



# You Don't Know WHIM Syndrome (A Chronic Neutropenic Disorder)

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# Resource Information

## About This Resource

These slides are one component of a continuing education program available online at MedEd On The Go titled [WHIM Syndrome \(A Chronic Neutropenic Disorder\): Uncouple the Complex for HCPs and Patients](#)

## Program Learning Objectives:

- Gain an understanding of WHIM syndrome as a rare PID/ chronic neutropenic disorder with diverse clinical presentations
- Implement strategic measures to improve the early identification of WHIM syndrome patients for prompt assessment and diagnosis to avoid potential complications and long-term sequelae
- Understand the CXCR4 pathway dysregulation and how it relates to the underlying causes of WHIM syndrome
- Garner an understanding of the limitations of current approaches for WHIM syndrome and potential new approaches for patients

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# WHIM Is a Serious Disease with Diverse Presentations

- The classic tetrad may not be present in all patients
- Prevalence of clinical findings in a large international cohort:

	Mean age at recognition or onset:
• Neutropenia 98%	3.8 years
• Lymphopenia 88%	5.0 years
• Infections 88%	1.6 years
• Hypogammaglobulinemia 65%	7.3 years
• Warts 40%	12.1 years

- Only 23% of patients in the cohort presented with all features of the WHIM acronym
  - Not counting myelokathexis, used only as a confirmatory feature

# WHIM Is a Serious Disease Associated with Morbidity and Mortality

- Infections:
  - Pneumonia (63%), otitis media (68%), cellulitis, urinary tract infection, omphalitis, osteomyelitis, deep soft tissue abscess, cellulitis, sepsis/meningitis (13%)
  - Bacterial pathogens include, but are not limited to, *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Proteus mirabilis*.
  - Viruses: HPV, EBV
- Vicious cycle of recurrent lung infections  
↕  
bronchiectasis



# WHIM Is a Serious Disease Associated with Morbidity and Mortality

- Sequelae of infections:
  - Hearing loss
  - Pulmonary insufficiency
  - Virus-related cancers: EBV-associated lymphomas, HPV-positive genital and anal cancers
  - Periodontal disease
- Autoimmune disease (21%)
  - cytopenias (ITP, AIHA, Evans syndrome), type 1 diabetes, thyroiditis, vitiligo, arthritis, hepatitis
- Heart disease
  - Tetralogy of Fallot, patent ductus arteriosus, right-sided aortic arch, tricuspid valve insufficiency, aortic valve insufficiency, Wolff–Parkinson–White syndrome

AIHA, autoimmune hemolytic anemia; ITP, immune thrombocytopenic purpura.

Kawai T & Malech HL. *Curr Opin Hematol*. 2009 Jan; 16(1): 20–26; Geier CB, et al. *J Clin Immunol*. 2022; 42(8): 1748–1765;

Moulin C, et al. *Br J Haematol*. 2024; 204(4):1383-1392.

# WHIM Is a Serious Disease Associated with Morbidity and Mortality

- Psychosocial morbidities
- Hospitalizations
- Absences from school/work
- Underemployment
- Social stigma
- Mortality:
- Meningitis/sepsis
- HPV-related carcinomas: genital, head/neck
- Bone marrow transplant
- **Low mortality with proper treatment**

# Early diagnosis and treatment is essential

- Irreversible end-organ damage, including bronchiectasis and hearing loss, was significantly more common in patients with late vs early diagnosis
- Median age at diagnosis 5 years: 27% developed bronchiectasis ( $n = 9$ ) and hearing loss ( $n = 3$ ) secondary to infections
- Median age at diagnosis 1 year: 8% (one patient) with bronchiectasis and none developed hearing loss



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