

# Disease statistics

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# WISKOTT-ALDRICH SYNDROME

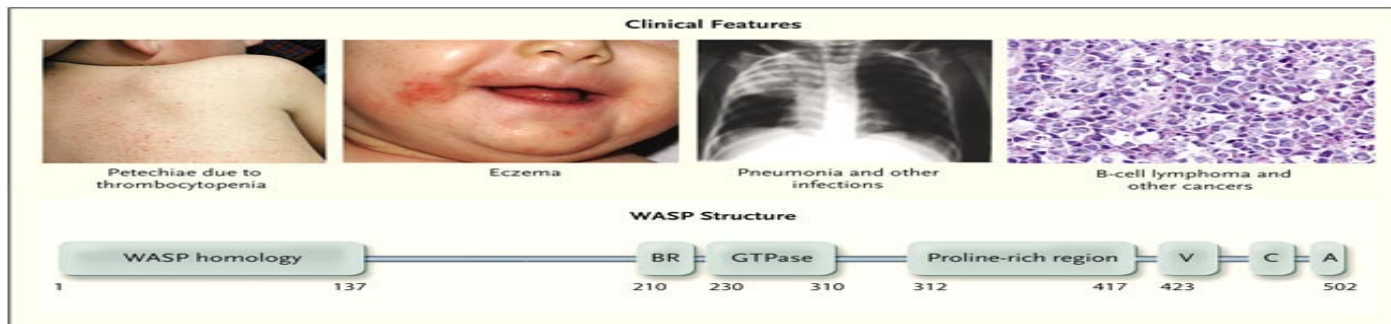
An X-linked Primary Immunodeficiency

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# WHAT IS WISKOTT ALDRICH SYNDROME?

**Wiskott-Aldrich Syndrome (WAS)** is a serious medical condition that causes problems both with the immune system and with blood clotting. Patients with WAS may be very susceptible to infections caused by bacterial and fungal organisms and eczema. The problems with easy bruising and bleeding in patients with WAS result from having low counts of small, non-functional platelets, the cells in the blood that clump together to form blood clots.

Children with WAS are diagnosed most commonly in the first 1-2 years of life because of easy bruising, abnormal bleeding, or low platelet counts. Patients may also have severe or frequent infections, including bacterial ear infections, sinus infections, pneumonia, blood infections, or viral infections.



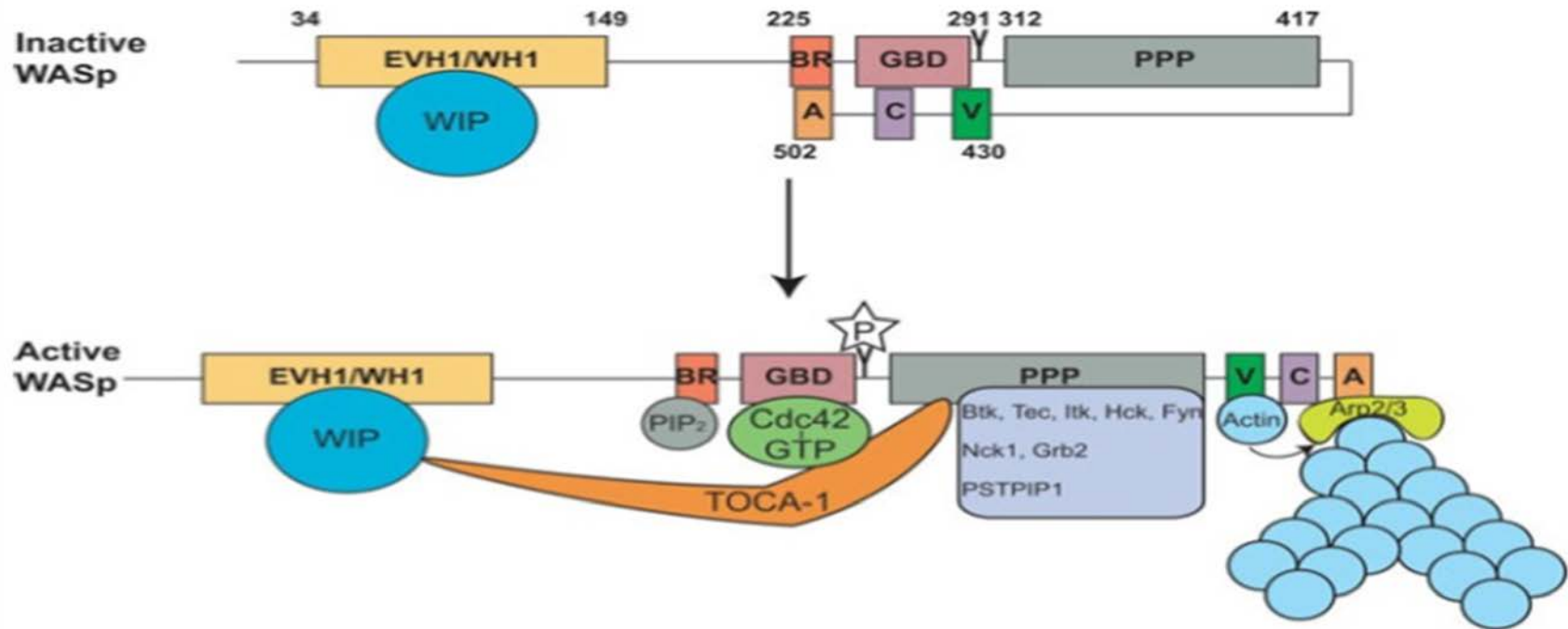
# TYPES OF WAS

Patients show a wide variation in the severity of the disease and four types have been identified:

- 1. Classic or Severe WAS:** This is the most severe form of WAS.
- 2. X-Linked Thrombocytopenia (XLT):** This is milder form of WAS where the platelets are affected but there is little or no immunodeficiency. Sometimes the symptoms of WAS and XLT overlap, making the distinction between the two unclear.
- 3. Intermittent Thrombocytopenia:** The mildest form called where the platelet abnormalities are intermittent and there is no immunodeficiency.
- 4. X Linked Neutropenia:** This is the rarest form in which the platelets are normal but there is a serious defect in the neutrophils (a kind of white blood cell). Patients can have serious and recurrent infections.

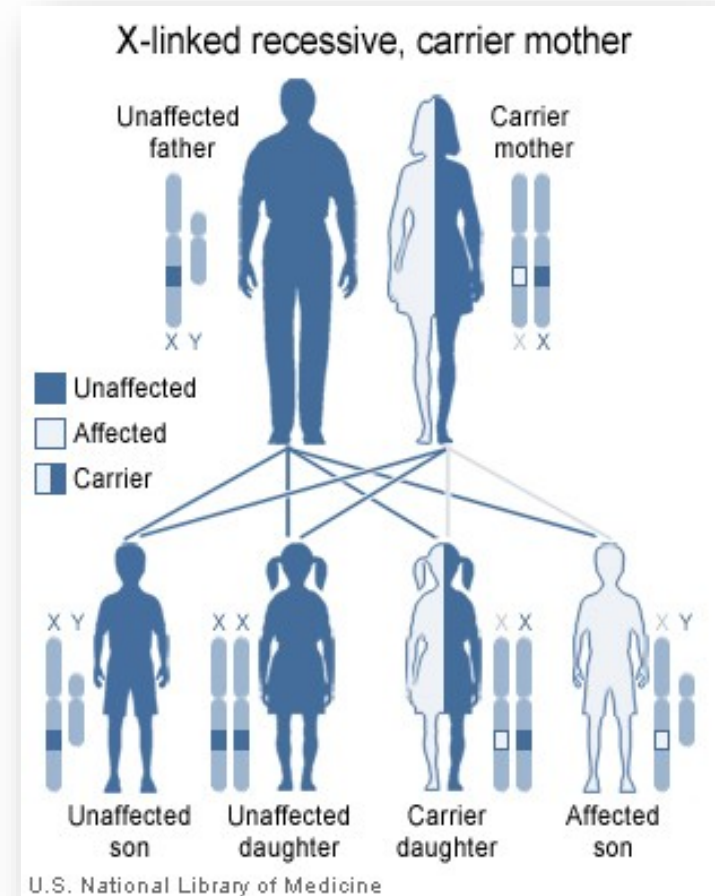
# WHAT CAUSES OF WAS ?

WAS is caused by a mutation in the WAS gene that is located on the X chromosome. The production of the WAS protein is controlled by the WAS gene. This gene instructs cells to make the WAS protein. When this gene is mutated, it results in patients having abnormal, reduced or absent protein causing WAS.



# HOW DO PEOPLE INHERIT WISKOTT-ALSRIICH SYNDROME?

- This condition is inherited in an X-linked pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes.
- In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell may or may not cause the disorder.
- In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell causes the disorder. In most cases of X-linked inheritance, males experience more severe symptoms of the disorder than females.



# STATISTICS OF WAS

- Life expectancy of 15 years in a patient lacking WAS protein expression.
- Affects 1 in 10 of every 1 million male newborns can occur in females only when X-chromosome containing the functional allele is inactive.
- 90 % manifest thrombocytopenia at presentation.
- 20% only have hematopoietic abnormalities.
- 5% only have infectious manifestations.
- 0% only have eczema

# CLINICAL MANIFESTATION OF WISKOTT-ALDRICH SYNDROME

In its classic form, WAS is typically characterized by the following basic clinical features:

- I. Increased tendency to bleed caused by a significantly reduced number of platelets( Thrombocytopenia)
- II. Recurrent bacterial, viral and fungal infections.
- III. Eczema of the skin
- IV. Auto Immune manifestations
- V. Malignancies( Cancer)

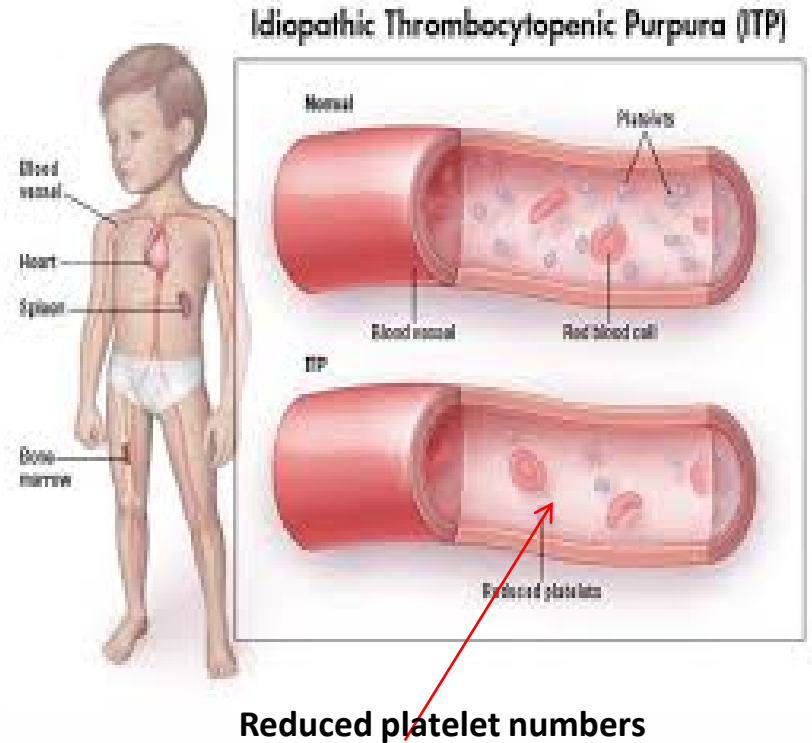


# I. Bleeding Tendency

**Thrombocytopenia** (a reduced number of platelets) is a common feature of patients with WAS. In addition to being decreased in number, the platelets themselves are small and dysfunctional, less than half the size of normal platelets. As a result, patients with WAS may bleed easily, even if they have not had an injury. Bleeding into the skin may cause pinhead sized bluish-red spots, called petechiae, or they may be larger and resemble bruises.

## Common manifestations:

- i. Bloody bowel movements (especially during infancy).
- ii. Bleeding gums, and prolonged nose bleeds.
- iii. Brain Hemorrhage.

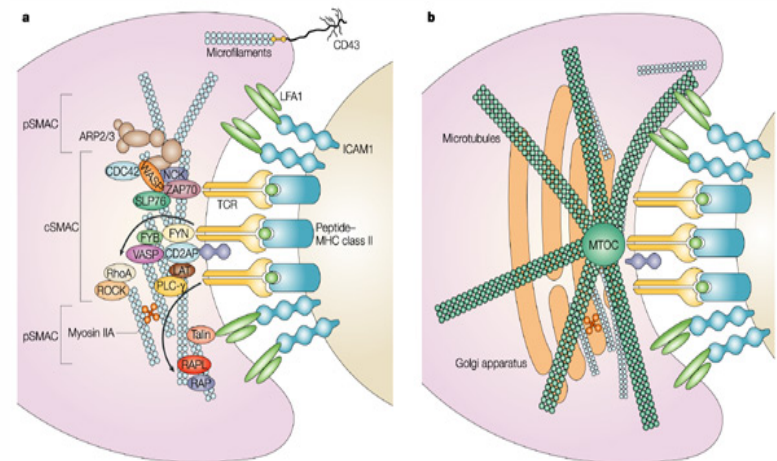


# II. INFECTIONS

The immunodeficiency associated with WAS causes the function of both B- and T-lymphocytes to be significantly abnormal. As a result, infections are common in the classic form of WAS and may involve all classes of microorganisms

## Common manifestations:

- i. Respiratory Infections such as ear infections, sinus and pneumonia.
- i. Sepsis (blood poisoning)
- ii. Meningitis
- iii. Severe viral and bacterial infections



Nature Reviews | Immunology

Michel J. Massaad, Narayanaswamy Ramesh, and Raif S. Geha. Wiskott-Aldrich syndrome: A comprehensive review. Ann. N.Y. Acad. Sci. 2013.

# III. ECZEMA

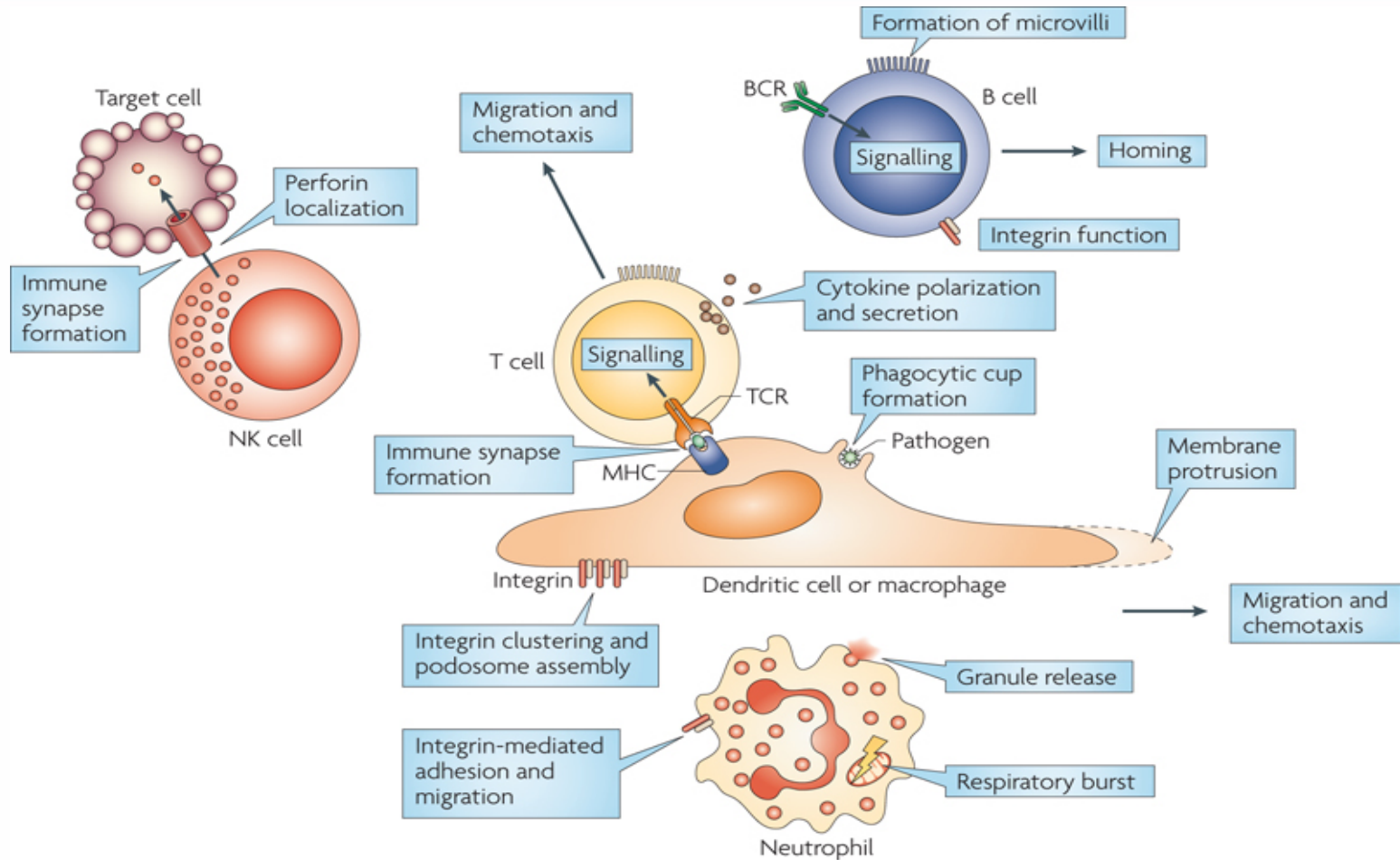
An eczema rash is common in patients with classic WAS. In infants, the eczema may occur on the face or scalp and can resemble “cradle cap.” It can also have the appearance of a severe diaper rash, or be more generalized, involving the arms and legs.



# IV. AUTOIMMUNE MANIFESTATIONS

MOST COMMON	LESS COMMON
Autoimmune hemolytic anemia	Inflammatory bowel syndrome
Cutaneous vasculitis	Idiopathic thrombocytopenic purpura
Arthritis	Neutropenia
Nephropathy	

# CLINICAL MANIFESTATION: IMMUNE DEFICIENCY

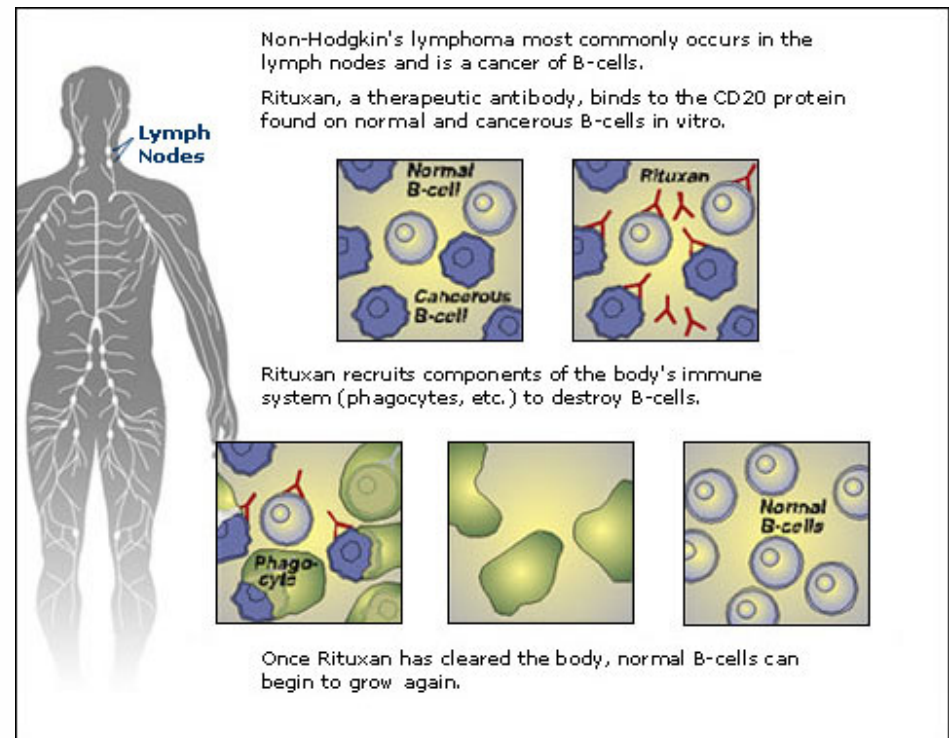


# V. MALIGNANCIES

Patients with WAS have an increased risk of malignancies (cancer) compared to normal individuals. Overall, it has been estimated that 15-20% of patients eventually develop malignancies.

## Common manifestations:

- I. Lymphomas or leukemia
- II. The most common with Non-Hodgkins lymphoma making up the majority of cases.



# DIAGNOSIS OF WAS

Once the diagnosis of WAS is clinically considered, the following laboratory tests may be ordered:

- Complete Blood Counts (CBC with differential) :This test includes the count and size of platelets. WAS patients present with platelet size that is significantly smaller than normal.
- Immunoglobulin levels (IgG, IgM, IgA, IgE) : Immunoglobulins (antibodies) levels in blood may be low in WAS.
- Specific antibody titers: these tests may detect decreased antibody response to vaccines, in particular to the Pneumovax, and low levels of antibodies to red cells (isohemagglutinins) normally present in all people.
- WAS protein levels in white blood cells : Absent, decreased or abnormal intracellular WASP in the white blood cells is also used as a screening tool for early diagnosis of WAS.
- Specific genetic testing - Confirmation of the diagnosis of WAS is done by testing for mutations in the WASP gene on the X chromosome.

# CURRENT TREATMENT AVAILABLE FOR WAS

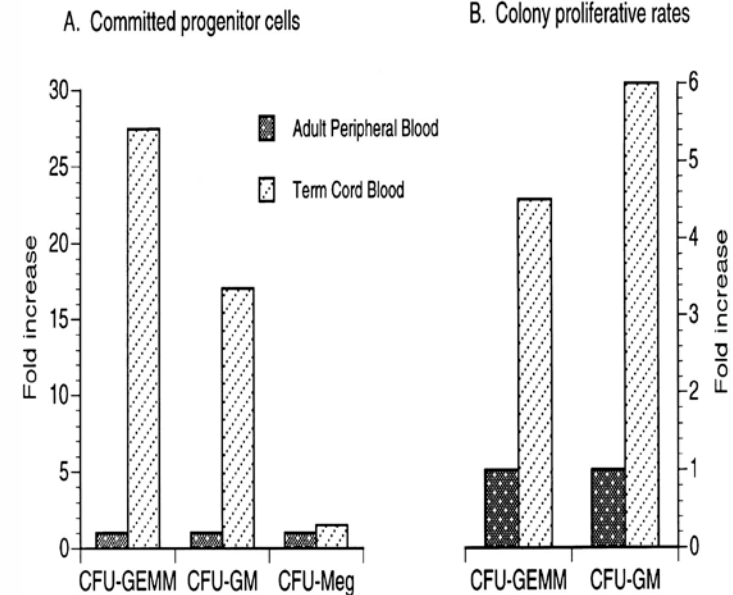
- Medications –especially *antibiotic, antifungal, and antiviral* medications to treat or prevent active infections.
- Using a helmet to reduce the risk of head trauma and intracranial hemorrhage.
- Avoid nonsteroidal anti-inflammatories such as Ibuprofen (Motrin) that can further impair platelet function.
- Use immunoglobulin supplementation (IVIg) when specific antibody responses are not developed
- Hematopoietic stem cell transplantation(HCT).

# HEMATOPOIETIC CELL TRANSPLANT

Currently, a [Hematopoietic Cell Transplant \(HCT\)](#) is the only proven curative treatment available for Wiskott-Aldrich Syndrome.

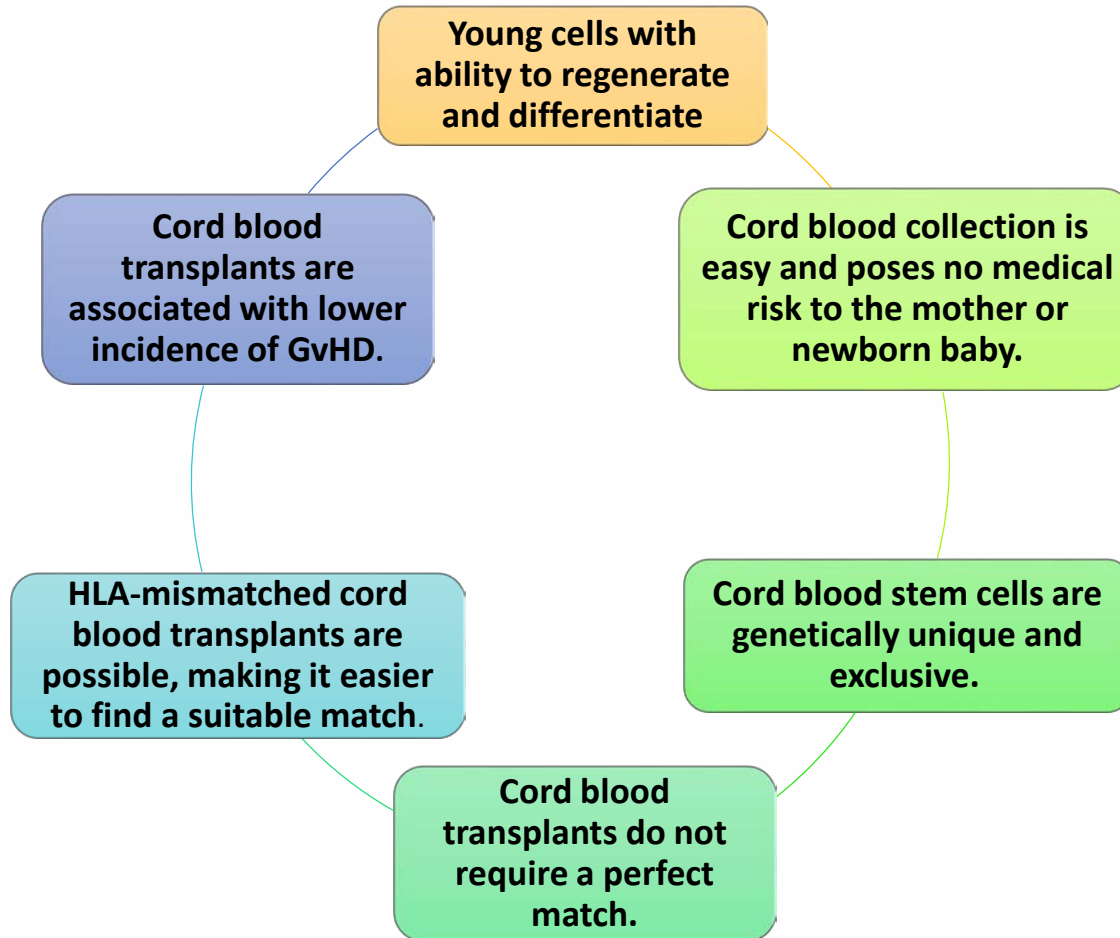
During a transplant for WAS, at least three major things happen:

- ✓ The patient's blood-forming stem cells are destroyed using medicines. It also destroys the patient's immune system, allowing the patient's body to accept the donor cells. The process is known as **Pre-operative regimen**.
- ✓ The donor cells are given to the patient.
- ✓ The donor cells grow and multiply, curing the patient.
- ✓ Stem cells can be obtained from three different sources:
  - a) Bone marrow
  - b) Peripheral blood
  - c) Umbilical cord blood





# THE ADVANTAGES OF UMBILICAL CORD BLOOD TRANSPLANTATION OVER BONE MARROW OR PERIPHERAL BLOOD



For comparison chart please click here :

<http://www.nationalcordbloodprogram.org/qa/comparison.html>

# UCB TRANSPLANTATION PROCEDURE



## Step 1

- Collection, Storage and Cryopreservation of Umbilical Cord Blood



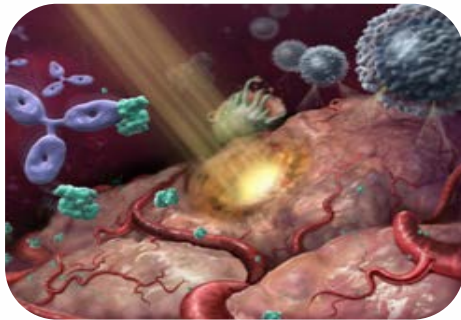
## Step 2

- Day -30 to -11: HLA typing and donor/recipient matching



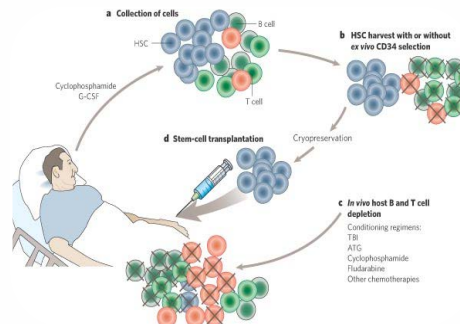
## Step 3

- Day -10: Patient Admission and Isolation in ICU Room



## Step 4

- Day -8: Pre Transplantation conditioning Regimen for 8-10 day before transplantation



## Step 5

- Day 0: Umbilical Cord Blood transplantation in Patient



## Step 6

- Day 1 to Day 25: Post Transplantation follow up and Monitoring

# TRANSPLANT DATA

**The first successful Haematopoietic Stem cell transplant for WAS took place in 1968.**

Significant advances in the field of HCT in the last two decades has improved the success rate for transplants. 5 year survivals for children transplanted under the age of 5 years with a perfect sibling match approaches 90%. When the transplant is done at experienced centers, a closely matched unrelated transplant is almost as successful as a MSD transplant in patients under 5.

## RESEARCH PUBLICATIONS ON APPLICATION OF UMBILICAL CORD STEM CELLS IN WAS

1. Hematopoietic Cell Transplantation for Wiskott-Aldrich Syndrome: Advances in Biology and Future Directions for Treatment  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2930258>
2. Use of two unrelated umbilical cord stem cell units in stem cell transplantation for Wiskott–Aldrich syndrome  
<http://onlinelibrary.wiley.com/doi/10.1002/pbc.20450/full>
3. Umbilical cord blood transplantation in Wiskott Aldrich syndrome  
<http://www.sciencedirect.com/science/article/pii/S0022347603000623>
4. Umbilical cord blood infusion in a patient for correction of Wiskott-Aldrich syndrome.(PMID:7749101)  
<http://europepmc.org/abstract/MED/7749101>
5. Outcome of unrelated umbilical cord blood transplantation in 88 patients with primary immunodeficiency in Japan  
<http://www.ncbi.nlm.nih.gov/pubmed/21569009>
6. Umbilical cord blood transplantation in Wiskott Aldrich syndrome.  
[http://www.researchgate.net/publication/10752526\\_Umbilical\\_cord\\_blood\\_transplantation\\_in\\_Wiskott\\_Aldrich\\_syndrome](http://www.researchgate.net/publication/10752526_Umbilical_cord_blood_transplantation_in_Wiskott_Aldrich_syndrome).

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