Reference for Management of low Immunoglobulin levels in Adults

What are Immunoglobulins?

Immunoglobulins are proteins made by B cells and Plasma cells that help protect against infection.
The standard immunoglobulin profile consists of Immunoglobulins IgG, A and M.
In Sheffield Immunology laboratory we routinely perform serum electrophoresis on all Immunoglobulin requests. Serum electrophoresis may identify evidence of monoclonal Immunoglobulin (overproduction of a single immunoglobulin by one specific plasma call population). This is known as a monoclone or paraprotein and can be seen in conditions such as Monoclonal Gammopathy of Undetermined Significance (MGUS) or Myeloma

STEP 1: Request and review serum/urine electrophoresis

Is there a monoclone in the serum or urine?

yes → **See Haematology paraprotein guidelines**

no

STEP 2 : History of **S**evere, **P**ersistent, **U**nusual, or **R**ecurrent (**SPUR**) infections

yes

Could other conditions be contributing to infections i.e. structural lung disease /asthma?

If infections persist / not possible to treat underlying cause for infections:
If IgG 4-6g/L consider discussing with Immunology StR prior to referral.
If IgG is <4g/L refer to Immunology clinic
Isolated recurrent urinary infections (UTIs) are not usually associated with immune deficiency. Do not refer to the Immunology clinic.

STEP 3: Which Immunoglobulin is low?

Low IgG (+/- low IgA and/or low IgM)

CONSIDER SECONDARY CAUSES

- Lymphoproliferative disease
- Protein loss:
  - *Check urine dipstick*
  - *Does the patient have chronic diarrhoea?*
- Iatrogenic Drug related (Box 1)
  - Immunosuppressants
  - Antipsychotics
  - Antiepileptics

Isolated low IgM

Isolated low IgM unlikely to be significant.

CONSIDER SECONDARY CAUSES

- Advancing age even in the absence of underlying pathology.
- Very rarely lymphoproliferative disease.*
- Uraemia
- Immunosuppressive drug therapy

Isolated low IgA

A. Review for features of autoimmunity / coeliac disease. Manage according to relevant guidelines
B. Provide patient with IDUK information leaflet for IgA deficiency
Immunodeficiency UK - Selective IgA deficiency

Secondary Cause Found

- Correction of secondary cause
- If B-type symptoms or lymphadenopathy/ clinically palpable splenomegaly - liaise with Haematology
- If it cannot be corrected follow →

NO Secondary Cause Found

- For borderline low IgG (4-6g/L) or low IgM where there is no clear secondary cause and no history of severe, persistent, unusual, or recurrent (SPUR) infection:
  It is likely that these are incidental findings.
  Recommend monitor serum Immunoglobulins and urine electrophoresis annually
- If IgG <4g/L **or** SPUR infections or panhypogammaglobulinemia - refer to Immunology

Box1: Drugs that can cause Low IgG		
Immunosuppressants	Antipsychotics	Antiepileptics
Abatacept Azathioprine Cyclophosphamide (Other alkylating agents) Gold D-Penicillamine Methotrexate Mycophenolate Prednisolone Rituximab (other B cell depleting treatment) Imatinib Sulphasalzine	Chlorpromazine Clozapine	Carbamazepine Lamotrigine Phenytoin Sodium Valproate

Sources of further information:

1. IDUK Website: Information on immune deficiencieshttp://www.immunodeficiencyuk.org/
2. Sheffield Protein Reference unit website: https://www.immqas.org.uk/TestItem.asp?id=487 – Information regarding sample requirements, reference ranges and interpretation of Immunoglobulin results

This pathway was created by:
Dr S Denness Consultant Immunologist CIAU Northern General Hospital Sheffield Teaching Hospitals

Draft amendments Dr.Sabiha Atcha GP/ BEST website lead Barnsley
July 2025