IPOPI
INTERNATIONAL
PATIENT ORGANISATION
FOR PRIMARY IMMUNODEFICIENCIES

PRIMARY **IMMUNODEFICIENCIES**

A GUIDE FOR **INTERNAL MEDICINE SPECIALISTS**

KEY ABBREVIATIONS

CT	Computerised tomography
Ig	Immunoglobulin
IPOPI	International Patient Organisation for Primary Immunodeficiencies
IVIG	Intravenous immunoglobulin
PID	Primary immunodeficiency
SADNI	Selective antibody deficiency with normal immunoglobulins
SCID	Severe combined immunodeficiency

Primary immunodeficiencies: A guide for internal medicine specialists (1st edition).

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INTRODUCTION

This booklet introduces the complex presentation of adult patients with primary immunodeficiencies (PIDs) who are often referred for internal medicine services with multiple, sometimes non-specific symptoms. Clinical indicators that may raise a suspicion of a PID are reviewed as is the need for a multidisciplinary team to optimise care for such patients.

Primary immunodeficiencies (PIDs) are rare diseases that occur when components of the immune system are either not present or are not functioning normally, rendering the patient susceptible to potentially life-threatening infections. The presentation of a PID is often complex with clinical indicators suggestive of multiple potential diagnoses. Such patients will often be referred to an internal medicine specialist with multiple, non-specific symptoms. Internal medicine specialists are, therefore, uniquely placed to identify patients with PIDs ensuring they receive a timely diagnosis and intervention to minimise the chronic effects and morbidity in PIDs by initiating prophylactic therapies.

The following sections review the often complex clinical presentations of patients with PIDs and the clinical indicators that may raise a suspicion of PIDs. Management strategies, including building a multidisciplinary team, are also explored.

PIDs: NOT JUST A PAEDIATRIC DIAGNOSIS

To date, over 354 different PIDs have been identified, according to the 2017 International Union of Immunological Societies (IUIS) publication, ranging from the very rare (e.g. severe combined immunodeficiency [SCID]) to the relatively common (e.g. selective immunoglobulin A deficiency).

PIDs can be diagnosed throughout the lifespan of a person and may affect around 1 in 2000 persons. The most severe forms of PIDs are usually diagnosed in childhood. However, others are frequently recognised during adulthood because of their late onset and because they have been misdiagnosed or undiagnosed.

PIDs can have widely differing presentations, from relatively mild to life-threatening. Some develop over time and worsen as late manifestations or complications appear. People with PIDs are more susceptible to infections, allergies, autoimmunity, malignancies and complications resulting from infections and inflammation. Many patients with PIDs remain undiagnosed for several years, during which time they are often treated several times with antimicrobial agents. The relatively non-specific nature of the presentation of PIDs can mean that they are referred for internal medicine evaluation with an array of chronic symptoms.

CLINICAL INDICATORS FOR PIDs

Clinical indicators include a family history of PIDs, repeated severe, refractory or unusual infections, bronchiectasis and therapy-resistant asthma (or other allergies) and autoimmune/inflammatory comorbidities.

CLINICAL INDICATORS FOR PIDS
Recurrent pneumonia
>4 bacterial infections per year
Bronchiectasis
Therapy-resistant asthma
Abscesses (skin or organs), recurrent sinusitis, two or more middle ear infections within a year
Infections in unusual locations, unusual (opportunistic) infections or infections that are more severe/prolonged than might be expected
Persistent oral candidiasis or fungal skin infections
Recurrent and/or severe viral infections
Complications associated with routine vaccinations
A family history of PID
Inflammatory bowel-like symptoms
Autoimmune symptoms
Granulomas

ACHIEVING A DIAGNOSIS OF PID

Initial investigations that may have been performed in the primary care setting include complete blood count including leucocytes and differentiation, IgA, IgM, IgG and IgE. A computerised tomography (CT) scan should be requested in cases of recurrent pulmonary infections to assess lung damage.

Additional tests that should be undertaken once a patient has been referred for specialist evaluation include a vaccination response in case of recurrent infections. In a patient with normal Ig levels an impaired vaccination response may point to a selective antibody deficiency with normal immunoglobulins (SADNI). Microbial diagnosis should also be undertaken by RNA, DNA or direct antigen testing to confirm a diagnosis, especially if a patient has hypogammaglobulinaemia or has already been initiated on Ig therapy. It may be necessary to involve additional specialists to achieve a diagnosis, usually a clinical immunologist, but possibly also a specialist in infectious diseases or a haematologist. A key step is to rule out haematologic malignancy as an alternative diagnosis.

BUILDING A MULTIDISCIPLINARY TEAM FOR PATIENTS WITH PIDs

Patients with PIDs may present with comorbid conditions (such as type 2 diabetes mellitus, autoimmune cytopenias, colitis and bronchiectasis) which may require the involvement of additional specialist physicians. Additional complications such as congestive heart disease during IVIG can cause a problem due to volume overload and the presence of haemolytic anaemia may require input from cardiology and haematology specialists. Patients with PIDs are more vulnerable to the development of malignancies, especially malignant lymphoma. Oncology specialists may need to be included as part of a multidisciplinary team.

Referral to centres specialising in the management of PIDs may be appropriate where available.

KEY MESSAGES FOR INTERNAL MEDICINE SPECIALISTS

- PIDs affect an estimated 1 in 2000 persons.
- While more severe PIDs are usually diagnosed during childhood, PIDs can present throughout a person's lifetime.
- Improved medical care during life resulted in more elderly with PIDs with the development of age-related diseases such as type 2 diabetes, heart disease etc
- Patients with complex, non-specific conditions are often referred for specialist evaluation by internal medicine physicians for whom a variety of clinical indicators can raise the suspicion of PIDs.
- Clinical indicators include a family history of PIDs, repeated severe, refractory or unusual infections, bronchiectasis and therapy-resistant asthma (or other allergies) and autoimmune/inflammatory comorbidities.
- Patients with PIDs may require care from a range of specialties depending on their individual symptoms and the organ systems affected.

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 national patient organisations active 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**

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