

Get to know immunodeficiency disorders in depth Fight against infectious diseases with ease



Introduction of secondary immunodeficiency disease and subcutaneous immunoglobulin replacement therapy

## What are immunodeficiency disorders?

Immunodeficiency disorders occur when the immune system becomes dysfunctional, leading to impaired immunity. Consequently, the body becomes less effective to fight against bacteria, viruses, fungi or other mutant cells, including cancer cells.<sup>1-3</sup>



#### **Primary Secondary** immunodeficiency disease (PID) immunodeficiency disease (SID)

Primary immunodeficiency disease refers to dysfunction of the immune system, primarily caused by genetic mutations. The majority of cases are hereditary, while other sporadic cases result from de novo genetic mutations.<sup>1,4</sup>

Secondary immunodeficiency disease refers to the state of compromised immune system. Various factors can damage or weaken the immune system (such as lowering the levels of immunoglobulin), hence increasing the risk of other diseases or complications.<sup>1,5,6</sup>

# What factors can cause secondary immunodeficiency disease?

Various factors may cause secondary immunodeficiency disease. The most common causes are taking certain classes of drugs or receiving certain therapies.<sup>5,6</sup>

#### Drugs targeting the immune system<sup>5,6</sup>

These drugs are usually used in treating immunology, hematology, rheumatology and oncology disorders. They may weaken or damage the immune system.

#### Other drugs<sup>5,6</sup>

Drugs that are not targeting the immune system, such as certain anti-epileptics, can reduce antibody levels and weaken immunity.





Malnutrition

#### Symptoms of immunodeficiency disease

Symptoms of primary and secondary immunodeficiency diseases are similar.<sup>8</sup> The most common ones are serious, recurrent or chronic infections, such as periodontitis, diarrhoea and dermatitis. Some uncommon or atypical microorganisms may cause these infections or even result in complications, such as sinusitis, bronchitis and pneumonia.<sup>1</sup>

## What investigations would doctors perform?

Doctors usually conduct blood tests to determine the patient's immune function, subject to changes according to the patient's situation and medical history.<sup>1,2</sup>



Doctors may also perform vaccine response tests for patients, through which the levels of antibodies in patients before and after the vaccination can be compared, in order to determine the degree of impairment of their immune system.



### Ways to treat immunodeficiency disorders

Treatment goals and drug therapies vary among patients with different immunodeficiency disorders.<sup>8</sup> One of the treatments is immunoglobulin replacement therapy.<sup>1</sup>

Immunoglobulin replacement therapy is a blood-based treatment which aims to increase the levels of immunoglobulin G (IgG) in serum.<sup>9</sup> This replacement therapy makes up for the inadequate numbers of IgG in patients, boosting their immune system to neutralise and fight against viruses, bacteria and parasites.<sup>9</sup>

The replacement therapy supplies IgG intravenously or subcutaneously, with an overall aim to prevent future infections.<sup>9</sup>



Apart from immunoglobulin replacement therapy, doctors can also adopt other measures to lower the infection risk, according to the patient's condition<sup>1</sup>:



What is the difference between intravenous and subcutaneous injection of immunoglobulin?



IVIg infuses immunoglobulin intravenously into the circulation, maintaining the levels of immunoglobulin in blood.<sup>1,9</sup> This method is more traditional and has been used since 1970s.<sup>9</sup>

Patients are required to receive intravenous infusion every 3 to 4 weeks, 2 to 4 hours each time.<sup>9,10</sup>



SCIg is the novel route for immunoglobulin replacement therapy.<sup>9</sup> This treatment supplies immunoglobulin subcutaneously into the circulation, increasing the levels of immunoglobulin in blood.<sup>9,11</sup>

Most of the patients self-administer immunoglobulin at home every week. The process takes at most 2 hours.<sup>9,10</sup>

#### Tips about immunoglobulins<sup>12,13</sup>

Immunoglobulins (also known as antibodies) are protein molecules secreted from activated and differentiated immune cells. Immunoglobulins appear in various body fluids, such as blood and mucus.



#### Immunoglobulins play a crucial role in fighting pathogens in our body.<sup>12</sup>

They recognise different microorganisms and infected cells, helping the immune system to eliminate pathogens.<sup>12</sup>

## If patients are prescribed immunoglobulin replacement therapy, which route of administration shall they choose?

Patients with immunodeficiency disorders shall discuss with specialists to choose the suitable route of administration.  $^{\rm 5}$ 

The subcutaneous route can stabilise the number of immunoglobulins in the long term and raise the minimum levels of immunoglobulins.<sup>14</sup> In addition, SCIg offers greater flexibility than IVIg, improving patients' quality of life.<sup>14</sup> They could choose the appropriate time for self-administration, even when they are abroad.<sup>215</sup>

#### Intravenous vs subcutaneous immunoglobulin replacement therapy at a glance

| Therapy  | lVlg   | SCIg  |
|--|--|---|
| Route of administration <sup>9</sup>                         | Intravenous  | Subcutaneous  |
| Treatment setting <sup>10</sup>                              | Hospital   | Home (Self-administration)  |
| Injection frequency <sup>10</sup>                            | Monthly  | Weekly  |
| Treatment efficacy <sup>10</sup><br>(Future infection rates) | Similar  | Similar   |
| Post therapy levels of<br>immunoglobulin <sup>9,10,15</sup>  | <ul> <li>More fluctuations in<br/>immunoglobulin levels:<br/>a quick increase is observed<br/>after IVIg, then gradually<br/>drops until the next dose</li> <li>The minimum level of<br/>immunoglobulin achieved<br/>with IVIg is lower than<br/>that with SCIg</li> </ul> | <ul> <li>Fewer fluctuations in<br/>immunoglobulin levels:<br/>More stable immunoglobulin<br/>levels are achieved</li> <li>The minimum level of<br/>immunoglobulin achieved<br/>with SCIg is higher than<br/>that with IVIg</li> </ul> |

Changes in immunoglobulin levels after intravenous or subcutaneous administration<sup>16</sup>



From Jolles, et al. (2011)

## Steps of subcutaneous immunoglobulin replacement therapy <sup>11,17</sup>

Healthcare professionals would guide patients on the administration steps and provide adequate training and support once the subcutaneous route is selected for immunoglobulin therapy.



Choose the site(s) of injection. If multiple sites are required, keep injection sites at least 5 cm apart.



Step 3

Connect a needle to a syringe and pull back on the plunger to withdraw the IgG solution.



# SHARPS \*

Insert the needle into the tissue below your skin after sterilisation and start the therapy.

Step 3

Step 4

Remove and sterilise the needle after use and dispose of it in the sharps box.

Questions and suggested solutions related to subcutaneous immunoglobulin replacement therapy<sup>17</sup>

| Questions   | Suggested solutions  |
|---|--|
| Local skin irritation<br>(e.g. redness,<br>swelling, itching) | <ul> <li>Most of the allergic reactions are mild and should resolve within 24 hours. If the reaction becomes more serious than expected, or if the reaction persists for a long period of time, patients can discuss with immunology specialists and try the following:</li> <li>Decrease the volume per injection site and/or prolong the administration time</li> <li>Change the length of the needle</li> <li>Keep the needle dry before inserting into the skin</li> <li>Practise self-injection technique such as the way to place and remove the needle</li> <li>Gently rub the skin after injection or apply warm or cold compress after therapy</li> </ul> |
| Leakage at site   | <ul> <li>Leakage can be caused by a lot of factors, such as the choice of the needle, needle placement, needle length and injection technique. If leakage occurs, please consider the following:</li> <li>Secure positioning of the needle</li> <li>Choose a site with adequate fatty tissue for injection</li> <li>Choose a suitable needle length</li> <li>Avoid high infusion volume</li> </ul>   |
| Long infusion time  | <ul> <li>Check the infusion tubing and needle</li> <li>Discuss the number of injection sites and the volume per site with immunology specialists</li> <li>Choose an appropriate injection site and do not inject into skin with scars, injuries, swelling or inflammation</li> <li>Check the infusion rate settings, whether the tubing size and length matches infusion rate, needle gauge, pump and battery functions</li> </ul>   |
| Serious anaphylactic<br>reactions                             | Discontinue immediately and seek medical attention   |

#### Immunoglobulin replacement therapy: Frequently asked questions

#### Q: Is regular assessment or follow-up required after receiving immunoglobulin replacement therapy?

Ans Follow-up is required every few months to half a year after initiation of immunoglobulin replacement therapy, subject to individual needs. Regular follow-up allows doctors to assess treatment progress and response.<sup>2</sup> If significant improvement in immune system is observed, doctors could consider ceasing the therapy.<sup>8</sup>

#### Q: What precautions should be taken during immunoglobulin replacement therapy?

Every immunoglobulin product is different. Patients may experience adverse or allergic reactions owing to compositions in each product.<sup>17</sup> Therefore, immunology specialists would assess the patient's conditions and monitor their progress before and throughout the therapy.

#### Q: What are the possible adverse reactions of immunoglobulin replacement therapy?

Ans Adverse reactions following immunoglobulin replacement therapy are uncommon, so the therapy is generally recognised as safe. However, occasional adverse reactions might occur, such as pain and swelling at injection site, redness, headache, fever and chills, nausea and vomiting, muscle and joint aches. Rare adverse reactions include serious anaphylactic reactions, renal or pulmonary complications and thromboembolism.<sup>17</sup>









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#### Select the most suitable immunotherapy. Minimise the risk of infectious diseases.

This booklet is for reference only.

If you wish to learn more about secondary immunodeficiency disease and subcutaneous immunoglobulin replacement therapy, please consult your doctor.

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