Memory and Naive B-Cell Testing

Indications for Ordering

- Screens for common variable immunodeficiency (CVID)
- Assesses B-cell subset reconstitution after bone marrow or stem cell transplant

Test Description

Immunoglobulins (IgA, IgG, IgM), Quantitative – quantitative nephelometry

B-Cell Memory and Naive Panel – flow cytometry

- Measures
  - B cells (CD19+)
  - Total memory B cells (CD19+ CD27+)
  - Class switched memory B cells (CD19+ CD27+ IgD- IgM-)
  - Nonswitched/marginal zone memory B cells (CD19+ CD27+ IgD+ IgM+)
  - IgM only memory B cells (CD19+ CD27+ IgD- IgM+)
  - Naive B cells (CD19+ CD27- IgD+)

Tests to Consider

Primary tests

Immunoglobulins (IgA, IgG, IgM), Quantitative 0050630

- Initial test in the workup of suspected immunoglobulin disorders
- Order in conjunction with serum protein electrophoresis and immunofixation to rule out plasma cell dyscrasia in adults and older children (>15 years) with suspected hypogammaglobulinemia

B-Cell Memory and Naive Panel 2008901

- Assess B-cell subsets of immunodeficiencies
- Supports the diagnosis of CVID and may help predict the clinical phenotype
- Assess B-cell reconstitution after bone marrow or hematopoietic stem cell transplantation
- Not recommended for rituximab monitoring
  - Refer to B-Cell CD20 Expression (0092099)

Related tests

Lymphocyte Subset Panel 6 – Total Lymphocyte Enumeration with CD45RA and CD45RO 0095862

- Useful for assessing primary T-cell immunodeficiency disorders
- T-cell and B-cell immunodeficiency testing profile includes
  - CD4
  - CD45RO
  - CD4:CD8 ratio
  - CD19
  - CD45RA
  - CD8
  - CD3
  - NK cells

Streptococcus pneumoniae Antibodies, IgG (14 serotypes) 0050725

- Evaluate the ability of a patient to produce antibody to pure polysaccharide vaccines (Pneumovax) or protein conjugated vaccines (Prevnar)

Diphtheria & Tetanus Antibodies, IgG 0050595

- Evaluate the ability of a patient to produce antibody to pure protein vaccines after vaccination to rule out antibody deficiency

TACI-Associated Common Variable Immunodeficiency *(TNFRSF13B)* Sequencing 2007569

- Use to identify *TNFRSF13B* variants in individuals with clinical phenotype for common variable immunodeficiency

Disease Overview

Prevalence of CVID

- 1/25,000-60,000 Caucasians
- 1/100,000 Japanese

Age of onset – bimodal peaks (childhood, 10-29 years)

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Symptoms

- Hypogammaglobulinemia with impaired ability to produce antibodies after vaccination
- Recurrent respiratory tract infections
- Intermittent or chronic diarrhea
- Splenomegaly
- Lymphadenopathy
- Nodular lymphoid hyperplasia of small bowel
- Autoimmune symptoms are common
  - Autoimmune cytopenias
    - Hemolytic anemia
    - Thrombocytopenia
  - Rheumatoid arthritis
  - Vitiligo
  - Alopecia
  - Granulomatous disease
- Associated with increased risk of lymphoid and nonlymphoid malignancies

Physiology

- Most individuals with CVID have normal number of peripheral blood B cells
  - B cells appear immature
  - Reduced number of memory B cells
    - Identified by surface marker CD27
- Low serum immunoglobulins associated with reduction of class-switched memory B cells (CD19+ CD27+ IgD- IgM-)
- Most individuals with high risk for splenomegaly and granulomatous disease show
  - Marked reduction of class-switched memory B cells

Genetics

Genes – *BAFF, CD19, CD20, CD21, CD81, ICOS, TNFRSF13B*

Inheritance – autosomal recessive

Variants – affect B-cell function

Test Interpretation

B-cell phenotyping can help with

- Disease classification
- Prediction of complications

Results

- Positive – after bone marrow transplantation, functionally immature naïve B cells and decreased memory B cells indicate delayed recovery of functional B cells and an immunodeficient state
- Abnormal – in memory B cells and/or class-switched memory B cells
  - Indicates the need for further correlation with clinical presentation and other immunological and genetic laboratory testing to confirm CVID
  - Nearly absent B cells (< 1%) represents severe defect of early B-cell differentiation
  - Severely reduced number of switched memory B cells
    - Indicates defect in germinal center development
    - Found in inducible costimulator (ICOS) or CD40L deficiency