Review article

The Importance of IgM and IgG Antibodies Testing in Infectious Diseases

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Abstract

There are five major classes of Immunoglobulins (Igs) or antibodies (Abs) in the human body: IgA, IgM, IgD, IgG and IgE. IgM and IgG play crucial roles in the immune response to infections. This paper aims to review briefly the production, functions, clinical significance and limitations of IgM and IgG antibodies testing in infectious diseases. Some available scientific research on IgM and IgG was reviewed using specialized databases such as PubMed and Google Scholar. IgM is typically the first antibody produced in response to an infection, while IgG provides long-term immunity and protection against reinfection. IgM and IgG antibody testing is a critical component of diagnosing and managing infectious diseases. These tests provide valuable insights into the immune response, allowing clinicians to identify recent infections, assess immunity, and make informed public health decisions. IgM and IgG antibody testing lies in the integration of innovative technologies and targeted research efforts. By addressing current limitations and exploring new testing methodologies, the field can enhance diagnostic accuracy, improve patient outcomes, and contribute to more effective public health strategies in the management of infectious diseases.

Keywords: *Immunity, Immunoglobulins, IgM, IgG, Infectious Diseases.*

Introduction

The field of immunology began with the work of scientists like Louis Pasteur and Emil von Behring late 19th Century, who explored the role of antibodies in protection against infections. In 1890, von Behring developed the first serum therapy, demonstrating that antibodies in serum could confer immunity. In 1930s-1950s, the classification of immunoglobulins (Ig) into different classes (IgG, IgM, IgA, IgE, and IgD) was established during this period [1]. In the 1930s, the first clear distinction between IgG and IgM was made, leading to the understanding that they play different roles in immune responses [2]. In 1940s-1960s, the use of serological tests to detect antibodies in patients became more prevalent. Techniques like agglutination tests, complement fixation tests, and later enzyme-linked immunosorbent assays (ELISA) were developed reviewed in [3].

IgM was identified as an early response antibody, typically present during acute infection, while IgG indicated a more prolonged or past infection [4]. However, serological assays remained essential for understanding population immunity and epidemiology. In 2000s to present, the investigation of IgM and IgG antibodies has been pivotal in the study of emerging infectious diseases, including SARS, MERS, and most recently, COVID-19 [5]. The rapid development of antibody tests for COVID-19 highlighted the importance of IgM and IgG assays in diagnosing infections, understanding immunity, and guiding public health responses [5].

Definition of immunoglobulins (human antibodies)

Immunoglobulins (Ig), or antibodies, are essential components of the adaptive immune system, responsible for identifying and neutralizing pathogens such as bacteria, viruses, and toxins. Ig are glycoproteins produced by B cells in response to antigens (Ags) [6,7]. IgM and IgG are the most abundant Abs classes in the human immune system, each with distinct roles in immune defense. Understanding the dynamics of IgM and IgG responses during infection can provide insights into disease progression, diagnosis, and immunity [6].

Structure and function of IgM and IgG

Among the five major classes of immunoglobulins, IgM and IgG play pivotal roles in the immune response, each with distinct structural characteristics and functional capabilities [7]. IgM is the first antibody produced in response to an infection, primarily serving as a key player in the early stages of the immune response. It is characterized by its pentameric structure, which allows for the simultaneous binding of multiple antigens. This structural configuration enhances its ability to agglutinate pathogens and activate the complement system, facilitating the destruction of invaders [4,8]. In contrast to IgM, IgG is the most abundant antibody in the bloodstream and plays a crucial role in the secondary immune response. It is produced after IgM and reflects a more mature and specific immune reaction [9]. The monomeric structure of IgG allows it to effectively neutralize toxins and viruses, opsonize pathogens for phagocytosis, and activate the complement system. Importantly, IgG is the only antibody class capable of crossing the placenta, providing passive immunity to the developing fetus [9], as shown in table 1.

Table 1. The structure and function of IgM and IgG

Feature	IgM	IgG
Structure	Pentameric (five Y-shaped units) No subclass	Monomeric (single Y-shaped unit) Subclasses (IgG1, IgG2, IgG3, IgG4)
Molecular weight	Largest antibody in size (~900kDa)	Smaller than IgM (~150kDa)
Forms	Present as a monomer on B cell surface and a pentameric in serum	Present only as a monomer in serum
Half-life	5-7 days	21-28 days
Function	First antibody produced in response to an infection activates the complement system effective agglutination of pathogens induces B cell activation	provides long-lasting immunity after infection or vaccination Neutralization Opsonization activates the complement system cross the placenta, providing passive immunity to the fetus
Location	In blood and lymph	In blood, extracellular fluid, and tissues
Role in vaccination	Rarely used for monitoring vaccine response	Key indicator of vaccine efficacy and response

Taken together, IgM and IgG provide a comprehensive immune defense strategy, with IgM initiating responses to newly encountered antigens and IgG sustaining long-term immunity. Understanding the structure and function of these antibodies is vital for insights into immune responses, vaccine development, and therapeutic interventions against infectious diseases.

IgM and IgG response in infectious diseases

The kinetics of IgM and IgG production and their respective roles in various infectious diseases underscore their importance in both clinical diagnosis and therapeutic interventions [7]. Elevated levels of IgM can indicate acute infections such as those caused by viruses or certain bacteria, while IgG levels reflect past infections or successful vaccination responses [8,10,11]. The interplay between these immunoglobulins is crucial in shaping the host's immune landscape, influencing susceptibility, disease progression, and recovery [12,13]. Table 2 represents some examples of IgM and IgG responses in various infectious diseases.

Table 2. Examples of IgM and IgG responses to some infectious diseases

Infectious diseases		IgM response	IgG response
Viral infections	COVID-19 [14]	Detectable within days of symptom onset, indicating recent infection	Appears later and correlate with protective immunity against reinfection
	Hepatitis Virus [15]	IgM antibodies against hepatitis A virus (anti-HAV IgM) indicate acute infection	IgG antibodies signify past infection or vaccination
Bacterial infections	Streptococcal Infections [16,17]	Elevated IgM may indicate recent streptococcal infection (e.g., rheumatic fever)	In Syphilis the presence of IgG indicates a chronic infection or past exposure
	Mycoplasma pneumonia [18]	IgM indicates acute infection	Borrelia burgdorferi: IgG indicates past Lyme disease infection
Parasitic infections	Malaria [19]	IgM levels rise early in infection	IgG levels can provide evidence of past infections and immunity development, especially in endemic areas
Protozoan infections	Chagas Disease [20]	IgM indicates acute infection	IgG suggests chronic infection or past exposure

Overall, understanding the distinct yet interconnected roles of IgM and IgG in infectious diseases enhances our knowledge of immune mechanisms and aids in the development of vaccines and diagnostic tools, ultimately contributing to improved public health outcomes.

Clinical significance of IgM and IgG testing

IgM and IgG tests are commonly used in clinical diagnostics to assess immune response and diagnose various infections and diseases [21,22]. Table 3 shows a summary of clinical significance of IgM and IgG testing.

Table 3. Shows a summary of clinical significance of IgM and IgG testing

IgM Testing	IgG Testing
Early Detection of Infection IgM is the first antibody produced in response to an infection. Elevated IgM levels can indicate a recent or acute infection [6].	Determination of Past Infection IgG antibodies are produced later than IgM and persist long-term, making them useful for detecting past infections or immune status [11].
Assessment of Inflammatory Conditions Elevated IgM levels can also be associated with autoimmune disorders and chronic inflammatory conditions [23].	Vaccination Monitoring IgG levels can be used to assess the effectiveness of vaccinations and determine immunity status [24].

Diagnostic Utility in Specific Infections IgM testing is crucial for diagnosing infections like Lyme disease, dengue fever, and toxoplasmosis [25].	Chronic Infection Assessment Persistent IgG levels can help in diagnosing chronic infections such as hepatitis B, hepatitis C, and HIV [26].

Combined use of IgM and IgG testing

Testing both IgM and IgG can help differentiate between acute and chronic stages of infections [27]. For instance, the presence of IgM with absence of IgG often indicates a recent infection [22], whereas the presence of both suggests an ongoing or past infection. The patterns of IgM and IgG production provide insights into the immune response and disease progression [7,8].

Monitoring disease progression

Monitoring disease progression through IgM and IgG levels provides critical insights into the status of infections and the effectiveness of immune responses. The decline of IgM antibodies over time typically indicates the resolution of an acute infection [28]. This decline can be monitored to assess whether a patient is recovering from an infectious disease [8]. Tracking IgM levels can help clinicians make informed decisions about treatment duration and further diagnostic testing, particularly in acute infections such as viral or bacterial diseases [4]. On the other hand, an increase in IgG levels over time is often indicative of a successful immune response to an infection or vaccination [24,29]. The presence of IgG suggests that the immune system has recognized the pathogen and is producing antibodies to combat it [9,26,30].

Importance of assessing IgG levels

Assessing IgG levels post-vaccination helps evaluate the immune response and effectiveness of vaccines (e.g., measles, mumps, rubella) [7,31]. Furthermore, monitoring IgG levels can help in assessing the efficacy of vaccines, especially in populations with varying immune responses (e.g., elderly, immunocompromised individuals) and monitoring of IgG levels can be particularly important for healthcare workers [32]. In addition to the importance of IgG levels, low IgG levels post-vaccination may indicate the need for booster doses to ensure sufficient protection against diseases. Also, it can guide public health decisions (population-wide IgG level assessments can inform public health policies regarding vaccine distribution and booster programs) [33]. Overall, assessing IgG levels post-vaccination is essential for understanding the efficacy and longevity of the immune response to vaccines. This evaluation aids in public health strategies and individual patient care, ensuring that populations remain protected against infectious diseases.

Limitations of IgM and IgG antibodies testing

IgM and IgG antibody testing is commonly used to diagnose infectious diseases, assess immune responses, and determine exposure to certain pathogens. However, there are some limitations of these tests as discussed accordingly. First, timing of detection, IgM antibodies typically develop within a few days to weeks after infection, while IgG antibodies take longer (generally several weeks). If a sample is taken too early in the infection, IgM may not be detectable, leading to false negatives [34]. Second limitation, cross-reactivity, studies demonstrated that many IgM and IgG tests can cross-react with antibodies from other infections, resulting in false-positive results. This issue is especially prominent with diseases that share antigenic similarities [35,36]. Next, IgG persistence, IgG antibodies can persist for months or years after infection, making it difficult to distinguish between current and past infections. This is particularly problematic in populations with high prevalence rates of specific infections [37]. Limited information on infectivity is one of IgM and IgG limitations, while IgM and IgG tests indicate exposure or immune status, they do not provide information about the current infectious state of an individual. This is crucial for managing outbreaks and preventing transmission [34,38]. Moreover, the interpretation of IgM and IgG results can be complex and often requires correlation with clinical symptoms and other diagnostic tests. Relying solely on antibody tests without considering the clinical context can lead to incorrect conclusions [38]. IgM and IgG testing lack to the sensitivity and specificity which can vary widely based on the assay used, the target population, and the prevalence of the disease. This variability can affect the reliability of test results [39,40]. In addition to the above-mentioned limitations some IgM and IgG tests can be expensive, and the required laboratory infrastructure may not be available in all settings, limiting access to testing, especially in low-resource environments. While IgM and IgG antibody tests are valuable tools in diagnosing and understanding infections, their limitations mean they are often used in conjunction with other diagnostic methods to provide a more accurate picture of an individual's health status. Overall, understanding the above limitations is crucial for clinicians to make informed decisions regarding patient care and public health measures. The future of IgM and IgG antibody testing lies in the integration of innovative technologies and targeted research efforts. By addressing current limitations and exploring new testing methodologies, the field can enhance diagnostic accuracy, improve patient outcomes, and contribute to more effective public health strategies in the management of infectious diseases.

Conclusion

IgM and IgG antibody testing is a critical component of diagnosing and managing infectious diseases. These tests provide valuable insights into the immune response, allowing clinicians to identify recent infections, assess immunity, and make informed public health decisions. Understanding both the strengths and limitations of IgM and IgG antibody testing is crucial for healthcare providers, researchers, and public health officials. While these tests are invaluable tools in infectious disease management, their interpretation requires a nuanced approach that considers individual patient circumstances and broader epidemiological trends. As the field continues to evolve, integrating new technologies and addressing existing knowledge gaps will be essential in enhancing the effectiveness of serological testing and ultimately improving patient care and public health outcomes.

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