Primary immunodeficiencies

Autoimmunity and autoinflammation

IPOPI
INTERNATIONAL
PATIENT ORGANISATION
FOR PRIMARY IMMUNODEFICIENCIES

List of some common abbreviations

APECED	Autoimmune polyendocrinopathy candidiasis ectodermal dystrophy
CAPS	Cryopyrin-associated periodic syndrome
CGD	Chronic granulomatous disease
CINCA	Chronic infantile neurological cutaneous and articular syndrome
CRMO	Chronic recurrent multifocal osteomyelitis syndrome
CVID	Common variable immunodeficiency
FCAS	Familial cold autoinflammatory syndrome
FMF	Familial Mediterranean fever
HIDS	Hyperimmunoglobulinemia D and periodic fever syndrome
Hyper IgM	Hyper IgM syndrome
IBD	Inflammatory bowel disease
IL	Interleukin
IPEX	Immune dysregulation, polyendocrinopathy and enteropathy, X-linked
MWS	Muckle-Wells syndrome
NOMID	Neonatal onset multi-system inflammatory disease
NSAIDS	Non-steroidal anti-inflammatory drugs
PAPA	Pyogenic arthritis, pyoderma gangrenosum and acne syndrome
PID	Primary immunodeficiencies
SCID	Severe combined immunodeficiency
TNF	Tumour necrosis factor receptor
TRAPS	TNF receptor-associated periodic fever syndrome
XLA	X-linked (or Bruton's) agammaglobulinaemia
WAS	Wiskott-Aldrich syndrome

Primary immunodeficiencies — Autoimmunity and autoinflammation (1st edition).
December 2013

Published by IPOPI: www.ipopi.org

Introduction

This booklet provides background information on autoimmune and autoinflammatory diseases in patients with primary immunodeficiencies.

Primary immunodeficiencies (PIDs) are a group of rare diseases caused when some components (mainly cells and/or proteins) of the immune system do not work properly. PIDs are caused by defects or mutations in the genes, many of which are hereditary. Over 250 specific types of PIDs have been identified.

The immune system normally helps protect the body from infections caused by micro-organisms, such as bacteria, viruses or fungi. As the immune system is altered in people with PIDs, it makes them more likely than other people to catch infections. It also makes it more difficult to fight infections.

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

The innate immune system is normally your first line of defence against many common micro-organisms. It comprises various types of cells and molecules that react immediately to invading micro-organisms, regardless of whether your body has encountered them before. These cells include:

- Mast cells and leukocytes (white blood cells, e.g. eosinophils and basophils), which release agents that produce inflammation and are toxic to invading micro-organisms
- Phagocytic cells (white blood cells, e.g. neutrophils and macrophages), which recognise, swallow and kill invading micro-organisms
- Natural killer cells, which kill infected body cells, produce inflammatory proteins and are also phagocytic.

The adaptive immune system is based on memory. The first time the body is exposed to a new micro-organism it recognises as foreign (an 'antigen'), it takes a few days to build up production of specific antibodies to the antigen. If the body is later exposed to the same antigen, the response is very quick because of the immunological memory. The main cells involved are:

- T cells, which attack invading micro-organisms inside your body's own cells and produce chemicals called cytokines that help to gather and organise other immune cells.
- B cells, which produce immunoglobulins (or 'antibodies'), which kill specific micro-organisms and help phagocytic cells to work.

Some people with PIDs are also affected by autoimmune and autoinflammatory diseases. Constant stimulation of the immune system is responsible for both disorders. However, different components of your immune system are 'overactivated' and responsible for your symptoms - your adaptive immune system in autoimmune disorders and your innate immune system in autoinflammatory disorders.

Understanding autoimmune diseases

Autoimmune diseases arise when your immune system mistakenly identifies your body's own cells as foreign and attacks tissues that it would normally ignore, causing damage to them, as well as changes to organs and the way they function and grow. In the majority of cases, they occur as a result of a person's genetic make-up; they can also be triggered by bacteria or viruses.

There are more than 80 types of autoimmune disorders and people may have more than one disorder at a time. In people with PIDs, autoimmune complications are not unusual – for example, they affect more than a quarter of people with common variable immunodeficiency (CVID).

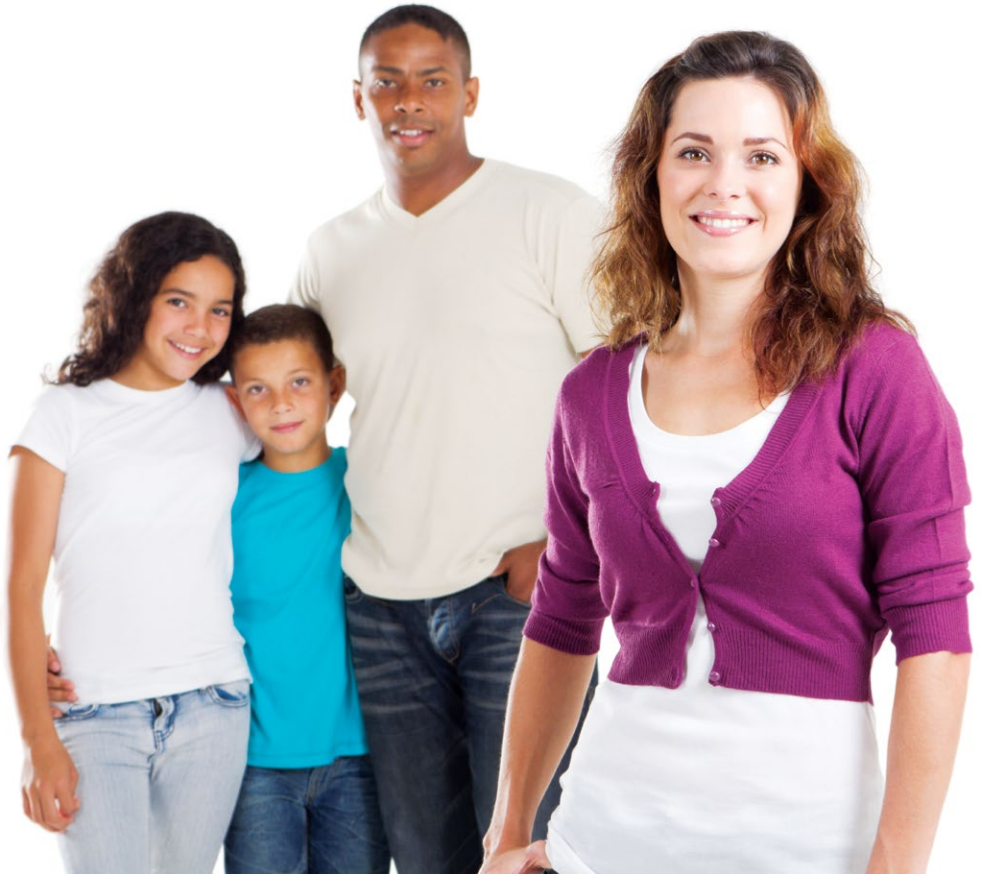
Examples of autoimmune diseases include:

- Addison's disease
- Pernicious anaemia
- Coeliac disease - sprue (gluten-sensitive enteropathy)
- Reactive arthritis
- Dermatomyositis
- Rheumatoid arthritis
- Graves disease
- Sjogren syndrome
- Hashimoto's thyroiditis
- Systemic lupus erythematosus
- Multiple sclerosis
- Type I diabetes
- Myasthenia gravis

Autoimmune disorders can affect one or more organs or tissues and the symptoms vary, depending which are involved. Symptoms can include, for example, fatigue, muscle aches, a low fever and a general feeling of being unwell. If you are experiencing these symptoms, discuss them with your doctor specialised in PID so that they can check and recommend the most appropriate course of treatment for you.

Areas of the body commonly affected by autoimmune diseases include:

Organs and tissues	Symptoms
Joints	Pain and swelling (arthritis)
Skin	Rashes, swelling and eczema
Liver	Enlargement of liver (hepatomegaly)
Spleen	Enlargement of spleen (splenomegaly)
Intestine	Inflammatory bowel disease (IBD) and lymphoid hyperplasia
Red and white blood cells	Anemia, thrombocytopenia, neutropenia and blood clotting disorders



Some of the most common autoimmune disorders experienced by people with PIDs are shown in the following table.

Possible autoimmune symptoms in people with PIDs

PID	Possible autoimmune disorders
Common variable immunodeficiency (CVID)	• Thrombocytopenia • Evans syndrome • Haemolytic anaemia • IBD • Neutropenia • Rheumatoid arthritis • Haemolytic or pernicious anaemia • Systemic lupus erythmatosus • Psoriasis
Severe combined immunodeficiency (SCID) (especially in Omenn syndrome)	• Alopecia • Dermatitis • Thrombocytopenia
X-linked chronic granulomatous disease (CGD)	IBD
X-linked (or Bruton's) agammaglobulinaemia (XLA)	• Juvenile rheumatoid arthritis • Rheumatoid arthritis/dermatomyositis
Wiskott-Aldrich syndrome (WAS)	• Haemolytic anaemia • Dermatitis • IBD • Vasculitis
Hyper IgM syndrome (hyper IgM)	• Autoimmune neutropenia • IBD • Rheumatoid arthritis • Uveitis
Immune dysregulation, polyendocrinopathy and enteropathy, X-linked (IPEX)	• Cytopenias (thrombocytopenia, anaemia, neutropenia) • Dermatitis • Enteropathy (intestinal disorder) • Juvenile diabetes
Autoimmune polyendocrinopathy candidiasis ectodermal dystrophy (APECED)	Endocrine

Understanding autoinflammatory diseases

Autoinflammatory diseases are a group of rare, hereditary inflammatory disorders that occur in the absence of any infection. The cells of your innate immune system induce an inflammatory response even though they have not encountered antigens in the body. Autoinflammation can also be trigged by infections or by natural bacteria in the intestines and airways.

People with autoinflammatory diseases typically have intense and recurring attacks of inflammation, which cause symptoms such as fever, rash, joint swelling, abdominal pain, diarrhoea, fatigue and weight loss. If you think you have these symptoms, discuss them with your doctor for advice on management and treatment.

There are several different types of autoinflammatory diseases and some examples and their symptoms are shown below.

Disease	Symptoms
Familial Mediterranean fever (FMF)	• Short duration of fever (24–48 hours) • Abdominal and chest pain • Erysipelas (super infection of the skin)
Tumour necrosis factor (TNF) receptor-associated periodic fever syndrome (TRAPS)	• Recurring fevers • Muscle, abdominal and chest pain • Rash • Nausea, vomiting, diarrhoea • Sore eyes
Hyperimmunoglobulinemia D and periodic fever syndrome (HIDS)	• Recurring fevers • Abdominal pain • Vomiting, diarrhoea • Joint pain • Skin lesions • Headache
Cryopyrin-associated periodic syndrome (CAPS): • Familial cold autoinflammatory syndrome (FCAS) • Muckle-Wells syndrome (MWS) • Neonatal onset multi-system inflammatory disease (NOMID)/ chronic infantile neurological cutaneous and articular syndrome (CINCA)	• Headache • Rash • Joint and muscle pain • Fever after cold exposure (FCAS) • Kidney impairment (MWS) • Hearing problems (MWS) • Conjunctivitis (MWS) • Organ damage (NOMID)
Blau's syndrome	• Rheumatoid arthritis • Inflammation of the eye • Skin rash and granuloma
Crohn's disease	• Diarrhoea • Abdominal pain • Fatigue • Weight loss • Blood and mucus in stools
Pyogenic arthritis, pyoderma gangrenosum and acne syndrome (PAPA)	• Pus-producing arthritis • Skin ulcers • Cystic acne
Chronic recurrent multifocal osteomyelitis syndrome (CRMO)	• Recurring fevers • Bone pain and lesions
Majeed syndrome	• Recurring fevers • Bone pain • Skin inflammation

Treatment of autoimmune and autoinflammatory diseases

Treatment of autoimmune or autoinflammatory diseases depends on a number of factors, particularly the type and severity of your condition, and your doctor specialised in PID will be able to provide the best advice and discuss your options. There are so many types of autoimmune and autoinflammatory disorders and each one has its own specific therapeutic requirements.

For many people with PIDs and autoimmune disorders, as well as receiving immunoglobulin replacement therapy for the treatment of your PID, the first step in treatment is often to take corticosteroids. These suppress the immune system and reduce inflammation, however, long-term use is associated with serious side-effects and careful management by your physician is required. You may benefit from taking supplements, such as calcium and vitamin D, and proton pump inhibitors, which protect the stomach from ulcers. The dose of the corticosteroid may also be altered to reduce any side-effects.

Your doctor may also prescribe other immunosuppressive therapies (azathioprine, leflunomide, methotrexate, mycophenolate, tacrolimus, cyclophosphamide or cyclosporine).

For patients with autoinflammatory conditions, anti-inflammatory products (non-steroidal anti-inflammatory drugs [NSAIDS], colchicine or immunomodulators) may initially be prescribed to reduce your symptoms.

For both autoimmune and autoinflammatory disorders, if the above options are not effective for you, your doctor may recommend biological therapies, which are suitable for a number of conditions. These therapies include:

- tumour necrosis factor (TNF) inhibitors, such as etanercept, infliximab or adalimumab
- interleukin (IL)-1 and IL-6 targeted therapies, such as anakinra, canakinumab, rilonacept or tocilizumab
- Other biological therapies, such as rituximab or belimumab.

These medicines should always be used under the guidance of your doctor, who will regularly monitor you to check if there is any change in your disease and if you develop any side-effects.

If you have any questions about treatment availability in your country, contact your local patient organisation for assistance.

Primary immunodeficiencies

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**.

Provided by

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.

Support us by becoming a member of Immunodeficiency UK. It's free and easy to do via our website. Members get monthly bulletins.

Immunodeficiency UK is reliant on voluntary donations. To make a donation, please go to **www.immunodeficiencyuk.org/donate**

Baxter

Supported by an educational grant from Baxter Healthcare Corporation

www.immunodeficiencyuk.org
hello@immunodeficiencyuk.org
0800 987 8986