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**Updates on Assisted Reproductive Therapy for Pregnancy in Turner Syndrome**

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*A woman with TS and her family*

**Points to ponder about parenthood in Turner syndrome**

Women with Turner syndrome (TS) often express an interest in becoming a parent through adoption, surrogacy, or their own pregnancy. Research related to TS and parenthood was published recently by Erin Falsey, a graduate student in genetics counseling from the MGH Institute of Health Professions. TSSUS supported recruitment for this study by distributing her online research survey of attitudes towards pregnancy, adoption, and surrogacy; this will be summarized at a later date for the TSSUS newsletter.

We wrote this article for the TSSUS Newsletter to highlight new techniques to achieve pregnancy in women with TS, at the same time reminding readers about the need for psychological and health screenings.

**Pregnancy in Turner syndrome**

Spontaneous pregnancy occurs in fewer than 10% of women with TS. This usually occurs in those who have “mosaicism” which refers to a mixture of both 45,X and 46,XX cells. However, the majority of women with TS wanting to become pregnant pursue Assisted Reproductive Technologies (ART) which includes in vitro fertilization (IVF) and egg donation.

**Update on the use of egg retrieval and cryopreservation**

For many years, women with TS and also in the general population have been interested in fertility preservation using a technique called cryopreservation, which is a process of freezing oocytes or eggs. Egg retrieval and cryopreservation has been a successful option for many years in women without TS who want to preserve eggs, but information specific to TS was minimal.

For most women with TS, fertility preservation and ART may be the only way to become pregnant. The technique typically requires hormonal stimulation of the ovarian follicles (eggs) for up to 2 weeks, followed by laparoscopy to retrieve the eggs for cryopreservation. Laparoscopy is a minimally invasive procedure in which a few small incisions are made in the abdomen to insert a small tube that has an attached camera and light that is used to carefully remove the eggs. While this procedure of egg retrieval and preservation is the same in all women, outcomes in women with TS are still unknown. In general, the ability for IVF to achieve pregnancy in TS is similar to the general population.

A recent report from Belgium published in the Journal of Assisted Reproduction and Genetics focused on a 29-year-old woman with TS mosaicism whose child is the first to be conceived with IVF using her own eggs preserved through cryopreservation. Although we are unable to share the full article, you [may access the abstract](https://link.springer.com/article/10.1007/s10815-022-02420-4) https://link.springer.com/article/10.1007/s10815-022-02420-4

**The health and genetics of the woman in the study**

*Background*

Diagnosed with TS at age 11 years, this woman had mosaicism for TS. She had a very low level of 45,X in 14% of her cells and 46,XX in 86% of her cells. A second test called “FISH analysis” found the level of 45,X to be slightly higher (36%). She had no structural heart or kidney defects. As a reminder, “TS mosaicism” does not always mean the person will be mildly affected since there is a lot of variation in appearance and performance.

*Hormone Treatments*

The woman in this report was treated with growth hormone for short stature. She did not require estrogen because she had spontaneous puberty at age 13 with regular menstrual cycles. This was an important clue that her ovaries could contain healthy eggs.

**The path to fertility using egg retrieval**

Since she wanted to preserve her eggs for potential future use, at the age of 24 years, her eggs were removed for rapid freezing. At age 29 years, she continued to have normal menstrual cycles but was unable to conceive after more than 12 months. Thawing of the eggs was successful, and viable eggs were fertilized with her partner’s healthy sperm, yet this first attempt of implantation was not successful. Surprisingly, a few weeks later, she conceived naturally resulting in a healthy baby boy. A year later the woman used Assisted Reproductive Therapy for the second time and successfully became pregnant using the frozen eggs. A healthy girl was born.

**Pregnancy risks for women with Turner syndrome**

Women with TS should only pursue pregnancy after a thorough evaluation of their cardiovascular risk. Those with a bicuspid aortic valve, coarctation of the aorta, and/or hypertension have an increased risk of aortic dissection or rupture during pregnancy and in the immediate postpartum period. The risk of death may be as high as two percent. Moreover, women with TS, including those with mosaic karyotypes, have a higher risk of pregnancy loss and obstetric complications. This occurs whether or not the pregnancy is achieved with the woman’s own or donated eggs. There are clinical guidelines for the optimal care of women with TS who desire pregnancy.

**Lessons learned from this research**

The authors of this research study commented that egg cryopreservation is a suitable choice for individuals with TS mosaicism who have experienced spontaneous menarche (periods). They must be psychologically mature enough to undertake the procedures involved. They recommended that all girls with TS who have experienced natural menstruation be evaluated for their ovarian reserve. This is important if they think they may pursue a pregnancy in the future. Many reproductive endocrinologists are willing to evaluate women with TS and discuss potential future options, including their eligibility for cryopreservation. It is important that patients and families receive guidance from a team of professionals who can care for their cardiac, hormonal, and psychological well-being. Ideally, a team should begin reproductive discussions and evaluations with the parents of young children and adolescents, as well as women prior to conception. If a team misses the opportunity for discussions and evaluations preconception, then they should begin at the current stage of pregnancy. After pregnancy, whether spontaneous or with IVF, the TS mother should have a postnatal cardiac evaluation.

Research papers usually report more than the results of a study, and in this article, the authors share advice about medical care. Specialists from the TS community, including Dr. Vaneeta Bamba and Dr. Angela Lin, supported by Cindy Scurlock as TSSUS President, felt compelled to endorse the study recommendations by sending a letter to the journal’s editor. They reminded that, “Women with TS and their providers recognize that medical care before pregnancy (pre-conception) should include standard cardiovascular monitoring. This care continues diligently throughout the pregnancy and postnatally (afterwards) to monitor for potentially devastating cardiac consequences. Such care will also contribute to favorable outcomes.” They emphasize the diligence necessary to care for a pregnant woman who has TS. Also important is the self-advocacy that may be necessary to ensure the best outcomes in this community.

**Future Directions**

There has been much conversation about options to preserve fertility in individuals with TS. We still do not have clear evidence that fertility preservation is effective for everyone. Readers might wonder if a younger woman is more likely to have suitable eggs, or if this procedure should be performed in children. Research teams in many countries are investigating how the ovaries function in women with TS, how we may preserve fertility over time, and when to perform these procedures.

Under the leadership of Veronica Gomez-Lobo, M.D., chief of the [NICHD’s Pediatric and Adolescent Gynecology (PAG) program](https://www.nichd.nih.gov/research/atNICHD/Investigators/gomez-lobo), and Dr. Tazim Dowlut-McElroy, a medical team at the National Institutes of Health (NIH) are conducting a [clinical trial](https://clinicaltrials.gov/ct2/show/NCT04948658) about egg harvesting in children with TS. They will remove ovarian tissue in an effort to learn more about these topics. <https://www.nichd.nih.gov/newsroom/news/042522-ovarian-tissue-cryopreservation>. This is an exciting development for TS families and their providers.

**Thoughts about this research for the TS community**

For anyone with a medical condition, it is important to be a good advocate for yourself. When considering a fertility procedure, ask your current health care providers if they are aware of fertility specialists who have experience in caring for women with TS. When you meet with a fertility specialist, ask if they are aware of the multidisciplinary guidelines for pregnancy and TS, and if they are able to implement them. Inquire if they have treated other women with TS and if so, how did the women respond to the procedures. As this Newsletter article explains, women with Turner syndrome can have medical complications during and after pregnancy. Your doctor should discuss and evaluate these risks to guide you appropriately.

Future articles will continue to discuss aspects of pregnancy as well as other family planning options.