

Genetic Disorders and Congenital Defects in Latin America and the Caribbean

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Socioeconomic Indicators

- 560 million inhabitants in 35 countries
- Average gross national income per capita: \$3,580 (USA: \$41,000)
- Average annual per capita health expenditure: \$262 (USA: \$5,700)
- Half the population lives in poverty and 27.6% earns less than \$2 per day
- 78% of the population lives in urban areas
- Poor educational levels, low status of women
- Authoritarian traditions, rigid religious directives
- Great health and socioeconomic disparities between and within countries

Health Profiles

- Infant mortality rate fell from 61 to 24 per 1000 over the last 20 years (2006 rates range: 6.5 (Cuba) -78 (Haiti))
- Epidemiologic accumulation: coexistence of diseases of poverty (infections and nutritional), with a rise in NCD (cardiovascular, cancer, diabetes, obesity, mental illness)
- Health services concentrated in big cities, significant inequities in access, privatization by for-profit entities

Reproductive Health Indicators

- Fertility rate declined from 4.1 in 1980 to 2.4 in 2006 (2.0 in USA)
- Maternal mortality: 90 per 100,000 lb, range: 17.3 (Chile), 523 (Haiti) (12 in USA)
- Births at maternal ages over 35 years: 13.5%. Range: 4.3% (Cuba), 22.5% (Peru)
- Low use of contraceptives,
- Induced abortion largely illegal, high rate of induced abortions: 50 per 100,000 (10-20 in industrialized countries), unsafe abortion is responsible for 25% of maternal mortality

Latin American Collaborative Study of Congenital Malformations

- In existence since 1967
- Network of maternity hospitals in South America where 200,000 live births per year are examined.
- All major and minor malformations diagnosed in live births weighing 500 g or more are detailed and registered, along with key demographic and pregnancy information on index cases and controls

Latin American Collaborative Study of Congenital Malformations

- Case-control analysis of demographic, pregnancy and newborn data
- Database of over 100,000 malformed infants and controls
- DNA bank of major malformations since 1998
- Has produced some of the finest epidemiologic data on congenital malformations in South America

Epidemiology of Genetic Disorders and Congenital Defects

- Prevalence at birth of congenital defects is similar to developed countries, except for higher prevalence of chromosome abnormalities (due to higher proportion of advanced maternal ages, prenatal diagnosis less available).
- Similar overall prevalence of single-gene conditions, with wide variations in specific conditions due to carrier selection, genetic drift, founder effects, consanguinity.
- No particular single gene disorder has an outstanding prevalence, but high prevalence clusters exist
- Common NCDs with genetic contribution rising

Selected Examples of Geographic Clusters

- Congenital malformations:
 - microtia in Quito (Ecuador) and Cordoba (Argentina),
 - hypospadias in Brazil,
 - cleft lip in La Paz (Bolivia)
- Mendelian Disorders:
 - Huntington in Maracaibo Lake, Venezuela
 - SCA-2 in Holguin province, Cuba
 - 5-hydroxi-reductase deficiency in Dominican Republic
 - GM-1 gangliosidosis in Cordoba, Argentina
- Complex disorders:
 - Bipolar disorders in Costa Rica
 - Alzheimer disease in Colombia, Dominican Republic

Genetic Science in Latin America

- Centers of excellence in genetics/genomics research in several countries:
 - Nucleotide Sequencing and Analysis network in Brazil sequenced the genome of the bacterium *Xylella fastidiosa*, a pathogen of citrus crops
 - Cancer Genome Project in Brazil, aiming at identifying ESTs associated with various types of cancer
 - Genome sequencing of Trypanosome *Cruzi* in Argentina
 - Biotechnology industry applied to health in Cuba

Gap Between Genomic Science and Health Applications

- Genomics research is not connected to prevention programs, nor with health services for people with genetic conditions
- There are major hurdles in the setting and implementation of policies for the prevention and management of congenital defects and genetic disorders

Current Status of Genetic Services in Latin America

- Reasonably well developed services in tertiary care centers in major cities
- Major inequities in access
- Emphasis on individual diagnostic services
- Newborn screening for selected conditions only in major cities and with low coverage
- Poor coordination with other health services
- Competition for funds with other programs
- Lack of population-based prevention programs

Some Current Programs of Primary Prevention of Congenital Defects

- Expansion of rubella immunization
- Folic acid fortification
 - Chile: Since January 2000, wheat flour is enriched with 220 $\mu\text{g}/100\text{g}$ of folic acid (427 μg of folic acid per day). The prevalence at birth of NTDs declined from 17 per 10,000 in the pre-fortification period (1999-2000) to 9.9 per 10,000 in 2001-2002 (42% reduction).
- Avoidance of potential teratogens: public and professional education, teratogen information centers
- Campaigns against alcohol consumption in pregnancy

Some Current Initiatives on Expanding Genetic Services

- Latin America Human Genetics Network (RELAGH) launched an initiative for quality assurance and regionalization of genetic tests
- The Ministry of Health of Argentina created a National Commission on Genetics and Health to conduct a needs assessment, fill identified gaps and implement a regionalized network of genetic services with base in PHC
- The Ministry of Health of Brazil is incorporating genetic services into it's Unified Health System
- Cuba is linking primary health care with genetic services
- Costa Rica has regionalized genetic services

The Program on
Genetics in Public Health and
Human Rights
for Latin America and the
Caribbean
of the Pan American Health
Organization

Background:

The W.H.O. Consultation on
Community Genetics Services in
Latin America and Regional Network
of Medical Genetics.
Porto Alegre, 2003

(Community Genetics, Special issue, 7:2004)

Recommendations of the Porto Alegre Consultation

- Conduct of epidemiological research in LAC on the prevalence and types of congenital defects, genetic disorders and genetic predispositions to common diseases;
- Lobby for increased governmental funding for services, research and education in medical genetics;
- Education of health professionals in genetics;
- Education of genetic professionals in community health and public health genetics;
- Foster dialog between clinical geneticists, public health personnel, primary health care workers and community organizations;
- Better planning of regionalized genetic services to avoid duplication and inefficiency

(Kofman-Alfaro & Penchaszadeh. *Community Genet* Special issue 7:2004)

PAHO Program: General Objective

- This regional program is based in the Buenos Aires PAHO Office and its general objective is to articulate, promote, and develop more effective ways of using genetics and genomics in the promotion, protection, and repair of health at population level in Latin America and the Caribbean, with a human rights approach and respect for human dignity.

Specific Objectives

1. To heighten awareness among health policy makers of LAC about the burden of disease determined by genetic disorders and congenital defects in the Region
2. To foster dialog among health policy makers (ministers, ministries staff, legislators), clinical geneticists and other stakeholders in LAC about how best to reduce the burden of disease caused by genetic conditions and congenital defects.
3. To provide a forum to discuss potential benefits and limitations of genetic approaches to public health.

Strategies

- To stimulate the conduction of epidemiologic research in countries of LAC in relation to the public health burden of congenital defects and genetic disorders.
- To stimulate the conduction of country surveys on the status of existing genetic services: distribution and organization of clinical and laboratory resources
- To constitute a regional network of advisors in medical genetics and public health of LAC capable of assessing the clinical validity and utility of genetic technologies and advise policymakers on their applicability for the protection and promotion of health at the population level.
- To promote in LAC the widest public health application of genetic technologies and services that are proven to be effective and safe.

Instruments: Policy Documents I

Policy documents will be produced on specific genetic issues addressing peculiarities of, and differences within LAC:

1. Burden of disease from congenital defects and genetic disorders
2. Objectives and organization of genetic testing and counseling services
3. Linkage between clinical genetics services and primary health care
4. Genetic testing. It's role in public health, methods to assess their clinical validity and utility, quality control and ethical aspects
5. Newborn screening of congenital disorders: criteria, requirements, indications, organization and quality control;

Instruments: Policy Documents II

6. Registries of congenital malformation and their articulation with genetics policies in health
7. Prenatal diagnosis of genetic disorders: criteria, requirements, indications, quality control
8. Ethical issues in genetics and health, with emphasis on the right to access to genetic services and genetic discrimination

Instruments: Work of Experts, Dissemination and Discussion Forums

- Commission, circulation, discussion and consensus development by experts on policy papers
- Disseminate policy papers to health policy makers
- Organize workshops and forums with health policy makers and other stakeholders (educators, patient organizations, health providers and payers)

Next meetings

- Rio de Janeiro, June 20, 2007: Presentation and discussion of the PAHO Public Health Genetics Program with experts from Mexico, Cuba, Costa Rica, Colombia, Ecuador, Chile, Brazil and Argentina
- Quito, July 25-28, 2007: Congress of Human Genetics Society of Ecuador.
- Buenos Aires, fall 2007: Workshop on priorities in health research in genetics. Sponsored by the Ministry of Health of Argentina.