World PI Week 22-29 April 2018

Tackling the diagnostic challenge can change the lives of people with PI

Around the world, Primary Immunodeficiencies (PI) are largely underdiagnosed and underreported with an estimated 70-90% of people living with PI remaining undiagnosed[1]. Similar to other diseases, early testing and diagnosis are essential first steps towards appropriate life-enhancing care and treatment for patients.

The eighth World Primary Immunodeficiency Week (World PI Week), celebrated from the 22nd to the 29th of April 2018 with the theme "*My future starts with early testing and diagnosis of PI*" has the objective to raise awareness of early testing and diagnosis of PI worldwide.

PI are "rare diseases" and a group of inherited and genetic disorders of the immune system that is either partly or totally missing or does not function properly. People with PI are more prone to a wide range of infections that are often chronic, persistent, debilitating and affect different parts of the body. Over 350 forms of PI exist[2] and they can lead to an increased susceptibility to autoimmune disorders, autoinflammatory diseases, allergy diseases and cancer, in parallel with recurring infections.

Because of the commonalities between PI symptoms and other "common" infections, diagnostic is complex, and practitioners often treat the infections missing the underlying cause. The increasing number of PI being recognized, a relatively low awareness of PI and the lack of diagnostic facilities also delay a timely diagnosis. There is often a perception that recurring infections are part of a child's normal development causing difficulty for non-immunologists to identify PI and diagnose it early. Diagnostic delays are not only damaging to patients' health but also have an impact on healthcare systems due to excessive use of health resources caused by various visits to a variety of different specialists.

The PI diagnostic pathway starts with a detailed evaluation of the immune system through several types of testing. The most severe forms of PI are more frequent in infancy and early childhood and when a family history of PI exists, it can facilitate the early detection. Yet, in other cases, patients can live with the symptoms and recurring infections for years before the correct tests and diagnostic are made. Since defects in genes are involved in the mal or non-functioning of the immune system and contribute to the complex nature of PI[3], recent advances in genetic technology have contributed to diagnosis[4]. However, genetic testing is not available in many countries, in particular in the developing world.

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[1] Primary Immunodeficiencies (PID) - Driving Diagnosis for Optimal Care in Europe, European Reference Paper.

[2] Bousfiha A, Jeddane L, Picard C, Ailal F, Bobby Gaspar H, Al-Herz W, Chatila T, Crow YJ, Cunningham-Rundles C, Etzioni A, Franco JL, Holland SM, Klein C, Morio T, Ochs HD, Oksenhendler E, Puck J, Tang MLK, Tangye SG, Torgerson TR, Casanova JL Sullivan KE. The 2017 IUIS Phenotypic Classification for Primary Immunodeficiencies. J Clin Immunol. 2018 Jan;38(1):129-143. doi: 10.1007/s10875-017-0465-8. Epub 2017 Dec 11

[3] IPOPI, Primary immunodeficiencies — Diagnosis of primary immunodeficiencies (1st edition). December 2012

[4] Chapel H, Prevot J, Gaspar HB, Español T, Bonilla FA, Solis L, Drabwell J and The Editorial Board for Working Party on Principles of Care at IPOPI (2014) Primary immune deficiencies – principles of care. Front. Immunol. 5:627. doi: 10.3389/fimmu.2014.00627

The exact prevalence of PI worldwide is still unknown[5] and it is unclear whether the incidence and frequency of PI at national levels have been estimated accurately. Proper studies at country levels and national registries are valuable tools to assess the proportion of affected individuals in a general population. These tools can guide policy-making by Governments to tailor national policies to the needs of the country.

In order for healthcare professionals to recognize different patterns of clinical presentations of PI, there is a need for greater public awareness of symptoms and medical research, increased education among primary and specialist care providers, and an enhanced recognition of the role of awareness campaigns, patient organisations and scientific societies. Improved training of immunologists is essential in facilitating improved diagnosis of people living with PI. Political and financial efforts also play a key role in educational efforts aimed at the medical and nursing communities[6].

It is crucial to develop better diagnostic facilities and guarantee patient access to them, as well as ensure greater availability of laboratory tests to investigate newly described PI. Upscaling screening in patients with recurrent infections, irrespective of age, and ensuring that routine newborn screening programmes for severe forms including Severe Combined Immunodeficiency (SCID) are implemented in both public and private healthcare settings worldwide are of upmost priority. Access to genetic testing should be made available to patients and widespread in all medical specialties to provide earlier detection of PI and diagnose unknown forms of the diseases.

The scientific, patient and advocacy communities have taken a number of initiatives to decrease time to diagnosis. These include raising awareness of the warning signs of PI, the development of "Red Flags"[7] lists to alert and educate healthcare professionals and of a multi-stage diagnostic protocol for screening of PI designed for non-immunologists[8] such as adult physicians and pediatrics.

Timely diagnosis and appropriate treatment remain the keys to successful management of people with PI[9]. While they can be complex, healthcare authorities, governments and state agencies in all countries should work in collaboration with public and private healthcare providers and other healthcare actors to establish the policies and financial measures needed to facilitate an early diagnosis of people with PI and ensure their access to services, in order to manage the impact of PI on their lives.

[5] N.Rezaei and al. Primary Immunodeficiency Diseases: Definition, Diagnosis, and Management. Second edition, Springer. 2017

[6] Chapel H, Prevot J, Gaspar HB, Español T, Bonilla FA, Solis L, Drabwell J and The Editorial Board for Working Party on Principles of Care at IPOPI (2014) Primary immune deficiencies – principles of care. Front. Immunol. 5:627. doi: 10.3389/fimmu.2014.00627

[7] Red Flags for Primary Immunodeficiency. Immunodeficiency Canada, Scientific Director and Medical Advisory Board. 2014

[8] E. De Vries, Clinical Working Party of the European Society for Immunodeficiencies (ESID). Patient-centred screening for primary immunodeficiency: a multi-stage diagnostic protocol designed for non-immunologists. 2006

[9] N.Rezaei and al. Primary Immunodeficiency Diseases: Definition, Diagnosis, and Management. Second edition, Springer. 2017