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.[2]

Prevalence of Manifestations, Laboratory Findings, and Associated Complications[2,3]

Classic WHIM Manifestations*

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.[2]

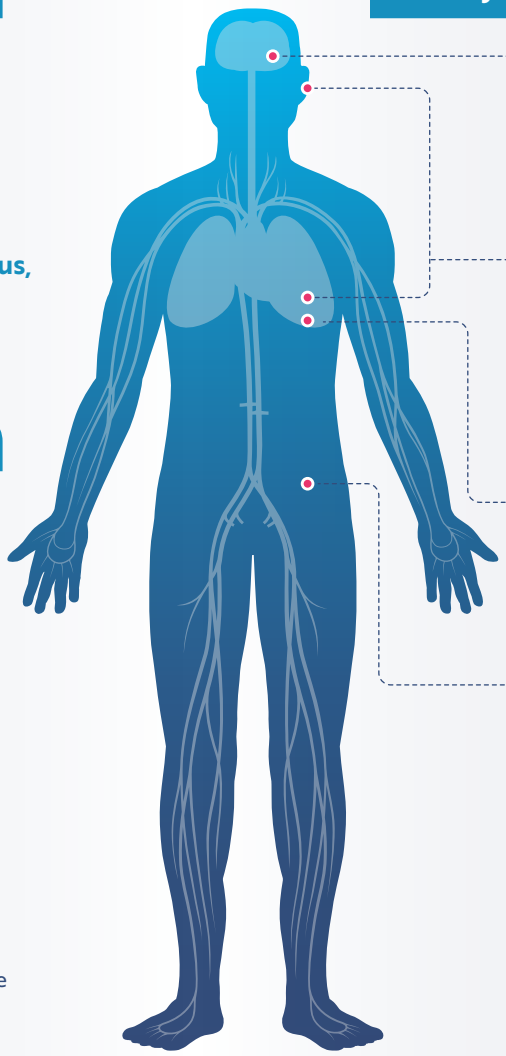
Frequent Laboratory Findings*

Neutropenia 98%

Lymphopenia 88%

Monocytopenia
Exact prevalence unknown

WHIM syndrome should be suspected in any case of chronic neutropenia with lymphopenia and/or monocytopenia.[4]



Multisystemic Complications*

Sepsis
13%
Resulting from bacterial meningitis and bacteremia

End-organ damage
20%
Bronchiectasis and hearing loss

Pneumonia
63%

Cancer
30%
Estimated 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=60 patients, as described in *Beaussant Cohen et al.*

Suspect your patient might have WHIM?
Connect with an X4 Diagnostic Liaison to learn more.

SCAN ME **WhatIfItsWHIM.com**

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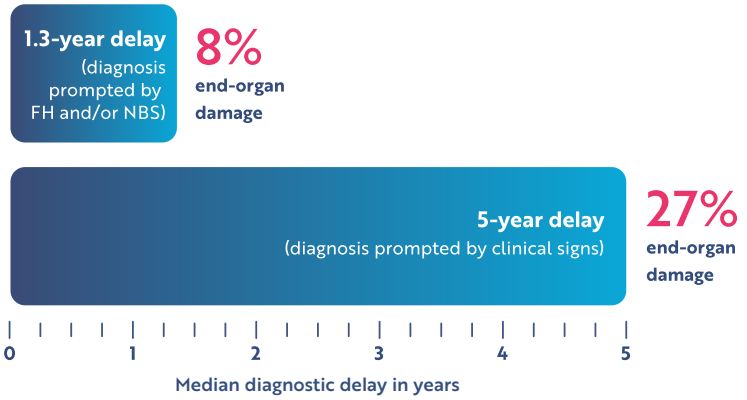
Early Diagnosis of WHIM Syndrome is Essential

Incidence of End-Organ Damage Based on Diagnostic Delay[2]

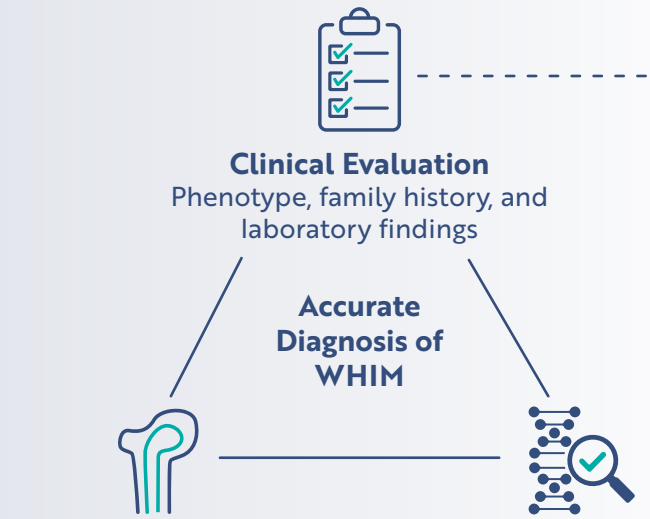


FH=family history. NBS=newborn screening.

- In a retrospective analysis, earlier diagnosis and treatment resulted in fewer hospitalizations and lower incidence of end-organ damage, including bronchiectasis and hearing loss.[2]
- An early, definitive WHIM diagnosis can help inform and guide patient management, improve outcomes, and may help reduce potential antibiotic resistance and long-term complications.[2,5]

WHIM Syndrome 3-Point Diagnosis

Clinical evaluation, bone marrow biopsy and/or genetic testing can help inform a WHIM syndrome diagnosis[2]



Phenotype and Patient/Family History[2,6]

Frequent Infections

- Recurrent sinopulmonary and upper respiratory tract infections
- History of frequent childhood ear infections
- Subcutaneous abscesses
- Absence of classic opportunistic infections

Recalcitrant Warts

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

Laboratory Findings[2,4]

Neutropenia

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

Lymphopenia

- ALC <1500 cells/μL (age appropriate)

Monocytopenia

Hypogammaglobulinemia

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

SCAN ME **Order no-cost genetic testing to diagnose or rule out WHIM syndrome through Path4Ward**

References: 1. Dale DC, Firkin F, Bolyard AA, et al. Results of a phase 2 trial of an oral CXCR4 antagonist, mavorixafor, for treatment of WHIM syndrome. *Blood.* 2020;136(26):2994-3003. **2.** 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. **3.** 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. **4.** Badolato R, Donadieu J; WHIM Research Group. How I treat warts, hypogammaglobulinemia, infections, and myelokathexis syndrome. *Blood.* 2017;130(23):2491-2498. **5.** Kawai T, Malech HL. WHIM syndrome: congenital immune deficiency disease. *Curr Opin Hematol.* 2009;16(1):20-26. **6.** 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.

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