The History of von Willebrand Disease

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The first case of VWD was described and published in 1926 by Erik von Willebrand. Therefore, 2026 marks its centenary anniversary.

This infographic explores the history of the diagnosis and management of the disease.

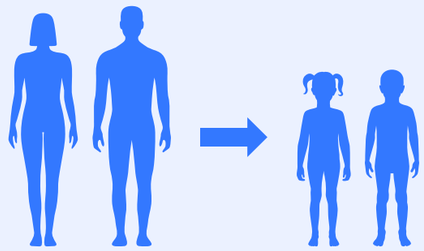
Introduction to von Willebrand Disease

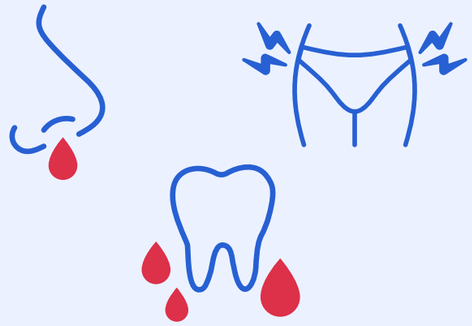
VWD is the most common inherited bleeding disorder worldwide. It is caused by a mutation on the VWF gene on **chromosome 12** (12p13).[1]

There are three main types:

1. **Type 1** is the most common type of VWD and appears in around 70–80% of cases. Patients produce less VWF, which leads to mild bleeding symptoms.[1]
2. **Type 2** has a stronger bleeding phenotype and affects around 15–20% of patients. The cause here are defects in the VWF protein. Based on the type of VWF defect, Type 2 is further divided into four subtypes (2A, 2B, 2M, and 2N).[1-3]
3. **Type 3** is the most severe form, but, at <5%, it is the rarest and is characterised by a total deficiency of VWF protein.[1]

Types 1 and 2 are **autosomal dominant** (approximately 50% risk if one parent is affected), while Type 3 is **autosomal recessive**; however, the alleles show variable penetrance and expressivity, so some individuals with quantitative alleles have normal levels and no bleeding.[4]





Symptoms can include frequent **nosebleeds**, **bleeding gums**, **heavy periods**, **prolonged bleeding after minor injuries**, and **bruising easily** amongst others.[5]

History of von Willebrand Disease

First Description

In 1926, **Erik von Willebrand** published his first paper on a bleeding disease he had observed in a 5-year-old girl and her family, from Föglö, a municipality of the Åland Islands in the Gulf of Bothnia.[6]

The girl was admitted to the Deaconess Hospital in Helsinki, Finland, in April 1924, for a severe haemorrhaging and the condition was first described as 'hereditary pseudohaemophilia.'

1924–1926

Naming of the Disorder

It was originally called von Willebrand-Jürgens thrombopathy as the defect was initially thought to be a platelet function disorder.[6]

1930s–1940s

Identification of the Plasma Protein Defect

Swedish researchers, including Inga **Marie Nilsson** and **Margareta Blombäck**, demonstrated that a plasma fraction corrected bleeding in VWD, identifying the factor later termed VWF.[7]

1957

von Willebrand Factor

Zimmerman et al.[8] characterised **factor VIII-related antigen** deficiency in VWD, distinguishing it immunologically from haemophilia A.[8,9]

1971

VWD ≠ HAEMOPHILIA A

Factor VIII Separated from von Willebrand Factor

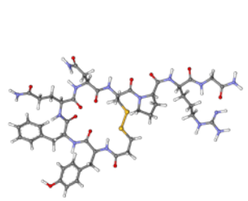
Harvey J. Weiss and colleagues demonstrated that ristocetin-induced platelet aggregation was defective in some types of VWD.[10]

1973

Desmopressin is Developed

Desmopressin was shown to raise factor VIII and reduce bleeding in mild haemophilia and VWD.[11] Reviewers have flagged more advances have occured since 1977.

1977



von Willebrand Factor in Weibel-Palade Bodies

VWF was identified as the main cargo of Weibel-Palade bodies in endothelial cells by **Denisa Wagner**. This compartment provides the stored pool of VWF that is released in circulation upon desmopressin treatment.[12]

1982

Cloning of the VWF Gene

VWF gene was cloned by four separate Dutch and American teams, which enabled genetic investigations into VWD and production of recombinant VWF therapeutics.[13-16]

1985

First in Human Clinical Trial

First in human clinical trial of recombinant VWF in patients with Type 3 VWD.[17]

2013

Abbreviations: Cas 9: CRISPR-associated protein 9; siRNA: small interfering RNA; VWD: Von Willebrand disease; VWF: Von Willebrand factor.

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Where Are We Today?

Desmopressin is commonly used in treatment. It is an analogue of vasopressin that stimulates the release of **endogenous factor VIII and VWF protein**.[18]

Research is exploring siRNA therapies and CRISPR/Cas9-based gene editing, with a focus on personalised treatments tailored to each patient's genetic profile, inspired by advances in gene therapy for haemophilia A and B.[19]