

## IgG SUBCLASSES – GUIDELINES FOR INVESTIGATION

There are 4 subclasses of IgG. IgG1 and IgG3 mature earliest (in the first few years of life) and are important in responses to protein antigens e.g. tetanus. IgG2 and IgG4 mature much more slowly and are important in defending against carbohydrate antigens e.g. pneumococcus and Hib.

In adults with low total IgG concentrations, secondary immune deficiency must be considered (secondary to protein loss via kidneys, gut or skin, malignancy, malnutrition, chemotherapy, radiotherapy etc.) It is also vital to check serum and urine for monoclonal proteins.

### Situations where measurement of IgG subclasses may be useful

- Total IgG should be in the normal range for age.
- The major clinical indication for measuring IgG subclasses is the occurrence of abnormally frequent and/or prolonged or severe infections that cannot be explained by the usual clinical and laboratory data, especially in patients in whom the possibility of IgG treatment is considered.
- Children with symptoms that could be associated with isolated IgG subclass deficiency. These are recurrent infection with pneumococcus, Hib or meningococcus with normal or low normal total IgG concentration; bronchiectasis and severe, recurrent stages of otitis media, sinusitis, pneumonia and bronchitis. The possibility of an IgG subclass deficiency should be considered in all children with recurrent infections and chronic obstructive bronchitis. However, it should be kept in mind that IgG subclass deficiencies in children may be transient. The levels of IgG2 increase relatively late in childhood. Thus, when low IgG2 levels are found in children below the age of 2-3 years, it is advisable to monitor this level in the course of time, since it may be due to a temporary maturation block.
- Suspected specific antibodies deficiencies – pre and post vaccination may be a more appropriate way of investigating these patients
- IgG4 related disease (IgG4-RD) is an immune-mediated fibroinflammatory condition characterized histopathologically by three hallmark features in involved tissue: obliterative phlebitis, storiform fibrosis, and a dense lymphoplasmacytic infiltrate. IgG4-RD can affect any organ with common presentations including Riedel's thyroiditis, autoimmune pancreatitis, sclerosing cholangitis, sialadenitis, dacryoadenitis, periaortitis, an eosinophilic rash, and pseudotumor of the lung, lymph nodes, or orbits. However, serum IgG4 quantification lacks sensitivity for IgG4-RD and is most useful as a predictor of relapse in patients who have been treated for IgG4-RD.

### Situations where measurement of IgG subclasses is not indicated

- Patients with polyclonally raised IgG e.g. patients with HIV, persistent infections, liver disease, autoimmune diseases.
- Patients on immunoglobulin replacement
- Asymptomatic patients with low total IgG concentrations will have low IgG subclass concentrations therefore measurement of IgG subclasses in patients with low total IgG concentrations not indicated.