Primary immunodeficiencies

Vaccines and primary immunodeficiencies

IPOPI
INTERNATIONAL
PATIENT ORGANISATION
FOR PRIMARY IMMUNODEFICIENCIES

List of some common abbreviations

BCG	Bacillus Calmette-Guerin
CGD	X-linked chronic granulomatous disease
DTP	Diphtheria, tetanus, pertussis
Hib	*Haemophilus influenza* type B
HPV	Human papillomavirus
IG	Immunoglobulin (antibody)
IPV	Inactivated polio vaccine
LAD	Leukocyte adhesion deficiency
MBL	Mannose-binding lectin
MMR	Measles, mumps, rubella
OPV	Oral polio vaccine
PID	Primary immunodeficiencies
SCID	Severe combined immunodeficiency
VZV	Varicella zoster vaccine
WAS	Wiskott-Aldrich syndrome

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Introduction

This booklet provides general guidance on vaccinations that should be considered by patients with primary immunodeficiencies.

Primary immunodeficiencies (PIDs) are a large group of rare diseases caused by some components (mainly cells and proteins) of the immune system not working properly. PIDs are often diagnosed in childhood, but can also remain undiagnosed until adulthood. Many are caused by inherited genetic defects in the immune system.

Normally, the immune system helps protect the body from infectious diseases caused by micro-organisms, such as bacteria, viruses or fungi. As the immune system is altered in patients with PIDs, it makes them more likely to catch infections than other people.

The immune system is divided into two systems: 'innate' (non-specific) and 'adaptive' (specific) immunity:

- **Innate immune system.** This system is present from birth and is the first line of defence against many common micro-organisms.
- **Adaptive immune system.** This system builds a specific immune response every time it encounters a new foreign micro-organism in the body (an 'antigen') and it 'remembers' that encounter. The system is quickly activated if the same antigen is found in the body again. Active immunity can be acquired naturally or by vaccination.

Many people with PIDs receive immunoglobulin (IG) replacement therapy, which helps protect against infections (passive immunity) by providing normal levels of antibodies. You may also need medicines to treat or prevent infections caused by bacteria (antibiotics), viruses (antivirals) or fungi (antifungals). As with all prescribed medicines, it is important to follow the instructions given by your doctor, pharmacist or nurse.

Most patients with PIDs who are receiving IG replacement therapy do not need vaccines. However, vaccinations should be considered in the following situations:

- as part of routine childhood immunisation programmes
- where a bacterial or influenza infection might make the underlying condition worse
- international travel.

Recommendations will vary between patients and specialist advice should always be sought before receiving any vaccinations.

Vaccination and vaccines

Vaccination (or immunisation) is the administration of a vaccine that contains components of an infectious organism. These stimulate the immune system to make antibodies or T cells that provide protection against subsequent infections by that organism (adaptive immunity).

Vaccines are produced using micro-organisms that have been killed (inactivated) or altered (attenuated) in some way so that they resemble the normal bacteria or virus but should no longer cause disease. Attenuated vaccines are also known as live vaccines. Importantly, most patients with PIDs should not be given live-attenuated vaccines as they may cause them to have infections.

Live-attenuated vaccines that protect against viruses include:

- rotavirus
- oral polio vaccine (OPV)
- measles, mumps and rubella (MMR)
- varicella zoster vaccine (VZV)
- intranasal influenza
- yellow fever.

The only commonly used live-attenuated vaccine for bacterial infections is bacillus Calmette-Guerin (BCG), a tuberculosis vaccine.

Most patients with PIDs should not receive live-attenuated vaccines.

Childhood and travel vaccinations

Routine childhood immunisation programmes vary from country to country but will, in general, include vaccinations that provide protection against the following preventable childhood infections:

- diphtheria
- tetanus
- polio
- pertussis (whooping cough)
- meningitis due to *Haemophilus influenza* type b (Hib)
- pneumococcus and some types of meningococcus
- rotavirus
- chickenpox
- measles
- mumps
- rubella.

Children diagnosed with a PID should not routinely receive live-attenuated vaccines as part of their childhood immunisation programmes. However, there are certain PIDs where it may be safe for children to receive them. Your specialist doctor will discuss this with you and advise on which vaccines are safe for your child.

Other vaccinations that may not be routinely available in your area could be considered for some patients with PIDs. These include influenza, BCG and human papillomavirus (HPV).

For infections that mutate from year to year, such as influenza, your IG replacement therapy may not provide protection as the donated plasma is likely to have been collected prior to the virus altering its state. If exposed to influenza, it may be advisable to take antivirals to prevent infection.

Having a PID should not prevent you from travelling internationally; however, you do need to take certain precautions. Before travelling, discuss plans with your specialist doctor who will advise you on safety issues and the need for vaccinations. Travelling to countries with a high risk of infection should be avoided for most patients.

Travel-related and country-specific infections not covered by routine childhood immunisation programmes in all countries include:

- typhoid
- cholera
- hepatitis A
- hepatitis B
- yellow fever
- rabies
- Japanese encephalitis
- tick-borne encephalitis.

Further details on specific vaccines can be found at the end of this leaflet.

General vaccination guidance for patients, families and carers

The following section provides general guidance on which vaccines may be appropriate for children and adults with PIDs, and also for their families, siblings and close contacts. Your specialist doctor will review your specific condition and discuss what is appropriate for you.

People with PIDs

In general, vaccinations that may benefit people with PIDs should be given and not avoided. However, patients with severe PIDs (especially T cell disorders) should not be given live-attenuated vaccines as these can cause infections. Vaccines are less likely to be beneficial in patients receiving IG replacement therapy.

If you are a parent or carer of children or teenagers with PIDs, their school should tell you if vaccination programmes are taking place or if there are any outbreaks of infections (such as measles, influenza, chickenpox, meningitis or food poisoning).

Recommendations on appropriate vaccines for you or your children should be based on individualised advice from your doctor.

Family, siblings and close contacts

The families of people with PIDs should normally be vaccinated in order to protect patients catching infections from them. However, the following general principles should be applied:

- administration of live-attenuated vaccines (except MMR and BCG if recommended) to household contacts of people with the most severe PIDs (such as profound combined immunodeficiencies) should be avoided
- if recommended, patients with PIDs and their household contacts should receive inactivated polio vaccine (IPV) rather than OPV
- Many people with PIDs should not have any contact with children vaccinated with OPV for the first 24 hours after administration and should avoid close physical contact for approximately 4–6 weeks after administration, although IG replacement therapy should provide protection.

General vaccination guidance according to PID

While PIDs are generally classified into eight groups, in this leaflet they have been categorised into four broader groups, depending on which part of the immune system is affected:

- **B cells:** Produce IGs (or 'antibodies'), which kill invading micro-organisms and help phagocytic cells to recognise, ingest and kill them.
- **T cells:** Attack invading micro-organisms inside the body's own cells and produce chemicals called cytokines that help to gather and organise other immune cells.
- **Complement:** Proteins that kill micro-organisms and help other cells in the immune system.
- **Phagocytes:** White blood cells (e.g. neutrophils and macrophages) that recognise, swallow and kill invading micro-organisms.

The following table provides general guidance on which vaccines are should be avoided or are recommended in people with PIDs. Recommendations will vary depending on your PID, IG levels and whether you are able to produce antibodies to vaccines.

Category	Example of PID	Not recommended	General recommendations
T cell	SCID WAS Hyper IgM syndrome	All live vaccines BCG OPV Rotavirus in SCID and in infants where family members have SCID until tested for immunodeficiency	IPV not OPV should be used
B cell	CVID XLA IgG subclass specific	No information on use of VZV vaccine Yellow fever OPV	All childhood vaccines can be given (DTP, Hib, IPV, meningococcal, MMR) as per routine schedule IPV not OPV should be used Conjugated pneumococcal vaccine initially, followed by polysaccharide vaccine aged >2 years Administer inactivated influenza vaccine annually from 6 months of age BCG when indicated
Complement	C2, C3, C4, C8, C9 deficiencies Properdine, factor B or factor D deficiencies	-	Many specialists recommend extra vaccinations against Hib, pneumococcus and meningococcus
Phagocytic function	CGD LAD	BCG Live *Salmonella typhi* vaccine	All other vaccines, including live vaccines can be given

BCG, bacillus Calmette-Guerin; CGD, X-linked chronic granulomatous disease; DTP, diphtheria, tetanus, pertussis; Hib, *Haemophilus influenza* type B; IgA, immunoglobulin A; IgM, immunoglobulin M; IPV, inactivated polio vaccine; LAD, leukocyte adhesion deficiency; MBL, mannose-binding lectin; MMR, measles, mumps, rubella; OPV, oral polio vaccine; SCID, severe combined immunodeficiency; WAS, Wiskott-Aldrich syndrome; VZV, varicella zoster vaccine.

Common vaccines

	Type of vaccine	Disease/symptoms
Routine vaccines		
BCG	Live	Tuberculosis
DTP	Combined, killed	Acute infectious disease of upper respiratory tract (diphtheria); acute disease characterised by generalised rigidity and spasm of skeletal muscles (tetanus); whooping cough (pertussis)
Hib	Polysaccharide, killed	Meningitis
HPV	Killed	Genital warts and anogenital cancers
Influenza	Killed Live-attenuated	Acute viral infection of respiratory tract
IPV/OPV	IPV, killed OPV, live	Acute illness with symptoms ranging from fever to aseptic meningitis or paralysis
Meningococcal	Killed	Meningitis or septicaemia or both
MMR	Combined, live-attenuated	Acute illnesses characterised by rash (measles), and swelling of the parotid (salivary) gland (mumps); mild disease characterised by a rash (rubella)
Pneumococcal	Killed	Sinusitis, otitis media, pneumonia, systemic (invasive) infections including bacteraemic pneumonia, bacteraemia and meningitis
VZV	Live-attenuated Live-attenuated	Chickenpox Shingles

	Type of vaccine	Disease/symptoms
Travel vaccines		
Cholera	Oral, killed	Acute diarrhoeal illness
Hepatitis A	Killed	Infectious disease of the liver leading to jaundice in most patients
Hepatitis B	Killed	Infectious disease of the liver characterised by flu-like symptoms
Japanese encephalitis	Killed	Illness ranges from asymptomatic infection to severe encephalitis
Rabies	Killed	Insidious onset resulting in death from respiratory paralysis
Tetanus	Killed	Generalised rigidity and spasms of skeletal muscles
Tick-borne encephalitis	Killed	Fever and flu-like symptoms followed by central nervous system involvement
Typhoid	Oral, live Injection, killed	Symptoms range from mild fever, diarrhoea, myalgia and headache to severe disseminated disease with multi-organ involvement
Yellow fever	Live	Ranges from non-specific, self-limiting symptoms of fever, malaise, photophobia and headache to a sudden onset illness with fever, vomiting and prostration progressing to jaundice and haemorrhage

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Further information and support

This booklet has been produced by the International Patient Organisation for Primary Immunodeficiencies (IPOPI). Other booklets are available in this series. For further information and details of PID patient organisations in 47 countries worldwide, please visit **www.ipopi.org**.

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