually, they contain agents mostly cause sperm immobilization.
- The cream is introduced high in the vagina soon before coitus, at least 5 minutes prior to intercourse.
- In isolation, it is not effective (18–29)

The pearl index

- The pearl index is the number of unwanted pregnancies per 100 women using the method of contraception for 1 year



HIV = human immunodeficiency virus; IUD = intrauterine device

*Other methods include fertility awareness-based methods and the lactational amenorrhea method (LAM) that can be used during the first 6 months of breastfeeding. Discuss these options with your health care provider.

Combined oral contraceptives (COCs)



- The most effective reversible method of contraception

Combined oral contraceptives (COCs)—

- 1. Containing an oestrogen and a progestogen.**
- 2. Progestogen-only pills (POPs)—**
these are a suitable alternative where **oestrogens** are **contraindicated** or not tolerated but they have a higher failure rate than COCs.
 - The typical failure rate is **5%** for both pill types.

COCP

- COCP provides reliable, effective contraception
- Modern COCPs all contain **ethinylestradiol** (20–35 micrograms) and are classified by type of **progestagen** they contain.
- The newer COCP **Qlaira** is an exception; it contains estradiol valerate.

Commercial names	Composition		No. of tablets
	Progestins (mg)	Estrogen (μg)	
1. Mala N (Govt of India)	Levonorgestrel 0.15	Ethinyl estradiol 30	21 + 7 iron tablets
2. Mala-D	Levonorgestrel 0.15	—do—	21 + 7 iron tablets
3. Loette (Wyeth)	Desogestrel 0.15	Ethinyl estradiol 20	21
4. Yasmin (Schering)	Drospirenone 3 mg (p. 531)	Ethinyl estradiol 30	21

Depending on the amount of ethinyl estradiol (E) and the types of progestin (P) used, pills are defined as : **1st generation** — with E 50 μg or more; **2nd generation** — with E 20–35 μg and P as levonorgestrel or norgestimate; **3rd generation** — with E 20–30 μg and P as desogestrel or gestodene; **4th generation** — E as third generation, with P as drospirenone, dienogest or nomegestrol. Low dose pills have E less than 50 μg .

Third generation progesterones

- **Increase risk of venous thrombosis**
- Reduce the incidence of: Acne, Headache, Weight gain, Breast symptoms, Breakthrough bleeding

Risk of venous thromboembolism

- Background risk is 5 in 100 000
- **On COCP**
- **Second generation** is 15 in 100 000
- **Third generation** is 25 in 100 000
- **In pregnancy** is 60 in 100 000

Progesterone content in COCPs

- **First and second generation**
Levonorgestrel, Norethisterone
- **Third generation** Desogestrel,
Gestodene, Norgestimate
- **Fourth generation** Drospirinone,
Dienogest, Nomegestrol

COCPs

- **Oestrogen content in COCPs**
- **Low** = 20 μg
- **Standard** = 30–35 μg
- **High** = 50 μg

Combined oral contraceptive pill: regimes

- 1 day of cycle.
- If first pill is after day 5, other contraception is needed for 7 days.
- Take the pill the same time every day.
- One pill daily for 21 days followed by 7 pill-free days.

Contraindications

- Pregnancy
- Post partum
- Breastfeeding <6 weeks post partum
- Non-breastfeeding <3 weeks post partum
- Smoking >15/day above the age of 35
- BMI >35
- Arterial disease: >2 risk factors for cardiovascular disease, Ischaemic heart disease, Stroke

Contraindications

- Hypertension: Systolic BP >160 mmHg, Diastolic BP >95 mmHg
- Valvular heart disease with:
Pulmonary hypertension, Subacute bacterial endocarditis
- Venous thromboembolism
- Migraine with aura
- Cancer

Non-contraceptive benefits of contraception

- **Combined oral contraceptives:**
- Lighter, regular, and less painful periods
- Decreased risk of benign breast disease
- Decreased ovarian cysts
- Decrease in both ovarian and endometrial cancer
- Decrease in acne

COCP

Decreased risk

- Ovarian cancer by 40–80% in user >10 years
- Endometrial cancer

Increased risk of

- Breast cancer
- Cervical cancer (unclear at the moment)

Missed pills

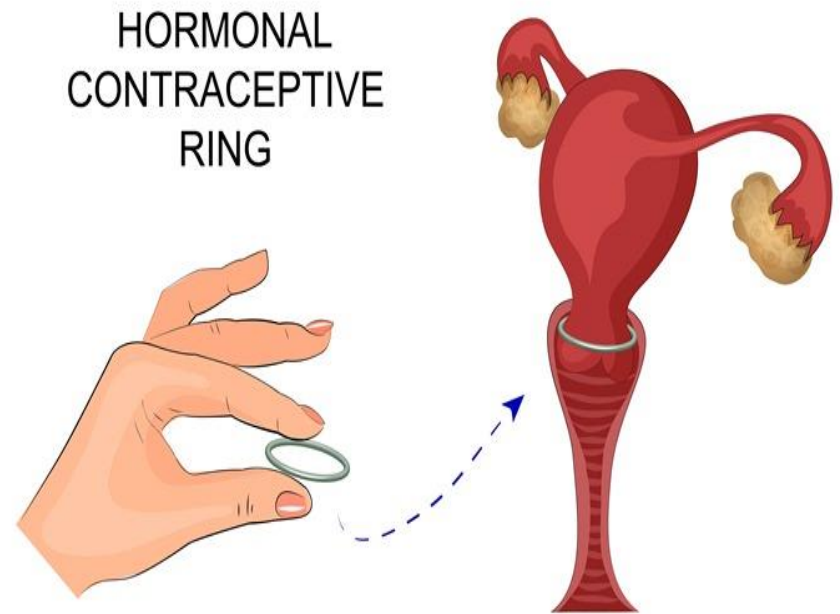
- Missed pills may lead to failed contraception.
- The risk of pregnancy is greatest at the beginning of the pack

Missed pill rules

- **If 1 pill is missed**
- Take the missed pill as soon as possible. Continue the rest of the pack as usual. No additional contraception is required.
- **If 2 or more pills are missed**
- Take the most recent missed pill as soon as possible. Continue the rest of the pack as normal. Additional contraceptive cover is required until 7 consecutive pills have been taken.

Vaginal ring

- The vaginal ring is a small plastic ring that is placed inside the vagina and releases oestrogen and progestogen.
- The ring remains in place for 3wks and is removed for the fourth. A new ring is used each month.
- Side effects include \uparrow vaginal discharge, irritation, or infection.
- The perfect-use failure rate is $<0.3\%$ and the typical-use failure rate is 2% .



Vaginal ring



progestin only contraception

- It contains low dose of a progestin
- Mechanism of action: It works mainly by making cervical mucus thick, thereby prevents sperm penetration. Endometrium becomes atrophic.

Benefits

- Side effects attributed to estrogen in the combined pill are totally eliminated
- No adverse effect on lactation
“Lactation Pill”
- It may be prescribed in patient with hypertension, fibroid, diabetes, smoking and history of thromboembolism

LARC

means...

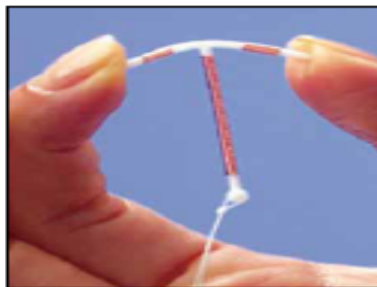
Long Acting Reversible Contraceptives. There are now 3: the Implanon implant, the Mirena IUD and the ParaGard IUD.



Implanon Implants *The Etonogestrel Implant*
Implanon implants are inserted under the skin, where they remain effective for 3 to 4 years, maybe longer.* Irregular spotting and bleeding improves over time. The total days of bleeding a woman experiences are diminished by Implanon. Implanon suppresses ovulation almost completely throughout the first 3 years after insertion.



Mirena IUD *The Levonorgestrel Intrauterine Device*
Mirena is placed into a woman's uterus, where it is effective for 5 to 7 years, maybe longer.* Mirena has so many non-contraceptive benefits. It is used to prevent or treat menstrual pain, menstrual blood loss, endometrial cancer, uterine fibroids, endometriosis and dysfunctional uterine bleeding (DUB). After the first year, 50 to 75% of women using Mirena IUDs are ovulating.



ParaGard IUD *The Copper T 380-A Intrauterine Device*
ParaGard is placed into a woman's uterus, where it is effective for 10 to 12 years, maybe longer.* While causing increased bleeding and/or pain in the first several months, in the long run, ParaGard has minimal effects on the physiology of a woman's periods, including the likelihood of ovulation. ParaGard IUDs are, by far, the most effective emergency contraception and may be inserted within 5 to 7 days of unprotected sex. In a British study, not one of 1,963 women who received a ParaGard IUD for emergency contraception became pregnant.*

*Non-FDA-approved use.

INJECTABLE PROGESTINS

- The preparations commonly used are depomedroxyprogesterone acetate (DMPA) and norethisterone.
- Both are administered intramuscularly within 5 days of the cycle.
- DMPA in a dose of 150 mg every three months or 300 mg every six months

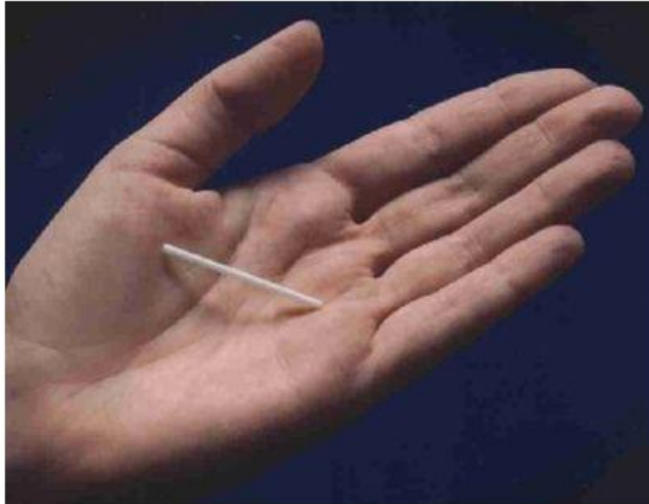


Implanon

- Implanon is a progestin only delivery system containing Ketodesogestrel (etonorgestrel).
- It is a long-term (up to 3 years) reversible contraception.
- It releases the hormone about 60 mcg, gradually reduced to 30 mcg per day over 3 years.
- Mechanism of action: It inhibits ovulation

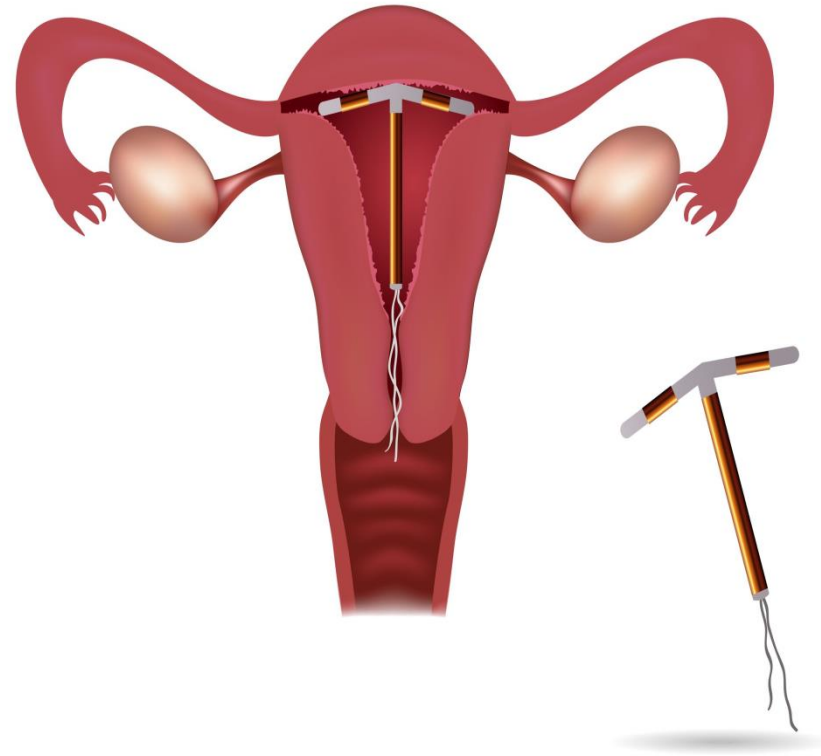
Nexplanon/Implanon

- Implanon approved by FDA in 2006
- An implant
 - One rod (Norplant-six)
 - Inserted under skin, inner arm
 - Can feel implant
- Low-dose progestin release
- Good for three years



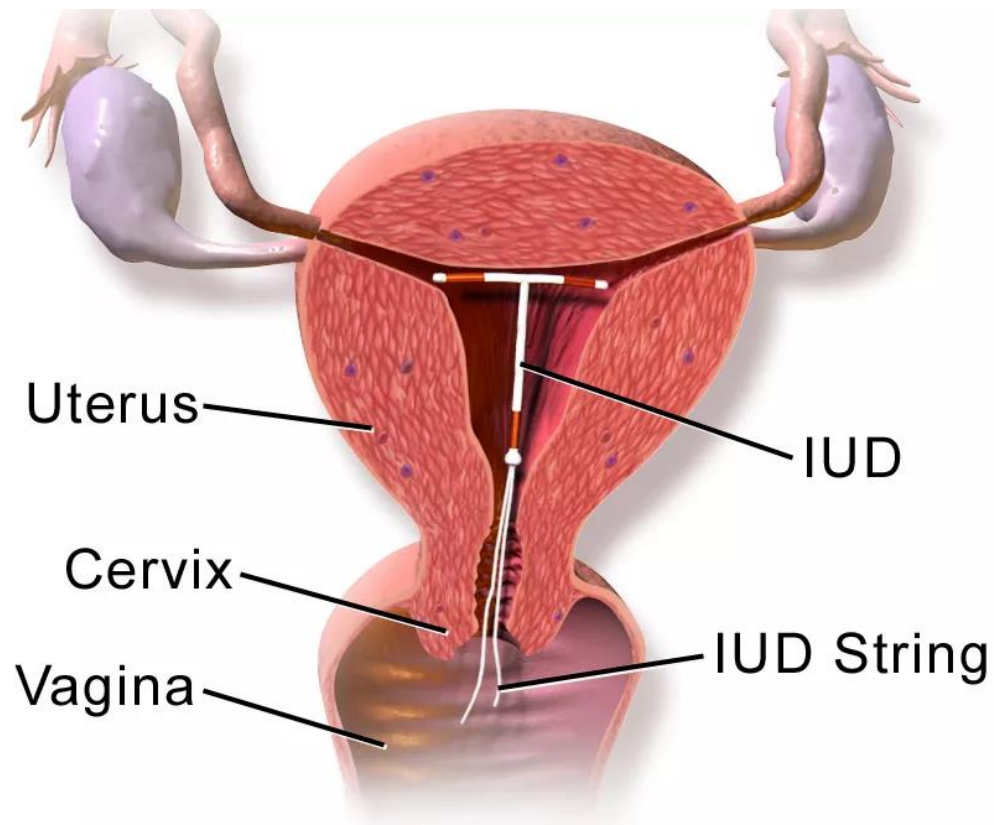
IUD

- Provides long-term reversible contraception.
- Very effective (failure rate of 0.6–0.8 per 100 woman-years).
- **Mode of action:** Foreign body reaction in the endometrium prevents implantation.



Complications

- **Irregular bleeding**, especially first 3–6mths.
- **Risk of infection**: screen for infection prior to insertion.
- **IUD expulsion**: most common in the first 3mths after insertion.
- **Perforation**.
- **Dysmenorrhoea**.



Intrauterine Device (IUD)

Mirena® IUS


- The LNG-releasing system has a T-shaped rod containing 52mg LNG (20 micrograms released daily).
- Due to its progestagenic content, menstrual blood loss is decreased by >90%, and it is as effective as endometrial ablation in the management of menorrhagia.

Emergency contraception

- **Levonorgestrel** 1500 mcg (within 72 h of unprotected sexual intercourse)
- **Intrauterine device** (within 5 days of unprotected sexual intercourse or within 5 days of ovulation)

Emergency contraception

- **Levonorgestrel** 1500 mcg
- Efficacy of use:
 - within 24 h = 95% effective
 - 24–48 h = 85% effective
 - 49–72 h = 58% effective
- **Side effects:** Nausea, Bleeding within 7 days of taking



**Emergency
Contraceptive
Consilient**
1500 microgram tablet
levonorgestrel

For oral use
1 tablet

1 tablet
For oral use

*Reduces the chance
of pregnancy
after unprotected sex*

*Not for regular
birth control*



After Pill[™]

Levonorgestrel Tablet, 1.5 mg



Emergency Contraceptive

*Contains the emergency contraceptive
medicine doctors recommend most*

Contains One 1.5mg Tablet

NDC 51285-769-93

Plan B[®]

(LEVONORGESTREL)
tablets 0.75 mg

Emergency Contraceptive

Reduces the chance of pregnancy after unprotected sex (ie, if a regular birth control method fails or after sex without birth control). Not Intended To Replace Regular Birth Control. Plan B[®] Should Be Used Only In Emergencies

Rx only for age 17
and younger



Take the first tablet as soon as possible within 72 hours of unprotected sex. The sooner you take the first tablet, the more effective Plan B[®] will be. Take the second tablet 12 hours later.

2 Levonorgestrel Tablets
0.75 mg each

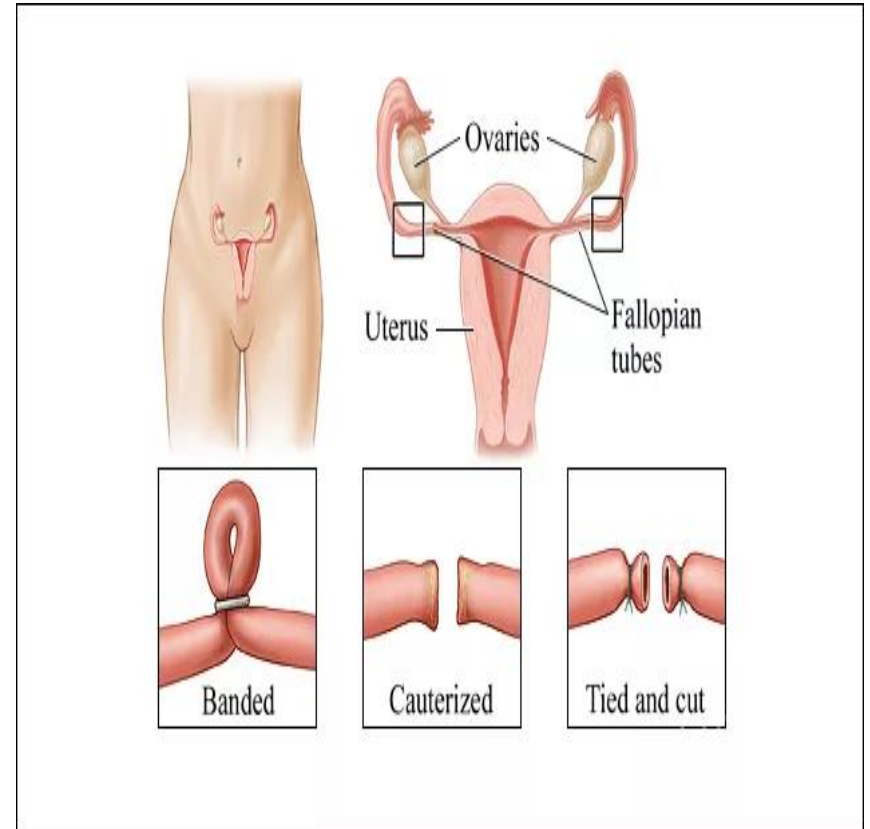
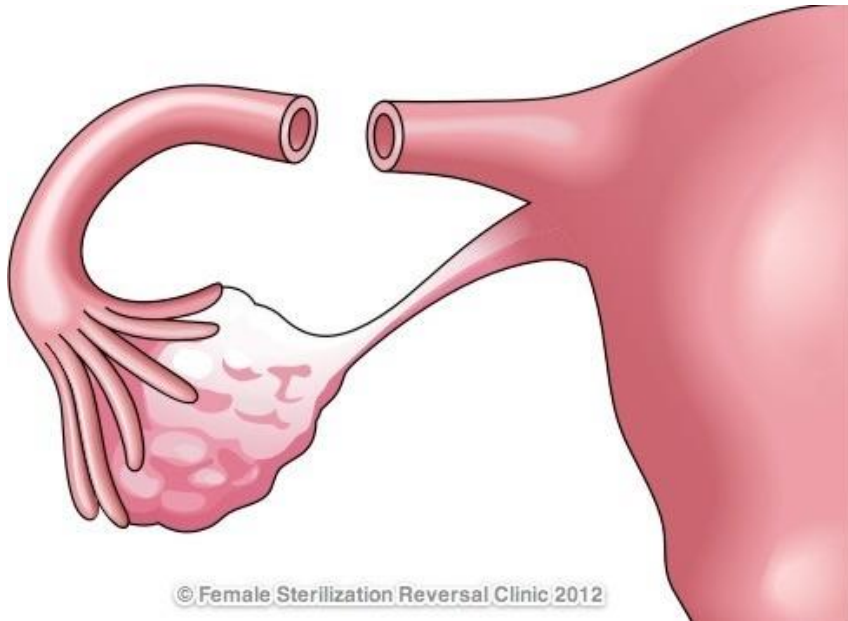
Belarus



Permanent methods

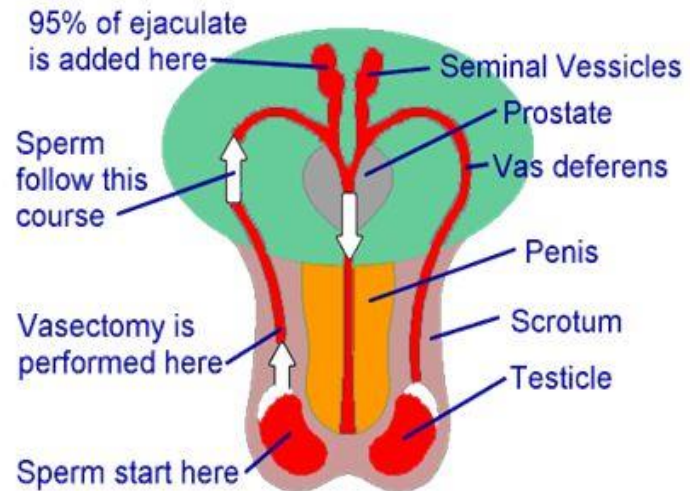
- **Female sterilization methods**
- **Male sterilization methods**

Female sterilization



Sterilization: Vasectomy

- Vasectomy blocks sperm from traveling through the vas deferens, preventing sperm from mixing into semen
- No glands or organs are removed
- Effectiveness: 99%+
- Considered irreversible



HORMONAL THERAPY IN GYNECOLOGY

- **Stimulation of ovulation**
- **Inhibition of ovulation**
- **HRT**

Stimulation of ovulation

- **Clomiphene citrate**
- **Mode of action:** In the hypothalamus, clomiphene citrate binds to estrogen receptors, occupies the nuclear site for a long time (weeks).
- The negative feedback of endogenous estrogen is thus prevented.

- Clomiphene therapy is simple, safe and at the same time cost-effective.
- Most centers use an initial dose of 50 mg daily.
- The actual starting day of its administration in the follicular phase varies between day 2 and day 5 and therapy is given for 5 days.

Inhibition of ovulation

- **Gonadotrophin antagonist**
- **GnRH agonist**
- **COC**

Danazol

- **Gonadotrophin antagonist**
- Acts on the pituitary gland and inhibits LH and FSH causing inhibition of ovarian steroidogenesis, resulting in decreased secretion of oestradiol
- Does not affect pituitary hormones
- Used to treat **Endometriosis, Uterine fibroids , Menorrhagia** (induces amenorrhoea)
- Side effects: Fluid retention, Weight gain , Masculinizing side effects

Buserelin

- **GnRH agonist**
- Acts on the pituitary, initially causes increase of LH and FSH levels
- Eventually after 21 days receptor downregulation occurs, LH and FSH levels decrease
- Used to treat: **Endometriosis, Uterine fibroids**
- Maximum duration of treatment is 6 months
- Side effects: Menopausal symptoms, Osteoporosis

Hormone replacement therapy

- **Oestrogens** used in HRT chemically synthesized from soya beans or yams, are molecularly **identical to the natural human hormone**
- **Progestagens** used in HRT are almost all synthetic and derived from plant sources. They are structurally different from progesterone.

HRT

- **Types of systemic oestrogen-based HRT**
- **Oestrogen alone** in hysterectomized women.
- **Oestrogen plus progestagen** in non-hysterectomized women.

Routes of administration

Oestrogen: oral, transdermal, vaginal.

Progestagen: oral, transdermal, intrauterine (levonorgestrel).

Benefits of HRT

- Vasomotor symptoms.
- Urogenital symptoms and improved sexuality.
- Risk of osteoporosis.
- Risk of colorectal cancer.

Tibolone

- Is a selective tissue oestrogenic activity regulator (STEAR)
- Used as HRT or Osteoporotic prevention
- **Has oestrogenic, progestogenic, and androgenic properties**
- Functions: Relieves climacteric symptoms, prevents osteoporosis,
**No endometrial stimulation,
Non-oestrogenic effects on
breast tissue**

Infertility

- Infertility is defined as a failure to conceive within one or more years of regular unprotected coitus.
- **Primary infertility** denotes those patients who have never conceived.
- **Secondary infertility** indicates previous pregnancy but failure to conceive subsequently.

Causes of infertility

- Conception depends on the fertility potential of both the male and female partner.
- The male is directly responsible in about 40 percent,
- The female in about 40 percent
- Both are responsible in about 10 percent cases.
- The remaining 10 percent, is unexplained, in spite of thorough investigations with modern technical knowhow.

CAUSES OF FEMALE INFERTILITY

- Tubal and peritoneal factors (25–35%),
- Ovulatory factor (30–40%)
- Endometriosis (1–10%).

TUBAL AND PERITONEAL FACTORS

- The obstruction of the tubes may be due to
- **Pelvic infections**
- **Previous tubal surgery or sterilization**

Ovarian factors

- **Anovulation**
- **Decreased ovarian reserve**
- **Luteal phase defect (LPD)**

Investigations

- **Semen analysis:** This should be the first step in investigation because, if some gross abnormalities are detected (example being absence of sperm), the couple should be counseled for the need of assisted reproductive technology.

TABLE 16.4**DIAGNOSIS OF OVULATION****Indirect**

- ◆ Menstrual history
- ◆ Evaluation of peripheral or endorgan changes
 - BBT
 - Cervical mucus study
 - Vaginal cytology
 - Hormone estimation (see Table 16.6)
 - Serum progesterone
 - Serum LH
 - Serum estradiol
 - Urine LH
 - Endometrial biopsy
- ◆ Sonography (TVS)

Direct

Laparoscopy

Conclusive

Pregnancy

BBT

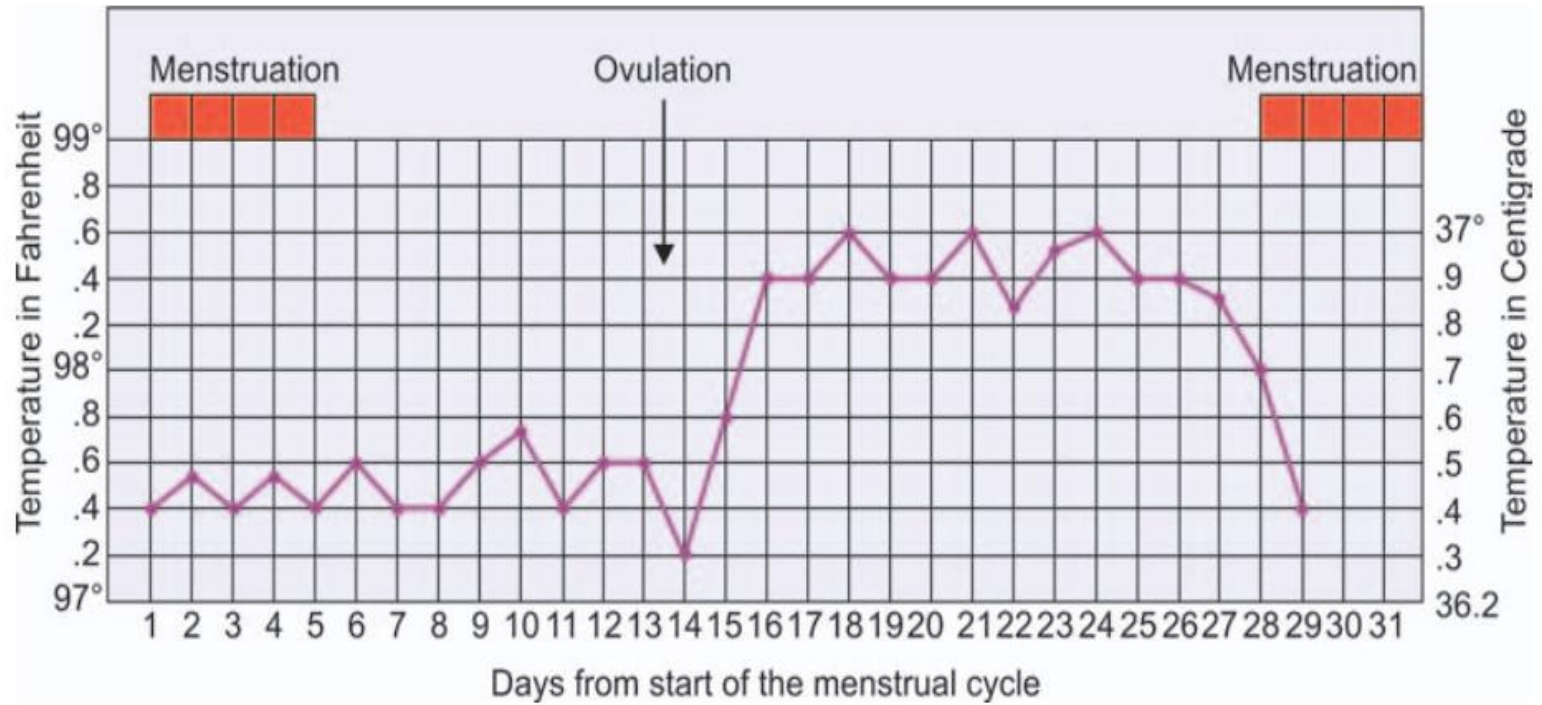


Fig. 16.1: Biphasic BBT chart

Tubal factors

- **Hysterosalpingography**
- **laparoscopy and chromopertubation**

Cervical factor

- **Postcoital Test**
- PCT is to assess the quality of cervical mucus and the ability of sperm to survive in it.
- This test is done several hours after (within 8–12 hours) sexual intercourse.
- Presence of at least 10 progressively motile sperm signifies the test is normal.

Self study

- IVF