

The Role of Laboratory Testing in Evaluating Immune Function in Chronic Illnesses

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Abstract:

Laboratory testing plays a crucial role in assessing immune function among individuals with chronic illnesses. Chronic diseases often involve dysregulation of the immune system, leading to either an overactive or underactive immune response. Tests such as complete blood counts (CBC), immune panels, and specific cytokine assays help measure the levels and activity of various immune cells, such as T-lymphocytes, B-lymphocytes, and natural killer cells. These tests can provide insight into the underlying immunological mechanisms contributing to a patient's condition, guiding therapeutic strategies and monitoring the effectiveness of treatment interventions. Moreover, certain tests can help identify underlying infections or autoimmune processes that may complicate the clinical picture, allowing for a more targeted and effective management approach. Furthermore, laboratory testing can aid in evaluating the impact of chronic illnesses on immune function over time. For instance, serial testing of immunoglobulin levels can reveal trends in immune competency, indicating how well a patient's immune system is functioning in response to ongoing treatment. By understanding the immune status of a patient, healthcare providers can refine treatment plans, tailor immunotherapies, and implement preventive measures against potential infections that patients might be more susceptible to. This personalized approach not only improves patient outcomes but also enhances the overall quality of life for individuals grappling with chronic illnesses by addressing their unique immunological needs.

Keywords: laboratory testing, immune function, chronic illnesses, complete blood count (CBC), immune panels, cytokine assays, T-lymphocytes, B-lymphocytes, natural killer cells, immunoglobulin levels, immunotherapy, personalized treatment, autoimmune processes.

Introduction:

Chronic illnesses represent a significant burden on healthcare systems worldwide, affecting millions of individuals and leading to substantial morbidity and mortality. Conditions such as autoimmune disorders, chronic infections, metabolic syndromes, and malignancies are often characterized by complex interactions between immune function, environmental factors, and genetic predispositions. Understanding how immune function is compromised or dysregulated in these conditions is critical for effective diagnosis, management, and treatment. Consequently, laboratory testing has emerged as a fundamental tool in the evaluation of immune function in individuals with chronic illnesses [1].

Laboratory testing for immune function can be broadly categorized into two types: functional assays that assess the activity of immune cells and biomarker assays that measure the presence of specific immune-related molecules. These tests can provide comprehensive insights into the dysregulations that occur within the immune system and establish correlations between immune parameters and clinical outcomes. An array of laboratory techniques, including flow cytometry, enzyme-linked immunosorbent assays (ELISA), multiplex cytokine analyses, and genomic profiling, are routinely used to analyze various components of the immune system, including T and B lymphocytes, cytokines, natural killer (NK) cells, and antibodies [2].

The importance of these evaluations is underscored by the growing body of evidence linking immune dysfunction to chronic illnesses. For instance, in autoimmune diseases such as rheumatoid arthritis and lupus, laboratory tests can reveal alterations in lymphocyte populations, increased levels of pro-inflammatory cytokines, and the presence of autoantibodies, all of which can help identify disease activity and inform treatment strategies. In cases of chronic infections, such as those associated with human immunodeficiency virus (HIV) or hepatitis C virus (HCV), specific immune markers can indicate the stage of infection and the effectiveness of antiretroviral therapies [3].

Furthermore, laboratory testing can help elucidate mechanisms of immune evasion employed by pathogens or tumors, thereby guiding the development of novel therapeutic approaches. For example, the identification of immune checkpoint molecules, such as PD-1/PD-L1, through laboratory tests has revolutionized the treatment of various cancers by providing targets for immunotherapy [4].

In metabolic syndromes, increasing evidence suggests a link between chronic inflammation and immune dysregulation, underscoring the role of laboratory testing in evaluating immune parameters that may contribute to disease progression. Markers of inflammation, such as C-reactive protein (CRP) and interleukin-6 (IL-6), can provide valuable information about the systemic inflammatory state of patients, enabling clinicians to tailor interventions aimed at reducing inflammation and enhancing immune function [5].

While laboratory testing is invaluable in the assessment of immune function, it also poses challenges. The interpretation of results requires a comprehensive understanding of the individual's clinical context, including medical history, symptomatology, and current therapies, as biological markers can vary significantly across different diseases and populations. Additionally, advancements in technology continuously improve the precision and breadth of laboratory testing, but inconsistencies in methodology and variability in assay results can complicate conclusions [6].

Given these complexities, a multidisciplinary approach involving immunologists, laboratory specialists, and clinical practitioners is essential for accurate interpretation and integration of laboratory findings into patient management. Significant efforts toward standardization, validation, and understanding the clinical significance of various immune markers are necessary to enhance the utility of laboratory testing in chronic illnesses [6].

Overview of Laboratory Testing Methods for Immune Evaluation:

The immune system plays a critical role in maintaining health by defending the body against pathogens, including viruses, bacteria, fungi, and parasites. Anomalies in immune function can lead to various disorders, including autoimmune diseases, immunodeficiencies, and allergies. To understand these conditions and monitor immune status, laboratory testing methods for immune evaluation have become an essential part of clinical medicine [7].

Serological Tests

Serological tests are among the most common laboratory methods for evaluating immunological conditions. These tests detect antibodies or antigens in serum, the liquid component after blood has clotted. Antibodies are proteins produced by B cells in response to foreign antigens, while antigens are substances that provoke an immune response [7].

1. Enzyme-Linked Immunosorbent Assay (ELISA)

ELISA is a highly sensitive technique used to quantify specific antibodies or antigens in a sample. This method involves coating a microplate with an antigen and then adding patient serum. If the antibodies against the antigen are present, they will bind. A secondary enzyme-linked antibody is then added, which binds to the captured antibodies, allowing for quantification through a substrate that produces a measurable signal, often a color change.

Applications: ELISA is extensively used in various scenarios, including diagnosing infections (e.g., HIV, hepatitis), evaluating autoimmune diseases (e.g., rheumatoid arthritis), and detecting specific allergies.

Limitations: While ELISA is a powerful tool, its sensitivity can lead to false positives, and interpretation may vary depending on the assay calibration and the presence of cross-reactive antibodies [8].

2. Western Blotting

Western blotting is another serological technique primarily used for the detection of specific proteins in a sample. Following gel electrophoresis, proteins are transferred to a membrane, and specific antibodies are used to probe for the target protein, providing qualitative and quantitative data [9].

Applications: This method is particularly vital for confirming HIV diagnoses after initial positive ELISA tests. It is also used for research to study protein expression profiles.

Limitations: The procedure is labor-intensive and time-consuming compared to ELISA, and results can be influenced by the specificity of the antibodies used in the assay.

Functional Assays

Functional assays evaluate the performance of various immune cells, providing insights into cellular immune responses [10].

1. Flow Cytometry

Flow cytometry is a technique that allows for the rapid analysis of individual cells suspended in a fluid stream. Cells are tagged with fluorescent antibodies that specifically bind to cell surface markers. The flow cytometer uses lasers to excite the fluorescent tags and detect emitted light, enabling the quantification of various cell populations.

Applications: This method is crucial for assessing lymphocyte subsets (e.g., CD4⁺ and CD8⁺ T cells) in HIV patients, evaluating immune reconstitution after stem cell transplantation, and diagnosing hematological malignancies.

Limitations: Flow cytometry requires expensive equipment and specialized knowledge for data interpretation, limiting its widespread use in all clinical settings [11].

2. Lymphocyte Proliferation Assays

These assays measure the ability of lymphocytes, typically T cells, to proliferate in response to specific stimuli, such as antigens or mitogens. Common methods include the MTT assay, which measures the metabolic activity of live cells, or the incorporation of radioactive thymidine into newly synthesized DNA [12].

Applications: They are primarily used in research settings to explore immune responses to infections, vaccines, or tumors.

Limitations: The necessity for radioactive materials and complex cell culture techniques can limit their practicality in standard clinical laboratories.

Molecular Techniques

Molecular techniques, including polymerase chain reaction (PCR) and next-generation sequencing (NGS), have revolutionized immune evaluation by allowing for the detection of specific genetic material related to immune responses [13].

1. Polymerase Chain Reaction (PCR)

PCR is a technique used to amplify specific DNA sequences, enabling the detection of low-abundance pathogens or genetic mutations related to immune function. This method can be qualitative or quantitative (qPCR) depending on the objective [14].

Applications: PCR is vital for diagnosing infections (e.g., tuberculosis, COVID-19), detecting genetic predispositions to immune diseases, and monitoring minimal residual disease in cancer patients [15].

Limitations: PCR can sometimes yield false-negative results in the presence of inhibitors, and the technical expertise required can be a barrier to its widespread application.

2. Next-Generation Sequencing (NGS)

NGS technologies allow for the simultaneous sequencing of millions of DNA fragments. This high-throughput method can provide comprehensive insights into various immune cells' genetic diversity and functional capabilities.

Applications: NGS is increasingly used in immunology to study the repertoire of antibodies or T-cell receptors, identify genetic variations associated with immune diseases, and understand the host response to infections and vaccines.

Limitations: Despite its cost-effectiveness decreasing, the complexity of data analysis remains a significant hurdle for many laboratories, requiring substantial bioinformatics expertise [16].

Key Biomarkers in Immune Function Assessment:

The human immune system serves as an intricate network of cells, tissues, and organs that work collaboratively to defend the body against pathogens, autoimmune diseases, and other health threats. Understanding immune function is crucial for diagnosing, monitoring, and treating various medical conditions, including infections, inflammatory diseases, and cancers. One of the most effective ways to evaluate immune function is through the assessment of specific biomarkers—molecular indicators that reflect the activity of the immune system.

Biomarkers are defined as measurable indicators of biological processes, conditions, or pharmacologic responses within an organism. In the context of immunology, biomarkers can be cellular, molecular, or biochemical factors that indicate the status or function of the immune system. The identification and measurement of these biomarkers allow healthcare professionals and researchers to gauge immune responses, identify dysfunction, and predict disease outcomes. Biomarkers can be derived from various sources: blood, tissue biopsies, urine, and even saliva [17].

Types of Immune Biomarkers

Immune biomarkers can be categorized into several types, including cytokines, chemokines, cellular markers, and antibody levels. Each type serves a unique function in the assessment of the immune system [18].

1. Cytokines

Cytokines are small proteins produced by immune cells that mediate and regulate immune and inflammatory responses. Key cytokines used as biomarkers in immune function assessment include:

- **Interleukins (ILs):** For example, IL-6 is a pro-inflammatory cytokine that plays a significant role in immune response and is often elevated in chronic inflammatory conditions such as rheumatoid arthritis. IL-10, on the other hand, is an anti-inflammatory cytokine involved in limiting immune responses.
- **Tumor Necrosis Factor-alpha (TNF- α):** This cytokine is another prominent marker that reflects inflammation. It is often upregulated in various autoimmune diseases and is targeted by specific therapies in conditions like rheumatoid arthritis and inflammatory bowel disease [18].

2. Chemokines

Chemokines are a subset of cytokines that specifically direct the migration of immune cells to sites of inflammation or infection. Biomarkers like CCL2 (MCP-1) and CXCL10 (IP-10) are important for understanding immune cell recruitment during diseases such as cancer and chronic infections like HIV [19].

3. Cellular Markers

Flow cytometry has enabled the detailed quantification of immune cells and their subtypes. Important cellular markers include:

- **CD4+ and CD8+ T Lymphocytes:** These subsets are critical T cell populations in adaptive immunity. The CD4+ T cells are often referred to as helper T cells and play crucial roles in orchestrating the immune response, while CD8+ T cells are primarily responsible for killing infected or cancerous cells. The ratio of CD4+ to CD8+ T cells can provide insights into immune health.
- **B Cells and Antibodies:** The levels of specific antibodies (immunoglobulins) in the serum can also be indicative of immune function. Elevated or diminished levels of IgG, IgM, and IgA can signal autoimmune disorders or immunodeficiencies, respectively [19].

4. Immune Activation Markers

Markers such as soluble CD14 (sCD14) and programmed cell death protein 1 (PD-1) can indicate immune activation or exhaustion. Elevated sCD14 often signifies monocyte activation and is associated with systemic inflammation, while PD-1 levels can indicate T cell exhaustion in chronic infections and cancers [20].

Clinical Significance

The assessment of immune biomarkers has substantial clinical implications. For instance, accurate measurement of cytokine levels can help physicians decide on therapeutic interventions in conditions like cytokine release syndrome, which can occur during certain cancer treatments. Moreover, immune biomarkers have proven invaluable in predictive medicine, allowing clinicians to determine prognosis and therapeutic responses in oncology. For example, measuring PD-1/PD-L1 expression can help ascertain a patient's response to immunotherapy in lung cancer.

In autoimmune diseases, specific biomarkers can assist in diagnosing conditions like lupus and multiple sclerosis, as well as in monitoring disease progression and response to therapy. The use of biomarkers in the context of infections can not only guide treatment decisions but also enhance understanding of pathogen-host interactions [21].

Future Directions in Immunology Research

As technology and methodologies advance, the field of immunology is poised to significantly benefit from the continuous exploration of immune biomarkers. Genomic and proteomic profiling offer promising avenues for the identification of novel biomarkers. Additionally, the advent of personalized medicine and targeted therapies underscores the need to delve deeper into understanding individual immune profiles.

Researchers are also exploring the potential of microbiome-related biomarkers. The gut microbiome plays a pivotal role in modulating immune responses; thus, profiling microbial metabolites may yield insights into immune function and dysregulation.

Furthermore, the integration of artificial intelligence and machine learning into immunology is expected to enhance biomarker discovery, leading to more precise immune assessments. By analyzing vast datasets and recognizing patterns, AI can uncover potential biomarkers that have previously gone unnoticed [22].

The Diagnostic Role of Complete Blood Counts (CBC):

Complete Blood Count (CBC) is a pivotal clinical tool widely employed in medical diagnostics, serving as a fundamental component in the assessment of an individual's overall health. It encompasses a comprehensive analysis of the cellular components of blood, providing invaluable insights into various physiological and pathological conditions [23].

Understanding Complete Blood Count (CBC)

A Complete Blood Count typically consists of several key parameters:

1. **Red Blood Cells (RBCs):** The primary function of RBCs is to transport oxygen from the lungs to the body tissues and facilitate the return of carbon dioxide back to the lungs. The CBC quantifies RBC concentration (measured in millions per microliter of blood), hemoglobin (the oxygen-carrying protein), and hematocrit (the proportion of blood volume that is occupied by RBCs) [24].
2. **White Blood Cells (WBCs):** WBCs are essential components of the immune system, tasked with defending the body against infections and foreign substances. The CBC counts the total WBCs and differentiates them into subtypes like neutrophils, lymphocytes, monocytes, eosinophils, and basophils. This differential count provides insight into various immune responses.
3. **Platelets:** These cellular fragments play a crucial role in the coagulation process. The CBC reports platelet count, crucial for assessing bleeding disorders or thrombotic events.

4. **Indices:** CBC also includes several indices, such as Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), and Mean Corpuscular Hemoglobin Concentration (MCHC), which provide information about the size, weight, and concentration of hemoglobin in red blood cells [24].

Interpretation of CBC Results

Interpreting CBC results requires clinical acumen and an understanding of the technical aspects of hematology. Normal ranges for each component can vary by factors such as age, sex, and individual health. For example, normal ranges for hemoglobin are generally 13.5 to 17.5 grams per deciliter for males and 12.0 to 15.5 grams per deciliter for females. Deviations from these norms can signal underlying medical conditions [25].

- **Elevated RBC Count:** Often indicative of polycythemia vera or other conditions leading to increased erythropoiesis.
- **Decreased RBC Count or Anemia:** This may point toward iron deficiency, chronic disease, or bone marrow disorders.
- **WBC Count:** A high WBC count may suggest infection, inflammation, or neoplastic disorders, while a low count might indicate bone marrow issues or immune disorders.
- **Platelet Count:** Thrombocytopenia (low platelet count) can lead to bleeding issues, while thrombocytosis (high platelet count) may increase the risk of thrombosis [25].

Clinical Applications of CBC

The practical applications of CBC are extensive and multifaceted. CBC is often one of the first tests ordered during routine examinations, for pre-operative assessments, or when patients present with symptoms such as fatigue, fever, or unexplained bruising. Some key clinical applications include:

1. **Diagnosis of Anemia:** CBC is instrumental in diagnosing different types of anemia, distinguishing between iron deficiency anemia, hemolytic anemia, and megaloblastic anemia based on specific RBC indices and morphology [26].
2. **Infection and Inflammatory Response:** Changes in WBC counts and differential counts help in identifying infections, guiding antibiotic therapy, and assessing inflammatory diseases.
3. **Hematological Disorders:** Various blood disorders, including leukemias and lymphomas, can initially be identified through abnormal CBC results, prompting further investigations like bone marrow biopsy or flow cytometry.
4. **Monitoring Treatment and Disease Progression:** In patients undergoing chemotherapy, a regular CBC is crucial to monitor bone marrow function and adjust treatment regimens accordingly.
5. **Evaluating Coagulation Status:** Platelet counts and other coagulation parameters guide the management of patients with bleeding disorders and help assess risks before surgical procedures [26].

Limitations of CBC

Despite its widespread utility, CBC is not without limitations. It is essential to recognize that while CBC can indicate certain conditions, it often does not provide a definitive diagnosis. The results need to be interpreted within the context of clinical findings and may require supplementary tests for confirmation. For instance:

- **False Positives and Negatives:** Various factors can influence CBC results, including hydration status, recent physical activity, or even time of day. These factors can lead to misinterpretation without thorough evaluation [27].
- **Lack of Specificity:** CBC can indicate a problem but is often not specific enough to confirm a diagnosis. For instance, a high WBC count may suggest infection, but it could also be related to stress or other non-infectious causes.
- **Laboratory Variability:** Variations in laboratory protocols, instrumentation, and quality control can result in inconsistency among results, emphasizing the importance of sending samples to accredited laboratories [27].

Significance of Cytokine Profiles in Chronic Disease Management:

Chronic diseases, characterized by their prolonged duration, generally slow progression, and often complex interactions with various biological systems, pose significant challenges for healthcare systems worldwide. Examples of chronic diseases include diabetes mellitus, cardiovascular diseases, obesity, autoimmune disorders, and chronic respiratory diseases. These conditions frequently overlap and are interrelated, contributing to morbidity and mortality rates that are alarmingly high in many populations. The quest for effective strategies in their management has led to a greater understanding of the underlying mechanisms, notably the role of cytokines in inflammation and immune response [28].

Cytokines are small signaling proteins produced by various cells, influencing the behavior of other cells. They play a crucial role in mediating inflammation, cell growth, and tissue repair. The cytokine profile—an array of cytokines

present in a given biological sample—provides insight into the immunological status of an individual. Changes in cytokine profiles can reflect the ongoing pathological processes in chronic diseases, aiding in diagnostics and therapeutic decision-making. As such, the significance of cytokine profiles in chronic disease management cannot be overstated [29].

To appreciate the role of cytokine profiles in chronic diseases, it is imperative to understand the types of cytokines involved. They can be broadly categorized into pro-inflammatory and anti-inflammatory cytokines. Pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), and interferon-gamma (IFN- γ), promote inflammation and are typically elevated in chronic inflammatory states. Conversely, anti-inflammatory cytokines such as interleukin-10 (IL-10) help regulate the immune response and mitigate inflammation [30].

The balance between pro-inflammatory and anti-inflammatory cytokines is crucial for maintaining homeostasis. Disruption of this balance often leads to a chronic inflammatory state, which is a common pathway in various chronic diseases. For example, in rheumatoid arthritis, the persistent elevation of pro-inflammatory cytokines is linked to joint damage and systemic symptoms. Similarly, in conditions like type 2 diabetes, inflammatory cytokines contribute to insulin resistance, exacerbating metabolic dysregulation [31].

One of the most significant applications of cytokine profiles in chronic disease management is in diagnosis and prognosis. Measuring the levels of specific cytokines can aid in the differentiation of disease states. For instance, elevated IL-6 levels are commonly associated with chronic inflammatory diseases and can also indicate disease activity, thus serving as a potential biomarker for monitoring treatment response. C-reactive protein (CRP), another inflammatory marker often used alongside cytokines, provides a broader picture of the inflammatory status in the body [32].

Furthermore, cytokine profiling holds promise for predicting disease progression. Clinicians can tailor treatments based on the identified cytokine profiles, customizing therapy to modulate the immune response. For instance, rheumatoid arthritis therapies that target TNF- α have shown efficacy in driving down inflammation by interrupting the cytokine signaling cascade. By stratifying patients based on their cytokine profiles, healthcare providers may be able to identify those who are likely to respond to specific therapies, thus improving outcomes and resource allocation [33].

The evolution of personalized medicine hinges on understanding the unique biological profiles of patients, and cytokine profiling stands at the forefront of this paradigm. As research reveals the interconnectedness of various cytokines and their roles in different chronic diseases, therapeutic strategies can become more directed and effective. For example, targeting specific cytokines implicated in inflammatory pathways has yielded some success in managing chronic diseases. Monoclonal antibodies designed to inhibit TNF- α , IL-1, or IL-6 have transformed the treatment landscape in autoimmune diseases, reducing symptoms and disease progression in conditions like psoriasis and ankylosing spondylitis. Ongoing research into other cytokines, such as IL-17 and IL-23, opens new avenues for treatment and reveals the multifaceted nature of immune responses [34].

Moreover, cytokine profiles can inform decisions regarding adjunct therapies. For instance, patients exhibiting a specific cytokine imbalance may benefit from lifestyle modifications such as dietary changes, exercise regimes, or psychological interventions to help mitigate stress-induced inflammatory responses. In this context, the role of cytokines extends beyond mere markers of disease; they become central in therapeutic decision-making processes [35].

Despite the promising role of cytokine profiles in chronic disease management, challenges persist. The complexity of cytokine interactions is not fully understood, and factors such as genetic predispositions, environmental influences, and comorbidities can complicate cytokine profiling efforts. Moreover, standardizing assay techniques for measuring cytokines remains a critical hurdle to broad clinical application. Future research must aim to establish reliable methodologies and validate the clinical utility of cytokine profiling in various chronic conditions [36].

Furthermore, longitudinal studies will be needed to track changes in cytokine profiles in response to treatment and disease progression over time. Understanding how these profiles evolve allows for an agile approach to treatment, potentially adapting therapies in real time to better address disease manifestations [37].

Interpreting Immunoglobulin Levels in Chronic Illness:

The immune system plays a critical role in maintaining health and warding off diseases. Among the various components of the immune system are immunoglobulins (Ig), also known as antibodies, which are crucial for identifying and neutralizing pathogens such as bacteria and viruses. The body produces several classes of immunoglobulins, including IgG, IgA, IgM, IgE, and IgD, each serving unique functions in the immune response. In individuals suffering from chronic illnesses, understanding the levels of these immunoglobulins can provide valuable insights into the patient's immune status, the presence of underlying infections, or even the response to therapies [38].

Immunoglobulin Structure and Functions

Immunoglobulins are glycoproteins produced by plasma cells, derived from B lymphocytes. The five primary classes of immunoglobulins—IgG, IgA, IgM, IgE, and IgD—each plays a distinct role in immune function:

1. **IgG:** The most abundant antibody in circulation, IgG constitutes approximately 75-80% of the total immunoglobulins. It is vital for long-term immunity, with the ability to neutralize toxins, opsonize pathogens for easier identification by phagocytes, and activate the complement system [39].
2. **IgA:** Predominantly found in mucosal areas, such as the respiratory and gastrointestinal tracts, as well as in secretions like saliva and breast milk, IgA is essential for mucosal immunity and protecting mucosal surfaces from pathogens.
3. **IgM:** The first immunoglobulin produced in response to an infection, IgM is critical for initiating the immune response. It forms pentamers, making it effective in agglutinating pathogens and activating the complement system.
4. **IgE:** Although present in small amounts, IgE plays a significant role in allergic reactions and responses to parasitic infections. Elevated levels of IgE are often associated with allergic diseases such as asthma, hay fever, and eczema.
5. **IgD:** The least understood immunoglobulin, IgD is believed to have a role in the activation and regulation of B cells but is found in very low concentrations in serum [40].

Clinical Use of Immunoglobulin Testing

Immunoglobulin levels can be quantified through serum assays, which measure the concentration of each immunoglobulin class. The interpretation of these levels requires an understanding of the normal ranges, which can vary depending on age, sex, and specific laboratory reference ranges. Clinicians typically assess immunoglobulin levels in patients with chronic illnesses to determine the presence of immune dysfunction, identify specific deficiencies, or monitor the disease's progression [41].

Scenarios of Testing

1. **Autoimmune Diseases:** Conditions such as rheumatoid arthritis and systemic lupus erythematosus (SLE) often lead to alterations in immunoglobulin levels. Patients with autoimmune disorders may exhibit elevated IgG and IgM levels due to chronic stimulation of the immune system. Furthermore, some patients may experience hypogammaglobulinemia, a reduction in serum immunoglobulin levels, which can predispose them to recurrent infections.
2. **Infections:** Chronic infections, such as HIV, tuberculosis, or chronic hepatitis, can lead to significant alterations in immunoglobulin profiles. In HIV-infected individuals, for instance, immunoglobulin levels can be preserved or even elevated in early stages of infection but eventually may decline with the progression of immunosuppression [41].
3. **Allergic Diseases:** In patients suffering from chronic allergic conditions, such as asthma or atopic dermatitis, evaluation of IgE levels can be particularly informative. An elevated IgE level can suggest the presence of an ongoing allergic response, while normalization may indicate effective management of the condition.
4. **Hospitalized Patients:** Individuals with chronic conditions who are hospitalized for other health issues may be assessed for immunoglobulin levels to help guide treatment, particularly if they display signs of infection or systemic inflammatory response [42].

Implications of Immunoglobulin Levels in Chronic Illness

Diagnosing Immune Deficiencies

One of the essential roles of immunoglobulin testing is the diagnosis of primary or secondary immunodeficiency disorders. Patients presenting with recurrent infections, particularly in the absence of other known causes, may be evaluated for conditions such as common variable immunodeficiency (CVID) or specific antibody deficiency (SAD). These conditions can manifest as low serum immunoglobulin levels, necessitating timely intervention, including immunoglobulin replacement therapy [43].

Knowledge of immunoglobulin levels can significantly influence treatment strategies. For instance, in chronic autoimmune conditions, elevated immunoglobulin levels may indicate a need to adjust immunosuppressive therapy to prevent further damage. Alternatively, in cases of hypogammaglobulinemia, intravenous immunoglobulin (IVIG) therapy may be initiated to restore adequate immunological function and prevent recurrent infections.

Periodic measurement of immunoglobulin levels can aid in monitoring disease progression and response to therapy. In autoimmune diseases, fluctuations in IgG and IgM levels may indicate changes in disease activity, guiding clinicians on the appropriateness of therapeutic adjustments. In some cancer patients, immunoglobulin levels may also be used to monitor the effectiveness of treatments like chemotherapy that can impact the immune system [43].

Integrating Laboratory Findings into Clinical Practice:

The understanding of human immunity and its complex mechanisms has substantially evolved over the decades, driven by advancements in immunology, molecular biology, and technology. As we move deeper into the 21st century, the integration of laboratory results into clinical practice regarding immunity evaluation becomes increasingly critical [44].

Significance of Evaluating Immunity

Immunity is a multifaceted defense system that enables the body to resist infections and diseases. Evaluating an individual's immune status has profound implications in various clinical settings, including management of chronic diseases, infectious diseases, and conditions related to immunodeficiency or autoimmunity. For example, understanding a patient's immune profile can inform vaccination strategies, guide treatment decisions for immunocompromised patients, and assist in diagnosing autoimmune disorders.

Laboratory tests that evaluate immunity can provide critical insights into immunological health, which is essential for personalized medicine approaches. As healthcare moves towards more individualized treatment plans, the role of laboratory testing in assessing and understanding immune functions cannot be overstated [45].

Types of Laboratory Tests for Immunity Evaluation

Laboratory tests aimed at evaluating immunity can be classified broadly into several categories:

1. **Serological Tests:** These tests are designed to detect antibodies or antigens in the blood, allowing clinicians to assess immune responses to infections or vaccinations. Common examples include enzyme-linked immunosorbent assay (ELISA) tests, which quantify specific immunoglobulin levels, and neutralization assays that determine the functionality of antibodies in neutralizing pathogens [46].
2. **Cell-Based Assays:** These assays evaluate the cellular components of the immune response, such as T cells and natural killer (NK) cells. Flow cytometry is an essential tool in this realm, allowing for the quantitation and characterization of specific immune cell populations. This can provide insights into T cell activation, memory response, and overall cellular immunity.
3. **Polymerase Chain Reaction (PCR) Tests:** PCR has revolutionized the diagnosis of infectious diseases. By amplifying specific nucleic acid sequences, PCR can detect the presence of pathogens, and in turn, inform clinicians about the immune system's interactions with these pathogens [46].
4. **Functional Immunoassays:** These tests evaluate the functional capacity of immune cells. For example, the lymphocyte proliferation assay can assess the ability of T cells to proliferate in response to specific antigens, thereby providing insights into the cell-mediated immune response.
5. **Genetic and Molecular Testing:** Advances in genetics enable the identification of hereditary immunodeficiencies that may alter immune function. Genetic tests can reveal mutations in specific genes related to immune processes, aiding clinicians in diagnosing primary immunodeficiencies [46].

Interpreting Laboratory Results

The interpretation of laboratory test results requires a comprehensive understanding of immunology and the context of clinical data. Various factors—including age, sex, medical history, and the presence of comorbid conditions—must be considered to accurately assess immunity through laboratory findings. For instance, a serological test result showing elevated antibody levels may indicate effective vaccination but could also reflect past infections. Thus, correlating these results with clinical symptoms and other diagnostic information is crucial to avoid misdiagnosis or inappropriate treatment [47].

Laboratory results often follow trends rather than isolated readings, so monitoring changes over time assists physicians in evaluating the effectiveness of therapies or the progression of diseases. In some cases, follow-up testing may be required to establish a clearer picture of immune status, especially during disease flare-ups or after significant clinical events [48].

Translating Results into Clinical Practice

Integrating laboratory findings into clinical decision-making enhances patient care and outcomes. Immune evaluations inform a range of clinical practices, including:

1. **Vaccination Strategies:** Laboratory tests can assess a patient's immune response to previous vaccinations, guiding decisions on whether booster doses are necessary. For example, in individuals with autoimmune diseases or those receiving immunosuppressive therapy, serological assessments can dictate tailored vaccination schedules to enhance protective immunity [49].
2. **Clinical Management of Infections:** In patients with recurrent infections, identifying underlying immunodeficiencies through laboratory tests allows for early intervention. This might include prophylactic therapies or immunoglobulin replacement in those with primary immunodeficiencies.

3. **Guiding Treatment for Autoimmune Disorders:** Laboratory evaluations help identify autoimmune conditions associated with improper immune responses. Results from cellular assays can dictate the use of immunomodulatory therapies and assist in monitoring disease activity [50]
4. **Personalized Medicine:** Advances in understanding the human genome have facilitated the move towards precision medicine, wherein lab results can help identify specific immune profiles that require tailored treatments based on an individual's genetic makeup.
5. **Research and Public Health:** On a larger scale, laboratory tests play a critical role in epidemiological studies and public health initiatives aimed at understanding population immunity, particularly in contexts such as vaccinations during outbreaks [51].

Future Directions in Immune Function Testing for Chronic Illnesses:

The immune system plays a crucial role in maintaining health and combating diseases. It is a complex network of cells, tissues, and organs that work in concert to protect the body from pathogens. Chronic illnesses, such as autoimmune diseases, chronic infections, and allergies, arise when the immune system's function is compromised, leading to longer-term health challenges. The need for effective diagnosis and monitoring strategies has never been more crucial as the prevalence of chronic illnesses continues to increase globally. One promising avenue for improving care and management in this area is through advanced immune function testing [52].

The future of immune function testing will likely be shaped by several emerging technologies that have the potential to enhance our understanding of the immune system's dynamics in relation to chronic illnesses. Traditional methods, such as complete blood counts and serum antibody assessments, have limitations in complexity and resolution. Recent advancements, including flow cytometry, mass cytometry, and next-generation sequencing, offer deeper insights into the cellular and genetic dynamics of the immune system [52].

Flow Cytometry allows for the detailed analysis of immune cell populations, measuring parameters such as size, granularity, and surface protein expression. This technology enables clinicians to identify specific immune cell types and assess functional responses, which can be critical for diagnosing immune dysregulation in chronic conditions like rheumatoid arthritis or lupus [53].

Mass Cytometry, or CyTOF, further expands this capability by allowing researchers and clinicians to measure over 40 parameters simultaneously at the single-cell level. This increases the depth of information obtained from samples, offering a high-resolution view of cellular function and immune profile alteration in chronic diseases.

Next-Generation Sequencing (NGS) applications, including T-cell receptor sequencing, allow for the assessment of the diversity and repertoire of T-cell populations. This can help in tracking how well the immune system responds over time to treatments or changes in disease state. The ability to analyze genetic information rapidly and cost-effectively opens new avenues for understanding the role of immune function in chronic illnesses on a personalized level [53].

The Role of Biomarkers in Immune Function Testing

Biomarkers are crucial for assessing immune function and disease progression. Future directions in immune function testing will involve the development of novel biomarkers that can address the multifaceted nature of chronic illnesses. Traditional biomarkers, such as C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR), provide limited insights into specific immune mechanisms [54].

Emerging research is focusing on developing biomarkers that reflect specific immune pathways and dysfunctions. For example, the discovery of cytokines like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α) as crucial mediators in inflammation has allowed for targeted therapeutic interventions in autoimmune diseases.

Moreover, the exploration of **immune signatures**—combinations of multiple biomarkers indicative of specific immune states—presents an avenue for refining diagnostic criteria and developing tailored treatment plans. Advances in machine learning and artificial intelligence (AI) are also supporting the identification of patterns among diverse immune markers, potentially revealing new associations that can inform clinical decisions [55].

An emerging trend in chronic illness management is the integration of holistic approaches, encompassing not just the immune system but the body as a whole, including mental health and lifestyle factors. Future immune function testing will likely incorporate assessments of psychosocial factors, nutrition, and environmental exposures [56].

Research has increasingly shown how stress and lifestyle choices can impact immune function. For instance, chronic stress can lead to immune dysregulation, contributing to exacerbated symptoms in chronic illnesses. Future testing paradigms may include psychoneuroimmunology assessments that evaluate the interplay between psychological well-being, lifestyle habits, and immune function to provide a more comprehensive view of a patient's health.

Additionally, nutritional immunology is emerging as a critical area that informs immune system health. Nutrient deficiencies have been linked to impaired immune function, prompting research into personalized nutritional interventions to support immune health in individuals with chronic illnesses. Testing panels that assess vitamin D

levels, zinc status, and other nutritional biomarkers could prove beneficial for tailoring interventions to enhance immune resilience [57].

Perhaps the most significant future direction of immune function testing lies in its implications for personalized medicine. Chronic illnesses often present with unique manifestations, and as such, standardized treatment approaches can be inadequate. Highly individualized immune function testing has the potential to inform more targeted therapies based on a patient's specific immune profile.

With the advent of precision medicine, providers can utilize immune function tests to select the most appropriate treatment strategies for patients. For instance, immune profiling may guide the use of biologic therapies in diseases like multiple sclerosis or inflammatory bowel disease, ensuring that individuals receive treatments that are more likely to be effective based on their immune characteristics [58].

Furthermore, continuous immune monitoring through advanced testing technologies can aid in real-time adjustments to treatment plans. For patients with chronic infections such as HIV or hepatitis, monitoring immune responses can provide early indications of treatment efficacy, enabling timely modifications that can improve health outcomes [59].

However, the transition to a personalized approach will also necessitate thoughtful considerations regarding data management, ethical considerations surrounding genetic information, and addressing disparities in access to advanced testing technologies. As these methodologies evolve, health systems will need to establish frameworks to ensure equitable access while safeguarding patient privacy [60].

Conclusion:

In conclusion, laboratory testing is indispensable for evaluating immune function in individuals with chronic illnesses. By providing critical insights into the immune system's status and functionality, these tests facilitate the identification of dysregulations that may exacerbate chronic conditions. Through measures such as complete blood counts, cytokine profiles, and immunoglobulin assessments, healthcare providers can gain a comprehensive understanding of a patient's immunological health. This knowledge not only aids in diagnosis and monitoring but also informs treatment strategies tailored to the unique needs of each patient. As our understanding of the immune system evolves, continuous advancements in laboratory testing methodologies will improve the precision and efficacy of interventions, ultimately enhancing patient outcomes and quality of life in those affected by chronic illnesses. The integration of these findings into clinical practice will be essential for optimizing care and ensuring patients receive the most effective and personalized approaches to managing their health.

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