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The relevance of collaborative work: the Latin American Society for Immunodeficiencies (LASID) registry model

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The Latin American Society for Immunodeficiencies (LASID) registry was established in April 2009 with the support of the European Society for Immunodeficiencies (ESID), the Jeffrey Modell Foundation, Baxter Bioscience and Conselho Nacional de Pesquisa e Desenvolvimento Científico (CNPq, Brazil).

The mission of LASID is to educate and increase awareness of primary immunodeficiencies (PIDs), and educate doctors in Latin America to recognize PIDs according to the different phenotypes.

The LASID registry has evolved from 25 centres in seven countries in April 2009, to now include 93 centres in 14 countries in July 2014. In total, 5203 PID cases have been reported. To date, the rate of response has been highest in Argentina, with 1942 (37%) reported cases, followed by Brazil with 1175 (23%) cases, Mexico with 854 (16%) cases and Columbia with 817 (16%) cases. Of the 5203 cases, antibody defects were recorded in 56% of patients, followed by well-established syndromes with immunodeficiency in 18% of patients, combined immunodeficiency in 10% of patients and phagocytic disorders in 9% of patients.

Based on an estimated frequency of one PID case for every 10 000 people in Latin America, and the patients currently recorded in the registry, we can estimate the number of patients still to be identified in each country. For example, Argentina has identified the greatest proportion of PID cases, with 1942 cases of an expected total of 3900 cases identified. In comparison, 1175 of 18 600 have been identified in Brazil, 854 of 10 600 have been identified in Mexico and 817 of 4200 have been identified in Columbia.

Evaluation of hyper-immunoglobulin (Ig)M syndrome is one of three clinical epidemiological projects developed within the LASID registry programme [1]. Hyper-IgM syndrome is a group of disorders characterized by normal to elevated levels of IgM, and absent or decreased levels of IgA, IgE and IgG. CD40 ligand (CD40L) deficiency is the most common form of hyper-IgM syndrome, which is estimated to represent 75% of cases [1]. Another form of hyper-IgM is a deficiency of activation-induced cytidine deaminase (AID). Patients with AID-deficiency are susceptible to extracellular bacterial infections, while patients with CD40L-deficiency are additionally susceptible to viral, fungal and intracellular bacterial infections [1,2].

A recent publication from the LASID registry summarizes the clinical and molecular characteristics of a cohort of 58 hyper-IgM patients [1]. In this cohort, genetic defects were found in 37 patients, 35 of whom were CD40L-deficient (causing an X-linked form of hyper-IgM syndrome) and two were AID-deficient. Following genetic analysis, five novel mutations which abolished CD40L protein production on activated $CD4^+$ T cells were identified [1]. The most frequently observed clinical manifestation of hyper-IgM syndrome was pneumonia, which affected 80% of CD40L-deficient patients. *Pneumocystis jirovecii* was the most frequent cause of pneumonia, followed by cytomegalovirus, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, parainfluenza virus type II and other unknown pathogens. Other common clinical manifestations of hyper-IgM syndrome included upper respiratory tract infections (63%), neutropenia (48%) and chronic diarrhoea (46%) [1].

Our study identified several microorganisms that were not previously associated with hyper-IgM syndrome, including *Aspergillus* spp., *Microsporidium* spp. and *Isospora belli*, which caused infections such as severe pneumonia and chronic diarrhoea in CD40L-deficient patients. In addition, CD40L-deficient patients frequently developed other fungal infections such as paracoccidioidomycosis. Recent studies have found that paracoccidioidomycosis, an infection endemic to South America which has been previously associated with a mutation in the beta 1 subunit of the interleukin-12 receptor, can also occur in CD40-deficient patients [1–3].

It should be noted that the different clinical phenotypes observed may be attributed to different environmental pressures. For instance, the occurrence of fungal infections may

be higher in Latin America due to the prevailing warm and humid conditions.

In conclusion, the LASID registry programme has evolved significantly to become a centralized resource for clinical immunologists throughout Latin America and beyond. The clinical epidemiological data are beginning to indicate that PIDs may present with distinct clinical features, which must be communicated to Latin American physicians in order to achieve early diagnosis and treatment.

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Disclosure

A. C. N. has no conflicts of interest to disclose.

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