The First Major Outbreak of Dengue Hemorrhagic Fever in Delhi, India

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An outbreak of dengue hemorrhagic fever/dengue shock syndrome (DHS/DSS) occurred in 1996 in India in and near Delhi. The cause was confirmed as dengue virus type 2, by virus cultivation and indirect immunofluorescence with type-specific monoclonal antibodies. This is the largest such outbreak reported from India, indicating a serious resurgence of dengue virus infection.

An outbreak of dengue hemorrhagic fever/ dengue shock syndrome (DHF/DSS) occurred in Delhi, India, and its adjoining areas, from August through November 1996. We confirmed the etiologic agent of this outbreak as dengue virus type 2 by virus cultivation and indirect immunofluorescence with type-specific monoclonal antibodies. This is the largest culture-confirmed outbreak of DHF/DSS in India and indicates a serious resurgence of dengue virus infection in this country.

Dengue fever occurs worldwide, in nearly all tropical and subtropical countries (1). Dengue virus was first isolated in India in 1945 (2). All four virus types circulate and cause epidemics, but only occasional cases of DHF/DSS have been reported in India (3).

Delhi, situated in the northern part of India, had outbreaks of dengue virus infection due to different dengue virus types in 1967, 1970, 1982, and 1988, but no culture-confirmed cases of DHF/DSS were reported during these epidemics (4-7). Some cases of DHF were seen for the first time in 1988 (7). These were confirmed only serologically, by the hemagglutination inhibition test.

Delhi had its largest outbreak of DHF/DSS in 1996. The outbreak started the last week of August and continued until the end of November, peaking in mid-October (8,9). A total of 8,900 cases were reported, with a death rate of 4.2% (9). We report results of virologic testing of samples received at the All India Institute of Medical Sciences from patients with suspected dengue fever or denguelike illness from Delhi and its adjoining areas, along with a profile of the culture-confirmed cases.

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Virus isolation was carried out on 149 samples received on ice from patients with acute illness. Serum was separated aseptically and stored at -70º C. The standard method of virus cultivation, which used the C6/36 clone of *Aedes albopictus* cell line, was followed with some modifications (10).

On days 5 and 10, cells were tested by indirect immunofluorescence assay (IFA) by using monoclonal antibodies to dengue virus types 1-4. If IFA was negative for dengue viruses on first passage, a second passage was made, and cells were again harvested on days 5 and 10 for IFA. All four dengue virus types (from the National Institute of Virology, Pune, India) were included as positive controls, and uninfected C6/36 cells were kept as negative controls.

Dengue viruses were isolated in C6/36 cells from 27 (18.1%) of 149 samples processed for virus isolation. Of the 27 isolates, 26 were identified as dengue virus type 2 and one as dengue virus type 1. Sixteen of the 27 isolates were from patients with DHF/DSS, while 11 were isolated from patients with uncomplicated dengue fever. Of the 27 culture-positive patients, 11 (40.7%) were in the 5- to 12-year age group (Table). However, the isolates were nearly equally distributed among children (<12 years) and adults. The ratio of male to female in these 27 cases was 12:15. The median duration of fever at the time of viral isolation was 4 days, on the basis of 24 culture-positive cases for which the duration of fever was available. After 5 days of

Table. Age distribution of patients with culture-positive dengue

Age (years)	No. of cases
0-1	2
>1-5	1
>5-12	11
>12-20	7
>20-30	4
>30	2

fever, virus isolation was possible only from one patient. The median duration of viremia in dengue type 2 infection was also found to be 4 days in a detailed study on dengue viremia from Jakarta, Indonesia (11). Testing for immunoglobulin (Ig) M antibodies to dengue virus was performed on 270 serum samples by MAC-ELISA according to a standard protocol (12). Of 270 sera tested for antibodies to dengue virus by MAC-ELISA, 140 (51.9%) showed anti-dengue IgM antibodies. All samples from patients with a duration of fever ≥ 5 days were tested for anti-dengue IgM antibodies. In some samples, antibodies could be detected as early as the fifth day of fever. Three of the culture-positive acute-phase samples were also positive by MAC-ELISA.

Analysis of the outbreaks of dengue virus infection in Delhi indicates a seasonal trend. All outbreaks (including the one reported here) occurred during the monsoon (rainy) season (August to November) and subsided with the onset of winter. Dengue virus types 1, 2, and 3 have been isolated during dengue fever outbreaks (without DHF/DSS) in Delhi. Serologic studies have also shown that dengue infection has been endemic in this region (13). During the 1996 outbreak of DHF/DSS, we were able to identify dengue virus type 2 as the etiologic agent. This is the first culture-confirmed outbreak of DHF/DSS from Delhi and its adjoining areas and the largest reported outbreak of DHF/DSS from India.

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