

# Inborn errors of metabolism in Latin America: challenges and opportunities

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**Abstract** Latin America includes more than 40 countries and possessions, and its population of 570 million has an important representation of the three main human races. The area is experiencing an economic improvement, progressively bringing the inborn errors of metabolism (IEM) to a higher level among health priorities. Challenges to the progress of the IEM field include the huge disparities, the high prevalence of malnutrition and infections, the co-existence of very different models of public health services, the unstable socio-economic and political conditions, and the difficulties in integrating the countries. However, a rapidly changing social and economic environment is presenting many opportunities to the IEM field, like the improvements in infrastructure, the concentration of the population in urban areas, the continuous growth of

neonatal screening, the use of filter paper samples, the availability of internet communication, and the interest in IEM by the new population medical genetics discipline. Analyzing this picture, several proposals are presented, such as the development of activities of provision of health services, education and research as an integrated package, the increase in training of human resources, the expansion of access to diagnostic tests, and the use the neonatal screening framework to expand the provision of services. In a continent with few IEM centers, there is a major need for such groups to work in collaboration, complementing each other's capabilities, providing training of human resources, and developing joint projects. The integration of these groups into a large transnational network of reference centers would be a major task for the coming years.

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## Latin America

Latin America includes 33 independent countries and 11 possessions, geographically spread over 21 million km<sup>2</sup> across South America, Central America, North America and the Caribbean ([www.wikipedia.org](http://www.wikipedia.org)).

In Latin America, there is important representation and heavy miscegenation of the three main human races (Sans 2000). The dominant cultural heritage, however, is much more homogeneous, due to the—sometimes ruthless—imposition of European culture over many centuries. In due course, the population of 570 million inhabitants has developed two predominant languages: Spanish (2/3 of the population, spoken in the vast majority of countries) and Portuguese (which, although spoken only in Brazil, is the native language of 1/3 of the population).

The heterogeneous distribution of the ethnic groups leads to important differences in disease incidences. Taking

phenylketonuria (PKU) as an example, its incidence of around 1:15,000 in the Southern Cone, where the presence of European descendants is higher, contrasts with a much lower figure (around 1:50,000) in some northern areas where the proportion of descendants of blacks and native Americans is more important (Borrajó 2007)

The area is experiencing an economic improvement in the last decades, with some countries very close to the “developed country” status based on per capita gross national income (GNI), as shown in Table 1 (source: [www.geo.worldbank.org](http://www.geo.worldbank.org)). Also, most countries are classified as having high “human development index” scores, with no country showing a low score, typical of least developed nations (United Nations Development Programme, [www.undp.org](http://www.undp.org)).

The predominant occidental culture, miscigenated ethnicity and economic background of recent development but still with huge disparities makes Latin America an interesting case of mixed challenges and opportunities in the IEM field.

## Challenges

The overall characteristics of Latin America impose several challenges in the field of IEM, including:

### 1) Disparities:

The economic improvement apparently is not significantly contributing to shorten the huge gap between the rich and the poor on this continent. Impressive disparities are noticed not only among nations (US\$ 10,000 of GNI per capita in Mexico vs US\$ 500 in Haiti—[www.geo.worldbank.org](http://www.geo.worldbank.org)) but also among affluent and marginalized groups in each country. These disparities reflect on the different availability in the provision of health services from country to country, and also on different access to these services by different groups inside the same country. Neonatal screening is an example of program which is provided free of charge and available to almost 100% of newborns in countries like Chile, Costa Rica, Cuba, and Uruguay, and is available

**Table 1** Selected data (information refers to 2007 data) of Latin American countries, ranked by per capita gross national income (GNI) (the table includes only independent countries with over 1,000,000 inhabitants)

	GDP <sup>a</sup> (billion US\$)	Population (million)	GNI <sup>b</sup> per capita (US\$)	Child mortality (under 5/1,000)	Life expectancy (years)	HDI <sup>c</sup>
Mexico	1022	105	9,400	35	75	0.854
Chile	163	17	8,160	9	78	0.878
Uruguay	24	3.3	6,620	14	76	0.865
Venezuela	228	27	7,550	19	74	0.844
Brazil	1333	190	6,060	22	72	0.813
Argentina	262	40	6,040	16	76	0.866
Costa Rica	26	4.4	5,520	11	79	0.854
Panama	19	3.3	5,500	23	76	0.812
Cuba	54 <sup>d</sup>	11	4,900 <sup>d</sup>	7	78	0.863
Jamaica	13	2.7	4,420	31	73	0.766
Colombia	208	44	4,100	20	73	0.807
Rep. Dom.	41	9.7	4,070	38	72	0.777
Peru	107	28	3,340	20	73	0.806
El Salvador	20	5.9	3,200	24	71	0.747
Ecuador	46	13	3,150	22	75	0.806
Guatemala	34	13	2,470	39	70	0.704
Paraguay	12	6.0	1,710	29	72	0.761
Honduras	12	7.1	1,590	24	70	0.732
Bolivia	13	10	1,220	57	66	0.729
Nicaragua	5.7	5.6	990	35	73	0.699
Haiti	6.7	9.6	520	58	61	0.532

<sup>a</sup> Gross domestic product (source: [www.geo.worldbank.org](http://www.geo.worldbank.org))

<sup>b</sup> Gross national income, per capita (source: [www.geo.worldbank.org](http://www.geo.worldbank.org)): low income US\$ 905 or less; low middle income US\$ 906–3,595; upper middle income US\$ 3,596–11,115; high income US\$ 11,116 or more

<sup>c</sup> Human development index (sources: [www.unpd.org](http://www.unpd.org) and [www.wikipedia.org](http://www.wikipedia.org)): very high HDI (developed countries) 0.900 or more; high HDI (developing countries) 0.800–0.899; medium HDI (developing countries) 0.500–0.799; low HDI (least developed countries) 0.499 or lower

<sup>d</sup> Source: [www.indexmundi.com](http://www.indexmundi.com)

only on a limited basis in most of the remaining countries (Borrajó 2007). An even higher heterogeneity occurs in the access to the treatment of metabolic diseases, with limited availability in most countries.

## 2) Low priority of genetic metabolic diseases:

This is not difficult to understand, as most of these countries still face important problems like malnutrition and infectious diseases, leaving metabolic diseases down on the priority list. However, the decline in child mortality over the last decades in most Latin American countries (and positive changes in several other indicators) suggests that this situation will improve in the coming years (Mathers and Loncar 2006)

## 3) Heterogeneous templates of health services:

There is no predominant model of health service in Latin America, with major countries presenting different solutions. While in Cuba there is an universal health assistance with no choice, in Chile there are different services according to the citizen option (and payment capacity). In between, Brazil has only one public health service, with many deficiencies (Ocké-Reis and Marmor 2010), but available to all, with a supplementary private health insurance to those who can afford the payment. In this scenario, it is difficult to make a proposal for an IEM approach suitable for all or almost all countries.

## 4) Economic and political instability:

Even experiencing a democratic period in most countries, Latin America is still far from social, economic, and political stability. Crises are present in the recent history of many Latin American countries, and some are still in turmoil. This brings difficulties to any project which needs support in the long-term, as well as sustained policies. As many Latin Americans experience, it is usually less difficult to purchase an expensive item of equipment than to keep it running with regular maintenance and regular supply of consumables. It is also difficult to hire personnel to provide technical support in the long term, as short-term policies linked more to the government than to the nation are the rule.

## 5) Difficulty in integrating countries in a large transnational community:

While the idea of a community of nations was historically present, it is still a distant dream. In practical terms, it is very difficult to establish collaborative efforts, and even the simple shipment of samples from one country to another faces an incredible list of sanitary and administrative barriers. The same applies to doctors, scientists and patients who want to take advantage of the expertise of a reference center located in a foreign country.

## Opportunities

Despite the difficulties, the Latin American historical conditions and recent changes bring several opportunities in the field of IEM, which include:

### 1) Infrastructure improvements:

A noticeable development in infrastructure has occurred in most Latin American countries in the last decades, especially in communications, transport, and energy. Nowadays, mobile phones are available to most people in Latin America, and travel to reference centers has become easier with better roads and low-cost flights.

### 2) Large urban concentrations:

The growth of Latin America resulted in the migration of a large part of the population from the rural areas to the cities, with the formation of very large urban agglomerates in most countries. The formation of these mega-cities brings several problems (such as, for example, housing and transportation) but, on the other hand, could help the delivery of health services as populations are living closer to the health centers and other modern facilities.

### 3) Neonatal screening programs:

The emergence of neonatal screening programs in most Latin American countries is contributing, among other benefits, to show that a public health program for rare diseases could be delivered to the population. In some cases, the enlargement of such programs is enabling the population to benefit from facilities for the diagnosis and treatment of many more metabolic diseases (Borrajó 2007).

### 4) Samples in filter paper:

The difficulties with shipment of samples, not only between countries but also inside countries with large areas and/or logistic problems, accelerated the expansion of the use of filter paper samples. A pioneer work by Chamoles et al. (2001) in Argentina with dried blood spots for the diagnosis of LSDs is well known worldwide, and recent developments in Colombia and Brazil (Uribe et al. 2009) in the use of dried urine will also be a major contribution to overcoming the logistic problems with the transportation and importation/exportation of biological samples for IEM investigation.

### 5) Internet:

The worldwide web is bringing professionals from different parts of the continent much closer. This is very important, especially if we consider that it is difficult for everyone to accumulate experience with rare diseases like IEM. A growing trend to exchange messages, images, laboratory results and much other information, very

important for the correct diagnosis and appropriate management, is observed almost universally in Latin America.

#### 6) Population medical genetics

The population genetics approach to medical genetics problems is bringing new possibilities to the Latin

American teams which work with inborn errors of metabolism. Well-known examples such as the one of GM2 gangliosidosis in Argentina (Kremer et al. 1985) have multiplied, with indications of clusters of Niemann-Pick B disease in Chile, MPS II in Bolivia, and MPS IV A in Colombia, among others. A recent report indicates an increased incidence of MPS VI in Northeast Brazil.



**Fig. 1** Map of Latin America, indicating the location of the most important reference centers for diagnosis of IEM (based on scientific output, not a complete list)

## Comments and proposals

Observing how the groups working with IEM in Latin America overcame the challenges and took advantage of the opportunities, it is possible to list some proposals which could contribute to increase the rate of success of such groups:

- 1) Integrate activities of provision of health services, education and research:

When working in countries where instability is the rule, to depend on one major funding source is usually risky. Successful groups usually have a diversified funding source. Having support from the health sector, research agencies and educational funds could be very helpful when there are budget cuts (very common in the Latin American countries) which usually affect some sectors more than others.

- 2) Increase investment on training of human resources on diagnosis and treatment of IEM:

Trained personnel is a need, and a major effort should be dedicated to appropriately educate technicians, through traditional education programs but also with training in established IEM centers. The Latin American School of Medical and Human Genetics ([www.cladegen.org](http://www.cladegen.org)) is an initiative already in practice which is contributing to this goal.

- 3) Expand information supply and access of health professionals acting on the area of IEM to reference centers:

Despite the presence of well-established reference centers in some countries (Fig. 1), the information provided by these centers should be easily available to health professionals. Also, access to tests should be facilitated, not only in terms of costs involved but also in the operational logistics of collection and transportation.

- 4) Use the neonatal screening framework to expand the provision of diagnostic and management services for high-risk patients:

The successful experience of identifying IEM through newborn screening is a very good example on how to integrate diagnosis and management of metabolic diseases with a public health approach. Its progressive expansion to include other diseases besides PKU would be a major contribution to the IEM field.

- 5) Work with government authorities to overcome difficulties to transport samples across borders:

The increased mobility of people and goods across borders over the last decades generated a reaction by

customs and health authorities to increase control, generating delays and difficulties with the transportation of samples, patients, and even technical staff. There is an urgent need of the IEM community, along with other groups, to approach authorities and obtain exemptions and special rules for the case of rare metabolic diseases, following the successful examples of initiatives from other groups, like HIV and neonatal screening laboratories.

- 6) Networks:

The organization of networks involving the groups which work with IEM in Latin America, although still very preliminary and mostly restricted to domestic groups inside some countries, would be a rational way to optimize the use of available resources. An example of such a network is the RELAGH (Latin American Network of Human Genetics) created in 2001 (Giugliani and Matte 2004). Another initiative is the MPS Brazil Network, established in 2004 as a partnership of nine Brazilian services which are active in the diagnosis and/or treatment of mucopolysaccharidoses in Brazil. This network has diagnosed over 1,000 MPS patients since then, doubling the previous rate of diagnosis by offering easy information and free access to diagnostic tests (Schwartz et al. 2008).

Finally, in a continent with few reference centers for IEM, there is a major need for such groups to work in collaboration, complementing each other's capabilities, providing training of human resources and developing joint projects, also in the research area. Integrating these groups into a large transnational community of reference centers would be a major advance, enabling different groups to take reciprocal advantage of its strengths to accelerate the growth of this area on the continent. The coordinators of these centers and the Latin American Society of Inborn Errors of Metabolism and Neonatal Screening could have a fundamental role in pushing this proposal forward.

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