



X-linked immunodeficiency with magnesium defect, Epstein-Barr virus infection, and neoplasia

X-linked immunodeficiency with magnesium defect, Epstein-Barr virus infection, and neoplasia (typically known by the acronym XMEN) is a disorder that affects the immune system in males. In XMEN, certain types of immune system cells called T cells are reduced in number or do not function properly. Normally these cells recognize foreign invaders, such as viruses, bacteria, and fungi, and are then turned on (activated) to attack these invaders in order to prevent infection and illness. Because males with XMEN do not have enough functional T cells, they have frequent infections, such as ear infections, sinus infections, and pneumonia.

In particular, affected individuals are vulnerable to the Epstein-Barr virus (EBV). EBV is a very common virus that infects more than 90 percent of the general population and in most cases goes unnoticed. Normally, after initial infection, EBV remains in the body for the rest of a person's life. However, the virus is generally inactive (latent) because it is controlled by T cells. In males with XMEN, however, the T cells cannot control the virus, and EBV infection can lead to cancers of immune system cells (lymphomas). The word "neoplasia" in the condition name refers to these lymphomas; neoplasia is a general term meaning abnormal growths of tissue. The EBV infection itself usually does not cause any other symptoms in males with XMEN, and affected individuals may not come to medical attention until they develop lymphoma.

Frequency

The prevalence of XMEN is unknown. Only a few affected individuals have been described in the medical literature.

Causes

XMEN is caused by mutations in the *MAGT1* gene. This gene provides instructions for making a protein called a magnesium transporter, which moves charged atoms (ions) of magnesium (Mg^{2+}) into certain T cells. Specifically, the magnesium transporter produced from the *MAGT1* gene is active in CD8+ T cells, which are especially important in controlling viral infections such as the Epstein-Barr virus (EBV). These cells normally take in magnesium when they detect a foreign invader, and the magnesium is involved in activating the T cell's response.

Researchers suggest that magnesium transport may also be involved in the production of another type of T cell called helper T cells (CD4+ T cells) in a gland called the thymus. CD4+ T cells direct and assist the functions of the immune system by influencing the activities of other immune system cells.

Mutations in the *MAGT1* gene impair the magnesium transporter's function, reducing the amount of magnesium that gets into T cells. This magnesium deficiency prevents the efficient activation of the T cells to target EBV and other infections. Uncontrolled EBV infection increases the likelihood of developing lymphoma. Impaired production of CD4+ T cells resulting from abnormal magnesium transport likely accounts for the deficiency of this type of T cell in people with XMEN, contributing to the decreased ability to prevent infection and illness.

Inheritance Pattern

This condition is inherited in an X-linked recessive pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation would have to occur in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition

- immunodeficiency, X-linked, with magnesium defect, Epstein-Barr virus infection, and neoplasia
- XMEN

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
[/primer/testing/geneticTesting](#)
- Genetic Testing Registry: Immunodeficiency, X-Linked, with magnesium defect, Epstein-Barr virus infection, and neoplasia
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3275445/>

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22X-linked+immunodeficiency+with+magnesium+defect%2C+Epstein-Barr+virus+infection%2C+and+neoplasia%22+OR+%22primary+immunodeficiency%22>

Other Diagnosis and Management Resources

- MedlinePlus Encyclopedia: Epstein-Barr Virus Test
<https://medlineplus.gov/ency/article/003513.htm>
- MedlinePlus Encyclopedia: T Cell Count
<https://medlineplus.gov/ency/article/003516.htm>

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Epstein-Barr Virus Test
<https://medlineplus.gov/ency/article/003513.htm>
- Encyclopedia: T Cell Count
<https://medlineplus.gov/ency/article/003516.htm>
- Health Topic: Immune System and Disorders
<https://medlineplus.gov/immunesystemanddisorders.html>
- Health Topic: Lymphoma
<https://medlineplus.gov/lymphoma.html>

Genetic and Rare Diseases Information Center

- X-linked immunodeficiency with magnesium defect, Epstein-Barr virus infection and neoplasia
<https://rarediseases.info.nih.gov/diseases/10907/x-linked-immunodeficiency-with-magnesium-defect-epstein-barr-virus-infection-and-neoplasia>

Additional NIH Resources

- National Institute of Allergy and Infectious Diseases: Primary Immune Deficiency Diseases
<https://www.niaid.nih.gov/diseases-conditions/primary-immune-deficiency-diseases-pidds>
- National Institute of Allergy and Infectious Diseases: Scientists Identify the Genetic Mutation Causing "XMEN" Disease
<https://www.niaid.nih.gov/diseases-conditions/scientists-identify-mutation-xmen-disease>

Educational Resources

- Centers for Disease Control and Prevention: About Epstein-Barr Virus
<https://www.cdc.gov/epstein-barr/about-ebv.html>
- MalaCards: immunodeficiency, x-linked, with magnesium defect, epstein-barr virus infection, and neoplasia
https://www.malacards.org/card/immunodeficiency_x_linked_with_magnesium_defect_epstein_barr_virus_infection_and_neoplasia
- Orphanet: X-linked immunodeficiency with magnesium defect, Epstein-Barr virus infection and neoplasia
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=317476

Patient Support and Advocacy Resources

- Immune Deficiency Foundation
<https://primaryimmune.org/>
- Jeffrey Modell Foundation
<http://www.info4pi.org/>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28xmen%5BALL%5D%29+OR+%28%28immunodeficiency%5BALL%5D%29+AND+%28magn1%5BALL%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>

Catalog of Genes and Diseases from OMIM

- IMMUNODEFICIENCY, X-LINKED, WITH MAGNESIUM DEFECT, EPSTEIN-BARR VIRUS INFECTION, AND NEOPLASIA
<http://omim.org/entry/300853>

Medical Genetics Database from MedGen

- Immunodeficiency, X-Linked, with magnesium defect, Epstein-Barr virus infection, and neoplasia
<https://www.ncbi.nlm.nih.gov/medgen/477076>

Sources for This Summary

- Brandao K, Deason-Towne F, Perraud AL, Schmitz C. The role of Mg²⁺ in immune cells. *Immunol Res.* 2013 Mar;55(1-3):261-9. doi: 10.1007/s12026-012-8371-x. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/22990458>
- Chaigne-Delalande B, Li FY, O'Connor GM, Lukacs MJ, Jiang P, Zheng L, Shatzer A, Biancalana M, Pittaluga S, Matthews HF, Jancel TJ, Bleesing JJ, Marsh RA, Kuijpers TW, Nichols KE, Lucas CL, Nagpal S, Mehmet H, Su HC, Cohen JI, Uzel G, Lenardo MJ. Mg²⁺ regulates cytotoxic functions of NK and CD8 T cells in chronic EBV infection through NKG2D. *Science.* 2013 Jul 12; 341(6142):186-91. doi: 10.1126/science.1240094.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23846901>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3894782/>
- Li FY, Chaigne-Delalande B, Kanellopoulou C, Davis JC, Matthews HF, Douek DC, Cohen JI, Uzel G, Su HC, Lenardo MJ. Second messenger role for Mg²⁺ revealed by human T-cell immunodeficiency. *Nature.* 2011 Jul 27;475(7357):471-6. doi: 10.1038/nature10246.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21796205>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3159560/>
- Li FY, Chaigne-Delalande B, Su H, Uzel G, Matthews H, Lenardo MJ. XMEN disease: a new primary immunodeficiency affecting Mg²⁺ regulation of immunity against Epstein-Barr virus. *Blood.* 2014 Apr 3;123(14):2148-52. doi: 10.1182/blood-2013-11-538686. Epub 2014 Feb 18. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24550228>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3975255/>
- Li FY, Lenardo MJ, Chaigne-Delalande B. Loss of MAGT1 abrogates the Mg²⁺ flux required for T cell signaling and leads to a novel human primary immunodeficiency. *Magnes Res.* 2011 Sep;24(3):S109-14. doi: 10.1684/mrh.2011.0286. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21983175>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3732466/>
- Wolf FI, Trapani V. MagT1: a highly specific magnesium channel with important roles beyond cellular magnesium homeostasis. *Magnes Res.* 2011 Sep;24(3):S86-91. doi: 10.1684/mrh.2011.0288. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21947671>

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