

## Primary Immunodeficiencies

### A Comprehensive Approach to Diagnosis

#### About Primary Immunodeficiencies

Primary immunodeficiency disorders (PIDD) impair the function of the immune system, and are not due to secondary factors such as viruses or chemotherapy. Patients with intrinsic (genetic) defects have increased susceptibility to recurrent and persistent or unusual infections, and they may have autoimmune or cancer related symptoms.

**Because most PIDDs are life long conditions, requiring therapies such as intravenous gamma globulin infusions, antibiotic therapies, or bone marrow transplantation, it is very important to perform a detailed diagnostic evaluation before initiating therapies that will be continued in an open-ended fashion.**

#### Advanced Diagnostic Laboratories (ADx) at National Jewish Health: A comprehensive approach to PIDD



#### Early indicators of immunodeficiency disease [1]:

- Eight or more new ear infections within one year.
- Two or more serious sinus infections within one year.
- Two or more months on antibiotics with little effect.
- Two or more pneumonias within one year.
- Failure of an infant to gain weight or grow normally.
- Recurrent, deep skin or organ abscesses.
- Persistent thrush in mouth or elsewhere on skin, after age one.
- Need for intravenous antibiotics to clear infections.
- Two or more deep-seated infections.
- A family history of Primary Immunodeficiency.

#### ADx recommends the following panel as an initial screen:

Serum immunoglobulin levels	WBC with differential
Specific antibody titers to vaccine antigens	Neutrophil staining, morphology
Flow cytometry to enumerate lymphocyte subsets	CH50 (total hemolytic complement activity)
Cutaneous delayed hypersensitivity	AH50 (alternative pathway hemolytic activity)

## PIDD is a Diverse and Underdiagnosed Set of Disorders

Most PIDDs are rare: the most common diagnosis is IgA deficiency, with a frequency of about one case per 500. Excluding developmental delay of immunoglobulin production (transient hypogammaglobulinemia of infancy), the next most common is DiGeorge syndrome (about 1 in 3000 live births). Other commonly recognized syndromes are X-linked Agammaglobulinemia (Bruton's Disease), Common Variable Immune Deficiency, and Severe Combined Immune Deficiency (boy-in-the-bubble disease).

More than 150 PIDDs have been described, involving over 100 genes and more than 4,500 mutations [2, 3]. Since 1997, when the World Health Organization listed 60 diseases, new disorders have been recognized at an accelerated rate and the genetic defects for most PIDs have been identified.

Estimated conservatively, about 25,000 – 50,000 new cases of PIDD are diagnosed annually in the US. However a recent study estimates a prevalence of 160,000 – 350,000 diagnosed cases, and a population frequency of 1:1200 [4]. The NIH estimates that at least 500,000 US cases of PIDD remain undiagnosed.

Primary immunodeficiencies are frustrating to patients, families and clinicians alike because the diagnosis is often not made before the occurrence of severe infections, permanent damage to organs such as the ears or lungs, physical disability, or even tragic loss of life. The healthcare costs of undiagnosed PID are high: a 2007 study commissioned by the Jeffrey Modell Foundation [1] estimates:

- Each undiagnosed patient with an underlying PID costs the healthcare system an average of \$102,736 annually.
- Each diagnosed patient with a recognized PID costs the healthcare system an average of \$22,696 annually.
- The economic impact of PID diagnosis (vs undiagnosed) represents an average savings of \$79,942 per patient.

The ADx team of laboratory experts stand ready to assist clients with education, interpretation, and selection of follow-up testing. With over 100 years of combined experience, these leaders may be accessed through the ADx Decision Support Line:

- Patsy Giclas, PhD
- Ronald Harbeck, PhD, D (ABMLI)
- Ashley Frazer-Abel, PhD
- Vijaya Nagabhushanam, MD, PhD

**Contact us at 800.550.6227 or online at [njlabs.org](http://njlabs.org)**



### References:

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