XX MALE SYNDROME

De La Chapelle Syndrome, Xx Testicular Disorder Of Sex Development, Dsd

The male sex chromosomal disorder characterized by a spectrum of clinical presentations, ranging from ambiguous to normal male genitalia.

Diagnosis Male

Related Diagnoses:
Azoospermia | Erectile dysfunction | Non-obstructive azoospermia | Hypogonadism | Idiopathic male infertility | Testicular failure | Gonadal dysgenesis

About XX male syndrome

The 46, XX disorder of sex development (DSD) is a rare form of sex reversal in infertile men, that was first described by la Chapelle et al. in 1964 and occurred 1:20 000 in newborns. Usually, it is caused by unequal crossing-over between X and Y chromosomes during meiosis in the father, which results in the X chromosome containing the normally-male SRY gene. When this X combines with a normal X from the mother during fertilization, the result is an XX male.

46,XX males are phenotypically and psychosexually male. Clinical phenotypes about 46, XX DSD have been identified to three groups, including males with normal phenotype, males with genital ambiguities and males with true hermaphrodites. Approximately 80% of individuals with 46,XX testicular DSD present after puberty with normal pubic hair and normal penile size, but small testes, and sterility resulting from azoospermia.

The sex-determining region Y gene (SRY) locating in Y chromosome, plays a major role in encoding a testis determining factor (TDF). About 90% of DSD patients have Y chromosomal material including the SRY gene that is usually translocated to the distal tip of the short arm of X chromosome or autosomal chromosomes. About 10% of 46, XX males are negative for SRY gene, which could carry different degrees of masculinization.

There are several pathogenic mechanisms explaining 46, XX testicular DSD patients:

- translocation of Y sequences, including the SRY gene, to an X chromosome or to an autosome;
- mutation in a gene in the testis-determining pathway triggering testis differentiation in SRY-negative XX males;
- hidden Y chromosome mosaicism limited to the gonad

Associated disease

- sterility
- azoospermia
- gonadal dysgenesis
- hypospadias

Complications

Long-term complications include: low libido, erectile dysfunction, decreased secondary sexual characteristics and depression.

Risk factors
There are no risk factors because it is generally a result of random unequal crossing over between X and Y chromosomes.

Impact on fertility

The heterogeneous nature of chromosomal abnormalities and the potentially complex reproductive result make it indispensable for the geneticist and clinician to be knowledgeable of the modern practice of fertility, both for diagnosis and couple counseling as to natural conception or by assisted reproduction. If sperm is available but the male bears a chromosomal abnormality, there is a higher risk than that of the normal population of an invisible conceptus occurring, or a liveborn with deficiencies. In some cases, the genotype may present a null perspective for the recovery of sperm, for example, as in some 46,XX males, and in these cases, other options should be discussed, such as the use of donor sperm or adoption.

Prevention

The XX male syndrome cannot be prevented.

Symptoms

Symptoms usually include small testes and subjects are invariably sterile. Individuals with this condition sometimes have feminine characteristics, with varying degrees of gynecomastia but with no intra-abdominal Müllerian tissue. Most of XX males are not stereotypically feminine and are typical boys and men although other reports suggest that facial hair growth is usually poor and libido is diminished, with notable exceptions.

Therapies

Self therapy

Although there is no cure for XX male syndrome, there are various resources to help manage the condition physically, psychologically, and emotionally.

Conventional medicine

Pharmacotherapy

When these individuals reach puberty, they require treatment with the male sex hormone testosterone to induce development of male secondary sex characteristics such as deepening of the voice and facial hair (masculinization). To help prevent breast enlargement (gynecomastia), hormone treatment is also useful.

Surgical therapy

There is no surgical therapy to treat XX male syndrome itself, although if gynecomastia is severe enough, breast reduction surgery is possible.

Assisted reproduction

When the SRY gene is present on the X chromosome, it almost always causes infertility due to
azoospermia. In such cases, there is possibility to extract sperm by technique called TESE - testicular sperm extraction.

Testicular sperm can be retrieved via percutaneous aspiration of testicular tissue. The doctors remove a small portion of tissue from the testicle under local anesthesia and extracting the few viable sperm cells present in that tissue for intracytoplasmic sperm injection (ICSI). Sperm obtained by these methods are subsequently used for ICSI. If no sperm are available, then the possibility of using sperm donation should be considered.

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Find more about related issues

**Diagnoses**

- **Azoospermia**
  Complete absence of sperm in the ejaculate of a man.
  Learn more at: [www.fertilitypedia.org/therapy/diag/azoospermia](http://www.fertilitypedia.org/therapy/diag/azoospermia)

- **Erectile dysfunction**
  The inability (that lasts more than 6 months) to develop or maintain an erection of the penis during sexual activity.
  Learn more at: [www.fertilitypedia.org/therapy/diag/erectile-dysfunction](http://www.fertilitypedia.org/therapy/diag/erectile-dysfunction)

- **Non-obstructive azoospermia**
  Complete absence of sperm in the ejaculate due to testicular failure.
  Learn more at: [www.fertilitypedia.org/therapy/diag/non-obstructive-azoospermia](http://www.fertilitypedia.org/therapy/diag/non-obstructive-azoospermia)

- **Hypogonadism**
  A medical term which describes a diminished functional activity of the gonads – the testes and ovaries.
  Learn more at: [www.fertilitypedia.org/therapy/diag/hypogonadism](http://www.fertilitypedia.org/therapy/diag/hypogonadism)

- **Idiopathic male infertility**
  A condition in which fertility impairment occurs spontaneously or due to an unknown cause.
  Learn more at: [www.fertilitypedia.org/therapy/diag/idiopathic-male-infertility](http://www.fertilitypedia.org/therapy/diag/idiopathic-male-infertility)

- **Testicular failure**
  The inability of the testicles to produce sperm or testosterone.
  Learn more at: [www.fertilitypedia.org/therapy/diag/testicular-failure](http://www.fertilitypedia.org/therapy/diag/testicular-failure)

- **Gonadal dysgenesis**
  Any congenital developmental disorder of the reproductive system characterized by a progressive loss of germ cells on the developing gonads.
  Learn more at: [www.fertilitypedia.org/therapy/diag/gonadal-dysgenesis](http://www.fertilitypedia.org/therapy/diag/gonadal-dysgenesis)

**Organs**

- **Testes**
  Male gonads which produce both sperm and androgens, such as testosterone, and are active throughout the reproductive lifespan of the male.
  Learn more at: [www.fertilitypedia.org/edu/organs/testes](http://www.fertilitypedia.org/edu/organs/testes)

**Reproductive cells**

- **Spermatogonium**
  An undifferentiated male germ cell with self-renewing capacity representing the first stage of spermatogenesis.
  Learn more at: [www.fertilitypedia.org/edu/reproductive-cells/spermatogonium](http://www.fertilitypedia.org/edu/reproductive-cells/spermatogonium)
Biological control

Progesterone
Steroid hormone, secreted by the ovaries, whose function is to prepare the uterus for the implantation of a fertilized ovum and to maintain pregnancy.
Learn more at: www.fertilitypedia.org/edu/biological-control/progesterone

Reproductive functions

Fertilization
The fusion of an ovum with a sperm to initiate the development of a new individual organism.
Learn more at: www.fertilitypedia.org/edu/reproductive-functions/fertilization

Spermatogenesis
Process in which spermatozoa are produced from male primordial germ cells in testicles by way of mitosis and meiosis.
Learn more at: www.fertilitypedia.org/edu/reproductive-functions/spermatogenesis

Symptoms

Depression
The emotional state characterized by persistent feel of low self-esteem, loss of interest, sadness and negative attitude.
Learn more at: www.fertilitypedia.org/edu/symptoms/depression

Gynecomastia
A disorder of the endocrine system in which there is a non-cancerous swelling of the breast tissue in boys or men.
Learn more at: www.fertilitypedia.org/edu/symptoms/gynecomastia

Hypospadias
A birth defect of the urethra in the male where the urinary opening is not at the usual location on the head of the penis.
Learn more at: www.fertilitypedia.org/edu/symptoms/hypospadias

Infertility
The failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.
Learn more at: www.fertilitypedia.org/edu/symptoms/infertility

Low facial and body hair growth
Decrease of facial and body hair in males.
Learn more at: www.fertilitypedia.org/edu/symptoms/low-facial-and-body-hair-growth

Lowered libido
The absence of sexual appetite.
Learn more at: www.fertilitypedia.org/edu/symptoms/lowered-libido

Small testes
Abnormally small testicular volume.
Learn more at: www.fertilitypedia.org/edu/symptoms/small-testes

Therapies

Egg donation
Process by which a woman donates eggs for purposes of assisted reproduction or biomedical research.
Learn more at: www.fertilitypedia.org/edu/therapies/egg-donation
ICSI
A micromanipulative fertilization technique in which a single sperm is injected directly into an egg.
Learn more at: www.fertilitypedia.org/edu/therapies/icsi

Micro TES
Microsurgical method used to identify areas of sperm production within the testes with the aid of optical magnification.
Learn more at: www.fertilitypedia.org/edu/therapies/micro-tese

PESA
Sperm aspiration procedure in which a needle is inserted into the epididymis in order to retrieve sperm.
Learn more at: www.fertilitypedia.org/edu/therapies/pesa

Preimplantation genetic diagnosis
Technology that allows couples with a family history of monogenic disorders, X-linked diseases and chromosomal abnormality have a healthy baby.
Learn more at: www.fertilitypedia.org/edu/therapies/preimplantation-genetic-diagnosis

Sperm donation
The procedure in which a man (sperm donor) provides his sperm for fertility treatment.
Learn more at: www.fertilitypedia.org/edu/therapies/sperm-donation

Standard IVF
A process in which an egg is fertilised by sperm outside the body: in vitro. Own or donated gametes may be used.
Learn more at: www.fertilitypedia.org/edu/therapies/standard-ivf

TESE
Removal of a small portion of testicular tissue in order to extract a few viable sperm.
Learn more at: www.fertilitypedia.org/edu/therapies/tese

Gallery

Meiosis crossover
The offspring gets a set of chromosomes from each parent so that, half comes from each parent. But the two sets of chromosomes are not identical with the parental chromosomes. This is because they are changed during a process called crossing over.

XX male
Because of crossing over, part of male chromosome with SRY gene (blue part of X chromosome) responsible for testicular development is translocated on X chromosome. The karyotype is feminine with masculine phenotype.

Sources
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