Family Planning and Assisted Reproductive Technologies (ART)

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Assisted Reproductive Techniques

- Donor Egg (with at risk/affected female)
- Donor Sperm (with at risk/affected male)
- Embryo Donation
- Preimplantation Genetic Diagnosis (either at risk/affected male or female)
- Pregnancy with prenatal testing of fetus (CVS or amniocentesis)
- Adoption
- Surrogacy

Donor Egg

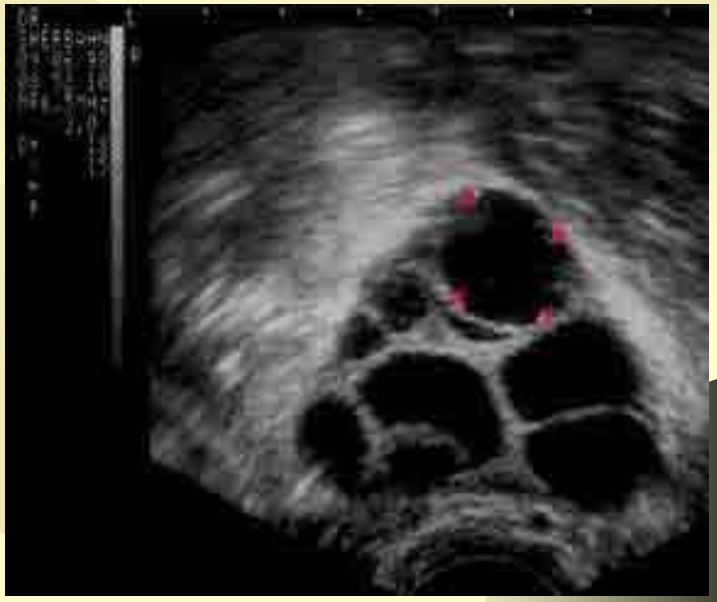
- Usually obtained through the following sources:
  - Donor programs affiliated with academic institutions
  - Donor programs affiliated with community hospitals
  - Private practices
  - Independent egg brokers

Egg donors

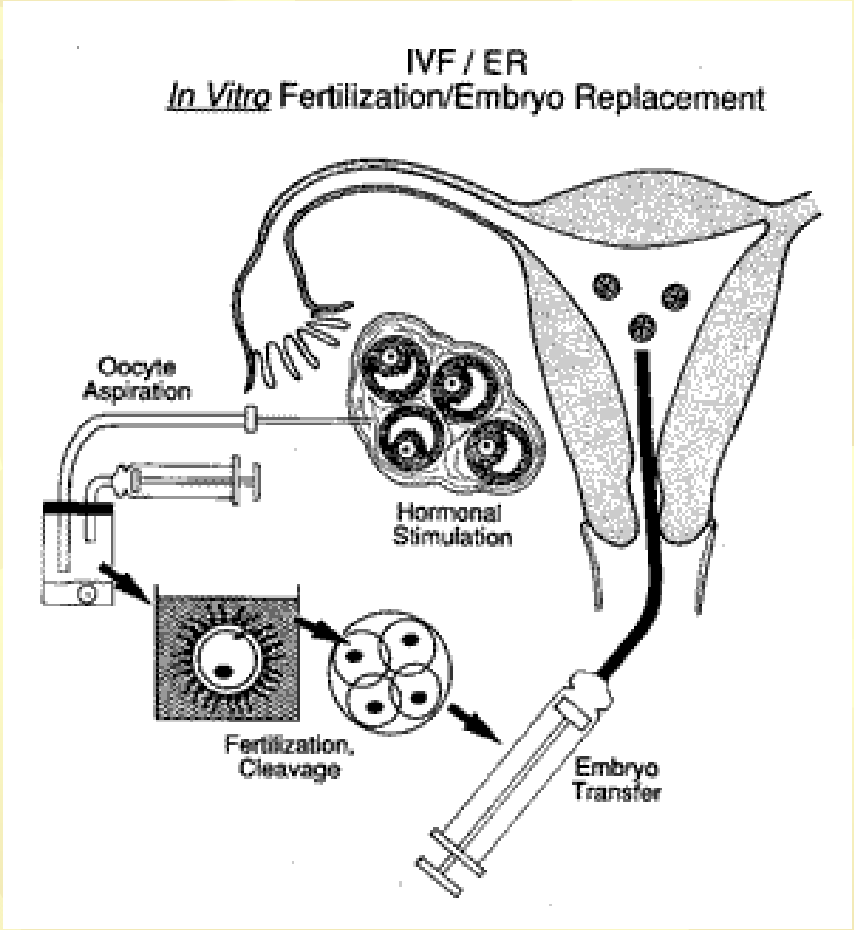
- Infertility patients who are undergoing *in vitro fertilization* (IVF) and who are willing to donate extra eggs
- Women planning other reproductive surgery (tubal ligation), who are willing to undergo ovarian stimulation in order to harvest eggs and egg retrieval prior to the procedure
- Relatives or friends of the prospective parents
- Healthy women recruited specifically to donate eggs.

Donor Egg Procedure

- Mother undergoes ovarian hyperstimulation using drugs in order to facilitate production of more than one egg per cycle.
- Eggs are harvested and fertilized with father's sperm
- Embryos are implanted into mother's womb



In Vitro Fertilization



Donor Egg

- The use of the donor egg with result in a child who will have inherited 50% of its genes from the biological father.

Donor Sperm

- Usually obtained from three sources:
  - Large semen banks that ship frozen specimens nationwide
  - Regional or local semen banks with a more limited distribution area
  - Individual practitioners who have established a pool of donors

Donor Sperm

- The use of donor sperm will result in a child who will have inherited 50% of its genes from the biological mother.

Donor Sperm Procedure

- Mother undergoes ovarian hyperstimulation using drugs in order to facilitate production of more than one egg per cycle.
- Eggs are harvested and fertilized with father's sperm
- Embryos are implanted into mother's womb

Note of Caution

- Few sperm banks or egg donor programs screen and/or test their donors for genetic disease

- A case has been seen in which an at risk individual was serving as a sperm donor; a case has also been reported in which an at risk individual served as a surrogate mother/egg donor.

Embryo Donation

- Frozen embryos that are left over after a couple using assisted reproduction has completed their family may be donated
- In this case, the child will have no genetic link with either of its parents unless the embryos are donated by a relative

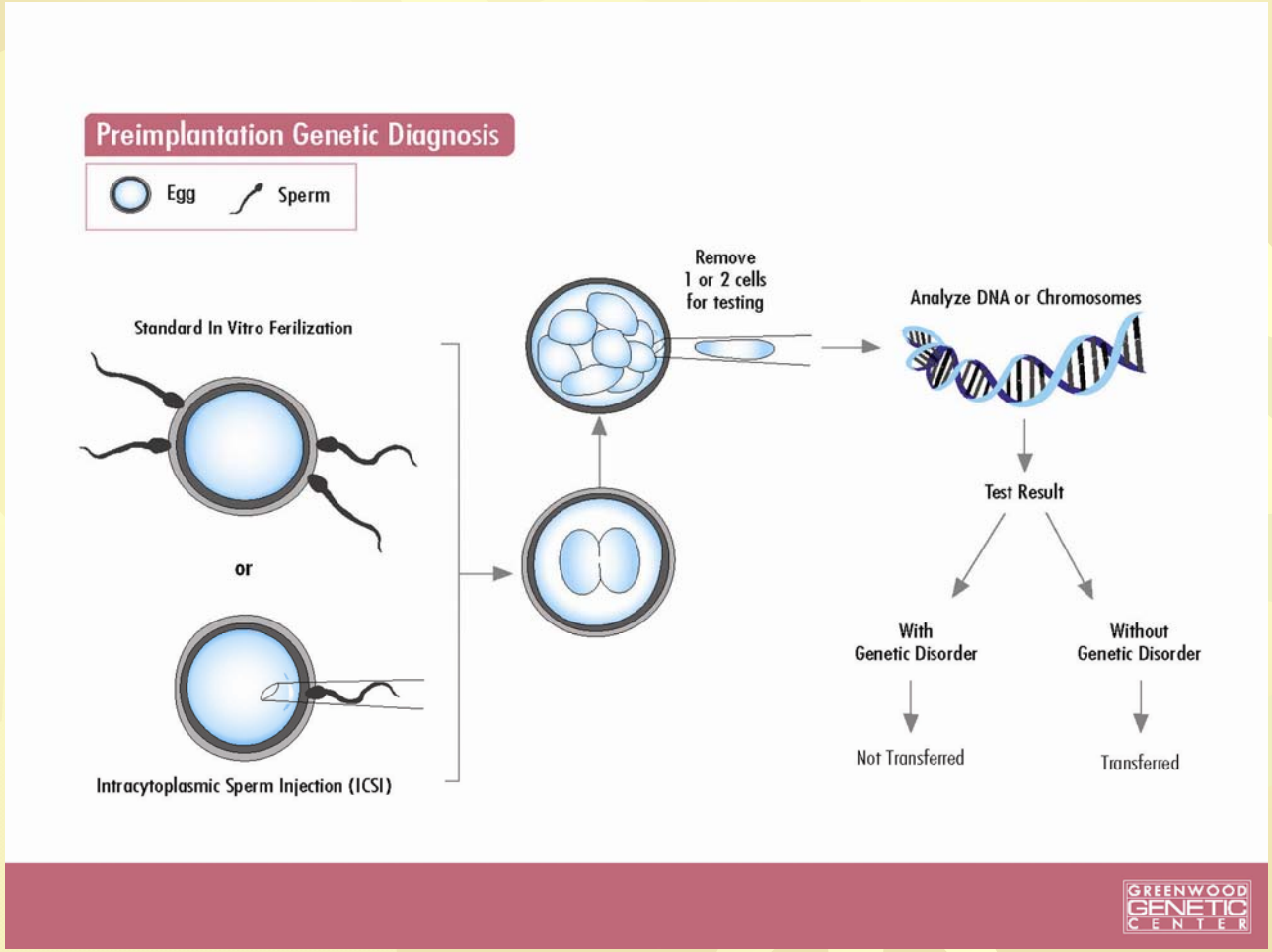
Egg Donation Procedure

- Thawed embryos left over after IVF are implanted in the mother's womb

Preimplantation Genetic Diagnosis

- Ovarian hyperstimulation and harvest of mother's eggs
- Eggs fertilized with father's sperm
- Resulting embryos permitted to grow to about the 8 cell stage
- One cell is removed from each embryo and tested for the presence or absence of the HD mutation
- Only those without the HD mutation are implanted

Preimplantation Genetic Diagnosis

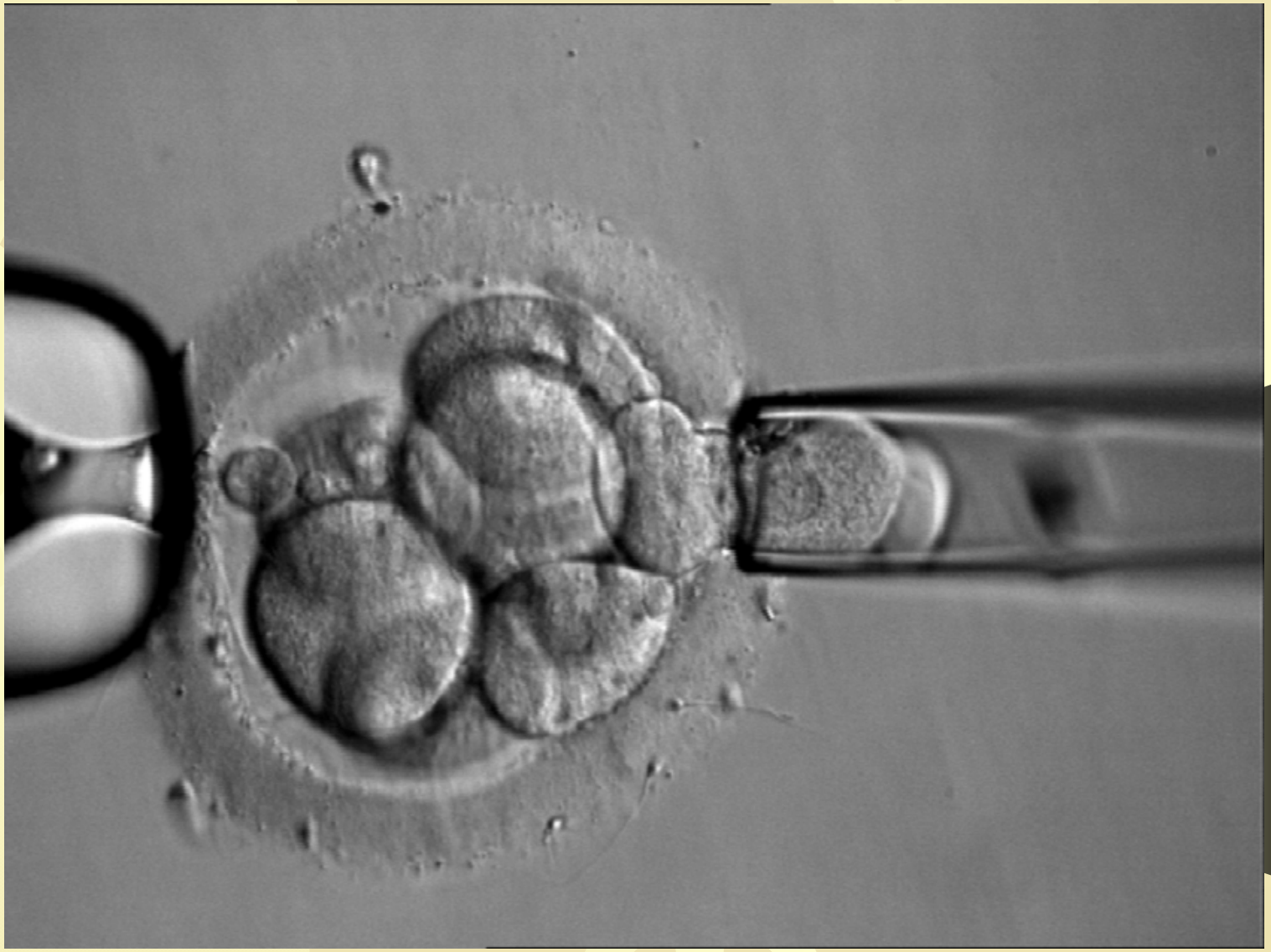


Testing

- Following fertilization, embryos grow in culture for further 3 days until they reach the 8-10 cells stage.
- At that time the embryo is at the cleavage stage, and one or two cells may be carefully removed for genetic analysis without causing any damage to the future development of the embryo.

Testing

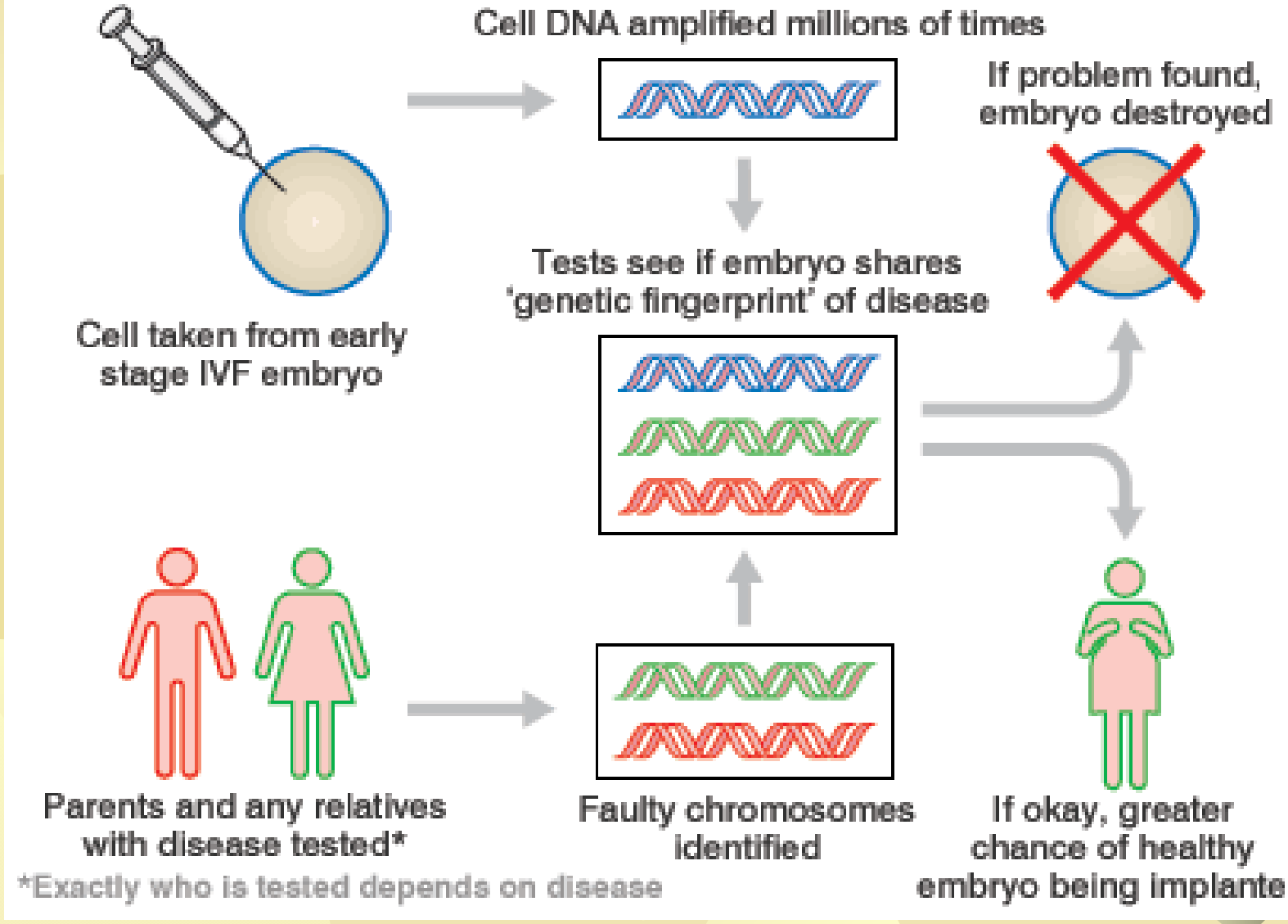
- With the embryo held still by gentle suction using the holding pipette, an opening is made in the outer shell, called the zona pellucida, using a laser. Afterwards, a micropipette aspirates carefully and very gently a single cell (blastomere).
- At this early stage of embryo development, all of the cells have the same potential for development, therefore, removal of one or two cells from the embryo is not detrimental and the embryo can continue its normal development following the procedure.

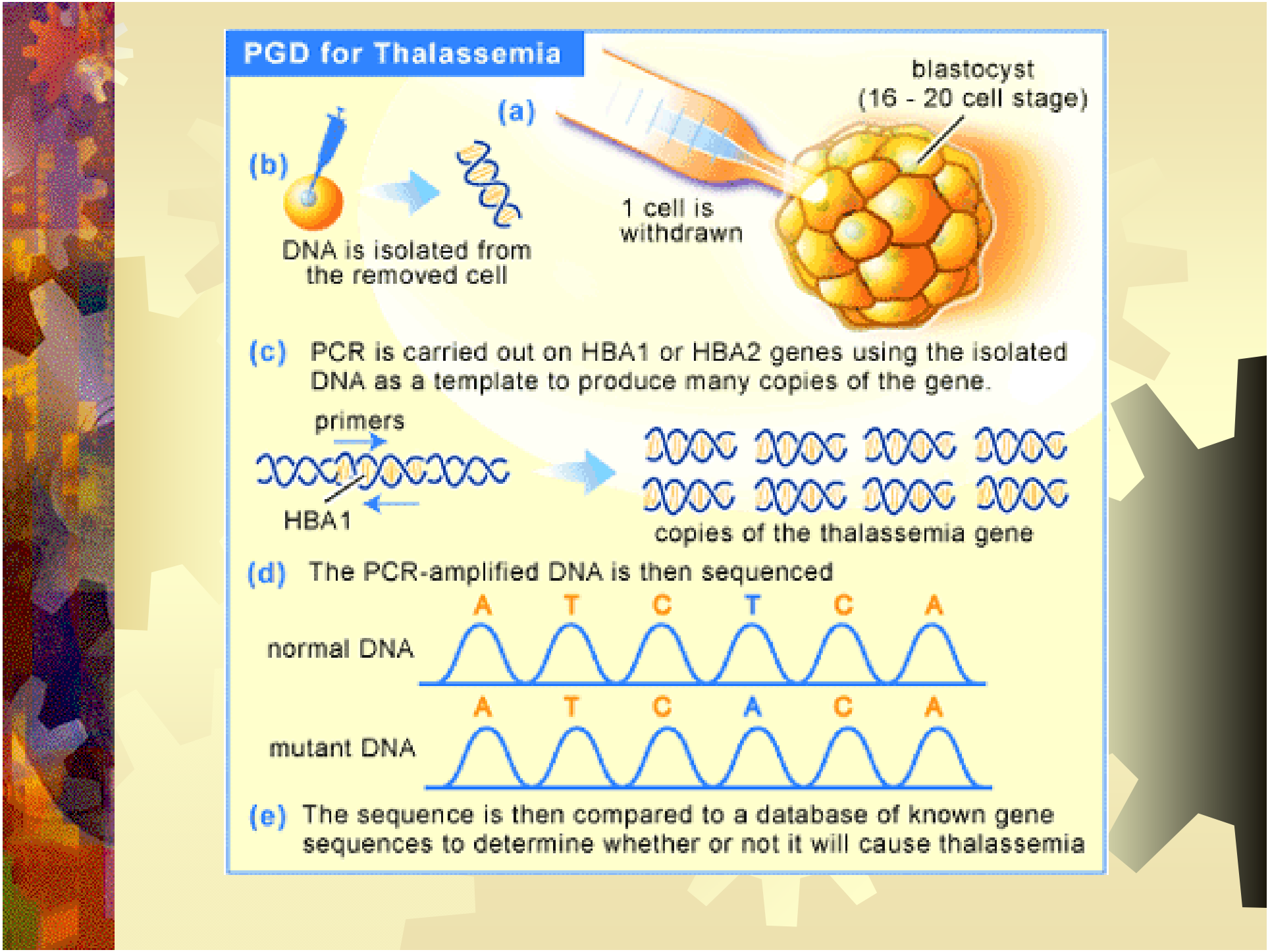


Testing

- The cell that has been removed is then tested for the presence of a gene or chromosome condition.

NEW EMBRYO TEST: PRE-IMPLANTATION GENETIC HAPLOTYPING




PGD for Thalassemia
(a)
blastocyst
(16 - 20 cell stage)
1 cell is
withdrawn
(b)
DNA is isolated from
the removed cell
(c) PCR is carried out on HBA1 or HBA2 genes using the isolated DNA as a template to produce many copies of the gene.
primers
HBA1
copies of the thalassemia gene
(d) The PCR-amplified DNA is then sequenced
normal DNA
A T C T C A
mutant DNA
A T C A C A
(e) The sequence is then compared to a database of known gene sequences to determine whether or not it will cause thalassemia

Preimplantation Genetic Diagnosis

- You do not have to be tested prior to pursuing this option, but you consider the medical risks involved
- IVF with PGD usually costs between $9,000 and $18,000
- Some insurance plans may pay for this procedure, while others may not

Selecting an ART Program

- Qualification of clinic and personnel
- Support services available
- Cost
- Success rates of specific programs

Pro and Cons for PGD

Pros

1. Only embryos diagnosed as free of the specific genetic disease are transferred into the woman for pregnancy.
2. It eliminates the need for an adult who is 'at risk' for a serious adult-onset genetic disease to undergo testing that would determine if he/she has the gene and will eventually develop the condition.
3. In most cases, this enables the family to avoid the decision of whether or not to end the pregnancy once it is established.
4. PGD is approximately 96-98% accurate

Cons

1. It does not always result in a pregnancy.
2. PGD is significantly more expensive than conceiving a pregnancy the usual way and undergoing prenatal testing.
3. This technology is still considered experimental.
4. PGD is approximately 96-98% accurate

Pregnancy and Prenatal Testing

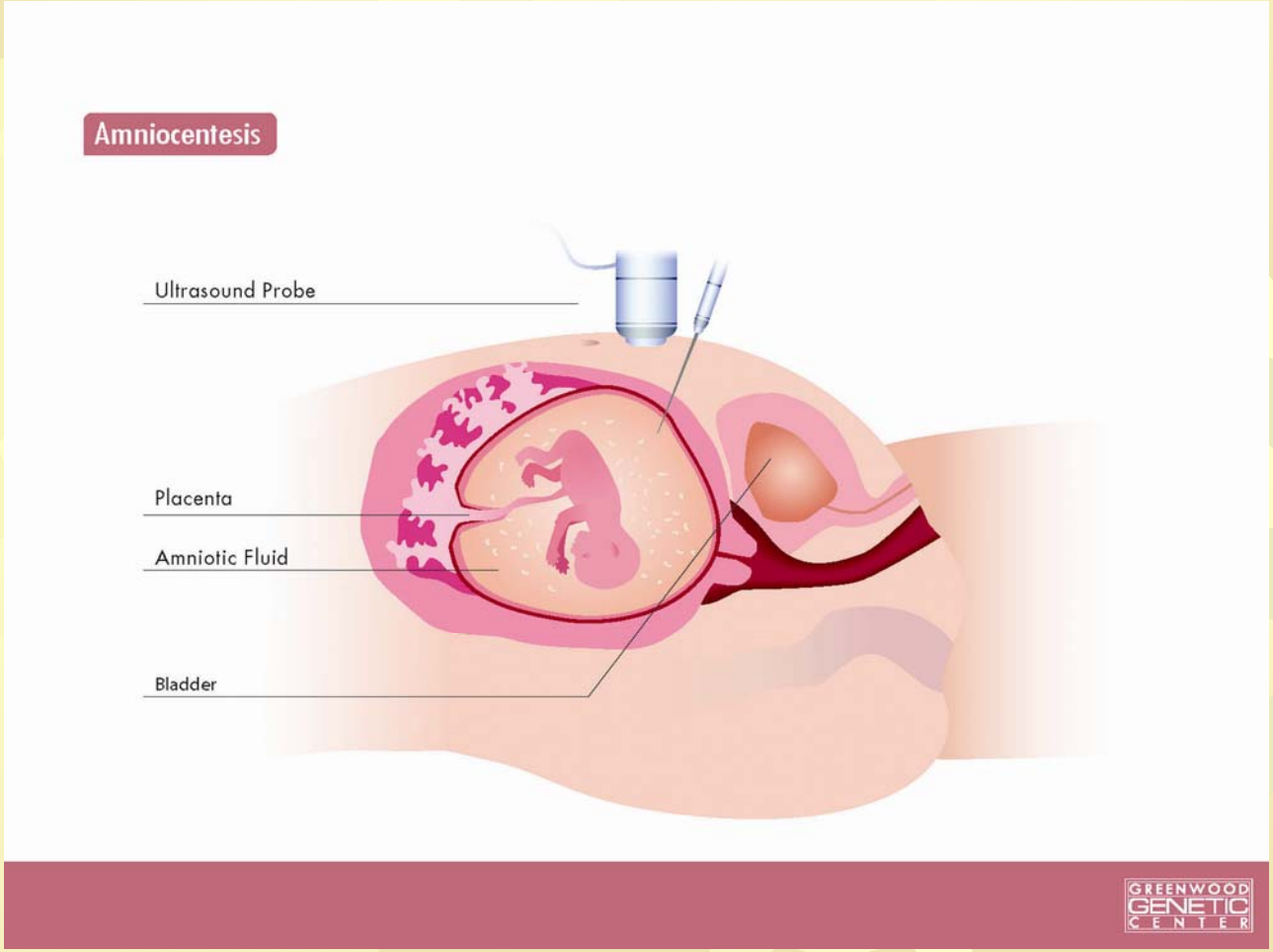
- The fourth option is to proceed normally with a pregnancy and request prenatal testing once the pregnancy has been established.

- Testing can be done using:
  - Amniocentesis
  - Chorionic villus sampling (CVS)

Amniocentesis

- A sample of amniotic fluid is removed from the womb by a syringe placed in the abdomen and uterus
- The amniotic fluid contains fetal cells that can be grown for diagnostic tests
- Performed on an outpatient basis typically around the 15^{th}-16^{th} weeks of pregnancy

Amniocentesis



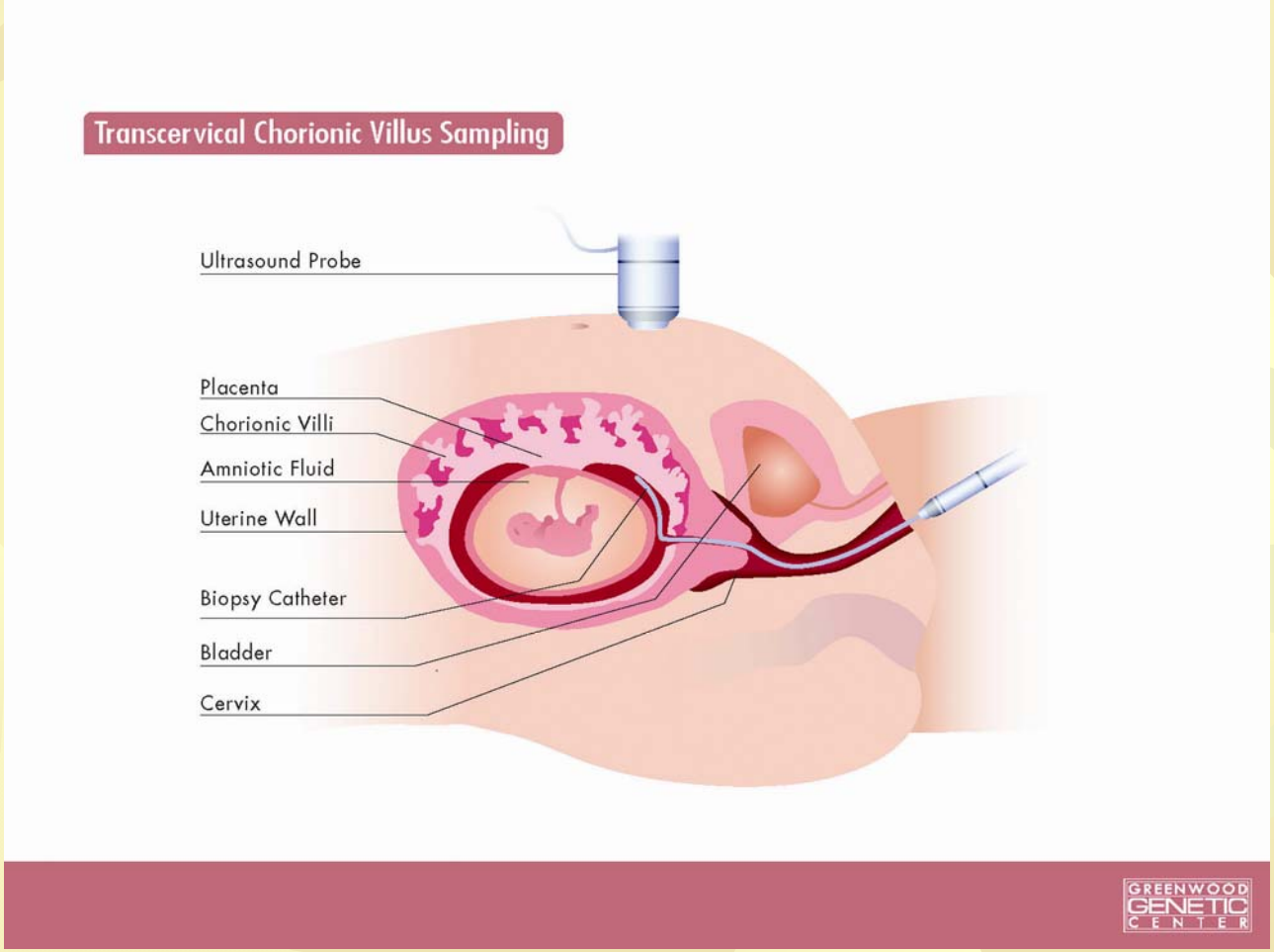
Complications of Amniocentesis

- Risk of miscarriage: 0.5%
  - Population risk of miscarriage (any woman who is pregnant): 2%-3%
- Other complications (rare):
  - Leaking of amniotic fluid, infection, injury to fetus, spotting or bleeding
  - Contact physician if complications arise

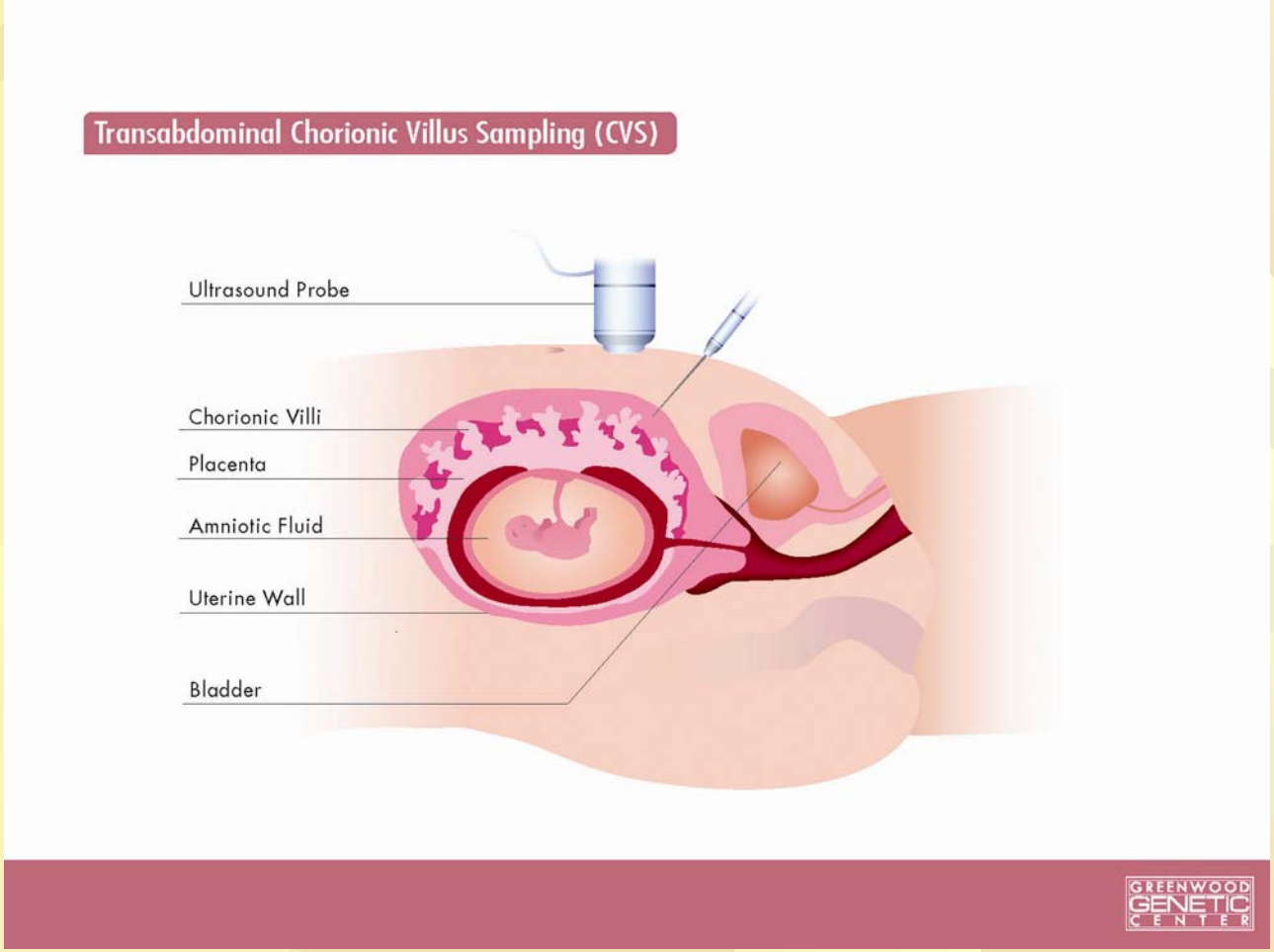
Chorionic Villus Sampling (CVS)

- Biopsy of tissue from the villous area of the chorion through the cervix or abdomen
- Usually performed between the 10^{th}-12^{th} weeks in pregnancy
- Allows results to be available at an earlier stage of pregnancy than with amniocentesis

Transcervical CVS



Transabdominal CVS



Complications of CVS

- Risk of Miscarriage: 0.5%-1%
  - Population risk of miscarriage at 7-12 weeks: 2-5%

- About 2% of the time the procedure may yield results that are ambiguous, thus requiring a follow-up amniocentesis

Adoption

- Some individuals at risk for HD have encountered difficulties in the adoption process based on their risk for developing HD
- Children who are put up for adoption are not genetically tested for the presence or absence of the HD mutation

Surrogacy

- For couples where the woman is unable to carry a pregnancy to term delivery.

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Huntington's Disease Society of America

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