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# MANAGEMENT OF DENGUE EPIDEMIC

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*Report of a Technical Meeting, SEARO, New Delhi  
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## **EXECUTIVE SUMMARY**

*Dengue/dengue haemorrhagic fever (DEN/DHF) is highly endemic in Indonesia, followed by Thailand and Myanmar. Its incidence is moderate in India and Sri Lanka. Bangladesh and Maldives continue to be a silent area since 1964 when the first episode was recorded. Bhutan and Nepal have not reported any incidence so far. The South-East Asia Region of WHO (SEAR) continues to show increased incidence and geographic spread. However, the case fatality rate has come down from five per cent to about two per cent due to improved management of hospital services.*

*Risk factors for DEN/DHF epidemics have been attributed to basic geographic receptivity governed by climatic conditions, vectorial competency of *Aedes aegypti* and extent of its prevalence, virus/host interactions, migration of the host and resultant epidemiological scenario.*

*To respond to emergent situations like DHF epidemics, administrative machinery must work at its optimal efficiency. It was, therefore, considered necessary to have a mechanism of creation of a multi-disciplinary emergency action committee (EAC) and a rapid action team (RAT) at national, state and local levels. While EAC will mobilize all resources of health and non-health sectors, the media, NGOs, schools/colleges, student manpower and communities to coordinate all required actions for emergency interventions, RAT will carry out urgent epidemiological and entomological investigations and undertake appropriate control measures. Official spokesmen (Public Information Officer) should also be designated at national, state and local levels to provide correct information to the mass media and to promote community participation for control of DHF outbreaks.*

*For prevention of mortality due to dengue during epidemics, and when panic situation develops, there is need for organizing emergency management as well as developing standardized management of clinical cases. For emergency crisis management, there is a need for appointment of a coordination committee with the primary purpose of providing outpatient medical service, in-patient service with adequate provision of equipment and medicines, organizing laboratory support, and arranging skilled manpower at each echelon of hospital care system.*

*Clinical management emphasizes early and accurate diagnosis of DHF before the critical stage or before the shock occurs, using thrombocytopenia and concurrent haemoconcentration, which represent abnormal haemostasis and plasma leakage respectively. Early volume replacement when haematocrit rises can significantly prevent the shock and modify the severity of the disease.*

*For the control of DHF outbreaks, emergency vector control becomes essential in order to reduce the load of the disease in the community and to check its further spread. Emergency control priorities chemical control supplemented by an all-out effort at source reduction by individuals, families, communities and social and non-governmental organizations with the active support of the mass media. Chemical control aims at immediate knock-down of infected mosquitoes by (i) space spraying using cold aerosol or ultra low volume (ULV) spraying, thermal fogging, and (ii) application of chemical and bio-larvicides in breeding containers to eliminate breeding. Legislation is an essential counterpart of all actions promoted and implemented by the *Aedes* control programme.*

*For the prevention and control of DEN/DHF epidemics, it is essential to have a full understanding of the epidemiological pattern of the disease based on an effective disease surveillance system at regional, national and local levels. Disease surveillance shall comprise of (i) active (proactive), and (ii) passive (reactive) surveillance. Passive surveillance should be mandatory by law which makes DEN/DHF a notifiable disease. This should be strictly on clinical basis, and need not require laboratory confirmation. Active surveillance should be laboratory-based, where clinical samples should be processed on a regular basis, supported by serological and virological methods. The information so gathered will reflect any increased activity of the virus, the time of occurrence, location, serotype and disease severity and will have predictive capabilities.*

*Vector surveillance is an integral part of disease surveillance and the two should always be linked together to identify transmission in time and space. Vector surveillance will determine the distribution of vector(s), the extent and intensity of breeding and seasonal fluctuations and delimit the areas of high risk. Vector surveillance will also identify the types of breeding habitats which support vector population for rationalizing control strategies and for invoking community participation in source reduction activities.*

*Based upon the information generated under disease surveillance and vector surveillance, countries of the Region should develop appropriate DEN/DHF control programmes at national, state and local levels. Control strategies in the first place be based upon source reduction and environmental management methods adequately backed by legislation, intersectoral coordination, community participation at various levels and the mass media. Countries of the Region may consider merging dengue control with existing disease control programme of other infections, particularly where mosquitoes are the vectors and breeding is overlapping, with a little extra inputs in terms of infrastructure, equipment and material.*

*DEN/DHF control programme must be supported by capacity-building programme on a continuing basis to add to and update new skills in the programme. There is an urgent need for research support in areas where information is lacking or in areas which can improve management of clinical cases or vector control strategies which can increase sustainability.*

*WHO/SEARO's role has been identified as crucial in helping the Member Countries in their tasks in many ways. The existing 'rapid response team' at SEARO needs to be strengthened to assist the Member Countries for emergency management of DHF as requested. Reinforcement should be made at the Regional Office in respect of (i) collecting and collating regional epidemiological data, undertaking trend analysis and providing the feedback; (ii) developing manuals and guidelines on disease management and control strategies; (iii) arranging intercountry workshops for exchange of experience and dissemination of knowledge; (iv) developing standard training modules in all disciplines connected with management and control of DEN/DHF to boost capacity-building efforts of the Member Countries; (v) designating additional WHO collaborating centres and strengthening existing centres; (vi) standardizing existing rapid diagnostic test kits, and (vii) arranging for making an inventory of dengue viruses.*

## **1. INTRODUCTION**

Dengue fever (DEN), with its severe manifestations such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) has emerged as a major public health problem in recent years. Outbreaks of epidemic proportions resulting in high morbidity and mortality are now more frequent in endemic countries. According to estimates, more than 2.5 billion people are at risk of infection in over 100 countries. Tens of millions of cases of dengue, and at least five hundred thousands cases of DHF/DSS with a mortality of about 5 per cent, occur each year worldwide. A majority of cases (around 95 per cent) are among children of less than 15 years of age in many countries of South-East Asia. DHF has become the leading cause of hospitalization and death among children. The disease is not only showing geographic spread but its incidence is also increasing.

Deeply concerned by these developments the World Health Assembly, in 1993, passed a resolution which urged Member States to strengthen their national and local programmes for the control of DEN/DHF and to specifically develop and implement cost-effective control strategies for achieving an interruption of transmission. In response to this resolution, a global strategy for vector control of DEN/DHF was developed during a consultation held at Geneva in June 1995. This was followed by a regional consultation at SEARO, New Delhi, in October 1995, and necessary regional guidelines were provided to Member States for the preparation of national action plans for the control of DEN/DHF.

Meanwhile, many countries of the Region, especially India and Sri Lanka, experienced the outbreak of DHF in 1996. Control efforts made to meet such emergencies highlighted the deficient preparedness of countries both for management of cases and for achieving quick interruption of transmission. The present meeting attempts to address these problems in order to enhance their capacities for taking more coordinated and timely actions to arrest the build-up of such epidemics.

## **2. OBJECTIVES**

- (1) To review and revise the administrative arrangements and requirements for intersectoral collaboration, vector control and organization of medical services during the dengue epidemic;
- (2) To identify the role and functions of public information, media, and community during the epidemic;
- (3) To review the requirements for standard case management of dengue/DHF/DSS;
- (4) To develop a mechanism to monitor control activities during and after the epidemic, and
- (5) To review short-and long-term prospects of prevention of dengue infection.

## **3. INAUGURATION**

The meeting was inaugurated by Dr Uton Muchtar Rafei, Regional Director, WHO/SEARO. Dr Uton, while welcoming the participants, emphasized the heightened concern about emerging and re-emerging infections, viz. recent outbreak of plague in India, and the Ebola virus epidemic in Zaire during 1995 and 1996. He referred to the dramatic increase in the global incidence of dengue and its severe manifestations such as DHF and DSS. In many countries of South-East Asia, DHF had become the leading cause of hospitalization and death, and therefore characterized it as a problem of major

importance among the vector-borne diseases in humans. He identified poor vector control activities, rapid demographic changes and ill-planned sanitation, increase in frequency and volume of air traffic and general deterioration in public health services as major contributory factors. Finally, he expected that the deliberations will help to bring out the technical deficiencies and constraints faced by countries of the South-East Asia Region to meet such epidemic situations and make suitable recommendations for building more efficient capabilities.

Professor, Natth Bhamarapravati was nominated as Chairperson, Professor Thein Thein Myint as Co-chairperson and Mr N.L. Kalra as Rapporteur.

Professor Natth Bhamarapravati, thanked WHO/SEARO for arranging the meeting which was very truly essential. He hoped that, based on the current knowledge with some consensus-building and good management, the South-East Asian countries would be able to keep dengue epidemics in check. He expressed his frustration that even after 40 years of the epidemics, South-East Asia had not been able to build up the necessary manpower in different disciplines related to dengue.

#### **4. MAGNITUDE OF DEN/DHF PROBLEM IN SOUTH-EAST ASIA**

Out of the ten countries in the WHO/SEA Region, DEN/DHF is highly endemic in Indonesia followed by Thailand, and Myanmar while it is moderate in India and Sri Lanka. Bangladesh experienced an outbreak in 1964 and the presence of dengue antibodies in high a percentage of the population implies the country's receptivity to DEN/DHF outbreaks. A similar situation exists in Maldives. Bhutan and Nepal, however, have not reported the incidence of dengue. The number of reported cases and deaths of DEN/DHF in SEAR by country for the years 1985-1995 are given in Figure (see details in Annex 1). It is apparent that the Region continues to be endemic for DEN/DHF as the number of cases shows a definite increase at an interval of 3 to 5 years. However, the case fatality rate has been brought down from five per cent to nearly two per cent due to improved management of hospital services.

India experienced a severe outbreak of DHF in Delhi during September/October 1996 which reported a toll of 378 lives with 8866 hospitalizations, giving a case fatality rate of 4.3 per cent.

## 5. RISK FACTORS OF DEN/DHF EPIDEMICS IN SEAR COUNTRIES

The epidemic proneness of an area depends upon basic receptivity and vulnerability, breeding potential of vector species, circulating viraemia and availability of susceptible individuals. These aspects are briefly discussed below.

### 5.1 Basic Receptivity of SEAR to Dengue Infection

The countries of the South-East Asia Region can be divided into four ecological zones depending upon the rainfall and temperature. Zone-wise receptivity of countries of South-East Asia is given in Annex 2. It is apparent that the receptivity to DEN/DHF increases as one moves from west to east because of increasing rainfall and reduction in (i) day-and-night temperature, and (ii) seasonal variation.

### 5.2 Vectorial Competency of DEN/DHF

*Aedes aegypti*, a domestic-container habitat species, been incriminated as the major vector of DEN/DHF/DSS. *Ae. albopictus*, although experimentally highly susceptible to all serotypes of DEN has not been involved except in some localized situations, primarily being feral and indiscriminate feeder. Vectorial competency of *Aedes aegypti* in any region would depend on the following:

#### (1) Taxonomic status of *Aedes aegypti*

Three sub-species and varieties of *Aedes aegypti* were reported as follows:

- (a) *Aedes aegypti* SSP formosus (black in colour)

Distribution: feral species restricted to very humid parts in Africa, south of Sahara. No role in the transmission of dengue infection.

- (b) *Aedes aegypti* s.str. type form (intermediate in colour)

Hydrophilic, domestic or semi-wild and adapted to human habitations.

Distribution: Predominant in Indo-Malayan region, the Pacific and in parts of New World. Less common in the Mediterranean, India and Australia.

- (c) *Aedes aegypti* var *queenlandensis* (pale variety)

Drought resistant, exclusively domestic and highly anthropophilic.

Distribution: same as type form. But more common in the Mediterranean, drier parts of India and Australia.

Vectorial competency of two ecological variants is governed by the bio-ecological characteristics of each in different ecological zones.

#### (2) Extent and Intensity of Breeding Potential of *Aedes aegypti*

The extent and intensity of *aegypti* breeding is of importance for delimitation of dengue risk-prone areas. While the extent of breeding can be measured by House Index (HI), the intensity of breeding can be judged by Container Index (CI) and Breteau Index (BI) (Annex 4).

Many attempts have been made to correlate the critical levels of *aegypti* breeding and the intensity of virus transmission. For example, in India, and in all recorded outbreaks the Container Index was above 20, while in Singapore it was estimated at nine, and in Thailand it was estimated at a much higher level. Three epidemiological situations with different container indices of vectors with disease were described as (i) areas with *Aedes aegypti* infestation without reported dengue; (ii) areas where dengue was endemic, and (iii) areas where dengue was present as an epidemic. From the above it is apparent that more sensitive indices are required for understanding the transmission dynamics to determine potential risk areas.

### **5.3 Virus-host Interaction**

There are four fundamentals: (1) dengue infections are relatively silent in children; (2) in adults dengue infections nearly always produce symptoms; infection: apparent disease ratios are nearly 1, (3) some primary as well as secondary dengue infections in adults may result in severe gastrointestinal haemorrhages but without increased vascular permeability. Many adults infected with dengue 1 in Taiwan in 1988 had underlying peptic ulcer disease, and (4) some secondary dengue infections produce DHF, more commonly in children.

The above four fundamentals produce at least five different epidemiological scenarios:

(1) Epidemic dengue in a totally susceptible population: Dengue fever is the principal disease and is seen in adults of all ages; depending upon the dengue strain, some adults have gastrointestinal bleeding but without increased vascular permeability, and are often diagnosed as DHF.

(2) Epidemic dengue in a population where (as an example) nearly all adults over the age of 40 are immune to the infecting type: Dengue fever is principally seen in adults, but only between ages of 20 and 40.

(3) Endemic dengue with only one type circulating: Infection rates start high in infants and fall progressively due to cumulative protective immunity. Essentially no disease is seen.

(4) Endemic dengue with two or more types circulating at high rates: When the second virus is of South-East Asian origin, this scenario produces classic South-East Asian DHF in children with little or no disease in adults.

(5) Endemic dengue with two or more types circulating at low infection rates: This produces a mixture of DHF in children at relatively low hospitalization rates - with a high median age at hospital admission - and dengue fever in adults. Some adults may have severe g.i. bleeding but without increased vascular permeability and will be reported as DHF. This gives the appearance of DHF across a wide age range.

## **6. ADMINISTRATIVE ARRANGEMENT AND REQUIREMENTS FOR INTERSECTORAL COLLABORATION AND LOGISTIC SUPPORT**

Dengue outbreaks, particularly when these are associated with severe manifestations of DHF/DSS, are responsible for high morbidity and mortality in a short span of time. They always create panic and people expect urgent action from government. Therefore, at such times it becomes essential to have preparedness and flexibility in the administrative structure at central, provincial and local levels so that it can respond to emerging situations as quickly as possible. Such arrangements require setting up of priorities for the control of DEN/DHF/DSS epidemics. Administrative requirements are as follows:

**(1) Emergency Action Committee (EAC) and Rapid Action Team (RAT)**

For contingency planning of DHF control, it is essential that a mechanism is embodied at national, state and local levels for creation of a multidisciplinary emergency action committee (EAC) and a rapid action team (RAT). The EAC will be entrusted with all administrative actions and will coordinate all activities aimed at emergency interventions. The RAT will undertake epidemiological investigations and control measures (Annex 5).

**(2) Declaration of dengue as notifiable disease**

Under the prevalent "Epidemic Acts" of the countries of the Region, dengue should be made a notifiable disease so that people, private practitioners, nursing homes and government and private hospitals report all cases to the government as per guidelines. This will serve the twin purpose of (i) early management of the cases in hospitals to prevent deaths, and (ii) to cut further transmission of the disease as hospitals are kept free of *Aedes* infestation.

**(3) Reporting system**

- Peripheral health units report to district/municipal health officer
- Confirmation of epidemic by chief, MOD/DOH
- Report to chief administrator of district/municipal corporation
- Report to provincial and national level.

**(4) Activities: Contingency plans would require the following:**

- Delimitation of epidemic areas
- Mobilization of men, materials and equipment
- Intersectoral meeting at district/city level
- Providing information to communities through mass media
- Implementation of action plan for control measures.

**(5) Case management:**

Adequate provision of hospital beds, diagnostic facilities, drugs and other requirements. Hospital premises to be kept free of *Aedes* infestation.

**(6) Vector control:**

To be based upon (i) insecticide fogging; (ii) application of larvicides and, (iii) source reduction. All-round efforts to be made to involve communities, schoolchildren and NGOs, etc.

**(7) Intersectoral collaboration:**

This requires the following: (i) political commitment and providing all required resources; (ii) constitution of intersectoral committees for combined activities, and (iii) maximizing the use of mass media for urgent actions by communities, schoolchildren, and NGOs.

**7. ROLE AND FUNCTIONS OF PUBLIC INFORMATION, MEDIA AND COMMUNITY**

**7.1 Public Information**

Public information is vital for allaying the fears of the community at the time of outbreaks or epidemics. Public information therefore should be exhaustive, clear and should explain how the disease is caused, how it spreads, how to control it, and where to get the treatment. Preferably comprehensive communication guidelines on the treatment and control of dengue epidemic, including the "Dos and Don'ts" should be developed for information of the public. This will also take care of information generated by other sources, which may not be always correct.

**7.2 Role of the Media**

It is an acknowledged fact that the media can play a positive role in the disease control programme or epidemic control. For the media to be effective it is essential that the media should be given information quickly, correctly and comprehensively. The information should be given through an authorized outlet of the ministry of health or municipal/district health officer so that there is no mix up or contradictory information. The health ministry should also publicize the complete addresses of the authorized outlets for the benefit of the media so that accredited media persons do not gather information at their own from sources which cannot provide authentic information. Whenever the media has no access to reliable and timely information it has a tendency to sensationalize as happened in India during the plague outbreak in 1994. It is also important that all government sources speak the same language and send the same message. It would be desirable to reach the media outlets through press releases rather than interviews. There is the obvious advantage that printed statements are less likely to be misinterpreted or misquoted. In short, governments should make the mass media as an ally against its fight to control epidemics.

**7.3 Community Participation**

Adequate disease prevention and control cannot be achieved without the cooperation and involvement of the community. Health managers must understand the social and cultural beliefs of the population regarding dengue fever, the relationship of mosquito to dengue and the benefit they perceive from the vector control.

Community participation is therefore essential to (i) extend the coverage of the vector control activities; (ii) make the campaign more efficient with greater coordination of resources, activities and efforts; (iii) make the campaign effective through pooling of efforts to achieve determined goals, objective plans and strategies for action; (iv) promote equity through sharing of responsibilities, and (v) promote self-reliance and increase people's sense of control over issues.

In DEN/DHF prevention and control campaigns, the communities are required to undertake source reduction measures such as emptying of water containers, removal of solid waste material including used tyres and its proper disposal, preventing breeding in man-made breeding places, viz. cisterns and wells and undertaking personal protection methods, e.g. use of mosquito nets, coils, etc., to prevent vector bites.

For the success of any campaign which requires community participation the relationship should be maintained by continuous dialogue and should be made sustainable by linking it with (i) existing well-organized programmes; (ii) income-generating schemes, and (iii) by mobilizing societal forces and organizations, both within and outside the health sector, for initiating and maintaining dengue control activities.

## **8. MEDICAL AND LABORATORY SERVICES AND STANDARD CASE MANAGEMENT OF DEN/DHF/DSS DURING EPIDEMICS**

### **8.1 Appointment of Coordination Committee**

During an outbreak of dengue haemorrhagic fever (DHF) there will be a large number of patients with dengue fever (DEN). Furthermore, with panic in the public there will be even greater number of patients with non-dengue febrile illness seeking medical care. Outpatient and inpatient facilities may be overwhelmed and medical care staff can rapidly become exhausted. In these circumstances it is essential to establish a coordination committee within hospital management to facilitate interdisciplinary and interagency communication.

### **8.2 Outpatient Medical Service**

As the prognosis of DHF depends on early diagnosis, and since during the early febrile phase DHF resemble DEN in many respects, patients with high fever and positive tourniquet test should be suspected of having DHF. They should be followed up for thrombocytopenia and rising hematocrit which are constant findings and essential for the diagnosis of DHF. These simple laboratory tests should be done at the *outpatient departments*. Since only about a third of DHF patients will develop shock and the critical period is reached by the time the temperature drops, patients who are suspected to have DHF can stay at home during the febrile phase and come back for follow up, and for proper treatment when there is significant leakage of plasma. Patients who live far away from hospital or whose parents or relatives cannot be relied to observe the clinical changes should be kept for observation as outpatients. An observation unit of approximately 10-20 beds should be set up to accommodate these patients who will be followed up until diagnosis of DHF is confirmed. Dengue fever and some mild cases of DHF can be treated at outpatient departments for 12-24 hours' period. This observation unit will help avoid over-crowding of wards and assure that persons who have DHF and genuinely require hospital care are admitted.

It is essential that the observation unit is well staffed and should have microhaematocrit equipment and microscopes for platelet estimation.

### **8.3 Inpatient Service**

A DHF special unit should be established for the convenience of providing care to patients who have the same disease and need the same pattern of clinical care. As patients in shock require intensive round-the-clock nursing and physician care, they should be grouped together. The unit should be staffed with well-trained nurses to provide care for patients in shock. There should be about 20-30 beds with adequate equipment and supplies needed for taking care of DSS patients. Paramedical workers or parents can assist by giving oral fluid therapy or by monitoring the rate of intravenous administration and the general status of patients.

#### **8.4 Laboratory Support**

Laboratory studies that are necessary for clinical diagnosis and management should be set up. Laboratory investigations for total white blood count, platelet count, and haematocrit determinations are essential for clinical diagnosis. It is recommended that laboratory facilities for this purpose should be available at the outpatient departments at all times. Microcentrifuge for haematocrit determination and a microscope for platelet estimation should be available at all institutions providing care for DHF patients.

#### **8.5 Equipments and Medications**

A blood pressure manometer, with different sizes of arm-cuff for children in different age groups, are required for Tourniquet test and follow-up B.P.

Based on the assumption that about 20-30 per cent of DHF patients will be in shock and about half of the grade I-II patients may require intravenous therapy with isotonic salt solution, about 10% of the patients may require blood transfusion. The following are examples of the preparations needed:

- |  |   |  |
|--|---|--|
| 100 cases of DHF                             | - | 200-300 litres of normal saline or Ringer acetate solution |
| 30 cases with shock                          | - | 30 litres of volume expander, e.g. Dextran 40, plasma      |
| 10 cases of DHF with significant haemorrhage | - | approximately 10-20 units of fresh whole blood             |
- Oral electrolyte solution: as used in diarrhoea
  - Solution for volume replacement: 5% D in NSS, 5% D in 1/2 NSS
  - Ringer's Lactate or acetate, Plasma expander, Dextran 40

#### **8.6 Training**

- (1) Hospital staff, doctors and nurses should be briefed or trained (short course/seminar) to recognize shock and diagnose cases of DHF and provide proper management using WHO criteria and guideline.
- (2) Laboratory workers should be trained to do haematocrit and platelet counts or estimation by examination of peripheral blood smears and coagulogramme.
- (3) Virus laboratory workers should be trained to collect blood specimens, acute and convalescent, for serological diagnosis and/or virus isolation.

#### **8.7 Prevention of Death**

Prevention of death can be achieved by early hospital admission, diagnosis and proper management. As only about a third of DHF cases will progress to develop shock, the parents or attendants of patients should be given thorough instruction for taking care of the patient at home during the febrile phase and to recognize early warning signs of shock.

## **8.8 Management of Dengue Haemorrhagic Fever**

The major pathophysiologic hallmarks that distinguish DHF from DEN and other diseases are abnormal haemostasis and increased vascular permeability that leads to leakage of plasma. The clinical features of DHF are rather stereotyped, with acute onset of high (continuous fever) haemorrhagic diathesis (most frequently on skin), hepatomegaly, and circulatory disturbance (in most severe form as shock - dengue shock syndrome). It is thus possible to make an early and yet accurate clinical diagnosis of DHF before the critical stage, or shock, occurs, by using the pattern of clinical presentations together with thrombocytopenia and concurrent haemoconcentration, which represent abnormal haemostasis and plasma leakage respectively.

The management of DHF is entirely symptomatic and supportive and is directed towards replacement of plasma losses for the period of 24-48 hours. Survival depends on early clinical recognition and frequent monitoring of patients for pathophysiologic changes. Early volume replacement when haematocrit rises can significantly prevent shock and/or modify disease severity. In shock cases, satisfactory results have been obtained with the following regimen:

- (a) Immediately and rapidly replace plasma losses with isotonic salt solution and plasma or plasma expander (in cases of profound shock).
- (b) Continue to replace further plasma losses to maintain effective circulation for the period of 24-48 hours.
- (c) Correct metabolic and electrolyte disturbance (metabolic acidosis, hyponatremia, hypoglycemia or hypocalcemia).
- (d) Give blood transfusion in cases of significant bleeding.

At the Children's Hospital in Bangkok, where a great number of DHF cases are being received every year, the treatment with this regimen (without using steroid or any vasopressor drugs) has resulted in a steady decline in the case fatality rate of shock cases from about 5 per cent in 1971 to 2 per cent in 1984 and to 0.2 per cent in 1991. The result of studies from various places on the use of corticosteroid in treating DSS showed no benefit either in the fatality rate or any reduction in the volume of fluid therapy or duration of therapy.

### **Pearls and pitfalls in the management of DHF**

- In a child with acute onset of high fever: flushed face without coryza, with petechiae and/or positive tourniquet test should suggest the possibility of dengue infection.
- Additional hepatomegaly (=tenderness) increases the possibility of DHF.

- Serial platelets and HCT determinations for a drop in platelets and rise in HCT, which represent major pathophysiological changes (abnormal haemostatic and plasma leakage), are essential for early diagnosis of DHF.
- Rising HCT by 20 per cent or more simultaneously with or shortly after a drop in platelet count (that occurring before subsidence of fever or onset of shock) reflects significant plasma losses and indicates a need for volume replacement.
- Early replacement of plasma losses with isotonic salt solution can prevent shock and/or modify severity.
- I.V. fluid therapy before leakage as prophylaxis for shock is not recommended as it may do some harm.
- Antipyretic helps in reducing the height of fever, but cannot shorten the duration of fever: recommend to use paracetamol (with caution); aspirin is contraindicated.

#### **Pearls and pitfalls in the management of shock**

- DSS is hypovolemic shock due to plasma losses: volume replacement with isotonic salt solution, plasma or plasma substitute for the period of plasma leakage (24-48 hours) is life-saving.
- Volume replacement should be monitored according to the rate of plasma leakage (as reflected by HCT, vital signs, urine output) to avoid fluid overload (the rate of leakage is more rapid in the first 6-12 hours).
- Dextran 40 is as effective as plasma (maximum dose 30 ml/kg/day), with some advantages.
- Over-replacement with more volume and/or for longer period of time will cause pulmonary congestion/oedema, particularly when reabsorption of extravasated plasma occurs.
- Stagnant acidemia blood promotes occurrence/enhances severity of DIC; acidosis must be corrected. Coagulogram should be evaluated.
- Platelet-rich plasma transfusion as prophylaxis for bleeding in all shock cases is not recommended.
- There are abnormal haemostatic changes that potentiate bleeding in DHF/DSS, severe bleeding (may be concealed) often occurs in cases with prolonged shock and further perpetuates shock.
- Refractory shock despite adequate volume replacement and a drop in HCT (at any rate, e.g. from 50 per cent to 40 per cent) indicates significant bleeding and a need for FWB transfusion (10 ml/kg/dose if HCT >35 vol%).

#### **8.9 Serological Diagnosis and Support During an Epidemic**

Five basic serological tests are used for diagnosis of dengue infection: haemagglutination-inhibition (HI), complement fixation (CF), neutralization test (NT), IgM-capture enzyme-linked immunosorbent assay (MAC-ELISA) appears to be the most important serological test for a rapid diagnostic technique. Commercial test kits for anti-dengue IgM and IgG antibodies are available. However, further standardization is required (See Annex 6). The most sensitive method for dengue virus isolation assay is the mosquito inoculation technique. However, although it is less sensitive, the mosquito cell cultures are recommended for routine virus isolation because it is more convenient and economical. The indirect fluorescent antibody (IFA) test which uses serotype-specific monoclonal antibodies is recommended for virus detection.

## **9. VECTOR CONTROL FOR CONTAINMENT OF EPIDEMIC**

Dengue/dengue haemorrhagic fever outbreaks, whenever they occur, build up in a short time; thus early actions are required to immediately exterminate the infected mosquitoes to interrupt transmission and to reduce or eliminate new breeding grounds of *Aedes aegypti*. Mobilization of government resources to meet such emergencies are always slow and before they come into operation much damage is already done. In countries where no *Aedes aegypti* control programme exists, the things are still worse. This was exemplified by the dengue outbreak in some cities of Member Countries in 1996 as the local authorities were caught unawares and it took a couple of weeks before a full-scale effective vector control campaign could be put into action. Therefore, to meet such emergencies it is essential that everybody at all levels, viz. individual, family, community and government, can contribute to arrest the spread of the epidemic. In the following paragraphs an attempt is made to highlight the actions which everybody can take as and when the first case of DEN/DHF is detected.

### **Development of Emergency Vector Control Programme**

#### **(A) Self-reliance action for vector control and personnel protection**

##### **Individual level**

- Knock down adult mosquitoes by making use of commercially-available safe aerosols (pyrethroid-based). Spray each bedroom for few minutes and close the room for 15-20 minutes. The timing of spray should coincide with peak biting time, i.e. two hours after sunrise and two hours before sunset.
- Empty all water containers, scrub them and dry them. Scrubbing is essential to eliminate eggs glued to the sides of the containers before drying and refilling. This should be followed every week.
- Remove all solid waste materials holding rain water and dispose it of in a way that they cannot hold rain water. For example, turning down of large drums upside down or storage under shed.
- Roof gutters or drainage pipes of sunshades and porch of building should be cleared so that there is no stagnation of water.
- All water containers in the house should be covered to prevent fresh egg-laying.

- All essential waters in the house, i.e. flower vases, ant traps, desert water coolers (in India) should be removed on weekly basis following the same principle of emptying, scrubbing and drying to maintain sustainability.

#### **At Family level**

- Families should use mosquito nets to prevent mosquito bites. Infants should be made to sleep under nets during day time.
- All members of family should be encouraged to use big-sleeve shirts and full-length pants, socks and boots to avoid mosquito bites.
- Family members either staying at home or going for work should use commonly available repellents during day time and also make liberal use of mats, coils, etc., during the night.
- Women should get together and form themselves into "women's groups" to create awareness about the disease in other families and together inspect houses in the locality for removal of breeding foci. Weekly checks are essential to maintain sustainability.

#### **At School Children level**

Schoolchildren should be provided health education on all aspects of dengue fever, i.e. what is dengue fever, how it spreads, role of mosquito and how they breed and how they can be controlled. After health education school children should be organized to detect and eliminate breeding of *Aedes aegypti* in schools, around schools, in houses and also in the neighbourhood.

#### **At Community level**

At the community level the people should form welfare groups and supplement the efforts at family/individual levels. Welfare societies can identify commercial groups, viz. traders dealing in used tyres, water-based commercial establishments (curing tanks for cement-based industries), timber merchants with mandatory maintenance of drums of water to meet fire emergencies water storage trolleys in places of congregation (cinema houses, religious places, etc. and create awareness about dengue and seek their cooperation for removal of breeding places at weekly intervals.

#### **(B) Action by local authorities**

##### **(1) Chemical Control**

For control of epidemics chemical control of the vector is the only way to interrupt the transmission. The following actions should be organized to achieve the goal. There are two main methods of space spraying for adult mosquito control: **(i) cold aerosol, and (ii) thermal fogging.** Guidelines for space spraying with adulticides and equipment which have been experimentally proven to be effective in the control of DEN/DHF outbreaks are included in Annex 7.

##### **(2) Cold aerosol or ultra-low-volume (ULV) spraying**

Technical grade of malathion or fenitrothion at the rate of 0.5 litre per hectare. For smaller areas, among aerosol generators tested and recommended are vehicle-mounted ULV generators, backpack with ULV nozzle or portable mist blower.

**(3) Thermal fogging**

A number of synthetic pyrethroid compounds as well as malathion or fenitrothion in different formulations have been tested, after mixing with diesel oil, with or without pyrethroid mixture. This approach has more operational constraints than ULV but has deeper penetration in crowded urban areas or where vegetation is dense. Swing fog machine and vehicle-mounted generator were once widely distributed in the South-East Asia Region.

**(4) Focal spraying**

Based on epidemiological information, a limited focal spraying is recommended to cover the surrounding area of each reported case of dengue/DFH within a radius of 500 metres. This approach is based on bionomics of *Aedes aegypti*, having a limited flight range of 500 metres or less. Focal spraying with 3-5% malathion thermal fogging in diesel oil had been once widely practiced throughout Indonesia, especially where houses were scattered. This is an ideal approach for taking up immediate action against a local outbreak and for giving public a sigh of relief.

**(C) Technical considerations for success of control operations**

To be successful and effective in interrupting an outbreak of DEN/DHF, the following criteria should be taken into account to make the efforts cost-effective otherwise an epidemic may continue until all adults of dengue vector species in the entire affected area are completely eliminated.

**(1) Space spraying**

- The size of the area to be sprayed should be large enough to cover the entire affected area.
- Space spraying must be repeated 2 to 4 times at an interval of 3 to 5 days within a period of 1 to 2 weeks, commencing as soon as an outbreak is declared.
- Space spraying must be carried out thoroughly under tight technical supervision in terms of dosage, particle sizes and their density.
- Space spraying must be carried out when adult mosquitoes are active, i.e. in the forenoon.
- Space spraying must be directed or concentrated indoors.

**(2) Larvicidal application**

Water containers which cannot be emptied for various reasons should be treated with temephos (abate), 1% sand core granules applied at a dosage of 1 ppm (10 grams of granules in 100 liters of water) can provide effective control of *Ae. aegypti* for 8-12 weeks if water is not removed/changed.

### **(3) Source reduction**

House-to-house searches should be organized for "detection and elimination" of all breeding places in the affected localities. This alone will reduce the breeding load of *Aedes aegypti*.

### **(4) Legislative measures**

Legislation is an essential counterpart of all the actions promoted and implemented by dengue/*Ae. aegypti* control programme. Provisions of legislation enacted by a country for epidemic disease control should be invoked and strict compliance of the provisions relating to vector control should be ensured.

## **10. MANAGEMENT OF POST-DHF EPIDEMICS**

Any activity during the post-epidemic period may look odd and wasteful but it is most essential for further improvement of the dengue control programme and for better management of epidemics. Besides, a retrospective study of an outbreak would provide essential material for case studies for teaching purposes.

### **Retrospective Study of Epidemic - Learning Lessons**

A retrospective study should cover all aspects of hospital care and case management, departure of clinical signs and symptoms from the already known pattern, response to chemotherapy/management success rate in reducing case fatality rate, and all administrative points connected with the adequacy of hospital management to meet such emergencies.

The epidemiological study should cover in depth the agent-host and vector interaction and collect all information on morbidity and mortality figures, prevalence of infection by age and sex, professions, socio-cultural factors promoting outbreaks, vector prevalence, types of containers promoting breeding and evaluation of all *aegypti* control strategies, factors related to cost-effectiveness and sustainability, degree of community participation, degree of governmental preparedness to control such epidemics and all other factors which will enhance the future capabilities of all those involved in epidemic control.

## **11. PROSPECTS OF DENGUE PREVENTION AND CONTROL**

Prospects of DEN/DHF prevention and control are not very promising because of epidemiological complexities of the infection which are not fully understood yet. However, important factors responsible for its geographical spread and intensity of occurrence are briefly summarized below:

- (1) Most of the countries have no regular dengue control programme while in others it is non-existent.

- (2) The Control strategy is based upon ULV space spraying which is inadequate in many situations to control *Aedes aegypti*.
- (3) Uncontrolled urbanization and population growth resulting in reduction of per head supplies of domestic water thereby encouraging storage practices.
- (4) Spread of *Aedes aegypti* along with rural water schemes.
- (5) Inadequate disposal of solid waste littered around houses and retaining rain water and breeding *Ae. aegypti* and *Ae. albopictus*.
- (6) Increased travel permitting rapid importation of dengue virus.
- (7) Deterioration of health infrastructure and following a "crisis mentality" in dealing with DHF outbreaks.
- (8) Lack of technology for early detection of dengue cases.

However, development of dengue vaccine and establishment of an efficient disease and vector surveillance system can go a long way in meeting the challenge.

### **11.1 Vaccine**

Since 1980, SEARO and the Rockefeller Foundation have supported the development of a live attenuated tetravalent dengue vaccine by investigators at Mahidol University, Thailand. For developing the tetravalent vaccine, the DEN-1, 2, 3 and 4 vaccines were combined and inoculated at one or two sites into a small number of susceptible adults; it was reported that the seroconversion rates were satisfactory. The tetravalent live attenuated vaccine has been licensed to the Pasteur-Merieux Company for commercial production. Studies are now in progress to test the immunogenicity and reactogenicity of this experimental tetravalent vaccine in susceptible children but the results have not yet been published.

While a broadly protective dengue vaccine seems to be at hand, there are unfortunately several major problems that remain to be solved which may delay the deployment of at least the current generation of vaccines. A great deal of work remains to be done to select the optimum age at which to administer the dengue vaccine and to determine if the vaccine is appropriately immunogenic.

It appears that the dengue vaccine can only be used in countries willing to adopt an "eradication" strategy implying the near-complete control of dengue virus transmission and saturation immunization to achieve herd immunity in all age groups; individuals who are solidly immune will not transmit the virus to a competent vector mosquito. But the purchase and use of limited quantities of dengue vaccine through the private sector is not likely to interrupt the dengue virus transmission and may place incompletely immunized vaccines at risk of infection and may perhaps result in enhanced disease.

If a country places total dependence on vaccine use rather than on vector control, populations of a dangerous vector will be able to initiate transmission again as the vaccination programme wanes. This has occurred in Africa in the form of urban yellow fever in an area where vaccination was inadequate and the vector densities remained high.

## **11.2 Disease and Vector Surveillance**

Disease surveillance is essential to determine the risk of impending outbreaks, ensuring early detection and identifying the location and size of areas at risk or areas infected as a basis for directing the vector control operations.

The surveillance system should comprise of (a) epidemiological surveillance, and (b) entomological surveillance. Epidemiological surveillance will comprise active (proactive) and passive (reactive) actions and should include (i) clinical surveillance of the disease; (ii) serological surveillance, and (iii) virological surveillance. Entomological surveillance would help stratify the high risk areas for vector control measures.

### **11.2.1 Epidemiological surveillance**

The epidemiological surveillance will comprise the following components:

*Passive (reactive surveillance):* For the development of passive surveillance system, DEN/DHF should be a notifiable disease mandated by law. Such a system will require reporting of all clinical cases by hospital dispensaries, private physicians and all other health centres providing medical care to the population at risk (Annex 8). The information so collected will help define trends in dengue transmission and detect any increase in dengue incidence.

*Active (proactive) surveillance:* The active surveillance has necessarily to be laboratory-based to provide early and precise information on four aspects of increased dengue activity, i.e. time, location, virus serotypes and disease severity. The main characteristic of this type of surveillance is its predictive capability.

Trend analysis of data, based on rapid diagnosis of cases, and identification of serotype provide the necessary information for initiating vector control measures well in advance to prevent outbreaks.

### **11.2.2 Vector surveillance**

Vector surveillance is an integral part of epidemiological surveillance and should be linked together to identify dengue transmission in time and space. Vector surveillance is always used to determine changes in the geographical distribution of the vectors, to obtain data and measurement of population over time to facilitate appropriate and timely decisions regarding methods of intervention. Vector surveillance will also permit delimitation of areas of high density as well as period of population fluctuations.

The parameters commonly applied for assessing levels of larval and adult population are included in Annex 4. However, selection of appropriate sampling methods depends on the surveillance objectives. Some guidance as to the choice of methods is given below:

**Sampling Methods for Assessing Levels of Larval and Adult Populations**

Objectives	Methods					
	Larval	Human	Resting	Ovitrap	Tyre	Adult
Susceptibility Baseline infestation surveys	X					X
Control programme monitoring: level > 5%	X					X
Low infestation levels: < 5%	X			X	X	X
Surveillance against reinfestation	X			X	X	X
Verification of eradication	X	X		X	X	X
Evaluation of control methods*	X	X	X	X	X	X

\* Choice depending on intervention used.

### 11.3 Research

Dengue/dengue hemorrhagic fever prevention and control, as stated earlier, has a very complex epidemiology. For a better comprehension of transmission dynamics a great deal of research input is essential for predictive research for developing cost-effective and sustainable control programmes. Some crucial areas of research have been identified as follows:

#### 11.3.1 Dengue/DHF Virus

Important research areas on dengue viruses which may help in predicting epidemics of dengue/DHF include: (i) study of neutralizing antibodies in one or more child cohorts; (ii) dengue virus activity; (iii) periodic cohort or age-stratified dengue neutralizing antibody surveys; (iv) silent dengue transmission, (v) dengue serotypes and genotype distribution temporarily and in association with DHF/DSS, and (vi) relation of dengue infection enhancing antibodies to disease outcome.

#### 11.3.2 Control of DHF

There is a need for developing more sensitive sampling methods of the *Aedes* population for predictive research. These may include: (i) use of pupal indices to assess the relative adult population; (ii) type of most preferred containers acting as mother foci and the containers utilized by the species for geographical spread locally or in new areas, for assessing the suitable intervention type, and (iii) ways and means to enlist community participation for control of DHF.

### 11.4 Regional Guidelines for Management of Epidemics

On the basis of the deliberations at the meeting, it is proposed to prepare comprehensive generic guidelines for the management of DEN/DHF epidemics which countries in the Region can adapt as per prevailing local conditions and resources.

## **12 RECOMMENDATIONS**

### **12.1 Administrative Arrangements for Control of DHF Epidemics**

It is necessary that a mechanism be established at national, state and local levels for the creation of a multi-disciplinary emergency action committee (EAC) and a rapid action team (RAT). EAC will mobilize all resources of health and non-health sectors, the media, NGOs, school/colleges, student manpower and communities at large in order to coordinate prompt actions for emergency interventions. The rapid action team, under the direction of EAC, should have the capacity to be mobilized at short notice to carry out epidemiological investigations and control measures.

#### **Recommendations**

##### **A. For WHO/SEARO**

The existing regional rapid response team at SEARO should be strengthened and expanded to include Member States to support emergency management of DHF as requested or required by country(ies).

##### **B. For Member States**

- (1) The EAC and RAT should be established at national, state and local levels to take early action for management of DHF outbreaks.
- (2) Inter-sectoral partnerships should be established at national and local levels with all related sectors to control epidemics.
- (3) An official spokesperson, (i.e. public information officer) should be designated at national, state and local levels, to provide accurate information to the public through inter-personal communication and the mass media regarding DHF outbreaks.

### **12.2 Preparation and Organization of Medical Care Before and During Epidemics**

During the past two decades the DEN/DHF incidence has been increasing every year in the countries of the Region. However, where DHF has appeared as a newly emerging disease, the case fatality rates are high, apparently due to lack of awareness of the standard management of cases. It is essential that DHF management skills need to be improved not only among health personnel but also in the management and organization of medical care services before and during epidemics. Recommendations are made as follows:

##### **A. For WHO/SEARO**

- (1) To develop standard comprehensive training modules for use in emergency preparedness for case management of DHF/DSS.

- (2) The revised version of the 1986 manual on diagnosis, treatment and control of DHF should be made available to the Member Countries as early as possible.
- (3) WHO should support Member Countries on research and training by way of expertise and for exchange visits of scientists within the SEA Region.

**B. For Member Countries**

- (1) Health personnel, especially physicians, should be oriented to the standard clinical case diagnosis and management by (i) providing WHO Case Management Guidelines for DEN/DHF/DSS; (ii) conducting training courses using standard training modules, and (iii) incorporating DEN/DHF into the curriculum in medical schools, schools of nursing and schools of public health as a long term measure.
- (2) Ensure that medical facilities where dengue patients are admitted are free from *Aedes* mosquitoes by eliminating breeding sources (e.g. a distance of 500 meters circumference) and equipped with mosquito screens to prevent further transmission of infection.

**C. For provincial/municipal/district health authorities**

- (1) Health facilities including private practitioners in peripheral areas where basic laboratory and treatment facilities are not available, health personnel should be trained to recognize important signs and symptoms of DEN/DHF/DSS and should refer the patients to hospital when suggestive signs of haemorrhagic manifestation or shock are detected.
- (2) A suitable referral system with appropriate transport facilities should be established.

**12.3 Standard Case Management of DHF/DSS**

For effective individual case diagnosis and management of DHF/DSS, laboratory support is essential. The following steps are recommended:

**A. For Member Countries**

- (1) The guidelines for Clinical Diagnosis and Management of Dengue and Dengue Hemorrhagic Fever in the WHO/SEARO Monograph No. 22 are appropriate for use by all physicians. It should be strictly followed, particularly for monitoring of platelet counts and haematocrit value and the amount and period of fluid replacement. Invasive procedures like gastric intubation is contraindicated as it causes haemorrhage. The use of salicylate analgesic (i.e. aspirin) is strongly contraindicated.
- (2) During outbreaks, all patients with high fever (38.5°C or higher) should be screened for dengue by Tourniquet test using appropriate-size sphygmomanometer cuff. All health facilities should be encouraged to establish at least one *observation room* for observing suspected cases of DHF for early detection of haemorrhagic manifestations and/or shock.

- (3) Clinical laboratory services should be established to function on 24-hours basis in order to monitor platelet and haematocrit levels and to start early fluid replacement, if indicated. It is desirable that separate arrangements (units, ward) for DHF/DSS patients be established and specially trained staff should be deployed to properly monitor and manage DHF/DSS cases. Basic laboratory facilities (microhaematocrit, microscopes, microcentrifuge) for total differential cell counts and haematocrit platelet counts should also be attached to the DHF/DSS wards.
- (4) Laboratory support should be strengthened for the diagnosis and management of dengue. Two types of laboratory tests are used for different purposes: (i) For individual case diagnosis and management, basic laboratory tests are essential in all health facilities. The hospital laboratory should also have the capability to test blood coagulogram, blood electrolytes, blood gas and liver function tests, and (ii) serological tests should be used for specific, etiological diagnosis and epidemiological surveillance. A small sample (5%) of all suspected dengue cases should be sufficient. Attempts should be made to collect paired samples at acute stage on admission and at convalescent stage on discharge. Virus isolation should be considered a special study.

#### **12.4 Laboratory Diagnostic Facilities**

At present there is no standardized rapid test for dengue infection. For MAC-ELISA and other serological tests, timely availability of reagents is necessary. Therefore, there is a need for timely supply of required reagents. The recommendations are as follows:

##### **A. For WHO/SEARO**

- (1) SEARO should consider designating additional arboviral WHO collaborating centres in the Region and strengthening existing centres in order to support increased production of viral reagents.
- (2) Rapid diagnostic test kits should be standardized by a WHO panel of experts which can provide rapid, dependable results.

##### **B. For Member States**

National virology reference centres should be strengthened and the availability of necessary reagents and other laboratory supplies which are required for the timely determination of virus serotypes should be ensured.

#### **12.5 Disease Surveillance System**

In order to prevent and control epidemics, it is essential to have a full understanding of the epidemiological patterns based on an effective disease surveillance system established at regional, national and local levels. The recommendations are:

##### **A. For WHO/SEARO**

SEARO should assist Member Countries to strengthen and coordinate surveillance activities on a regular basis in order to determine trend analysis, provide feedback to Member Countries and exchange information.

**B. For Member Countries**

Countries of the Region should develop and strengthen their disease surveillance systems on a regular basis to determine trends and early warning signs of the disease outbreak. DHF should be declared as a reportable/notifiable disease. Existing legal frameworks should be reviewed and steps taken to empower local authorities and/or state governments to monitor, prevent and control epidemics.

**C. For Provincial/Municipal/District Authorities**

Approximately 5 per cent of the clinical diagnosis of dengue/DHF cases should be confirmed at the beginning of the transmission season by laboratory diagnosis. The information can be linked to vector control measures in order to reduce vector population.

**12.6 Vector Surveillance and Control**

In the absence of any vaccine or drug for treatment of infection, the choice for prevention and control of DEN/DHF epidemic falls on vector control. Information about vectors and their control is required to develop cost-effective control strategies. The recommendations are:

**A. For WHO/SEARO**

- (1) SEARO should develop a manual and guidelines on contingency vector control to deal with the epidemic situation.
- (2) SEARO should organize intercountry workshops on vector surveillance and its control so that Member Countries can adopt appropriate strategies suiting local conditions.

**B. For Member Countries**

- (1) Member Countries should carry out vector surveillance in epidemic potential areas to bring out information on vector dynamics and possible risk factors.
- (2) It is necessary for countries to develop appropriate entomological assessment for effective implementation in order to monitor vector control activities and assess the impact on vector population.

**C. For Provincial/Municipal/Districts Authorities**

- (1) During the dengue outbreaks, immediate action is essential to identify local areas where transmission is occurring. Local authorities should develop mechanisms to conduct epidemic investigation and apply remedial vector control measures.

- (2) Local authorities should convey a clear message that members within communities should undertake source reduction measures in and around their houses and protect themselves by using available protective measures. They should be encouraged during DHF epidemics to cooperate with municipal health authorities with regard to control activities.

## **12.7 Capacity-Building**

A cadre of trained workers and scientists forms the backbone for the success of any disease control programme, and DHF control is no exception. Therefore, there is a need for building up competency-based course curricula and arranging trainers' training programme in all aspects of disease surveillance and outbreak management. The recommendations are:

### **A. For WHO/SEARO**

- (1) SEARO should organize a workshop to design a study on silent dengue transmission. Where resources permit, Member Countries may choose to establish a prospective study of a selected population in a study site. DEN/DHF cases, dengue transmission patterns, vector densities and other parameters of epidemiological significance should be correlated to determine factors favourable for silent dengue transmission.
- (2) Technical guidelines for epidemic management of DHF should be developed by SEARO for the Member States to adopt according to local capacity.

### **B. For Member Countries**

- (1) National dengue prevention and control programmes should be established and existing programmes should be further strengthened at each infrastructural level with the appointment of qualified staff. In countries where urban malaria programmes exist, merging of dengue control with these programmes may be considered.
- (2) Logistical support for the management of outbreaks in the Member Countries should be further strengthened at regional, national and local levels. Manpower mobilization should be strengthened by creating awareness through workshops and seminars to fight epidemics.
- (3) Training courses should also be developed to improve the competency of health personnel at all levels in order to implement effective DHF epidemic control measures.

## **12.8 Research on DEN/DHF/DSS**

There was an urgent need for developing basic research to understand the epidemiological complexities of the disease and operational research and training was required to develop cost-effective control strategies and their implementation. Socio-cultural habits, beliefs and prejudices of communities not only promote building up of breeding potential for dengue vector but also come in the way of implementing control strategies. The recommendations are as follows:

### **A. For WHO/SEARO**

SEARO should arrange to make an inventory of dengue viruses isolated from DEN/DHF cases in each country and coordinate genotyping studies at WHO collaborating centres.

**B. For Member Countries**

- (1) Countries should investigate the distribution of the genotype of dengue viruses in collaboration with SEARO and WHO collaborating centres.
- (2) Countries should conduct a study to identify their early warning system for detection of virus circulation, based on local capacity, by which future epidemics may be determined before they become explosive outbreaks.
- (3) To identify indicative signs/symptoms or simple laboratory tests which can predict haemorrhage or shock in dengue cases.
- (4) Study reliable rapid laboratory diagnostic technology.
- (5) There was a need for developing more sensitive and applicable entomological parameters to correlate mosquito population densities with dengue transmission rates.
- (6) Current vector control survey methods need to be reassessed to take into consideration prevailing socio-cultural conditions and vector control measures to determine which can be utilized effectively in a cost-effective and sustainable manner.
- (7) An in-depth study on the bioecology of the two ecological variants of *Aedes aegypti* be conducted in order to determine ecological consequences of environmental changes and vector breeding as related to dengue transmission and to develop rational control strategies.
- (8) Ways and means by which communities can be mobilized for DEN/DHF outbreaks should be considered. In this regard a well-defined and simple community action for control of vectors should be prepared, and how the same should be communicated to the people needs to be defined.
- (9) Social/behavioural research should be strengthened to improve communication at the community level for better prevention and control of DHF: knowledge, attitude, belief and practice (KABP), including culturally-sensitive health messages.

## Annex 1

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### Annex 3

#### RECEPTIVITY OF SOUTH-EAST ASIA TO DENGUE INFECTION

Ecological Zones	Geographic Regions	Breeding Potential of <i>Aedes aegypti</i>	Receptive for DEN/I
<p><b>arid less than &gt;50 cm Rainfall</b></p> <p>temperature                      ssion season:2-3 months</p>	<p>North West India</p>	<p>Breeding restricted to urban towns Rural areas generally free within towns species depict "Annual Pulsation</p>	<p>" <b>Very low.</b> Sporadic and inte transmission by single serotyp manifestation of classical Den;</p>
<p><b>us Dry and Wet</b></p> <p>=50-150cm                      : temperature                      ssion season 4-5 months</p>	<p>Most of central and South India</p>	<p>Same as above <i>Aedes aegypti</i> extend to few urbanized villages Areas above 500 meters free of <i>Ae. aegypti</i> infestation. <i>Ae. albopictus</i> has no role in transmission</p>	<p><b>Low:</b> Low grade transmission two serotype. All adult mostly Clinical symptoms remain unc children. During years of high extended rainfall transmission occurrence of DHF epidemic.</p>
<p><b>l Monsoon</b></p> <p>&gt;150cm                      : temperature                      ermit year round                      ssion</p>	<p>North East India (Valleys)                      Myanmar,Thailand and Sri Lanka</p>	<p><i>Aedes aegypti</i> wide spread in urban and rural areas. Extent and intensity of breeding high. <i>Ae. albopictus</i> involvement suspected.</p>	<p><b>High:</b> Hyper endemic conditic maintained by extended transr more than one sero type. DHF (&gt;15 year common).</p>
<p><b>ial</b></p>			

<p>&gt;200cm e climate, Transmission out the year.</p>	<p>Indonesia</p>	<p>Year round breeding of <i>Ae.aegypti</i>. Extent and intensity very high. Temperature favour year round transmission. <i>Ae.</i> <i>albopictus</i> involvement suspected.</p>	<p><b>V.High.</b> Hyper endemic condi Transmission year round. DHI common</p>
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## Annex 4

### ENTOMOLOGICAL PARAMETERS

#### Larval population

- (1) *House (premises) index (HI)*: Percentage of houses infested with larvae and/or pupae

$$HI = \frac{\text{Infested houses}}{\text{Houses inspected}} \times 100$$

- (2) *Container index (CI)*: Presence of water-holding containers infested with larvae or pupae.

$$CI = \frac{\text{Containers positive}}{\text{Containers inspected}} \times 100$$

- (3) *Breteau index (BI)*: Number of positive containers per 100 houses inspected.

$$BI = \frac{\text{Number of positive containers}}{\text{Houses inspected}} \times 100$$

#### Adult population

- (1) *Landing/Biting collection (per man-hour)*: These are sensitive parameters to detect low levels of infestation and is an indicator of proximal hidden breeding site. Rates of capture using handnets or aspirators are expressed as landing/biting counts per man-hour.

- (2) *Resting collection*: During the period of inactivity mosquitoes are collected as resting population by various techniques, and can be expressed as number of adults (both male and female) per house or number of adults per man-hour.

## Annex 5

### FUNCTIONS OF EMERGENCY ACTION COMMITTEE (EAC) AND RAPID ACTION TEAM (RAT)

#### (A) Emergency Action Committee (EAC):

Constitution: EAC will be comprised of administrators, epidemiologists, entomologists, clinicians and laboratory specialists, school health officers, health educators, and representatives of other related sectors.

##### **Functions:**

- (a) To take all administrative actions and to coordinate activities aimed at management of serious cases in all medical care centres and undertake emergency vector control intervention measures.
- (b) To draw urgent plans of action and resource mobilization in respect of medicines, intravenous fluids, blood products, insecticides, equipment and vehicles.
- (c) To liaise with intersectoral committees to mobilize resources of non-health sectors, viz. urban development, ministry of education, ministry of information, legal department, water supply, waste disposal, information for elimination of breeding potential of *Aedes aegypti*.
- (d) To interact with the news media and NGOs for dissemination of information related to health education and community participation.

#### (B) Rapid Action Team (RAT):

##### **Constitution:**

RAT at state/provincial levels will be comprised of epidemiologists, entomologists and laboratory specialist at state and local levels.

##### **Local Levels:**

Medical officer, public health officer, non-health staff, local government staff.

##### **Functions:**

- Undertake urgent epidemiological and entomological investigations.
- Provide required emergency logistical support, e.g. delivery of medical and laboratory supplies to health facilities.
- Provide on-the-spot training in case management for local health staff.
- Supervise elimination of breeding places and applying vector control measures.
- Carry out health education activities.

- Sampling collection of serum specimens.

## Annex 6

### RELATIVE SENSITIVITY AND INTERPRETATION OF SEROLOGICAL TESTS

#### (1) Haemagglutination Inhibition (HI)

- Ideal for seroepidemiology; sensitive; easy to perform; minimal equipment; reliable; best for most flaviviruses, well-standardized.
- Remove non-specific inhibitors and agglutinins from serum; lack of specificity of serotypes; usually paired serum samples.

#### Interpretation of Dengue Haemagglutination-Inhibition Antibody Response<sup>a</sup>

Antibody response	Convalescent		Convalescent titre <sup>c</sup>	Interpretation
	S1-S2 interval <sup>b</sup>	Titre <sup>c</sup> <<1		
>4-fold rise	≥7 days		≤1:1280	Acute flavivirus infection, primary
≥4-fold rise	≥Any specimen		≥1:2560	Acute flavivirus infection, secondary
>4-fold rise	≥7 days		≤1:1280	Acute flavivirus infection, either primary or secondary
No change	Any Specimen		≥1:2560	Recent flavivirus infection, secondary
No change	≥7 days		≤1:1280	Not dengue
No change	≤7 days		≤1:1280	Uninterpretable
Unknown	Single specimen		≤1:1280	Uninterpretable

Clarke OH, Casals J. American journal of tropical medicine and hygiene, 1958, 7:561-573.

- These criteria were derived empirically from data accumulated at the US Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand. Individual laboratories should assess the sensitivity of their assay with standard sera from WHO collaborating centres. Laboratories should also establish baseline data for the population they serve during a period of little or no flavivirus transmission. Test results should be transformed to reduce variance: results that are two standard deviations greater than the geometric mean may be presumed to indicate recent dengue infection.
- Interval in days between acute (S1) and convalescent (S2) specimens.
- Against any dengue antigen.

#### (2) Complement Fixation (CF)

- More specific
- More difficult, longer, less widely used; highly-trained personnel.

**(3) Neutralization Test (NT)**

- Most specific and sensitive; mostly used PRNT
- Detects past infection, expensive and time-consuming

**(4) IgM-capture (Mac-ELISA)**

- New, simple, RAPID, IgM, only one sample needed, screening many samples.
- Less sensitive than HI

**Interpretation of MAC-ELISA Results<sup>a</sup>**

<b>IgM antibody response</b>	<b>S1-S2 interval<sup>b</sup></b>	<b>IgM to IgM ratio</b>	<b>Interpretation<sup>c,d</sup></b>
Increase in molar	2-14 days	High	Acute flavivirus infection, primary
		Low	Acute flavivirus infection, secondary
Elevated, no change or decrease in molar fraction	2-14 days	High	Recent flavivirus infection, primary
		Low	Recent flavivirus infection, secondary
Elevated	Single	High	Recent flavivirus infection, primary
	specimen	Low	Recent flavivirus infection, secondary

- (a) These criteria were derived empirically from the data accumulated at the US Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand. Individual laboratories should assess the sensitivity of their assay with standard sera from WHO collaborating centres. Test results should be transformed to reduce variance: results that are two standard deviations greater than the geometric mean may be presumed to indicate elevated levels of anti-dengue IgM or IgG.
- (b) Guidelines do not apply to intervals between acute (S1) and convalescent (S2) specimens greater than 14 days.
- (c) To infer that dengue virus elicited anti-flavivirus IgM laboratories must test with a regionally appropriate panel of flavivirus antigens. Laboratories must also determine appropriate criteria for categorizing primary and secondary sero-responses.
- (d) Sera for standardization of the assay are available from Chief, Department of Virology, US Armed Forces Research Institute of Medical Sciences, 315/6 Rajvithi Road, Bangkok 10400, Thailand (fax 66-2-247-6030).

**(5) IgG-EIA (Indirect IgG ELISA)**

- insensitive

**(6) Dot Blot Immunoassay**

- Reagents and test procedures are evolving.
- Needs standardization.

## Annex 7

### GUIDELINES FOR EQUIPMENT AND CHEMICAL SPACE SPRAYING

*Aedes aegypti* is the main vector of DEN/DHF which has been responsible for all urban epidemics of this disease. *Ae. albopictus* is also mainly involved in dengue transmission in South-East Asia and the Western Pacific regions. *Ae. aegypti* has a close association with man and it is a highly domestic species with more than 90 per cent resting on no sprayable surface in the house. Therefore, indoor residual treatment of houses is not generally recommended. *Chemical control using insecticide generally has very little impact for long-term control of DEN/DHF. The use of insecticide should be discouraged for long-term prevention and control. However, experiments on the control of Ae. aegypti in several countries in SEA Region has shown that thorough treatment at an interval of 1-2 weeks with portable fogging applicators together with truck-mounted applicators yielded control of Ae. aegypti. Space spray with insecticide should be considered as an epidemic contingency measure.* Total coverage should be targeted for, however attention should be focused inside the house and in the places where high vector densities have been recorded. Space spray should be implemented in a compact community and it should be within the radius of 400-500 metres from the affected house.

Equipment used for ULV/thermal fogging are listed below:

<b>Equipment</b>	<b>Possible Daily Coverage</b>
Vehicle-mounted cold fogger, e.g. LECO	225 ha
Vehicle-mounted thermal fogger, e.g. Dyna-Fog	150 ha
Back-pack ULV mist blower, e.g. Fontan	30 ha
Hand-carried thermal fogger e.g. Swing Fog	5 ha
Hand-carried indoor ULV aerosol generator,e.g. Mity Moe	5 ha or 250 houses

Suitable insecticides for thermal and cold aerosols are indicated in the table.

**Insecticides suitable as cold aerosol sprays and for thermal fogs for mosquito control**

Insecticide	Chemical	Dosage of ai.b (g/ha)		Toxicity: oral LD <sub>50</sub> fai. <sup>b</sup> for rats(mg/kg body weight)
		Cold	Thermal	
Chlorpyrifos	OP	10-40	150-200P	135
Cyfluthrin	PY	1-2	-	500
Ypermethrin	PY	1-3	-	7180
Cyphenothrin	PY	2-5	-	2250-2640
Deltamethrin	PY	0.5-1.0	-	>2940 <sup>c,d</sup>
D-phenothrin	PY	5-10	-	>10,000
Etofenprox	PY	10-20	10-20	>40,000
Fenitrothion	OP	250-300	270-300	503
Fenthion	OP	150	-	330 <sup>d</sup>
Malathion	OP	112-693	500-600	>4000
Naled	OP	56-280	-	430
Permethrin <sup>e</sup>	PY	5-10	-	>4000 <sup>c,d</sup>
Pirimiphos-Methyl	OP	230-330	180-200	2018
Propoxur	C	100	-	95
Zeta-Cypermethrin	PY	1-3	-	86

a PY = Synthetic pyrethroid, OP = organophosphorus, and C= Carbamate

b ai.= active ingredient

c Because of their low dermal toxicity and on the basis of experience with their use, these products have been classified in the WHO Hazard Classification in Class III, Table 5 (WHO/PCS/94.2).

d Dermal toxicity

e Also used in mixtures with knock-down agents or synergists

## Annex 8

### CLINICAL CASE DEFINITION FOR DENGUE HAEMORRHAGIC FEVER

#### All must be present:

1. Fever, or recent history of acute fever.
2. Thrombocytopenia ( $100,000\text{mm}^3$  or less).
3. Haemorrhagic tendencies, as evidenced by at least one of the following:
  - (a) Positive tourniquet test.
  - (b) Petechiae, ecchymoses or purpura.
  - (c) Bleeding from mucosa, gastrointestinal tract, injection sites, or others.
4. Plasma leakage due to increased capillary permeability as manifested by at least one of the following :
  - (a) Hematocrit on presentation that is  $\geq 20\%$  above average for that age and population.
  - (b)  $\geq 20\%$  drop in haematocrit following treatment.
  - (c) Commonly associated signs of plasma leakage: Ascites Hypoproteinemia  
Pleural effusion

### CLINICAL CASE DEFINITION FOR DENGUE SHOCK SYNDROME

All four criteria above plus evidence of circulatory failure manifested by all of the following :

- Rapid and weak pulse
- Narrow pulse pressure (20mmHg or less) or hypotension for age
- Cold clammy skin and altered mental status.

### REPORTABLE CASES OF DHF OR DSS WILL HAVE THE ABOVE, PLUS

One of the following:

- (1) Virological or serological evidence of acute dengue infection, or
- (2) A history of exposure in dengue endemic or epidemic areas (recognizing that during epidemic or significant levels of endemic transmission it is unlikely that many cases will have laboratory confirmation).

**Annex 9****RECOMMENDATIONS FROM INFORMAL CONSULTATION ON  
PREVENTION AND CONTROL OF DEN/DHF, WHO/SEARO  
New Delhi, October 1995**

- (1) A regional strategy and plan of action for its implementation should be developed by the South-East Asia Regional Office and its Member States for the prevention and control of DF/DHF.
- (2) Every Member State of the Region should be encouraged to develop and strengthen its own national strategy and plan of action to control DF/DHF. The creation and implementation of such plans should be monitored and evaluated; the formation of national planning committees to oversee and assist in the implementation should be encouraged.
- (3) The funding sources, both national and international should be identified and funds sought from the potential donors; SEARO should assist the endemic countries in the preparation of requests and identification of the potential donors.
- (4) A regional as well as national training should be developed for all categories of health personnel dealing with DF/DHF. Where possible, clinicians/paediatricians experienced in the management of DHF/DSS should be recruited as trainers for the national and regional courses dealing with the clinical diagnosis and treatment of DHF/DSS; emphasis should be given to train personnel from countries with high case fatality rates.
- (5) The disease surveillance related to the distribution and seasonal incidence of the infection, its serotypes, and the occurrence of DHF and DSS syndromes should be improved at the national level; this should be supported by capable national laboratories using accurate diagnostic methods. The training courses in new techniques as well as the provision of reagents and equipment for diagnostic laboratories should be supported.
- (6) The intensified vector surveillance should include the distribution and seasonal variations in population densities of the vectors, determination of their preferred larval habitats and their contribution to the overall vector densities, and surveys of their insecticide susceptibility.
- (7) The control programmes must be planned, supervised, implemented, and evaluated by well-trained professionals and involve all levels of the community in their planning and implementation; this will ensure intersectoral collaboration in control measures.
- (8) The governments should ensure that adequate budgets are allocated for vector and disease surveillance, and for the manpower and materials required for vector control.
- (9) research must be an integral component of the surveillance, diagnosis, treatment and control programmes; SEARO should support such research with the provision of information, literature, equipment, supplies and, where necessary, with technical advisers.
- (10) WHO should continue to support the development of dengue vaccine and also ensure its efficacy and safe use at low cost.

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