Introduction

Dengue hemorrhagic fever (DHF), first described in 1957 by Hammon in the Philippines (1), causes high morbidity and mortality in some parts of the world (2) and constitutes a significant threat to public health. Until 1981, this disease had been limited to Southeast Asia and the Western Pacific. No epidemics of DHF had occurred in the Americas, despite circulation of dengue viruses in our Region for the previous 25 years or so (3, 4), and only sporadic cases had been reported in that period (5, 6).

In the summer of 1981, however, Cuba was struck by a major dengue epidemic that included numerous DHF cases and fatalities. This constituted the first time in this century that confirmed DHF cases had occurred in the Americas and one of the few occasions on which DHF had been detected outside of Southeast Asia and the Western Pacific (7). Previously published articles have dealt with various aspects of this epidemic (8-12), but none has described the principal indicators detected during the outbreak or their evolution, which is the purpose of this report.

Within this context, it should be mentioned that the DHF epidemic in Cuba merits thorough study, because it offers a unique opportunity to augment our theoretical and practical knowledge of the disease.

Between 1945 (13) and the 1970s dengue was unknown in Cuba, and it was not until 1977 that dengue virus reappeared and produced a large-scale dengue epidemic coinciding with a concurrent dengue-1 pandemic in the Caribbean (14). Then came the 1981 epidemic, caused by dengue-2 virus, that led to the appearance of DHF. Because of this sequence of events, we have been given the opportunity to study hemorrhagic dengue under a well-defined set of epidemiologic circumstances within the parameters of conditions prevailing in the Caribbean. These conditions contrast sharply with those prevailing in Southeast Asia, where the four dengue virus serotypes circulate simultane-
ously—a state of affairs creating obvious difficulties for data interpretation.

**Report on the Epidemic**

**Early Developments**

The epidemic was first detected in late May 1981, several weeks after the onset of the rainy season, on the outskirts of the city of Havana, where a growing number of people were coming down with fever; abdominal, retroocular, and muscular pains; intense headache and asthenia; rashes; and occasionally a hemorrhagic picture accompanied by shock that in some cases led to death. At the time the epidemic was recognized, high indexes of *Aedes aegypti* infestation existed in almost all the country’s urban centers.

The first cases were deemed to be meningococceemia, partly because this disease is endemic in Cuba, and partly because there were no previously reported cases of DHF in our country. However, these first cases were quickly followed by an explosive epidemic, with cases being reported throughout the island.

At this time the Pedro Kourí Institute of Tropical Medicine was asked to diagnose the illness and identify the virus. Within 24 hours the health authorities were presented with a presumptive seroepidemiologic diagnosis, and a few days later the dengue-2 virus was isolated and identified, using a methodology previously described (8).

**Clinical Symptoms**

The clinical picture of typical DHF cases was characterized by fever, vomiting, hepatomegaly, and abdominal pains. The hemorrhagic manifestations most common in children were petechiae and hematemesis, while those most common in adults were purpura, metrorrhagia (in women), and hematemesis. Shock, when it developed, occurred most frequently on the fourth day of clinical symptoms. Among the children who died, hemorrhaging predominated; while among the adults who died, shock predominated.

An interesting fact about the disease in adults is that even though the course of the disease was generally favorable and few cases of shock were observed, when shock was present the evolution was almost invariably fatal. In contrast, children with the disease who exhibited shock more commonly recovered, a circumstance that could indicate an important difference between children and adults regarding the mechanisms that produce shock.

**Morbidity**

Figure 1 shows the numbers of dengue cases recorded over the course of the epidemic. In all, 344,203 cases were registered and reported (on a daily basis) to the Ministry of Public Health. The week of highest incidence extended from 30 June through 6 July, when a daily average of 9,447 cases was reported; and the day of highest incidence was 6 July, when 11,400 cases were reported.

A gradual decline in morbidity that began the second week in July was due, in our opinion, to an intense anti- *Aedes* campaign that was launched.
across the country in the month of June, producing a rapid drop in the indexes of vector infestation.

Overall, the epidemic lasted from the end of the month of May until 10 October, when the last case was reported. Around the latter time a national dengue surveillance system was established that is still in existence; after more than three years of operation, it allows us to affirm that the country is entirely free of this disease.

### Hospitalizations and Case Severity

Table 1 shows the number of dengue patients hospitalized during each month of the epidemic. As may be seen, the Ministry of Public Health adopted a liberal hospital admission policy for dengue cases, with the result that 116,151 patients (33.7% of all those with reported cases) were admitted. This policy appears to have played a significant role in reducing fatalities; in other epidemics elsewhere, where the index of hospitalization was typically much lower, patients were hospitalized when they were already in shock, and the indexes of mortality and lethality were higher (15).

Table 2 shows the prevalence of "serious" and "very serious" cases per month. In general, the classifications "serious" and "very serious" corresponded, respectively, to levels III and IV

<table>
<thead>
<tr>
<th>Month</th>
<th>No. hospitalized</th>
</tr>
</thead>
<tbody>
<tr>
<td>June</td>
<td>16,302</td>
</tr>
<tr>
<td>July</td>
<td>51,813</td>
</tr>
<tr>
<td>August</td>
<td>46,455</td>
</tr>
<tr>
<td>September</td>
<td>1,499</td>
</tr>
<tr>
<td>October</td>
<td>82</td>
</tr>
<tr>
<td>Total</td>
<td>116,151</td>
</tr>
</tbody>
</table>
TABLE 2. Numbers of cases classified as “serious” or “very serious” in a manner corresponding to levels III and IV, respectively, in the classification established by the WHO Technical Advisory Committee on DHF for the South Asian and Western Pacific regions (16), by month.

<table>
<thead>
<tr>
<th>Month</th>
<th>Serious cases</th>
<th>Very serious cases</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>June</td>
<td>1,660</td>
<td>221</td>
<td>1,881</td>
</tr>
<tr>
<td>July</td>
<td>5,508</td>
<td>715</td>
<td>6,223</td>
</tr>
<tr>
<td>August</td>
<td>1,949</td>
<td>171</td>
<td>2,120</td>
</tr>
<tr>
<td>September</td>
<td>85</td>
<td>2</td>
<td>87</td>
</tr>
<tr>
<td>October</td>
<td>1</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>9,203</td>
<td>1,109</td>
<td>10,312</td>
</tr>
</tbody>
</table>

in the classification established by the World Health Organization Committee of Experts for Hemorrhagic Dengue in Southeast Asia and the Western Pacific (16). As may be seen, a total of 9,203 serious cases and 1,109 very serious cases were recorded, with the highest numbers of both types occurring in July.

TABLE 3. Distribution by race of 98 patients (72 children and 26 adults) dying of DHF in the 1981 epidemic.

<table>
<thead>
<tr>
<th>Race</th>
<th>Racial distribution of the Cuban population</th>
<th>Distribution by race of 98 patients dying of DHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>66.0%</td>
<td>80.4%</td>
</tr>
<tr>
<td>Mulatto</td>
<td>21.9%</td>
<td>11.3%</td>
</tr>
<tr>
<td>Black</td>
<td>12.0%</td>
<td>8.2%</td>
</tr>
<tr>
<td>Asiatic</td>
<td>0.1%</td>
<td>—</td>
</tr>
</tbody>
</table>

a This racial distribution, found by the National Housing and Population Census of 1980, was based on skin color.
b The race of each of the 98 patients, obtained from the patient's clinical history, was likewise determined according to skin color.

Mortality Patterns

A total of 158 deaths were reported, yielding an overall mortality of 1.59 deaths per 100,000 inhabitants and a lethality index (deaths per 1,000 dengue cases) of 0.46, the lowest lethality index reported until then for a dengue epidemic involving confirmed DHF. The ages of the patients who died ranged from three days to 80 years, the modal age being four years. In all, 101 children and 57 adults died. The high proportion of adult deaths deserves particular attention, because DHF morbidity and mortality among adults is uncommon in Southeast Asia and the islands of the Western Pacific.

Table 3 shows the distribution by race of the 98 fatalities for whom clinical histories were available. These figures appear to indicate that there was a statistically significant (p < 0.05) predominance of fatalities among whites, relative to the proportion of whites within the Cuban population. To date, no explanation for this observation has been found.

Regarding the sex of those fatally afflicted, no significant female predominance was evident—an observation that contrasts with reports from countries where DHF is endemic (2). However, data on serious and fatal cases among both children and adults indicated that certain inherited or partly inheritable conditions—including asthma, diabetes, and sickle cell anemia—constituted risk factors for both serious disease and death from DHF.

Another interesting point is brought out by considering the specific ages of the 72 children who died of DHF. As Figure 2 shows, no recorded deaths occurred among children one or two years old—children who had not been
Figure 2. The age in years of 72 children who died of dengue hemorrhagic fever during Cuba's 1981 epidemic.

Born at the time of the 1977 dengue-1 epidemic and so would not have been infected by the dengue-1 virus. In other words, for these children a dengue-2 infection would not have constituted a secondary infection with a new dengue virus serotype. This observation provides substantial support for Halstead’s view that DHF can result if a person previously infected with dengue experiences a second infection with another dengue virus serotype (17). In this regard, it should also be noted that it was very uncommon to find any children in this age range with serious cases who had obvious DHF symptoms. It is true (as Figure 2 indicates) that four infants (children under one year old) died of DHF; but in this instance maternal antibodies to prior dengue infection could have created an immunologic situation similar to that produced by previous primary infection of the infant with dengue-1.

Concluding Remarks

In summing up, it seems appropriate to direct attention to a number of basic findings relating to the Cuban epidemic that could prove useful in interpreting epidemiologic data from other countries. These findings are as follows:

- Epidemic hemorrhagic dengue can occur under the ecologic conditions prevailing in the Caribbean.
- The Cuban epidemic broke out suddenly, soon after the beginning of the rainy season.
- Heavy infestation with an efficient mosquito vector (*Aedes aegypti*) was a necessary factor in making the epidemic possible.
- The Cuban population had little protection against the dengue viruses involved.
- The sequence of viruses causing dengue epidemics on the island...
was dengue-1 (in 1977) and dengue-2 (in 1981).

- The interval between the first and second dengue infections was about three years.
- Hemorrhagic dengue was found to occur among both children and adults, depending on their immunologic status.
- Hemorrhagic dengue was found to occur among whites, blacks, and mulattoes, although the serious and fatal cases appeared to occur predominantly among whites.
- Both dengue-1 in 1977 and dengue-2 in 1981 caused large numbers of disease cases, and in 1981 these cases were concentrated within less than a four-month span of time. These observations point to widespread and rapid dengue virus circulation during both of these epidemics.

ACKNOWLEDGMENT

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SUMMARY

The dengue epidemic that struck Cuba in 1981 deserves special attention. Quite aside from the fact that it caused over 300,000 cases of dengue, this epidemic was the only one in the history of the Americas to cause numerous confirmed cases of dengue hemorrhagic fever (DHF) and shock syndrome, a development leading to 158 recorded deaths. It was also the only major epidemic involving DHF known to have occurred away from areas where viruses belonging to all four dengue serotypes were in simultaneous circulation, and so it has afforded a unique opportunity to study hemorrhagic dengue in well-defined epidemiologic circumstances where the circulation of multiple dengue virus serotypes has not impeded interpretation of the data.

Some of the points about this epidemic that seem especially noteworthy are as follows: An unusually large proportion of those dying (36%) were over 15 years of age. Hemorrhagic symptoms in children most often took the form of petechiae and hematemesis, while in adults they most often took the form of purpura, metrorrhagia (in women), and hematemesis. Not many cases of shock were observed among adults, but those that occurred were almost invariably fatal.

It should also be noted that the 1981 epidemic, caused by dengue-2 virus, followed another major dengue epidemic in Cuba, that of 1977 caused by dengue-1 virus. The only childhood age groups without DHF fatalities in 1981 were the one and two year age groups—groups that were never exposed to the dengue-1 virus during the 1977 epidemic and ones that did not include significant numbers of breast-feeding infants who could conceivably have been receiving dengue-1 antibodies from their mothers. Hence, the absence of fatalities (and a near-absence of any DHF symptoms) in these age groups tends to support the theory that DHF is a possible result of serial infection with two different dengue virus serotypes.
REFERENCES


