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: CBC and differential, serum immunoglobulins, antibody titres to immunizations with protein antigens, as well as polysaccharide antigens, (at >24 months of age), PCR 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, 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 with significant antibody deficiency require doses of IVIG between 0.4-0.8 g/kg every 3 to 4 weeks (or the equivalent given in divided doses once or twice a week subcutaneously) in order 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 two weeks, and/or the dose may be increased.
4. In patients with 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 unprotective levels upon cessation of treatment.

5. The first 3 infusions should be ideally given in a qualified centre 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 pre-treatment serum IgG trough levels should be obtained monthly and follow up with Immunology specialist should be at least every 6 months to monitor treatment effectiveness and complications. More frequent visits with the Immunologist and/or other specialists may be necessary in individual patients.
7. In the case that patients experience severe adverse reactions to a licenced IVIG product, a different brand of IVIG or subcutaneous IgG should be tried. If adverse reactions persist, premedications with corticosteroids, anti-histamines and/or anti-pyretics is frequently effective. Slowing down infusion rate should alleviate minor reactions. If it has been established that certain patients only tolerate 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 in patients who have poor IV access. Because subcutaneous Ig can be safely self-administered 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. Yearly assessment including pulmonary function test and a bi-annual CT scans are recommended as a minimal monitoring regimen. Aggressive antibiotic treatment is needed during acute exacerbations of lung disease. Prolonged or continuous antibiotic treatment may be helpful in chronically infected patients, and adjuvant therapies such as

physiotherapy, bronchodilators/inhaled corticosteroids, and percussion devices to promote pulmonary toilet are often needed in such patients . If bronchiectasis is localized and cannot be adequately controlled with IVIG and antibiotics, a lobectomy should be considered.

10. Indications for IgG replacement include: CVID, XLA, autosomal-recessive agammaglobulinemia, hyper-IgM syndromes, dysgammaglobulinemia, or antibody deficiencies associated with syndromes such as Wiskott Aldrich Syndrome, Ataxia telangiectasia and others.

† In Canada it is recommended that analysis and interpretation will 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).

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