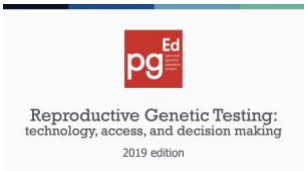
VIDEO TRANSCRIPT

Reproductive Genetic Testing: Technology, Access, and Decision Making

Link to video.

Slide 1



This PGED lesson aims to examine how genetic testing might offer hope to individuals wishing to have children as well as some of the ethical implications of that testing.

Slide 2

Before we get started, take a moment to consider these questions:

If you could choose specific traits or qualities that you would want your child to have, what would you choose? Why?

Are there traits you would not want your child to have? What are they? Why?

You may want to pause here to think about your own answer to this question.

Typically answers to these questions vary widely. What is important to realize though is that many physical, mental and behavioral traits are very difficult to predict or ensure. This is because such traits are the result of an individual's environment and lifestyle as well as an individual's genetic

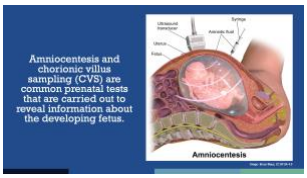
makeup. In addition, the genetic basis of many traits is extremely complex and beyond our current understanding.

Slide 3

The reproductive technologies presented in this lesson can be used in a variety of ways:

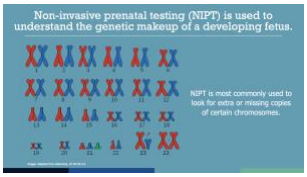
- To gain genetic information about an embryo or unborn fetus
- To help people conceive
- To identify medical conditions that might be treated in utero or, in other words, "in the womb, before birth"
- To allow people to select embryos based on their genetic makeup
- And, in the future, to possibly alter human DNA

Slide 4



Two common forms of reproductive genetic testing are Amniocentesis and chorionic villus sampling - or CVS. These prenatal tests are carried out to reveal information about the developing fetus. Both are considered invasive procedures. An amniocentesis, typically performed between 15-20 weeks of pregnancy involves inserting a large needle through a pregnant person's abdomen, uterus and then the amniotic sac to obtain fetal DNA from the amniotic fluid. CVS, typically offered at 11-13 weeks of pregnancy, is performed vaginally or via a needle through the abdomen to collect fetal tissue from the placenta. Both procedures carry a small risk of miscarriage.

Slide 5



Non-invasive prenatal testing - or NIPT - is another type of reproductive genetic testing that is used to understand the genetic makeup of a developing fetus.

NIPT has been available for clinical use in the US since 2011. The technique is most commonly used to look for extra or missing copies of certain chromosomes (a condition known as "aneuploidy"). One of the most common of these conditions is Down syndrome, which is characterized by having three copies of chromosome 21 in the fetal cells.

It is important to note that NIPT results are not definitively diagnostic. NIPT results may suggest the presence of aneuploidy, but more invasive forms of prenatal testing (such as amniocentesis or CVS) are needed for diagnosis. Similarly, one could receive an NIPT result that suggests a chromosomal condition is less likely, but it cannot completely rule them out. The likelihood that a positive NIPT result is truly positive varies for different conditions and for individuals of different age groups.

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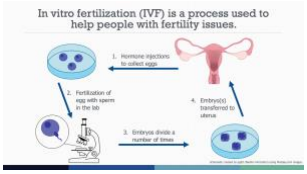
So how exactly does NIPT work? And what makes it a non-invasive procedure?

All of us have small fragments of DNA circulating in our bloodstream that are released from cells in our body. When a person is pregnant, a small fraction of this cell-free DNA originates from cells of the placenta, an organ formed by embryonic cells that connects the developing embryo (and later fetus) to the uterus. By obtaining a blood sample from the arm of the pregnant person, physicians and researchers can analyze its cell-free DNA to reveal information about the developing fetus. NIPT can be performed as early as week 9

of the pregnancy. Because NIPT is done on a blood sample taken from a vein, it is considered a non-invasive procedure that does not, by itself, increase the risk of miscarriage.

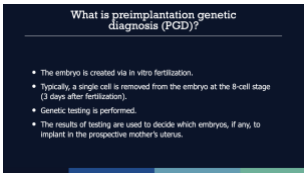
Slide 7



A reproductive genetic technology that people might be familiar with is In Vitro Fertilization - or IVF.

IVF is a process used to help people with fertility issues. In the IVF process, hormone injections are administered to stimulate the ovaries to produce mature eggs. These eggs are fertilized in a lab by the addition of sperm in a petri dish. One or more of the resulting embryos are then transferred to the uterus. IVF was first performed in 1978, and is estimated to account for 1-2% of US births annually.

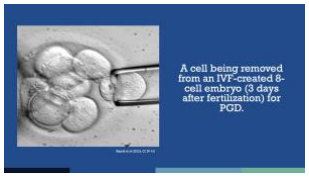
Slide 8



A form of reproductive genetic testing that can be combined with IVF is Preimplantation Genetic Diagnosis - or PGD.

PGD can be used to screen embryos during IVF to make a decision about which embryos to implant. PGD gives people who carry variants for serious genetic diseases the opportunity to prevent passing these on to their offspring. Such genetic disorders include deadly childhood diseases, such as Tay-Sachs, as well as adult–onset diseases, such as Huntington's disease and certain inherited forms of breast cancer. Typically, a single cell is removed from an 8-cell embryo and screened for specific disease-causing variants. Any embryo that is free of the particular variant is then considered for transfer into the uterus.

Slide 9



This slide shows an image of a cell being removed from an IVF-created 8-cell embryo - which is 3 days after fertilization - for the purpose of PGD.

Slide 10

First performed in 1990, PGD was brought into the public eye by the Nash family. Pictured are siblings Molly and Adam Nash. Molly was born in 1994 with a deadly disorder called Fanconi Anemia (FA), a genetic condition that disrupts the ability of cells to repair their DNA and often leads to specific types of cancer like leukemia.

As a young child, Molly needed a stem cell transplant to save her life. Her parents wanted another baby and decided to use PGD with the goal of conceiving a child who would be free from FA and a perfect donor match for Molly. When Adam was born in 2000, stem cells from his umbilical cord were transplanted into Molly's bone marrow. Since the transplant, Molly has recovered, and both children are doing well.

The Nash family was one of the first in the United States to go public with their use of PGD for donor matching. While many people were supportive, the Nashes also faced criticism that Adam was a "designer baby" and suffered unjust risks, conceived only to help his sister.

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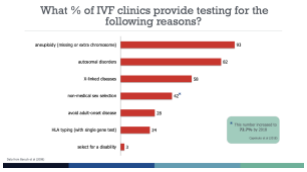
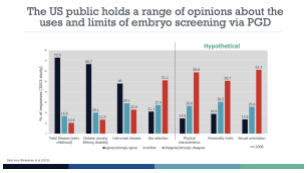


IVF clinics that provide PGD use this technology to test for a number of traits, ranging from serious genetic disorders to non-medical sex selection.

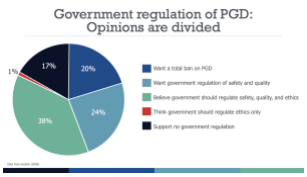
In a 2008 US-based study of 137 clinics, 42% of the surveyed clinics offer to assess the sex of the embryo for "non-medical reasons." For example, parents want a boy or a girl based on preference and not because they wish to avoid a genetic condition that is typically associated with one sex or the other. This number increased to almost 73% by 2018. The study also shows that 3% of clinics allow families to select embryos with traits that others might see as a disability, such as deafness or dwarfism.

Slide 12



People have a wide range of opinions about the uses and limits of embryo screening, including the use of donor matching (as the Nash family did). In a 2015 study, a majority of the Americans surveyed thought it was acceptable to use PGD to select embryos in order to avoid serious illness or disability, or to identify a match for stem cell donation. Note that close to 20% of people stated it would be acceptable to screen for personality traits and other complex characteristics, even though those options are purely hypothetical. The genetic contributions to complex traits such as personality, intelligence, sexual orientation, and strength are poorly understood, making these characteristics unsuitable to this sort of technology.

Slide 13

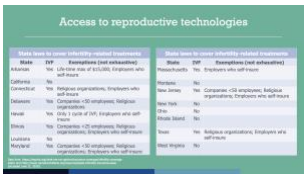


In the same way that opinions on the uses of PGD varied widely, the same is true for opinions on the need for government regulation of PGD.

Currently, there is little US government regulation of what embryonic and fetal traits can be examined via genetic technologies. The government regulates drugs, medical equipment, and the licensing of practitioners, which are all required to perform the described technologies. However, the genetic testing procedures themselves, such as PGD, are not regulated by the federal government. The American Society for Reproductive Medicine issues guidelines, but they do not sanction any violations of their guidelines.

In the study highlighted on the slide, published in 2006, 62% of people surveyed thought there should be some government regulation, while 17% believed the government should have no role in regulating PGD and that the patient or doctor can make any decision related to the embryos.

Slide 14



The access to as well as the cost of various reproductive technologies varies greatly.

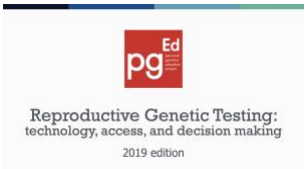
In 2020, the price of NIPT ranges between $300-$8,000 US. However, NIPT is increasingly covered by insurance companies, as more doctors are recommending the test for their patients.

The average cost of IVF is $10,000-15,000 US, a cost that many people cannot afford. As outlined on the slide: sixteen US states require health insurance companies to either cover or offer coverage for infertility-related treatments, the specifics of which vary highly from state-to-state. These state

laws do not apply to public health programs such as Medicaid, which provides health insurance to low-income families. Only 9 of those 16 states mandate coverage of IVF, many of which award exemptions to small business or on the basis of religious grounds. Many insurance companies cover IVF only for married heterosexual couples, excluding the use of donated gametes and denying access to IVF for single parents and same sex couples. The variation of the rules and regulations state-by-state and for different contexts makes it challenging for individuals to determine their insurance coverage, creating additional barriers for those who do not have the resources to do the necessary research.

The average cost of IVF combined with PGD is $20,000-30,000 US. In the United States, PGD is not covered under the majority of public and private health care companies. Moreover, individuals who pursue PGD often do not have infertility problems, and would not otherwise be seeking IVF to become pregnant. Therefore, under many coverage guidelines, the costs for the required IVF treatment are also not covered.

Slide 15



The advances in reproductive genetic testing technologies may offer hope to people who are trying to have children. We explored some of the benefits of these technologies as well as the ethical implications. Opinions on the use and regulation of embryo screening vary widely and the inconsistencies in insurance coverage as well as the sometimes-prohibitive costs means that some people who could benefit from reproductive genetic testing are forced to go without.