

Medical genetic services in Cuba

Dra. Araceli Lantigua Cruz,¹ Dra. María Teresa Lemus Valdés² y Dra. Beatriz Marcheco Teruel³

ABSTRACT

The present paper describes the history and the current state of Medical Genetics in Cuba. Initial investigations developed by the National Center of Scientific Research and the Medical Genetics Department, of the Institute of Basic and Preclinical Sciences "Victoria de Girón", which belongs to the Higher Institute of Medical Sciences of Havana; contributed to insert medical genetics into the Cuban Health System, in 1981. Nowadays, Cuba possesses a Medical Genetics Network, extended even to the most remote communities. The Genetic Program is aimed to primary, secondary and tertiary prevention of genetics disorders in the country and it is supported by several conditions, such as: (a) legality of the induced abortion, (b) services of health free, (c) special education is available and free to everyone who need it and (d) there is a system in charge of the social care and support of people with disabilities and their families.

Key words: Clinical genetics, community genetics, neonatal screening, prenatal screening, congenital defects, public health, genetics education.

RESUMEN

Se recorrió el desarrollo histórico de la genética médica y clínica en Cuba y sus características actuales. La integración de los conocimientos aportados por la Genética Médica en el sistema de salud cubano, comienza en el año 1981, teniendo como antecedentes los resultados de investigaciones iniciales desarrolladas por el Centro Nacional de Investigaciones Científicas y el Instituto de Ciencias Básicas y Preclínicas «Victoria de Girón» del Instituto Superior de Ciencias Médicas de La Habana. Hoy día, existe en Cuba una red de genética médica que involucra a los 169 municipios del país. El programa genético está dirigido a la prevención primaria, secundaria y terciaria de enfermedades genéticas y defectos congénitos en la nación. Sus fortalezas son: (a) el aborto inducido es legal, (b) la atención médica es gratuita, (c) la educación especial está disponible para cada persona que lo necesite, y (d) existe un sistema de cuidado y apoyo social para las personas discapacitadas y sus familias.

Palabras clave: Genética Clínica, Genética Comunitaria, pesquiasaje neonatal, pesquiasaje prenatal, defectos congénitos, Salud Pública, Educación Genética.

With a surface of 110 922 km², the Republic of Cuba, the largest island of the West Indies, is an archipelago located at the Caribbean Sea. For many years it was occupied by the Spaniards, who introduced black people from the central region of Africa, to work as slaves. In addition, during the second half of the XIX century, a significant quantity of Asian immigrants, mainly Chinese, arrived. Therefore, Cuban genome is the combination of Aboriginal, Spaniards, Africans and Asian genomes.

Demographic, economic situation and health characteristics of the Cuban Population

Cuba has a population of 11 257 105 inhabitants, 24.7 % in the rural area, and 75.3 % in the urban area. The population younger than 15 years represents 14.9 % of the total. A gross national product (GNP) of 36452.7 millions of dollars.¹

Birth-rate in the last five years was 12.9 for 1 000 inhabitants. In the last six years 99.9 % of deliveries occurred in institutions and the 9.8 % of births corresponds to mothers older than 35 years,² Infant mortality average was 6.7 per 1000 in the last five years (5.8 in 2004 and 6.2 in 2005). Direct maternal mortality average was 2.9 per 10 000 liveborns, in the last three years.² Congenital malformations are the second cause of death during the first year of life with a rate of 1.7 and 1.6 for 1000 liveborns in 2004 and 2005, respectively. Cuban life expectancy at birth is 76.15 years (74.20 for males and 78.23 for females).

The island comprehends 14 provinces and 169 municipalities, subdivided in several health areas in accordance with the territorial extension and population density. Every health area has a polyclinic for primary assistance. Cuban Health System is public and completely financed by the state. There are 67 079 physicians (59.6 physicians per 10000 inhabitants, Dec.

¹ Physician Doctor. Clinical Geneticist. Full Professor. National Centre of Medical Genetics.

² Medical Doctor. Clinical Geneticist. National Centre of Medical Genetics.

³ Physician Doctor. Clinical Geneticist. National Centre of Medical Genetics.

2002 data), among them, 16 662 s functions as Family Physician (specialist in Integral General Medicine) in the community, each one cares about 120 families.²

Clinical Genetics as a medical specialty in Cuba

Clinical Genetics was recognized as a medical specialty by the Cuban Ministry of Public Health in 1975. Over the past 20 years, the National Center of Medical Genetics (CNGM) of the Higher Institute of Medical Sciences of Havana (Medical University) has graduated more than 100 clinical geneticists from all over the country. Such specialist has received additional training at the Departments of Medical Genetics of foreign universities or medical institutions of England, France, Holland, Sweden, Italy, United States, Spain, Denmark, Germany, Hungary and Mexico.

The training to become a specialist in clinical genetics lasts four years and it is an option for physicians either as a primary specialty or following completion of a residency in Integral General Medicine. In either case, high academic index is required. Besides, in 1996, the CNGM began to train health professionals in genetic counselling.³ So far, 543 health professionals obtained the degree of Master in Genetic Counselling (523 of them in the last 4 years) and 32 obtained a Master in Medical Genetics. All of these graduates are involved in the clinical genetics services, most of them were initially specialized in Integral General Medicine and other medical specialties such as Gynaecology, Obstetrics, Paediatrics, Psychiatry, neurology and ophthalmology, although there are also nurses, special educators and biologists.

Teaching Genetics in Medical Sciences

Medical Genetics has been taught in Medicine career since 1972. Nowadays, Medical Genetics course represents 54 hours of the fourth semester of Medicine and it is also taught in Dentistry, Nursing, and Health Technology.

Organization of genetic services

Clinical genetics services in Cuba began to organize in the early 80's in Havana City, capital of Cuba, and extended progressively during 1986 and 1988. At the present, there is a national network of medical genetics which covers the whole country and it is directed by CNGM, located in the capital and

inaugurated on August 2003, by the president of Cuba. It coordinates the work of provincial medical genetics centres and the genetic services linked to primary assistance in the municipalities. It hosts 105 professionals and technicians, 12 of them are certified clinical geneticists. It has been recently equipped with state-of-the-art equipment to perform metabolic and chromosomal disorders testing. The type and number of DNA-based diagnosis will increase in the early future. This centre is the main methodological adviser for the teaching Medical Genetics in Cuba.

Every component of the medical genetics network is responsible for the diagnosis, prognosis, treatment and prevention of the genetic disorders and birth defects in their own region. They serve general population and patients referred from special education or social services. People at risk of having a liveborn affected by a genetic disease are submits to an assessment consult. Medical genetics centres attend individuals diagnosed as positive in the newborn screening program.

Provincial centres services are conducted by a clinical geneticist and a Master in Genetic Counselling, helped by Family Physicians. Their work consists in genetic screening and the education of local population in accordance with the genetic and environmental situation of the community. Every provincial centre is able to perform hemoglobin electrophoresis for sickle cell carriers screening and use Ultra-Micro Analytic System (Cuban-designed analytic tool for automated clinical laboratory testing).⁴ Six provincial laboratories are equipped to perform chromosome analysis of amniotic fluid and peripheral blood samples. In the next few months, some of these labs will be provided with state-of-the-art cytogenetic equipment.

Provincial medical genetics centres have specific functions determined by their demographic and epidemiological characteristics, such as population density and prevalence of genetic disorders.

All provincial medical genetic centres send information about the epidemiological situation and their specific needs to CNGM and the Ministry of Public Health. Genetic services include teleconsults via INTERNET (www.sld.cu). Patients without a clear diagnosis or adequate treatment plan are consulted with specialists in Cuba and abroad.

National screening of genetic disorders

National Maternal and Child Health Program of the Ministry of Health, includes screening of genetic

disorders during prenatal and neonatal periods. The decision of what to screen for is based on epidemiological knowledge, the origins of the Cuban genome and international guidelines.

Prenatal genetic screening includes:

- Quantification of alpha-foetus-protein in maternal blood for the detection of open neural tube defects and other foetal anomalies. This program began in 1982⁵ and so far, 3 007 266 pregnancies have been screened (99 % of coverage, 6.86 % positives), using national equipment and diagnosis kits⁴. Two percent of positive cases were confirmed by ultrasound.
- Hemoglobin electrophoresis of pregnant women peripheral blood, in order to identify couples with increased risk of having an offspring with sickle cell (the most frequent genetic disease in Cuba, carrier frequency 3.7 %).^{6,7}
- Foetal ultrasound of pregnancies at 20-22 weeks of gestation for the detection of foetal anomalies. Yearly, about 150 000 foetal ultrasound evaluations (more than 99 %) are performed. Furthermore, around 30 % of the pregnancies are subjected to a second ultrasound before the end of gestation.⁸
- Cytogenetic prenatal diagnosis of Down syndrome in pregnant women over 38 years of age. In 2004, 3 901 amniotic fluid chromosome analyses were performed at the CNGM, 4.6 % of them were abnormal. This is the most expensive program and has the smallest coverage. The annual number of prenatal chromosome analyses for the entire country is between 3 000 and 3 500.⁸

Newborn screening includes:

- Detection of phenylketonuria (PKU) and hyperphenylalaninemia (96 % of coverage) Prevalence at birth is 1 in 50 000 liveborns. So far, 50 PKU patients have been diagnosed and treated.⁸
- Detection of congenital hypothyroidism (100 % coverage of newborns). Prevalence at birth is 1 in 3 393 liveborns. Until April 2004, 683 babies have been detected and treated.³
- Detection and registry of congenital malformations. The Cuban Registry of Congenital Malformations (RECUMAC) covers 95 % of liveborns. Prevalence of malformations detectable at birth is 1 %.⁸

All mentioned programs were implemented after pilot studies in several regions of the country and were relevant and feasible. They were conducted with strict observance of the ethical principles of autonomy, beneficence and justice, as well as the recommendations of the National Program for Neonatal Screening (NPNS). In all cases genetic counselling is offered. When results of prenatal studies are abnormal, the couple's decision to continue or interrupt the affected pregnancy is supported in a non-judgmental manner.⁹ The termination of pregnancy in Cuba is legal. For babies with positive newborn screening tests, treatment and follow-up are provided freely.⁸

Research

CNGM conducts several research projects geared in order to improve the diagnostic capabilities, to determine the origin of most common mutations causing genetic disorders in Cuba, to contribute to the phenotype delineation of specific genetic diseases, and to establish to genotype-phenotype correlations. New prenatal and neonatal for genetics disorders screening programs have been planned. Other research projects are aimed to improve epidemiological knowledge about the relative roles of genetic and environmental aetiology on birth defects, reproductive failure of genetic origin, predisposition of common and complex diseases and disabilities due to genetic or prenatal environmental causes.

Recently a comprehensive project guided to detect developmental disabilities in the Cuban population concluded. It took less than two years and 10 897 family physicians, 8 051 psychologists from special education, 102 masters in Genetic Counselling, 81 clinical geneticists, 11 200 professionals of different specialties, and 121 genetic counselling students; were involved. Results are properly preserved on protected databases fulfilling the ethical principle of the confidentiality of personal information. Subjects were included in the study after signing the informed consent, nobody refused to participated, 366 864 affected persons, were visited and evaluated.¹⁰ Prevalence of all types of disability in the general population was of 3.23 % (Table 1).

Mental retardation was detected in 140 489 persons (prevalence: 1.25 %), 15.9 % of the cases due to genetic causes, mainly Down syndrome with a prevalence of 4.3 per 10 000 in the general population and 6.8 per 10 000 children under 5 year old.¹⁰

Table. The prevalence of specific disabilities in Cuba

| Developmental disabilities | Prevalence |
|--|--------------------------|
| Physical disabilities | 8,2 in 1 000 inhabitants |
| Blindness and poor vision | 4,1 in 1 000 inhabitants |
| Deafness | 2,1 in 1 000 inhabitants |
| Psychosis without mental retardation | 8,6 in 1 000 inhabitants |
| Mixed (mental retardation plus another described disability) | 2,2 in 1 000 inhabitants |

Special Research Programs

A new National Program for Registry and Care of People with Disability and the Development of Medical Genetics started in 2001. This program is supported by the government; it is addressed to prevention and treatment of disabilities. Evaluation, medical care and social support will be provided to everyone who needs it. On the other hand, this program will update the epidemiological data about the genetic and environmental factors that could cause disability.

Special centres has been founded in response to regional health problems, a good example is the Center for Research and Care of Hereditary Ataxias (CIRAH), located in Holguín province. This place has a high prevalence of spinocerebellar ataxia type 2 (SCA2), an autosomic dominant disease result of founder effect.¹¹⁻¹³ In the whole country there are 101 affected families, 757 identified affected individuals (553 live in Holguín province) and 7 068 persons at risk (25-50 %) of having inherited the defective gene. CIRAH provides integral medical care for the affected individuals including genetic counselling and offers of presymptomatic and prenatal DNA diagnosis to healthy individuals at risk.

Research projects conducted by the centre follow ethical principles that take into consideration the opinions of patients and families, and includes the estimation of risk factors that modify the onset and natural history of disease, new treatments (including neuro-rehabilitation), and animal models.

Perspectives of Medical Genetics in Cuba

The achievements obtained so far, in the organization of genetics services into the socio-economic system, will allow:

- To improve the clinical genetics services according to regional demands.
- To consolidate the automation of Genetics network in the country.
- To increase the quality of services and the coverage of the current national screening programs.
- To develop specialized resources directed to the incorporation of new approaches for screening and treatments of genetic disease, birth defects and conditions of genetic predisposition.
- To enhance teaching of medical genetics in Medical Sciences Programs.
- To extend genetics education to the population through the mass media.
- To promote better conditions for developing integral genetic research projects, adapting the technology to the needs of society.

Conclusions

Cuban government has the vision that genetic disorders and birth defects are particularly sensible determinants of disease, disability, suffering and death. At the same time, the public health authorities are addressing the prevention of these disorders and conditions of genetic predisposition, such as cardiovascular diseases, mental illness, malignancies and other common diseases.

The public health authorities have organized genetic services in a comprehensive and integrated manner, with roots at the primary health care level, because they are convinced that the key to the success of any future genetic program. Finally, the organization of genetic services in Cuba is based in international guidelines and advised by experts of the World Health Organization for the prevention and management of genetic disorders and birth defects in developing countries.¹⁴

Acknowledgements

The authors want to thanks Marcia Cobas-Ruiz, Director of National Program for Attention and Register of Disability People and Development of Medical Genetics and Professor Dr. Francisco Morales-Calatayud. We specially thank Professor Dr. Rolando Hernández-Fernández for encourage us to write this paper, review it and for his useful comments.

REFERENCES

1. Oficina Nacional de Estadística. Anuario Estadístico de Cuba 2005. Visitado: Noviembre, 2005. URL disponible en: www.sld.cu/sitios/dne
2. Ministerio de Salud Pública. Anuario Cubano de Salud. La Habana: Ministerio de Salud Pública de Cuba; 2004.
3. Penchaszadeh VB, Heredero L, Pinales-Morejón D, Rojas I, Pérez ET: Genetic counseling training in Cuba. *Am J Hum Genet* 1997;61(4):1099.
4. Sistema Ultramicroanalítico. Programas Nacionales. Tecnología SUMA. Visitado: April 15, 2004. URL disponible en: www.tecnosuma.com
5. Rodríguez L, Sánchez R, Hernández J, Carrillo L, Oliva J, Heredero L. Results of 12 years' combined maternal serum alpha-fetoprotein screening and ultrasound foetal monitoring for prenatal detection of foetal malformations in Havana City, Cuba. *Prenat Diagn* 1997;4:301-4.
6. Granda H, Gispert S, Dorticos A, Martín M, Cuadras Y, Calvo M. et al. Cuban programme for prevention of sickle cell disease. *Lancet* 1991; 337:152-4.
7. Granda H, Gispert S, Martínez G, Gómez M, Ferreira R, Collazo T, et al. Results from a reference laboratory for prenatal diagnosis of sickle cell disorders in Cuba. *Prenat Diagn* 1994;14:659-62.
8. Ministerio de Salud Pública de Cuba. Programas de Prevención Materno Infantil. La Habana: Dirección Nacional Materno Infantil; Informe 2002.
9. Dorticós-Balea A, Martín-Ruiz M, Hechevarría-Fernández P, Robaina-Castellanos MS, Rodríguez-Blanco M, Moras-bracero F, et al. Reproductive behaviour of couples at risk for sickle cell disease in Cuba: A follow-up study. *Prenat Diagn* 1997;17:737-42.
10. Colectivo de Autores: Por la vida. Estudio psicosocial de las personas discapacitadas y estudio psicopedagógico y clínico genético de las personas con retraso mental en Cuba. La Habana: Casa Editora Abril; 2003.
11. Auburger G, Orozco Díaz G, Capote RF, Sánchez SG, Pérez MP, Estrada del Cueto M, et al. Autosomal dominant ataxia: genetic evidence for locus heterogeneity from a Cuban founder-effect population. *Am J Hum Genet* 1990;46:1163-77.
12. Velázquez L, Santos-Falcón N, García-Zaldívar R, Paneque-Herrera M, Echeverría-Pupo RR. Epidemiology of Cuban hereditary ataxia. *Rev Neurol* 2001;32:606-11.
13. Velázquez-Pérez L, García R, Santos FN, Paneque HM, Medina HE, Hechavarria PR. Hereditary ataxias in Cuba. Historical, epidemiological, clinical, electrophysiological and quantitative neurological features. *Rev Neurol* 2001;32:71-6.
14. Penchaszadeh VB, Christianson AL, Giugliani R, Boulyjenkov V, Katz M. Services for the prevention and management of Genetic disorders and Birth defects in developing countries. *Community Genet* 1999;2:196-201.

Recibido: 4 de diciembre de 2006. Aprobado: 28 de diciembre de 2006.

Dra. Araceli Lantigua-Cruz. Email: lantigua@infomed.sld.cu