



Understanding Mannose-Binding Lectin Deficiency

This common medical condition can cause recurrent infections in children and adults.

By Dana Henry

BETWEEN FIVE AND 30 out of every 100 people have a deficiency that many have never heard of: mannose-binding lectin deficiency, also known as MBL deficiency.¹ People with this condition have low levels of MBL in their blood.² Part of the complement system that helps protect the body from infection, MBL plays an important role in defending the body against invading microorganisms, including yeasts, parasites, viruses and some types of bacteria.^{3,4,5} MBL is produced by the liver and released into the blood, where it recognizes mannose residues present on a wide range of common pathogens and binds to them. This binding initiates complement activation of the lectin

pathway,^{6,7} which is the first part of the complement system to react to invading microbes.⁸

“In many individuals, MBL deficiency is asymptomatic (since the other pathways of complement activation are still intact), but in some people, it can lead to recurrent bacterial infections,” says Bob Geng, MD, MA, assistant professor in the division of allergy and immunology at the University of California, San Diego. “However, deficiency in MBL can predispose individuals to develop more severe symptoms if they have chronic inflammatory conditions. In addition, MBL deficiency in addition to another known defect of the immune system can lead to more

severe and frequent bacterial infections” such as pneumonia and meningitis.

MBL deficiency is diagnosed with a blood test, and is then classified as mild, moderate or severe based on how low the MBL levels are. Depending on the type of infection, symptoms vary in frequency and severity,² and treatment is based on the severity of symptoms.¹

MBL Deficiency in Children

Since the 1970s, researchers have recognized that MBL deficiency affects children, namely those between ages 6 months and 18 months. Early research revealed that failure to thrive and recurrent infections characterized by severe local inflammation were associated with the deficiency.⁹ Current research supports that MBL deficiency is especially hard on children, whose immune systems are immature and who therefore have an increased susceptibility to infections.³

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Pneumonia is common in children, and recent studies suggest impairments of the innate immune system may account for these infections.⁶ “It is crucial to identify patients with such impairments to better manage and prevent future complications,” say immunologists Michelle Halbrich, MD, Moshe Ben-Shoshan, MD, and Christine McCusker, MD, who add that even in cases with mild clinical presentations, a high level of suspicion of an underlying immune deficiency is needed.⁶

For some children, issues with MBL deficiency can persist beyond 18 months old. One parent describes her struggle with her two daughters, both of whom have MBL deficiency: “My girls are now 9 and 10, and after years of chasing this down, both are doing much better.” She credits early detection and treatment of infections with her children’s improvement. “I am more aware, as well as doctors, so antibiotics are immediate — no waiting until they are really sick,” she says. One child is also on

long-term low-dose antibiotics to help combat her infections, the same measure that is sometimes also taken with other forms of immunodeficiency.¹⁰

MBL Deficiency in Adults

Initially, MBL deficiency was believed to exclusively affect children, not adults whose immune systems have matured. Before discussing the potential issues MBL deficiency can have in the adult population, it’s important to contextualize that conversation. For many people, a low MBL level, in and of itself, causes no health issues. In an online question-and-answer about the condition, Phil Lieberman, MD, clinical professor of medicine and pediatrics in the Departments of Internal Medicine and Pediatrics at the University of Tennessee College of Medicine, underscores this point. “First, I think it is important to understand that many individuals who have mannose binding lectin (MBL) deficiency do not suffer any adverse symptoms related to the diminished levels of MBL,” he writes.¹¹

MBL deficiency can, however, cause issues for some adults. The view that the condition only affects children was first challenged in 1995. A group of researchers showed that adults with the condition could have severe and unusual infections in which MBL gene mutations were the only identified cause of immunodeficiency.⁹ These infections included skin abscesses, chronic diarrhea associated with a type of parasite, meningococcal meningitis with recurrent herpes simplex, and a form of fatal necrotizing pneumonia. The patients ranged in age from 15 years to 56 years and were both male and female.⁹

Since that study, MBL deficiency in adults has also been associated with recurrent bacterial sinusitis, more severe forms of recurrent community-acquired pneumonia, pneumococcal sepsis, E. coli-induced pyelonephritis, fallopian tube infections and persistent hepatitis B.^{9,11}

A 2013 study paints a clear picture of what it can be like to suffer myriad health issues at significantly higher rates than those who don’t have the condition. These include higher rates of:¹²

- Bacterial infections of the vagina
- Bronchitis
- Common cold
- Conjunctivitis
- Cystitis
- Gastritis
- Gingivitis
- Esophagitis
- Onychia

- Otitis media
- Pharyngitis
- Pneumonia
- Prostatitis
- Sinusitis
- Stomatitis
- Tracheitis
- Urethritis

The study also showed that those with MBL deficiency had a 43 percent chance of having suffered from recurrent and severe episodes of infections, compared with only 16 percent in the control group. And, antibiotic treatment was significantly more common among MBL deficiency patients.¹²

Certain groups of adults are at greater risk when they have MBL deficiency. These include patients with suppressed immune systems such as those who have another form of immunodeficiency in addition to the MBL deficiency. Dr. Lieberman recommends people with low MBL deficiency look for associated immunological defects such as hypogammaglobulinemia.¹¹ Also at greater risk are those who have had an organ transplant, and those who are undergoing chemotherapy.^{3,11}

Adults with autoimmune diseases can also be negatively affected by MBL deficiency. Diseases such as systemic lupus erythematosus and rheumatoid arthritis have a more severe course in the presence of MBL deficiency. In cases of cystic fibrosis, MBL deficiency leads to a poorer prognosis.³

Therapies for MBL

Treating MBL deficiency isn't a one-size-fits-all approach. For those who don't have health issues associated with the condition, treatment is unnecessary.^{1,11} For those with associated health issues, a three-pronged approach is employed. First, antibiotics, including prophylactic antibiotics, are used for infection control. Second, vaccinations are recommended. And third, patients are encouraged to have their antibodies checked to determine if an additional form of immunodeficiency is present.^{13,14}

"Both recombinant (synthetically made) and plasma-derived MBL products are commercially available, but are still currently under research investigation as a form of replacement therapy," says Dr. Geng. "The most likely indication for this investigational therapy may be patients diagnosed with MBL deficiency plus another known defect of the immune system who are suffering from severe acute bacterial infections." However, according to Terry O. Harville, MD, PhD, medical director in the Special Immunology Laboratory at the University of Arkansas for Medical Sciences, "because these

therapies have a very short half-life, they are not practical except perhaps in acute illnesses."

In the future, because a certain gene has been found to cause this condition, gene therapy may be a viable treatment.¹⁵

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Living with MBL

"MBL deficiency and treatment remains controversial," explains Dr. Harville. "Data indicate that 30 percent of the population in Denmark are MBL deficient without excessive complications, so many are not convinced it is a problem." Nevertheless, it is one of the most common human immunodeficiencies, and several studies have shown that deficiency of MBL increases the overall susceptibility of an individual to infectious disease. As such, more research is needed to better treat those diagnosed who do suffer from recurring infections. ■

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