

Future methods of fertility regulation

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1. Improvement of existing methods

Efficacy, side-effects, duration of action, manufacturing process, cost

2. New approaches

Mode of action

3. New targets for contraception



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1. Improvement of existing methods



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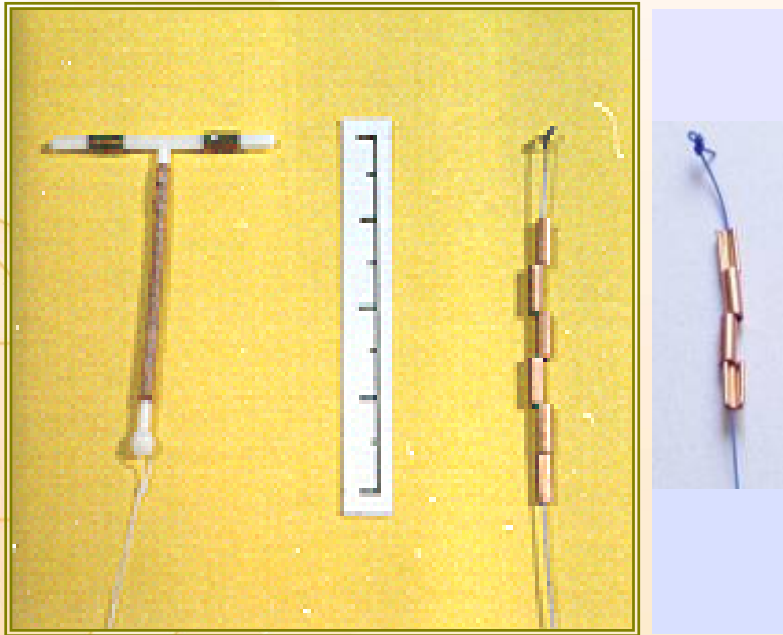


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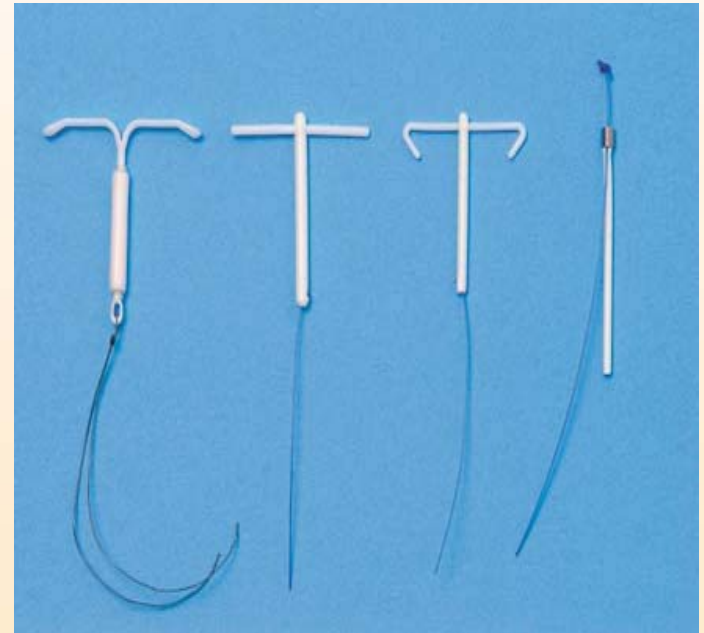


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Intra-uterine devices



Copper-releasing



Levonorgestrel-releasing



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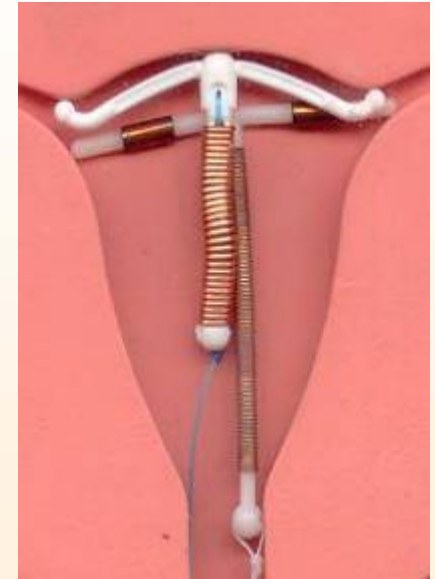


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Intra-uterine devices

Also under development:

- Swing: copper-releasing with coil stem
- IUD releasing a progesterone receptor modulator (CDB-2914)
- Copper IUD releasing indomethacin



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Contraceptive implants

- **Jadelle:**

levonorgestrel, 2 rods, 5 years

- **Implanon:**

etonogestrel, 1 rod, 3 years

- **Nestorone:**

pure progestogen, 1 rod, 2 years



Injectables (1)

Improved pharmacokinetic profile :

- **Biodegradable microspheres:**
norethisterone, norgestimate, progesterone
- **Controlled particle size distribution:**
DMPA, levonorgestrel butanoate

Decreased side-effects :

- **Monolithic macrocrystals:**
progesterone, 17-beta- estradiol, testosterone
combined for once-a-month administration



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Injectables (2)

Safer delivery system :

- Provision of Cyclofem in non-reusable disposable syringes (Uniject, Soloshot)



Contraceptive vaginal rings

- **Progestogen only**
(for continuous use)
 - **Progering** - Silesia (3 months)
 - nestorone - Pop.C. (12 months)
- **Estrogen-progestogen**
(3 weeks in /1 week out)
 - **Nuvaring** - Organon (1 month)
 - nestorone/EE - Pop.C. (12 months)



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Transdermal systems

- Patch releasing an estrogen and a progestogen:
 - EVRA: norelgestromin 150 μg + ethinyl estradiol 20 μg
 - levonorgestrel + ethinyl estradiol
 - gestodene 50 μg + ethinyl estradiol 18 μg (Angeliq - Schering)
- Patch releasing a progestogen:
 - nesterone (also being developed as gel and spray)
 - norgestimate



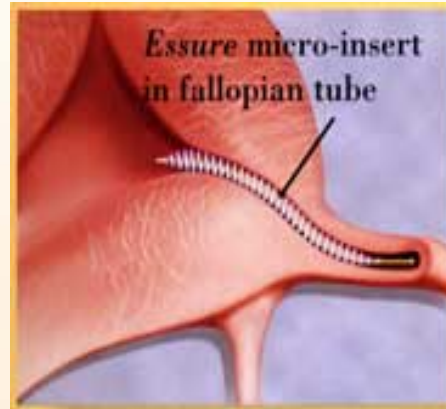
Natural methods

- Standard days method, based on abstinence/protection from cycle day 8 to cycle day 19.
- "Two days" method, based on cervical mucus observation



Female sterilization

- Essure
- Adiana
- Ovabloc
- Quinacrine



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Male condoms



Polyurethane: Avanti, eZ.on, Supra
Styrene-based plastic: Tactylon, Unique, Unisex



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Female condoms



Femidom

FC2

Under development:

- polyurethane (PATH)
- natural latex (Reddy, other)
- plastic



V-Amour



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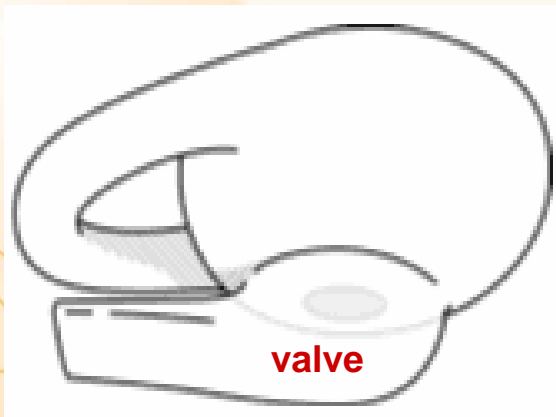


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New diaphragms



**Lea's
Shield®**



SILCS



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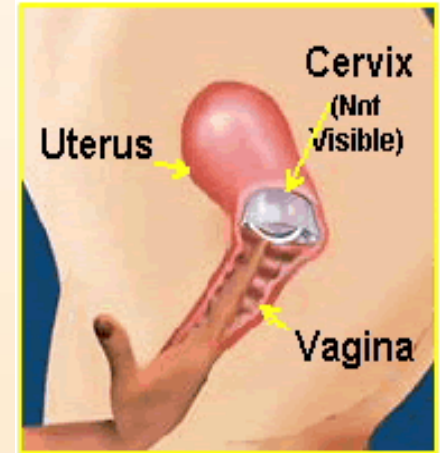
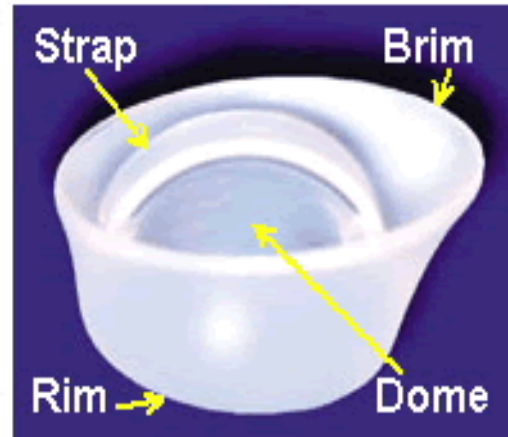


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New cervical caps



Ovès



FemCap™



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2. New approaches



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Microbicides with contraceptive action

- Products that create a **protective physical barrier** in the vagina: e.g. Sulfated and sulfonated polymers, such as cellulose sulfate, polystyrene sulfonate.
- Products which increase vaginal defense mechanisms by **maintaining natural acidity** (which immobilises sperm): e.g. BufferGel and Acidform.
- **Surfactant** products: e.g. acylcarnitine analogs, C31G.
- Products which block attachment of HIV to target cells and **sperm - zona pellucida fusion**: e.g. naphthyl urea derivatives.



Immunocontraceptives

Most advanced immunocontraceptives are based on hCG :

Their goal is to generate antibodies against hCG secreted by embryonic trophoblastic cells, necessary for maintenance of the corpus luteum and the continued production of progesterone:

hCG β Chain: whole or the 109-145 amino acid sequence of the C-terminal portion

+ diphtheria toxoid as carrier

+ muramyl dipeptide as adjuvant

+ squalene/mannide monooleate (4:1) as emulsifying agent

Other targets: - zona pellucida (permanent effect on ovaries)
- molecules on sperm surface, e.g. fertilin (PH-30), fertilisation antigen (FA-1), sperm protein (SP-10), LDH-C4



Anti-progestins for contraception

- Sequential regimen
 - Mifepristone + Norethisterone
 - Mifepristone + Medroxyprogesterone acetate
 - Mifepristone (days 1-15) + nomegestrol acetate (days 16-28)
- Continuous regimen: 0,1 to 10 mg/day
- Weekly use: 2,5 to 50 mg doses
- Monthly use: 200 mg 2 days after the LH peak
- Emergency contraception: 10 mg



METHODS FOR MALE CONTRACEPTION

- Prevent sperm production
- Prevent sperm transport
- Prevent sperm deposition
- Modify sperm function
- Prevent fertilization



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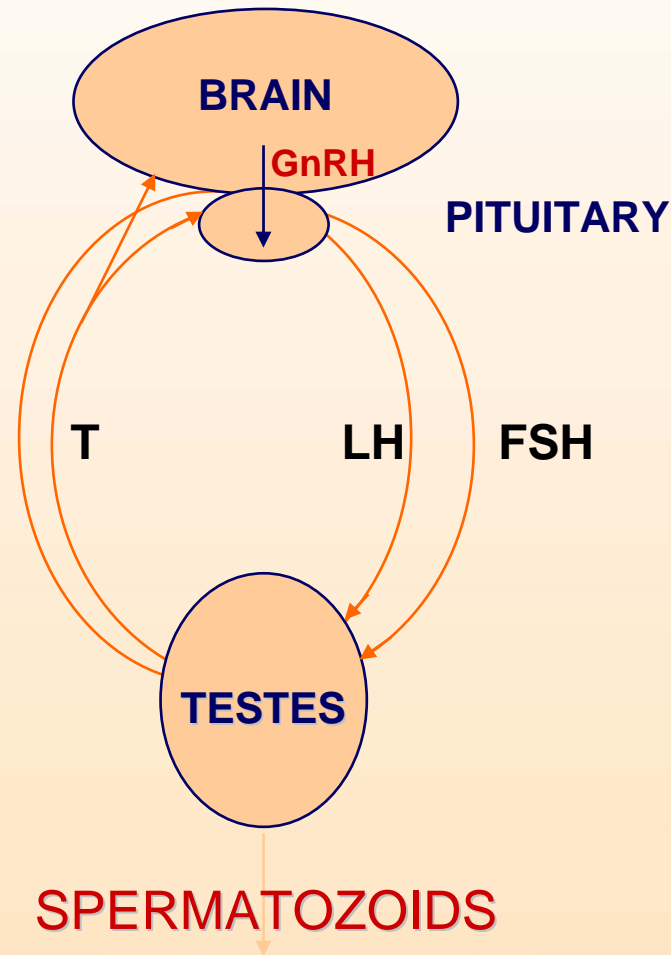


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Hormonal control of sperm production



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Methods to suppress sperm production

- Hormonal
 - Testosterone esters
 - progestogen or GnRH analogue + testosterone
- Immunological, based on antibodies against
 - GnRH, LH, FSH, their receptors



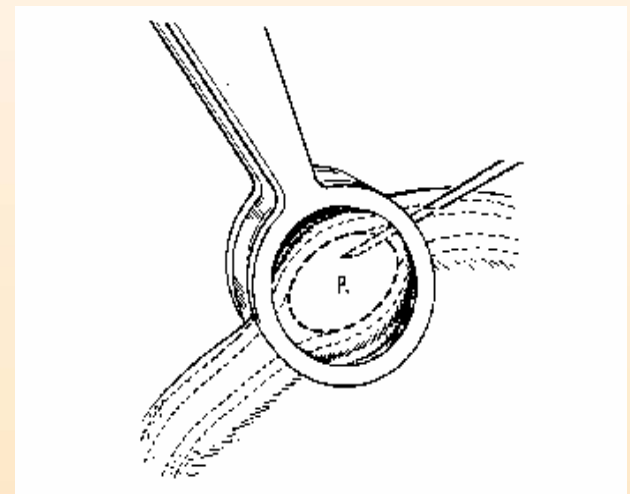
Methods for male sterilization

No scalpel vasectomy

Fascial interposition

Percutaneous vas occlusion

- Permanent, with **sclerosing agents**:
e.g. methylcyanoacrylate,
polyurethane
- Reversible, with **non-sclerosing agents**:
e.g. silicone plugs
or **resins**: e.g. maleic anhydride / styrene



3. New targets



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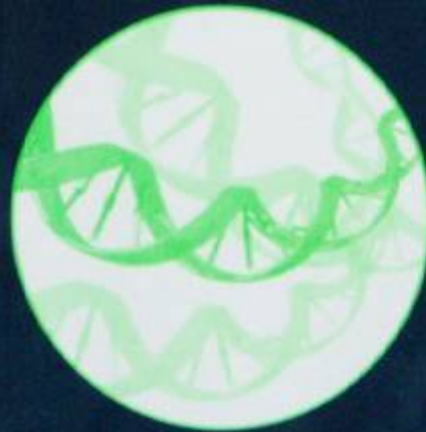
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Possible targets

- Gametogenesis
- Sperm motility
- Sperm capacitation
- Acrosomal reaction
- Follicular development
- Implantation



NEW FRONTIERS IN CONTRACEPTIVE RESEARCH



A
Blueprint
for
Action

INSTITUTE OF MEDICINE
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Some of the more promising leads

- Lonidamine analogues: deplete immature germ cells from seminiferous epithelium.
- Inhibitors of epididymal proteins: eppin and cystatin-11
- Inhibitors of testis-specific enzymes (GST, SAC)
- Inhibitors of fusion of sperm with zona pellucida: GnRH antagonists.
- Change in endometrial receptivity: LIF antagonists; antibodies against LIF, IL-11, or the IL-11 receptor; ebaF.
- Anti-angiogenic agents (magainin analogues, fumagillin).



Challenges for the development of new technologies

- Cost and time (10-15 years, US\$ 200-300 million)
- Industry involvement
- Perspectives of users and potential users, of different religious and socio-cultural backgrounds, and of new generations of women and men
- Access in resource-poor settings (cost, technology)

For women to benefit from these new technologies, they need better access to education and income and to have greater decision-making power.

