

# Patient Guide to Immunoglobulin Replacement Therapy



This booklet is to help you understand a little bit more about what is happening to your health at the moment and what we can do to try and help you stay well. We understand that coming to hospital can be a worrying time and you probably have some questions about your condition that you hadn't thought of when you were last with us. Some of the answers may be contained within the following pages. You may also have more questions to ask after reading this and we are always happy to answer any queries you have.

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# The immune system

The immune system is the body's natural defence mechanism, consisting of various cells, tissues and organs and is our way of protecting ourselves from harmful organisms such as bacteria, fungi and viruses. These are also known as antigens or pathogens. When you come into contact with them your body will try to defend itself and the Immune System is how it goes about it.

**White blood cells** (also known as leukocytes) make up a very important part of the immune system and have two main types:

- 1: Phagocytes:** these are basically cells that swallow up and digest any bugs or cells which have been identified as harmful. The most common type is the Neutrophil.
- 2: Lymphocytes:** there are two types of lymphocytes, which are B and T cells. Both are responsible for recognising and remembering antigens which you have come into contact with before. They are more specialised in how they work and help you to become "immune" to certain diseases.

## Basic anatomy of immune system

**Thymus** – involved in T-cell development and maturation

**Lymph nodes** – site of antigen and lymphocyte interaction and one of the sites of antibody production

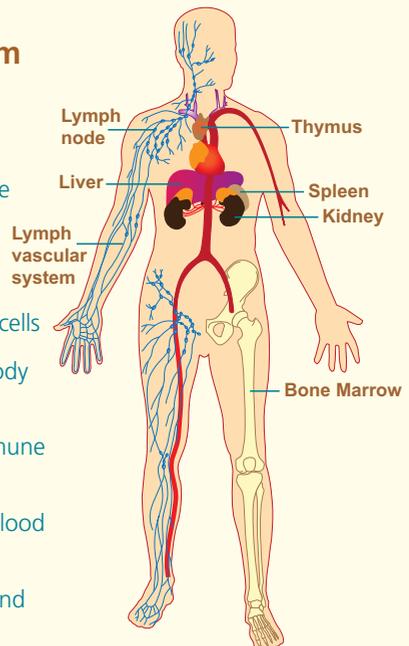
**Liver** – breaks down (metabolises) toxic substances and contains immunologically active cells

**Kidneys** – maintain fluid balance within the body and filters chemicals from blood into urine

**Bone marrow** – inner part of bone where immune cells and antibodies are produced

**Spleen** – site of B cell maturation and where blood cells, platelets and antigens are broken down

**Lymph vascular system** – carries antibodies and antigens throughout the body



## Immunoglobulins

Immunoglobulins are a type of protein and an important part of the immune system. They are made by B-cells and are also known as antibodies. There are three main types:

- 1: Immunoglobulin M (IgM)** antibodies are the first to react to the threat of antigens and are important for the first few days of infection.
- 2: Immunoglobulin A (IgA)** antibodies are found in the mucosal areas of the body and protect those areas with a high antigen concentration and where the physical barrier (mucous membrane) is less effective than the skin. The nose, mouth, digestive tract, and eyes are all areas where IgA can be found.
- 3: Immunoglobulin G (IgG)** antibodies are perhaps the most important of the antibodies and are found throughout the body. They are produced in far higher quantities and can recognise and attack particular antigens. Particular IgG antibodies will match up with the antigens and help destroy them. It can also signal other immune cells to come and help.

## Immunodeficiency

People with immunodeficiencies are less able to fight infections as their immune system is not working properly, either partially or not at all. They generally get infections more frequently and will also tend to take longer getting over them. The infections normally appear around the lungs (chest infections), the nasal passages (sinusitis) or the gut (diarrhoea). In the UK, roughly 5,000 people are thought to be affected, although this figure is steadily rising with greater understanding of the condition.

If you have been diagnosed with an immunodeficiency you do not need to panic. Most conditions that fall under the term can be managed very successfully with medical treatment.

Some patients may only need to have regular check-ups or clinic visits to have their blood tested. Others will need to take regular antibiotics to

limit the number of infections they have been having. A few will need to have essential antibodies replaced by intravenous (IV, which means into a vein) or subcutaneous (under the skin) infusions. This helps to boost the immune system to a level comparable with unaffected people. Some children with a severely compromised immune system can have it replaced with a healthy one by bone marrow transplantation. This is a well understood and mostly successful procedure, however, its use in adults is limited. New treatments, such as gene therapy, are also being developed for some more severe forms of immunodeficiency.

**Primary immunodeficiencies** (PIDs) are immunodeficiencies that people are born with or develop spontaneously later in life without any obvious reason. There are many different types of primary immunodeficiencies with varying degrees of severity. The causes are thought to be mostly genetic and will depend on the gene or genes affected and the amount of mutation present. About 20% of patients found to have a primary immunodeficiency will also have a close family member affected, although not necessarily with the same condition. There is a lot of research currently trying to discover more about the causes of immunodeficiencies, some of it carried out here at the Royal Free.

**Secondary immunodeficiencies** are those that are acquired later on in life and can be due to infections, some types of cancer or from certain drug therapies such as chemotherapy, immunosuppression, antimalarial treatment or epileptic medication.

**Important information about HIV** – A lot of people when they hear the term Immunodeficiency automatically think of HIV or AIDS. This is a completely different condition, caused by a virus, and is not the same. *Primary immunodeficiencies are not related to HIV or AIDS.*

## Treatment

There is much that is still not understood about problems with the immune system and consequently new treatments and research is being carried out all the time to improve the quality of life for people with immunodeficiencies. The new UCL Institute of Immunity and Transplantation at the Royal Free will have an important focus on research into primary immunodeficiency disorders to improve diagnosis and care.

The treatment for primary and secondary immunodeficiency is the same and usually involves infusions of antibodies to replace those not already present. This would typically be given straight into a vein (IVIg) or into the subcutaneous layer of tissue around the abdomen or upper thigh (SCIg). Treatment would either be on a day ward at a hospital or, if appropriate, training can be given to carry out infusions at home. Many patients find home therapy a convenient way to have treatment with minimal disruption to their day-to-day lives.

There are a number of different manufacturers making immunoglobulin replacement therapies and you may hear us refer to them as “products”. Naturally occurring antibodies (specifically IgG) found in human blood plasma are the essential components of all these products. This is obtained from screened donors and purified using a lengthy and complex filtering system to ensure that, as much as possible, any harmful components are removed. The main way these products differ is in the solution they are dissolved in and the concentration. For most patients, one product will be as good as another.

## Why do I need the treatment?

The term immunodeficiency means that your immune system is not working fully and therefore needs help to fight off infections caused by viruses and/or bacteria and/or fungi (pathogens). Usually your body produces immunoglobulin (antibodies) all the time to help keep you well but often an immunodeficient person is not able to do this and can become easily unwell. The antibodies that should be present in blood need to be replaced through infusions and this is where the term “replacement therapy” comes from.

As already mentioned, the replacement products are sourced from a large amount of donors, which means they contain a wide range of antibodies effective against most of the general pathogens within the population. This does not mean, however, that you will now be protected against all kinds of pathogens. At best, being on replacement therapy will mean that you have a similar chance of catching common infections as anyone else. This means it is vitally important you look after yourself by maintaining good hygiene, taking regular exercise (especially if you already have lung damage), eating a healthy diet and, most importantly, **not smoking**.



## Having your treatment

Before starting any treatment a doctor and one of the nurses will explain to you what this involves, giving you a chance to ask any questions you may have. If you are still unclear about anything, please use the details given at the back of the booklet to contact us. We are always happy to discuss issues relating to your treatment and understand that this may be a bewildering time for you and your family.

## On the ward

Initially your treatment will be given on the Institute of Immunity and Transplantation infusion ward on the second floor of the Royal Free Hospital but may be transferred to your local hospital if you don't live locally.

Once on the ward, one of the nurses will show you around and check that we have your contact details and next of kin listed correctly. Before you start your treatment one of our doctors will ask you to sign a consent form confirming that you understand what the treatment is and why it is necessary. They will also be able to answer any questions that you may have.

The first few times you have the treatment it will take between 4-6 hours. This slow starting rate is to make sure you can tolerate the infusion and will gradually be increased to a faster normal rate. You will also be given a small dose of hydrocortisone, a steroid, on your first two visits to lessen the effects of any potential reactions. We recommend that you be collected or take a taxi home after these first few sessions. It is important that you have breakfast and something to drink before your infusion. Lunch and other drinks will be provided for you throughout the day. Free Wifi is available on the ward during your stay.

## Side effects

There is a possibility that you may have a slight reaction to the product you are on, although this is not common. This could mean feeling faint or dizzy, lower back pain, short of breath, itchiness or a headache. Often, this will only happen the first few times you have an infusion but occasionally it can continue. If so, we may consider changing your immunoglobulin product. This is nothing to worry about. It only means that your body is a little sensitive to that particular solution and not to the essential ingredient (immunoglobulin) within it. Infusion reactions can also occur if you have an active infection. Sometimes we need to delay your infusion until your infection has been treated. Please let us know if you are unwell when you are due to have your infusion, so we can discuss whether to delay your infusions or not.

## Treatment options

The amount of monthly immunoglobulin is usually worked out by body weight. There are two ways of having an immunoglobulin infusion: IV (intravenous) or SC (subcutaneous) and both routes involve having the same amount of immunoglobulin over the course of the month. Each method is acceptable and has certain advantages over the other. The one you decide on will depend on your personal preference and we would support you whichever you choose. It is also possible to change from one to the other at any time.



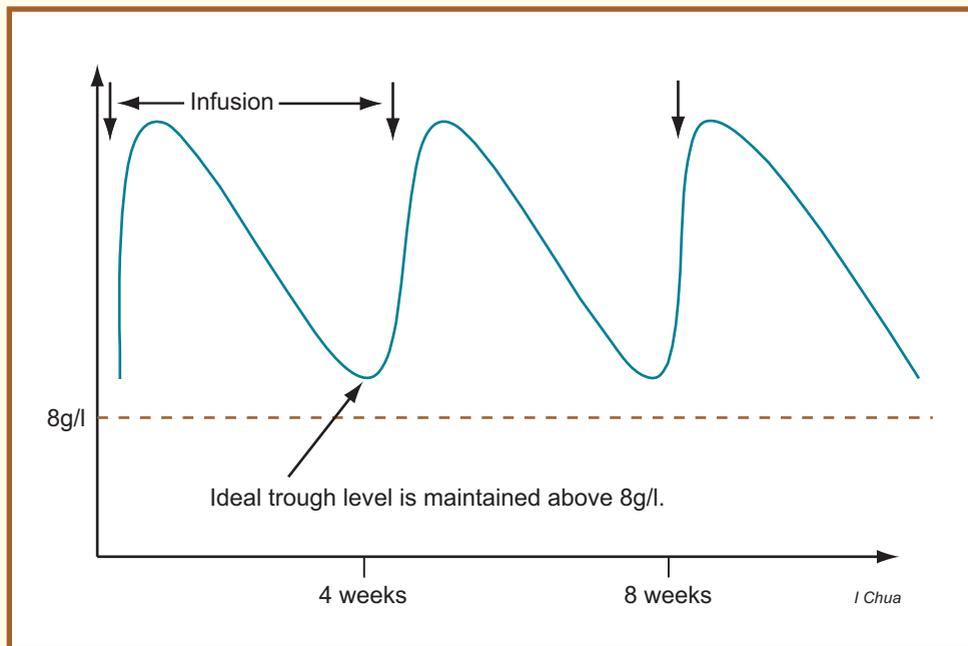
Intravenous infusions go directly into a vein in your arm or hand using a small butterfly needle. We try to rotate the veins used so they can be rested and kept working for as long as possible. Once established on a suitable IV product, your treatment will typically take place every 3-4 weeks and should take about 2-3 hours.

Having your infusion IV means that a higher dose can be given at once, which is why you only need to have treatment every 3-4 weeks. The downside to having IV treatment is that you need to have veins which can be accessed easily and the side effects mentioned above can be more noticeable due to the higher dose given in one infusion.

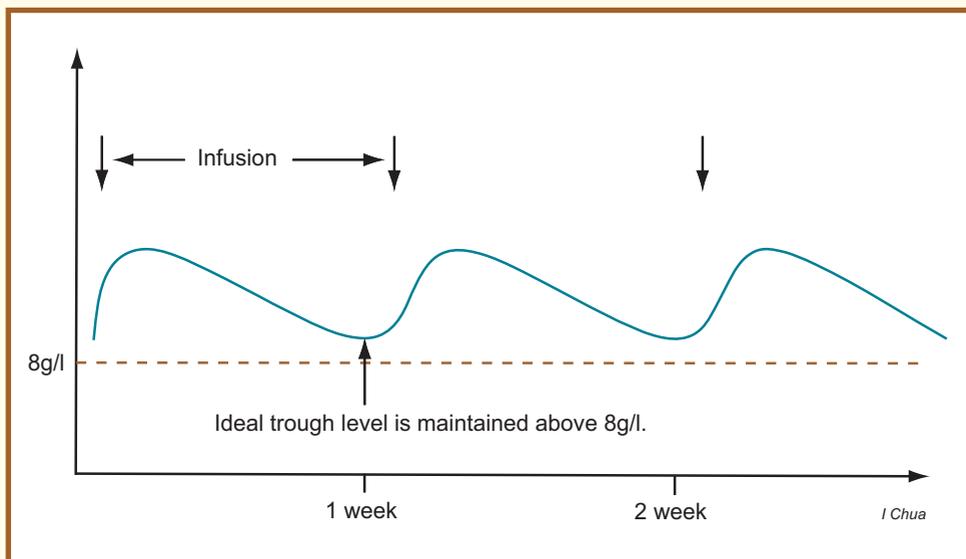
Some people don't have great veins to begin with or just may not like larger needles too much. For these patients subcutaneous treatment (SC) can be the preferred option. This method is still carried out with a needle, but a much smaller one which goes into the fatty layer of tissue under the skin around the abdomen or upper thighs, rather than into a vein. This means it takes longer for your body to absorb the liquid and consequently why a smaller, and more frequent, dose is needed. You may experience some side effects around the needle site such as swelling, itchiness and redness although this only lasts for a short while. SC is generally thought easier to do and, although carried out weekly, infusion time is less at about 90 minutes. Other advantages for SC therapy are that side effects are generally less marked, due to the smaller, but more frequent, doses. It will also give you a more even level of Immunoglobulins throughout the month.

## Differences between IV & SC treatment

### Simplified diagram of IgG levels after each infusion of IVIg



## Simplified diagram of IgG levels after SCIg



## Blood testing

Having blood taken is very necessary for us to monitor how your treatment is going. If you start on replacement therapy we will need to monitor the levels of immunoglobulins in your bloodstream approximately every three months. This allows us to find out if you're getting the right dose, as your needs may vary depending on the levels of infections you're having. The blood will also tell us about your liver function plus an indicator of infection called the CRP. We may, from time to time, ask you to give some blood to help in our research projects, but this will only be a small amount and only when you're already having blood taken. There is no obligation to give blood for research and we will always ask for written consent before doing so.

## Psychological treatment

Whilst the majority of people with immunodeficiencies are managing their condition and the impact on their life well, we know that this is not true for everybody. There is a link between physical health and mental wellbeing, and adults with chronic illnesses are at increased risk of

suffering from depression than the general population. Poor mental health can also affect an individual's ability to manage their physical health. Within the department, we have a psychology service that can provide short-term, talking therapy to patients with immunodeficiencies, or support patients to find other more suitable services locally. The treatment aims for those using the service vary and can include improvements in mood, general anxiety, specific health anxiety, sleep and fatigue, and having a space to reflect on the impact the illness has on their own and other's lives. We use a practical, cognitive-behavioural model of treatment which helps individuals to try out different techniques and skills which can make life easier. If you would like to find out more about the service or discuss the possibility of an assessment appointment please ask one of the team.

## **Jeffrey Modell Foundation**

Vicki and Fred Modell established the Jeffrey Modell Foundation (JMF) in 1987, in memory of their son Jeffrey, who died at the age of fifteen, from complications of primary immunodeficiency. Since 2009, the Royal Free Hospital is a JMF centre which means that we are dedicated to early diagnosis, meaningful treatments and, ultimately, cures through research, physician education, public awareness, advocacy, patient support and newborn screening.

## Glossary of terms

**Antibody:** a protein made by B cells which can destroy antigens. Also known as Immunoglobulins.

**Antigen:** general term for something that is recognised by your immune system as harmful and triggers a response. Common antigens can include particles from bacteria, viruses and fungi.

**B cell:** a protein and type of lymphocyte. Source of antibodies (immunoglobulins) which locks on to specific antigens, triggering their destruction with the help of other immune cells.

**Bone marrow:** inner part of bone where immune cells and antibodies are produced.

**Intravenous (IV):** literally means into a vein and is the most commonly used route for replacement therapy.

**Immunoglobulins:** proteins made by B cells. Also known as antibodies. Three main types: IgM, IgG and IgA. (see main text).

**Lymphocyte:** a type of white blood cell mostly produced in bone marrow. Also known as T or B cells. Both are responsible for recognising, remembering and helping to kill pathogens.

**Lymph nodes:** Site of antigen and lymphocyte interaction and one of the sites for antibody production.

**Lymph vascular system:** carries antibodies and antigens throughout the body.

**Neutrophil:** the most common type of phagocyte or 'cell eater'.

**Pathogens:** any kind of harmful agent, typically bacteria, viruses or fungi.

**Phagocyte:** a group of white blood cells which engulf and digest harmful cells.

**Replacement therapy:** term used to describe immunoglobulin infusions.

**Subcutaneous (SC):** refers to the fatty layer of tissue just under the skin and is the alternative route for replacement therapy.

**Spleen:** site of B cell maturation and where blood cells, platelets and antigens are broken down. Can become enlarged in some patients.

**T cell:** a protein and type of lymphocyte. Like antibodies, they react to specific antigens. Comes in 3 types:

- Killer T cells (CD8+): destroy cells invaded by bacteria or viruses but also cancerous cells and foreign tissue such as transplanted organs.
- Helper T cells (CD4+): activate killer T cells and stimulate B cells to make antibodies.
- Suppressor T cells: moderate the immune response and prevents the immune system going into overdrive that could lead to an 'autoimmune' response where the body's own healthy cells are attacked.

**Thymus:** small organ located behind the sternum and site of T cell maturation.

**White blood cells:** also known as leukocytes, are the main component of the immune system. The two main types are phagocytes and lymphocytes.

## Useful websites

[www.centreforimmunodeficiency.com](http://www.centreforimmunodeficiency.com) – This is our own website linked up with the paediatric service at Great Ormond Street Hospital. You'll find plenty of information here, especially about the specifics of your condition.

[www.ucl.ac.uk/immunity-transplantation](http://www.ucl.ac.uk/immunity-transplantation) – This is the website of the new Institute of Immunity and Transplantation based on the Royal Free Hospital. You can find lots of information about the research currently being conducted in immune-related conditions.

[www.pidpatients.org](http://www.pidpatients.org) – This is the website of the group formed to represent the interests of patients with Primary Immunodeficiency (PID) who are managed by the UCL Centre for adult PID at the Royal Free Hospital. You will find information about PIDs and patient's experiences of living with the illness.

[www.ipopi.org](http://www.ipopi.org) – This is the International Patient Organisation for Primary Immunodeficiencies website and has a broad range of information covering patient issues, drug and treatment developments, legislation and much more. A very good website.

[www.esid.org](http://www.esid.org) – Exchange of ideas and information among doctors, nurses, biomedical investigators, patients and their families concerned with primary immunodeficiency.

[www.ukpin.org.uk](http://www.ukpin.org.uk) – The UK Primary Immunodeficiency Network (UKPIN) is a multidisciplinary organisation of those caring for patients with primary immunodeficiencies. UKPIN aims to share methods of best practice, and to accredit immunology centres which practice in this way. Please explore these pages to see the wealth of reports, guidelines and other information available here.

## Contact us

### Nurses

**Andrew Symes** – Clinical Nurse Specialist.

andrewsymes@nhs.net

Tel: 020 7830 2140 or blp. 2029 via switchboard (020 7794 0500)

**Sarita Workman** – Research Sister.

sarita.workman@nhs.net

Tel: 020 7794 0500 ext. 33832 or blp. 2831

**Irene Wahlberg** – Immunology Nurse.

irene.wahlberg@nhs.net

Tel: 020 7794 0500 ext. 34001

**Mary Herman** – Ward Clerk.

mary.herman@nhs.net

Tel: 020 7794 0500 ext. 36231

### Consultants

**Dr. Ronnie Chee** – Consultant.

ronnie.chee@rnhs.net

Tel: 020 7794 0500 ext. 34519

**Dr. Siobhan Burns** – Consultant.

Siobhan.burns@ucl.ac.uk

Tel: 020 7794 0500 ext. 36662

**Dr. Suranjith Seneviratne** – Consultant.

Suranjith.seneviratne@nhs.net

Tel: 020 7794 0500 ext. 34519

**Jacqueline Glendinning** – Medical Secretary.

jacqueline.glendinning@nhs.net

Tel: 020 7830 2141

Tel: 020 7794 0500 ext. 34519

## **Registrars**

**Dr. Magdalena Dziadzio** – Special Registrar.

magdalena.dziadzio@nhs.net

Tel: 020 7794 0500 ext. 34807 or blp. 1168

**Dr. Nisha Verma** – Special Registrar.

nisha.verma@nhs.net

Tel: 020 7794 0500 ext. 34807 or blp. 1168

## **Psychologist**

**Dr. Mari Campbell** – Clinical Psychologist.

mari.campbell@nhs.net

Tel: 020 7794 0500 ext. 31467

## **Jeffrey Model Foundation**

**Paula Freitas** – JMF Project Coordinator.

paula.freitas@nhs.net

Tel: 020 7794 0500 ext. 34892



