Medical genetic services in Latin America: report of a meeting of experts[1]

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During the Ninth International Congress of Human Genetics which was held in Rio de Janeiro, Brazil, from 16 to 18 August 1996, a group of experts under the coordination of the authors discussed at length the state of medical genetics in Latin America. The facts and ideas presented at the meeting, which was sponsored by the Human Genetics Program of the World Health Organization (WHO) and the Maternal and Child Health Program of the Pan American Health Organization, are examined in this document under three broad headings. The first verses on the history and current status of medical genetics in selected Latin American countries. This is followed by a discussion of the general features of medical genetics in the Region and by a final section of recommendations for promoting medical genetics in Latin America.

GENETIC SERVICES IN SELECTED COUNTRIES[4]

Argentina

In the 1950s a few eminent physicians, among them Francisco Saez and Luis Varela pioneered the field of medical genetics in Argentina. Juan Valencia introduced cytogenetic studies and initiated the institutional development of medical genetics at the University of Buenos Aires. Subsequently, medical genetics sections were opened at the National Academy of Medicine (1960) and two pediatric hospitals (1963 and 1971) in Buenos Aires. The Argentine Ministry of Health established the Medical Genetics Center in 1969 for research, teaching, and service provision. In 1988, a medical genetics department was opened at the national pediatric hospital which is currently the main referral center for complex pathologies.

The Ministry of Health acknowledged genetics as a new medical specialty in 1991. Residence training in clinical genetics and cytogenetics is now available at the Medical Genetics National Institute. In Buenos Aires, medical genetics services are currently rendered to patients of all ages at this institute and the Hospital de Clínicas, where prenatal diagnosis is also offered. The Hospital de Clínicas has a Department of Molecular Genetics, which is under the School of Biochemistry, and performs research and services related to DNA analysis. The

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three existing pediatric hospitals in Buenos Aires have genetic departments; two have cytogenetics laboratories and the third performs DNA diagnostic testing.

Sarda Maternity Hospital specializes in identifying and performing cytogenetic studies of congenital malformations in newborns. Private genetic services are also provided at institutions such as the *Centro de Educación Médica e Investigación Clínica* (CEMIC) and the Medical Genetics Foundation. Most large urban centers within Argentina, such as Buenos Aires, La Plata, Cordoba, and Mendoza, have geneticists that provide clinical genetic services and perform different genetic tests. However, geneticists in smaller cities lack the resources with which to study patients and have few opportunities to improve and update their skills. Nationwide economic difficulties also hamper access to good medical genetic care.

Ethnicity and genetic epidemiology. Of Argentina's 32.5 million inhabitants, 85% are of European descent. Unlike other Latin American countries, Argentina has only a small Amerindian population and few mestizos.

Brazil

Medical genetics has been taught in postgraduate courses in Brazil since the late 1960s. The Sociedade Brasileira da Genética (SBG) and the Associação Médica Brasileira (AMB) together created the Sociedade Brasileira de Genética Clínica (SBGC) in 1986.

Today, medical genetics is one of 60 medical specialties recognized by the AMB and the Conselho Regional da Medicina. The SBGC administers qualifying examinations to certify physicians in the specialty. Four universities offer residencies in clinical genetics. The SBGC has 250 members from 14 Brazilian states—half of them, however, are from Rio Grande do Sul and São Paulo.

A 1996 survey found 33 medical genetics centers providing services to the public with a total of 118 clinical geneticists, 84 biologists, and 109 other professionals, including social workers, nurses, and psychologists. In 1995, they served around 35 000 patients and offered the following tests: lymphocyte karyotyping (23 centers), fetal karyotyping (10), clinical testing for inborn errors of metabolism (4), ancillary tests for various genetic diseases (11), newborn screening for phenylketonuria (PKU) and hypothyroidism (5), DNA analysis and/or fluorescence in situ hybridization (FISH) (13), teratogenic information services (2), registry and surveillance of congenital anomalies (8), tests for the diagnosis of some special genetic diseases (21), and management/therapy of special genetic diseases (15). Well-staffed private genetic clinics have recently begun offering prenatal diagnosis and other genetic services in the large urban centers. They send a significant number of tests overseas, but only a small portion of Brazilians can afford them.

Only a minority of patients with genetic diseases are seen by medical geneticists. Other medical specialists provide adequate treatment to additional patients but are not skilled in the nuances of genetic diagnosis or in dealing with family and reproductive risks. Brazil is currently undergoing an acute economic crisis, and the prospects are dim for wide availability of medical genetic services anytime soon.

Ethnicity and genetic epidemiology. Most of Brazil's 147 million inhabitants are bi- and trihybrids, mainly from the mixture of whites, blacks, and Amerindians. Current knowledge of the epidemiology of genetic diseases is minimal, but frequency data are available for hemophilia, Tay-Sachs disease, cystic fibrosis, hemoglobinopathies, PKU, and hypothyroidism. Data on congenital anomalies are more extensive. Some genetic diseases have been originally described in Brazilian patients. Classic examples are the Grebe-Quelce Salgado syndrome and acheiropodia.

Chile

Chile has only one accredited three-year training program for medical geneticists at the genetics department of the Hospital Clínico of the University of Chile in Santiago. Rotations in medical genetics are included in pediatrics, obstetrics and gynecology, and hematology programs. One postgraduate Master's program is available.

A total of 21 medical geneticists provide services in Chile's 13 medical genetics centers. Nine of the centers are in Santiago, which is home to a third of the nation's population. The centers provide services in a number of areas, such as genetic counseling, cytogenetics, birth defects, clinical genetics, prenatal diagnosis (in 4 centers), tissue culture (5), cancer genetics (4), infertility, dermatoglyphics, hematological cytogenetics (7), public health education, population genetics, paternity studies (1), twin studies, and teratogen identification.

Twenty-two specialized technicians work in nine cytogenetics laboratories, all but two of which are in Santiago. Most perform the following tests: sex chromatin; cordocentesis; amniocentesis; karyo-

typing of peripheral blood, trophoblast of spontaneously aborted uterine contents, and bone marrow; chromosomal fragility studies; and high resolution studies of prometaphase chromosomes and solid tumors. Four laboratories are implementing *in situ* hybridization techniques with fluorescence.

Scientific societies for geneticists are the Sociedad de Genética de Chile and the genetics division of the Sociedad Chilena de Pediatría (SPC). The SPC committee on chronic diseases also deals with genetic disorders. Most geneticists agree that the most significant problems in the field are lack of funds and ignorance on the part of other physicians and potential consumers concerning the goals and usefulness of medical genetics services.

Genetic characteristics and epidemiology. The population of Chile is 13 386 231, and the 1994 infant mortality rate was 14/1 000 live births. An analysis of 50 malformations in 106 457 successive births in eight Chilean maternity hospitals during 1982–1988 showed an annual incidence of congenital malformations of 2.97%, including live births and stillbirths. The stillbirth rate was 0.93%. The prevalence of congenital hypothyroidism is estimated to be 1 per 2 900 newborns, and that of classic phenylketonuria is 1 per 14 000 newborns.

Colombia

Clinical genetic and cytogenetic services were initiated at the Colombian National University Medical School in the 1960s. Genetics groups subsequently formed in the Colombian National Institute of Health, some public and private medical schools, the Colombian National Cancer Institute, and one public hospital in Bogotá. In the early 1990s, a nonprofit institution, the Gillow Foundation, established services in clinical genetics, cytogenetics, prenatal diagnosis, and biochemical genetics. Despite this history, the teaching of medical genetics is deficient in most Colombian medical schools, consisting only of short courses with little clinical application.

Medical genetics services are currently available in 10 of Colombia's main urban centers, but their degree of development varies. One privately run clinic offers newborn and prenatal screening programs for maternal serum alpha fetoprotein (MSAFP)/human chorionic gonadotropin (HCG). The Maternal and Child Health Institute, a public teaching hospital in Bogotá, conducts a neonatal screening program for hypothyroidism. There are no official guidelines for genetic testing. Most genetic units in Bogotá perform a few molecular genetic tests. Several faculty members from public and private universities throughout the country have independent private practices.

The Colombian Society of Genetics has been reorganized and its activities are expected to stimulate interest and competency in medical genetics. Medical geneticists in Colombia are concerned that the public may establish too close an association between prenatal testing and abortion, even though results are normal in the vast majority of cases. Interruption of pregnancy is illegal in Colombia, but first trimester abortions are performed at several centers, particularly in large urban areas.

Ethnicity and genetic epidemiology. Colombia's population of 37 million shows features resulting from the mixture of Amerindians, Spanish conquerors, and African slaves. The infant mortality rate was approximately 25/1 000 live births in 1995. Clusters for hemoglobinopathies have been confirmed in the regions where African descendants live. Small clusters of single gene and multifactorial disorders have also been observed. A large cluster of Vitamin D dependent rickets type II has been described in a semi-isolated black population in the southwestern region of the country.

From 1982 to 1992, the frequency of congenital malformations in newborns in a maternity hospital in Bogotá was 2.8%.

Cuba

In Cuba, human cytogenetics and inborn errors of metabolism were first studied in the late 1960s. In the 1970s, the National Center for Scientific Research organized a series of graduate courses in genetics. These courses, which were taught by visiting scientists from abroad, led to the creation of several human genetics centers with three main specialty areas: biochemical genetics, clinical genetics, and genetics and public health. Today, the Cuban National Center for Medical Genetics (NCMG) is a World Health Organization Collaborative Center for the Development of Genetic Approaches to Health Promotion.

The NCMG coordinates training in medical genetics as well as genetic research and services for the entire country. The standard medical curriculum includes 18 hours of general medical genetics. Nurses and health technicians are introduced to genetics in their undergraduate professional education. At the postgraduate level, clinical geneticists complete residencies in the National Center, during which they rotate through clinical disciplines (such as pediatrics, internal medicine, obstetrics, and gynecology) and gather experience in clinical ge-

netics, prenatal genetics, administration of genetic programs, and research. Recently, Master's level programs in genetic counseling and medical genetics have been implemented in response to the need for extending genetic services to the level of primary care.

Cuba's public health services have incorporated preventive interventions against genetic disease since the 1980s. The main goals are: detection of fetal anomalies by maternal serum alpha-fetoprotein (MSAFP) and ultrasound; prevention of sickle-cell disease by carrier detection, genetic counseling, and prenatal diagnosis; prenatal screening for fetal chromosomal anomalies in pregnant women over 38 years of age; newborn screening for PKU and congenital hypothyroidism; and clinical genetics and genetic counseling services for the population at large.

The main hospital in each of Cuba's 14 provinces has a genetics unit staffed by two clinical geneticists, an obstetrician, a pediatrician, and two nurses with training in genetics. Services are coordinated with the family physicians at the primary level. They include hemoglobin electrophoresis, MSAFP, and fetal ultrasonography for all pregnant women, as well as counseling in clinical genetics, teratogenicity, and general genetics. Pre- and postnatal chromosome analyses are performed in five of the 14 provincial services and at the NCMG. Regional laboratories for the diagnosis of PKU are located in Santiago and Havana. At the NCMG in Havana, a modest biochemical genetics lab performs some biochemical and enzyme assays.

The following national data provide an idea of the volume of services provided. In 1995, 109 985 pregnancies were monitored by MSAFP and 267 malformed fetuses were detected, resulting in 259 interrupted pregnancies. An additional 664 malformed fetuses were diagnosed by ultrasound (including 110 with cardiac defects), leading to 561 pregnancy terminations. During screening of 140 951 pregnant women for sickle cell trait, 202 at-risk couples were detected and 27 affected fetuses were diagnosed, resulting in 15 pregnancy terminations. A total of 574 prenatal chromosome diagnoses were performed and 12 abnormal fetuses identified, eight of which were aborted. The total number of postnatal clinical genetic consultations was 8 057.

Cuba's difficult economic situation increasingly hampers delivery of genetic services. This explains why the number of chromosomal diagnoses performed in 1995 was fewer than half the average number performed in previous years.

Ethnic and genetic epidemiology. Cuba's population numbers approximately 11 million. Sixty-six percent of the population is white; 22%, mestizo; 12%, black; and 0.1%, Oriental. Infant mortality is under 10/1 000. The prevalence at birth of sickle-cell disease is 1/1 700, the average carrier frequency of S hemoglobin being 3%. Cystic fibrosis has a birth prevalence of 1/1 836. A cluster of spinocerebellar atrophy type 2 in the province of Holguín shows a prevalence of 133 per 100 000 in the province.

The birth prevalence of anencephaly is 0.91 per 10 000; however, a study in Havana, which included terminations of affected pregnancies, showed a prevalence of 6.3 per 10 000. Spina bifida occurs with a birth prevalence of 3.63 per 10 000 (9.4 per thousand pregnancies, including terminations, in Havana proper). The following are the frequencies per 10 000 live births of other malformations: encephalocele: 0.49; microtia: 1.73; cleft lip: 6.33; cleft palate: 2.25; esophageal atresia: 1.92; anal atresia: 2.04; hypospadias: 16.35; limb reduction defects: 2.72; diaphragmatic hernia: 2.25; omphalocele: 1.03; gastroschisis: 0.49; Down's syndrome: 8.0.

Ecuador

In Ecuador, the specialty of medical genetics originated in 1984 with the creation of genetic services in two Quito hospitals. Today, three additional hospitals—one in Quito and two in Guayaquil—provide medical genetic and cytogenetic services that cover 23% of Quito's population and about 20% of the population of Guayaquil. Among the tests and procedures provided are chromosome analyses of peripheral blood cells, solid tumors, bone marrow, amniotic fluid, chorionic villi sampling, and effusions; diagnostic tests for PKU and other metabolic disorders; and molecular genetic tests for cystic fibrosis, leukemia (bcr-abl), human papillomavirus, certain oncogenes (NF2), and repair genes.

In Quito and Guayaquil, two public and one private university are involved in clinical genetics, genetic research, cytogenetics, molecular genetics, and genetics counseling. Clinical services, cytogenetic testing, and genetic counseling are also available in Cuenca, the third largest city in the country.

Medical genetics has not progressed very much in Ecuador. The Ministry of Public Health does not have a genetic health program, and there are only 15 clinical geneticists in the whole country. Undergraduate and postgraduate instruction in genetics is currently concentrated in universities in Quito. Postgraduate studies in biochemical sciences and the Master's program in genetics have been eliminated because of lack of funds. Demand for medical genetic services is small, probably because

there's little knowledge of their benefits among health professionals and the public at large. People tend to regard genetic disorders as untreatable and to conceal them for fear of being stigmatized.

However, there are indications of growing interest in genetics. An Ecuadorian Society of Genetics has been established, and attempts are being made to educate the public through newspaper articles and other means.

In Ecuador, abortions are generally performed only if two professionals agree that there is a compelling medical reason to perform them. This approach seems to be widely accepted by the public.

Ecuador is experiencing "biopiracy." Samples from Indian populations are being smuggled out of the country to developed nations for research purposes. Most geneticists wish to preserve the genetic patrimony while remaining open to collaborative research projects such as were proposed at the Earth Conference that was held in Rio de Janeiro, Brazil, in June of 1992.

Ethnicity and genetic epidemiology. Ecuador has a population of 10 million inhabitants and an infant mortality rate of 35.3 per 1 000. The main ethnic groups are mestizos, Amerindians (with high inbreeding), blacks, and whites. Birth defects affect about 3% of newborns. The most common congenital anomalies are microtia, congenital hip dysplasia (4 to 6 times higher than in the rest of Latin America), cardiac defects, chromosomal anomalies, cleft lip and palate, neural tube defects, and cryptorchidism. Chromosomal anomalies are similar to those reported worldwide, except for the high frequency (9%) of mosaicism in Down's syndrome babies born to young mothers.

Mexico

The first Mexican publications on cytogenetics and clinical genetics appeared in the 1960s after several Mexican physicians returned from training abroad. The Mexican Society of Human Genetics, which was founded in 1968, organized the Fifth International Congress of Human Genetics in Mexico City in 1976. At present the Society has 230 members. Graduate level genetics is taught in four courses in Mexico City, under the sponsorship of the Universidad Nacional Autónoma de México, and in public universities in Guadalajara and Monterrey.

In 1991, 131 specialists, 97 of whom were physicians, were certified by the Mexican Board of Human Genetics. Most (98) worked in the four largest cities in the country.

A survey conducted in 1995 identified 40 units dedicated to human genetics, 23 in public hospitals and the rest connected to universities. Fifteen engage systematically in research activities. In addition, a few private hospitals in Mexico City and other large cities provide limited genetic services. Genetic counseling is performed in all hospital-based units, almost exclusively by specialist physicians. The common diagnostic and biochemical genetic tests are readily available in most of these units. Prenatal diagnosis is available in a few private hospitals in the larger cities, but few people have access to it. Genetic screening for hypothyroidism in newborns has been compulsory since 1988, but many smaller hospitals are unequipped to perform the tests. Screening for PKU and other metabolic disorders is available in two or three cities.

Molecular genetic diagnostic techniques are regularly performed in large hospitals, usually for the study of cystic fibrosis, hemophilia, and muscular dystrophy. Molecular biology is just getting started in Mexico, but all genetic units either have the technology or are trying to develop it. Some universities are forming partnerships with hospitals: the former supply the necessary personnel, equipment, and expertise in molecular genetics, while the hospitals provide the patients.

If any further progress is to be achieved, Mexican medical genetics must overcome several obstacles. The public hospitals that provide genetic services charge very little, but there are few of them and most of the population lacks access. Sophisticated genetics laboratories are present only in the larger cities. The legal process for purchasing equipment for public institutions is unduly complicated and often results in the acquisition of cheaper, less reliable products.

Prenatal diagnosis is practically unavailable and genetic counseling is underdeveloped, largely due to a vocal minority's efforts to block attempts at modifying laws against abortion. In such a context, physicians may not have sufficient regard for patient autonomy. In a recent survey, 95% of geneticists agreed that counseling should be value-neutral. However, when presented with specific hypothetical situations involving 26 different fetal diagnoses, more than 70% said they would recommend continuing or interrupting the pregnancy, depending on how severe they perceived the problems to be.

Salaries for professional and technical personnel in government institutions are very low. As a result, many move into the private sector and some of the most talented go abroad. Of those who remain in public institutions, many take second jobs to supplement their incomes and this interferes with their academic development.

Ethnicity and genetic epidemiology. Mexico has close to 100 million inhabitants, 90% of whom are mestizos resulting from Amerindian-Spanish admixture. There are close to 5 million monolingual Indians and several small groups from different parts of the world, mainly Europe. In mestizos of middle to low socioeconomic status around 55% of ancestral genes are Indian, 40% white, and 5% black. In some coastal areas, however, as much as 40% black ancestry is present.

Nationwide monitoring between 1980 and 1988 revealed that approximately one out of every 50 live newborns and one out of every nine stillborns have one or more congenital malformations. In addition, sickle cell anemia and the A-type of glucose-6-phosphate dehydrogenase deficiency are common, with the Mediterranean type seen mostly in Oriental Jews. A few cases of Tay-Sachs' disease or Gaucher's disease have been observed in Ashkenazi Jews.

Paraguay

Medical genetics is in an embryonic stage in Paraguay. The country has no specialists in clinical genetics. The universities offer only general courses in genetics. There is only one cytogenetic laboratory (*Instituto de Investigaciones en Ciencias de Salud*), which is located at the Medical School of the National University at Asunción and offers training in cytogenetics.

Medical genetic services do not exist as such in Paraguay. Genetic counseling, diagnosis, and other services are performed in scattered hospitals and private practices. Prenatal amniocentesis to detect chromosome anomalies is performed by private laboratories. Specimens are sent outside the country for the diagnosis of other biochemical or molecular genetic disorders. The illegality of abortion is one reason that prenatal diagnosis is so restricted in scope.

The Ministry of Public Health and Welfare has an indirect role in medical genetics through institutes devoted to the rehabilitation of individuals with physical and mental disabilities. In addition, a number of foundations and volunteer associations provide services to the handicapped. These include physical therapy and special education for persons with speech and hearing disorders.

Changes that would boost medical genetics in Paraguay include: incorporation of genetic tests and interventions into public health services; significant financial allocations, especially for salaries; more emphasis on the prevention of genetic disorders; education in genetics for health personnel and the general population; and international support.

Ethnicity and genetic epidemiology. Paraguay's population is a little over 4 million inhabitants, the majority of which are indigenous (*guaraníes*) and mestizos. There are no reliable data at the national level on the prevalence or incidence of genetic disorders. A study carried out by the *Instituto de Investigaciones en Ciencias de Salud* revealed a prevalence of congenital hypothyroidism of 1 in 4 290 newborns. This study was conducted at the maternity ward of the National University in Asunción.

Puerto Rico

José M. García-Castro pioneered human and medical genetics in Puerto Rico in the 1970s. Today, all four medical schools on the island include genetics in their curricula but only the one in Ponce has a formal course in medical genetics. Postgraduate medical training in specialties such as pediatrics and obstetrics and gynecology covers very basic concepts of dysmorphology, Mendelian genetics, and cytogenetics. These programs also offer formal genetic training programs for interested physicians.

Puerto Rico has five certified clinical geneticists but only one genetic counselor. There are two established genetic clinics. The main one, which is at the university-affiliated pediatric hospital in San Juan, has been in existence since 1975 and sees approximately 1 600 patients a year. The San Juan Municipal Hospital has a clinic that provides genetic diagnosis and primary and ambulatory services.

A current initiative, known as *genética de atención primaria* (genetics in primary care), seeks to establish genetic clinics throughout the island. This initiative is being developed by the Hereditary Diseases Program of the Ministry of Health, with grant support from the United States Federal Government, with the goal of detecting and diagnosing patients with genetic diseases. As part of this program, clinics have been established at Carolina Regional Hospital, Ponce Regional Hospital, and Mayagüez Medical Center. The program includes a monthly genetic clinic for patient evaluation and educational services for residents in training. The quality of care for individuals with genetic disorders has markedly improved.

Financial, administrative, legislative, bureaucratic, and sociocultural issues are slowing the progress of medical genetics in Puerto Rico. Most or all current research is funded by U.S. Federal grants, mostly through the minority programs of the National Institutes of Health, which have suffered significant cuts. More commitment on the part of the Puerto Rican Government is badly needed.

An administrative infrastructure is critically needed to support efficiency and efficacy in genetic

services and to avoid duplication of labor and costs. Communication and coordination must improve between institutions, governmental agencies (particularly the Department of Health), and genetic health providers.

All Puerto Rican medical schools should establish medical genetics courses and encourage individuals who are interested in specializing in genetics. An M.D./Ph.D. program would foster biomedical research in general. The establishment of diagnostic laboratories (with molecular, cytogenetic, and biochemical testing capabilities) would result in faster test results, improved management and diagnosis of patients with genetic disorders, and greater genetic research.

Ethnicity and genetic epidemiology. Puerto Ricans, who number approximately 3.7 million, are the product of a mixture of three main ethnic groups: Europeans, Africans, and Taino Indians. As in the rest of the western Caribbean, many southern European nations contributed to the genetic pool of Puerto Ricans. There are no identifiable genetically isolated groups, but there is a considerable degree of consanguinity, especially in the island's central highlands.

Infant mortality in 1993 was 13.4 per 1 000 live births. Congenital anomalies were a very common cause of infant mortality, second only to the complications of low birth weight.

It is widely known that Puerto Rico has one of the world's highest incidence rates of oculocutaneous albinism I, which affects approximately 5 in every 10 000 individuals. Particularly frequent are also the Hermansky-Pudlack syndrome, the Jarcho-Levin syndrome, (a spondylothoracic dysplasia), and the Bardet-Biedl syndrome. A high frequency of metabolic disorders has been observed, but incidence data are available only for congenital hypothyroidism and PKU. In 1994–1995, near universal neonatal screening revealed a 25 in 10 000 incidence of hypothyroidism and a 59 in 100 000 incidence of PKU. Hemoglobinopathies (carriers and/or affected) were identified in 2.3% of neonates.

Venezuela

Medical genetics is not included in the core curricula of Venezuelan medical schools, and the subject is often entirely omitted from postgraduate education. The main pediatric post-graduate training programs in Venezuela have no formal medical genetics course.

Venezuela has 30 clinical geneticists in 13 genetic units located in seven of its 14 states. Most of these units provide only basic clinical and cytogenetic services. A few relatively simple biochemical tests are performed by a small number of centers. A single laboratory, at the Venezuelan Institute for Scientific Investigation (IVIC), performs some highly specialized biochemical tests. Molecular genetic studies are at an incipient stage. Prenatal diagnosis of chromosome anomalies in amniotic fluid is provided in five genetics units, one of which also performs chorionic villus sampling. Follow-up on positive prenatal diagnoses is problematic because abortion is illegal without exception.

Demand for medical genetics services is strong and on the rise in Venezuela, but the resources to meet it are scarce. More than 10 million Venezuelans lack access to services, and financial and personnel shortages limit the quality of care where services exist. Moreover, several factors justify being pessimistic in relation to the future. First, national and regional public health authorities do not consider genetic diseases to be important problems. They have not developed a single program for the prevention, diagnosis, or treatment of these conditions, nor is any office charged with doing so. Second, there is an increasing shortage of human resources, as senior geneticists are not being replaced by younger professionals. Finally, the Venezuelan medical community pays little attention to genetics or genetic diseases.

Ethnicity and genetic epidemiology. Venezuela's population is 21 million, and its infant mortality rate was 24.8 per 1 000 in 1992. It is difficult to assess current morbidity from genetic diseases, since there are no reliable national statistics. Most likely, however, they represent an important and under-recognized public health problem, considering the high mortality they cause as well as the following facts:

- In 1979, a study revealed that at least 8.9% of inpatients in the main pediatric Venezuelan hospital had a genetic disorder.
- Venezuela has 600 000 births per year. It is estimated that every year 700 Venezuelan babies are born with Down's syndrome, 2 400 with multiple congenital malformations, and 1 300 with open neural tube defects.
- In some isolated populations, there is a high prevalence of sickle cell trait (as high as 15% in Isla de Toas, Zulia State).
- In the past decade, two genetics units in Venezuela have managed approximately 10 000 patients with genetic diseases.
- Pilot studies in Caracas have documented an incidence of congenital hypothyroidism of 3 cases in 10 000 births.

GENERAL ISSUES IN LATIN AMERICAN MEDICAL GENETICS[5]

Birth defects registries

Latin America, with its population of 450 million producing 12 million births per year, has scant monitoring of congenital malformations. Only two hospital-based programs participate in the International Clearinghouse of Birth Defects Monitoring Systms (ICBDMS), a non-governmental organization that coordinates the information provided by malformation registries worldwide and provides global statistics for the incidence of congenital anomalies in newborns. The Latin American Collaborative Study on Congenital Malformations (ECLAMC), which is carried out at different sites in Argentina, Chile, Colombia, Panama, Paraguay, and Uruguay, covers about one percent of the Region's neonatal population. In Mexico, a tracking system known as *Registro y Vigilancia Epidemiológica de Malformaciones Congénitas Externas* (Registry and Epidemiologic Surveillance of External Congenital Malformations, or RYVEMCE) monitors 2% of the country's births.

Two countries, Cuba and Costa Rica, have national birth defects monitoring programs. Although each covers about 50% of all births, neither yet meets the requirements for membership in the International Clearinghouse of Birth Defects Monitoring Systems. Chile, Panama, and Uruguay should also have national programs, as their infant mortality rates are below 20 per 1 000, and they are only partially covered by the ECLAMC.

Diagnosis of inborn errors of metabolism

Inborn errors of metabolism (IEM) comprise more than 500 heterogeneous and rare disorders, which are extremely rare and diagnosable only by the use of sophisticated and costly laboratory methods. This report on the diagnosis of IEM in Latin America is based on a 1996 survey of 26 public and private laboratories in eight different Latin American countries (Argentina, Brazil, Chile, Cuba, Mexico, Peru, Uruguay, and Venezuela) conducted by Roberto Giugliani. The survey questionnaire did not address neonatal screening, but focused only on the diagnosis of IEM in high-risk patients with clinical findings.

The number of laboratories that test for IEM has increased at a faster pace in the past decade. Of 23 laboratories providing such data, five (22%) had been diagnosing IEM for more than 20 years, five (22%) for 10 to 20 years, and 13 for less than 10 years. In addition to the eight countries surveyed, Colombia and Costa Rica also have centers that provide IEM diagnostic services.

Nineteen (73%) of the 26 laboratories receive most of their funds from the central government, and the remaining nine from private clients. In recent years, six (32%) of the government-supported laboratories have begun to seek funding from the private sector as a result of reduced public expenditures. Most laboratories (72%) are linked to some type of teaching institution, nearly always a university or research center.

In addition to the diagnosis of IEM in high-risk patients, genetic counseling and treatment are offered by about 60% of the centers, usually through their departments of medical or human genetics. More sophisticated and costly procedures, such as carrier detection and prenatal diagnosis, are offered by only 33% and 22% of such services, respectively. Most genetics services performed biochemical screening tests (77%), qualitative electrophoresis and chromatography (77%), and quantitative spectrophotometric and/or fluorometric metabolite analysis (65%). A significant proportion of laboratories offer quantitative amino acid analysis (54%) and fluorometric and/or colorimetric enzyme assays (42%), which reflect a higher level of sophistication. Analysis of organic acids is performed by only 27% of laboratories, probably due to the high cost of equipment and to the fact that the importance of organic acidemias has only recently been recognized. Surprisingly, 19% of laboratories use molecular genetic techniques to diagnose selected disorders, which suggests these methods are gaining ground rapidly even in developing countries. The proportion of services (11%) performing radioisotopic analysis is small, probably because of the difficulty of obtaining radiolabeled material.

Sixteen laboratories provided data on their research on high-risk patients. The rate of diagnosed IEM in such patients was 4.9%, similar to that found in developed countries. However, the rate tended to increase over time, probably due to improvements in diagnostic techniques.

Phenylketonuria (PKU) was the most frequent IEM diagnosis because of the relatively high frequency of the disease, the simplicity of the diagnostic procedure, and the expansion of newborn screening programs (Table 1). Next most frequent were mucopolysaccharide (MPS) storage and amino acid disorders, especially maple syrup urinary disease (MSUD), cystinuria, homocystinuria, and

[5] The following authors provided information for the subsections indicated: Eduardo Castilla (Argentina), Birth defect registries; Roberto Giugliani (Brazil), Diagnosis of inborn errors of metabolism; Bernardo Beiguelman (Brazil), Postgraduate education; and Victor Penchaszadeh (United States of America), Medical genetics and bioethics.

tyrosinemia. Although they are more difficult to diagnose, organic acidemias, metachromatic leukodystrophy, and the glycogen storage disorders were identified frequently. Galactosemia and urea cycle disorders were less common, despite their importance. A few IEMs were seen frequently in just one or two centers. Some examples are fucosidosis in Cuba; Sandhoff disease in Cordoba, Argentina; GM1 gangliosidosis in southern Brazil; and Gaucher's disease and X-linked adrenoleukodystrophy in Buenos Aires, Argentina. Such a distribution may be explained by differential population frequencies, technical difficulties in developing some diagnostic techniques, or the special interests of the laboratories in those places.

Latin America lacks organized reference systems or systems for cross-verification of samples and patients. Remittance of samples from one Latin American country to another is rare and reflects the difficulties entailed in transporting samples across national borders. Moreover, there are no referral systems, even within the same country. Exchanging information, patients, and samples and creating a network would enable Latin American laboratories to make a more significant contribution to the understanding of IEM disorders.

TABLE 1. Inborn errors of metabolism reported most frequently by 26 genetics services in eight Latin American countries (each service reported only its five most frequent disorders)

Disorder reported	Cases (no.) ever reported	Centers (no.) ranking the disorder among the five most frequent
Phenylketonuria	592	15
Mucopolysaccharide storage disorders	423	18
Organic acidemias	176	6
Gaucher's disease	100	1
Glycogen storage disease	89	6
GM2 gangliosidosis (Sandhoff)	72	1
GM1 gangliosidosis	69	7
Maple syrup urine disorder	69	7
Metachromatic leukodystrophy	60	3
X-linked adrenoleukodystrophy	55	1
Cystinuria	30	4
Urea cycle defects	25	3
Homocystinuria	24	5
Fucosidosis	20	2
Galactosemia	18	3
Porphyrias	17	2
Tyrosinemia	16	4
Mucolipidosis	10	1
Mannosidosis	6	1
GM2 gangliosidosis (Tay-Sachs)	4	1

Postgraduate education

The current structure of Brazilian graduate programs reveals profound deficiencies with respect to the training of geneticists that may be instructive for other Latin American countries. Under the regulations of the Brazilian Council for Higher Education, Brazilian students must accumulate a large number of course credits—requiring, on average, 4 years of study—in order to obtain a Master's degree and qualify for entry into a doctoral program. The courses needed are so numerous and vary so much in their availability that, as a rule, students are compelled to take some if not many courses that are unrelated to their professional goals. The excessive length of classroom teaching delays the time when students finally begin to exercise creativity in their professional subjects. The situation is even more dramatic for medical students, who must complete 6 years of undergraduate medical education and 2 years of residency training prior to starting formal postgraduate studies. As a result, they may pass the age of maximum creativity before they commence active research.

Students' motivation is compromised, moreover, by two circumstances. First, legislation has made Master's and doctoral degrees mandatory for professional stability and promotion. Second, scholarships are plentiful and pay more than the meager salaries of beginning professionals. These factors encourage some students to go the distance in obtaining degrees even though they have no true scholarly goals.

Some of the implications of maximizing postgraduate schools' yield of good researchers are obvious. Clear goals should be established for Master's and doctoral degrees, and the former should not be a prerequisite for the latter. Candidates for graduate studies should be selected on the basis of creativity rather than the accumulation of knowledge. The course of study should be centered on the thesis project, rather than on any arbitrarily fixed number of credits. Mechanisms should be created for independent experts to participate in the evaluation of the thesis project, with double-blind review. Graduate programs should be made multidisciplinary to promote collaborative approaches to scientific problems.

In the specific case of medical genetics, Master's degrees should be conferred based on either the completion of a residency program or on graduation from a professional training program in genetic counseling or laboratory techniques. Residency in medical genetics and specialization courses in clinical genetics should be open exclusively to medical school graduates. Professional courses in genetic counseling and laboratory tech-

niques should be available to all graduates in the health sciences and related fields. No thesis or scientific publication should be mandatory to obtain a Master's degree. Doctoral programs in medical and human genetics should be open to graduates in appropriate fields, whether or not they have a Master's degree, provided that they have an obvious vocation and talent for scientific research. These candidates should present an original thesis project at the beginning of their doctoral studies and receive their degree after successfully defending their thesis.

Medical genetics and bioethics

In Latin America, as opposed to the industrialized world, medical genetics has been accorded relatively low priority and bioethics is rudimentary. A number of major ethical and social issues confound the practice of medical genetics in the Region. The most serious—as for health services generally—is inequality of access to services due to socioeconomic, cultural, and linguistic barriers. Only wealthy people can readily obtain diagnosis and treatment of their genetic problems.

In Latin America, more than in some other regions, the ability to diagnose and predict genetic diseases far outstrips the capacity to treat them. Under such circumstances, centers need to consider carefully before performing tests whose results, if positive, may place the patient at risk for stigmatization and discrimination with no possible benefit. Anecdotal reports indicate that such care is not always being taken.

Latin America lacks a tradition for quality control of clinical and laboratory services. This is an ethical issue in many branches of medicine, but particularly in genetics, given the potential consequences of inaccurate prenatal diagnosis.

Physician paternalism is still strong and linked to traditional patriarchal authoritarianism. Yet failure to respect patient autonomy is indefensible when reproductive decisions must be made in the face of genetic risks.

In industrialized countries, insurance companies and employers are interested in obtaining individuals' genetic information to maximize their profits or increase their competitiveness. The lag in technological development has retarded this trend in Latin America, but the traditional lack of respect for patient privacy and poor legal controls suggest that patients will ultimately face a very high risk of genetic discrimination and stigmatization.

Ethically, prenatal diagnosis must be universally accessible (like all genetic services) and voluntary and must be accompanied by non-directive counseling. In Latin America, unfortunately, prenatal diagnosis is generally available only to those who can afford private services. Moreover, the fact that abortion is illegal in most countries unjustifiably constrains parents' free choice when genetic testing detects serious fetal problems. The State's ethical onus to allow medical termination of affected pregnancies is still greater in light of the fact that medical care and social support for persons with birth defects and disabilities falls far short of adequate.

CONCLUSIONS AND RECOMMENDATIONS

The following conclusions and recommendations were arrived at by consensus after group discussions among all participating experts.

Clinical genetic services

The central goal of clinical genetic services is the comprehensive management of individuals affected with or at risk for developing and/or transmitting a genetic condition. Components of clinical genetic services include the diagnosis of genetic disorders and their predisposing factors, genetic counseling, prenatal diagnosis, psychosocial support, and long-term management of patients and their families. The following measures are recommended:

- Regionalizing clinical genetic services and organizing them into primary, secondary, and tertiary care levels. The latter should be endowed with expertise in clinical genetics, cytogenetics, biochemical genetics, and molecular genetics. Psychologists, social workers, and professionals trained in genetic counseling should be part of genetic medicine teams under the supervision of clinical geneticists.
- Providing services at the primary and intermediary levels of care in the screening of populations and in prenatal screening for genetic risks. Such services should be located in health centers and medium-sized hospitals and should employ the staff or be under the supervision of tertiary care centers.
- Establishing close links between clinical genetic services on the one hand, and genetic laboratories and the full range of medical specialties on the other, particularly obstetrics, pediatrics, neurology, and oncology.
- Instituting clinical genetics as a recognized medical specialty requiring special training and certification.

- Establishing newborn screening programs in countries where infant mortality is under 30 per 1 000. These programs should be supported with public funds for screening, diagnostic confirmation, counseling, treatment, and lifelong follow-up of affected individuals. Disorders under consideration for prenatal or neonatal screening should be clinically severe, highly prevalent, easily detectable, and amenable to early treatment.
- Offering, as part of genetic services, adequate prenatal care, maternal serum screening for neural tube defects and trisomies, fetal sonography, and fetal cell sampling techniques (amniocentesis, chorionic villus sampling, and cordocentesis) for the diagnosis of genetic disorders. Genetic counseling supervised by a clinical geneticist should be offered before performing the diagnostic procedures and after detecting any abnormal results.
- Making sure that genetic services are universally accessible (regardless of a patient's ability to pay), voluntary, respectful of patient autonomy, supportive of patient decision-making, and protective against stigmatization and discrimination.

Genetic diagnostic laboratories

The diagnostic genetic laboratory is an essential component of genetic services and should be equipped to perform analytic testing in cytogenetics, biochemical genetics, and molecular genetics. Thus, the following steps are recommended:

- Forming a directory of all genetic testing laboratories in Latin America;
- Conducting a needs assessment for deciding on the creation and regional distribution of different types of genetic testing laboratories;
- Creating mechanisms for close interaction between genetic testing laboratories and clinical genetics departments;
- Requiring that genetic testing laboratories perform the following: banded karyotyping as part of cytogenetics; testing for PKU and congenital hypothyroidism as part of neonatal screening; amino acid chromatography and/or electrophoresis, and analysis of mucopolysaccharides, sugars, oligosaccharides, and lysosomal enzymes as part of biochemical genetics; testing for hemoglobinopathies, fragile X, cystic fibrosis, and muscular dystrophies as part of molecular genetics;
- Encouraging voluntary quality control programs;
- Improving communication among genetic testing laboratories by using the Internet and electronic mail;
- Supporting the development of collaborative research projects with the participation of clinical geneticists, epidemiologists, and public health workers.

Training in human and medical genetics

Modernizing medical education, with an emphasis on prevention, primary care, and community medicine, is imperative in Latin America. Medical genetics is an essential component of a modern medical education. Thus, the following measures are recommended:

- Making the teaching of medical and human genetics mandatory for undergraduates wishing to enter medical school and for other health professionals. A basic human genetics course lasting a minimum of 60 hours should be offered throughout the years of preclinical training and should cover the clinical applications of genetics and community genetics programs;
- Incorporating a minimum of 60 hours of genetics in postgraduate medical education programs, such as residency training;
- Structuring postgraduate education in medical genetics so as to train:
  a) *clinical geneticists*: physicians trained in the diagnosis, prevention, and treatment of genetic diseases and in the genetic counseling of patients and their families;
  b) *laboratory geneticists*: physicians, biologists, or biochemists trained in cytogenetic, biochemical genetic, and/or molecular genetic testing;
  c) *genetic counselors*: various types of health professionals (physicians, nurses, psychologists, biologists, etc.) who are trained to provide genetic counseling under the supervision of clinical geneticists;
- Providing continuing education in medical genetics for health professionals and public health officials;
- Teaching genetics in primary and secondary schools and providing information to the public at large, and supporting associations of patients and their relatives.

Research in human and medical genetics

Scientific and technological research is improving in Latin America, as measured by indicators such as the numbers of researchers, peer-reviewed scientific publications, and graduate studies programs. Research should be an integral component

of medical genetics programs. Ideally, the following recommendations should be followed:

- Striving for a scientific policy that recognizes the importance of human genetics in every country of the Region;
- Conducting a survey in the Region of the human and material resources dedicated to research and training in human genetics;
- Publicizing existing opportunities for training and research in human genetics;
- Providing researchers with sufficient moral and material incentives to discourage them from abandoning the world of academia or migrating to industrialized countries;
- Improving the quality of scientific journals;
- Involving human geneticists in decisions regarding resource allocation and including them in forums for the establishment of scientific policy;
- Encouraging research on the epidemiology, causes, prevention, and treatment of genetic disorders and birth defects having a significant impact on human health and quality of life in the Region. Collaborative research should be based on mutual respect between developed and developing countries and should foster the transfer of technologies from the former to the latter;
- Promoting the creation of national committees to provide ethical guidelines for research in human genetics and its clinical applications;
- Engaging human genetics researchers in public education;
- Utilizing basic research in genetics to foster a creative scientific environment.

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SINOPSIS

Servicios de genética médica en América Latina

Durante el Noveno Congreso Internacional de Genética Médica que se celebró en Rio de Janeiro, Brasil, del 16 al 18 de agosto de 1996, un grupo de expertos bajo la coordinación de los autores examinó en detalle el estado de la genética médica en América Latina. Los datos y las ideas que se presentaron en esa reunión, que fue patrocinada por el Programa de Genética Humana de la Organización Mundial de la Salud (OMS) y por el Programa de Salud Maternoinfantil de la Organización Panamericana de la Salud (OPS), se presentan en este documento en tres secciones generales. La primera versa sobre la historia y el estado actual de la genética médica en todos los países de América Latina en que ese campo ha tenido cierto desarrollo. A ella le siguen una discusión de las características generales de la genética médica en la Región y una última sección de recomendaciones sobre cómo promover la genética médica en América Latina.

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