ASSISTED REPRODUCTIVE TECHNOLOGIES (ART)

Dr. Herve Lucas, MD, PhD,
Biologist, Andrologist
Dr. Taher Elbarbary, MD
Gynecologist-Obstetrician

Definitions of Assisted Reproductive Technologies

Techniques involving oocyte retrieval and ejaculated sperm:

- Gamete Intra-Fallopian transfer (GIFT), Peritoneal Oocyte Sperm Transfer (POST)
- Zygote Intra-fallopian Transfer (ZIFT).
- In Vitro Fertilization (IVF)
- Tubal Embryo Transfer (TET)

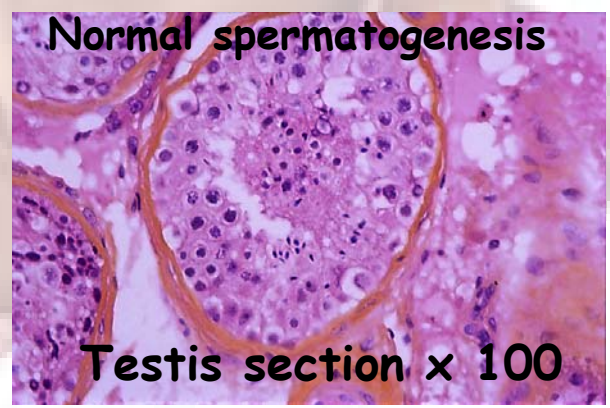
Techniques Including sperm retrieval:

- Testicular Sperm Aspiration (TESA)
- Per-cutaneous Epididymal Sperm Aspiration (PESA)
- Microsurgical Epididymal sperm Aspiration (MESA)
- Non-Scalpel Vasal Sperm Aspiration (NSVSA)

For injection:

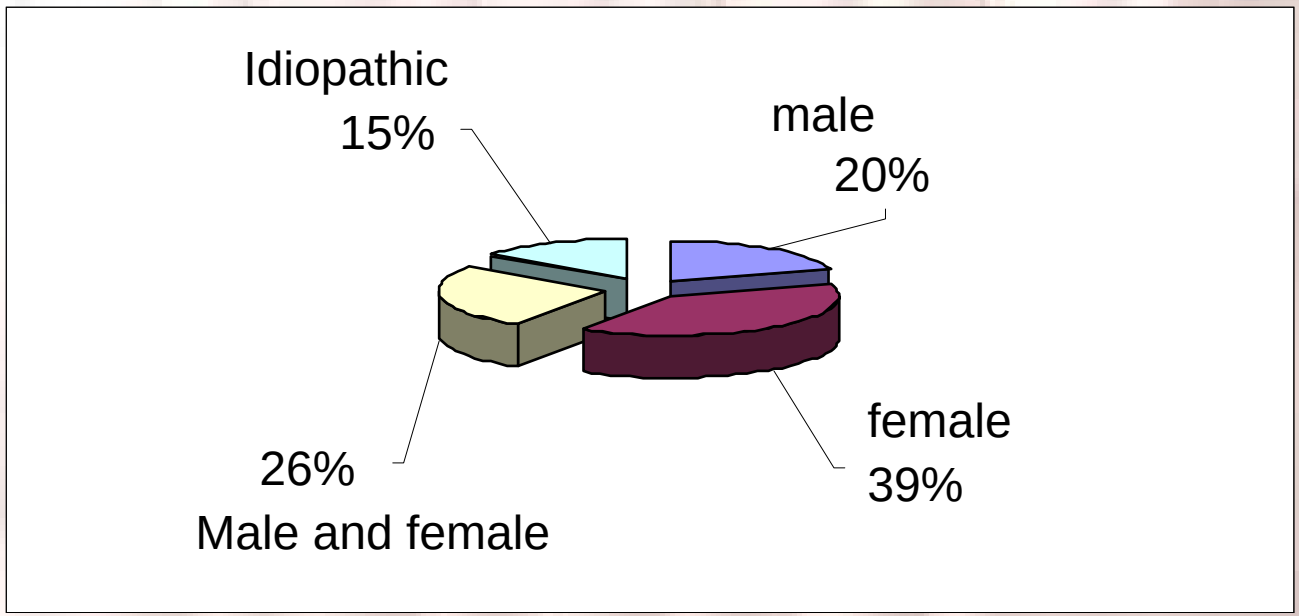
- Intra-Cytoplasmic Sperm Injection (ICSI)

Don't forget artificial Insemination…easy, low cost…!



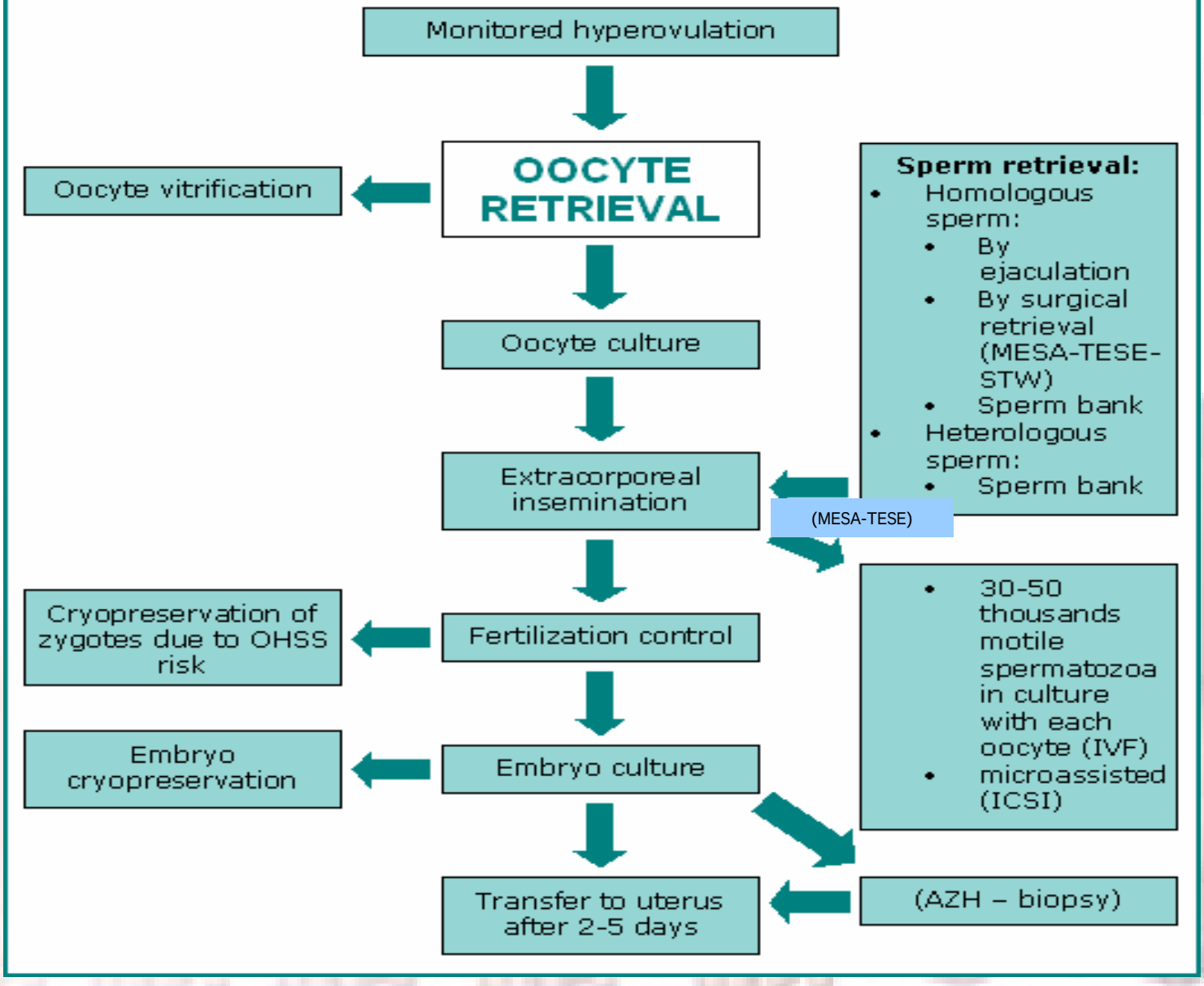
Who are the candidates of ART ?

15 % of European couples who want to conceive

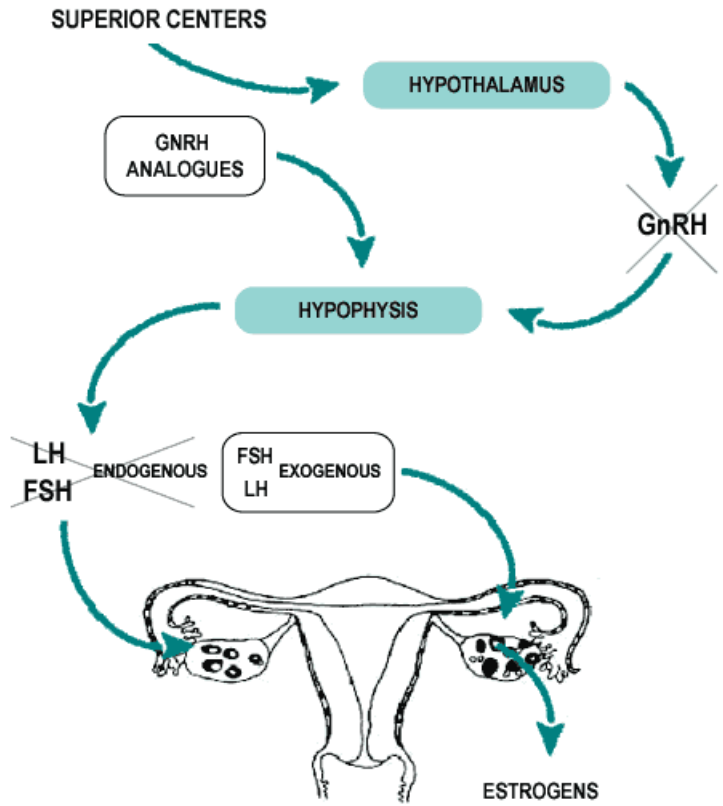


Indications for ART *including artificial inseminations…*

Steps of ART


Monitored hyperovulation
OOCYTE RETRIEVAL
Oocyte vitrification
Oocyte culture
Extracorporeal insemination
Cryopreservation of zygotes due to OHSS risk
Fertilization control
Embryo cryopreservation
Embryo culture
Transfer to uterus after 2-5 days
Sperm retrieval:
Homologous sperm:
By ejaculation
By surgical retrieval (MESA-TESE-STW)
Sperm bank
Heterologous sperm:
Sperm bank
(MESA-TESE)
30-50 thousands motile spermatozoa in culture with each oocyte (IVF)
microassisted (ICSI)
(AZH – biopsy)

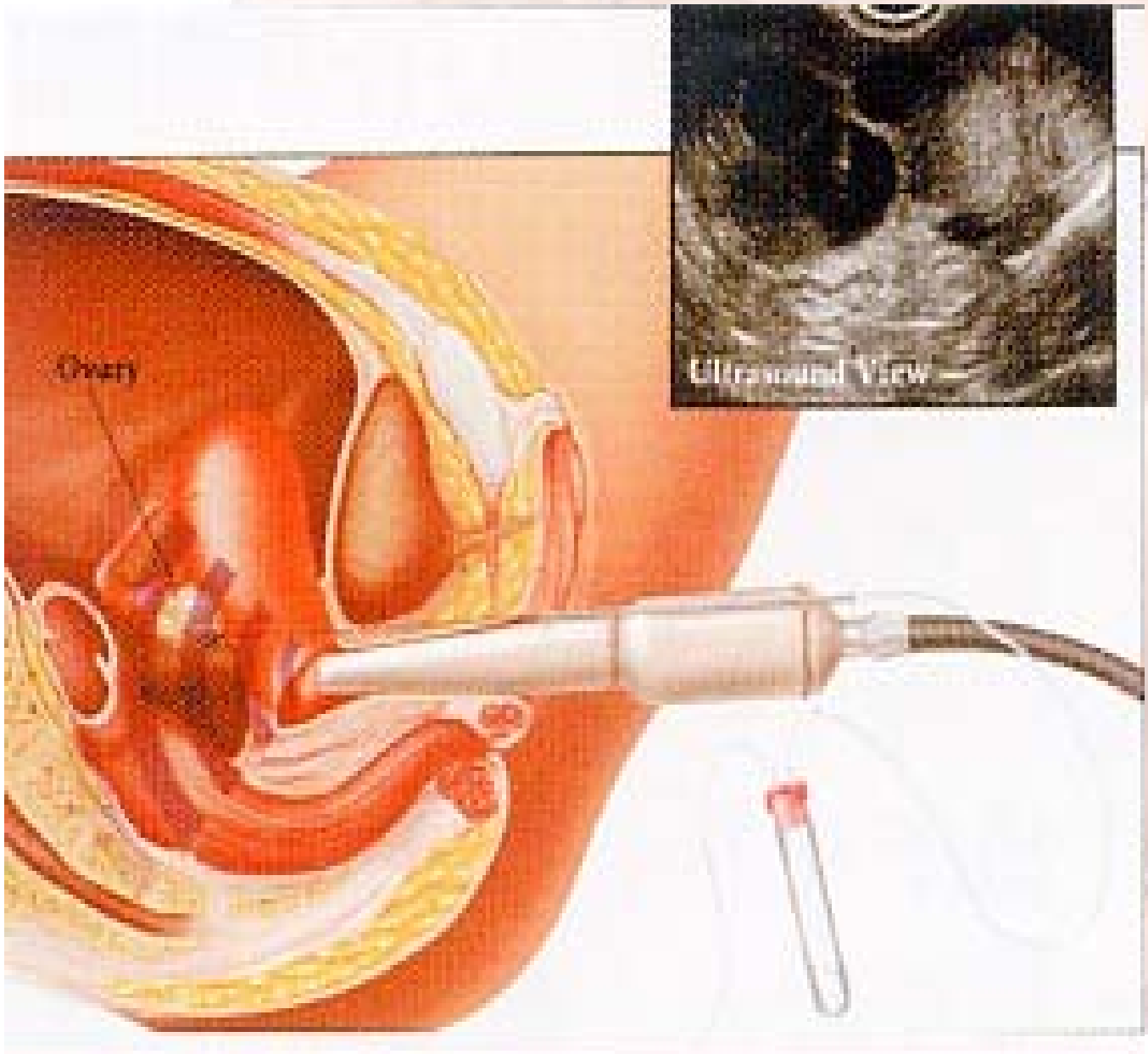
PATIENT STIMULATION



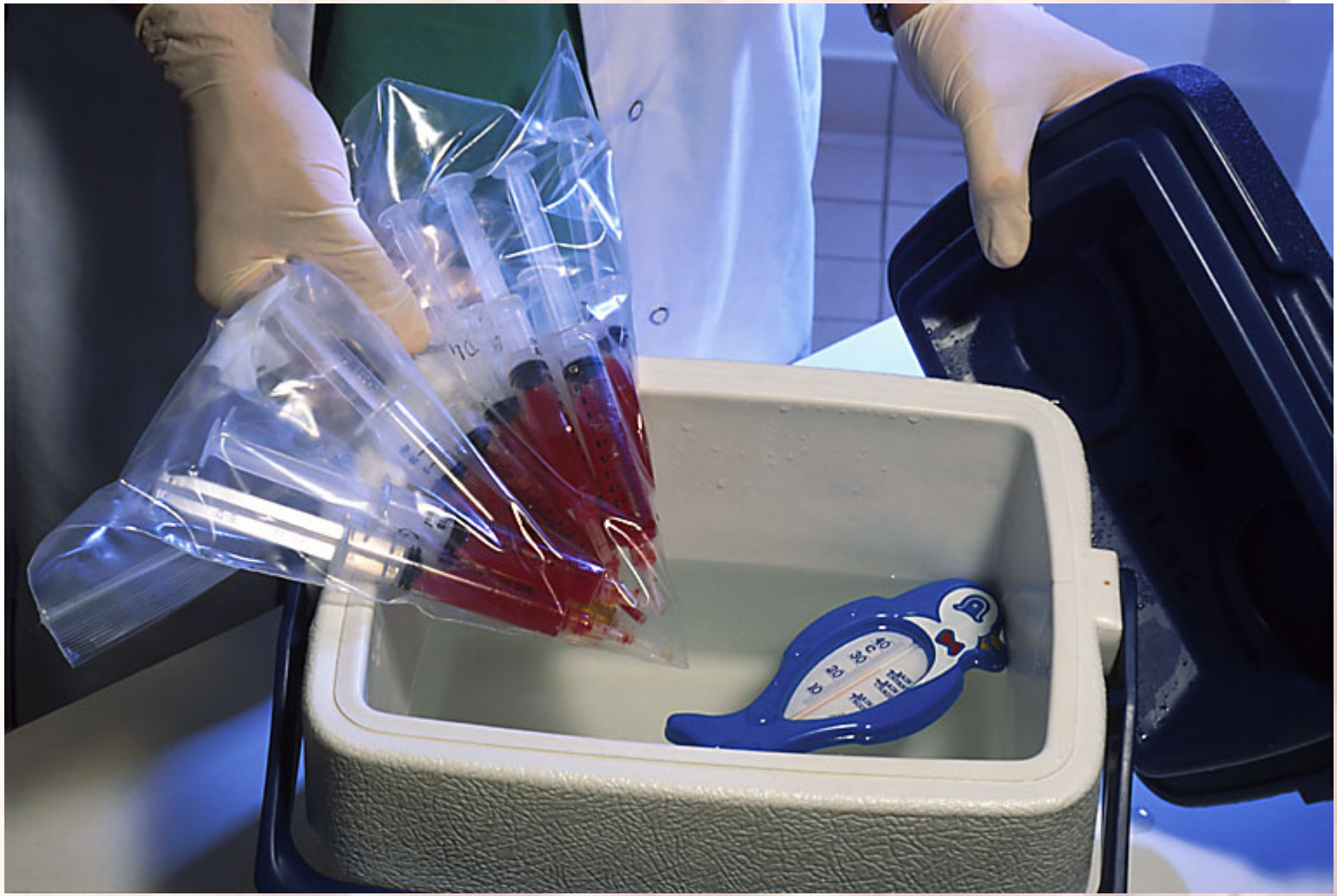
US image of multiple ovarian follicles

Serum estradiol level

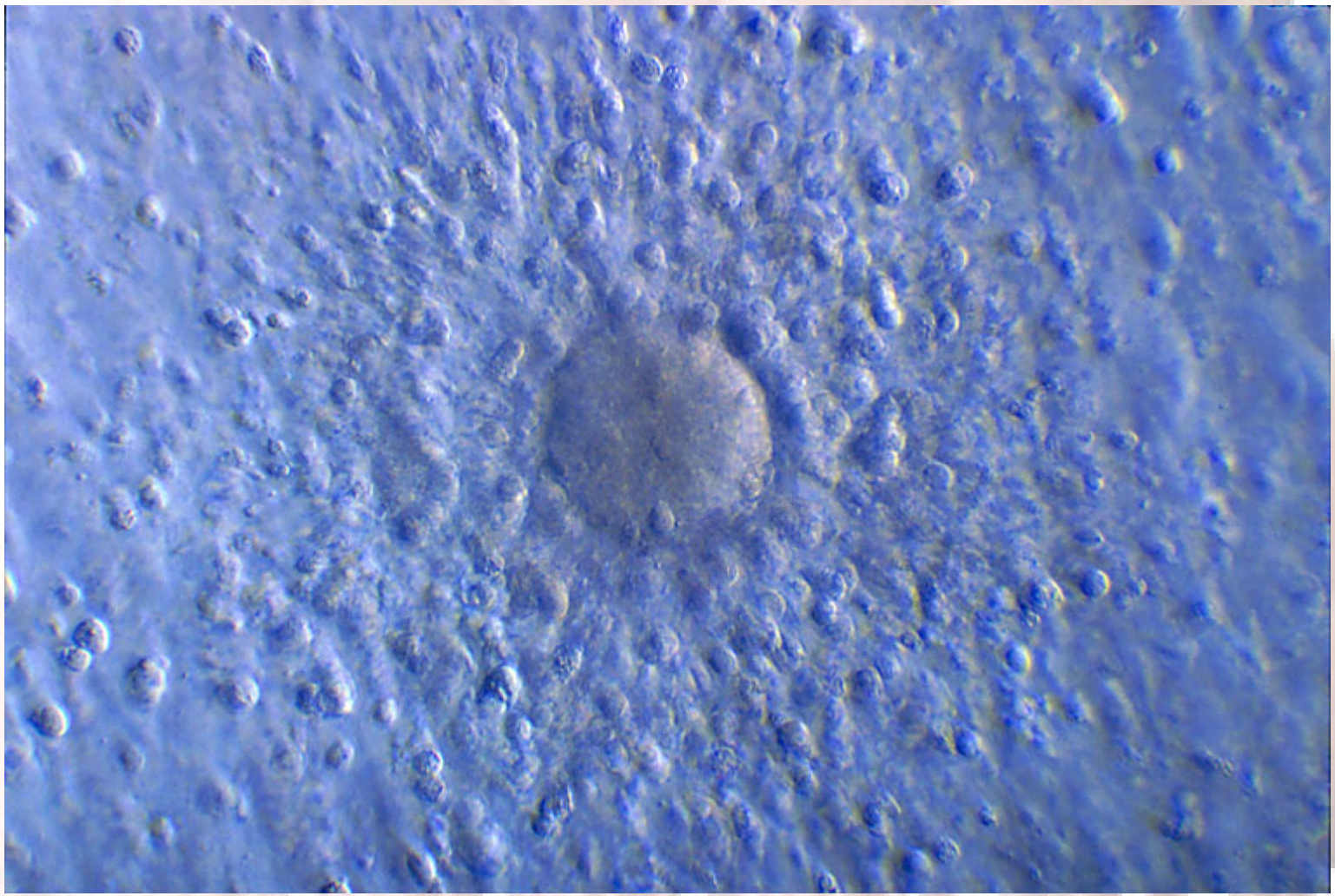
Oocyte retrieval



Syringes with cumulus-oocyte complex in follicular fluid



Cumulus-oocyte complex



Sperm preparation (various techniques for various utilisations, AI, IVF, ICSI, GIFT…)

1- Sperm retrieval

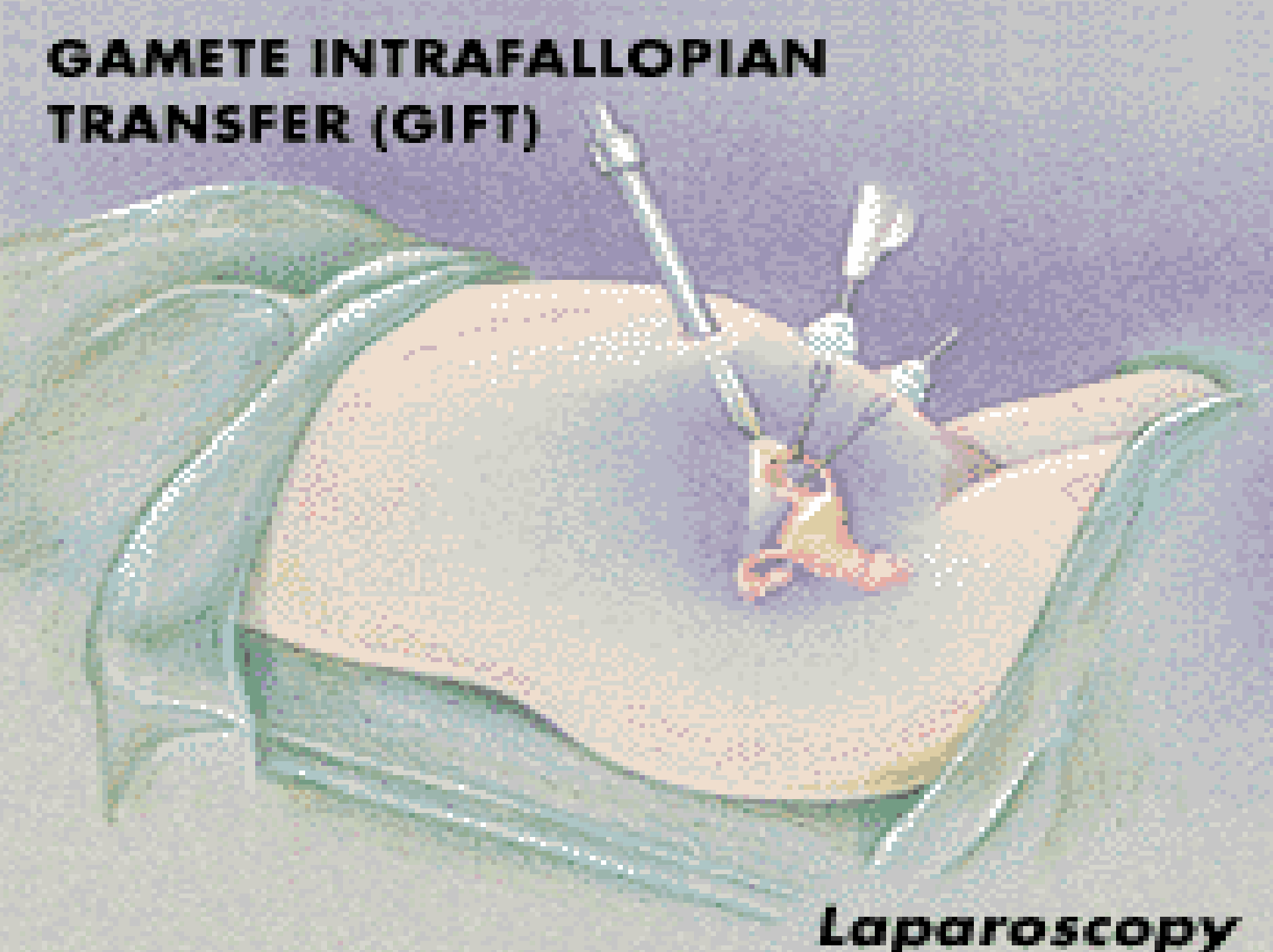
2- Sperm washing

Adaptation of the sperm preparation :

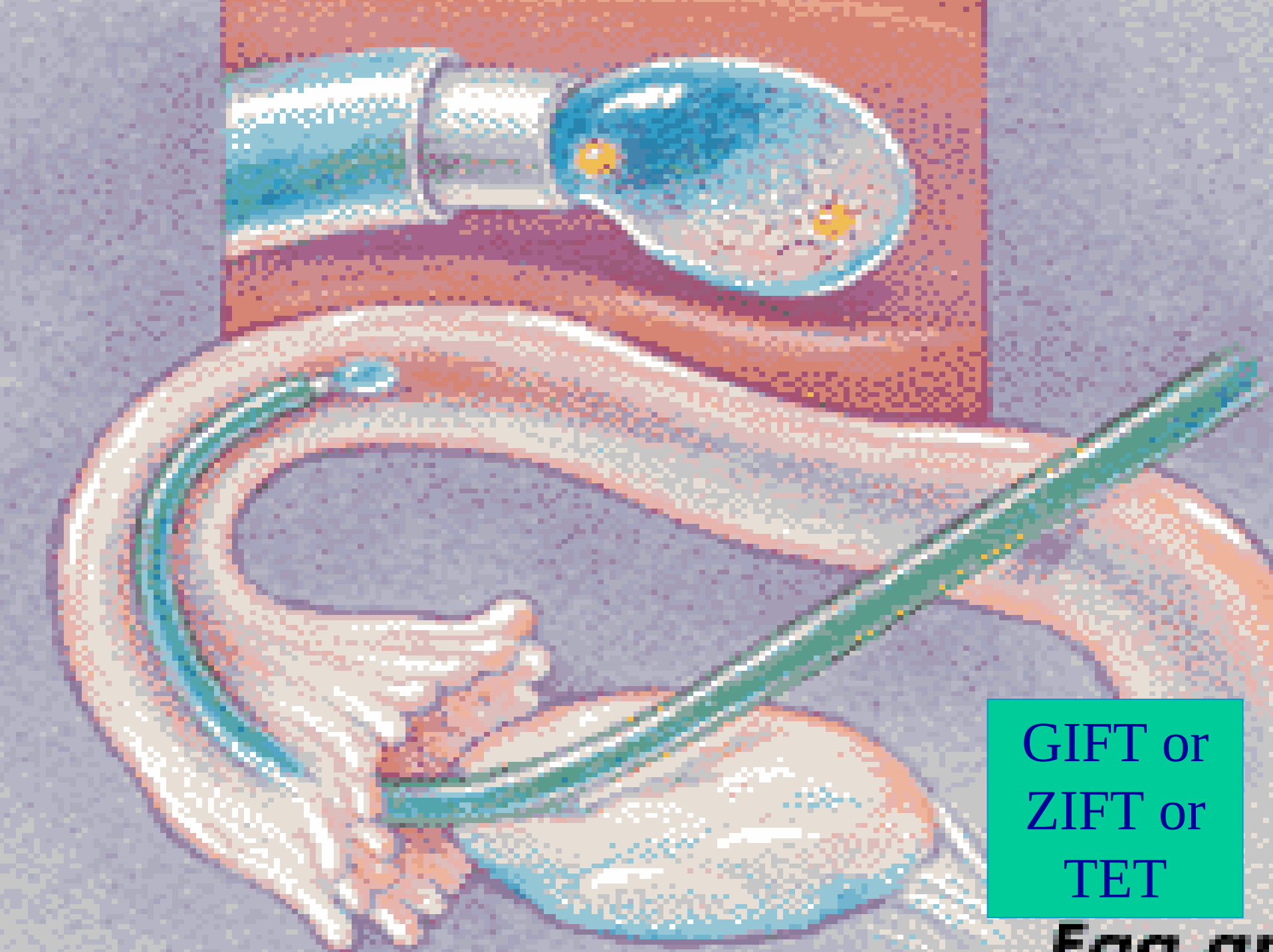
- **Ejaculate vs freezing-thawed,**
- **Very poor sperm vs normospermia,**
- **Ejaculate vs testicular or epididymal,**
- **Sperm with antisperm-antibodies,**
- **Retro-ejaculated sperm….**

Artificial inseminations (indication : >1M motile spz, tubes OK..)

GAMETE INTRAFALLOPIAN TRANSFER (GIFT)

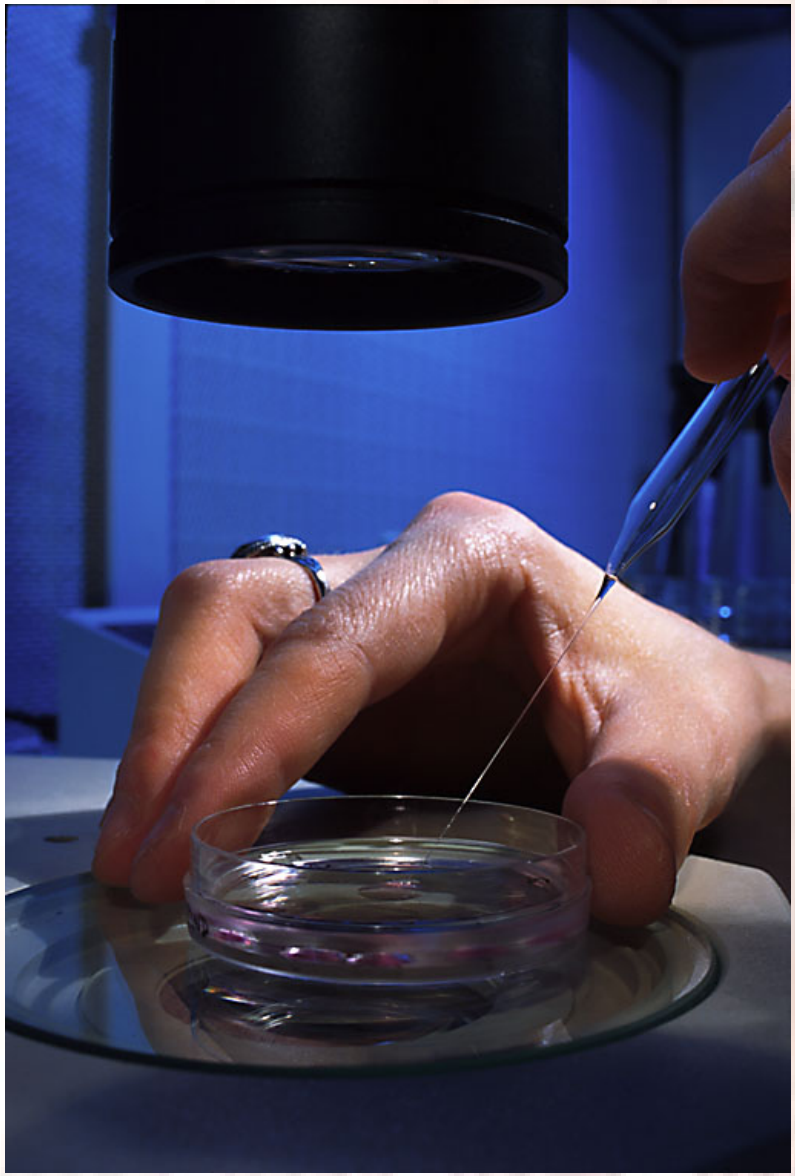


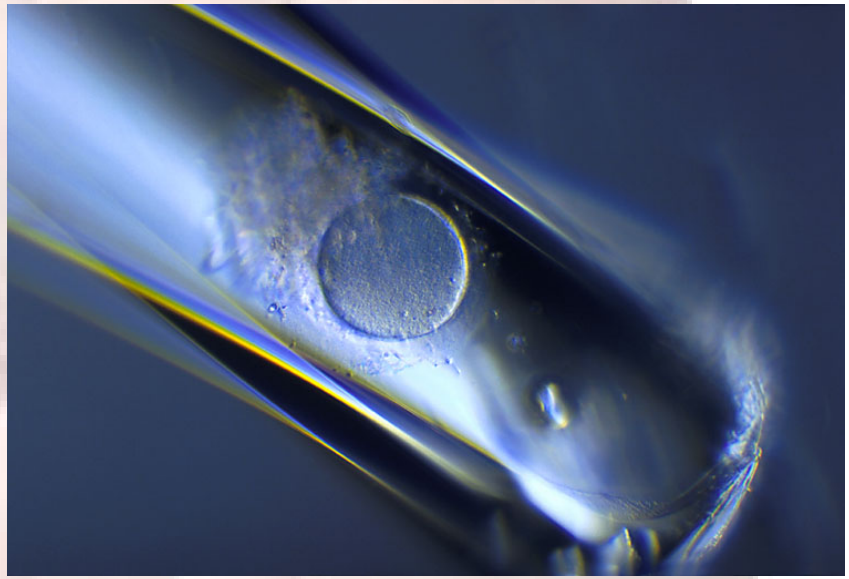
Laparoscopy


GIFT or
ZIFT or
TET

ICSI

Day (0): Decoronization of mature oocytes before injection (MII)

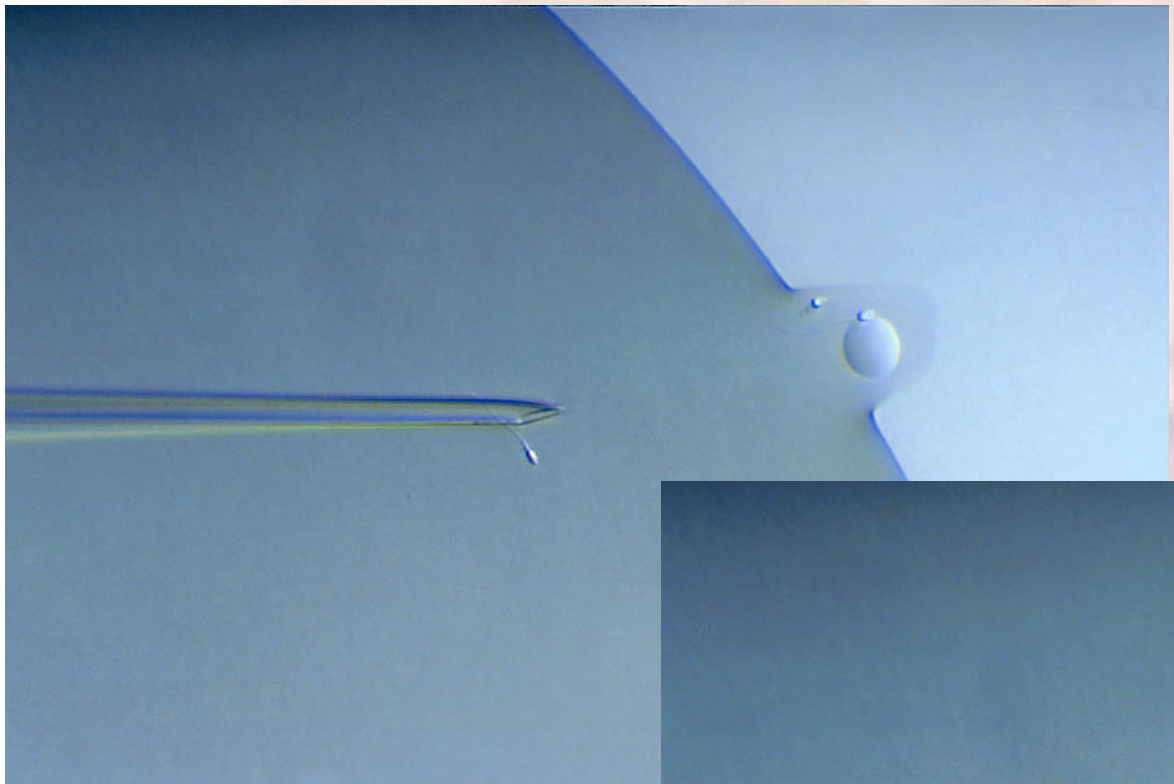


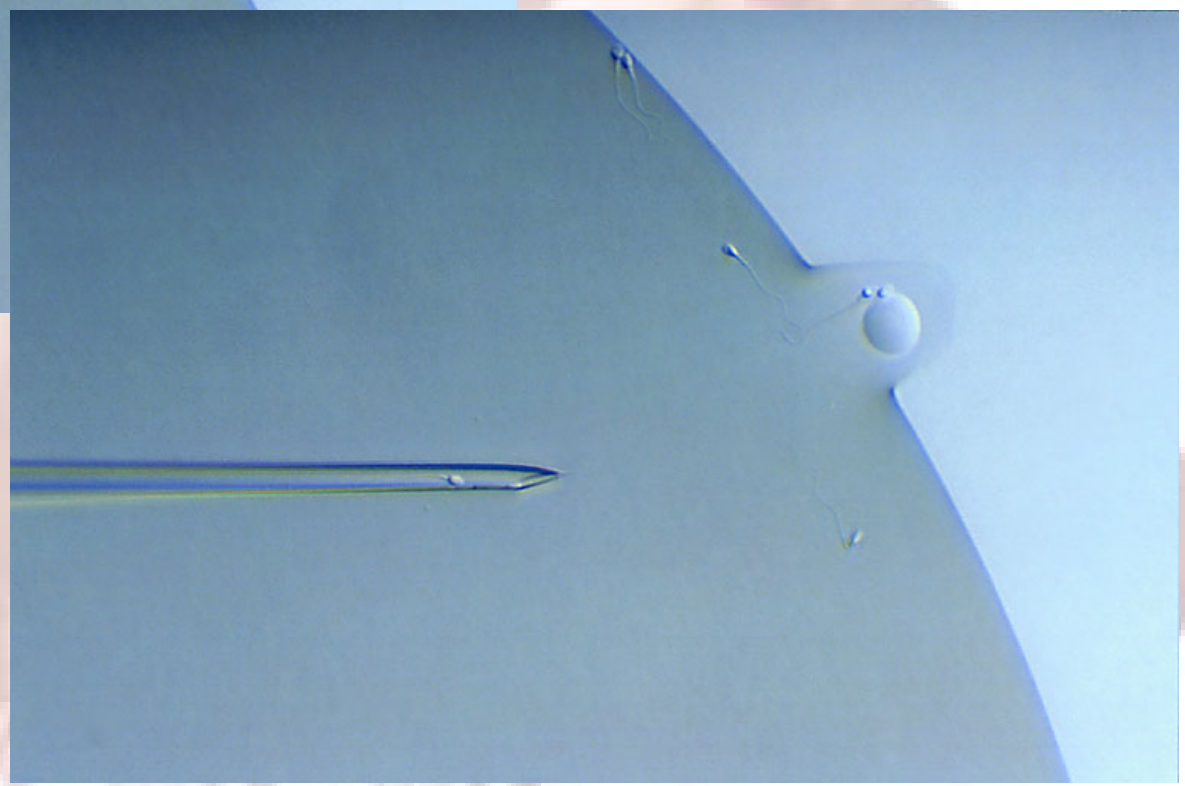


ICSI

Day (0)

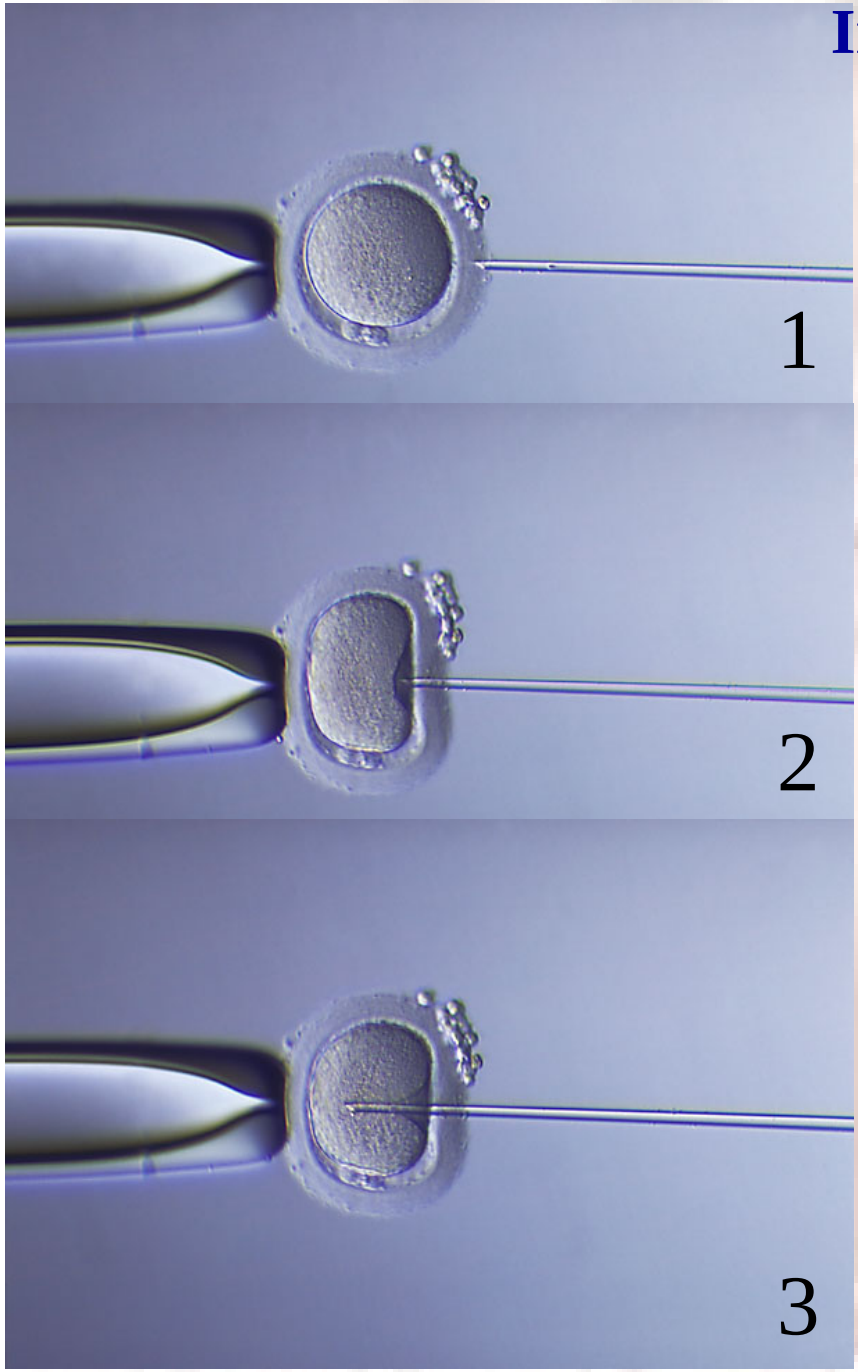
Day (0): Catch a single sperm with the injection pipette

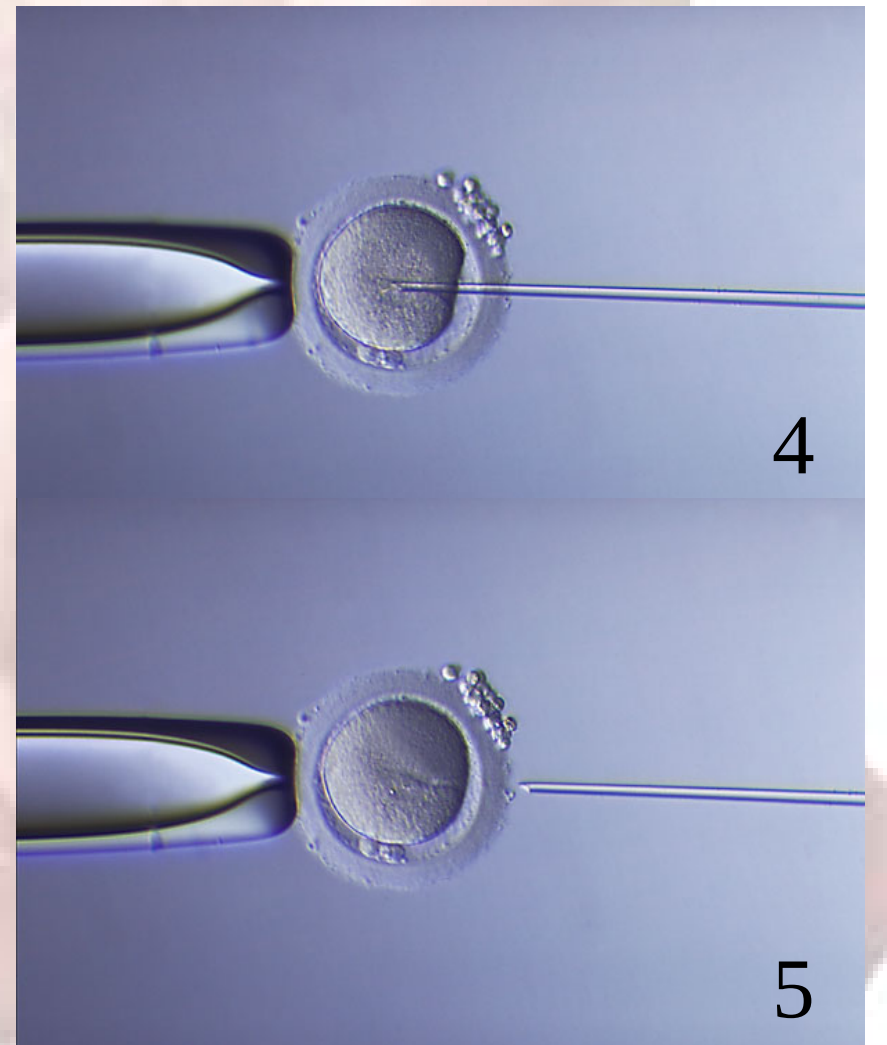




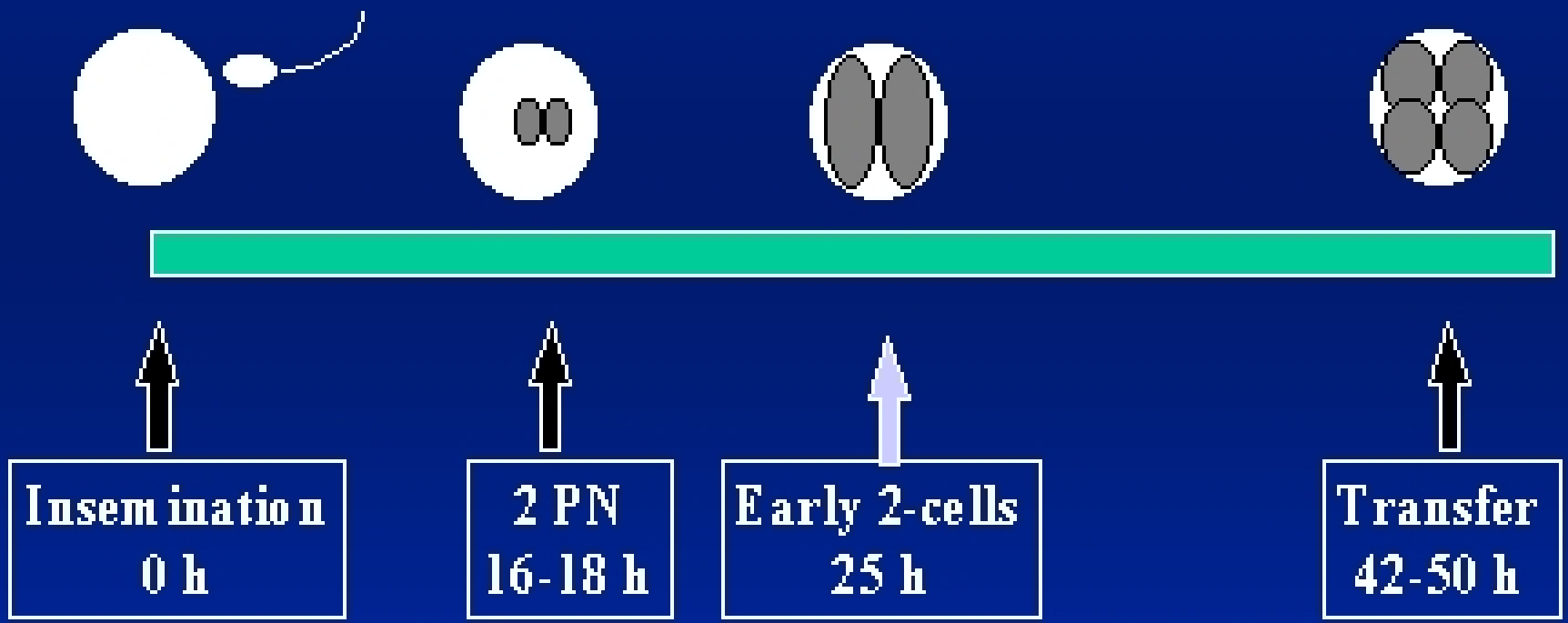
ICSI

Intra-Cytoplasmic Sperm Injection
Day (0)



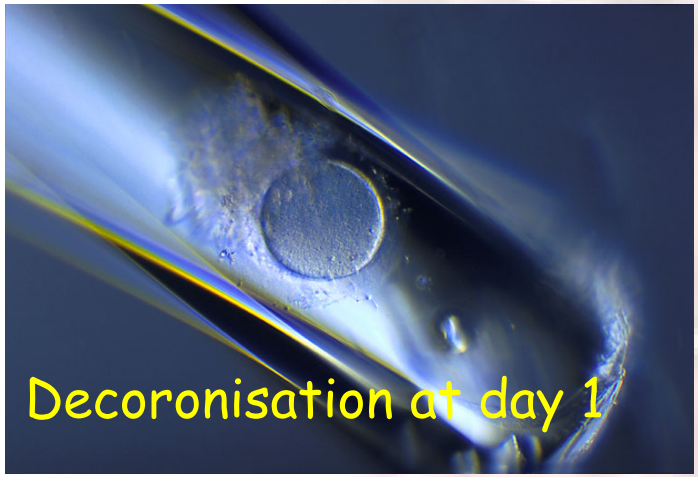


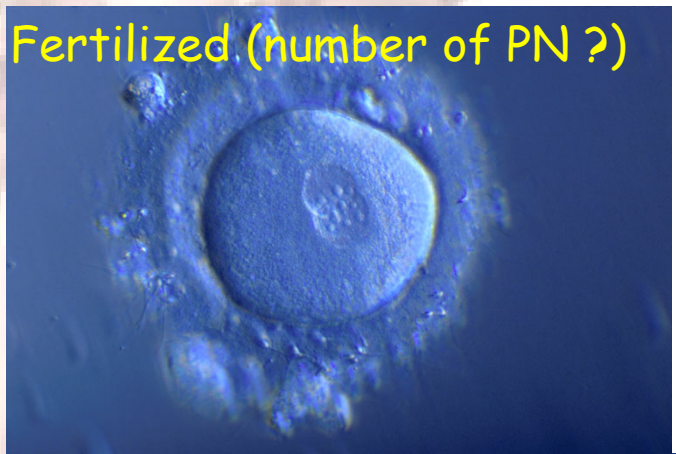
Fertilization control…and embryo development.



Observation of zygotes

Day (1) 16-18 h post-classical IVF





Fertilization rate :

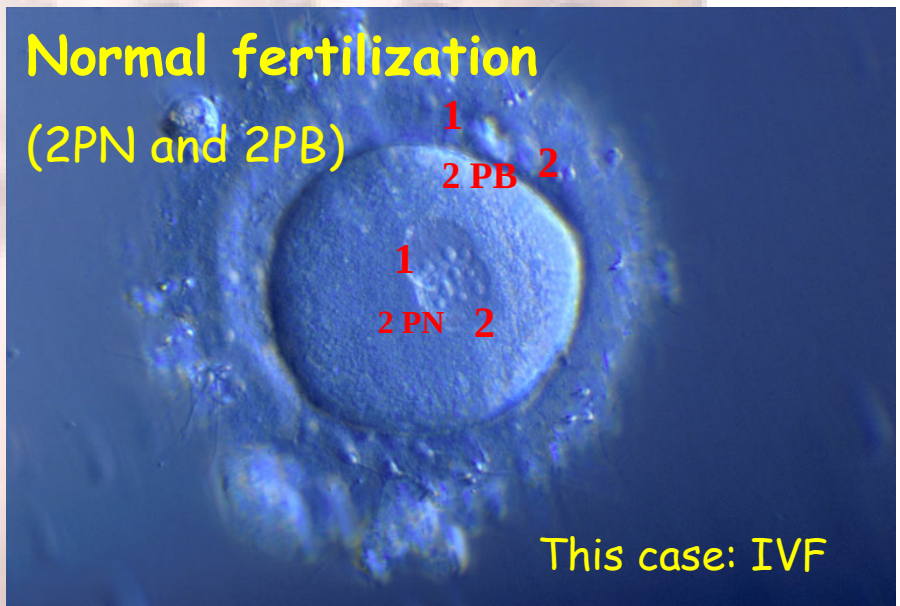
Observation of zygote

Day (1) 16-18h post IVF or ICSI

1 PN zygote : problem of oocyte activation ? (spz or nuclus oocyte origin ?).

3 PN after ICSI : non extrusion of the second polar body… by lesion of meiotic spindle ?

3 PN after IVF : polyspermia = too many spz inseminated or bad quality oocyte because abnormal cortical granules)

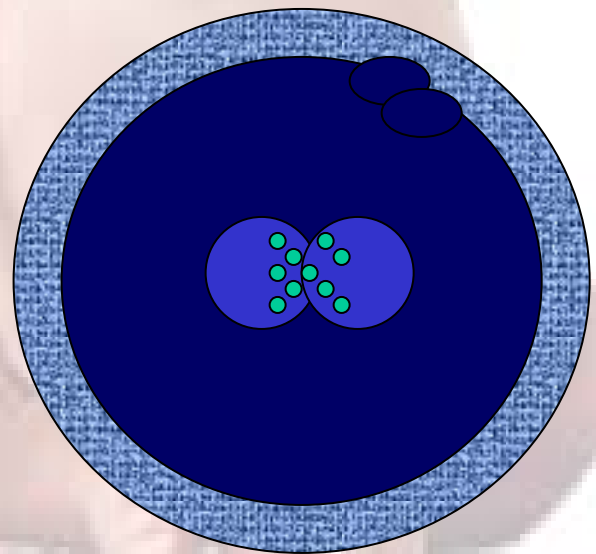


Scoring of zygotes…

Correlated with embryo quality (J2-J3)

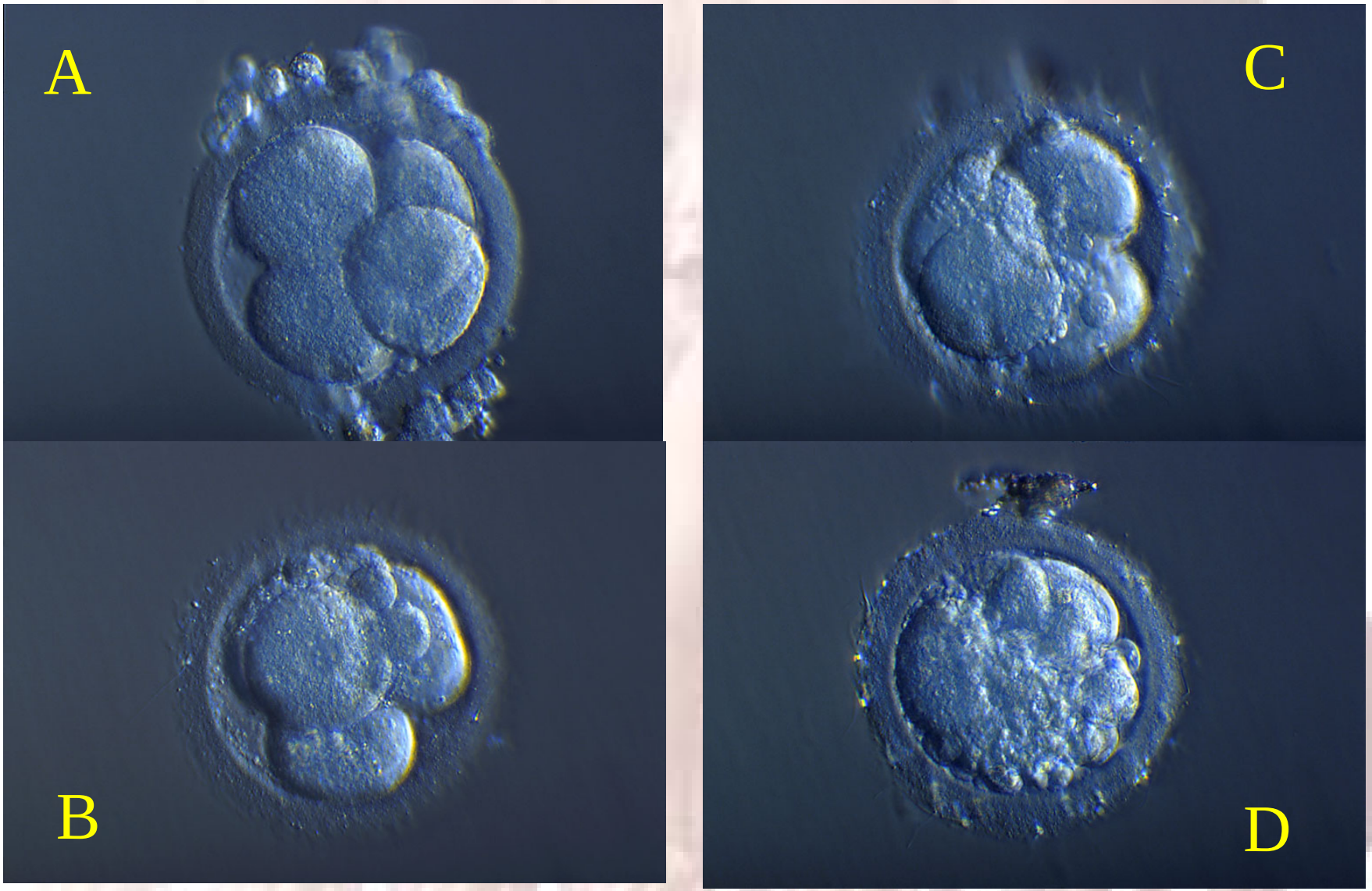
•Day (1) (PM) two cell embryo : the early cleavage (25 h),

The same indication :
good timing in embryo development.

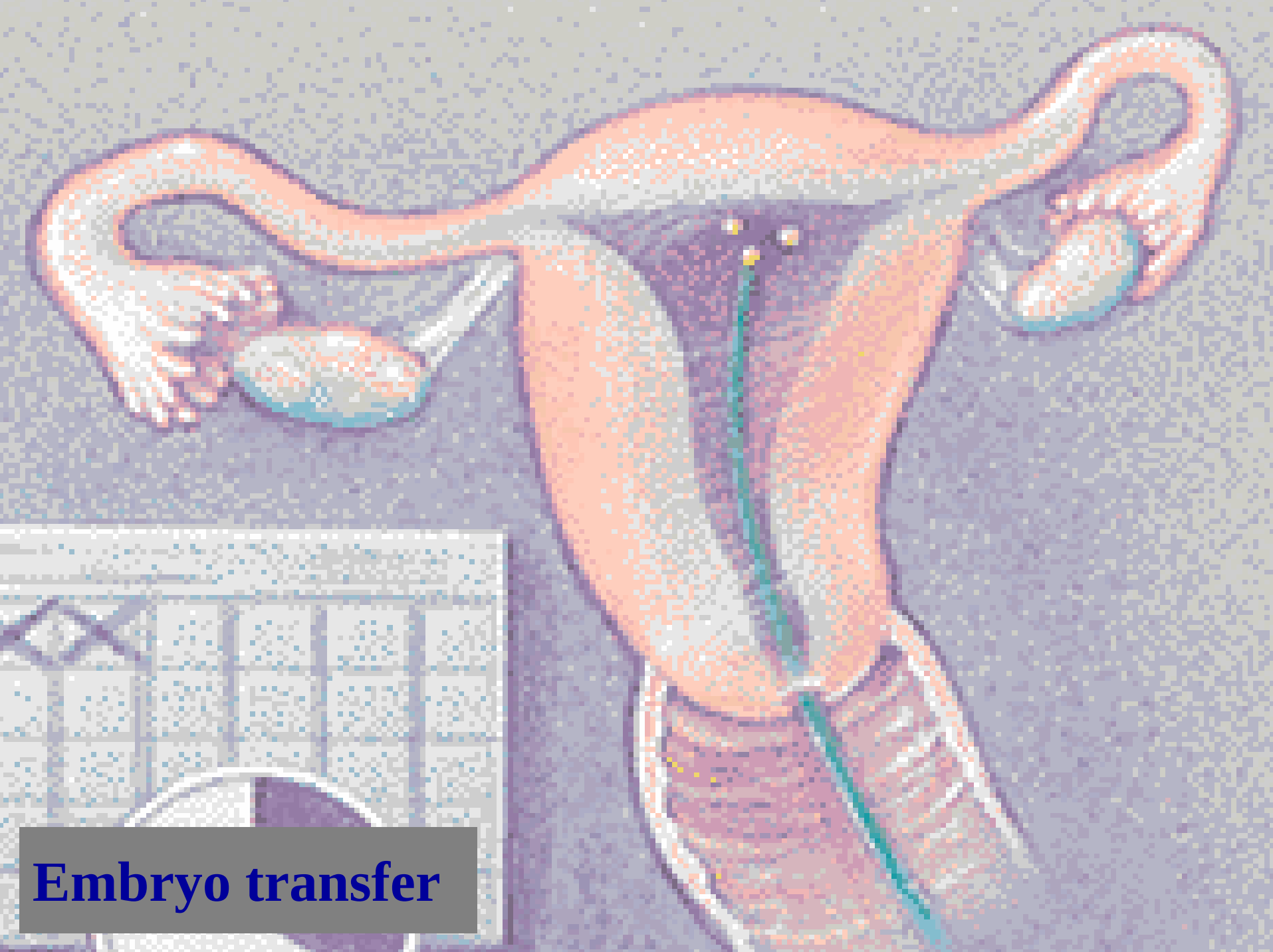


•Day (1) (AM) Zygote stage : best scoring zygote (16h),

Day (2): 4-cell stage embryo quality.



Day (4): Morula stage


Embryo transfer

What are the risks of ART ?

Risk due to ovarian stimulation ?

Risk due to oocyte retrieval ?

Risk due to embryo transfer ? Multiple pregnancies

Risk due to ICSI ? Increased !!!

Double in comparison with naturally obtained pregnancy (male genetic analysis in oligospermia)

Risk due to Classical IVF ?

Increased in comparison with naturally obtained pregnancy (bias of observation of the children ? Techniques *in vitro* ?)

What are the success rates of ART ?

IVF

Deliveries per retrieval …….. 29.1%

ICSI

In women < 35 years without male factor infertility…….. 35.7%

In women > 35 years with male factor infertility……... 35.1%

In women < 40 years without male factor infertility…….. 10.3%

In women > 40 years with male factor infertility……... 12.8%

GIFT

In women < 35 years without male factor infertility…….. 34.9%

In women > 35 years with male factor infertility……... 22.2%

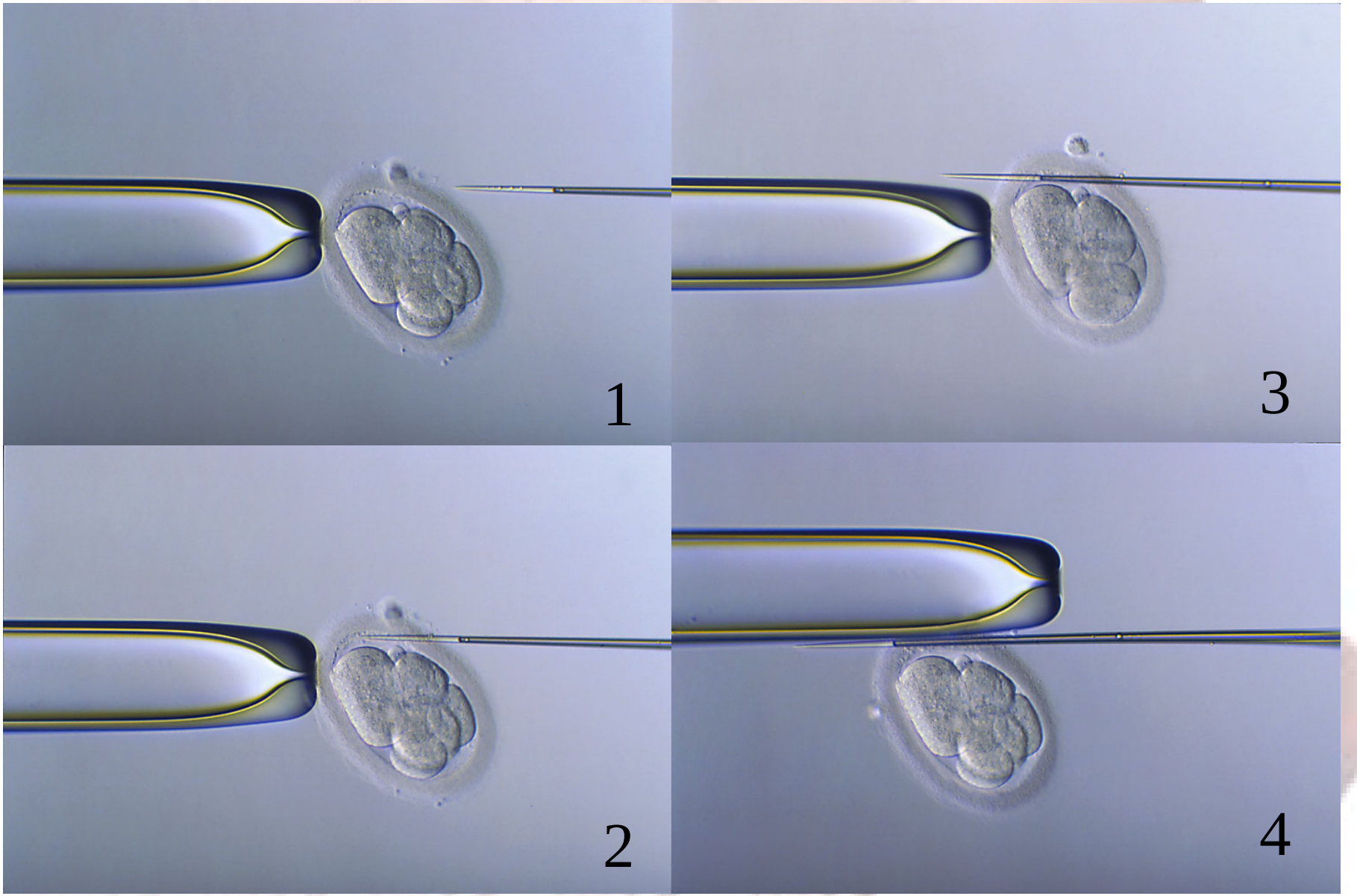
In women > 40 years without male factor infertility…….. 09.1%

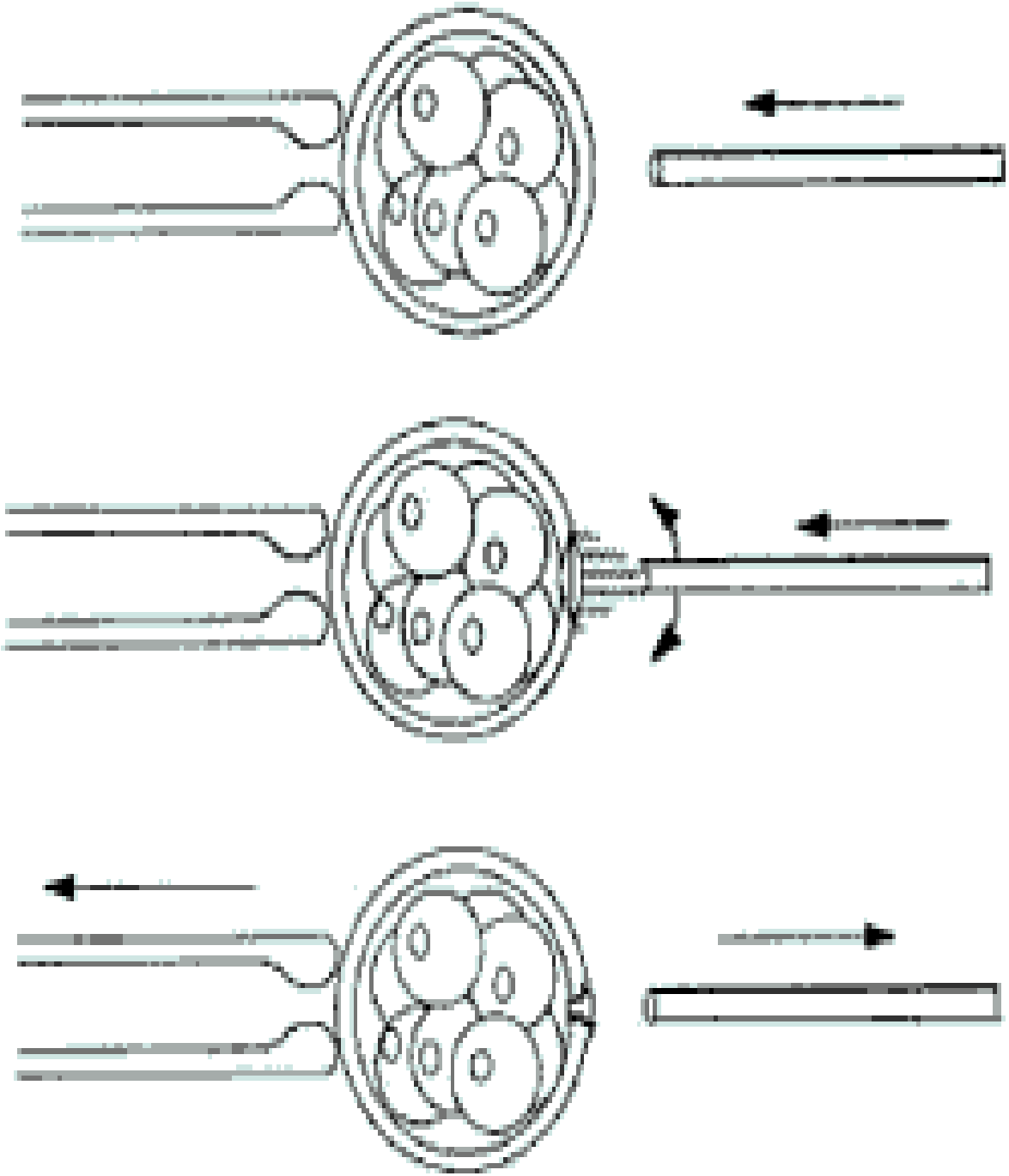
In women > 40 years with male factor infertility……... 11.1%

Nb of transferred embryos, indications, AI before IVF ???

ASRM/SART registry: 1998 results. Fertil Steril2002

Mechanical assisted hatching



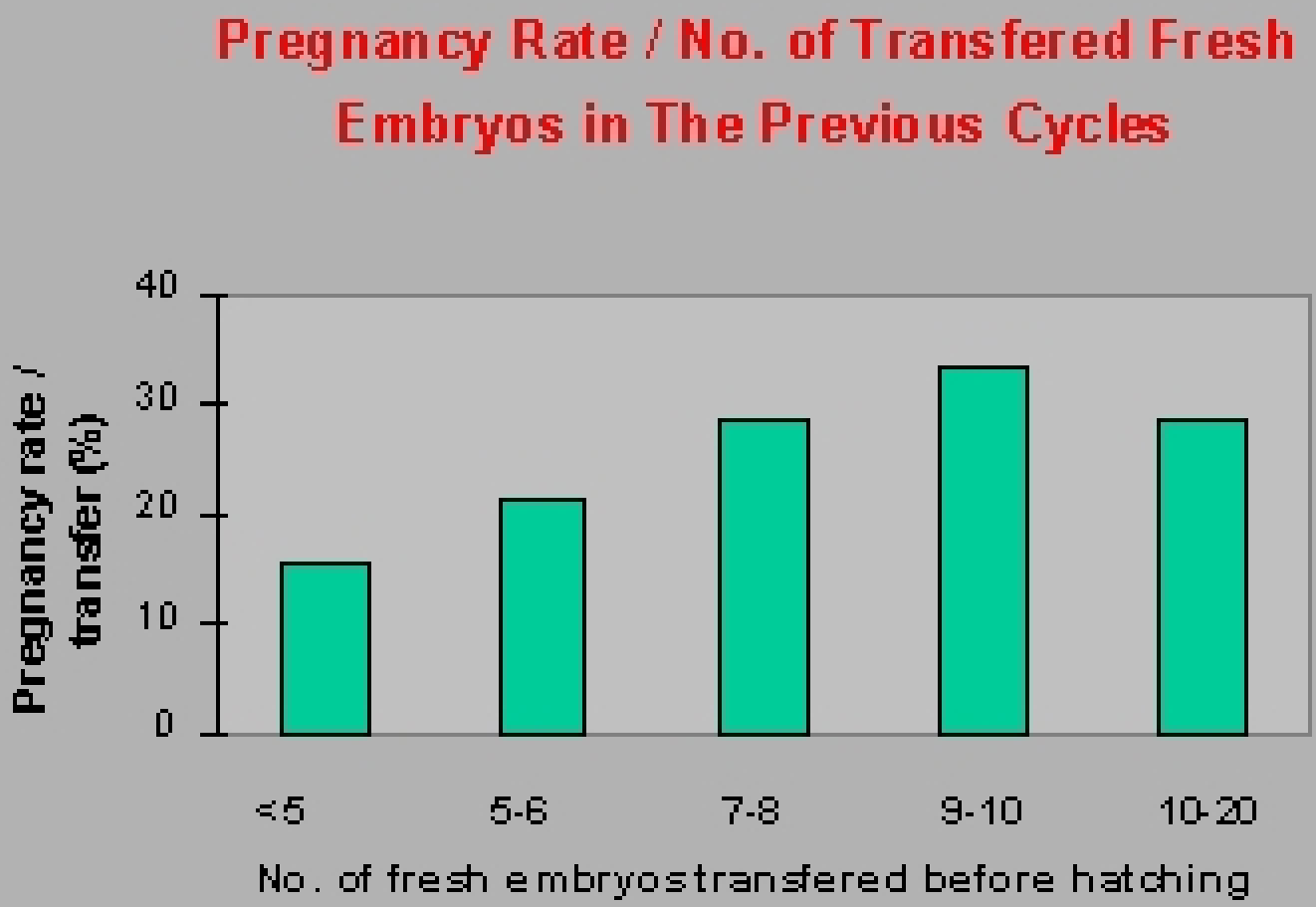


Assisted hatching

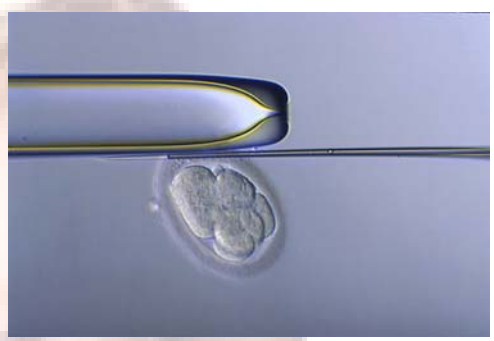
with acid solution…

now with LASER : safer technique!

Correlation Between the Number of Embryos Transferred in the Previous Cycles and the Pregnancy Rate After the Assisted Hatching



Our own experience
(Paris + Geneva)

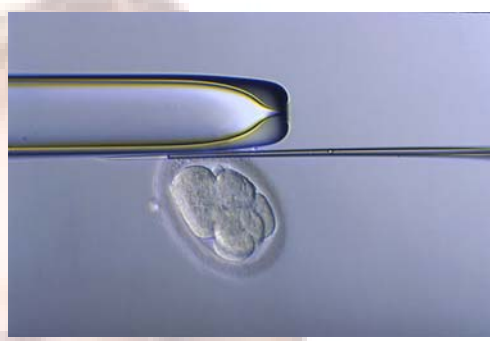


<u>Assisted Hatching indicated in :</u>

- Failed Embryo Transfer (more than 3 ET of 2 good quality embryos).

and/or

- Thick Zona Pellucida (>15 um)- Hard ZP

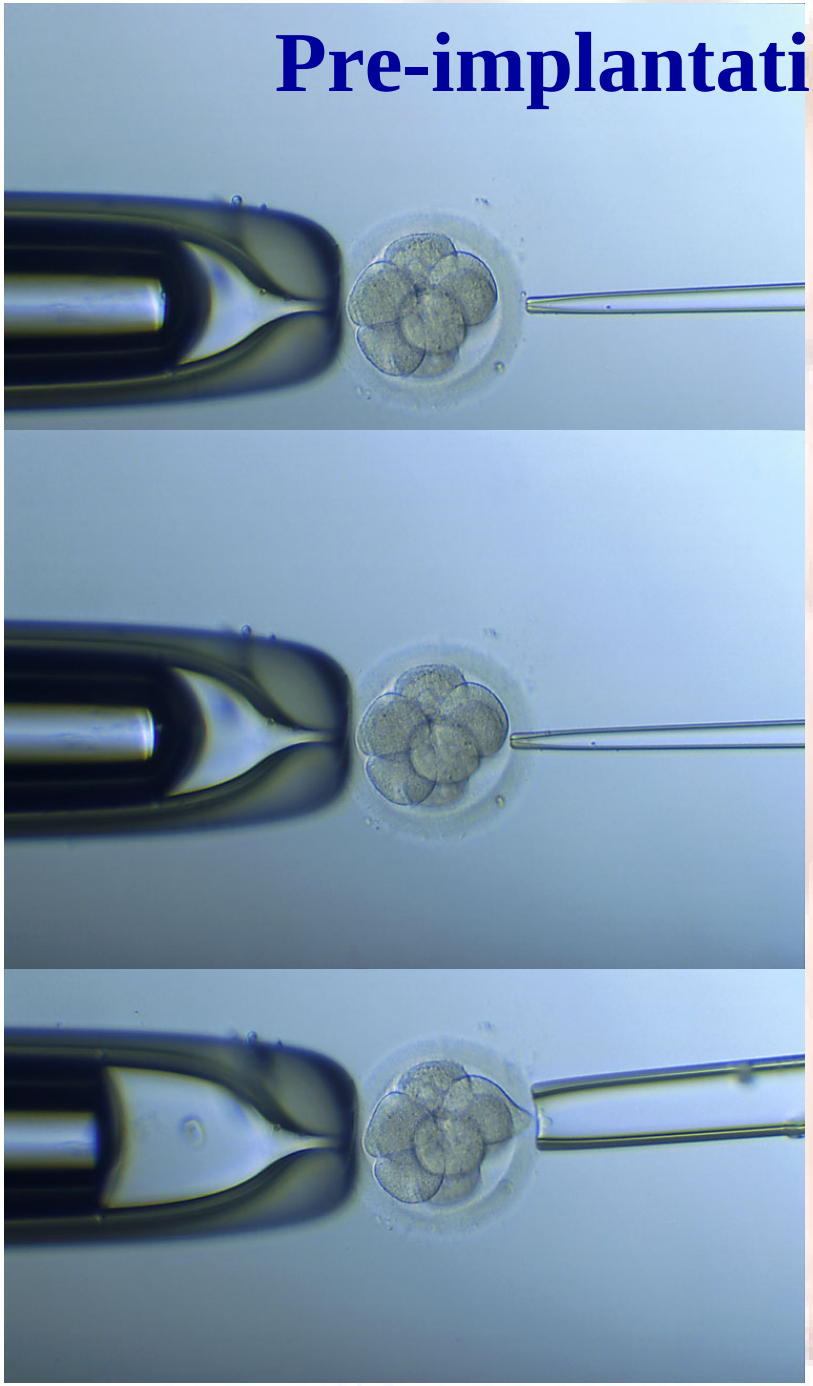


But …

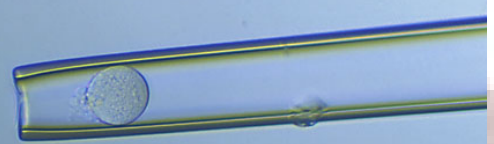
ESHRE analysis doesn't confirm the interest of Laser Assisted Hatching in any indication

Further study to conclude ?

Pre-implantation genetic diagnosis (PGD)



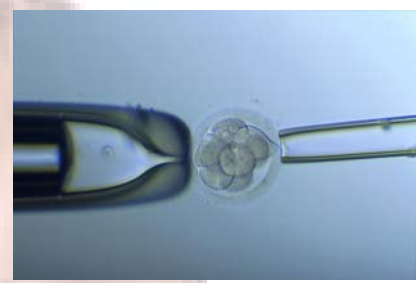
Genetic analysis (x2 cells):



Number of Chr. : FISH

Gene alteration : PCR

Pre-implantation Genetic Diagnosis (PGD)



- The benefits of PGD in infertile couple (2 Polar body, PCGD).
  - •Research of aneuploidy in older women (decrease miscarriage)
- The benefits of PGD in fertile/infertile couple.
  - •Sex embryo screening (Ethically discussed…)
- Who should have PGD ?
  - •Fertile or infertile couples with known and genetically detectable genetic desease.

Very good genetic laboratory needed !

What is the future in ART :

- Ovarian tissue cryopreservation and graft.
- In Vitro Oocyte Maturation.
- Reducing the number of embryo transferred (blastocyst culture development).
- Pre-Implantation Genetic Diagnosis.
- In Vitro maturation of male germinal cells.

What is the future in ART :

….To have primate model for evaluation of :

NEW BIOLOGICAL TECHNOLOGIES,

NEW MALE/FEMALE TREATMENTS,

….Before use in humans.