Dengue is a mosquito-borne disease, caused by serologically related but antigenically distinct single-strand positive-sense RNA viruses; the viruses have been grouped into four serotypes (DENV-1 through DENV-4) belonging to the genus Flavivirus (family Flaviviridae). Aedes aegypti is the primary mosquito vector; however, other species from the genus Aedes, such as Aedes albopictus, can also be vectors of dengue virus transmission.

The clinical spectrum of disease includes asymptomatic infection, mild dengue fever (DF), dengue hemorrhagic fever (DHF), or dengue shock syndrome, which is frequently fatal because of abnormal capillary permeability and plasma leakage. Unusual manifestations such as miocardiopathy, hepatic failure, and neurological disorders have also been reported. There is no specific treatment of dengue illness as yet, and vector control is the only preventive strategy.

Dengue incidence and prevalence are rising in endemic areas of the tropical and subtropical regions. On the basis of mathematical model estimates, approximately 50 million infections occur each year. Dengue infection occurs in more than 100 countries in the Asia-Pacific, Americas, the Middle East, and Africa, and cases continue to rise worldwide. In the past, the burden of the disease has fallen on countries in South-East Asia and the Western Pacific regions of the World Health Organization (WHO). However, a dramatic increase of cases has been reported since 1995. Recent dengue virus transmission has been reported in almost every country in this region, and Uruguay and continental Chile are the only countries without indigenous transmission in Latin America.

Although there is a perceived increase in disease burden, dengue epidemiology of the Americas region has not been well documented. Here, we characterize dengue disease dynamics during the last three decades and track the spread of dengue across the Americas.

INTRODUCTION

METHODS

To examine the disease patterns, we obtained the dengue infection records of WHO and of the Pan American Health Organization (PAHO), the regional body of WHO responsible for the 35 nations and 9 territories of the Americas. Because age and monthly distribution of cases are not routinely reported to PAHO, we obtained data from the Ministries of Health of selected countries to assess age distribution and seasonality patterns.

Annual PAHO reports of DF and DHF cases, reported according to the PAHO dengue case definitions, were analyzed by subregions and by country. Seven PAHO subregions were considered: North America (excluding Mexico), Central America/Mexico, Andean (i.e., Bolivia, Colombia, Ecuador, Peru, and Venezuela), Southern Cone (i.e., Argentina, Brazil, Chile, Paraguay, and Uruguay), Hispanic Caribbean, and Non-Hispanic Caribbean. Three time periods were considered: 1980 through 1989 (80s), 1990 through 1999 (90s), and 2000 through 2007 (2000–7). Population data from the U.S. Census Bureau Population Division, Department of Commerce for 1980 through 2006; population data were obtained from the Ministries of Health of selected countries to assess age distribution and seasonality patterns.

Because serotype identity had been systematically determined since 1995, serotype circulation could be assessed from PAHO records beginning in 1995. The identity and proportions of serotypes circulating in each country were compared. To examine case age distribution, we analyzed available data from Brazil, Venezuela, Honduras, and Mexico, because these countries reported the highest number of DF and DHF cases during the last two decades. Incidence rates by age-adjusted population (per 100,000 inhabitants) were calculated. The dengue case age distribution for Brazil was obtained from the MoH website for 2005 through 2007. We also reviewed data from the Secretariat of Health of Honduras.
(Dirección General de Vigilancia en Salud, [DGVS]) for 2004 through 2007. Mexican case, incidence and population data were obtained from the MoH, General Directorate of Epidemiology (GDE) website for 2002 through 2006. To examine seasonality, we obtained data from the Brazilian MoH and SINAN, and Mexican MoH, GDE, and the Honduran DGVS websites. We examined available gender distribution data from Mexico (2003 through 2007) and Brazil (2001 through 2005) at their respective MoH websites.

**RESULTS**

**Dengue disease patterns.** The total dengue cases reported in the Region were 1,033,417 (16.4/100,000) during the 80s, 2,725,405 (35.9/100,000) during the 90s, and 4,759,007 (71.5/100,000) during 2000–7. Similarly, the number of DHF cases increased over time from 13,398 (0.2/100,000) during the 80s, to 58,419 (0.8/100,000) during the 90s, to 111,724 (1.7/100,000) during 2000–7. The DHF cases as a percentage of total dengue cases also increased from 1.3% to 2.1% to 2.4% (Table 1). Epidemic cycles were observed every 3–5 years with an increased frequency of DHF cases and fatalities caused by dengue during epidemic years (Figure 1). From 1980 through 1987, 242 deaths were reported (1.8% of all DHF cases) compared with 1,391 deaths during 2000–7 (1.2% of all DHF cases).

The Southern Cone and Andean subregions reported the highest proportion of cases during the 90s: 55% (66.3/100,000) for Southern Cone and 20.7% (55.9/100,000) for Andean subregion. In 2000–7, the proportion of cases remained approximately the same but the incidence increased substantially: 64.2% (155.3/100,000) for Southern Cone and 19% (97.7/100,000) for Andean. Interestingly, two different regions reported the highest percentages of cases during the 80s: Hispanic Caribbean 39.1% (210.5/100,000), and Central America/Mexico 27.2% (28.7/100,000). In general, reported cases increased over time in most subregions. In contrast, the number of reported cases was highest in the 80s in the Hispanic Caribbean and declined over time (Table 1). Similarly, the majority of DHF cases and the highest incidence of disease occurred in the Hispanic Caribbean in the 80s: 77.5% (5.5/100,000); the Andean subregion reported the most DHF cases during the 90s (83.4% [4.8/100,000]) and 2000–7 (58.5% [7.1/100,000]).

The number of countries with an average incidence greater than 100/100,000 increased from 5 during the 80s, to 7 during the

<table>
<thead>
<tr>
<th>Subregion</th>
<th>1980–9 Total</th>
<th>1990–9 Total</th>
<th>2000–7 Total</th>
<th>Total Region</th>
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<tr>
<td>DF cases</td>
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<tr>
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<td>3,049,262</td>
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<tr>
<td>DF cases</td>
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<td>DHF cases</td>
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<td>1,257</td>
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<td>Fatalities</td>
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<td>46</td>
<td>73</td>
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<tr>
<td>Total region</td>
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<td></td>
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<td>Dengue total cases</td>
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<td>4,732,594</td>
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<td>111,724</td>
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<tr>
<td>Fatalities</td>
<td>242</td>
<td>577</td>
<td>1,391</td>
<td>2,210</td>
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</table>

*A total of 1,139 cases were not included because the country was not specified.
Deaths from 1990–4 are not reported.
90s to 15 during 2000–7 (Figure 2). Brazil reported the majority of dengue cases (54.5%) during the 27-year study period but ranked sixth in total DHF cases (Figure 3). Venezuela reported the highest number of DHF cases in the (35.1%) during the same period. During the 80s by contrast, Cuba experienced the highest number of dengue and DHF cases. By the end of 2007, only 2 countries (Uruguay and Chile) reported an absence of indigenous transmission. Endemic dengue transmission was reported in the Easter Island, a Chilean territory at the Pacific Ocean.

**Dengue serotypes.** During 1995 through 1999, all four serotypes were reported in Central America and the Caribbean subregions. Serotypes DENV-1, DENV-2, and DENV-4 were detected in the Andean subregion, but only DENV-1 and DENV-2 were circulating in the Southern Cone. By 2000–7, all four serotypes were circulating throughout the Americas, except for the Southern cone, where only DENV-4 was not detected during the period. The number of countries circulating ≥3 serotypes in any given year was 5 during 1995 through 1999 and rising to 15 during 2000–7.

The circulating serotypes reported most frequently during the 90s were DENV-1 and DENV-2. This pattern changed during 2000–7 when DENV-2 and DENV-3 were the most frequently reported serotypes (Figure 4). DENV-3 circulation increased throughout the Americas after its introduction in the Andean and Southern Cone subregions in 2000.

**Age distribution of cases.** In Brazil, the highest incidence of DF during 2000–7 was among young adults. In Venezuela, incidence was highest among 10- to 14-year-old children and adolescents, but peaked among 5 to 9 year olds in 2007 (570/100,000). In Honduras, the incidence across age groups was similar. In Mexico, children and adolescents 10 through 14 years of age had the highest dengue incidence rates followed by adolescents 16 through 18 years of age (Figure 5).

In general, DHF incidences by age group were similar to those observed for DF. However, in Venezuela the highest incidence rates were observed among infants starting in 2005 and peaking in 2007 (62.9/100,000). In Brazil, the highest DHF incidence rates were among young adults during 2001 through 2005 and were coincident with the highest incidence of DF. However, in 2006 the incidence rate among <5 year olds increased dramatically (0.47/100,000) and was higher than that observed among 10 through 19 year olds (0.36/100,000) and 20 through 39 year olds (0.46/100,000).

![Figure 1](image1.png)  
**Figure 1.** Number of dengue fever (DF) and dengue hemorrhagic fever (DHF) cases, Region of the Americas, 1980–2007.

![Figure 2](image2.png)  
**Figure 2.** Average dengue incidence per 100,000 by country, Region of the Americas, 1980–2007.
Other epidemiological features. A seasonal pattern was observed in the countries with available monthly case distribution data. In Brazil, most cases occur in the first half of the year, peaking in March–April. However, in Honduras and Mexico the cases began to increase in June–July, and most cases were concentrated in the second half of the year. In Mexico, cases peaked between August and October throughout 2000–7 (Figure 6).

The case reports indicate that women were more frequently infected with dengue than men. The male: female ratio ranged from 1:1.22 to 1:1.34 in Brazil during 2001–5 and from 1:1.27 to 1:1.41 in Mexico during 2003 through 2007.

DISCUSSION

The data reported herein suggest that the Americas region overall is trending toward the higher dengue incidence rate levels. The Region of the Americas reports the most WHO-reported cases of dengue worldwide (68%, 2000 through 2006). Although the greatest proportion of dengue-related deaths are reported in the South-East Asia and Western Pacific regions and some of these countries may underreport dengue-related disease by recording only DHF cases, the disease burden in the Americas is a significant public health concern. Over the last three decades, a 4.6-fold increase in reported cases was observed in the Americas (~1 million cases during the 80s to 4.7 million during 2000–7).

The endemo-epidemic nature of dengue in the Americas features recurring peaks of reported cases at 3- to 5-year intervals. Over time, the peaks have become progressively higher. More worrisome is the increasing trend of observed DHF cases. During the study period, DHF cases increased 8.3-fold, (~13,400 in the 80s to ~111,700 DHF in 2000–7).

Since 1980, the disease has broadly expanded throughout the region. The Southern Cone reported the most cases since 1990, with Brazil alone accounting for 63% of reported cases since 2000. In contrast, the Latin Caribbean and Central America/Mexico reported the highest number of DF and DHF cases after the emergence of dengue in Cuba in 1981. In the following two decades, the Andean subregion reported the majority of DHF cases, after a large epidemic in Venezuela in 1989.

The epidemiological patterns of dengue in the Americas Region may be related to outbreaks of disease caused initially by a single dengue serotype followed by infections by a different serotype. DENV-1 was reported for the first time in the region in 1977 causing an epidemic, which began in Jamaica expanded to Cuba, Puerto Rico, and Venezuela, and eventually to the rest of the Caribbean countries, Mexico, Central America, and the northern countries of South America. DENV-2 caused the first DHF epidemic in the region when reported in Cuba in 1981. During the same year, DENV-4 was introduced into the eastern Caribbean islands. This serotype then expanded to the rest of the Caribbean and Central, South America and Mexico. Despite the increasing number of dengue cases during 1981 through 1988, the incidence of
DHF in the region remained low until 1989 when a second DHF epidemic was reported in Venezuela. DENV-1, -2, and -3 serotypes were isolated from clinical samples with DENV-2 predominant. During the 80s, dengue started to circulate in Brazil, Bolivia, Paraguay, Ecuador, and other South American countries that had not experienced the disease before. In Brazil, the first laboratory-confirmed dengue outbreak was reported in 1981–1982 in Roraima state. This outbreak was contained after local vector control measures were implemented. No further dengue activity was reported until 1986 with the introduction of DENV-1 in Rio de Janeiro state.

In 1990, DENV-2 serotype was introduced in Rio de Janeiro during a period of DENV-1 serotype circulation. DENV-2 serotype in Brazil spread to other parts of the country with more severe clinical presentations, and the first fatal cases caused by secondary dengue infections. In 1994, DENV-3 virus was reintroduced in the Americas after an absence of 16 years. Colombia and Puerto Rico reported this serotype in 1977 and 1978, but it was not observed again until 1994 in Nicaragua and Panama. DENV-3 serotype initially expanded to Central American countries and Mexico, and later to Puerto Rico, other Caribbean islands, and South America.

In 2000, DENV-3 serotype was introduced in Rio de Janeiro causing a widespread, 3-year outbreak. Although DENV-3 was the predominant serotype and was the only serotype associated to fatalities, DENV-1 and -2 serotypes were also

**Figure 5.** Incidence rates per 100,000 of dengue fever (DF) and dengue hemorrhagic fever (DHF) cases by age: (A) Brazil, (B) Mexico, (C) Honduras, and (D) Venezuela.

**Figure 6.** Monthly distribution of dengue cases: (A) Brazil, (B) Mexico, (C) Honduras, and (D) Venezuela.
circulating. DENV-3 virus later spread more broadly in Brazil, and DENV-2 was reintroduced to Rio de Janeiro in 2007 and 2008 causing the majority of fatal cases during that time. These data suggest that a prior dengue infection may set the stage for a more deadly infection by a different serotype in a few years. Several seroepidemiological studies support this hypothesis.

Although the populations in Southeast Asia and the Americas are similar and that all dengue serotypes are endemic in both regions, DHF rates in the Americas are lower compared with those reported in Southeast Asia since World War II. One potential explanation may be the failure of clinicians in the Americas to collect data to fulfill the requirements of the PAHO case definition. Another explanation is the association of severe disease to a specific dengue genotype. The introduction of the DEN-2 Asian genotype in the Americas may have contributed to the increase of disease burden. Globalization, infrastructure, and a decreased access to health care has also contributed to the increase of disease burden.

In conclusion, the Americas Region evolved from a low dengue-endemic state to hyperendemic state with indigenous transmission now observed in almost all countries. The increasing trend in DHF cases and the occurrence of more severe cases in children is alarming. The only available control measures relies on vector control programs, which are costly and difficult to maintain. The development of effective vaccines to protect against the four dengue serotypes, in conjunction with the broad implementation of a PAHO initiative, the Integrated Management Strategy for Dengue Prevention, seem to be the most promising approaches for disease control.
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REFERENCES


