

M U N I
M E D

Department of Gynecology and Obstetrics
Brno University Hospital and
Masaryk University, Faculty of Medicine
head: doc. MUDr. Vít Weinberger, Ph.D



Infertility

Tvarožek S., Meixnerová I.

Obstetrics and Gynecology - lectures

2020

Infertility

- **Fertility** – biological ability to conceive within 6–9 months
- **Infertility** – disability to conceive after 12 months of unprotected sex
- 15–20 % couples, rapidly growing incidence in last decades
- evaluation should begin after 6 months of trying unsuccessfully to conceive

Fertility – physiology

- Ovulation
- Oocyte migration
- Sperm penetration
- Fertilization
- Embryo migration
- Implantation in uterine cavity

Infertility causes

Male factor (40%)

- **Abnormal sperm production or function**
 - undescended testicles, genetic defect, DM, infection, mumps
- **Sperm delivery problems**
 - premature ejaculation, cystic fibrosis, blockage of testicles, damage/injury
- **Damage related to cancer treatment**
 - radiation, chemotherapy
- **Immunological**
 - an autoimmunity to own sperm

Infertility causes

Female factor (40%)

- **Uterine:** polyps, shape abnormalities (septum...), fibroids
- **Tubal:** blocking or damage (inflammation, endometriosis, adhesion)
- **Ovulatory:** ovulation disorders, PCO, insufficiency, chemotherapy, hyperprolactinemia
- **Cervical:** polyps, occlusion
- **Immunological:** immunity to sperm, zona pellucida, ovary...
- **Endometriosis:** affect function of ovaries, uterus, fallopian tubes
- **Unexplained:** not diagnosed by any known medical procedure

Age and fertility

- Female fertility after 35 years of age **decreases 3 times** in comparison to women under 25 years of age
- **Causes:** ovarian dysfunction, endocrinologic factors, hypothalamic – pituitary factors, environmental changes

Diagnosis

- Always both partners
- Patient/family history
- Sexual habits (intercourse frequency)
- Laboratory tests (hormones)
- Genetic testing
- Semen analysis
- Ovulation testing (LH, P, prolactin)

Diagnosis

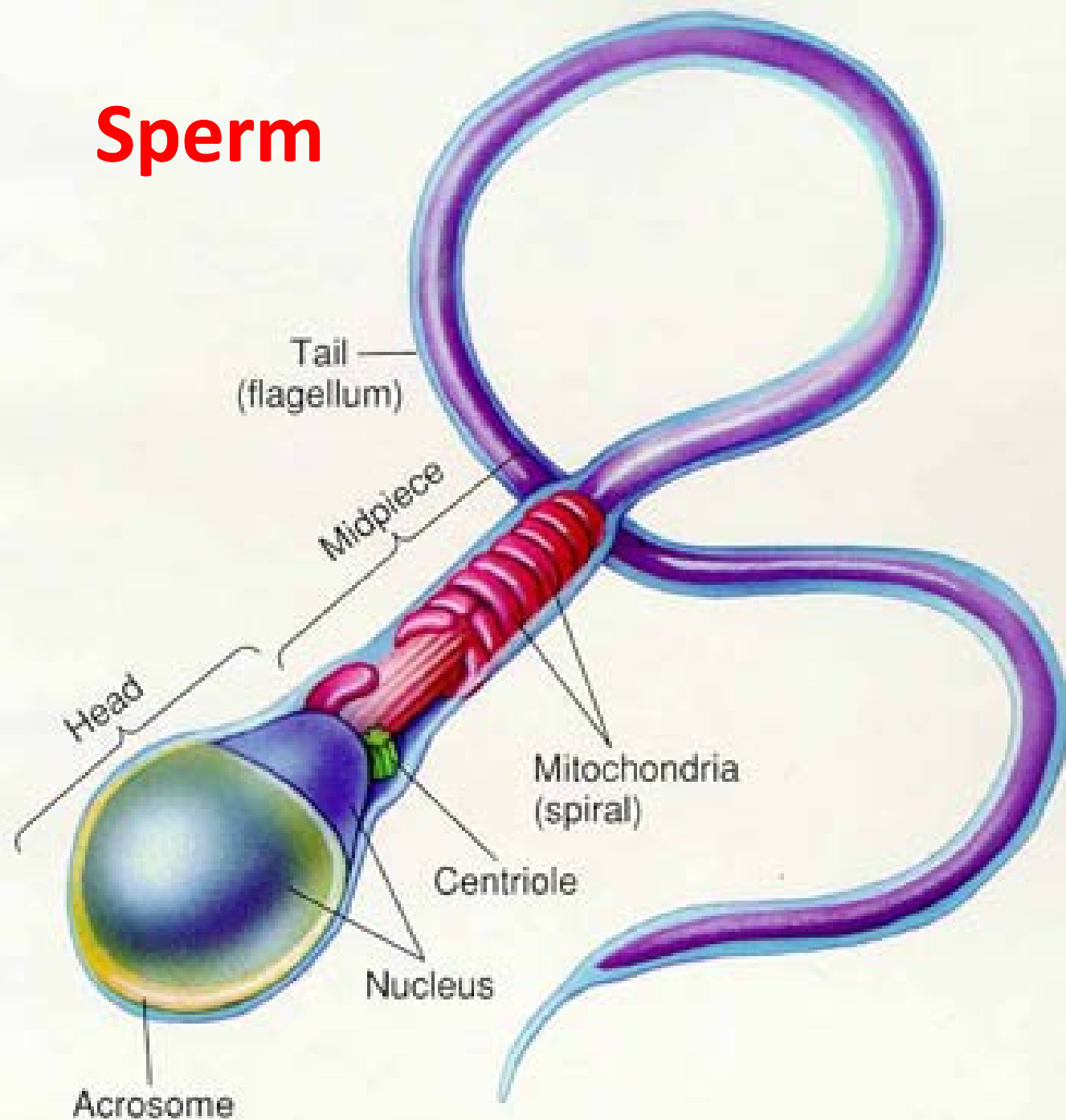
- Ovarian reserve testing (AMH)
- Ultrasound examination
- **Hysterosalpingography (SONO-HSG)**
- Hysteroscopy
- Diagnostic laparoscopy (DGL)
- **Chromopertubation** – blue dye solution introduction
- Other hormone testing (TSH, T3, T4, FSH...)

Sperm analysis

| | |
|-------------------------------------|------------------------------|
| Volume | ≥ 1.5 ml |
| Concentration | ≥ 15 millions/ml |
| Total sperm count | ≥ 40 millions |
| Motility/forward progression | ≥ 32 % |
| Morphology | ≥ 4 % normal and more |

- **Approximate concentration of total sperm cells:**
 - 1940 110 mil/ml
 - 1990 60 mil/ml

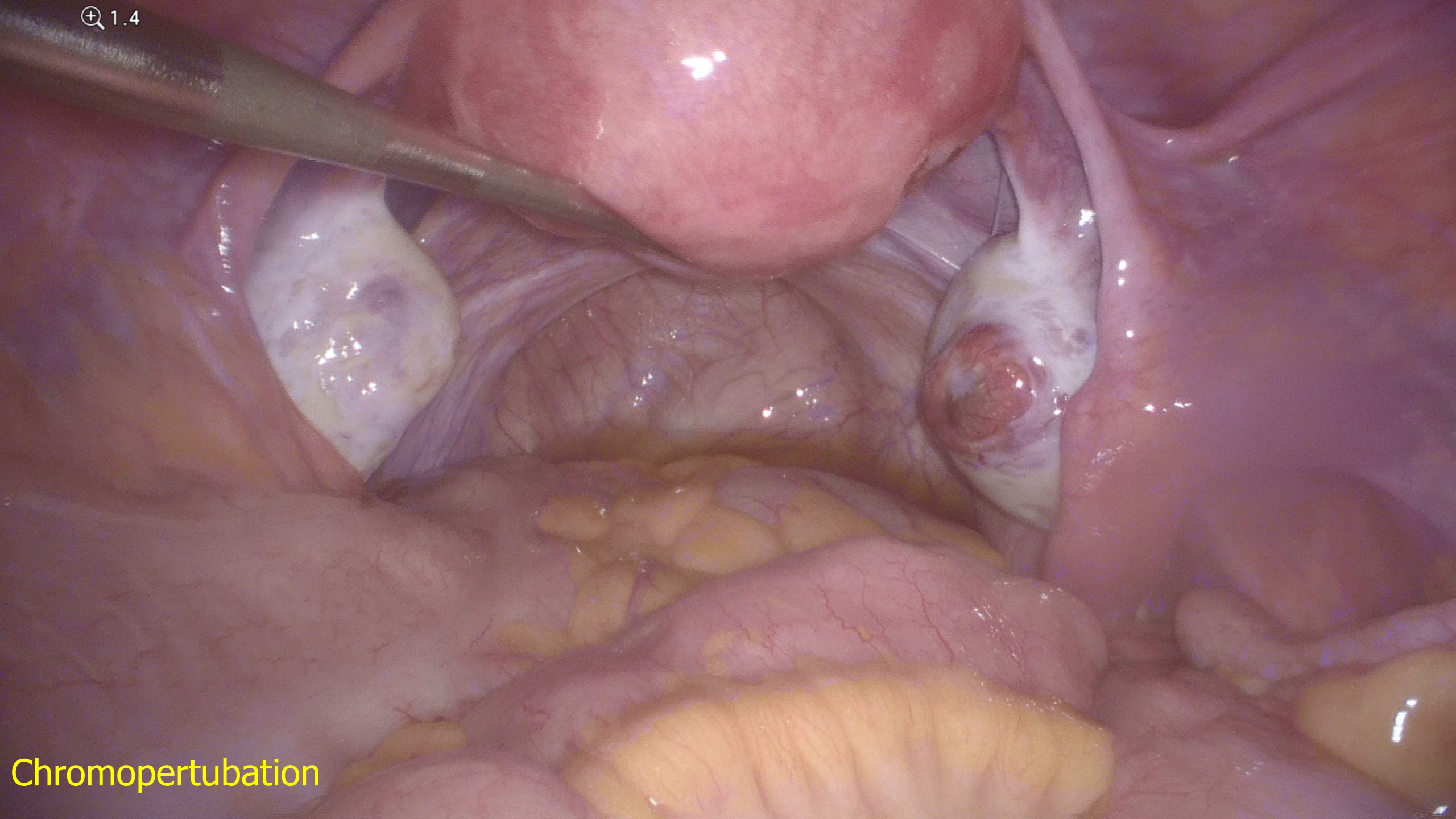
Sperm



Semen deficiencies - nomenclature

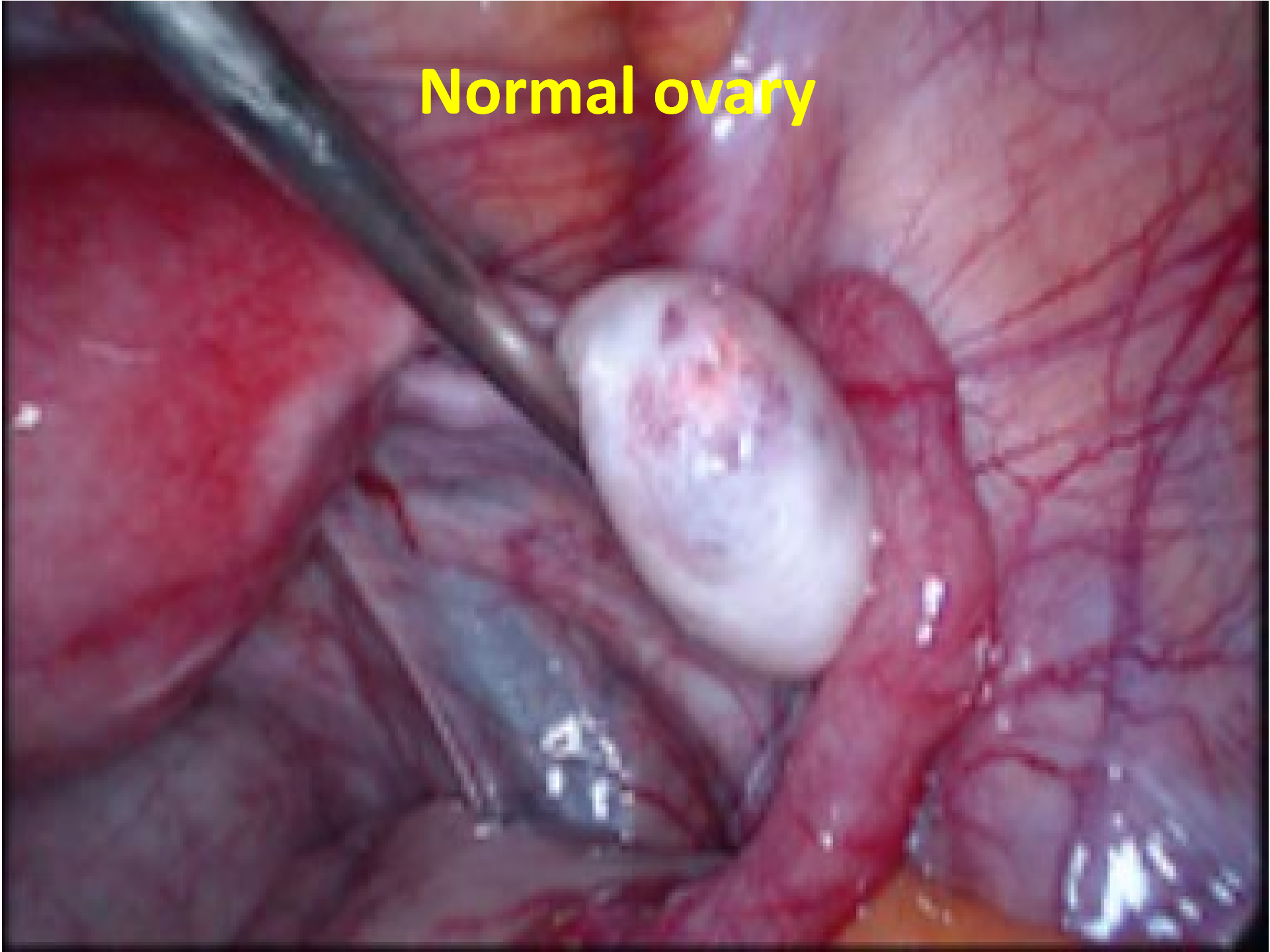
| | |
|--------------------------|--|
| Normozoospermia | normal result |
| Oligozoospermia | reduced concentration |
| Asthenozoospermia | reduced sperm motility |
| Teratozoospermia | abnormal morphology |
| Azoospermie | absence of spermatozoa (motile sperm cell) |
| Aspermia | complete lack of semen |

⊕ 1.4



Chromopertubation

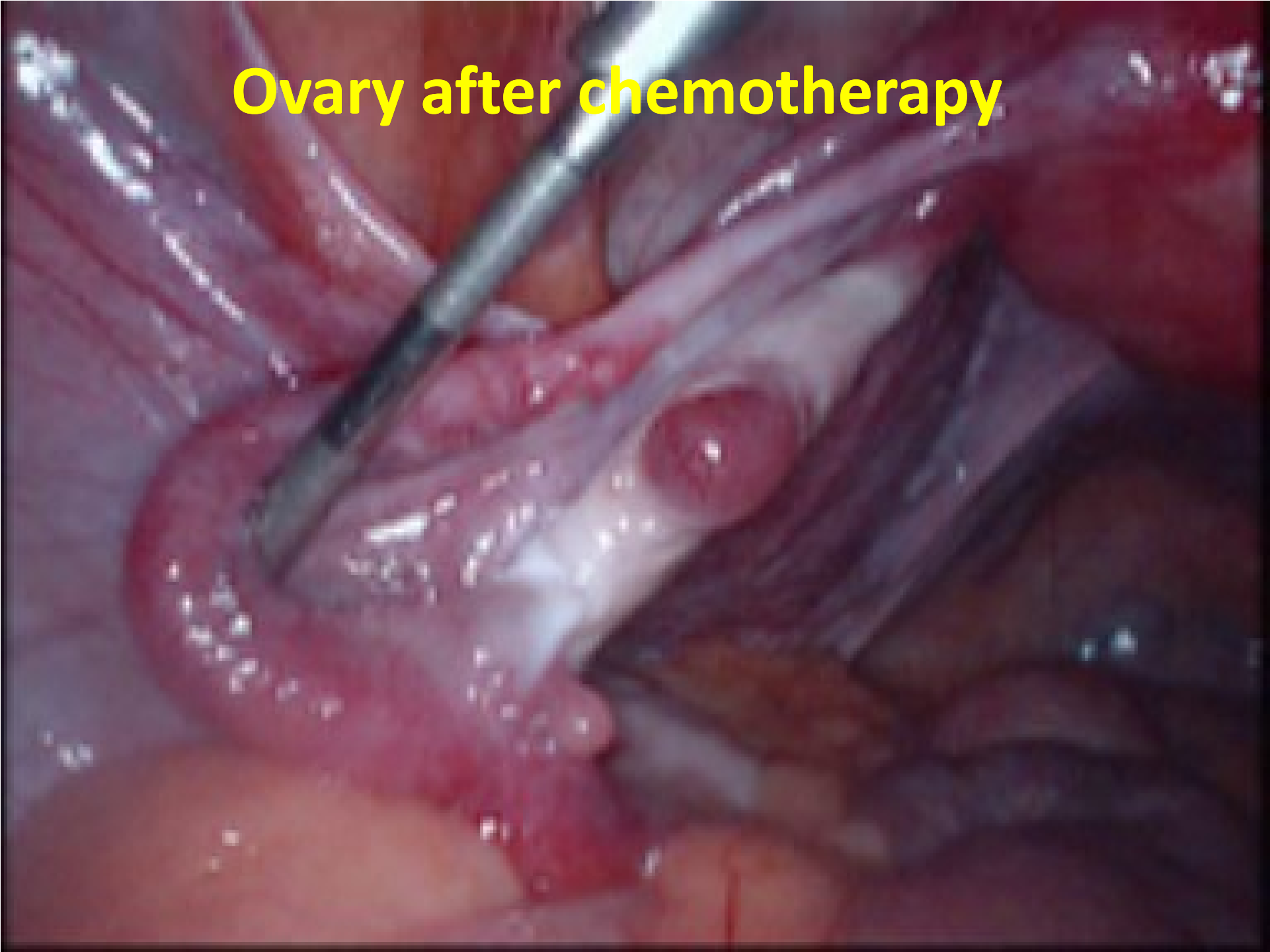
Normal ovary



Streak ovary (Turner sy.)



Ovary after chemotherapy



Ovary after ovarian cyst removal



Sactosalpinx



MUM
MED

RES
2D
75%
Dym R 58
P Off
Res

SONO HSG



5.0cm

SONO HSG - fimbriae

M U
M E

RS
2D
38%
Dym R 58
P Off
Res



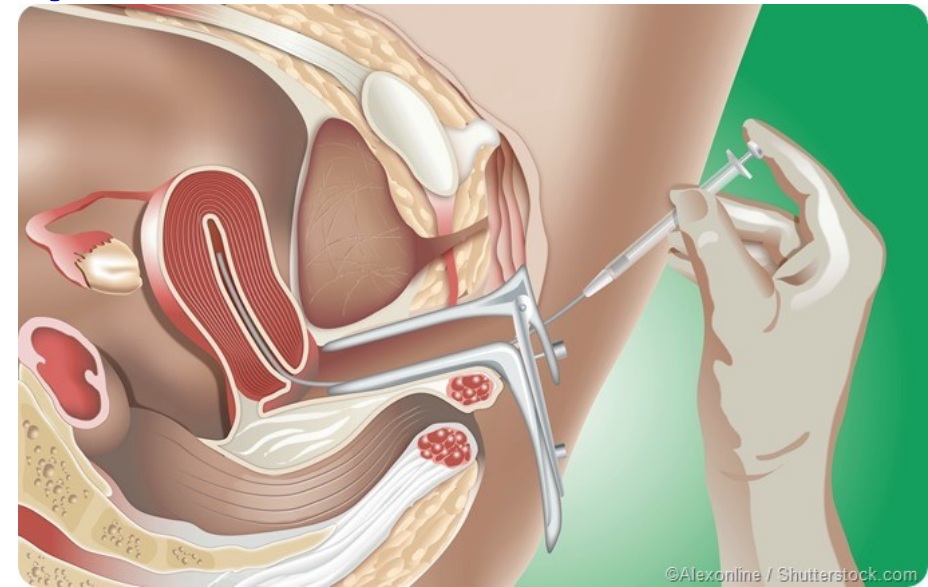
3.0cm

Assisted reproduction

- medical procedures used primarily to **address infertility**
- any procedure that involves the **handling of eggs, sperm, or both, outside the human body**
- includes artificial insemination, intrauterine insemination, in vitro fertilization, and ovarian stimulation

Assisted reproduction methods

- **Ovulation induction (stimulation)**
- **Artificial insemination (IUI) – introduction of sperm into uterus**
- **In-vitro fertilisation (IVF)**
- **Preimplantation genetic diagnosis (PGD)**
- **Donor conception**
- **Surrogacy**

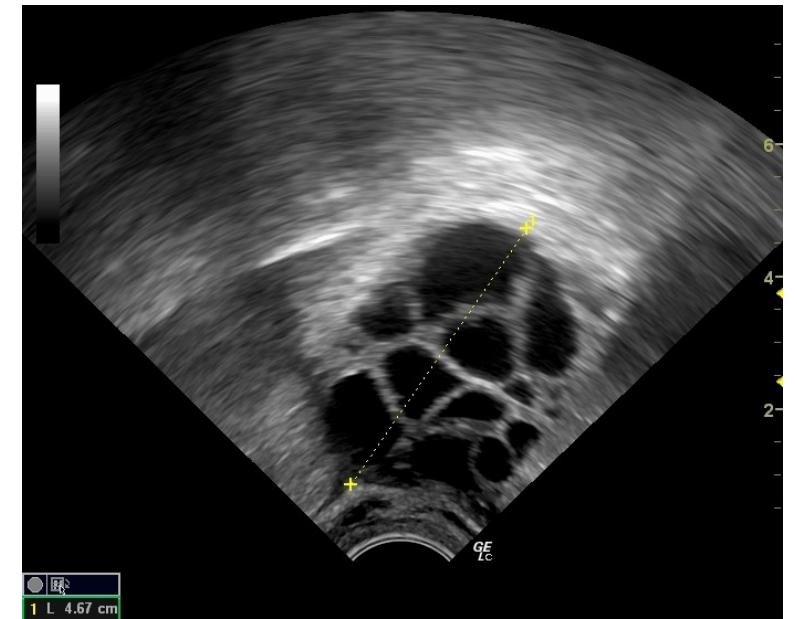


In vitro fertilisation

- A process of fertilisation outside the body (in vitro/glass)
- **Monitoring and stimulating** a woman's ovulatory process
- **Retrieving oocytes** from ovaries
- **Sperm and oocytes** placed in a liquid culture to **fertilise**
- **Embryo culture** – embryo is growing in an artificial medium
- **Embryo transfer/frozen embryo transfer** (to a uterus)

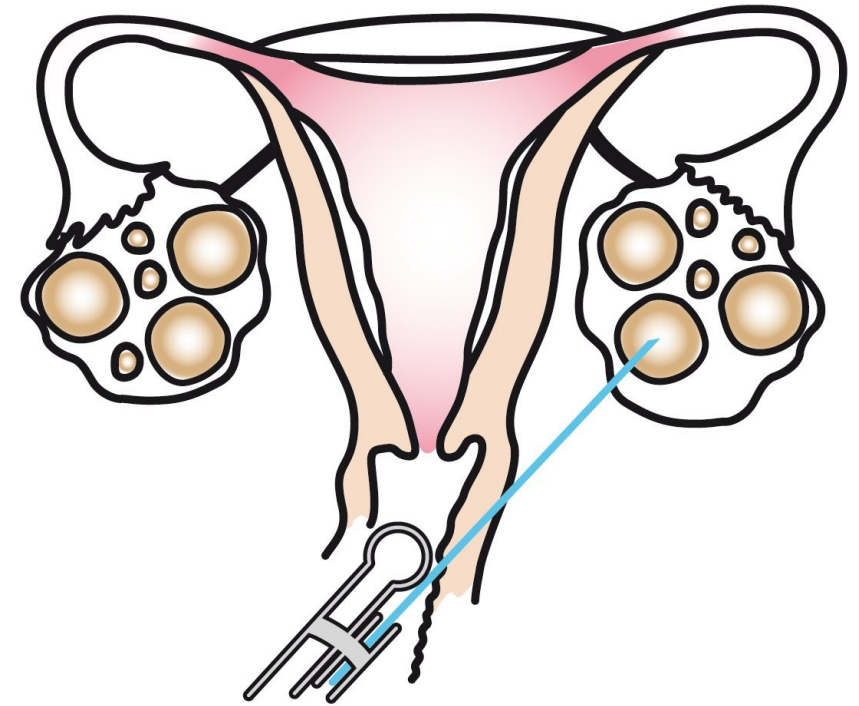
Ovulation induction (stimulation)

- Woman is not ovulating or not ovulating regularly
- Taking a hormone medication to stimulate ovulation
- Response to hormones is monitored with US
- **Timing of intercourse**
- At the beginning of **every IVF cycle**
- Th: clomifen citrate, FSH, hCG.....
- monitored by US folliculometry



Oocyte retrieval/egg collection

- transvaginal oocyte retrieval
- removing oocytes from the ovary in order to enable **fertilisation** or to egg freezing (**cryopreservation**)



Sperm retrieval techniques

Microsurgical method of sperm extraction MESA, TESE

Obstructive azoospermia

- microsurgical epididymal sperm aspiration – MESA

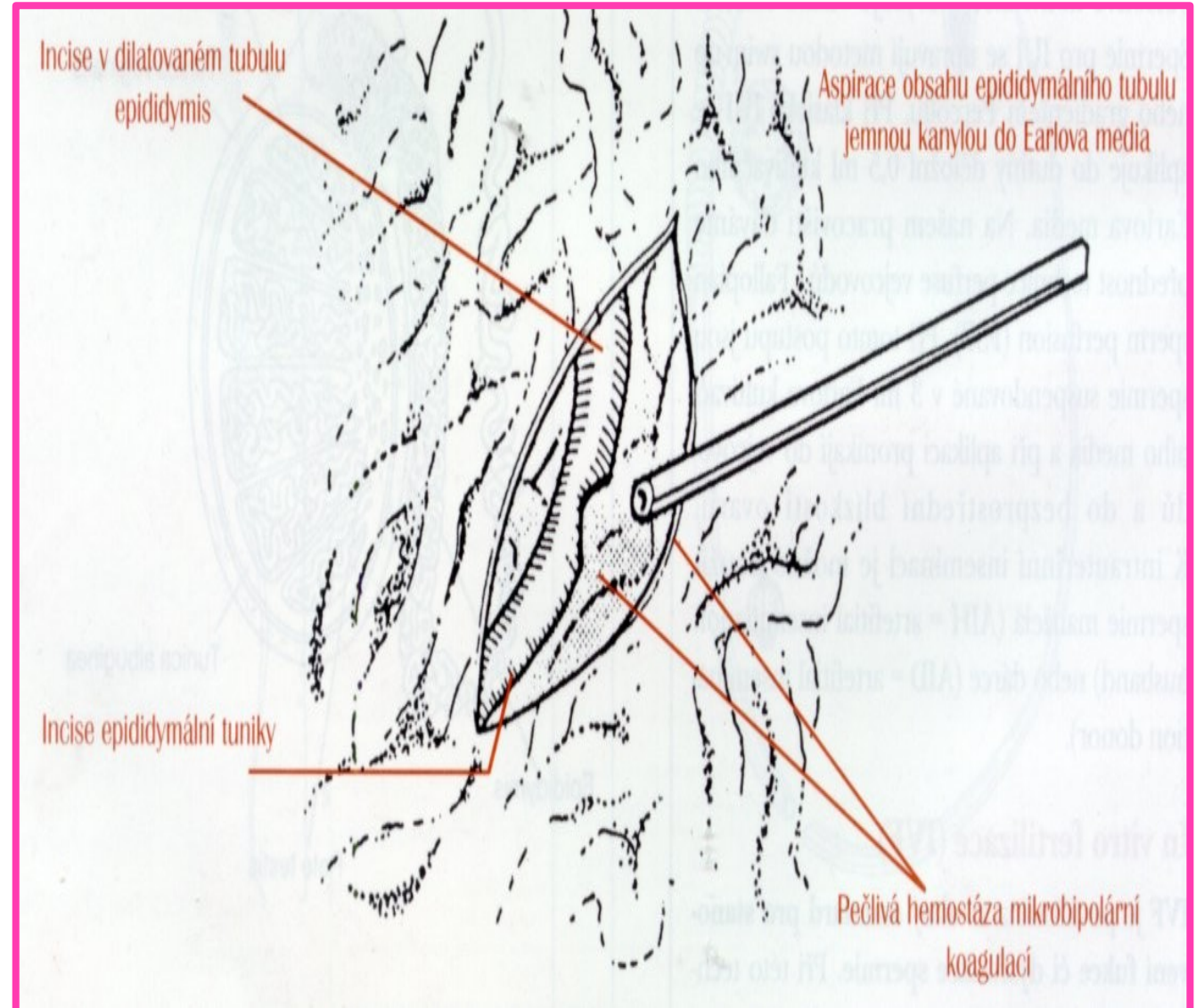
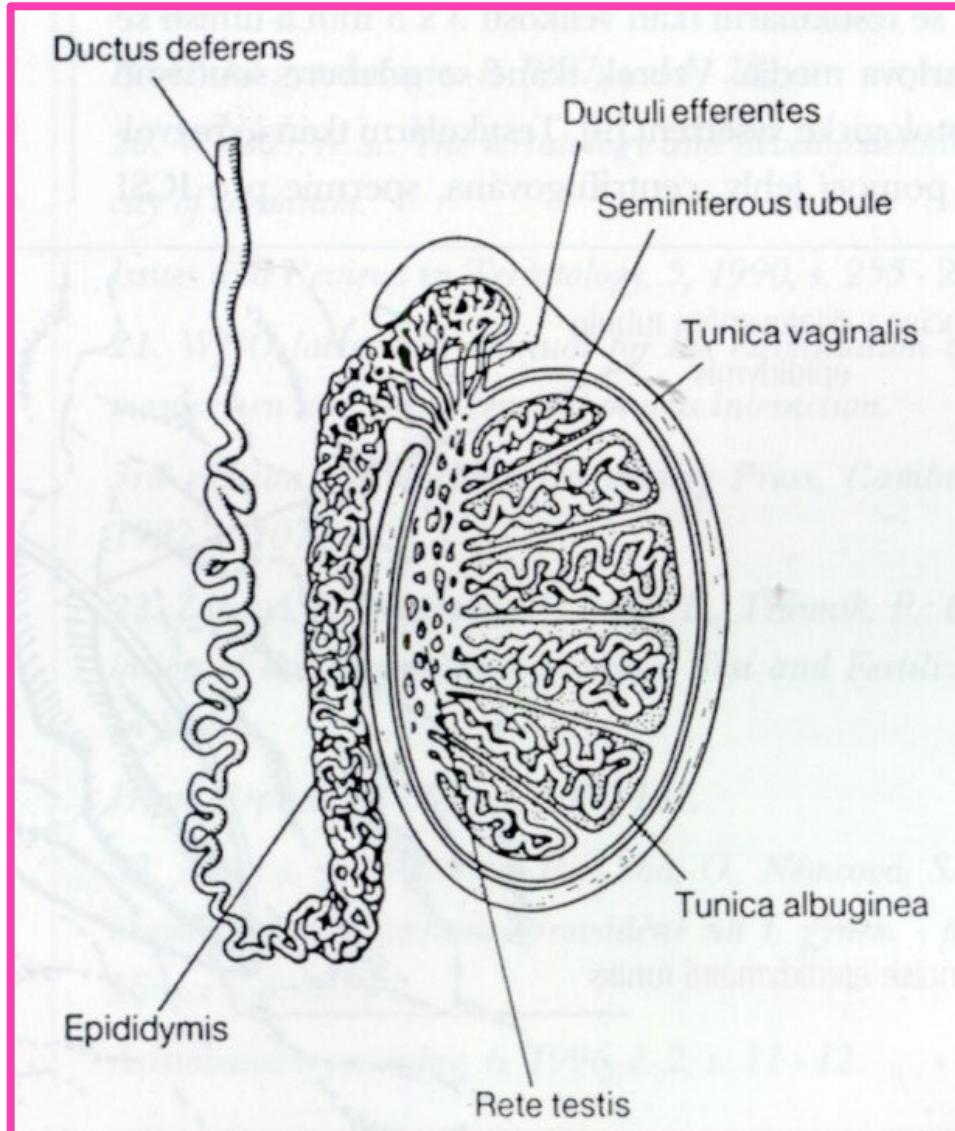
Non obstructive azoospermia

- testicular sperm extraction – TESE

Microsurgical epididymal sperm aspiration – MESA

- in case of occlusion between epididymis and urethra
- via 3 cm long scrotal incision, under general anesthesia
- liquid is aspirated from the ducts by pipette

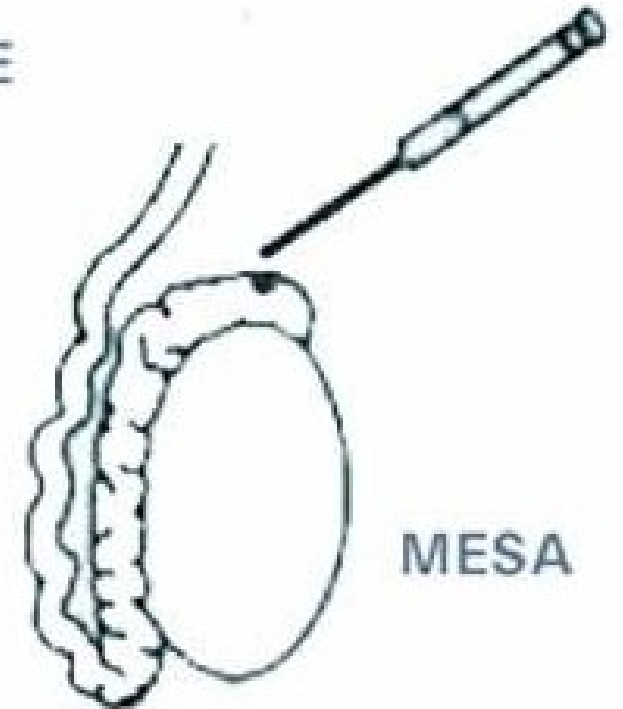
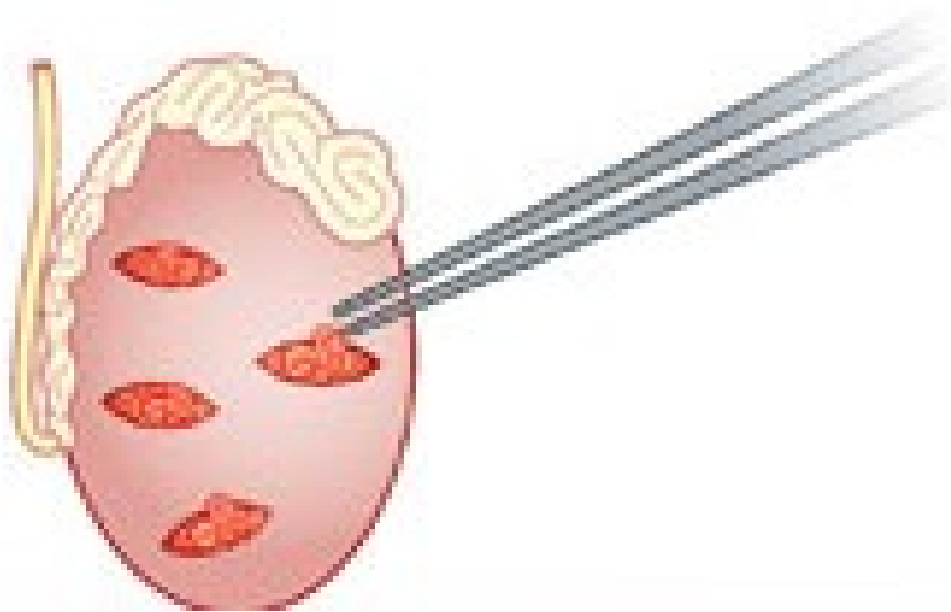
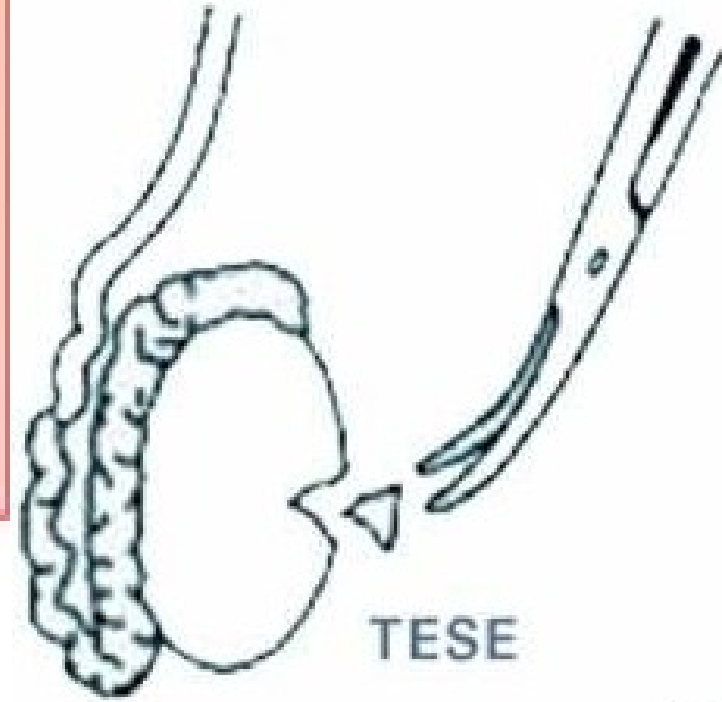
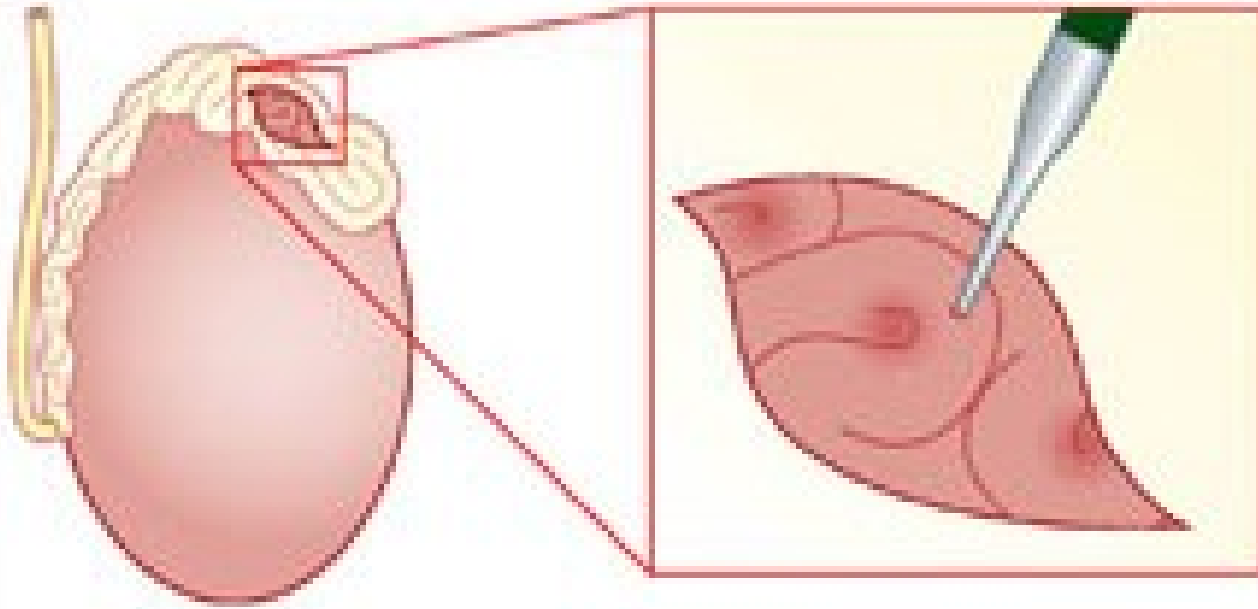
MESA



Testicular sperm extraction – TESE

- in case of no sperm was retrieved from MESA technique
- It allows for extracting sperm cells (if they are present) from the ducts of the germinal epithelium
- follows the previous MESA procedure
- small incisions are made in the testicular sheets
- a little of the testicular tissue is retrieved

MESA/TESE



In vitro fertilisation – advanced techniques

- **Intracytoplasmic sperm injection (ICSI)**
 - direct injection of a single sperm into each oocyte
- **Preselected Intracytoplasmic sperm injection (PICSI)**
 - transferring specially selected sperm
 - Sperm exhibits positive binding to hyaluronan gel
 - Hyaluronan is an important component of oocyte layer

In vitro fertilisation – advanced techniques

- **Magnetic activated cell sorting (MACS)**
 - selecting damaged spermatozoas with higher number of fragmented DNA
- **Assisted Hatching (AH)**
 - Embryo is surrounded by a hard layer of cell – zona pellucida
 - Creating small crack in the zona pelludica
 - AH help an embryo implant in the uterus

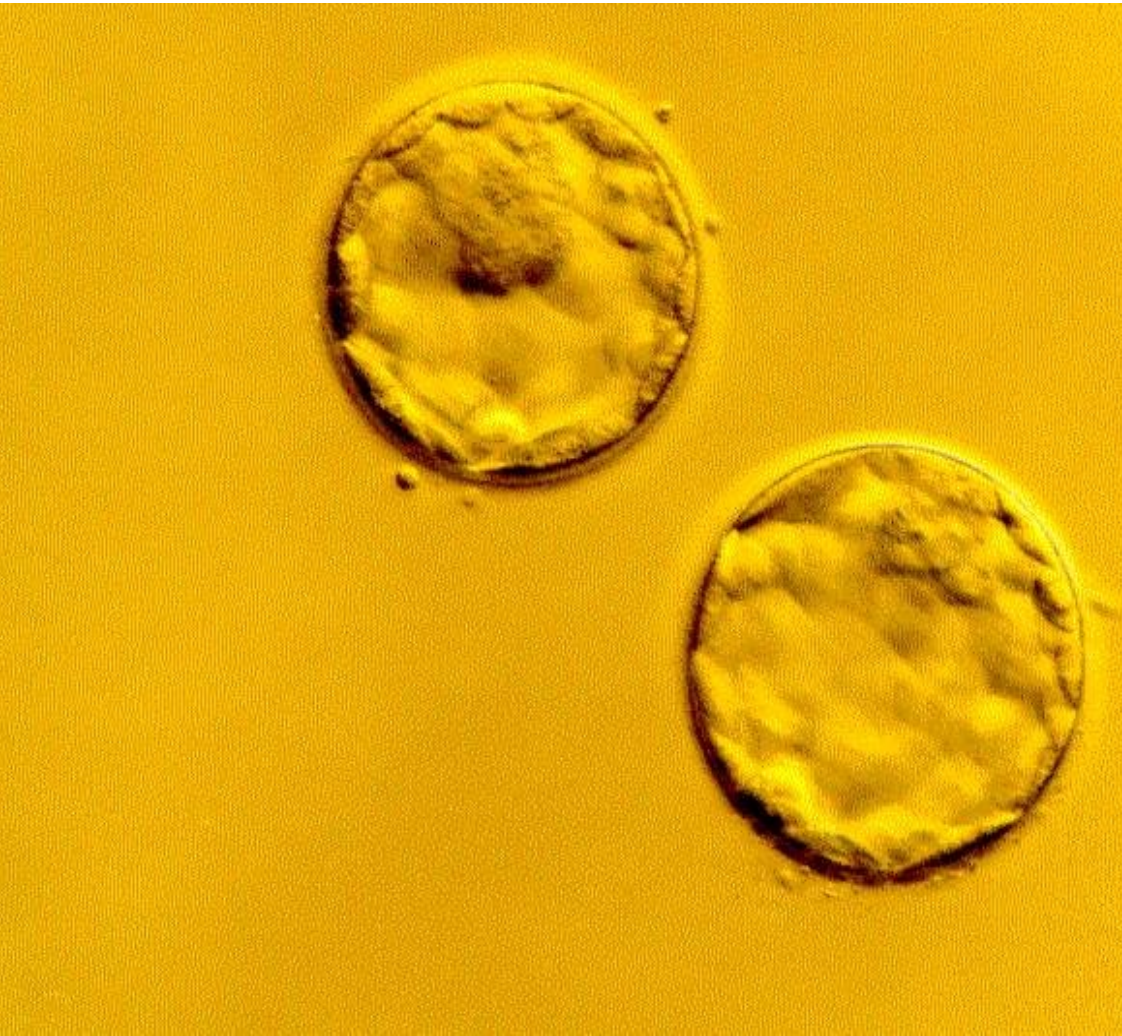
Zygote



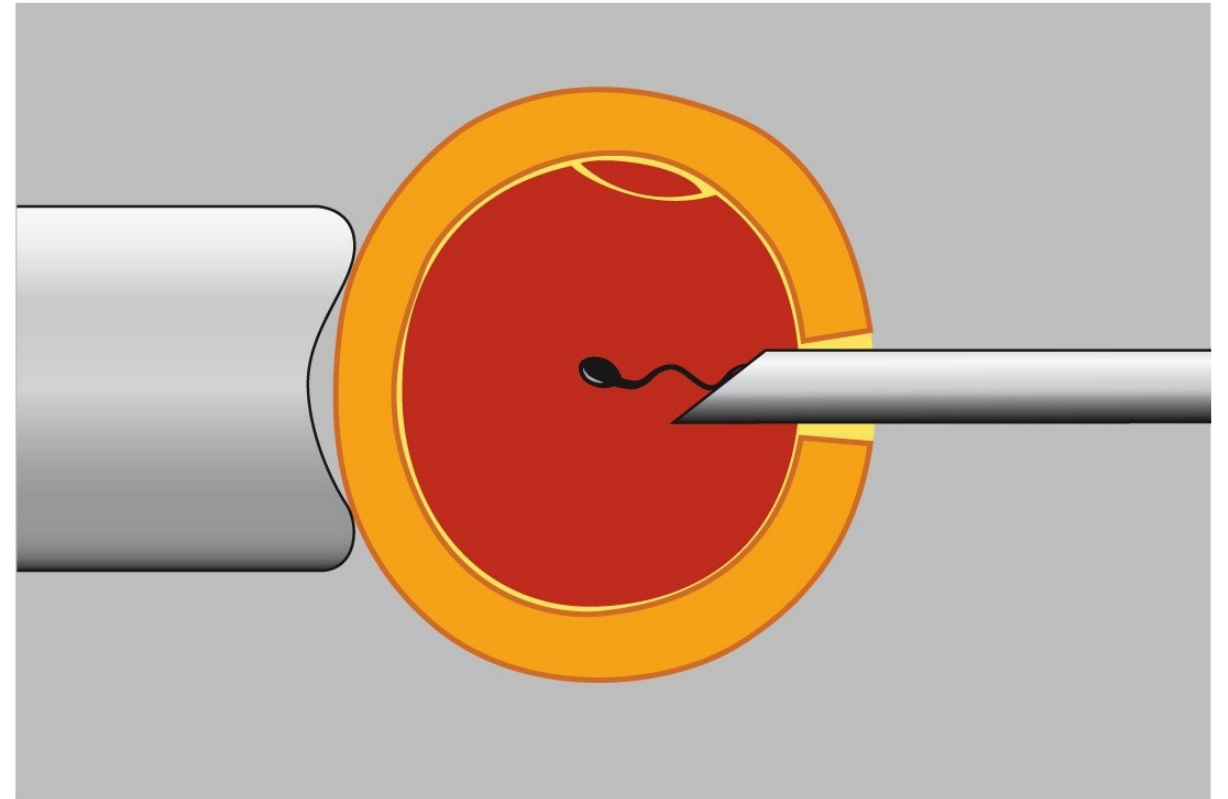
8-cell embryo after 72-hour-long cultivation



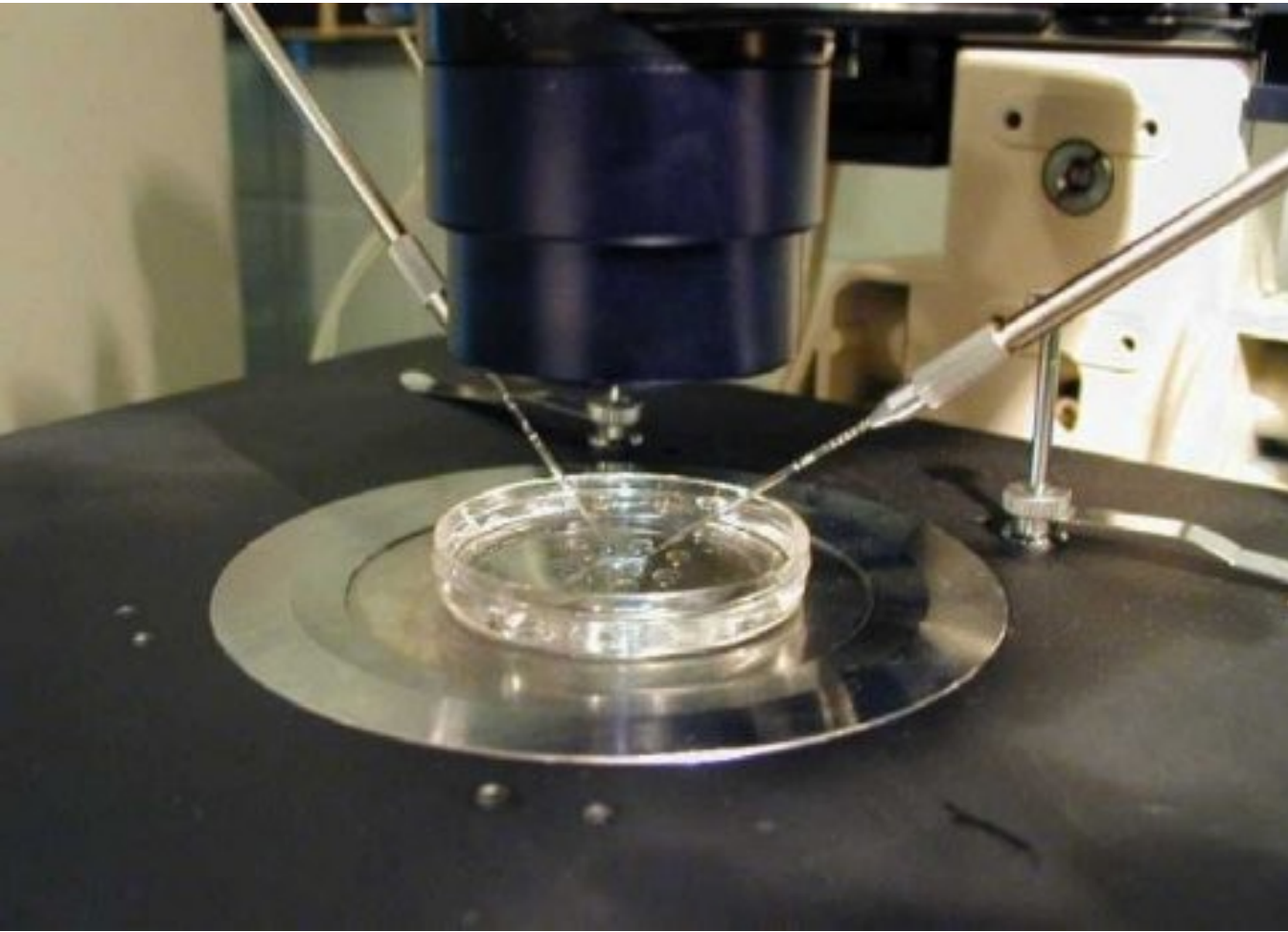
Blastocyst



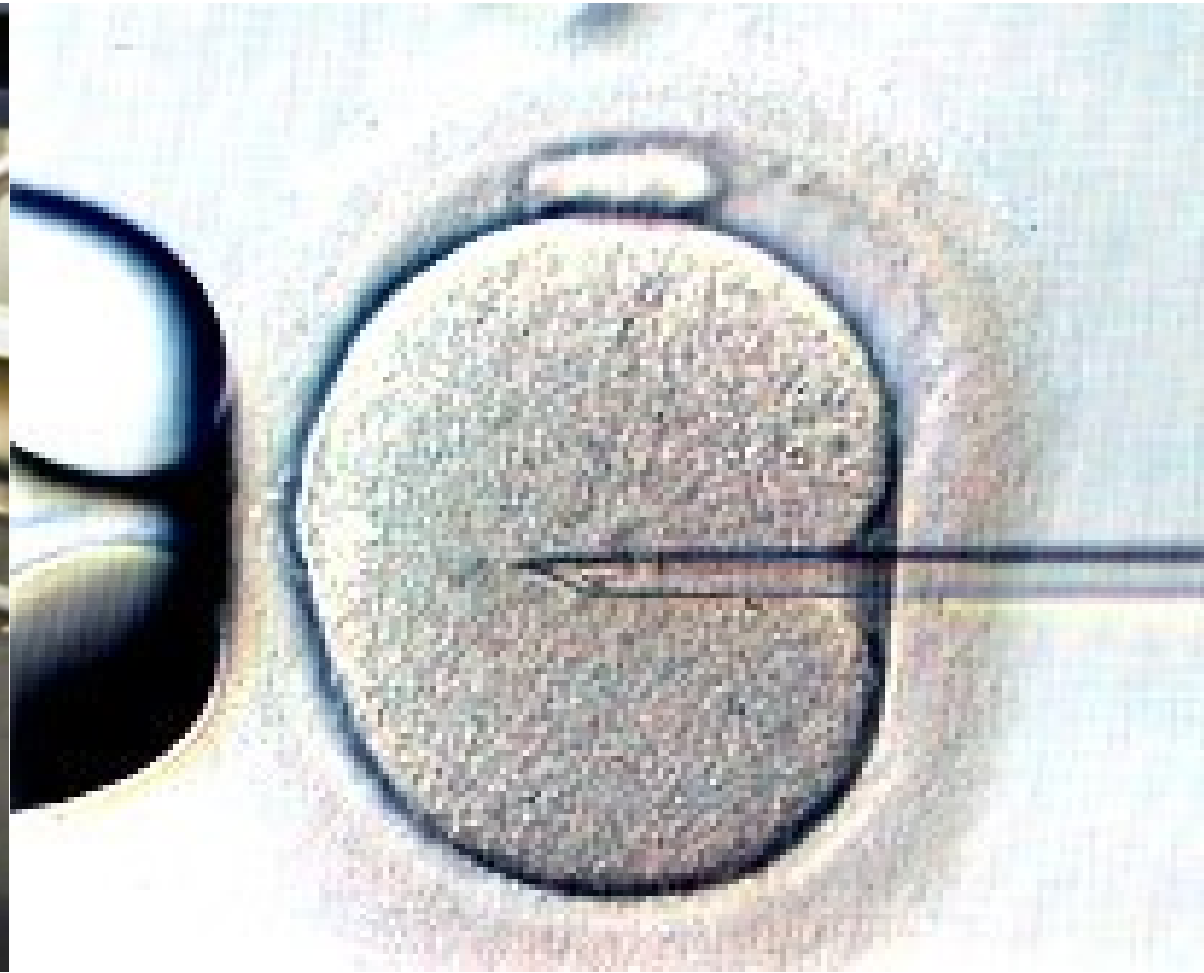
ICSI



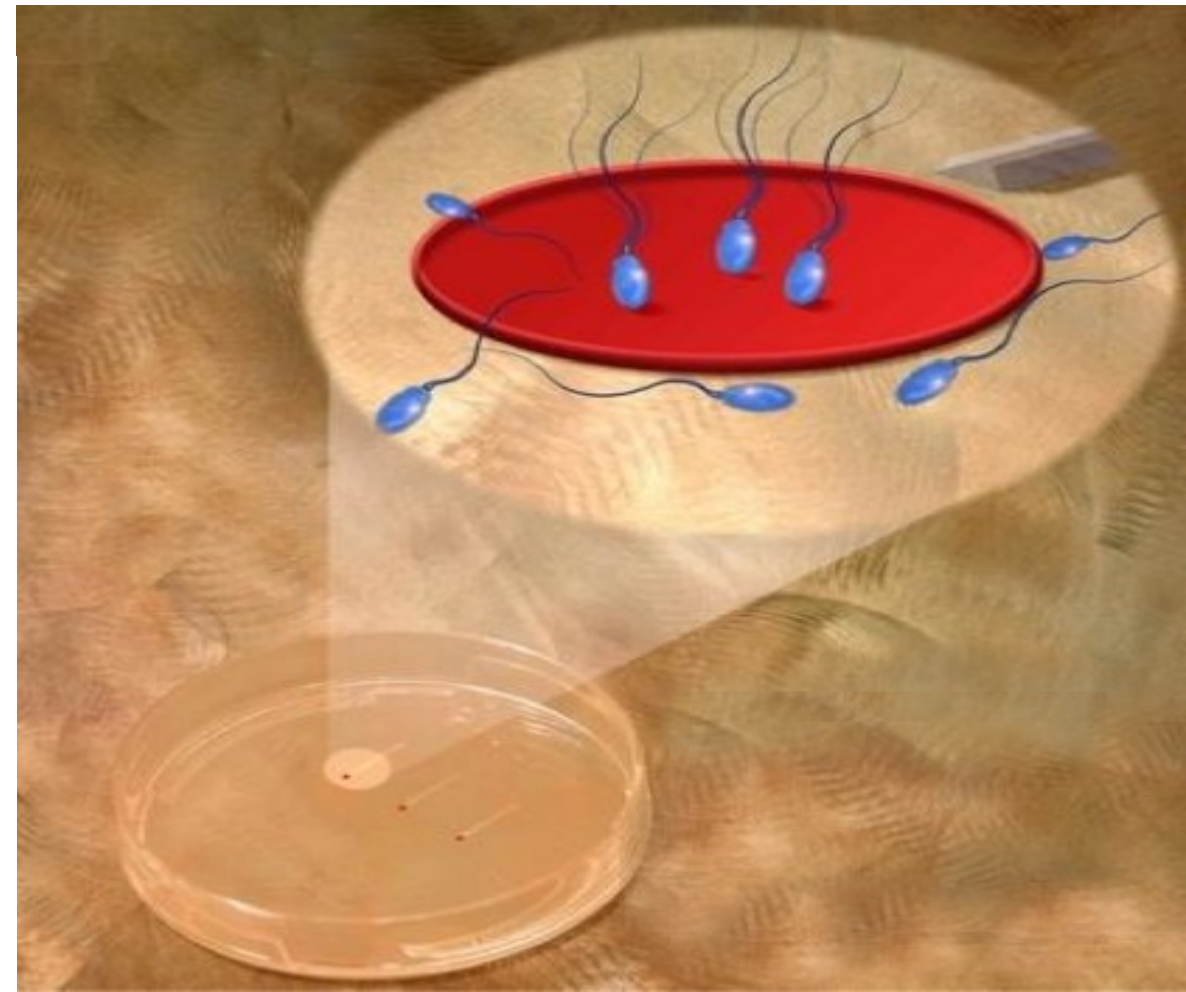
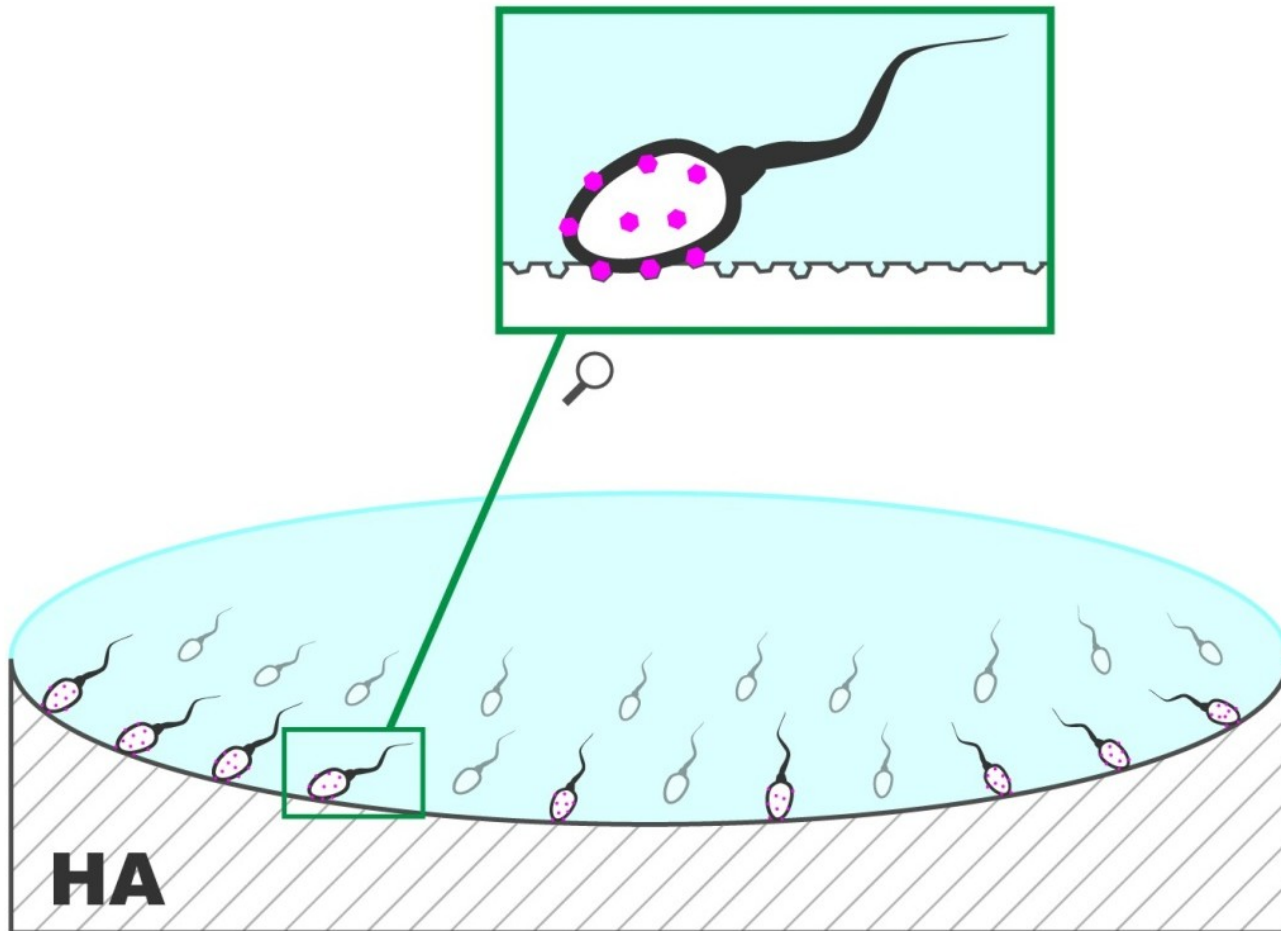
Micromanipulation pipettes



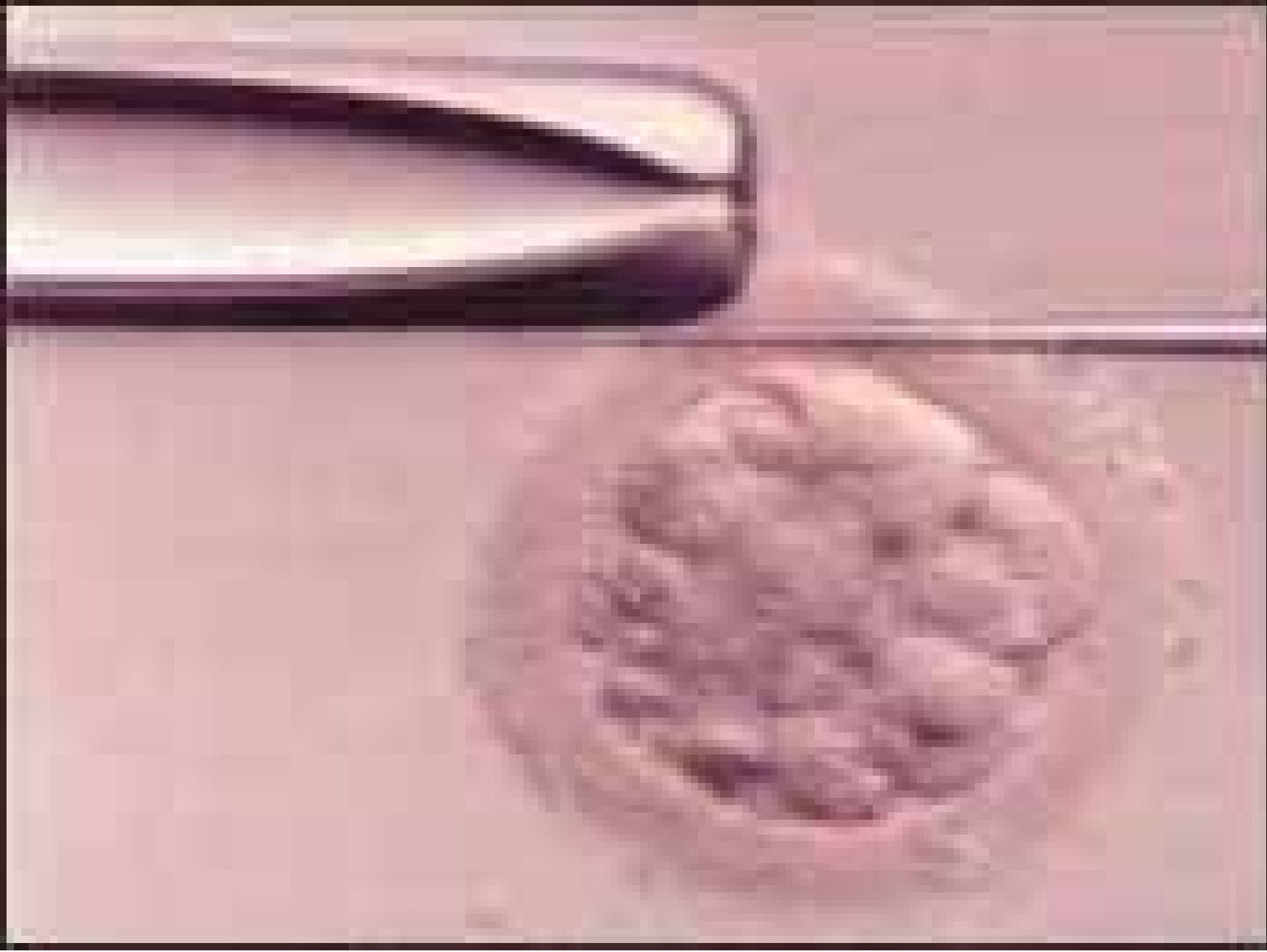
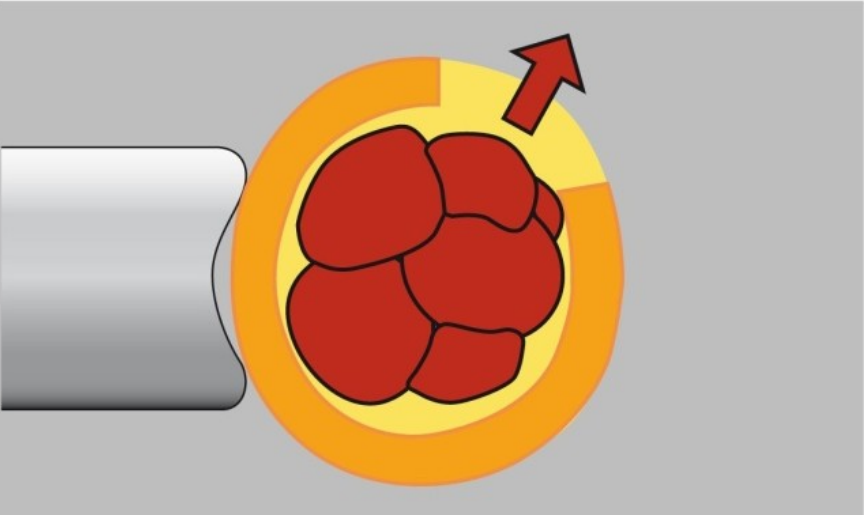
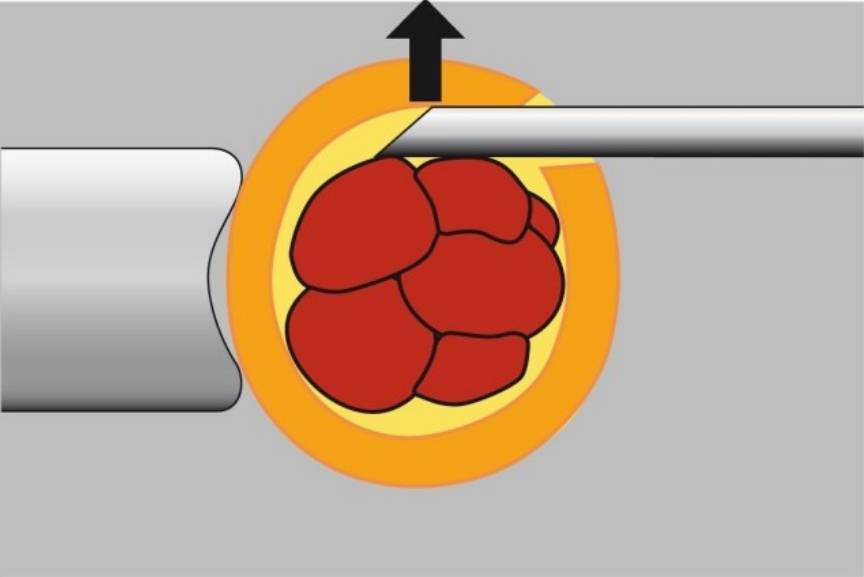
ICSI



Sperm selection – hyaluronan acid binding for PICSI

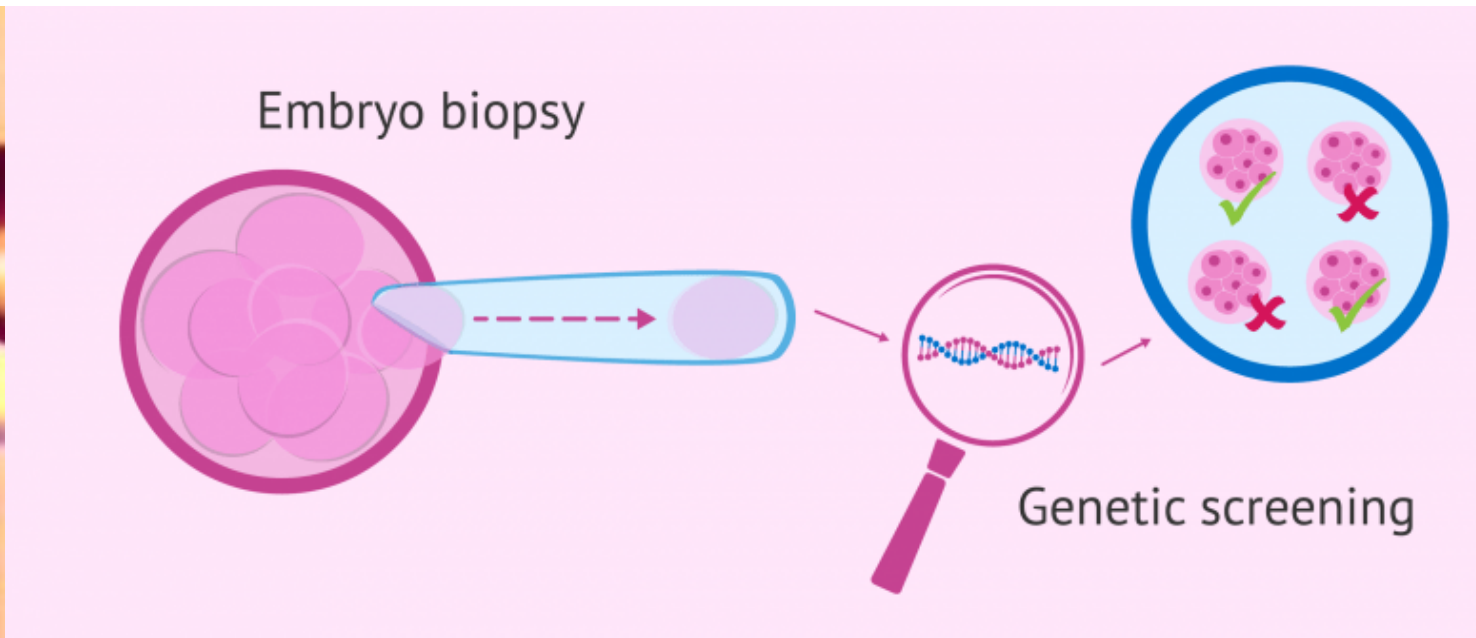


Assisted hatching (AH)



Pre-implantation diagnosis (PGD)

- the genetic profiling of embryos prior to implantation
- sampling on single cell taken from developing embryo
- usually takes place on the 5th day of the embryo's development



Cryoconservation (cryopreservation)

- process of freezing and storing embryos
- providing an additional chance for pregnancy
- saving embryos before certain treatments



Donor conception

- the eggs, sperm or embryos or both (double donation) from donors are used in order to conceive
- can be used in IUI or IVF
- donation is voluntary and anonymous
- some donor characteristics may be known (skin hair and eye color) – try to find the best match

Surrogacy

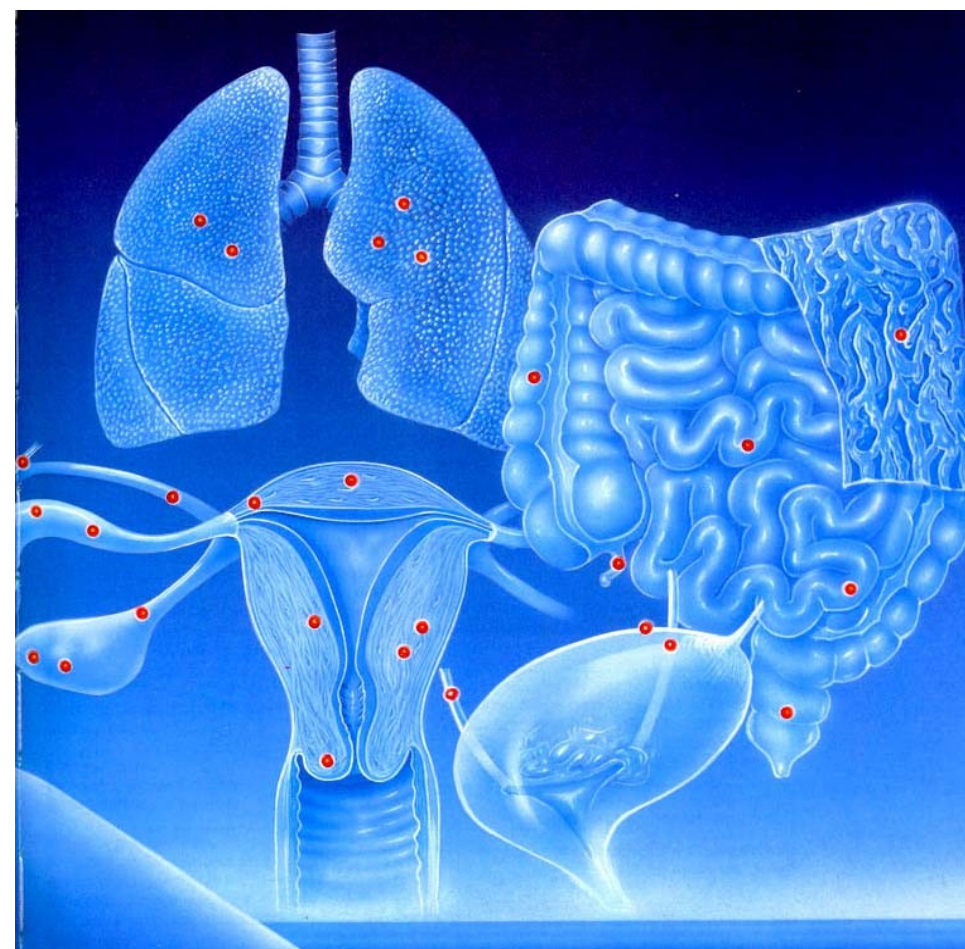
- arrangement, whereby a woman (the surrogate mother) agrees to bear a child for another person or person
- indications: abnormal uterus, post hysterectomy, congenital malformation of uterus, history of multiple miscarriages, (same sex couple)

Endometriosis

- The presence of **endometrial tissue in an abnormal anatomical location** (out of uterus)
- Endometrial tissue **respond to menstrual cycle** hormones, and bleed during the menstrual cycle
- between 6 and 10 percent of women of reproductive age worldwide
- Lot of theories of etiology (metaplastic, Sampson's retrograde menstruation theory, and many others)

Localisation of endometriosis

| | |
|--------------------------|-------------|
| Sacruterine ligg. | 63 % |
| Ovary | 56 % |
| C.Douglasi | 25 % |
| Vesica ur. | 20 % |
| Samps. Cyst | 20 % |
| Broad ligament | 8 % |
| Intestine | 6 % |



Risk factors

- **White race**
- **Early menarche**
- **Late menopause**
- **Nulliparity**
- **Obesity**
- **Short menstrual cycle**
- **Family history**

Symptoms

- 20-25% of women are asymptomatic
- **Pelvic pain/chronic pelvic pain**
- **Dysmenorrhea**
- **Dyspareunia**
- Dysuria
- Mittelschmerz – associated with ovulation
- **Infertility**
- diarrhoea/constipation
- Irregular/heavy period.....

Diagnosis

- Ultrasound examination / expert US examination
- DGL
- MRI
- Biopsy/histopathology

Therapy

- depends on: symptoms, age, fertility, stage, former therapy
- **Hormonal therapy:** COC, Progesterone, GnRH modulators
- NSAID
- **Surgery** – excision/resection endometrial endometriomas

**Thank you
for your
attention**



Questions

1. Normal sperm cell concentration is?

- A) 20 mil./ml
- B) 40 mil./ml
- C) 15 mil./ml.
- D) 35 mil./ml.

2. Ashenozoospermia means?

- A) reduced concentration
- B) reduced sperm motility
- C) abnormal morphology
- D) absence of spermatozoa (motile sperm)
- E) complete lack of semen

Questions

1. Normal sperm cell concentration is?

- A) 20 mil./ml
- B) 40 mil./ml
- C) 15 mil./ml.**
- D) 35 mil./ml.

2. Ashenozoospermia means?

- A) reduced concentration
- B) reduced sperm motility
- C) abnormal morphology
- D) absence of spermatozoa (motile sperm)
- E) complete lack of semen

Questions

1. Normal sperm cell concentration is?

- A) 20 mil./ml
- B) 40 mil./ml
- C) 15 mil./ml.**
- D) 35 mil./ml.

2. Ashenozoospermia means?

- A) reduced concentration (Oligozoospermia)
- B) reduced sperm motility**
- C) abnormal morphology (Teratozoospermia)
- D) absence of spermatozoa (motile sperm) (Azoospermia)
- E) complete lack of semen (Aspermia)

Questions

3. Which of the following does not belong to assisted reproduction methods?

- A) Ovulation stimulation
- B) In-vitro fertilisation
- C) Surrogacy
- D) Vasectomy

4. Infertility is ?

- A) Failure to achieve a pregnancy after two years of regular unprotected intercourse
- B) Failure to achieve a pregnancy after 6 months of regular unprotected intercourse
- C) Failure to achieve a pregnancy after 9 months unprotected intercourse
- D) Failure to achieve a pregnancy after one year of regular unprotected intercourse

Questions

3. Which of the following does not belong to assisted reproduction methods?

- A) Ovulation stimulation
- B) In-vitro fertilisation
- C) Surrogacy
- D) Vasectomy**

4. Infertility is ?

- A) Failure to achieve a pregnancy after two years of regular unprotected intercourse
- B) Failure to achieve a pregnancy after 6 months of regular unprotected intercourse
- C) Failure to achieve a pregnancy after 9 months unprotected intercourse
- D) Failure to achieve a pregnancy after one year of regular unprotected intercourse

Questions

3. Which of the following does not belong to assisted reproduction methods?

- A) Ovulation stimulation
- B) In-vitro fertilisation
- C) Surrogacy
- D) Vasectomy**

4. Infertility is ?

- A) Failure to achieve a pregnancy after two years of regular unprotected intercourse
- B) Failure to achieve a pregnancy after 6 months of regular unprotected intercourse
- C) Failure to achieve a pregnancy after 9 months unprotected intercourse
- D) Failure to achieve a pregnancy after one year of regular unprotected intercourse**

Questions

5. Which of the following does not belong to infertility diagnostic methods?

- A) Anti-Müllerian Hormon (AMH)
- B) SONO-Hysterosalpingography
- C) Curettage
- D) Diagnostic laparoscopy

6. MESA is indicated for sperm retrieval in case of?

- A) failure of TESA method
- B) occlusion between epididymis and urethra
- C) oligospermia
- D) Occlusion between ovarium and uterus

Questions

5. Which of the following does not belong to infertility diagnostic methods?

- A) Anti-Müllerian Hormon (AMH)
- B) SONO-Hysterosalpingography
- C) Curettage**
- D) Diagnostic laparoscopy

6. MESA is indicated for sperm retrieval in case of?

- A) failure of TESA method
- B) occlusion between epididymis and urethra
- C) oligospermia
- D) Occlusion between ovarium and uterus

Questions

5. Which of the following does not belong to infertility diagnostic methods?

- A) Anti-Müllerian Hormon (AMH)
- B) SONO-Hysterosalpingography
- C) Curettage**
- D) Diagnostic laparoscopy

6. MESA is indicated for sperm retrieval in case of?

- A) failure of TESA method
- B) occlusion between epididymis and urethra**
- C) oligospermia
- D) Occlusion between ovarium and uterus

Questions

7. Which is the most common symptom of endometriosis?

- A) missed periods
- B) rapid weight loss
- C) chronic pelvic pain
- D) vomiting

8. Which of the following is not a risk factor for Endometriosis?

- A) long menstrual cycle
- B) nulliparity
- C) late menopause
- D) early menarche

Questions

7. Which is the most common symptom of endometriosis?

- A) missed periods
- B) rapid weight loss
- C) chronic pelvic pain**
- D) vomiting

8. Which of the following is not a risk factor for Endometriosis?

- A) long menstrual cycle
- B) nulliparity
- C) late menopause
- D) early menarche

Questions

7. Which is the most common symptom of endometriosis?

- A) missed periods
- B) rapid weight loss
- C) chronic pelvic pain**
- D) vomiting

8. Which of the following is not a risk factor for Endometriosis?

- A) long menstrual cycle**
- B) nulliparity
- C) late menopause
- D) early menarche