

Insights Into MS

The Role of Immunoglobulins

Immunoglobulins and the immune system



- Antibodies, also known as immunoglobulins (Igs), function as part of the healthy immune system to destroy bacteria and viruses¹

IgG

- The most common of all antibodies (70% to 80%), they are produced during an initial infection or antigen exposure, rising in level for a few weeks before decreasing and then stabilizing¹
- IgG antibodies form the basis of long-term protection from microorganisms and can be rapidly reproduced when the body is exposed to the same antigen¹
- In the healthy immune system, sufficient IgG is produced to prevent reinfection¹

IgM

- Make up about 10% of all serum antibodies and are the body's first response to a new infection or "non-self" antigen before there are sufficient levels of IgG^{1,2}

IgA

- Comprising about 15% of serum antibodies, IgA provides protection against infection in mucosal areas of the body such as the respiratory tract (sinus and lungs) and the gastrointestinal tract (stomach and intestines)¹

IgD

- Present in small amounts, the role of IgD is not completely understood and it is not routinely measured^{1,2}

IgE

- Also present in small amounts, IgEs are associated with allergies, allergic diseases, and with parasitic infections¹
- IgE is measured as part of an allergy testing blood panel, but is typically not included as part of a quantitative immunoglobulin test¹

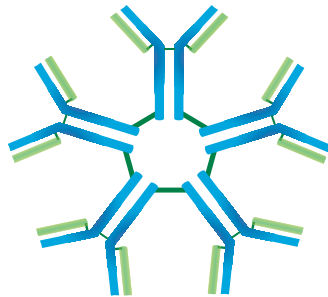
Immunoglobulins

IgG

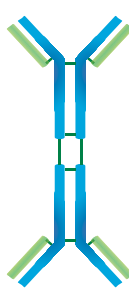


There are 4 IgG subclasses:
IgG1, IgG2, IgG3, IgG4

IgM

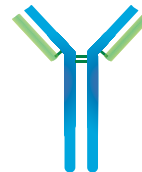


IgA



There are 2 IgA subclasses:
IgA1 and IgA2

IgD



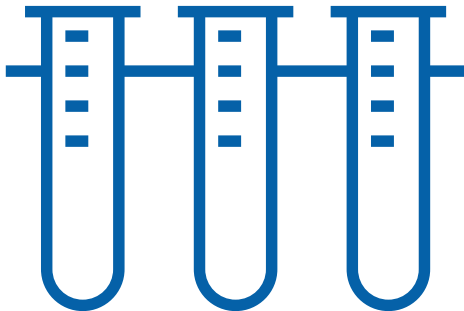
IgE



Immunoglobulin testing



- Immunoglobulin testing measures the total amount of each primary immunoglobulin class, IgA, IgM, and IgG, in blood without distinguishing between subclasses¹
- Separate testing can be performed to measure immunoglobulin subclasses (eg, IgG1, IgA1) and/or to detect and measure specific antibodies¹



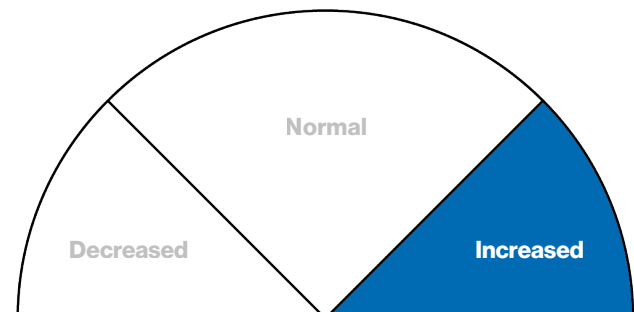
Immunoglobulins in MS



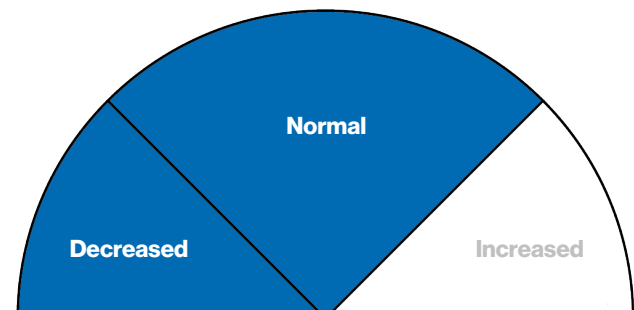
- Expanded IgG and IgM levels in the CSF, characterized by increased oligoclonal bands, are often used as a marker of inflammation in the diagnosis MS³
- The existence of oligoclonal bands within the CSF, but not the serum, is found in nearly all patients with clinically definitive MS³
- Serum Ig levels in patients with MS are variable, but low serum IgG levels have been reported in patients with all forms of MS, including relapsing-remitting MS, secondary progressive MS, and primary progressive MS^{4,5}

Patients With MS

IgG Level in CSF³



IgG Level in Serum^{4,5}



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Potential impact of low immunoglobulin levels



- Hypogammaglobulinemia (reduced blood concentration of IgG, IgM, and/or IgA) has been reported to lead to severe infections⁶
- The risk of infection is most likely when IgG levels drop to below 400 mg/dL⁵
- A recent study reported high prevalence rates of reduced serum IgG in patients with and without DMT, suggesting low serum Ig levels may be part of MS pathology for some patients⁵

Percentage of People With Low Serum Concentration of IgG (<700 mg/dL)⁵

Control Group (n=58): 3.5%




MS Patients Not on DMT (n=198): 8.1%



MS Patients on DMT (n=129): 26.4%



 percentage of people with low serum concentration of IgG (<700 mg/dL)

Lower Limits of Normal (LLN)⁵
 IgG <700 mg/dL
 IgM <40 mg/dL
 IgA <70 mg/dL

DMTs and immunoglobulins



- Some B-cell-depleting, anti-CD20 therapies have been shown to reduce IgG and IgM serum levels over 1 to 5.5 years, which is not observed with older first-line therapy DMTs⁷⁻¹⁰
- Severe hypogammaglobulinemia is associated with a higher likelihood of severe infections¹¹
- Most common infections in patients with MS include urinary tract infections and pneumonia¹²



Serum IgG levels should be monitored in patients on DMTs, especially anti-B-cell therapies, to ensure they stay within the normal limit^{5,11}

CSF, cerebrospinal fluid; DMT, disease-modifying therapy; Ig, immunoglobulin; MS, multiple sclerosis.

References

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