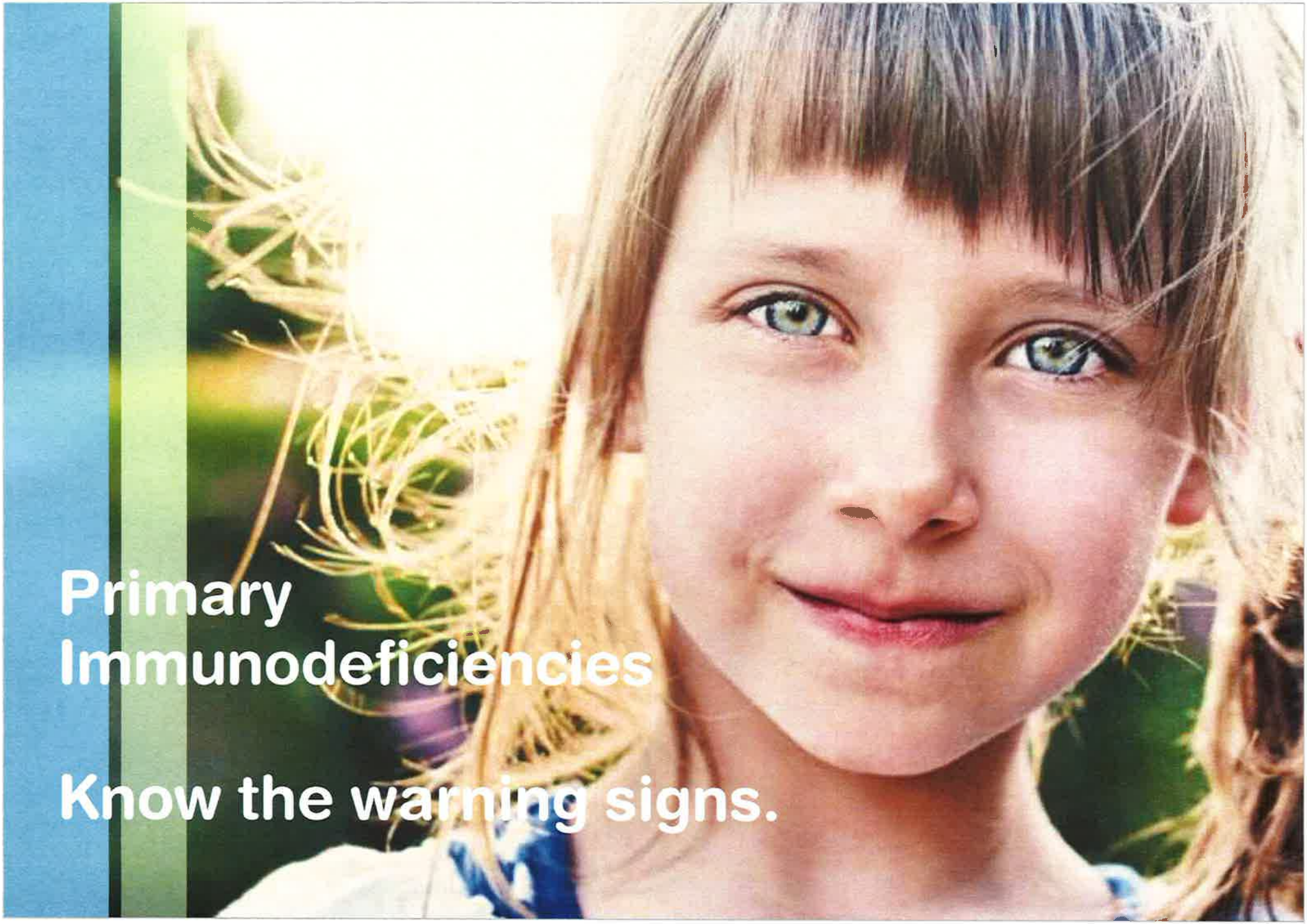
Primary
Immunodeficiencies
Know the warning signs.

What is Primary Immunodeficiency?

Primary Immunodeficiencies (PIs) are hereditary and genetic defects of the immune system that cause increased susceptibility to a wide range of infections, affecting the skin, ears, lungs, intestines and other parts of the body. PI often presents itself in the form of otherwise ordinary infections, which do not respond to treatment. Too often infections are treated while missing the underlying cause, allowing the illnesses to recur, and leaving the patient vulnerable to vital organ damage, physical disability, and even death. PIs may also predispose patients for allergies, autoimmunity and cancer.

Prevalence

Current diagnosis levels suggest that 1 in 8-10,000 people have a severe primary immunodeficiency that significantly affects their health and life expectancy. However, experts estimate that between 70-90% of PIs remain undiagnosed, and the true incidence of some PIs within the general population could be as high as 1 in 250-500.[1-3]

200

There are currently more than 200 identified PI conditions.[4]

70-90%

It is estimated that 70–80% of PIs remain undiagnosed, globally.

Early diagnosis is critical

From common infections and fevers to pneumonia and bronchitis, the symptoms of PI come in many different forms. Despite this challenge, diagnosis can be simple and inexpensive.

The principal clinical manifestation of immunodeficiency is increased susceptibility to infection.[L5] PIs are often overlooked because they are thought to be common infectious illnesses (e.g. sinus/ear infections, atypical febrile illness or bronchitis). If left undiagnosed or poorly treated, PIs can have a devastating effect on the lives of patients and their families. Recurrent infections are frightening and frustrating and may cause permanent damage to vital organs, resulting in disability or death. Children miss time from school and study while adult patients are forced to take time off work and may require care workers to look after them.[L6]

Early diagnosis and access to appropriate treatment enables people living with a PI to lead normal productive lives whilst significantly reducing healthcare expenditure. Lack of awareness of PI remains a major issue, and due to this problem the majority of patients are diagnosed too late.

Methods of detection

A careful history, physical examination and simple, inexpensive blood test known as CBC (Complete Blood Count) can identify the majority of patients. For precise diagnoses of PIs, more advanced immunological and genetic tests are required and must be administered by an experienced specialist.

An immunologist can help with diagnosis, evaluation and treatment.
For more information, or to find an immunologist in your area, please find the contact information on the back side of this brochure.

Importance of early detection and treatment

Accurate early diagnosis and proper treatment of PI may:

- Prevent severe complications and tissue damage
- Prevent chronic organ damage
- Decreased morbidity and mortality
- Avoid secondary costs due to illness
- Dramatically improve quality of life

CBC

On those potential patients detected, a simple and relatively inexpensive Complete Blood Count (CBC) test can identify over 95% of PI patients.[4]

Know the warning signs

A good first step in correctly diagnosing a Primary Immunodeficiency is a simple assessment of the 10 Warning Signs.

There are a number of signs and symptoms of a Primary Immunodeficiency disease. Patients with PI have an increased susceptibility to recurrent and persistent infections, varying in severity from ear and sinus infections to lung infections, meningitis and septicaemia, amongst others. Less commonly, patients with PI may have abscesses in internal organs, lymph nodes or skin, or infections in their bloodstream.

Other indications

There are particular infections caused by germs that primarily afflict immunodeficient patients, in which case the infection-causing pathogen itself may serve as a warning sign for PI. Patients with PI may also have a variety of autoimmune disorders, rheumatologic diseases or gastrointestinal problems. In some cases these problems can result from an intestinal infection; in others, they may be a reflection of an autoimmune or inflammatory disorder.

Adult warning signs

1. Two or more ear infections within 1 year
2. Two or more sinus infections within 1 year, in the absence of allergy
3. One pneumonia per year for more than 1 year
4. Chronic diarrhea with weight loss
5. Recurrent viral infections (colds, herpes, warts, condyloma)
6. Recurrent need for intravenous antibiotics to clear infections
7. Recurrent, deep abscesses of the skin or internal organs
8. Persistent thrush or fungal infection on skin or elsewhere
9. Infection with normally harmless tuberculosis-like bacteria
10. A family history of PI

Childhood warning signs

1. Four or more new ear infections within 1 year
2. Two or more severe sinus infections within 1 year
3. Two or more courses of antibiotic treatment with little effect
4. Two or more pneumonias within 1 year
5. Failure of an infant to gain weight or grow normally
6. Recurrent, deep skin or organ abscesses
7. Persistent thrush in mouth or fungal infection on skin
8. Need for intravenous antibiotics to clear infections
9. Two or more deep-seated infections including septicemia
10. A family history of PI

Suggested laboratory investigations in case of recurrent bacterial infections:

- *White blood cells with differential count (CBC test)*
- *Determination of the number of lymphocyte subsets*
- *Quantification of IgG, IgA, IgM, IgF*
- *Documentation of infection proneness (patient diary)*
- *Measurement of antibody responses to vaccine components (in children only)*

PI is treatable

Unlike with many other rare diseases, effective treatment options are available to allow many patients with PI to lead normal lives. None of these therapies, however, will reverse the damage of late diagnosis.

In undiagnosed or misdiagnosed patients, treatments are focused on the frequent and long-term use of antibiotics. Improved diagnosis of PI could therefore have a positive impact in reducing the use of antibiotics, minimising future infections, improved use of health care facilities, reduced costs and an improvement in the patient's quality of life.

A range of treatments are available

The first step in addressing PI is to treat the current infection, which can be done using antivirals, antibiotics and antifungals. In order to prevent future infections, patients with antibody deficiency can be prescribed prophylactic antibody replacement therapy, in which the patient receives an infusion with antibodies – so-called immunoglobulins – extracted from human plasma. The therapy is normally either infused intravenously or subcutaneously.

If treatment with immunoglobulins is instituted early and is individually tailored, antibody replacement therapy is effective in preventing infections and consequent damage due to repeated infections. Infection rates in people undergoing antibody replacement therapy are similar to infection rates of the normal population, and scientific studies have shown significant improvements in patient-reported health and quality of life for patients with PI. Home therapy has been shown to further improve the quality of life of patients and their families.[16]

More severe forms of PI may require bone marrow or stem cell transplantation, or even gene therapy, which aim at correcting the immunodeficiency through reconstitution of the normal immune system.

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Jeffrey Modell Foundation

ABOUT THE JEFFREY MODELL FOUNDATION

The Jeffrey Modell Foundation is a global non-profit organisation established in 1987 by Vicki and Fred Modell in memory of their son, Jeffrey, who died at the age of 15 after struggling with a Primary Immunodeficiency.

The Foundation is dedicated to basic and clinical research, physician education, patient support, public awareness and advocacy.

JEFFREY MODELL CENTERS NETWORK

The Jeffrey Modell Centers Network reaches all corners of the globe. It is comprised of Jeffrey Modell Diagnostic and Research Centers and a referral network of hundreds of Expert Immunologists at academic teaching hospitals and medical schools.

For more in-depth information, or to receive diagnostic assistance, contact your local JMF Center at:

(Who to contact + info about JMF and the local centre(s)...)

References

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