Androgen insensitivity syndrome

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 external 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 have a small chance of becoming 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.

The partial and mild forms of androgen insensitivity syndrome result when the body’s tissues are partially sensitive to the effects of androgens. People with partial androgen insensitivity (also called Reifenstein syndrome) can have genitalia that look typically female, genitalia that have both male and female characteristics, or genitalia that look typically male. They may be raised as males or as females and may have a male or a female gender identity. People with mild androgen insensitivity are born with male sex characteristics, but they are often infertile and tend to experience breast enlargement at puberty.

Frequency

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.

Causes

Mutations in the AR gene cause androgen insensitivity syndrome. This gene provides instructions for making a protein called an androgen receptor. Androgen receptors allow cells to respond to androgens, which are hormones (such as testosterone) that direct male sexual development. Androgens and androgen receptors also have other important functions in both males and females, such as regulating hair growth and sex drive. Mutations in the AR gene prevent androgen receptors from working properly, which makes cells less responsive to androgens or prevents cells from using these
hormones at all. Depending on the level of androgen insensitivity, an affected person’s sex characteristics can vary from mostly female to mostly male.

Inheritance Pattern

This condition is inherited in an X-linked recessive pattern. A condition is considered X-linked if the mutated gene that causes the disorder is located on the X chromosome, one of the two sex chromosomes in each cell. In genetic males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In genetic females (who have two X chromosomes), a mutation must be present in both copies of the gene to cause the disorder. Males are affected by X-linked recessive disorders much more frequently than females.

About two-thirds of all cases of androgen insensitivity syndrome are inherited from mothers who carry an altered copy of the AR gene on one of their two X chromosomes. The remaining cases result from a new mutation that can occur in the mother’s egg cell before the child is conceived or during early fetal development.

Other Names for This Condition

- AIS
- androgen receptor deficiency
- androgen resistance syndrome
- AR deficiency
- DHTR deficiency
- dihydrotestosterone receptor deficiency

Diagnosis & Management

Genetic Testing Information

- What is genetic testing? /primer/testing/genetictesting
Other Diagnosis and Management Resources

- Accord Alliance: Disorders of Sex Development (DSD) Guidelines
  http://www.accordalliance.org/dsd-guidelines/

- GeneReview: Androgen Insensitivity Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1429

- MedlinePlus Encyclopedia: Androgen Insensitivity Syndrome
  https://medlineplus.gov/ency/article/001180.htm

- MedlinePlus Encyclopedia: Intersex
  https://medlineplus.gov/ency/article/001669.htm

- MedlinePlus Encyclopedia: Reifenstein Syndrome
  https://medlineplus.gov/ency/article/001169.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Androgen Insensitivity Syndrome
  https://medlineplus.gov/ency/article/001180.htm

- Encyclopedia: Intersex
  https://medlineplus.gov/ency/article/001669.htm

- Encyclopedia: Reifenstein Syndrome
  https://medlineplus.gov/ency/article/001169.htm

- Health Topic: Infertility
  https://medlineplus.gov/infertility.html

Genetic and Rare Diseases Information Center

- Androgen insensitivity syndrome
  https://rarediseases.info.nih.gov/diseases/5803/androgen-insensitivity-syndrome

- Androgen insensitivity syndrome, mild

- Complete androgen insensitivity syndrome

- Partial androgen insensitivity syndrome
Educational Resources

- Boston Children's Hospital
  http://www.childrenshospital.org/conditions-and-treatments/conditions/a/androgen-insensitivity

- MalaCards: androgen insensitivity syndrome, mild
  https://www.malacards.org/card/androgen_insensitivity_syndrome_mild

- MalaCards: complete androgen insensitivity syndrome
  https://www.malacards.org/card/complete_androgen_insensitivity_syndrome

- Orphanet: Androgen insensitivity syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=754

- Orphanet: Complete androgen insensitivity syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=99429

- Orphanet: Partial androgen insensitivity syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Ln=EN&Expert=90797

Patient Support and Advocacy Resources

- Accord Alliance
  http://www.accordalliance.org/

- AIS-DSD Support Group
  http://aisdsd.org/

- InterACT Advocates for Intersex Youth
  https://interactadvocates.org/

- National Organization for Rare Disorders
  https://rarediseases.org/rare-diseases/androgen-insensitivity-syndrome-partial/

- Resolve: The National Infertility Association
  https://resolve.org/

Clinical Information from GeneReviews

- Androgen Insensitivity Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1429

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Androgen-Insensitivity+Syndrome%5BMAJR%5D%29+AND+%28androgen+insensitivity+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D
Catalog of Genes and Diseases from OMIM

- ANDROGEN INSENSITIVITY SYNDROME
  http://omim.org/entry/300068

Medical Genetics Database from MedGen

- Androgen resistance syndrome

Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/26182482

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10727996

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301602

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23392093

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22698698

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