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REPRODUCTIVE DECISION MAKING AND TSC

Deciding to start a family or grow an existing family is a life-changing decision, full of excitement and hope. However, if your family medical history contains a diagnosis of tuberous sclerosis complex (TSC), that excitement and hope can give way to fear and anxiety. Fortunately, geneticists can support families on reproductive decision-making.

The geneticist, along with their team of genetic professionals, tries to meet three goals with the family: diagnosis, prognosis, and recurrence risk. For the purposes of reproductive decisions, when the diagnosis of TSC is already known within a parent or family member, recurrence risk is often the most crucial information a family is seeking. A recurrence risk means the risk (or odds) that a subsequent child will be affected with the same condition.

In the case of diagnosing TSC, the genetic professional's job is to convey the genetic facts about TSC. TSC is a genetic disease caused by a change in the *TSC1* or *TSC2* gene that is causing it to no longer work. The non-working gene can then be passed on to future generations. However, it is important to remember that approximately two-thirds of the time when a child is diagnosed with TSC, neither parent has TSC.

If the change in *TSC1* or *TSC2* that causes TSC in a family member can be detected and identified, further testing can be performed on other family members or used for prenatal testing.

Pregnancy and TSC

Many women with TSC have normal, healthy pregnancies. However, there are some potential health complications to take into consideration when a woman with TSC becomes pregnant, including an exacerbation of her disease particularly related to lung and kidney involvement. Some women with TSC also have a disease called lymphangiomyomatosis (LAM) that involves a bundling of muscle cells within the lung that block air, blood, and lymph vessels, thus affecting the exchange of oxygen within the lungs. For reasons not clear, this condition often worsens during pregnancy causing potentially dangerous complications for the mother and baby. Additionally, there is evidence that angiomyolipomas (a TSC-related kidney tumor) increase in size during

Hope no matter how complex

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pregnancy, leading to renal complications. Therefore, it is critical that women know their renal status prior to pregnancy.

Reproductive Options

Reproductive decision making is one of the most sensitive topics a family must discuss, and the choices made are based on a family's beliefs, values, and faith. The TSC Alliance does not advocate for specific options but is committed to sharing the information so families understand all of their possibilities and can make informed choices. It is important to consider that some of these options are still relatively new and very expensive. Often, health insurance will not provide coverage for fertility treatments. If it does, many times the coverage is very limited. Each alternative needs to be considered within a legal and ethical context. Attorneys specializing in family law, perinatologists, reproductive endocrinologists, and geneticists offer professional guidance in supporting families to make the choices right for them.

Prenatal Diagnosis

When the change in the *TSC1* or *TSC2* gene is known, testing can be performed during the pregnancy to evaluate whether the fetus will have TSC. This can be done by one of two techniques: chorionic villus sampling (CVS), which is usually performed between weeks 10-12 of pregnancy; and amniocentesis, which is usually performed between weeks 15-18 of pregnancy. Both carry a small risk of miscarriage. The risk varies depending on the center performing the procedure.

Ultrasounds can also sometimes detect findings of TSC in the fetus; however, they cannot be used to rule out TSC.

Knowing whether the baby has TSC during the pregnancy can be helpful to some families. Some find it helpful so they can prepare for medical care, such as where they will deliver and what doctors they will see. Others also find it helpful emotionally. Although a very difficult decision, and depending on circumstances, some families will choose not to continue the pregnancy.

Prenatal diagnosis can give information about whether the baby has TSC; however, at this time, it cannot be used to predict what symptoms of TSC the baby will have (for example, if he/she will have seizures).

Preimplantation Genetic Diagnosis

When the change in the *TSC1* or *TSC2* gene is known, another option is preimplantation genetic diagnosis (PGD). PGD is technology used to identify a specific genetic change in an embryo created through in vitro fertilization (IVF) before implanting the embryo into the uterus. The purpose of PGD is to identify an unaffected embryo for implantation, thereby reducing or virtually eliminating the risk of having a child with certain genetic diseases.

There are different techniques used for certain indications and varying by center. In general, PGD involves extracting genetic material from the embryo for analysis. Removing

a cell from the embryo for genetic analysis does not hurt the embryo. The embryo compensates for the removed cell and continues to divide normally. This genetic material is then used to determine if the embryo has the change in the gene of interest.

Families with a high risk of having children with a genetic disorder or chromosome abnormalities and who wish to avoid elective pregnancy termination or to prevent the birth of an affected child following prenatal diagnosis may consider PGD. Performing genetic diagnosis prior to implantation of the embryo may reduce the potential for termination of affected fetuses diagnosed by prenatal testing.

There is no difference in pregnancy rates for couples going through IVF and PGD and couples doing IVF alone. The rates are age dependent, but as a general rule it is 30-40% per IVF cycle.

Adoption

Adoption is the process of taking a child into one's family and building a parent-child relationship. This relationship offers all the same rights and privileges of one's biological child. Steps to a successful adoption vary within the United States and internationally. Families typically work through private adoption agencies, social service agencies or religious organizations. Adoptions are legalized through the court system.

Surrogacy

Surrogacy is a method some couples choose as a reproductive option to create a family. It involves a legal contract whereby a woman agrees to become pregnant for the purpose of gestating and giving birth to a child for others to raise. The surrogate mother may be the baby's biological mother (use of the surrogate's eggs) or may be implanted with someone else's fertilized egg.

Egg and/or Sperm Donation

When a couple is concerned about potential risk of passing on a genetic mutation through her eggs or his sperm, options are now available using donor eggs and/or sperm. Donors are available through infertility clinics and private agencies. Egg donation is done in combination with in vitro fertilization (IVF). Sperm donation can be used in combination with IVF and intra-uterine insemination (IUI).

Resources

www.resolve.org: Provides education, advocacy, and support for people facing infertility, multiple miscarriages or having a difficult time with conception

www.sart.org: SART is the primary organization of professionals dedicated to the practice of assisted reproductive technologies (ART) in the United States. The mission of the organization is to set and help maintain the standards for ART in an effort to better serve our members and our patients.

www.adoptionresources.org: The primary purpose of Adoption Resources is to serve the best interests of children, so that each child will be raised in a permanent and loving family. Adoption Resources, strives to provide services that protect the dignity of children, birth parents, adoptive families, and foster families. Comprehensive services provide all those involved in adoption with support and counseling, before, during, and after placement.

www.theiar.org: International Adoption Resources (IAR) is an unbiased resource center for hopeful adoptive parents. IAR offers a wealth of information to provide prospective adoptive parents the insights they need to make informed and educated international adoption choices. In addition to education, IAR has established both grant and corporate partner travel programs to alleviate the financial barriers to international adoption

www.affordingadoption.com: Comprehensive resource list for people seeking financial assistance with adoption costs

www.kidshealth.org: Comprehensive resource list related to genetics and genetic counseling

www.marchofdimes.org: March of Dimes researchers, volunteers, educators, outreach workers and advocates work together to give all babies a fighting chance against the threats to their health: prematurity, birth defects, low birthweight.

<https://ghr.nlm.nih.gov/>: Genetics Home Reference provides overview of genetics, genes, chromosomes, and specific genetic disorders including TSC.

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