

The Physical and Genetic Components of Intersex

There are many types of Intersex. We have selected six types of Intersex to discuss in our presentation.

We are going to talk about two categories of Intersex:*

(*note that I have developed names for these categories in order to provide clarity for the different conditions – these are not widely defined categories*)

Meiosis-related Genetic Intersex

1. 47 XXX – Trisomy X or Triple X
2. 45 XO – Turner's Syndrome
3. 47 XXY – Klinefelter Syndrome

Hormonal-related Genetic Intersex

1. 5-alpha Reductase Deficiency
2. Congenital Adrenal Hyperplasia (CAH)
3. Androgen Insensitivity Syndrome (AIS)

47 XXX – Trisomy X or Triple X

Definitions and Facts

- This type of Intersex is an example of gamete carrying an extra X chromosome when it was fertilized (2 in one gamete, 1 in another = 3 Xs)
- 47 XXX is characterized by the presence of an additional (third) X chromosome in each of a female's cells (which normally have two X chromosomes)
- Some females with trisomy X have an extra X chromosome in only some of their cells; this is called 46,XX/47,XXX
- 47 XXX is not inherited, it is due to a random event during the formation of the gametes

Symptoms

- 47 XXX is associated with tall stature, learning problems, delayed development of speech and language, delayed development of motor skills, weak muscle tone, and other features in some girls and women
- Although females with this condition may be taller than average, this chromosomal change typically causes no unusual physical features
- Seizures or kidney abnormalities occur in about 10 percent of affected females
- Most females with triple X syndrome have normal sexual development and are able to conceive children

45 XO – Turner's Syndrome

Definitions and Facts

- Turner syndrome is a genetic disorder that affects a girl's development
- The cause is a missing or incomplete X chromosome
- Individual's with Turner's experience normal intelligence

Symptoms

- Girls who have Turner's are short, and their ovaries don't work properly
- Most are infertile
- They are at risk for health difficulties such as high blood pressure, kidney problems, diabetes, cataracts, osteoporosis and thyroid problems
- Short, "webbed" neck with folds of skin from tops of shoulders to sides of neck
- Low hairline in the back
- Low-set ears
- Swollen hands and feet

What am I? A cross-disciplinary lesson on Intersex

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47 XXY – Klinefelter Syndrome

Definitions and Facts

- Klinefelter's syndrome is a condition that occurs in men who have an extra X chromosome in most of their cells
- Klinefelter syndrome is named after Dr. Henry Klinefelter, who first described a group of symptoms found in some men with the extra X chromosome
- Because not every male with an XXY pattern has all the symptoms of Klinefelter syndrome, it is common to use the term XXY male to describe these men, or XXY condition to describe the symptoms

Symptoms

- The syndrome can affect different stages of physical, language and social development
- The most common symptom is infertility
- Because they often don't make as much of the male hormone testosterone as other boys, teenagers with Klinefelter's syndrome may have less facial and body hair and may be less muscular than other boys
- They may have trouble using language to express themselves
- They may be shy and have trouble fitting in

5-alpha Reductase Deficiency

Definitions and Facts

- 5-alpha reductase deficiency is a condition that affects male sexual development before birth and during puberty. People with this condition are genetically male, with one X and one Y chromosome in each cell, and they have male gonads (testes).
- Their bodies, however, do not produce enough of a hormone called dihydrotestosterone (DHT). DHT has a critical role in male sexual development, and a shortage of this hormone disrupts the formation of the external sex organs before birth.
- This condition is inherited in an autosomal recessive pattern, which means both copies of the *SRD5A2* gene in each cell have mutations.
- Although people who are genetically female (with two X chromosomes in each cell) may inherit mutations in both copies of the *SRD5A2* gene, their sexual development is not affected.
- The development of female sex characteristics does not require DHT, so a lack of steroid 5-alpha reductase 2 activity does not cause physical changes in these individuals.
- Only people who have mutations in both copies of the *SRD5A2* gene and are genetically male (with one X and one Y chromosome in each cell) have the characteristic signs of 5-alpha reductase deficiency.

Symptoms

- Many people with 5-alpha reductase deficiency are born with external genitalia that appear female.
- In other cases, the external genitalia do not look clearly male or clearly female (sometimes called ambiguous genitalia).
- Still other affected infants have genitalia that appear predominantly male, often with an unusually small penis (micropenis) and the urethra opening on the underside of the penis (hypospadias).
- During puberty, people with this condition develop some secondary sex characteristics, such as increased muscle mass, deepening of the voice, development of pubic hair, and a growth spurt.
- The penis and scrotum (the sac of skin that holds the testes) grow larger. Unlike many men, people with 5-alpha reductase deficiency do not develop much facial or body hair. Most affected males are unable to father a child (infertile).

Congenital Adrenal Hyperplasia (CAH)

Definitions and Facts

- People have 2 adrenal glands, one located on top of each of their kidneys. These glands make hormones, cortisol and aldosterone, that are essential for life. People with congenital adrenal hyperplasia lack an enzyme the adrenal gland needs to make the hormones.
- At the same time, the body produces more androgen, a type of male sex hormone. This causes male characteristics to appear early (or inappropriately).

Symptoms

- Symptoms will vary, depending on the type of congenital adrenal hyperplasia someone has and their age when the disorder is diagnosed.
 - Children with milder forms may not have signs or symptoms of congenital adrenal hyperplasia and may not be diagnosed until as late as adolescence.
 - Girls with a more severe form often have abnormal genitals at birth and may be diagnosed before symptoms appear.
 - Boys will appear normal at birth even if they have a more severe form.
- In children with the more severe form of the disorder, symptoms often develop within 2 or 3 weeks after birth.
 - Poor feeding or vomiting
 - Dehydration
 - Electrolyte changes (abnormal levels of sodium and potassium in the blood)
 - Abnormal heart rhythm
- Girls with the milder form will usually have normal female reproductive organs (ovaries, uterus, and fallopian tubes). They may also have the following changes:
 - Abnormal menstrual periods or failure to menstruate
 - Early appearance of pubic or armpit hair
 - Excessive hair growth or facial hair
 - Failure to menstruate
 - Some enlargement of the clitoris
- Boys with the milder form often appear normal at birth. However, they may appear to enter puberty early. Symptoms may include:
 - Deepening voice
 - Early appearance of pubic or armpit hair
 - Enlarged penis but normal testes
 - Well-developed muscles
- Both boys and girls will be tall as children but much shorter than normal as adults.

Androgen Insensitivity Syndrome (AIS)

Definitions and Facts

- This condition is inherited in an X-linked recessive pattern.
- Androgen insensitivity syndrome is a condition that affects sexual development before birth and during puberty.
- People with this condition are genetically male, with one X chromosome and one Y chromosome in each cell. Because their bodies are unable to respond to certain male sex hormones (called androgens), they may have mostly female sex characteristics or signs of both male and female sexual development.
- Complete androgen insensitivity syndrome occurs when the body cannot use androgens at all. People with this form of the condition have the external sex characteristics of females, but do not have a uterus and therefore do not menstruate and are unable to conceive a child (infertile).

- They are typically raised as females and have a female gender identity.
- Affected individuals have male internal sex organs (testes) that are undescended, which means they are abnormally located in the pelvis or abdomen. Undescended testes can become cancerous later in life if they are not surgically removed.
- People with complete androgen insensitivity syndrome also have sparse or absent hair in the pubic area and under the arms.
- A person with complete AIS appears to be female but has no uterus, and has very little armpit and pubic hair. At puberty, female sex characteristics (such as breasts) develop. However, the person does not menstruate and become fertile.
- Persons with incomplete AIS may have both male and female physical characteristics. Many have partial closing of the outer vaginal lips, an enlarged clitoris, and a short vagina.
- There may be:
 - A vagina but no cervix or uterus
 - Normal female breasts
 - Testes in the abdomen or other unusual places in the body

How common is Intersex?

47 XXX – Trisomy X or Triple X

- This condition occurs in about 1 in 1,000 newborn girls. Five to 10 girls with triple X syndrome are born in the United States each day.

47 XXY – Klinefelter Syndrome

- Scientists believe the XXY condition is one of the most common chromosome abnormalities in humans. About one of every 500 males has an extra X chromosome, but many don't have any symptoms.

45 XO – Turner's Syndrome

- This condition occurs in about 1 in 2,500 newborn girls worldwide, but it is much more common among pregnancies that do not survive to term (miscarriages and stillbirths).

5-alpha Reductase Deficiency

- 5-alpha reductase deficiency is a rare condition; the exact incidence is unknown. Large families with affected members have been found in several countries, including the Dominican Republic, Papua New Guinea, Turkey, and Egypt.

Congenital Adrenal Hyperplasia (CAH)

- Congenital adrenal hyperplasia can affect both boys and girls. About 1 in 10,000 to 18,000 children are born with congenital adrenal hyperplasia.

Androgen Insensitivity Syndrome (AIS)

- Complete androgen insensitivity syndrome affects 2 to 5 per 100,000 people who are genetically male. Partial androgen insensitivity is thought to be at least as common as complete androgen insensitivity. Mild androgen insensitivity is much less common.

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