Incidence of IDDM in Children Living in Puerto Rico

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OBJECTIVE — To determine incidence, geographic distribution, and seasonal variation of IDDM in children 0–14 years of age living in Puerto Rico. Because these data have been collected through the infrastructure of the World Health Organization's DiaMond project, these results are directly comparable with incidence data from other populations worldwide involved in this study.

RESEARCH DESIGN AND METHODS — Beginning in 1990, new cases of IDDM were registered retrospectively from 1985 and prospectively to 1994 by review of medical records from island hospitals. Included in the hospital registry are 1,527 cases of IDDM. Validation of the primary source was by three secondary lists of cases obtained through diabetic camps, surveys of schools, and a government registry. Log linear modeling (capture-recapture) was used to correct incidence.

RESULTS — Mean incidence of IDDM from 1985–1994 was 18.0 cases/100,000 children per year (95% CI 17.6–18.3). There was a slight female rather than male predominance: 51% of the cases were girls, and 49% were boys. Although Puerto Rico has marked variation in rainfall, altitude, and genetic markers, no significant differences are found in the incidence rates of different areas or seasons of the island.

CONCLUSIONS — This registry of Puerto Rican children is the largest IDDM registry of minority children in the U.S. The results of this study indicate that the annual incidence of IDDM of children living in Puerto Rico is higher than the incidence of other multiracial ethnic groups living in the U.S.

Epidemiological investigations in Spanish-heritage populations in the Americas are potential sources to quantitate effects of genetic admixture, socioeconomic conditions, and geography on IDDM. Migrant populations are exposed to environmental risks of IDDM in their areas of settlement but retain the genetic disposition of the founding ethnic group. Resulting incidence rates are often intermediate between country of origin and country of migration, as shown for Mexican-Americans in Colorado and Chicago (1,2). However, two studies that included small Puerto Rican populations both reported higher incidence rates for Puerto Ricans than were found in other Caucasians in the U.S. (2,3). No incidence data for the island of Puerto Rico are presently available to determine if this higher rate is found in the original population or if it occurs as the result of migration to the U.S. mainland.

The World Health Organization's (WHO's) DiaMond project is an investigation of IDDM incidence, genetics, and outcome that involves more than 120 centers in 69 countries and includes 5% of children with IDDM in the world (4). More than 35 centers include Hispanic and/or African-American heritage populations. Seven registries are located in the Caribbean and Mexico. Data from Puerto Rico provide an important component to the worldwide study of incidence of IDDM because the island has a mixed population of southern European, Amerindian, and African heritage, is located in the tropical Caribbean, and has a socioeconomic structure similar to that of the U.S.

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Abbreviations: WHO, World Health Organization.

Puerto Rico is located on the northeastern side of the Caribbean Sea (Fig. 1), and is a U.S. territory. The island population exceeds 3.5 million, and more than 2 million Puerto Ricans have migrated to the U.S. mainland. To determine IDDM incidence rates in Puerto Ricans on the island, we used the WHO DiaMond protocol to facilitate comparisons with IDDM registries of the U.S. and other areas of the world.

RESEARCH DESIGN AND METHODS

— In 1990, an island-wide registry of new cases of childhood IDDM was established retrospective to 1985. Hospital and outpatient clinic care are provided by 128 facilities. Eligible IDDM patients were identified by medical record review at the 57 island hospitals that admit pediatric patients. Records with Diagnostic Related Group Code (*International Classification of Diseases, Ninth Revision*) 250 were examined if the patient's age was <15 years. Patients were included if one parent was Puerto Rican and if the patient was discharged on insulin to a residence in Puerto Rico. These entry criteria are identical to other registries of the DiaMond project to permit direct comparisons.

To fulfill WHO protocol, the hospital registry was validated by secondary sources of cases: a voluntary government registry, summer diabetes camp lists, and survey forms sent to public and private schools. The government list originated in public drives to register all diabetic patients in the 1970s and 1980s. Diabetes camp lists were compounded by the nurse abstractor who attended the camp. The school survey is conducted annually by school nurses, who collect information about chronic diseases. If a child listed diabetes, a questionnaire was sent home for the parents to complete and give consent to participate in the study.

All registries record given name, paternal and maternal names, date of birth, and date of onset of diabetes. Other information is obtained according to the type of registry. To avoid multiple case counts, cases that matched previously reported cases by name and birth date were deleted from the registry.

The 1990 U.S. census recorded the population of Puerto Rico as 3,522,037, of which 958,219 were children <15 years of

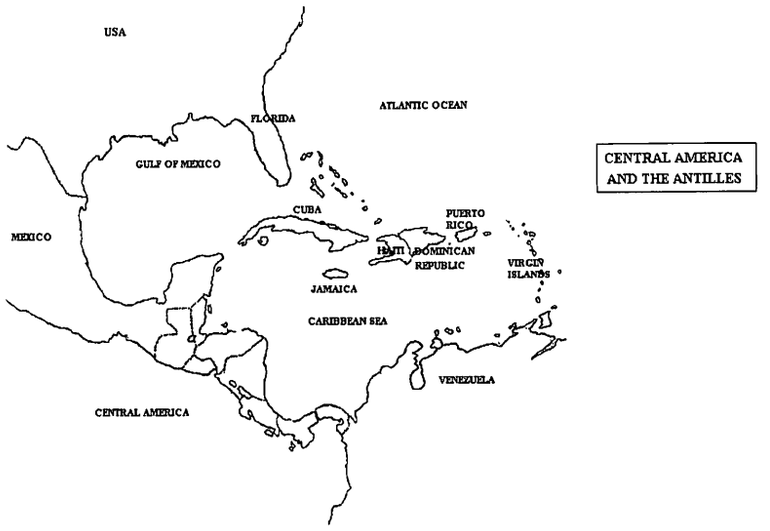

Figure 1—*Map of the Caribbean. Puerto Rico, an island of 40 × 100 miles 18°N of the equator, is 1,000 miles from Florida, 1,500 miles from New York, and 500 miles from Venezuela.*

age. This census defines all residents of Puerto Rico as Hispanics (5).

Capture-recapture methodology and log linear modeling were used to determine incidence and ascertainment (6,7); 95% confidence intervals are based on Poisson distribution (8).

RESULTS

Incidence

Forty-eight hospitals in Puerto Rico admitted at least one patient with newly diagnosed IDDM under the age of 15 years since 1985. Over a 10-year period, 1,527 cases of IDDM were identified through hospital records; 395 cases were extracted from a government registry of both IDDM and NIDDM; 863 cases were reported from the school registry; and 369 cases were identified from diabetes camps. A total of 1,602 cases were identified in all four registries. Integrating primary and validation sources, the mean incidence for the years 1985–1994 is 18.0 cases per 100,000 children per year (95% CI 17.6–18.3, ascertainment 92.4%). Analysis of the yearly incidence is shown on Table 1. No temporal trend of increasing or decreasing number of cases could be found in these data.

Seasonal variation

The climate of Puerto Rico is divided into drier springs and summers, and rainy autumns and winter months, including hurricane season from June to November. An increase in the incidence of IDDM is suggested in winter months, which would parallel the increased diagnosis rate in temperate zones. However, the 70 ± 6.4 cases/year (mean ± SD) in the summer months is not significantly different from the 76 ± 9.5 cases/year of the winter months.

Sex differences

Unlike other autoimmune diseases, IDDM often exhibits a slight male dominance in Caucasian populations. In contrast, African, Asian, and their heritage populations show higher incidence in females (10). Although predominantly a Caucasian population, Puerto Rico also shows a slight female predominance; the male-to-female ratio is 0.91. The mean age of onset in girls (± SEM) is 8.6 ± 0.1 years, with a peak number of diagnosis at 10–11 years of age; in boys, mean age of onset is 8.4 ± 0.1 years, with equal numbers of cases from 8–14 years of age.

Incidence in different health regions

In spite of the geographic and ethnic variations of the island, no significant differences were found in the incidence rates of IDDM in the different health regions.

CONCLUSIONS — Geographic location is a strong determinant of incidence of both acute and chronic illness. Worldwide incidence rates of IDDM vary more than any other chronic disease. There is a 30- to 60-fold difference between the high of 35 cases/100,000 children/year in Finland to 0.7 cases in Korea and Mexico (11). Concordance rate of identical twins of 25–35% during childhood indicates that both genetic and environmental factors account for this variation (12–15). The tenet of the WHO DiaMond project is that worldwide comparison of incidence rates and genetic factors in diverse populations will facilitate determination of the etiology of IDDM.

Puerto Rico is the smallest of the Greater Antilles islands of the West Indies, located 18° north of the equator. Land height changes from sea level to 3,000 feet, and annual precipitation varies 10-fold, from 30 inches in southern areas to 365 inches in the eastern rain forest. Located twice as far from Florida as from Venezuela, Puerto Rico became a U.S. possession after the Spanish-American War in 1898 and is one of three remaining American territories. European settlement of Puerto Rico began soon after discovery by Columbus in 1493. Although the Amerindian inhabitants, Tainos, were eliminated as a distinct culture, these descendants of the PaleoIndians made a significant genetic contribution to Puerto Ricans (16).

The modern genetic admixture of Puerto Rico is estimated to be 50–55% Southern European, 25–30% Western African, and 15–20% other, including Amerindian, Northern European Caucasian,

Table 1—*Cases and yearly incidence and 95% CIs of newly diagnosed IDDM cases by year in Puerto Rico in children <15 years of age, determined by log linear modeling*

	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
Cases	125	167	176	146	166	176	160	146	161	179
Incidence	13.1	17.4	18.4	15.2	17.3	18.4	16.7	15.2	16.8	18.7
95% CI	12.8–13.6	16.2–19.3	17.5–19.6	14.6–16.1	16.7–18.3	17.6–19.4	16.0–17.7	14.6–16.2	16.5–17.3	17.6–20.4

Demographic data are the number of children <15 years of age from the 1990 U.S. census of Puerto Rico, the midpoint of the decade examined.

and modern Asian immigrants. These estimates follow population records of settlers and slaves from the early 1800s when slave importation was prohibited. Although Puerto Rico participates in the U.S. Census every decade, no ethnic information is obtained, and all people living in Puerto Rico are defined as "Hispanic." Ninety-five percent of medical records do not record the ethnicity of the patient. For this reason, no effects of race or ethnicity could be ascertained by this study. Nonetheless, like other American cultures, Puerto Ricans exhibit marked variation in their genetic origins. But whereas the incidence of sickle-cell trait varied from 0.7 to 7.3% from the central to the eastern part of the island, no significant differences were found in incidence rates of IDDM across the island (9).

Socioeconomic conditions in Puerto Rico have changed rapidly over the last 100 years. At the beginning of the century, it had the lowest per capita income of the entire Caribbean, ranking below Haiti. After World War II, gross national product rose dramatically, and Puerto Rico currently ranks with Argentina as the highest per capita income in Latin America. Northern American culture has been extensively imported to Puerto Rico, most notably in the availability of grocery items, fast food, and television. Obesity rates parallel rates in the U.S. Medical practices in Puerto Rico are similar to those in the U.S.: medical schools and residency training programs are accredited by the same Liaison Committee for Medical Education and Residency Training. Twenty percent to 35% of physicians have completed residencies on the U.S. mainland.

The IDDM registry of Puerto Rican children is the largest population registry of minority children described in the U.S. This report provides information about effects of tropical geography on IDDM incidence in an affluent, primarily Caucasian, population. It is the third island, following Prince Edward Island and Sardinia, to report a higher incidence of IDDM than found on bordering mainlands. The findings of Puerto Rico contrast with the findings of the U.S. Virgin Islands, in which Tull et al. (17) reported 28 children diagnosed over a 5-year period and an incidence of 7.5/100,000 children per year. Furthermore, differing from the rest of Latin America, Puerto Rico is the first Hispanic population to report higher incidence rates than its major populations of origin, Spain (11.3–11.5/100,000) and Africa (5.7–10.9/100,000) (18,19).

The high incidence rates reported for mainland Puerto Rican children living in Philadelphia and Chicago, 15–18 cases/100,000 children per year, are similar to the incidence rate that we ascertained for the island, 18 cases/100,000 children per year (2,3). Although these mainland studies were based on small populations, the IDDM incidence rates of these migrant populations seem valid and equal to the rate of the population at the site of origin. The Puerto Rican community is therefore the only population reported in which incidence of IDDM does not appear to increase with migration to the U.S. mainland.

In summary, the Puerto Rican registry provides a unique perspective on environmental and genetic determinants of IDDM incidence. In contrast to previous reports of low-latitude countries, it documents a high incidence rate in a Hispanic population and indicates that this rate does not change with migration to the U.S. The relative contributions of a socioeconomic status similar to the mainland U.S. and the Puerto Rican genetic predisposition in causing these incidence rates remain to be determined.

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References

1. Hamman RF, Gay EC, Cruickshanks KJ, Cook M, Lezotte DC, Klingensmith GJ, Chase HP, Colorado IDDM Registry: Incidence and validation of IDDM in children aged 0–17. *Diabetes Care* 13:499–506, 1990
2. Lipman TH: Epidemiology of type I diabetes in children 0–14 years of age in Philadelphia. *Diabetes Care* 16:923–925, 1993
3. Lipton RB, Fivecoate J: High risk of IDDM in African-American and Hispanic children in Chicago, 1985–90. *Diabetes Care* 18:476–482, 1995
4. WHO Diamond Project Group: WHO Multinational Project for Childhood Diabetes. *Diabetes Care* 13:1062–1066, 1990
5. U. S. Bureau of the Census: *General Population Data Puerto Rico*. Bureau of the Census, Washington, DC, 1990
6. Cochi SB, Edmonds LE, Dyer K: Congenital rubella syndrome in the United States, 1970–85: on the verge of elimination. *Am J Epidemiol* 129:349–361, 1989
7. WHO DiaMond Project Group: *Methods of Operation: Parts I-IV, Incidence Study*. Version 2. June 1991
8. International Working Group for Disease Monitoring and Forecasting: Capture-recapture and multiple-record systems estimation II: applications in human diseases. *Am J Epidemiol* 142:1059–1068, 1995
9. Santiago-Borrero P, Valcarcel M, Caceres M, Montalvo F: Geographic distribution of abnormal hemoglobins in Puerto Rico. *Bol Asoc Med PR* 7:447–451, 1983
10. Rewers M, LaPorte, RE, King HM, Tuomilehto J: Insulin-dependent diabetes mellitus in childhood: international patterns and trends. *World Health Stat Q* 41:179–189, 1988
11. Karvonen M, Tuomilehto J, Libman I, LaPorte R, the WHO DiaMond Project: A review of the recent epidemiological data on the world-wide incidence of type 1 (insulin-dependent) diabetes mellitus. *Diabetologia* 36:883–892, 1993
12. Kyvic KO, Green A, Beck-Nielsin H: Concordance rates of insulin dependent diabetes mellitus: a population based study of young Danish twins. *BMJ* 311: 913–917, 1995
13. Kumar D, Gemayel, NS, Deapen D, Kapadia D, Yamashita PH, Lee M, Dwyer JH, Roy-Burman P, Bray GA, Mack TM: North American twins with IDDM. *Diabetes* 42:1351–1363, 1993
14. Matsuda A, Kuzuya T: Diabetic twins in Japan. *Diabetes Res Clin Pract* 24 (Suppl.): S63–S67, 1994
15. Kaprio J, Tuomilehto J, Koshenvue M, Romanov K, Reunanem A, Eriksson J, Stengard J, Kesaniemi YA: Concordance for type 1 and type 2 diabetes mellitus in population-based cohort of twins in Finland. *Diabetologia* 35:1060–1067, 1992
16. Thieme FP: The geographic and racial distribution of ABO and RH blood types and tasters of PTC in Puerto Rico. *Am J Hum Genet* 4:94–112, 1952
17. Tull ES, Roseman JM, Christian CLE: Epidemiology of childhood IDDM in U.S. Virgin Islands from 1979 to 1988. *Diabetes Care* 14:558–564, 1991
18. Serranos-Rios M, Moy CS, Martin Serrano R: Incidence of type I diabetes mellitus in subjects 0–14 years in the Comunidad of Madrid, Spain. *Diabetalogia* 33:422–424, 1990
19. Elamin A, Omer MI, Zein K, Tuvemo T: Epidemiology of childhood type I diabetes in Sudan, 1987–90. *Diabetes Care* 15:1556–1559, 1992