1. Introduction and Scope

Investigation of a possible deficiency includes assessment of the humoral immune system. The function of the humoral immune system can be assessed by measuring the antibody response generated by an antigen challenge. Bacterial antigens are predominantly either proteins or complex polysaccharides; thus, assessing a vaccination response to either protein or polysaccharide antigen can help evaluate antibody function.

A response to a polysaccharide vaccination requires functional B cells only. Vaccines used include the pneumococcal polysaccharide vaccine and the salmonella typhi Vi vaccine. A response to a protein vaccination requires both B and T cell function and an impaired response indicates that one or both may be abnormal. Vaccines used include tetanus and Hib.

The guideline applies to all members of the immunology team involved in the investigation and management of adult patients with antibody deficiency. It may be used as guidance for other medical and nursing staff involved in the care of these patients in conjunction with the input of specialist immunologists. For paediatric vaccination responses please refer to the guideline 'Investigating suspected primary immunodeficiency prior to immunology referral' on INsite.

Interpretation and application of clinical guidelines remains at the discretion of the individual practitioner depending on the clinical scenario.

2. Guideline Standards and Procedures

2.1 Patients who may have a vaccine response assessed

- Patients who are being assessed for a possible primary or secondary immune deficiency and are experiencing recurrent infections
- Patients with secondary immune deficiencies who may have recovered and are being reassessed

2.2 Requirements prior to vaccine administration

- Appropriate medical treatment, equipment and staff should be readily available for immediate intervention in case of an anaphylactic reaction following vaccination
- The medical doctor must prescribe the vaccine on the outpatient prescription sheet
- Staff administering the vaccination must have documented competency to do so and should follow local policies regarding vaccine administration
- Patients must be assessed by staff administering the vaccination prior tot giving the vaccine by enquiring the following:
- Allergies and any previous reactions to vaccination. Any concerns should be raised with the prescriber
- Their health on the day of the proposed vaccination. The vaccination may need to be postponed if the patient is experiencing a febrile illness

2.3 Assessing a vaccine response to polysaccharide antigens using pneumococcal polysaccharide vaccination (Pneumovax II)

Pneumococcal polysaccharide vaccination is available as the Pneumovax II vaccine which is manufactured by Merck & Co. Inc. It contains 23 pneumococcal serotypes.

A pre-vaccination pneumococcal antibody level must be taken either prior to the vaccination or on the day of the vaccination. **A vaccine response cannot be assessed without this.** At present serotype specific pneumococcal antibodies are available in the Trust which assesses 13 of the 23 serotypes contained within the Pneumovax II vaccine

A dose of 0.5ml is given intramuscularly. The recommended injection site is the deltoid region. The patient should be observed for 10 minutes after the vaccination

The patient should be given an immunology form to have post vaccination pneumococcal serotype specific antibodies taken 4 weeks after the vaccination. Ideally both pre and post vaccination pneumococcal antibody samples should be performed by the same laboratory to reduce variation

The response is assessed as follows:

- Adequate response – 9/13 serotypes achieve a two fold response as well as a titre above 0.35
- Suboptimal response – Between 8 – 3/13 serotypes achieve a two fold response as well as a titre above 0.35. This may be termed mild – moderate specific antibody deficiency
- Deficient response – 2/13 or fewer serotypes achieve a two fold response as well as a titre above 0.35. This may be termed definite specific antibody response

There are no internationally agreed guidelines with regard to an adequate response to pneumococcal polysaccharide vaccination and the above are guidelines used within the Immunology department in University Hospitals of Leicester NHS Trust.

Prevnar

Please note that vaccination with the conjugated pneumococcal vaccine (Prevnar 13) will affect these results as serotypes overlap. Prevnar is a conjugated vaccination and cannot be used to assess a polysaccharide vaccine response, although it can be used to provide some protection for patients who do not respond well to Pneumovax.

Revaccination

Re-vaccination may be considered for persons at increased risk of serious pneumococcal infection who were given pneumococcal vaccine more than five years earlier or for those known to have a rapid decline in pneumococcal antibody levels. For selected populations (e.g. asplenics) who are known to be at high risk of fatal pneumococcal infections, re-vaccination at three years may be considered

2.4 Assessing a vaccine response to polysaccharide antigen using Salmonella typhi Vi vaccine

Salmonella typhi Vi polysaccharide vaccination is available as the Typhim Vi vaccine which is manufactured by Sanofi pasteur. It contains purified Vi capsular polysaccharide of Salnonella typhi

A pre-vaccination salmonella typhi Vi antibody level must be taken either prior to the vaccination or on the day of the vaccination. **A vaccine response cannot be assessed without this**

A dose of 0.5ml is given intramuscularly. The recommended injection site is the deltoid region. The patient should be observed for 10 minutes after the vaccination

The patient should be given an immunology form to have post vaccination salmonella typhi Vi antibodies taken 4 weeks after the vaccination

The response is assessed as follows:

- Adequate response – A 3 fold response which also achieves a titre of >5.1 U/ml. Of note vaccine naïve patients are expected to have a titre <50 U/ml

There are no internationally agreed guidelines with regard to an adequate response to salmonella typhi Vi polysaccharide vaccination and the above are recommendations from the Immunology department in University Hospitals Birmingham NHS Trust

2.5 Assessing a vaccine response to protein antigens using tetanus vaccination

Tetanus vaccination is available in the combined vaccine, Revaxis (diptherria/tetanus/inactivated polio vaccine (Td/IPV) which is manufactured by Sanofi Pasteur

A pre-vaccination tetanus antibody level must be taken prior to vaccination. If this level is above the protective level of 0.15 IU/mL there is no indication for vaccination

A dose of 0.5ml is given intramuscularly. The recommended injection site is the deltoid region. The patient should be observed for 10 minutes after the vaccination. The patient should be given an immunology from to have post vaccination tetanus antibodies taken 4 weeks after the vaccination.

An adequate response is achieved if post vaccination titres are above the optimal protective level of 0.15 IU/mL

2.6 Assessing a vaccine response to protein antigens using Hib vaccine

Hib vaccination is available in the combined Hib/Men C vaccine. Menitorix which is manufactured by GlaxoSmithKline. This is a conjugated vaccine with tetanus toxoid as the carrier protein. Responses to this conjugate vaccine can be used to assess responses to protein antigens because the vaccine induces antibodies to the protein component of the conjugate

A pre-vaccination Hib antibody level must be taken prior to vaccination. If this level is above the optimal protective level of 1.00 IU/mL, there is no indication for vaccination

A dose of 0.5ml is given intramuscularly. The recommended injection site is the deltoid region. The patient should be observed for 10 minutes after the vaccination

The patient should be given an immunology form to have post vaccination Hib antibodies taken 4 weeks after the vaccination

An adequate response is achieved if post vaccination titres are above the optimal protective level of 1.00 IU/mL

2.7 Recommendations / cautions

Vaccine responses can be affected by the following:

- Older age
- Concurrent medications e.g. high doses of steroids or prolonged use of steroids, immunosuppressants, chemotherapy
- Usually vaccine responses are not assessed until a ptietn has been off of immunoglobulin replacement therapy for 4 months as antibodies within the product may interfere with testing. However there are negligible amounts of antibody to salmonella within the product and a response to salmonella typhi Vi vaccination can be assessed while on immunoglobulin

Undesirable effects of vaccination

- Local injection site reactions
- Headache, nausea
- Myalgia

- Allergic type reactions including urticarial and rash
- Anaphylaxis (very rare)

Pregnancy

- Vaccinations should not be given to pregnant women

3. Education

Staff administering the vaccination must have documented competency to do so and should follow local policies regarding vaccine administration

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting Arrangements
Review of the patients being considered for Immunoglobulin replacement to ensure correct vaccine response assessment	Patients records reviewed at Immunology MDT	Dr Shanti Mahabir	Monthly	Immunology MDT

5. Supporting References

1. Orange JS et al, Use and interpretation of diagnostic vaccination in primary immunodeficiency: a working group report of the Basic and Clinical Immunology Interest Section of the American Academy of Allergy, Asthma and Immunology JAC 2013:130:s1
2. Sorensen, R and Paris, K. Assessing antibody function as part of an immunologic evaluation. Feldweg, A,Ed. UpToDate. Waltham, MA: UpToDate Inc. https://uptodate.com Accessed 05/06/2019
3. Summary of Product Characteristics: Menitorix, GlaxoSmithKline UK, Feb 2016. Accessed via www.medicines.org.uk on 05/06/2019

6. Key Words

Vaccination, Immune deficiency

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Details of Changes made during review: **New Guideline**	