Preconception Genetic Carrier Screening IVF & PGD

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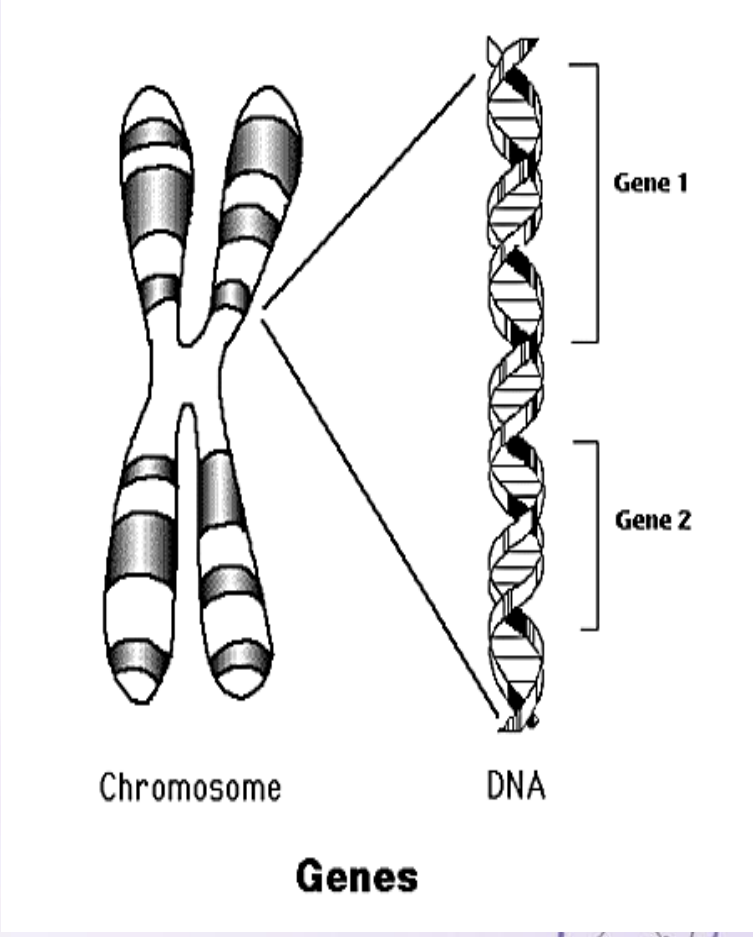
Preconception Genetic Carrier Screening

- Preconception Genetic Carrier Screening refers to pre-pregnancy testing that screens for serious genetic diseases such as Cystic Fibrosis (CF), Spinal Muscular Atrophy (SMA), Sickle Cell, Thalassemia and Tay-Sachs disease (TSD).

- These genetic diseases cannot be cured, but men and women who do screening *before* having children and test positive as *carriers* for the same condition, have a number of reproductive options available to them, including IVF coupled with preimplantation genetic diagnosis (PGD).

Genetics 101: Information

- **Gene** – basic unit of genetic information. Genes determine the inherited characters.
- **Genome** – the collection of genetic information.
- **Chromosomes** – storage units of *genes*.
- **DNA** - is a nucleic acid that contains the genetic instructions specifying the biological development of all cellular forms of life



Genetics 101: Inheritance and Disease

- Humans have 23 pairs of chromosomes (portions of DNA), each containing large numbers of genes.
- Genes code for specific protein synthesis by a cell.
- 22 of these chromosomal pairs are known as autosomes.
- The other chromosomal pair is known as the sex chromosomes.
  These special sex chromosomes are in large part responsible for determining our gender, and are named X and Y.

Genetics 101: Inheritance and Disease

- Individuals have two copies of every gene (one gene on each autosomal chromosome pair) - one inherited from their mother, the other from their father.
- The vast majority of gene pairs in the body are normal and function properly allowing for smooth protein synthesis and cell function.
- However, some genes may malfunction due to a change in their DNA structure - known as a genetic mutation.
- The preconception genetic testing screens for *mutations that will cause so-called single gene disorders*, if both parents are carriers of the same gene mutation.

Genetics 101: Inheritance and Disease

- A person with one normal gene copy and one mutant copy is known as a ***Carrier***.
- *Carriers* are healthy individuals with little or no disease symptoms, who nevertheless have a *mutant version of a recessive gene,* as well as a normal copy of the gene.
- For genetic diseases that are autosomal recessive, *both copies of the gene must contain a mutation* in order for an individual to be affected with the disease.
- The single gene disorders/diseases screened for by the preconception genetic testing have two primary inheritance patterns: autosomal recessive and X-linked recessive.

Genetics 101: Inheritance and Disease

Autosomal Recessive Inheritance

- Majority of diseases on Counsyl's Universal Genetic Test are autosomal recessive. (On chromosomes 1-22)
- Since carriers have no symptoms of the disease, the ***risk*** arises when two carriers conceive a child in the *absence of carrier testing.* If both parents are carriers for the same gene mutation/disease, their children will have a 1 in 4 (25%) chance of having the disease!
- Thousands of unsuspecting healthy parents are caught off guard when their children are born with *serious genetic disorders*, because each parent unknowingly was a carrier of the same recessive gene mutation.

Family History Is Not Enough !!!

- Some parents are aware of their increased risk of a given genetic disease due to a *positive family history of an affected child*.
- However, since the majority of genetic mutations are passed down quietly through the generations, more than 80% of children born with a preventable genetic illness lack a family history of that disease!
- As a result, *the only way to know your carrier status for certain is through genetic carrier testing.*

American College of Obstetricians and Gynecologists (ACOG)

Individuals of European Jewish Descent (Ashkenazi) should be offered carrier screening ideally before conception for:

- Tay Sachs disease
- Canavan disease
- Cystic Fibrosis
- Familial Dysautonomia.

Carrier screening is also available for:

- Mucolipidosis IV
- Niemann-Pick Disease type A
- Fanconi anemia group C
- Bloom syndrome
- Gaucher's disease.

This Ashkenazi genetic carrier screening is *often not performed due to extremely high cost. (Over $2000)*

* Chicago Center for Jewish Genetic Disorders *

What If Both Test Positive as Carriers? IVF / PGD

- If a man and woman are *both carriers of the same genetic disease*, there are ***preventative actions*** they can take to dramatically improve their chances of having a healthy baby.

- By undergoing in vitro fertilization (IVF) and genetically testing each embryo -- Preimplantation Genetic Diagnosis (PGD) for the single gene disorder, a couple can *virtually eliminate their chances of having a genetically abnormal child!*

- By transferring only those embryos that are genetically normal or carriers, the couple can have a healthy baby.

In Vitro Fertilization (IVF)

- Evaluate egg quality
- Bypass fallopian tubes
- Overcome male factor problems
- PGD

Procedural Steps in Basic IVF

- 1) Patient selection
- 2) Stimulation of multiple follicles for multiple eggs
- 3) Egg aspiration
- 4) Fertilization and culture
- 5) Biopsy of embryos (if doing PGD)
- 6) Transfer of embryos

Procedural Steps in Basic IVF

- **Patient selection** (Infertility vs PGD)
- Stimulation of multiple follicles for multiple eggs
- Egg aspiration
- Fertilization and culture
- Transfer
- Early pregnancy stages

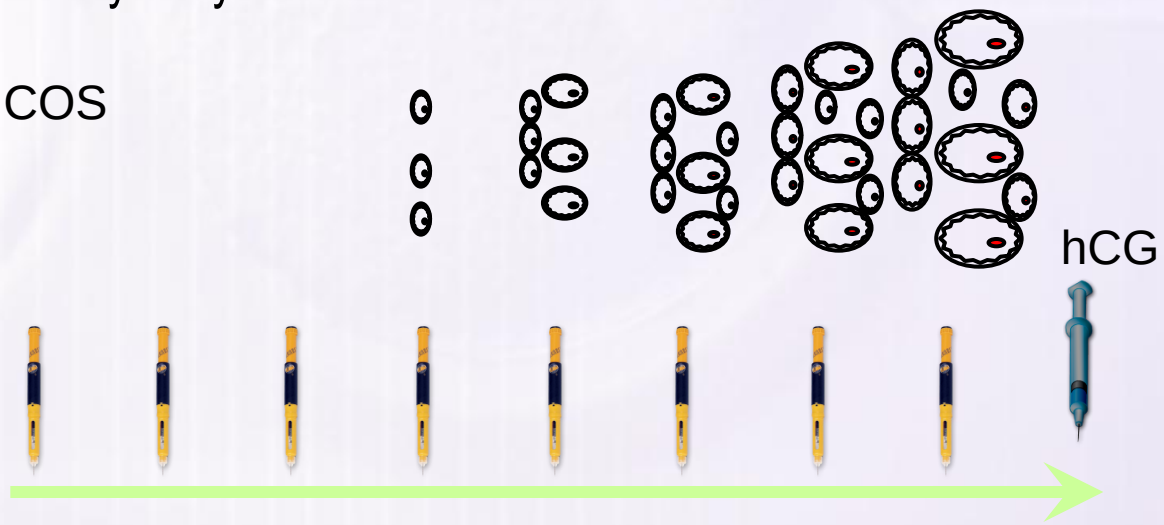
Procedural Steps in Basic IVF

- Patient selection
- **Stimulation of multiple follicles for multiple eggs**
- Egg aspiration
- Fertilization and culture
- Transfer
- Early pregnancy stages

Controlled Ovarian Stimulation (COS):

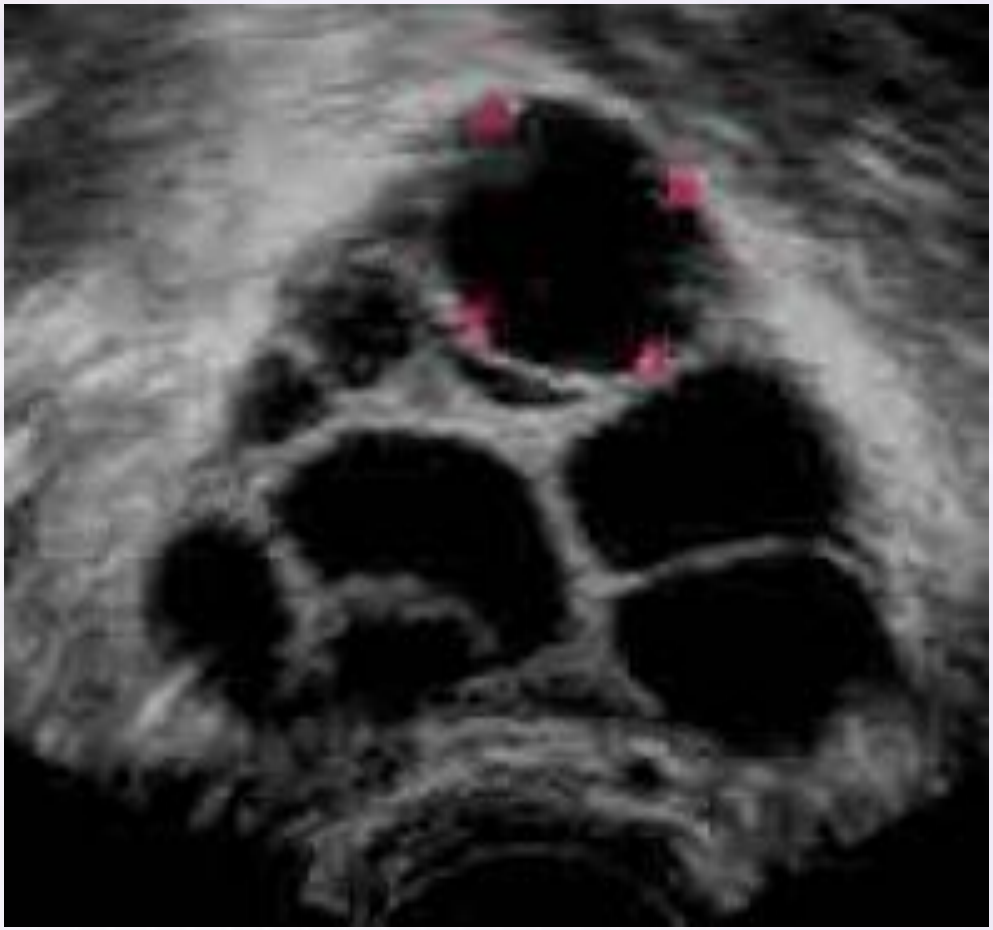
Gonadotropin (FSH) Treatment

- Starts with higher doses of gonadotropin injections
- Stimulation for 10-14 days
- Multiple Ultrasounds & Estrogen measurements
- Need “blocking medications” GnRH agonists or antagonists to prevent ovulation
- COS is followed by oocyte retrieval



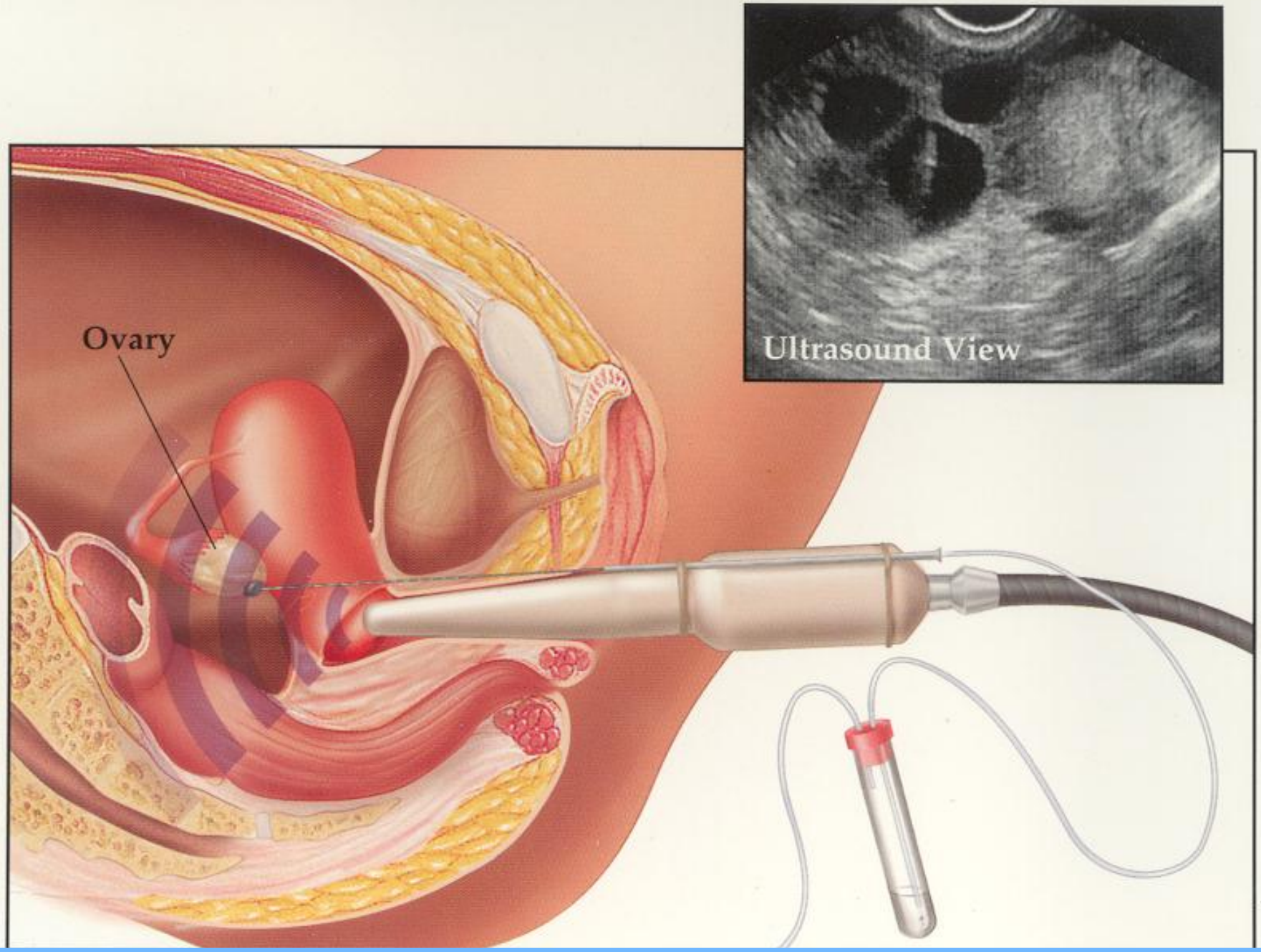
Arslan et al. *Fertil Steril*. 2005;84(3):555.
Borini and Dal Prato. *Reprod Biomed Online*. 2005;11:283.

Mature Follicles



Procedural Steps in Basic IVF

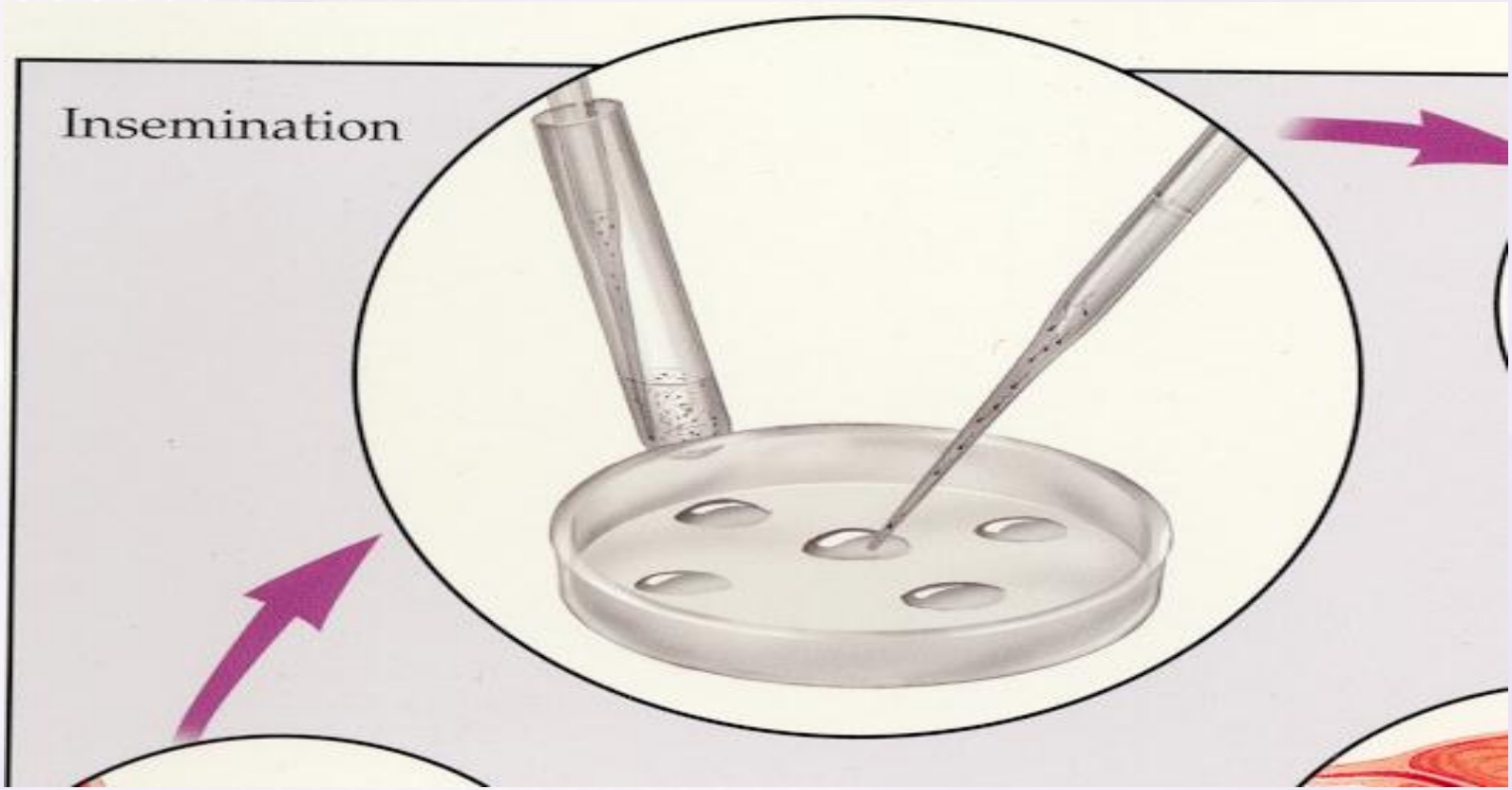
- Patient selection
- Stimulation of multiple follicles for multiple eggs
- **Egg aspiration (retrieval)**
- Fertilization and culture
- Transfer
- Early pregnancy stages

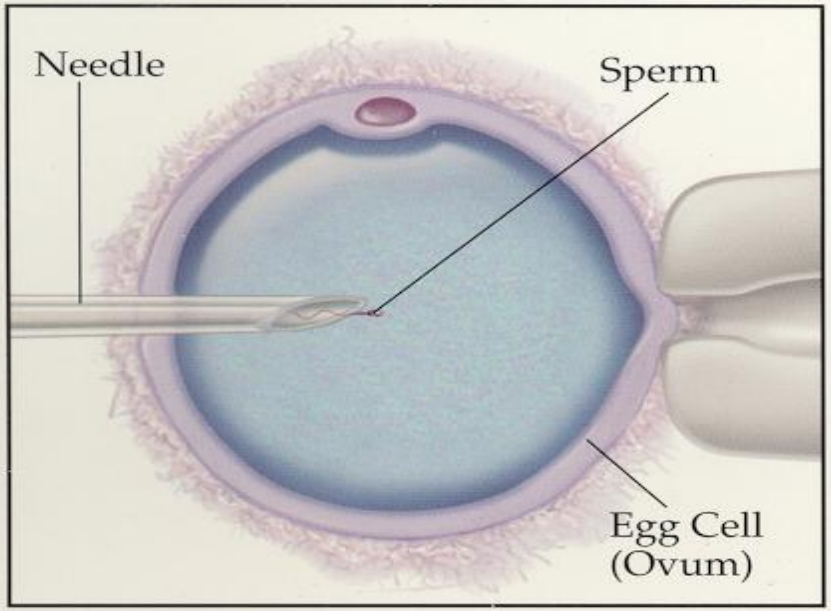


Transvaginal Oocyte Retrieval

Procedural Steps in Basic IVF

- Patient selection
- Stimulation of multiple follicles for multiple eggs
- Egg aspiration
- **Fertilization and culture**
- Transfer
- Early pregnancy stages


Insemination



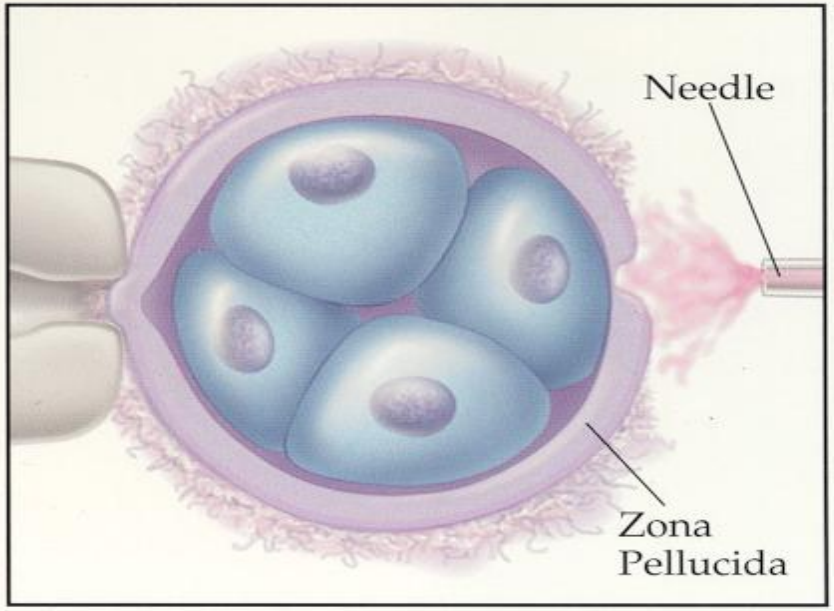
Enlarged View

ICSI
(Intracytoplasmic Sperm Injection)

A single sperm is injected into the egg.

Assisted Hatching

A portion of the egg shell is removed to allow the embryo to hatch and escape.

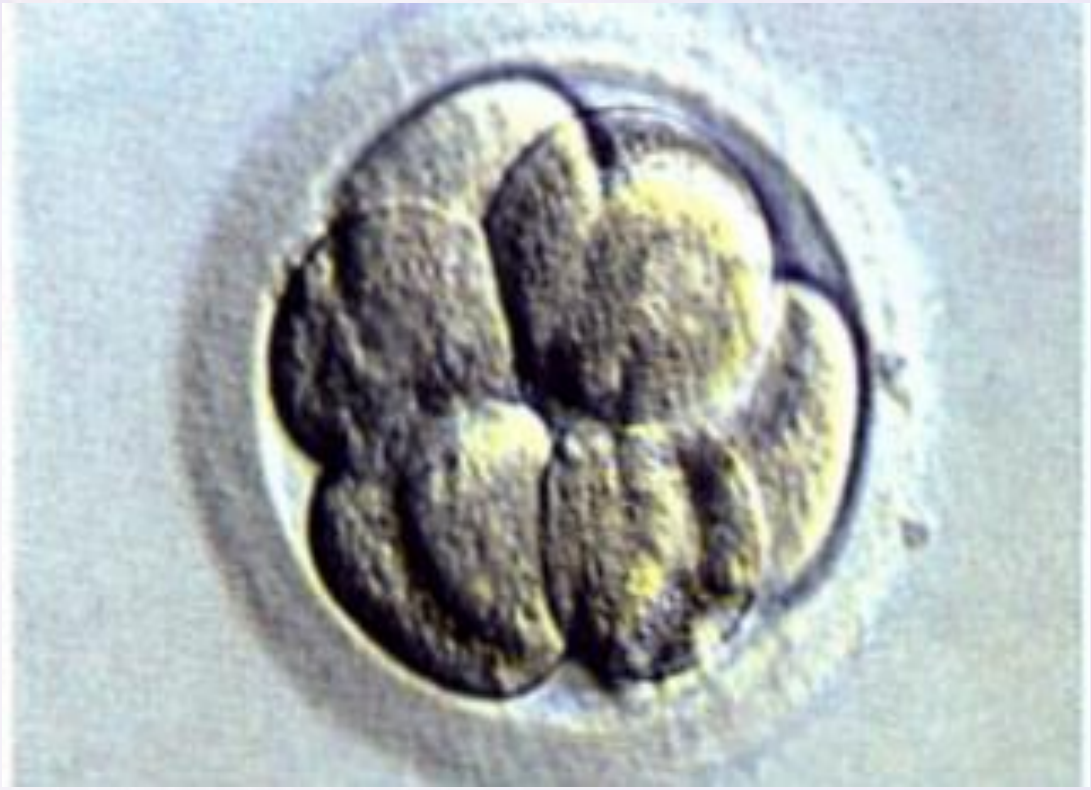


Enlarged View

Micromanipulation of Gametes and Embryos

Intracytoplasmic Sperm Injection (ICSI)

Normal Eight Cell Embryo



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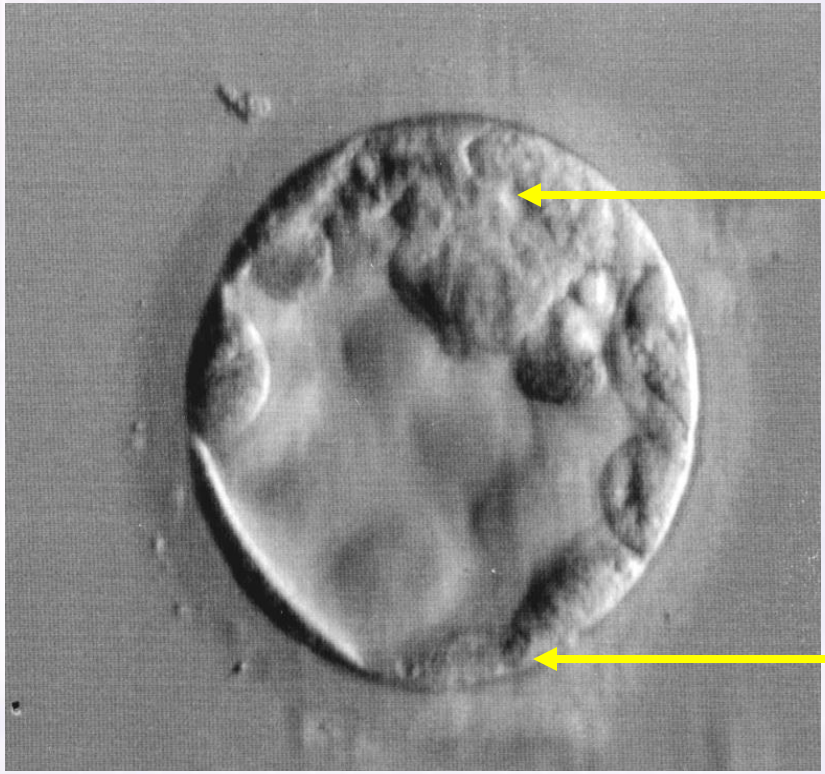
IVF & PGD: Blastocyst biopsies



Inner cell mass
(Fetal cells)

Trophectoderm
(Placental cells)

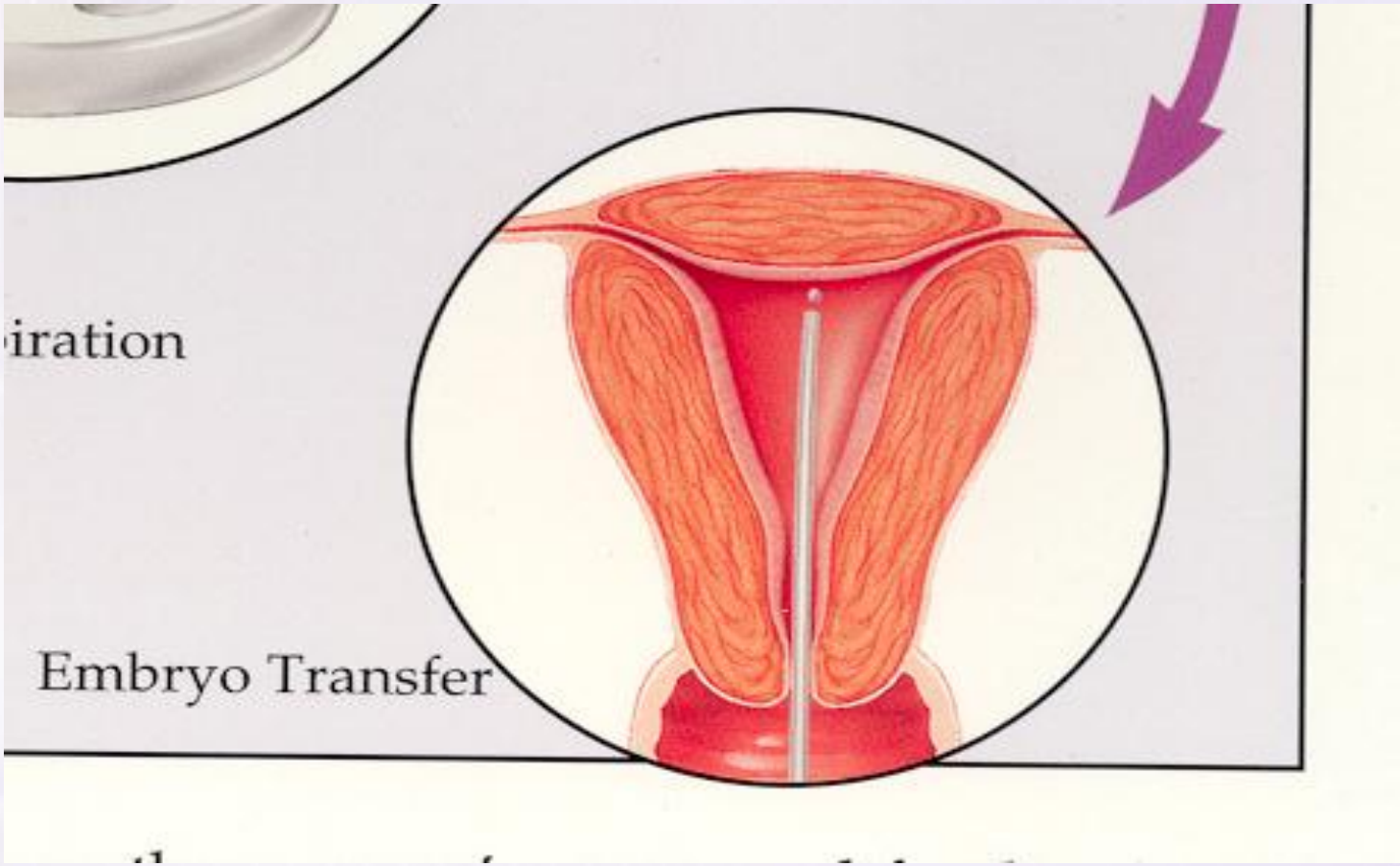
d5

Genetics Lab

- Embryo (d5 blastocyst) biopsy … several cells
- Cells are sent to the Genetics lab for PGD (single gene)
- Embryo is then frozen (Vitrification)
- Get Genetics report in 10-14 days

Procedural Steps in Basic IVF

- Patient selection
- Stimulation of multiple follicles for multiple eggs
- Egg aspiration
- Fertilization and culture
- **Transfer embryos**
- Early pregnancy stages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Embryo Transfer

IVF Controversy

- Donor Egg
- Donor Sperm
- Gestational Carriers (Surrogacy)
- Donor Embryos vs Adoption
- Frozen Eggs & Embryos
- Same Sex Couples

Thank You …

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