Immune Deficiencies Related to B Cells

Our immune system normally fights off things that are foreign (e.g., viruses, bacteria, fungi, etc.). **Immune deficiencies** (or immunodeficiencies) happen when the immune system is weakened. The patient may have **too many infections**, infections that are **difficult to cure**, **unusually severe** infections, or infections with **unusual organisms**.

B cells are responsible for antibody-mediated immunity. When there aren't enough B cells, or when there are problems with antibody production, the body's immune system cannot fight invaders as efficiently. Typical signs of B cell-related immune deficiencies are recurrent or severe infections.

In individuals with **hypogammaglobulinemia**, the IgG level is low. In those with **panhypogammaglobulinemia**, the levels of all the types of antibodies are low.

B cells levels and functions are typically normal in individuals with 22q11.2 deletion syndrome (22q11.2DS) and 22q11.2 duplication syndromes (22q11.2DupS), but a small number of people have deficiencies.

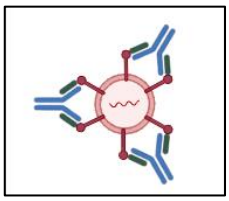
Methods for detecting B Cell Deficiencies

- Measure antibody levels in the blood and compare the results to **aged-matched** controls.
- Measure the function of antibodies (e.g. responses after vaccines)
- Check B cells counts and development using flow cytometry.

Visit the Laboratory Tests page from the Immune Deficiency Foundation to learn more.

Antibodies

- Also called **immunoglobulins (Ig)**.
- Immunoglobulins are mostly made by plasma cells (mature B cells) in the bone marrow.
- The human immune system can make antibodies that can bind to many types of bacteria and viruses. When an invader is "labelled" with antibodies, other immune cells work together to get rid of it. See figure on the right.
- Rarely, antibodies are made to wrongly target parts of our own bodies, leading to autoimmune disorders.



Antibodies binding to a virus.
Image created in https://BioRender.com

- Antibodies are classified based on chemical structure into IgA, IgD, IgE, IgG, and IgM.
  - IgG is the most common and most important in the fight against invading pathogens. It is our immune memory.
- Visit the Antibodies page from the Cleveland Clinic to learn more.

Antibody Deficiencies and 22q11.2DS

- A minority of children and adults with 22q11.2DS have:
  - A gradual loss of antibody function
  - A decrease in antibody levels
  - Frequent and long infections of the upper and lower respiratory tract
- Antibody deficiencies may be caused by the inability of T cells to activate B cells, but missing a copy of the *TBX1* gene may also play a role.
- The antibody dysfunction can arise at any age.

Antibody Deficiencies and 22q11.2DupS

- A minority of children and adults with 22q11.2DupS have:
  - Low levels of one or more types of antibodies
  - Low level of memory B cells
  - Rapidly decreased protection from vaccines compared to expected levels.
  - Frequent infections in many body systems
- Antibody deficiencies may be due to the extra dosage of the *TBX1* gene, but research is still ongoing
- Antibody deficiencies are more common than T cell deficiencies

Immune Deficiencies Related to B Cells (continued)

Treatment Options

Antibiotics

- Used to treat infections by bacteria (but not viruses) in people with and without immune deficiencies
- Also used to prevent or reduce bacterial infections in people with immune deficiencies
  - Breaks the cycle of repeated infections and tissue damage; also slows down infections to give patient time to seek medical help before an infection becomes life threatening
- Patients should take the full course of antibiotics to avoid the growth of antibiotic-resistant bacteria
- See the Antibiotics and immunodeficiency page from Immunodeficiency UK for more info

Immunoglobulin Replacement Therapy

- Individuals whose antibodies are deficient or do not work well may be eligible for immunoglobulin replacement therapy.
- IVIG involves injecting antibodies (Ig) intravenously (into the vein), and SubQ Ig or SCIg involves giving the antibodies subcutaneously (under the skin) to defend against infections.
- These products use antibodies that were extracted from blood donated by other people and highly purified.
- Injected antibodies only last about 1 to 4 weeks
  - Supplies the antibodies but does not fix the cause of the deficiency
  - Patient needs to receive injections regularly
- Benefits:
  - Can significantly improve the patient's quality of life
  - Decreases the frequency of infections
  - Even if a patient needs antibiotics, he/she may need them for a shorter time
- Visit the Immunoglobulin replacement therapy page on the website of the Immune Deficiency Foundation for more info, including manufacturing safety, tests required, and potential side effects

Antibiotics or Immunoglobulin Replacement Therapy?

Each treatment method has benefits and risks. Please discuss your situation with your healthcare provider.

IVIG or SCIg?

SCIG is done at a lower dosage more frequently, so the Ig levels in the blood does not fluctuate as much. It can also be done at home if the patient or caregiver can manage.

IVIG requires less frequent injection and only 1 infusion site, but must be given by a healthcare provider.

Recommendations

- Immunologic assessments: B cell counts, antibody levels, vaccine responses
- Patients with unusual infections should be referred to an immunologist
- Vaccines are at least partly effective for most people with antibody disorders

Resources

Immune Deficiency (not specifically 22q differences)

- Immune Deficiency Foundation: Decoding antibody deficiency diagnoses | Laboratory Tests | Immunoglobulin replacement therapy
- Immunodeficiency UK: Antibiotics and immunodeficiency

Immune Deficiency + 22q11.2 deletion or duplication syndrome

- The immune deficiency of chromosome 22q11.2 deletion syndrome – 2017
- Variable immune deficiency related to deletion size in chromosome 22q11.2 deletion syndrome – 2018
- Immunodeficiency in 22q11.2 duplication syndrome – 2021
- Immunologic, Molecular, and Clinical Profile of Patients with Chromosome 22q11.2 Duplications – 2023
- Updated clinical practice recommendations for managing [**children** | **adults**] with 22q11.2 deletion syndrome – 2023

Joanne C. Y. Loo, PhD and Kathleen Sullivan, MD, PhD; 12/2024