

# Management of Primary Antibody Deficiency with Replacement Therapy: Summary of Guidelines

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## KEYWORDS

- Primary antibody deficiency • IgG replacement
- Intravenous immunoglobulin

In managing primary antibody deficiency with replacement therapy, the following guidelines should be observed:

1. All patients should be referred to an immunologist for diagnosis and initiation of treatment. Long-term management can be shared with family physicians and pediatricians.
2. The following investigations should be performed as appropriate in individual cases:
  - Blood cell count and differential
  - Serum immunoglobulins
  - Antibody titers to immunizations with protein antigens, as well as polysaccharide antigens, (at age greater than 24 months)
  - Polymerase chain reaction assay for HIV and other chronic viral infections (hepatitis B and C)
  - Lymphocyte surface marker analysis
  - Lymphocyte function tests such as mitogen and antigen proliferation
  - Liver and renal function tests
  - Assessment of end-organ damage may be required including Lung function

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CT scans of lung and sinuses

Gastrointestinal endoscopy

Bone marrow and/or liver biopsy

Detailed mutation and additional molecular analyses of the immunologic defect should be considered when appropriate.

3. Patients who have significant antibody deficiency require doses of intravenous immunoglobulin (IVIG) between 0.4 and 0.8 g/kg every 3 to 4 weeks (or the equivalent given in divided doses once or twice a week subcutaneously) to achieve trough IgG serum levels of at least 5 g/L (ideally, 6.5–10 g/L). If IgG half-life is shorter than 3 weeks and/or if treatment effects are not satisfactory, the frequency of infusions may be increased to every 2 weeks and/or the dose may be increased.
4. In patients who have significant antibody deficiency, IgG replacement should be given regularly and should not be interrupted. IVIG should not be given intermittently because effective serum IgG trough levels may drop to nonprotective levels on cessation of treatment.
5. The first three infusions ideally should be given in a qualified center for monitoring of severe adverse reactions. Subsequent infusions can be administered by family physicians in community hospitals or at home by homecare nurses.
6. After replacement therapy has been established, pretreatment serum IgG trough levels should be obtained monthly and should be followed by an immunology specialist at least every 6 months to monitor treatment effectiveness and complications. Individual patients may require more frequent visits with the immunologist and/or other specialists.
7. If a patient experiences severe adverse reactions to a licensed IVIG product, a different brand of IVIG or subcutaneous IgG should be tried. If adverse reactions persist, premedication with corticosteroids, antihistamines, and/or antipyretics frequently is effective. Slowing the infusion rate should alleviate minor reactions. If it has been established that a patient tolerates only certain brands, the brand of IgG given to that patient should not be changed without obtaining permission from the responsible immunologist.
8. Subcutaneous IgG should be offered as substitute for IVIG for patients who have poor intravenous access. Because subcutaneous immunoglobulin can be self-administered safely at home, it has been offered as an alternative for selected patients.
9. Patients who have developed chronic lung disease (bronchiectasis) should receive special attention. The minimal monitoring regimen is yearly assessment including a pulmonary function test and biannual CT scans. Aggressive antibiotic treatment is needed during acute exacerbations of lung disease. Prolonged or continuous antibiotic treatment may be helpful in chronically infected patients, and these patients often need adjuvant therapies such as physiotherapy, bronchodilators/inhaled corticosteroids, and percussion devices to promote pulmonary toilet. If bronchiectasis is localized and cannot be controlled adequately with IVIG and antibiotics, a lobectomy should be considered.
10. Indications for IgG replacement include common variable immunodeficiency, X-linked agammaglobulinemia, autosomal-recessive agammaglobulinemia, hyper-IgM syndromes, dysgammaglobulinemia, or antibody deficiencies associated with syndromes such as Wiskott Aldrich syndrome, ataxia telangiectasia, and others.

It is recommended that analysis and interpretation be performed by immunologists in immunology service laboratories who have the experience, knowledge, and skill to perform DNA sequencing, protein immunoblotting, and, ideally, analysis of the functional pathway of the target gene.