

# Immunisations in Immunocompromised Patients and Close Household Contacts UHL Immunology Guideline

University Hospitals of Leicester 

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## 1. **Introduction**

### 1.1. **Background**

Immunosuppressed patients are in high risk for infection due to their diagnosis and also due to increased exposure to high risk environments (eg hospital). They can also be in risk if in contact with immune-competent individuals receiving live vaccinations, due to potential shedding of the live pathogens. On the other hand, appropriate immunisation of close contacts offers extra protection for the immunocompromised patient. Ensuring the immunosuppressed patient and their close contacts are fully and appropriately immunised, is the responsibility for any health care professional involved in their care. However decisions are complex and often need to be made on a case by case basis, guided by the Immunology Team.

### 1.2. **Who Guideline Applies to**

The scope of this document is to assist the Clinical staff of the Immunology Department working in the University Hospital of Leicester (UHL) NHS Trusts in decision making on Immunisation of the Immunocompromised patient and help with providing advice to patients and other health care professionals involved in their care. The guidance can be used for adult and paediatric patients.

The two main questions to be answered in making decisions on vaccinations for immunocompromised patients and/or their families, is regarding the safety and vaccine effectiveness mainly for any immunosuppressed patient.

This document does not cover immunisation recommendations for the immunocompetent individuals and this information can easily be accessed elsewhere ( green book from public health England, <https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book> )

### 1.3. **Definitions**

The term 'household contact' refers to individuals living in the same household with the immunosuppressed patient and who have direct contact with the immunocompromised person. That would include people living together in residential and nursing care homes. Immunisation of the personnel working at care homes is beyond the scope of this guideline.

(see Public Health Guidance for immunisations in healthcare staff [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/147882/Green-Book-Chapter-12.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/147882/Green-Book-Chapter-12.pdf) )

### 1.4 **Abbreviations**

PID: Primary Immunodeficiency	ISP: immunosuppressive
SID: Secondary Immunodeficiency	LAIV: live attenuated influenza virus
CVID: Common Variable Immune Deficiency	OPV: oral polio vaccine

slgAD: selective IgA deficiency	YF: yellow fever
SCID: Severe Combined Immunodeficiency	PCV: pneumococcal conjugated vaccine
WAS: Wiskott-Aldrich Syndrome	PPSV: pneumococcal polysaccharide vaccine
AT: Ataxia Telangiectasia	BCG: Bacillus Calmette-Guerin
CGD: Chronic Granulomatous Disease	MMR: Measles Mumps Rubella
LAD: Leukocyte adhesion deficiency	VZV: Varicella Zoster vaccine
MBL: Mannose Binding Lectin	MenACW135Y: Meningococcal groups A, C, W, Y MenB: Meningococcal B vaccine
MAC: Membrane Attack Complex	QIV: Quadrivalent Inactivated Influenza vaccine
IRT: Immunoglobulin Replacement Therapy	Hib: Haemophilus influenzae type b

## 2. **Guideline and Standards and Procedures**

### 2.1. **Decision making for Vaccinations in the Immunosuppressed individual**

#### 2.1.1. Consideration of **vaccinations prior to planned Immunosuppression** (eg initiation of medication) when feasible:

- Inactivated vaccines should be given at least two weeks in advance.
- Live vaccines should preferably be given four weeks in advance.
- Live vaccines should be avoided in the two weeks before immunosuppression is commenced.

#### 2.1.2. Decisions on **vaccinations for the already immunosuppressed** individuals, should be based on:

- Patient- specific factors: age, underlying diagnosis affecting the severity of immunodeficiency (PID, SID), general condition and comorbidities, medication (duration and dose).
- Vaccine- specific factors: degree of attenuation, immunogenicity, primary immunisation or booster.

In live vaccines, the balance between attenuation and immunogenicity is determined for healthy population and does not apply to the immunocompromised patients. All live vaccines, viral and bacterial are contraindicated in the severely immunodeficient patient.

In less severe immunosuppression decision should be made in a case by case basis.

## 2.2. Primary Immunodeficiency

**Table 1. Vaccination recommendations in PID**

Catergory	Examples of disease	Vaccine indication	Effectiveness of vaccines	Especially recommended
<b>Humoral deficiency</b>	Severe antibody deficiencies (eg CVID, Hypogammaglobulinaemia on IRT)  <i>*Severity of immunodeficiency in CVID varies. If evidence of adequate cellular immunity, live vaccines can be carefully considered.</i>	OPV, LAIV, YF, live bacterial (eg typhoid, BCG) No data for rotavirus or VZV  (CVID: very little evidence of viral vaccine-related infections)	Uncertain efficacy especially if on IRT (known to interfere with measles and possibly varicella immunization)  XLA: immunization is not contraindicated but it is unlikely to be effective.	QIV  PCV &/or PPSV23  Conjugated Hib
	Less severe antibody deficiencies (eg sIgAD, IgG subclass deficiency)	OPV, YF, BCG Other live vaccines appear to be safe	All probably effective, responses maybe attenuated	LAIV/ QIV in age appropriate patients  PCV &/or PPSV23  Conjugated Hib
<b>T cell and combined</b>	Severe (eg SCID, athymic DiGeorge, CHARGE syndrome)  SCID post HSCT with incomplete reconstitution or under ISP drugs	All live vaccines, viral and bacterial	All vaccines probably ineffective	Inactivated influenza  PCV &/or PPSV23  Conj. Hib
	Incomplete Di George, Combined Immunodeficiency WAS, AT	All live vaccines need careful consideration  Inadvertent MMR vaccination - no clinical infection  No data for rotavirus	MMR and VZV considered in adults if CD4 > 0.5x10 <sup>9</sup> /L  MMR, LAIV (if over 2 years) should be given in children if CD4 > 0.3x10 <sup>9</sup> /L	QIV for adults  PCV & /or PPSV23  Conjug.Hib
<b>Complement</b>	Properdin deficiency MAC deficiency MBL deficiency	None	All routine vaccines probably effective	PCV &/or PPSV23  Conjugated Hib  MenB MenACW135 Y

**Table 1 continued**

Category	Examples of disease	Vaccine contra-indication	Effectiveness of vaccines	Especially recommended
<b>Phagocytic defects</b>	CGD LAD Myeloperoxidase deficiency	Live bacterial vaccines (eg BCG)  LAIV	All inactivated bacterial safe and probably effective  Live virus probably safe and effective	As per routine apart from live bacterial vaccines
<b>IFN-γ-IL-12 pathway</b>		Live bacterial vaccines (eg BCG)	Sparse data on other live vaccines  No reported infection after live attenuated viral vaccines but with caution	
<b>Functional or anatomical asplenia</b>		None		PCV &/or PPSV23  Conjugated Hib  MenB MenACW135Y

## 2.3. Secondary Immunodeficiency

Vaccination contraindications depend on the level of Immunosuppression.

### 2.3.1. Levels of Immunosuppression

High level Immunosuppression:

- Currently on chemotherapy or radiotherapy, or such treatment within the previous six months
- Solid organ transplant within the previous two months
- On transplant- related immunosuppressants (eg Cyclosporine, Tacrolimus, Sirolimus, Mycophenolate mofetil)
- After HSCT (duration dependent on the type of transplant- longer for allogenic than for autologous, the presence of complications such as GVHD- until at least 24 months post-transplant and at least 12 months off all immunosuppressive treatment or longer where the patient has developed graft-versus-host disease.)
- HIV infection and CD4  $<0.2 \times 10^9$  /L in adults. HIV infection and CD4  $<15\%$  for infants and young children, in terms of absolute counts, CDC indicators of severe

immunosuppression are:      <12 months, CD4 count < 0.75 x10<sup>9</sup>/L,  
1-5 years CD4 count < 0.5 x 10<sup>9</sup>/L,  
6 years and above, CD4 count <0.2 x10<sup>9</sup>/L

- f) High dose daily corticosteroids and within three months after stopping treatment:
  - ✓ Adults receiving dose equivalent or greater than 40 mg of prednisolone for over a week, or 20 mg of prednisolone for over two weeks
  - ✓ Children receiving dose equivalent or greater than 2 mg/kg/day of prednisolone for at least one week, or 1 mg/kg/day for one month
- g) Currently on DMARDs (eg Azathioprine, cyclosporine, methotrexate, cyclophosphamide, leflunomide ) alone or in combination with lower doses of steroids and within 6 months after stopping treatment.
- h) Currently on biologics (such as anti-TNF, anti CD-20) and within 12 months of stopping treatment. Immunisation with live vaccine should also be delayed for 6 months, for babies born to mother who were receiving immunosuppressive biological therapy during pregnancy.

#### Mild/ Moderate Immunosuppression

- a) HIV infection: asymptomatic patients with CD4 cells 0.2 - 0.499 x10<sup>9</sup>/L (children 15-25%)
- b) Corticosteroid therapy :
  - ✓ Prednisolone >20 mg/day but duration less than 2 weeks (live vaccines to be given at least 2 weeks after the end of treatment)
  - ✓ Prednisolone <20 mg /day , for longer than 2 weeks
  - ✓ Depot cortisone regimes (depending on dose)
- c) Low dose immunosuppressants eg:
  - ✓ MTX <0.4 mg/kg/week
  - ✓ Azathioprine <3mg/ kg/day
  - ✓ Mercaptopurine <1.5 mg/kg/day
- d) Anatomical or functional asplenia
- e) Chronic Kidney disease
- f) Chronic Liver disease
- g) MS without treatment

h) Diabetes melitus (advanced disease, poor control)

#### Low level/ not clinically relevant immunosuppression

a. Corticosteroids :

- ✓ Short term (<2 weeks) low dose (<20 mg/day) of prednisolone (in children <0.5 mg/kg per day)
- ✓ Topical, Inhaled, intra-articular corticosteroids, physiological replacement dose

b. HIV infection : CD4 Tcells  $0.5 \times 10^9/L$  and above (children over 15%)

c. Tumour patient: in remission, last chemotherapy over 3 months ago (solid tumours), stable post SCT (individual assessment).

d. Autoimmune diseases not on immunosuppressive or immunomodulatory therapy

e. Diabetes melitus (type 1 and 2) well controlled.

#### **2.3.2. Vaccination recommendations in SID according to immunosuppression level**

##### **In patients with Low level immunosuppression:**

Inactivated vaccines are safe to be administered.

Live vaccines are considered in a case by case basis weighing risk and benefit . In HIV patients with CD4 T cells over  $0.5 \times 10^9/L$ , VZV and MMR should be considered as the disease maybe more severe. In children with HIV that are not severely immunosuppressed the UK vaccination schedule should be followed, including recommendations for MMR, VZV and LAIV.

In patients with chronic hepatitis B or C, HepA vaccination is recommended.

##### **In patients with Mild/Moderate Immunosuppression:**

Inactivated vaccines are safe to use.

Patients with chronic diseases (CVS, respiratory, renal, liver, GI, diabetes melitus) should be up to date with their immunisations (especially Inactivated Influenza, PCV &/or PPSV23 , HepB).

In acquired complement deficiencies (eg on anti-C5 treatment), recommended are: PCV &/or PPSV23, Conjugated Hib, MenB, MenACW135Y.

##### **In patients with High level immunosuppression:**

Inactivated vaccines can be administered but effectiveness is not guaranteed

Live vaccines generally contraindicated.

**Table 2. SID with significant Immunosuppression and recommended vaccines**

SID category	Recommended vaccines
High Immunosuppression examples (as previous list)	
HIV and CD4 count < 0.2x10 <sup>9</sup> /L (<15% for infants and young children)	Inactivated Influenza PCV &/or PPSV23 Conjugated Hib MenB MenACW135Y HepB
Blood malignancies during chemotherapy	Inactivated Influenza PCV &/or PPSV23 Conjugated Hib  MMR can be given in children 12 months into remission
HSCT During and up to 3 months post ISP, within the first 2 years post-transplant, in chronic GVHD	Inactivated Influenza PCV &/or PPSV23 Conjugated Hib
Solid organ transplant (especially within the first 2 months post)	Inactivated Influenza PCV &/or PPSV23 Conjugated Hib HepA and HepB in liver transplant
ISP medication (eg high dose, long term steroids, biologics)	Inactivated Influenza PCV &/or PPSV23

#### **2.4. Immunisations for the close household contacts of Immunosuppressed patients:**

Immunocompetent individuals living in the same household with immunocompromised patients can receive all the inactivated vaccines safely. Regarding the safety and recommendations on live vaccines:



**Table 3. Safety profile of live vaccines for household contacts**

<b>Safety of live vaccines administered to close contacts of immunocompromised patients</b>		
<b>Live vaccine</b>	<b>Pathogen shedding? If so, site?</b>	<b>Evidence of transmissibility from vaccinated immuno-competent individuals</b>
Measles, Mumps, Rubella	No No Yes (nasopharynx, in low titres in breast milk)	Generally no, only mother to infant transmission of rubella vaccine strain via breast milk
Polio oral	Yes (stool)	Yes, rare cases of vaccine associated paralytic poliomyelitis
Rotavirus oral	Yes (stool)	Yes but no reported cases of symptomatic infection
Typhoid oral	No	No
Varicella	Yes (skin lesions)	Rare, in cases that skin lesions develop post immunisation
Zoster	Yes (lesions at the injection site)	Not reported
Yellow fever	Yes (possibly in breast milk)	Yes (encephalitis in infants exposed to the vaccine through breast feeding)
Live attenuated Influenza	Yes (nasal secretions)	Rare (from a vaccinated toddler)
BCG	Yes (ulceration at injection site, also potentially via breast milk)	Sparse data

**Table 4. Recommended vaccinations for close contacts of immunocompromised**

<b>Vaccinations for immune-competent people living with immunocompromised</b>	
MMR	Should be given to eligible individuals
LAIV	Should be given instead of the inactivated, only If the household contact is healthy, not pregnant, between 2-18 years of age and the immunocompromised individual is over 6 months old
OPV	Should not be given
Rotavirus	Should be given to eligible infants but highly immunosuppressed patients should not handle the baby's nappies for four weeks post vaccination
Typhoid	Safe to give
Yellow fever	Safe to give apart from breastfeeding women
Zoster	In eligible adults. If skin lesions develop , to avoid contact with the immunosuppressed person until the lesions resolve
VZV	In eligible children. If skin lesions develop , to avoid contact with the immunosuppressed person until the lesions resolve
BCG	Discuss risk and benefit on a case by case basis

## **2.5. Vaccination in pregnant women expecting to have a child with primary immunodeficiency:**

Routine immunisations (Tdap, inactivated influenza).

In addition: Pneumococcal, Hib, meningococcal vaccines

## **3. Education and Training**

None

## **4. Monitoring Compliance**

<b>What will be measured to monitor compliance</b>	<b>How will compliance be monitored</b>	<b>Monitoring Lead</b>	<b>Frequency</b>	<b>Reporting arrangements</b>
Call logs for telephone advice given to other physicians	Periodic audit of call logs	Nafsika Sismanoglou	yearly	Departmental Immunodeficiency MDT discussion

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## 6. **Keywords**

Immunization, vaccination, immunodeficiency, immunocompromised

## 7. **Review records:**

Approved by the Primary Immunodeficiency MDT on 20/6/2019 and Immunology Quality meeting 5/3/20

First review due in 3 years.

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