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**INTERNATIONAL CONFERENCE ON
DENGUE HAEMORRHAGIC FEVER**

**Report of WHO/ICMR/DBT Meeting
and
National "Brainstorming" Session on Dengue**

**National Institute of Virology, Pune, India
7-8 February 1994**

**Sponsored by: Department of Biotechnology, Government of India
Indian Council of Medical Research
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1. INTRODUCTION

There is evidence that India has experienced major epidemics of dengue and dengue haemorrhagic fever in recent years; however, information regarding these outbreaks has generally not been well documented or formally presented in the scientific literature. Further, indications are that a wide divergence exists in local treatment practices of severe dengue infection, and that local clinicians may not be fully aware of proven successful procedures for the clinical management of these patients. The International Conference on Dengue Haemorrhagic Fever and the National Brainstorming Session on Dengue summarized here, reflects recognition by the Government of India of the need for more information on the current status on dengue, and for a coordinated approach to address this emerging problem. Through the generosity of the Rockefeller Foundation, the World Health Organization, the Department of Biotechnology, Government of India, and the Indian Council of Medical Research, international experts were able to meet with national leaders, scientists and clinicians to share experiences and formulate a plan of action for India. For two full and fruitful days, this group heard presentations by various experts from throughout India, and shared in the experiences of others from around the world. The conclusion was an enthusiastic endorsement by the group of several recommendations that offer specific actions that India can immediately institute to help address the problem of dengue and dengue haemorrhagic fever, as well as an organizational framework that will allow future work to be efficiently approached and coordinated.

It is noteworthy that over forty years after the Rockefeller Foundation assisted the Government of India in establishing the National Institute of Virology (then called the Virus Research Centre) in Pune, the Foundation should now play a seminal role in helping the Government of India to focus attention on a pending national crisis due to the emergence of dengue. But unlike in 1952, the National Institute of Virology today has matured and grown, and has taken its rightful role as a national resource fully capable of addressing the tasks ahead. It is fitting that this conference should be hosted by the National Institute of Virology, once again demonstrating the highly successful collaborations enjoyed between the Government of India, The Rockefeller Foundation and the World Health Organization.

2. BACKGROUND

Dengue has been known to exist in India for over a century. Indeed, two strains of dengue 1 virus were first isolated in India by Sabin in 1945, both from humans infected in Calcutta. When the National Institute of Virology was founded in Pune in 1952, only dengue and sandfly fever were recognized, and only dengue 1 had been isolated. Several references had been made to "7 day fever" outbreaks near Delhi and Patna during World War II, and the clinical descriptions leave little doubt that these were outbreaks of dengue. Since 1956, all 4 dengue serotypes have been isolated from India, frequently from humans and from vector mosquitoes, *Aedes aegypti* and less often from *Aedes albopictus*.

Despite frequent outbreaks of dengue, no report of haemorrhagic fever associated with dengue was made until 1963, when outbreaks occurred in Calcutta and Visakhapatnam, which appeared to be associated with both dengue and chikungunya viruses. In Calcutta, several thousand cases were estimated to have occurred, some of which were DHF-like and dengue serotypes 1, 2 and 4, as well as chikungunya virus, were isolated. The epidemic lasted from 1963 to 1965, and an estimated 100,000 cases of dengue may have resulted. Dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) were both documented during the epidemic.

More recently, serious outbreaks of dengue occurred in Delhi in 1988, and dengue and DHF were diagnosed reported cases in Madras in 1989, including many fatalities ascribed to DHF. A large outbreak of dengue 3 occurred in Calcutta in 1990, including cases of DHF, and another outbreak occurred in Delhi in 1991, but little information is available regarding the serotypes of dengue involved, or the attack rates.

Dengue is not a reportable disease in India, and no active surveillance system is in place. Consequently, outbreaks of dengue and DHF are not often documented, and of those which are reported only the largest outbreaks are likely to be investigated. There is a consensus that the incidence of dengue and DHF, which was primarily an urban disease in the 1970's, is now increasing in rural areas.

3. OBJECTIVES OF MEETING

Given the current situation regarding dengue in India, the following objectives were formulated for this meeting:

- 3.1 To have DHF and DSS experts meet and interact with Indian communicable disease epidemiologists, both national and from the key states where DHF has been reported (Tamil Nadu, Gujarat, Uttar Pradesh, Maharashtra, West Bengal and Andhra Pradesh).
- 3.2 To gather preliminary data on recent occurrences of DHF/DSS in India;
- 3.3 To meet and interact with key members of the Indian medical community, especially paediatricians who have cared for DHF/DSS patients;
- 3.4 To disseminate information on case definition and case management to Indian clinicians;
- 3.5 To discuss and propose recommendations on various topics, including:
 - Enhanced surveillance for DHF/DSS in India;
 - Methods of dissemination of WHO technical information on DHF/DSS throughout the Indian public health and clinical channels;
 - Publication of a series of articles on DHF/DSS in one or more Indian medical journals.
- 3.6 To formulate vector control measures.

4. SUMMARY OF PRESENTATIONS

- 4.1 A total of 41 abstracts of presentations were submitted and published in a booklet* distributed to participants during registration for the meeting. The meeting was organized into 8 sessions that focused on epidemiology (2 sessions), medical entomology (2), clinical aspects (1), immunology of dengue infection (1), strategies of dengue control (1), and a roundtable discussion. Following the formal presentations, the National Brainstorming Session on Dengue was held, during which the group broke into four sections to discuss clinical considerations of dengue, surveillance, medical entomology, and research. Each group formulated recommendations, which are summarized below under 5. Recommendations.
- 4.2 Two general themes dominated the meeting; the increasing number of dengue outbreaks, and the spread of the primary vector of dengue, *Aedes aegypti*.
- 4.3 Outbreaks of dengue fever have been known to occur in India for more than a century, but it has only been since the early 1960's that DHF/DSS have been seen. Over the past decade, a dramatic increase in number of DHF/DSS cases has occurred, and during the meeting information was presented on recent DHF/DSS outbreaks in 9 Indian States (Maharashtra, Gujarat, Karnataka, Andaman and Nicobar Islands, Assam, Nagaland, Harayana, Uttar Pradesh, and Tamil Nadu). All four serotypes of dengue have been isolated from acutely ill persons in India, and there was a strong suggestion that dengue was now present in nearly all States of India, and that the risk of DHF/DSS was present and growing. The age of the typical DHF/DSS patient appears to be decreasing, with most cases now seen in children. Outbreaks are increasing in frequency and magnitude, but continue to go unrecognized due to the lack of appropriate diagnostic capacity for much of the country. Dengue and DHF/DSS are not reportable in India, and when outbreaks are recognized, it is often based on clinical presentation alone. Few outbreaks are properly investigated, and when studied, it is often as transmission is waning and the epidemic nearly over. Treatment of the severe forms of dengue, DHF and DSS is not standardized, and it is clear that the general Indian medical community could benefit from provision of guidelines for the proper management of these diseases.
- 4.4 With regard to the status of vectors of dengue, several species of mosquitoes are present in India that may transmit dengue, but the principal vector species is *Aedes aegypti*. This species has traditionally been associated with urban centres in India, and is found virtually throughout the country. During the meeting, however, new information was reported to indicate that *Ae. aegypti* is increasingly abundant in rural settings, thus placing much more of the country at risk of dengue and DHF/DSS. Every presentation made that had data on mosquito densities collected over a period of years found that *Ae. aegypti* population densities were now high, with indications that they were getting higher. In some areas of India, where human migration to urban centres has led to over burdened housing, water supply, and refuse management, concomitant increases in vector mosquito populations have been especially dramatic. In spite of recognition of the increasing densities of vector mosquitoes, no nation-wide campaign exists for vector control, and when present, vector control is often limited to emergency measures, with no sustained programme of control. Thus, it appears that conditions are ripe for explosive epidemic dengue transmission.

* Available on request

5. RECOMMENDATIONS FROM BRAINSTORMING SESSION

5.1 Recommendations from the clinical group:

5.1.1 An educational campaign should be developed to raise the level of awareness for dengue and DHF/DSS among all segments of the Indian population.

- a. Guidelines encompassing the signs, symptoms and diagnostic procedures for dengue, DHF/DSS should be distributed to medical teachers/practicing clinicians, non-governmental organizations and health care workers. WHO should assist in the development and distribution of these guidelines.
- b. More stress should be placed on teaching dengue, DHF/DSS in medical schools, undergraduate, and graduate level courses.
- c. Continuing Medical Education (CME) courses should be developed and offered to practicing physicians to update their knowledge of dengue case management, epidemiology, prevention and control. ICMR should be approached to assist in meeting this objective.
- d. Practicing clinicians should be taught to rule out dengue in any febrile patient with flushed face and without signs or symptoms of upper respiratory tract infection, and proven not to have malaria. Antibiotic treatment should not be started unless indicated.

5.1.2 Treatment of dengue and DHF/DSS

- a. Tourniquet tests should be done on all suspect cases of dengue fever, DHF/DSS.
- b. A flow chart to guide the treatment of DHF/DSS cases should be made available to all hospitals and primary health centres.
- c. Administration of drugs such as aspirin, ibuprofen, steroids and heparin should be avoided when treating dengue fever and DHF/DSS patients.
- d. Minimum diagnostic facilities for dengue, such as haemagglutination inhibition tests or ELISAs, should be available in selected medical schools. Antigens for this test should be of high quality and supplied through a central source. The National Institute of Virology should coordinate and provide quality control over dengue diagnostic reagents.
- e. Multicentric research on dengue, DHF/DSS should be encouraged.

5.2 Recommendations from the surveillance group:

- a. Dengue Haemorrhagic Fever and Dengue Shock Syndrome should be reportable diseases.
 - WHO case definitions should be used;
 - Existing reporting networks, i.e., for polio, should be used whenever possible;
 - Each State should define its own areas of surveillance;
 - NICD should present a coordinated reporting system to National authorities.
- b. Each State should have laboratory diagnostic capabilities for dengue, DHF/DSS.
 - The National Institute of Virology should serve as a national reference centre to assist with technical problems and to maintain quality assurance and proficiency testing of the peripheral groups.
 - Other laboratories should be used as surveillance centres;
 - The IgM capture ELISA is the test of choice for routine diagnosis of dengue, DHF/DSS;
 - WHO should assist with initial acquisition of reagents and training.
- c. Entomological surveillance should be initiated and linked with vector control efforts.
 - Entomological surveillance data (ie, malaria control, *Aedes aegypti*, others) should be shared at the District level;
 - National summaries could be collated, distributed and stored at the Vector Control Research Centre, Pondicherry.
- d. Outbreak investigations should be linked to surveillance activities.
 - NICD should prepare guidelines for surveillance and outbreak investigations;
 - States should organize their own investigation teams.
- e. A training component should be included in all surveillance activities.

5.3 Recommendation from the epidemiology and research group:

- a. Improve Indian research capacity: There are a number of sources of research support in India, including the Indian Council of Medical Research (ICMR), the Department of Science and Technology (DST), the Council of Scientific and Industrial Research (CSIR), and the Department of Biotechnology (DBT). The ICMR funds clinical and epidemiological research; DST and CSIR fund basic research which supports biotechnology research that is product oriented.

There is an urgent need to develop and standardize research tests and reagents, and this in turn requires the training of scientists and designation and strengthening of present training centres. The WHO Collaborating Centre at the National Institute of Virology can assist in standardizing research test systems in India with those of the international community.

- b. Collaborative research should be stressed; research test protocols and reagents can best be developed through high quality research projects that have reagent production and training as a defined component. Such collaborations could be especially rewarding in the area of biotechnology, where modern techniques could be focused on reagent production.
- c. Clinical research should be linked with virological laboratory support through a multicentric approach.
- d. Epidemiological research should focus on development of several sites where prospective epidemiological studies on DHF/DSS may be undertaken. Both clinical and epidemiological studies will generate research specimens that will require characterization and contribution to virological, immunological and pathogenesis research.
- e. Basic pathogenesis research should be supported to contribute to human clinical pathogenesis studies.
- f. To strengthen scientific decision-making, a scientific symposium on DHF/DSS should be held with proceeds published in India.
- g. To strengthen the prevention and control strategies of dengue, reports in the media on the clinical burden of DHF/DSS should be published.
- h. To assist clinicians and public health workers, a video might be prepared that describes the clinical features of dengue, DHF/DSS, treatment and vector control strategies.

5.4 Recommendations from the vector control group:

- a. A nation-wide vector surveillance system based on existing institutions should be established to map and publish the present distribution of *Ae. aegypti*, and be used to restrict its spread to new areas.
- b. The ecological factors that encourage the increase or decrease of vector population densities should be investigated.
- c. An institute or agency should be designated to maintain a database of *Ae. aegypti*, including distribution, population densities, insecticide resistance and vector incrimination information.
- d. To ensure uniform reporting and utilization of information collected, standardized reporting of vector levels and indices should be used.

- e. Every effort should be made to increase the awareness of decision makers at national, state and municipal levels of the importance of *Aedes* transmitted disease, their public health and economic impact, to assure their support for establishing permanent vector control services.
- f. Vector control must be based on inter-sectorial collaboration and such cooperation should be ensured from the very beginning.
- g. Seventy-two entomological zonal units have existed in India in addition to the States and Central entomological components. These must be orientated towards *Aedes* surveillance and control. While professional staff positions are unfilled, replacements must be urgently recruited.
- h. Equipment, insecticides and transport should be available on a standby basis at a state level for immediate use in vector control should an epidemic outbreak occur.
- i. Uniform legislation should be enacted in all municipalities specifically related to *Aedes* control. Equally, legislation should be enacted which would present the creation of breeding sites for *Aedes aegypti*.
- j. Many aspects of the bionomics and control of the vector are yet unknown; research on vector biology and vector control through chemical, biological, genetic and molecular methods should be supported.

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