IPOPI
INTERNATIONAL
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FOR PRIMARY IMMUNODEFICIENCIES

PRIMARY **IMMUNODEFICIENCIES**

PIDS AND GASTROINTESTINAL DISORDERS

ABBREVIATIONS

6-MP	6-mercaptopurine
AR	Autosomal recessive
AZA	Azathioprine
CGD	Chronic granulomatous disease
CT	Computed tomography
CVID	Common variable immunodeficiency
GI	Gastrointestinal
IBD	Inflammatory bowel disease
IG	Immunoglobulin
IPEX	Immune dysfunction, polyendocrinopathy, enteropathy and X-linked syndrome
MRI	Magnetic resonance imaging
NLH	Nodular lymphoid hyperplasia
PID	Primary immunodeficiency
SCID	Severe combined immunodeficiency
WAS	Wiskott-Aldrich syndrome
XLA	X-linked agammaglobulinaemia

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INTRODUCTION

This booklet explains the gastrointestinal issues that patients with primary immunodeficiencies may encounter and their treatment options.

Primary immunodeficiencies (PIDs) are rare diseases that occur when components of the immune system are either not present or not working properly. There are over 250 variations with a wide range of symptoms.

Gastrointestinal (GI) disorders, affecting the mouth, throat, stomach and intestines, are common in many patients with PIDs. The GI system is constantly exposed to viruses, parasites and bacteria, all of which have the potential to cause irritation, inflammation and infection of the intestinal lining, particularly when the immune system is not functioning correctly.

Also, the GI system contains the majority of the body's lymphocytes (a type of white blood cell) and produces immunoglobulins (IGs) (antibodies) so it is quite likely that GI disorders may emerge when the immune system is not fully functional.

If you have a PID and develop GI symptoms, it is important to discuss them with your physician. Early diagnosis will enable appropriate treatments to be prescribed that will improve your health and your GI function.

Routine checks of your GI system may be beneficial, depending on the type and severity of your PID, and your physician will be able to provide you with information about these tests.

GASTROINTESTINAL DISORDERS

GI disorders can be broadly classified into four groups: infections, inflammatory conditions, autoimmune conditions and malignancies. In addition, GI symptoms may occur in response to certain treatments.

GI disorders can lead to serious problems in some people with PIDs so it is important that you discuss any new symptoms with your physician as they arise.

MAIN CAUSES OF GI DISORDERS IN PATIENTS WITH PIDS

Infections	*Infections can be bacterial, viral or parasitic.* Bacterial infections *Salmonella* species *Campylobacter jejuni* Bacterial overgrowth Viral infections Cytomegalovirus Coxsackievirus Echovirus Rotavirus Parasitic infections *Giardia lamblia* *Cryptosporidium parvum* *Entamoeba histolytica*
Inflammatory conditions	*In these conditions, there is excessive inflammation in the GI system.* Crohn's disease Inflammatory bowel disease (IBD) Ulcerative colitis
Autoimmune conditions	*In these conditions, the immune system mistakenly damages healthy tissues.* Coeliac disease Nodular lymphoid hyperplasia Pernicious anaemia
Malignancies	Colon cancer Pancreatic cancer Stomach cancer

GI SYMPTOMS

The symptoms of many GI disorders are the same as in individuals without PIDs. However, in PID patients, the development of the GI disease is likely to be different - symptoms can be long-standing and the conditions are sometimes difficult to diagnose and treat.

Typical symptoms of GI disorders

Prolonged or recurring diarrhoea, Mouth ulcers, Inflamed gums, Bloating, Blood in stool, Abdominal pain, Rectal ulcers, Failure to thrive, Weight loss

Some GI disorders are more prevalent than others in patients with specific PIDs. For example, bacterial infections often occur in patients with B-cell deficiencies and viral infections are more common in patients with T-cell deficiencies.

IMMUNODEFICIENCY	TYPICAL GI SYMPTOMS
Agammaglobulinaemia: X-linked (XLA) or autosomal recessive (AR)	GI disorders, especially those caused by the parasite, *Giardia lambia.* This may cause abdominal pain, diarrhoea and poor growth.
Common variable immunodeficiency (CVID)	Abdominal pain, diarrhoea, bloating, nausea, vomiting, weight loss, IBD, *Giardia lambia* infection.
Selective IgA deficiency	Some patients are more susceptible to infections than others. GI infections, chronic diarrhoea.
Hyper IgM syndromes	Diarrhoea, malabsorption, progressive liver disease.
Severe combined immunodeficiency (SCID)	Symptoms can be present from birth. Chronic diarrhoea, malabsorption, oral candidiasis (thrush), IBD.
Chronic granulomatous disease (CGD)	Bowel conditions due to inflammation (similar to Crohn's disease). Liver abscesses.
Wiskott-Aldrich syndrome (WAS)	Diarrhoea, malabsorption.
Immune dysfunction, polyendocrinopathy, enteropathy and X-linked syndrome (IPEX)	Autoimmune conditions with severe chronic diarrhoea.

GI EVALUATIONS

Depending on your PID and health status, your physician may recommend routine GI evaluations, which may include:

- Physical examinations to check for oral or anal ulcers, fluid or tenderness in the abdomen, enlarged or tender liver.
- Blood tests to look for signs of intestinal bleeding or inflammation, assess your nutritional status and check for liver irritation.
- Stool tests to identify inflammation and infections caused by bacteria, viruses or parasites.
- X-rays, ultrasounds, computed tomography (CT) scans or magnetic resonance imaging (MRI) scans to obtain images of the inside of your body.
- Liver or bowel biopsies to make definitive diagnoses of liver or bowel disease.
- Gastroscopic and/or colonoscopic procedures to view the mucosa and take biopsies.

If your physician can identify any problems early, then appropriate treatments can be started to improve your symptoms and your overall health.

GASTROINTESTINAL SYMPTOMS AS AN INDICATOR OF PIDS

A GI disorder (particularly chronic or acute diarrhoea, malabsorption, abdominal pain or IBD) may be the first sign that you have a PID, particularly if the disorder doesn't respond to conventional treatments and the symptoms keep returning.

It is important that physicians and gastroenterologists look for immunodeficiencies in patients with GI symptoms not responding to usual treatments.

If you have chronic diarrhoea or colitis, for example, your physician should check for infection with rotavirus, enteroviruses, *Campylobacter, Cryptosporidium, persistent Salmonella, Clostridium difficile* or recurrent giardiasis.

As well as initiating specific evaluations, it is important that your physician refers you to an immunologist.

TREATMENTS

If you receive intravenous or subcutaneous IG replacement therapy, this may provide you with some protection against many viruses and bacteria. However, it may not reverse or prevent the development of all GI diseases and you may require additional support.

Steroids are often the first choice of therapy, and in many cases, they can be sufficient to control symptoms. Antibiotics and anti-microbial treatments are also prescribed to treat infections.

As well as steroid treatment, other medicines that suppress the immune system are often required for severe autoimmune or inflammatory GI disorders. These can include immune modulators (such as azathioprine (AZA), 6-mercaptopurine (6-MP) or methotrexate) or biological therapies (such as infliximab or adalimumab). This process is very individual requiring a flexible treatment plan that your physician will discuss with you.

Typical treatments for a number of infections/conditions are described below.

INFECTION/CONDITION	TYPICAL TREATMENTS
Bacterial infections	As per non-PID patients but may require longer antibiotic courses and careful monitoring for complications.
Coeliac disease	Responsive to gluten withdrawal in IgA-deficient patients but not CVID patients.
Giardia *lamblia* infection	Metronidazole (may require several courses in patients with CVID). Steroid therapy but prolonged therapy not recommended. Other immune modulators, 6-MP or AZA can be used in addition to IG replacement therapy.
Colitis	Corticosteroids, 5-aminosalicyclic acid, 6-MP and AZA.
Asymptomatic IgG patients with GI symptoms	Treat as per non-PID patients but monitor for progression to CVID.
Neutropenia	Daily subcutaneous injections of the granulocyte colony-stimulating factor, filgrastim, may be effective in some patients.

If you have significant GI symptoms, it will be important for your healthcare team to involve a GI specialist to assist with diagnostic testing and directing treatment.

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 52 countries worldwide, please visit **www.ipopi.org**.

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IMMUNO DEFICIENCY UK

Supporting families affected by primary and secondary immunodeficiency

Immunodeficiency UK is a national organisation supporting individuals and families affected by primary and secondary immunodeficiency.

We are the UK national member of IPOPI, an association of national patient organisations dedicated to improving awareness, access to early diagnosis and optimal treatments for PID patients worldwide.

Our website has useful information on a range of conditions and topics, and explains the work we do to ensure the voice of patients with primary and secondary immunodeficiency is heard. If we can be of any help, please email us or call on the number above, where you can leave a message.

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