MONTHLY MEMO:

GENETICS IN REPRODUCTIVE SEX, CANCER RISK, AND WOMEN'S HEALTH

Overview

This memo aims to provide an educational account of various intersections between genetics and women's health, including the definition of biological sex and gender, differences in sexual development (DSD) conditions, and the BRCA mutations.

Sex, Gender, and Intersex Conditions

Sex is a complex biological concept that involves multiple factors, including genetics, anatomy, hormones, and physiology. While sex is typically assigned at birth based on external genitalia, this visible trait represents just one component of biological sex determination. Broadly, sex can be categorized into several dimensions:

- Genetic sex refers to the chromosomal makeup, such as XX (typically female) or XY (typically male).
- Gonadal sex pertains to the presence of testes, ovaries, or a combination of both.
- Hormonal sex reflects the timing and levels of sex hormone release, such as estrogen or testosterone.
- Morphological sex is defined by external genitalia.
- Physiological sex relates to secondary sex characteristics, such as body hair, breast development, or voice changes during puberty.

Differences in sex development (DSD), often referred to as intersex conditions, occur when a person is born with reproductive or sexual anatomy that doesn't align with typical definitions of male or female. An estimated 1.7% of babies are born with DSD, although the majority of cases are not identified until later in life. These variations may involve chromosomes, gonads, external genitalia, or hormone levels. Intersex traits are naturally occurring and highlight the diversity in how biological sex is expressed, underscoring that sex is not always strictly binary.

Consider this:

A significant amount of the population, 1–2 percent of people, do not fall into the strict categories of biological female or male.

FACT!

Being intersex is not a disorder, disease, or condition that needs treatment. However, some people who are intersex may pursue gender affirmation options.

Did you know?

The term "hermaphrodite" is an inappropriate and outdated term. Intersex and differences in sex development are preferred terms.

*Sources & links to corresponding websites are cited at the end of this memo.

What is the BRCA Mutation?

BRCA1 and BRCA2 are genes that produce proteins responsible for repairing damaged DNA. Individuals who inherit a mutation in BRCA1 or BRCA2 have an increased risk of developing breast and ovarian cancers, often at a younger age. Most people with a BRCA1 or BRCA2 mutation inherit a normal copy from the other parent, which typically provides some protection against cancer.

Women with a BRCA1 or BRCA2 mutation have a significantly higher lifetime risk of developing breast cancer—more than 60%, compared to approximately 13% in the general population. Additionally, 30–40% of individuals with a BRCA mutation who develop breast cancer will experience cancer in the opposite breast (contralateral breast cancer) at some point. Men with a BRCA mutation are also at risk, with 1–7% developing breast cancer, compared to about 0.1% in the general male population.

BRCA mutations also increase the risk of ovarian cancer. Approximately 39–58% of women with a BRCA1 mutation and 13–29% of those with a BRCA2 mutation will develop ovarian cancer in their lifetime, compared to only about 1.1% of the general female population.

In addition to breast and ovarian cancer, BRCA1 and BRCA2 mutations are associated with increased risks of pancreatic and prostate cancers, melanoma, endometrial cancer, and certain types of leukemia. However, BRCA mutations remain relatively rare, occurring in approximately 0.2–0.3% of the general population.

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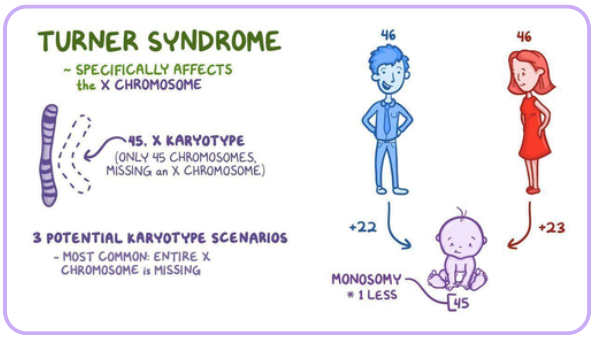
Taking a Closer Look at an Intersex Condition: Turner Syndrome



Turner Syndrome is a genetic condition that affects 1 in 2,500 babies assigned female at birth, characterized by the partial or complete absence of one X chromosome. This chromosomal anomaly leads to a wide range of developmental and medical challenges. Typically, females have two X chromosomes; however, in Turner Syndrome, one X chromosome is partially or partially missing. This chromosomal alteration occurs randomly and is not usually inherited.

Features of Turner Syndrome include: short stature, ovarian insufficiency leading to delayed or absent puberty, broad chest, small lower jaw, skeletal abnormalities, lymphedema, kidney abnormalities, hearing conditions, educational delays, and more.

A diagnosis of Turner Syndrome is confirmed through a karyotype test, which analyzes the number and structure of chromosomes. This test can be performed prenatally or after birth if there are suspicions based on features or growth patterns of the infant. There is no cure for Turner Syndrome, although hormone therapy can be used to increase height, promote secondary sexual development, support bone health, and more.

Genetics in Women's Health

Genetics plays a key role in many complex women's health conditions, including menopause, polycystic ovary syndrome (PCOS), and endometriosis. The timing of menopause is influenced by inherited factors, with certain genes affecting ovarian aging and hormone levels. PCOS, which impacts hormone balance and metabolism, tends to run in families, suggesting a strong genetic link. Endometriosis and uterine fibroids also have genetic components, with variations in genes related to inflammation and estrogen response contributing to their development. While genetics can increase the risk of these conditions, environmental and lifestyle factors also play a crucial role in how they manifest and progress.

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