Wiskott-Aldrich syndrome

Wiskott-Aldrich syndrome is characterized by abnormal immune system function (immune deficiency) and a reduced ability to form blood clots. This condition primarily affects males.

Individuals with Wiskott-Aldrich syndrome have microthrombocytopenia, which is a decrease in the number and size of blood cell fragments involved in clotting (platelets). This platelet abnormality, which is typically present from birth, can lead to easy bruising, bloody diarrhea, or episodes of prolonged bleeding following minor trauma. Microthrombocytopenia can also lead to small areas of bleeding just under the surface of the skin, resulting in purplish spots called purpura or rashes of tiny red spots called petechiae. In some cases, the bleeding episodes can be life-threatening.

Wiskott-Aldrich syndrome is also characterized by abnormal or nonfunctional immune system cells known as white blood cells. Changes in white blood cells lead to an increased risk of several immune and inflammatory disorders in people with Wiskott-Aldrich syndrome. These immune problems vary in severity and include an increased susceptibility to infection and eczema (an inflammatory skin disorder characterized by abnormal patches of red, irritated skin). People with Wiskott-Aldrich syndrome are at greater risk of developing autoimmune disorders, such as rheumatoid arthritis or hemolytic anemia, which occur when the immune system malfunctions and attacks the body's own tissues and organs. The chance of developing certain types of cancer, such as cancer of the immune system cells (lymphoma), is also increased in people with Wiskott-Aldrich syndrome.

Wiskott-Aldrich syndrome is often considered to be part of a disease spectrum with two other disorders: X-linked thrombocytopenia and severe congenital neutropenia. These conditions have overlapping signs and symptoms and the same genetic cause.

Frequency

The estimated incidence of Wiskott-Aldrich syndrome is between 1 and 10 cases per million males worldwide; this condition is rarer in females.

Genetic Changes

Mutations in the WAS gene cause Wiskott-Aldrich syndrome. The WAS gene provides instructions for making a protein called WASP. This protein is found in all blood cells. WASP is involved in relaying signals from the surface of blood cells to the actin cytoskeleton, which is a network of fibers that make up the cell's structural framework. WASP signaling triggers the cell to move and attach to other cells and tissues (adhesion). In white blood cells, this signaling allows the actin cytoskeleton to
establish interactions between cells and the foreign invaders that they target (immune synapses).

WAS gene mutations that cause Wiskott-Aldrich syndrome lead to a lack of any functional WASP. Loss of WASP signaling disrupts the function of the actin cytoskeleton in developing blood cells. White blood cells that lack WASP have a decreased ability to respond to their environment and form immune synapses. As a result, white blood cells are less able to respond to foreign invaders, causing many of the immune problems related to Wiskott-Aldrich syndrome. Similarly, a lack of functional WASP in platelets impairs their development, leading to reduced size and early cell death.

Because they all have the same genetic cause, Wiskott-Aldrich syndrome, X-linked thrombocytopenia, and severe congenital neutropenia are sometimes collectively referred to as WAS-related disorders.

Inheritance Pattern
This condition is inherited in an X-linked 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 males, who have only one X chromosome, a mutation in the only copy of the gene in each cell is sufficient to cause the condition. In females, who have two copies of the X chromosome, one altered copy of the gene in each cell can lead to less severe features of the condition or may cause no signs or symptoms at all. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition
- eczema-thrombocytopenia-immunodeficiency syndrome
- IMD2
- immunodeficiency 2
- Wiskott syndrome

Diagnosis & Management

Genetic Testing
- Genetic Testing Registry: Wiskott-Aldrich syndrome

Other Diagnosis and Management Resources
- GeneReview: WAS-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1178
- MedlinePlus Encyclopedia: Thrombocytopenia
  https://medlineplus.gov/ency/article/000586.htm
• National Marrow Donor Program
https://bethematch.org/patients-and-families/about-transplant/diseases-treated-by-
transplant/wiskott-aldrich-syndrome/

• Rare Disease Clinical Research Network: Primary Immune Deficiency Treatment
Consortium
http://www.rarediseasesnetwork.org/cms/pidtc/Learn-More/Disorder-
Definitions#WAS

General Information from MedlinePlus
• Diagnostic Tests
https://medlineplus.gov/diagnostictests.html

• Drug Therapy
https://medlineplus.gov/drugtherapy.html

• Genetic Counseling
https://medlineplus.gov/geneticcounseling.html

• Palliative Care
https://medlineplus.gov/palliativecare.html

• Surgery and Rehabilitation
https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus
• Encyclopedia: Thrombocytopenia
https://medlineplus.gov/ency/article/000586.htm

• Health Topic: Bleeding Disorders
https://medlineplus.gov/bleedingdisorders.html

• Health Topic: Eczema
https://medlineplus.gov/eczema.html

• Health Topic: Immune System and Disorders
https://medlineplus.gov/immunesystemanddisorders.html

Genetic and Rare Diseases Information Center
• Wiskott Aldrich syndrome
Additional NIH Resources

• National Heart, Lung, and Blood Institute: Thrombocytopenia
  https://www.nhlbi.nih.gov/health-topics/thrombocytopenia

• National Institute of Allergy and Infectious Diseases: Primary Immune Deficiency Diseases

Educational Resources

• Boston Children's Hospital: Autoimmune Diseases
  http://www.childrenshospital.org/conditions-and-treatments/conditions/a/autoimmune-diseases

• Boston Children's Hospital: Thrombocytopenia
  http://www.childrenshospital.org/conditions-and-treatments/conditions/t/thrombocytopenia

• Boston Children's Hospital: Wiskott-Aldrich Syndrome
  http://www.childrenshospital.org/conditions-and-treatments/conditions/w/wiskott-aldrich-syndrome

• Cleveland Clinic: Eczema
  https://my.clevelandclinic.org/health/diseases/9998-eczema

• Disease InfoSearch: Wiskott Aldrich syndrome
  http://www.diseaseinfosearch.org/Wiskott+Aldrich+syndrome/7514

• Immune Deficiency Foundation: Wiskott-Aldrich Syndrome
  https://primaryimmune.org/about-primary-immunodeficiencies/specific-disease-types/wiskott-aldrich-syndrome/

• MalaCards: wiskott-aldrich syndrome
  http://www.malacards.org/card/wiskott_aldrich_syndrome

• Orphanet: Wiskott-Aldrich syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=906

Patient Support and Advocacy Resources

• Immune Deficiency Foundation: Wiskott-Aldrich Syndrome
  https://primaryimmune.org/about-primary-immunodeficiencies/specific-disease-types/wiskott-aldrich-syndrome/

• Internation Patient Organisation for Primary Immunodeficiencies
  https://ipopi.org/

• National Organization for Rare Disorders (NORD): WAS Related Disorders
  https://rarediseases.org/rare-diseases/was-related-disorders/
• Platelet Disorder Support Association: Platelet Details
  https://www.pdsa.org/about-itp/platelet-details.html

• Rare Disease Clinical Research Network: Primary Immune Deficiency Treatment
  Consortium
  http://www.rarediseasesnetwork.org/cms/pidtc/Learn-More/Disorder-Definitions#WAS

• The Wiskott-Aldrich Foundation
  http://www.wiskott.org/

**GeneReviews**

• WAS-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1178

**ClinicalTrials.gov**

• ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Wiskott-Aldrich+syndrome%22

**Scientific Articles on PubMed**

• PubMed
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  +1080+days%22%5Bdp%5D

**OMIM**

• WISKOTT-ALDRICH SYNDROME
  http://omim.org/entry/301000

**MedGen**

• Wiskott-Aldrich syndrome

**Sources for This Summary**

• Blundell MP, Worth A, Bouma G, Thrasher AJ. The Wiskott-Aldrich syndrome: The actin
  DMA-2010-0735. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21178275
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3835520/

• Chandra S, Bronicki L, Nagaraj CB, Zhang K. WAS-Related Disorders. 2004 Sep 30 [updated 2016
  Sep 22]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD,
  Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA):
  NBK1178/
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301357


Reprinted from Genetics Home Reference:

Reviewed: March 2018
Published: April 3, 2018

Lister Hill National Center for Biomedical Communications
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