The First Step to Diagnosing WHIM Syndrome Is Suspecting It

WHIM syndrome is a rare, combined primary immunodeficiency and a chronic neutropenic disorder named for the manifestations of[1]:

Warts | **H**ypogammaglobulinemia | **I**nfections | **M**yelokathexis

Less than 1 in 4 patients with WHIM syndrome present with all 4 manifestations. The onset, severity, duration, and frequency of WHIM syndrome symptoms and potential resulting complications can be variable.[1]

Prevalence of Manifestations, Laboratory Findings, and Associated Complications[1-3]

Classic WHIM Presentation*

Warts 40%

Hypogammaglobulinemia 65%

Infections 92%

Myelokathexis† ~100%

WHIM syndrome is heterogeneous, and only ~23% of patients will typically present with the full tetrad of key manifestations.[1]

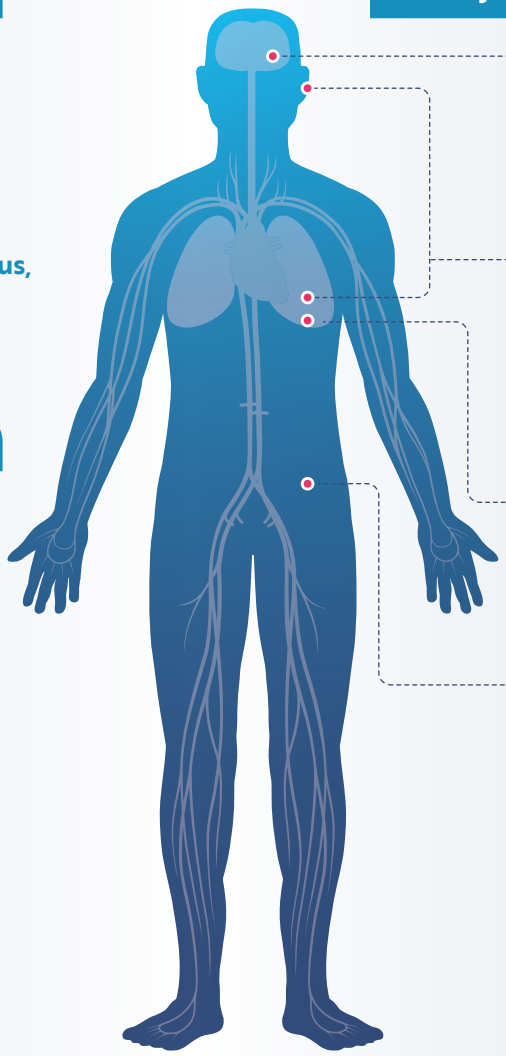
Frequent Laboratory Findings*

Neutropenia 98%

Lymphopenia 88%

Monocytopenia
Exact prevalence unknown

WHIM syndrome should be suspected in any case of chronic neutropenia with lymphopenia and/or monocytopenia.[3]



Multisystemic Complications*

Sepsis
13%
Resulting from bacterial meningitis and bacteremia

End-organ damage
20%
Bronchiectasis and hearing loss

Pneumonia
63%

Cancer‡
23%
Overall risk by age 40, including HPV- and EBV-associated malignancies

*Based on analysis of n=66 patients, as described in *Geier et al.*

†Includes leukopenia in cases where bone marrow biopsy was not performed.

‡Based on analysis of n=155 patients, as described in *Moulin et al.* Variable rates of cancer risk and prevalence in patients with WHIM are reported in the literature.

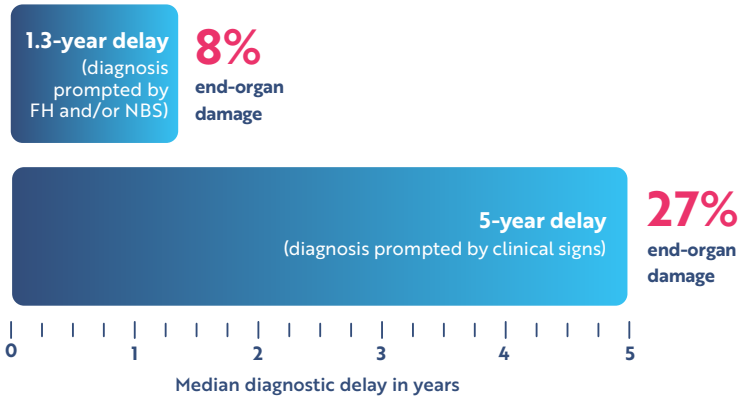
Suspect your patient might have WHIM? Connect with an X4 Rare Disease Specialist to learn more.

WHAT IF IT'S WHIM?

X4 PHARMACEUTICALS

Early Diagnosis of WHIM Syndrome Is Critical

Incidence of End-Organ Damage Based on Diagnostic Delay[#,1]



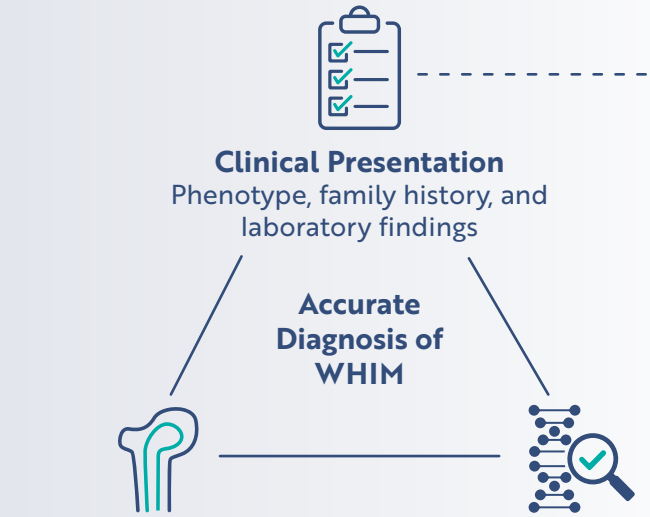
FH=family history. NBS=newborn screening.

[#]Diagnostic delay defined as the time from first date of recorded neutropenia to final molecular diagnosis of WHIM syndrome.

- In a retrospective analysis, earlier diagnosis and treatment resulted in fewer hospitalizations and lower incidence of end-organ damage, including bronchiectasis and hearing loss.[1]
- An early, definitive WHIM diagnosis may help inform and guide patient management, improve outcomes, and reduce the risk of potential long-term complications.[1,4]

WHIM Syndrome 3-Point Diagnosis

Clinical evaluation, bone marrow biopsy and/or genetic testing can help inform a WHIM syndrome diagnosis[1]



Phenotype and Patient/Family History[1,4,5]

Frequent Infections

- Recurrent sinopulmonary and respiratory tract infections
- History of frequent childhood ear infections
- Frequent infections of the skin and underlying tissue

Recalcitrant Warts

- Consistent presence of HPV warts
- Anogenital warts
- Resistance to therapy

Laboratory Findings[1,3,6]

Neutropenia

- ANC ≤1000 cells/μL (elevated during infection but low with recovery)

Lymphopenia

- ALC <1500 cells/μL (age appropriate)

Monocytopenia

- AMC <200 cells/μL (adults)

Hypogammaglobulinemia

- Low circulating levels of IgG, IgA, and/or IgM

References: 1. Geier CB, Ellison M, Cruz R, et al. Disease progression of WHIM syndrome in an international cohort of 66 pediatric and adult patients. *J Clin Immunol.* 2022;42(8):1748-1765. doi:10.1007/s10875-022-01312-7 **2.** Moulin C, Beaupain B, Suarez F, et al. *CXCR4* WHIM syndrome is a cancer predisposition condition for virus-induced malignancies. *Br J Haematol.* 2024;204(4):1383-1392. doi:10.1111/bjh.19373 **3.** Badolato R, Donadieu J; WHIM Research Group. How I treat warts, hypogammaglobulinemia, infections, and myelokathexis syndrome. *Blood.* 2017;130(23):2491-2498. doi:10.1182/blood-2017-02-708552 **4.** Kawai T, Malech HL. WHIM syndrome: congenital immune deficiency disease. *Curr Opin Hematol.* 2009;16(1):20-26. doi:10.1097/MOH.0b013e32831ac557 **5.** Heusinkveld LE, Majumdar S, Gao JL, McDermott DH, Murphy PM. WHIM syndrome: from pathogenesis towards personalized medicine and cure. *J Clin Immunol.* 2019;39(6):532-556. doi:10.1007/s10875-019-00665-w **6.** Beaussant Cohen S, Fenneteau O, Plouvier E, et al. Description and outcome of a cohort of 8 patients with WHIM syndrome from the French Severe Chronic Neutropenia Registry. *Orphanet J Rare Dis.* 2012;7:71. doi:10.1186/1750-1172-7-71

X4 PHARMACEUTICALS