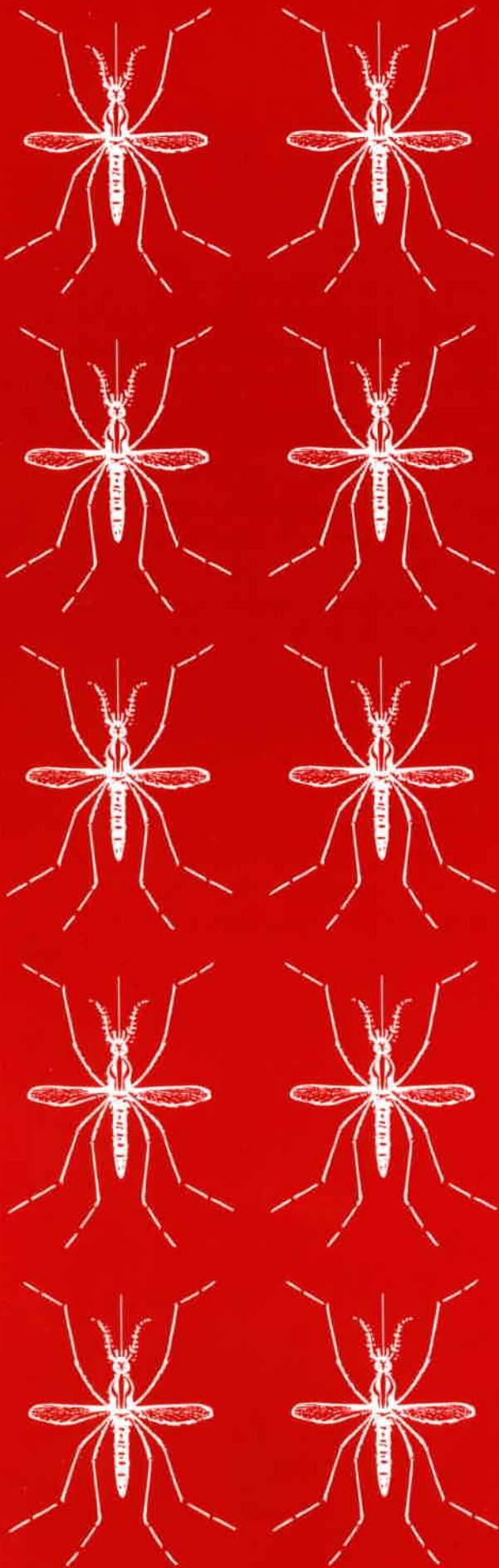


Scientific Publication No. 548

# **Dengue and Dengue Hemorrhagic Fever in the Americas: Guidelines for Prevention and Control**

PAN AMERICAN HEALTH ORGANIZATION



Dengue and its potentially fatal forms, dengue hemorrhagic fever and dengue shock syndrome, once more threaten much of the Region. Although the *Aedes aegypti* mosquito, the disease's main vector, was once virtually eradicated from the Americas, nearly all the countries were reinfected and suffered epidemics in the 1980s. As vector control programs fell victim to that decade's cutbacks in public health expenditures, the programs were left with scanty surveillance capabilities, and their response to dengue outbreaks tended to be too little too late. Moreover, the vertically structured traditional control programs in most countries were costly and difficult to manage. Clearly, a new approach was needed.

These guidelines have risen to that challenge by incorporating all aspects of the prevention and control of the disease and its vectors. In addition, because dengue is primarily a problem of domestic sanitation and household members can combat the problem inexpensively through physical means and without overusing chemicals, these guidelines emphasize ways to transfer the responsibility, capability, and motivation for dengue control and prevention to the community.

Prepared by experts in aspects of dengue prevention and control from the Region and by several PAHO staff members, this publication fills a critical niche in the fight against dengue in the Americas, and is an invaluable tool for health professionals working in vector control.



**Pan American Health Organization**  
Pan American Sanitary Bureau, Regional Office of the  
**World Health Organization**

# **DENGUE AND DENGUE HEMORRHAGIC FEVER IN THE AMERICAS: GUIDELINES FOR PREVENTION AND CONTROL**



Scientific Publication No. 548

**PAN AMERICAN HEALTH ORGANIZATION  
Pan American Sanitary Bureau  
Regional Office of the  
WORLD HEALTH ORGANIZATION**

525 Twenty-third Street, N.W.  
Washington, D.C. 20037  
U.S.A.

Also published in Spanish (1995) with the title:  
*Dengue y dengue hemorrágico en las Américas: Guías para su prevención y control*  
Publicación Científica de la OPS No. 548  
ISBN 92 75 31548 5

PAHO Library Cataloguing in Publication Data

Pan American Health Organization

Dengue and dengue hemorrhagic fever in the Americas :  
guidelines for prevention and control. — Washington, D.C.  
: PAHO, © 1994. — v, 98p. — (Scientific Publication ; 548)

ISBN 92 75 11548 6

I. Title II. (Series)

1. DENGUE—prev 2. AMERICA—epidemiol  
NLM WC528

First printing, 1997

ISBN 92 75 11548 6

The Pan American Health Organization welcomes requests for permission to reproduce or translate its publications, in part or in full. Applications and inquiries should be addressed to the Publications Program, Pan American Health Organization, Washington, D.C. U.S.A., which will be glad to provide the latest information on any changes made to the text, plans for new editions, and reprints and translations already available.

© Pan American Health Organization, 1994

Publications of the Pan American Health Organization enjoy copyright protection in accordance with the provisions of Protocol 2 of the Universal Copyright Convention. All rights are reserved.

The designations employed and the presentation of the material in this publications do not imply the expression of any opinion whatsoever on the part of the Secretariat of the Pan American Health Organization concerning the status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the Pan American Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

# CONTENTS

Preface .....	v
1. Introduction .....	1
2. Dengue and Dengue Hemorrhagic Fever .....	3
Historical Overview in the Americas .....	3
Clinical Manifestations and Diagnosis .....	8
Vector Distribution and Biology .....	15
Risk Factors for Dengue and Dengue Hemorrhagic Fever .....	19
Risk Factors for the Appearance of DHF/DSS .....	20
3. Surveillance .....	23
Disease Surveillance .....	23
Vector Surveillance .....	28
4. Strategies for Prevention and Control .....	33
The Success and Failure of the Hemispheric Eradication Program .....	33
Current Approaches for Surveillance and Control .....	34
Epidemiologic Stratification .....	37
5. Sustainable Prevention and Control Programs .....	39
Organization and Function of Control Activities .....	39
Vector Control Methods .....	49
6. Emergency Preparation and Response .....	59
Education of the Medical Community .....	60
Organization and Requirements for Medical Care .....	60
Case Management: Classification and Treatment of Patients .....	62
Emergency Vector Control .....	69
7. Evaluation and Prevention Control Programs .....	71
Epidemiologic Evaluation .....	71
Entomological Evaluation .....	73
Information Systems for <i>Aedes aegypti</i> Control Programs .....	73
8. Operational Research .....	77
9. Training in Dengue Programs .....	79
10. Recommendations for Dengue Programs .....	81
Bibliography .....	83

---

Annexes .....	89
Dengue Hemorrhagic Fever Record Sheet .....	89
Sample Dengue Case Investigation Form .....	90
Sample Size in <i>Aedes</i> Larval Surveys .....	91
Emergency Plan Guide .....	93
Handout for Patients with Dengue Fever .....	97
List of Participants at the Dengue Guidelines Meeting 16-20 December 1991, Washington, D. C. ....	98

## PREFACE

In the 1950s and 1960s, the spectacular success of the campaigns to eliminate urban yellow fever by eradicating the *Aedes aegypti* mosquito, also put a major dent in the transmission of dengue fever. Unfortunately, that situation has slipped since then.

As *Aedes aegypti* eradication campaigns deteriorated during the 1970s and 1980s, the mosquito proliferated and spread to nearly every corner of the Region. Not surprisingly, dengue activity increased, reaching staggering levels in that last decade.

During the 1980s, Bolivia, Brazil, Ecuador, Paraguay, and Peru, five countries that either had been free of dengue for several decades or had never recorded the disease, suffered explosive outbreaks. Moreover, in 1993, the only tropical Latin American countries that had remained free of dengue—Costa Rica and Panama—reported indigenous transmission of the disease. Millions of persons are estimated to have been infected during the outbreaks in those seven countries alone.

More alarming than the spread of dengue has been the fact that the disease's most severe form, dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS), has gained a foothold in the Americas. In 1981, Cuba succumbed to the most serious DHF/DSS outbreak ever recorded in the Region—344,203 dengue and DHF cases were reported, including 10,312 severely ill patients and 158 deaths. Venezuela suffered the second most serious outbreak in 1989–1990, with 5,990 DHF cases and 70 deaths, and smaller epidemics have been reported in El Salvador in 1987–1988 and in Brazil and Colombia in the 1990s. Excluding the figures from the DHF epidemic in Cuba, about 10,100 DHF cases and 165 deaths had been reported in the Region up to 1992. As DHF/DSS becomes endemic in several countries, the Americas might face a situation similar to Asia's, in which several hundred thousand cases are reported in certain years. In any event, the toll from this disease is already unacceptably high.

Dengue's meteoric rise made it imperative to have guidelines for the disease's prevention and control, especially since previously published guides, manuals, and plans of action were either incomplete or out-of-date. In order to fill this need, at the end of 1991 the Pan American Health Organization gathered experts in various aspects of dengue and DHF/DSS from several of the affected countries, so that they could update existing materials and develop a new set of guidelines. That meeting marked the birth of this book.

These guidelines break new ground by dealing with the vector as much as with the disease itself. In a fundamental departure from previous eradication efforts, this book's approach stresses a comprehensive vector control effort that brings together all possible safe, effective, and economical control methods to keep vector populations at acceptable levels. To that end, the importance of environmental management has been underscored.

Much consideration also has been given to the elements necessary for sustaining effective dengue prevention and control programs. Besides a comprehensive vector control effort, this complex endeavor will require political, financial, and legislative commitments, as well as a well-planned, decentralized program structure and cooperation within and outside the health sector. Last, but far from least, is the essential role to be played by the community and the importance of utilizing health promotion. Because dengue is basically a problem of domestic sanitation, these guidelines highlight the community's active involvement in dengue prevention and control activities.

The Pan American Health Organization has published these guidelines as a contribution to the ongoing battle against dengue, and in the hopes that the Region once again may be poised at the brink of the disease's control and, ultimately, its eradication.

**Carlyle Guerra de Macedo**  
Director

# 1. INTRODUCTION

Classical dengue, along with its more serious forms, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), is a serious health problem in many parts of the Americas, and it may harm national economies in the Region. Epidemics are extremely costly in terms of hospitalization, patient care, and emergency vector control efforts.

The Hemisphere-wide *Aedes aegypti* campaign succeeded in eradicating this dengue vector from most of Latin America during the 1950s and 1960s. However, the Region's drastic socioeconomic deterioration subsequently resulted in significant reductions in public expenditures for health, including vector surveillance, which led to a reinfestation in nearly all of the countries, subsequent epidemics of classical dengue in each one, and DHF epidemics in Cuba in 1981 and Venezuela in 1989-1990. Obviously, new approaches are needed to address this problem.

The traditional paternalistic, centralized, vertically structured programs that still exist in many countries, are largely ineffective, principally because they are neither affordable nor manageable. They overemphasize chemical control and attempt to cover all infested areas, but have insufficient resources to do so. Because there is no dengue surveillance capability that can detect an increased incidence and that would allow a timely response, most programs' reaction to outbreaks usually is too little and comes too late to significantly alter the epidemic's course. There is little collaboration with other departments within the health sector, or with other relevant government agencies, nongovernmental organizations, and the community at large.

Dengue is basically a problem of domestic sanitation. With little or no expenditure, the members of each household can easily eliminate the problem by physical means and without the use of chemi-

icals. The challenge is to find ways of transferring to the community the responsibility, capability, and motivation for the prevention and control of dengue.

Previously published guidelines, manuals, and plans of action for dengue programs are now obsolete or incomplete. The World Health Organization (WHO) manual, "Dengue Hemorrhagic Fever" (1986), is excellent, but includes very little information on vector control, and needs to be adapted to the conditions in the Americas. The PAHO document "*Aedes aegypti*: Biology and Ecology" (1986), also includes little control information. The 1982 document, "Emergency Vector Control after a Natural Disaster," deals only with that aspect of *A. aegypti* control, and the paper "*Aedes albopictus* in the Americas" (PAHO, 1986), presents a plan of action only for that species. Clearly, a comprehensive document that incorporates all of the aspects of prevention and control of the disease and the two *Aedes* vectors, was needed.

With the full support and endorsement of the Pan American Health Organization's Member Countries, a meeting was held at the Organization's Washington D.C. headquarters from 16-20 December 1991, specifically to prepare such a document. The meeting was attended by eighteen participants from Brazil, Cuba, Honduras, Mexico, Panama, the United States, and Venezuela and eleven staff members of the Pan American Health Organization, all with experience in some aspect of prevention and control of dengue or related disciplines. These guidelines constitute the report presented by that group. Subsequent to the meeting, Erik Martínez of the Hospital William Soler in Havana, Cuba, and Suchitra Nimmannitya of the Children's Hospital in Bangkok, Thailand, also provided invaluable assistance in the elaboration of these guidelines.



## 2. DENGUE AND DENGUE HEMORRHAGIC FEVER

### Historical Overview in the Americas

Dengue-like illness has been reported in the Americas for over 200 years. Until the 1960s, most dengue outbreaks occurred at intervals of one or more decades, but thereafter the intervals have shortened.

The first laboratory-documented epidemic of classic dengue fever in the Americas was associated with dengue-3 serotype, and affected the Caribbean Basin and Venezuela in 1963-1964. Prior to that, only dengue-2 virus had been isolated in the Region, in Trinidad in 1953-1954, in a non-epidemic situation. In 1968-1969, another epidemic affected several Caribbean islands, during which dengue serotypes 2 and 3 were isolated.

During the early and mid-1970s, Colombia was affected by extensive outbreaks associated with serotypes 2 and 3; during this period, these serotypes became endemic in the Caribbean. In 1977, dengue serotype 1 was introduced into the Americas, and after its initial detection in Jamaica, spread to most Caribbean islands, causing explosive outbreaks. Similar outbreaks were observed in northern South America (Colombia, Venezuela, Guyana, Suriname and French Guiana), Central America (Belize, Honduras, El Salvador, Guatemala), and Mexico. Indigenous transmission of dengue-1 also was documented in the state of Texas, U.S.A., during the second half of 1980. About 702,000 cases of dengue were reported by the affected countries during 1977-1980, in which dengue-1 was the principal serotype circulating in the Americas. It is likely, however, that during this period, millions of persons were infected with the virus, since in Cuba alone, 42% of its 10 million inhabitants were infected with dengue-1.

### **Increased Magnitude of the Dengue Problem in the 1980s**

During the 1980s, the dengue problem in the Americas increased considerably, and dengue

activity was characterized by a marked geographic spread in the Region (Table 1). In 1982, an epidemic caused by serotypes 1 and 4 occurred in northern Brazil; in 1986, a major outbreak of dengue-1 affected Rio de Janeiro, and, subsequently, the virus spread to several other Brazilian states. Four other countries with no previous history of dengue transmission or where the disease had not been observed for several decades, suffered extensive epidemics due to dengue-1: Bolivia (1987), Paraguay (1988), Ecuador (1988), and Peru (1990). During the Peruvian outbreak, dengue-4 also was isolated. Serologic studies suggested that several million persons were affected during these outbreaks, although only about 240,000 dengue cases were reported by the five countries during 1986-1990. During this period, there was a marked increase in the occurrence of dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS).

### **DHF/DSS in the Americas**

Table 2 summarizes the suspected and confirmed DHF/DSS cases reported during 1960-1991. To date, the 1981 outbreak of DHF/DSS in Cuba was the most important event in the history of dengue in the Americas. During this epidemic, associated with dengue-2 virus, a total of 344,203 cases of dengue were reported, including 10,312 classified as severely ill (WHO grades II to IV) and 158 deaths (of which 101 were children). In a 3-month period, the majority of the total of 116,143 persons were hospitalized. The Cuban government quickly implemented an effective *A. aegypti* control program that eliminated dengue and almost eradicated the vector.

The second outbreak of DHF/DSS occurred in Venezuela. The outbreak started in October 1989, peaked in January 1990, then showed a marked decline and apparently ended in April; however, cases of DHF continued to be reported in Venezuela throughout 1990. A total of 5,990 DHF cases

**Table 1. Number of reported cases of dengue and dengue hemorrhagic fever in the Americas, by country, 1980–1990.**

Subregion/country	Year										
	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990
Regional total	66,011	388,591	68,886	40,705	39,307	66,943	88,607	134,390	47,783	89,138	116,389
South America											
Bolivia	— <sup>c</sup>	—	—	—	—	—	—	1,994(1)	4,847(1)	—	—
Colombia	8,964(1,2) <sup>d</sup>	10,790(1)	6,776(1,2,4)	12,919(1,2,4)	7,540(1,4)	8,272(1,2)	7,881(1,2)	17,510(?)	16,308(1,2,4)	10,092	17,389(1,2,4)
Ecuador	—	—	—	—	—	—	—	—	25(1)	19	302
Paraguay	—	—	—	—	—	—	—	—	405(1)	41,800	—
Peru	—	—	—	—	—	—	—	—	—	—	7,858(1,4)
Venezuela	39	71(1)	39	6	20(1,2)	2(1,2,4)	...(1,2,4)	57(2,4)	12	4,025(1,2,4)	10,962
Brazil	—	—	12,000(1,4)	—	—	—	47,370(1)	89,394(1)	190(1)	5,334(1)	40,642(1,2)
Central American Isthmus											
Belize	4	7	482	26	127(1)	—	5	—	—	—	2(1)
El Salvador	2,060	5,185	5,166(4)	3,814(4)	560	425	916	2,836(1,2,4)	1,786	518	2,381
Guatemala	30	104	33	2	...	...	...	2,318(1)	5,175(1?)	7,448(1?)	5,757(1,2)
Honduras	2,078	1,612	1,217(1,2)	729(1)	378(1,2)	260(4)	569(1,2)	261(1,4)	844(1,2,4)	2,507(1,2)	1,700(1,2,4)
Nicaragua	—	—	—	—	—	17,483(1,2)	484	64	203	659	4,137(2)
Mexico	51,406(1)	17,046(1)	32,640(1,2)	19,028(1,2,4)	27,645(1,2,4)	13,688(1,2,4)	19,520(1,2,4)	13,371(1)	10,526(1,4)	7,120(1)	14,485(1,4)
Latin Caribbean											
Cuba	169(1)	344,203(2)	—	—	—	—	—	—	—	—	—
Dominican Republic	54	619	435(4)	538(4)	260(1,4)	92(2,4)	6(1,2,4)	20(1,2,4)	164(1,2,4)	7	39(2)
Haiti	255	44(4)	211(1)	483(1)	328(1,2)	20(2)	...(1)	...	...	...	...
Puerto Rico	921(1)	8,350(1,4)	9,536(1,4)	2,789(4)	1,865(1,2)	2,376(1,2,4)	10,659(1,2,4)	5,835(1,2,4)	6,539(1,2,4)	9,003(1,2,4)	9,450(1,2,4)
Caribbean <sup>a</sup>											
Anguilla	—	1	—	2	—	—	—	—	—	—	12
Antigua and Barbuda	1	77	5	1	—	—	—	—	—	—	1
Aruba	—	—	—	—	—	24,000(1)	—	—	—	—	—

Bahamas	—	—	—	—	—	—	—	—	87(2)	2	
Barbados	—	6(1)	99(1,4)	63(4)	63	—	78(2)	10(2)	45(2)	236(1)	
Bonaire	... <sup>e</sup>	...	...	...	...	6(1)	...	...	...	...	
Dominica	—	18	—	2	—	—	6	2	—	6(2)	
French Guiana	...	...(1)	...(4)	...	...	...	229(2)	...	...	...	
Grenada	—	2	7	6	3	—	—	4	—	1	
Guadeloupe	—	—	Sporadic	Sporadic	339	216	120	344	41	37	
Guyana	—	51(2,4)	—	—	—	—	—	—	—	—	
Jamaica	9	—	21(2,4)	72(2,4)	12(2)	3	3	3(2)	6	32	
Martinique	—	10	Sporadic (4)	Sporadic	Sporadic	Sporadic	—	—	97(1)	16	
Saint Kitts and Nevis	—	23	—	—	—	2	—	—	—	—	
Saint Lucia	6	—	31	—	—	—	164	1	2	4	
Saint Martin	...	7	...	...	...	2(2)	...	...	...	...	
Saint Vincent and the Grenadines	—	—	1	—	—	—	—	—	1	—	
Suriname	—	22(1)	25(1,4)	—	—	—	64(2)	1(2)	5(2)	4	
Trinidad and Tobago	—	15(1,2,4)	16(1,2,4)	117(2,4)	31(1,4)	5(1,2)	145(2)	125(2)	80(2)	11(2)	
Virgin Islands (USA)	—	127(1,4)	2(1,4)	1	73(1)	43(1)	74(2)	77(1,2,4)	380(1,2,4)	275(1,2)	
Virgin Islands (UK)	...	...	...	...	...	...	...	...	13	...	
North America											
U.S.A. <sup>b</sup>	15	201(1,4)	144(1,2,4)	107(1,2,3,4)	63(1,3)	48(1,4)	322(1,2,4)	95(1,3)	124(2,4)	94(1,2,3)	102(1,2,3)

**Source:** Country reports to PAHO. Puerto Rico, the Virgin Islands, Aruba, Bonaire, St. Martin, and French Guiana were obtained from Dengue Surveillance Summary, San Juan Laboratories, CDC, Puerto Rico. The source of the data from Colombia, 1981–1984, was Boshell, J. et al., Dengue in Colombia. *Biomedica* 6(3/4):101–106, 1986 (figures reported to the Ministry of Health, Colombia.) The source of the data from the Dominican Republic, 1981, was CAREC's Review of Communicable Diseases in the Caribbean, 1982.

<sup>a</sup>French Guiana, Guyana, and Suriname included in the Caribbean. No cases reported from Bermuda, Cayman Islands, Monserrat, and Turks and Caicos Islands.

<sup>b</sup>Imported cases.

<sup>c</sup>No cases reported.

<sup>d</sup>Virus serotypes.

<sup>e</sup>No data available.

**Table 2. Confirmed and suspected cases of dengue hemorrhagic fever reported in the Americas, 1960–1991.**

Country	1960–1980				1981–1991										
	1968	1975	1977	1978	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991
Aruba	—	—	—	—	—	—	—	—	2(2)	—	—	—	—	—	—
Brazil	—	—	—	—	—	—	—	—	—	3(3)	1(1)	—	—	274(8)	188(?)
Colombia	—	—	—	—	—	—	—	—	1(1)	—	—	—	1(0)	39(1)	96(0)
Cuba	—	—	—	—	10,312(158)	—	—	—	—	—	—	—	—	—	—
Curaçao	27(0) <sup>a</sup>	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Dominican Republic	—	—	—	—	—	—	—	—	—	—	—	4(2)	—	2(0)	7(0)
El Salvador	—	—	—	—	—	—	—	—	—	—	79(3) <sup>c</sup>	74(4) <sup>c</sup>	—	—	1(0)
French Guiana	—	—	—	—	—	—	—	—	—	—	—	—	—	—	15(3) <sup>f</sup>
Haiti	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Honduras	—	—	—	5(5) <sup>b</sup>	—	—	—	—	—	—	—	—	—	—	16(1) <sup>e</sup>
Jamaica	—	—	2(0)	—	—	—	—	—	—	—	—	—	—	—	—
Mexico	—	—	—	—	—	—	8(4)	—	—	—	—	—	4(1) <sup>d</sup>	—	2(0)
Nicaragua	—	—	—	—	—	—	—	7(7)	—	—	—	—	—	—	—
Puerto Rico	—	3(0)	—	—	—	—	—	2(0)	31(3)	17(1)	8(0)	12(5)	6(1)	14(1)	—
Saint Lucia	—	—	—	—	—	—	—	—	1(0)	—	—	—	—	—	—
Suriname	—	—	—	—	—	3(0)	—	—	—	—	—	—	—	—	—
Venezuela	23(23) <sup>b</sup>	—	—	—	—	—	—	—	—	—	—	—	2,665(27)	3,325(52)	1,980(26)

**Source:** Country reports to PAHO; scientific publications for cases from 1968–1978, 1981, and 1985 (Colombia); and Dengue Surveillance Summary, San Juan Laboratories.

<sup>a</sup>( ): No. of deaths; NA: Not available

<sup>b</sup>No laboratory or clinical investigations performed. Some deaths were also not confirmed in Puerto Rico.

<sup>c</sup>Only a few cases were laboratory confirmed.

<sup>d</sup>Clinically suspected, no laboratory confirmation.

<sup>e</sup>All 16 cases were laboratory confirmed; only 3 cases met WHO's case definition for DHF.

<sup>f</sup>Provisional figure.

(2,665 in 1989 and 3,325 in 1990) including 70 deaths<sup>1</sup> (18 in 1989 and 52 in 1990) were reported. Approximately two-thirds of these cases and fatalities were among children under 14 years of age. Isolations of serotypes 1, 2, and 4 were obtained during the outbreak.

Prior to the Cuban outbreak, only sporadic suspected cases of DHF were reported in the Americas. These reports originated from Curaçao and Venezuela in the 1960s and from Honduras, Jamaica, and Puerto Rico in the 1970s, where few cases were confirmed by laboratory. However, every year from 1981 through 1991, with the exception of 1983, confirmed cases of DHF that met the WHO case definition have been reported annually.

In addition to Cuba and Venezuela, the countries and other political units that reported cases of DHF or of severe hemorrhagic disease included Brazil, Aruba, Colombia, the Dominican Republic, El Salvador, Honduras, Mexico, Nicaragua, Puerto Rico, Saint Lucia, Suriname, and the U.S. Virgin Islands. Most countries have reported fewer than 10 cases, but others such as Brazil, El Salvador, Colombia, and Puerto Rico, have each had more than 40 cases. Puerto Rico has reported laboratory-confirmed cases of DHF/DSS every year from 1985 through 1991, and the disease is considered to be endemic on the island. Brazil reported a few sporadic cases associated with dengue-1 infection during 1986-1987.

Following the introduction of dengue-2 in 1990, an outbreak of DHF was reported in Rio de Janeiro in the latter part of 1990, with 274 cases and 8 deaths; an additional 188 cases were reported in 1991. In 1991, dengue-2 virus spread to two other Brazilian states, one of which was previously infected with dengue-1, but to date no hemorrhagic disease has been reported from these states. El Salvador reported 153 cases (7 fatal) of DHF in 1987-1988, and 1 in 1991, but few were laboratory-confirmed. Colombia reported 39 confirmed DHF cases in 1990 and an additional 96 cases in 1991. The fact that Venezuela reported 1,980 cases of DHF (26 deaths) in 1991, suggests that DHF is becoming endemic in that country.

Regarding the information on Table 2, it should be noted that several cases did not meet the WHO case definition for DHF (e.g., Curaçao, 1968; Jamaica, 1977; Aruba, 1985; Brazil, 1986) or the

clinical information was insufficient or absent to determine if they fulfilled this definition (e.g., Venezuela, 1968; Honduras, 1978; Nicaragua, 1985; El Salvador 1987-1988).

Thus, it appears that DHF/DSS is gradually becoming endemic in several countries of the Americas, following the trend observed in Asia. The marked increase of DHF/DSS incidence observed in several Asian countries during the past 10 years, as compared to the preceding years, illustrates the potential threat that American countries face in the future.

### Reports of Dengue Cases

Table 1 shows the number of reported cases of dengue by country in the Americas for 1980-1990 and the circulating dengue serotypes. With the exception of 1981, when there were 388,591 cases, numbers for the other years ranged from 39,307 (1984) to 134,390 (1987). The marked underreporting of dengue cases is illustrated in Ecuador, where only 25 cases were reported in 1988, although a serological survey in Guayaquil estimated that 422,000 of its inhabitants were infected. In 1986-1987, a similar situation was observed in Brazil, which reported 136,764 cases, although serological surveys estimated that more than one million infections occurred in Rio de Janeiro during this biennium. Again excluding 1981, when Cuba reported 344,203 cases, most dengue fever case reports during 1980-1984 came from Mexico. In 1985, Aruba and Nicaragua reported the most cases; in 1986-1987 and in 1990, the greatest number of cases were reported from Brazil, while Colombia and Paraguay reported the highest number of cases during 1988 and 1989, respectively.

### Dengue Virus

The dengue virus belongs to the family Flaviviridae; four serotypes can be distinguished by serologic methods, and are designated as dengue-1, dengue-2, dengue-3, and dengue-4. The infection in humans by one serotype produces lifelong immunity against reinfection with that serotype, but only temporary and partial protection against the other serotypes. All four serotypes have been isolated from autochthonous cases in the Americas; however, only dengue serotypes 1, 2, and 4 have circulated during the period 1978-1991, while dengue-3 was last isolated in Colombia and Puerto Rico in 1977. Although dengue-2 was

<sup>1</sup>The Ministry of Health of Venezuela previously reported 73 deaths between October 1989 and April 1990 (*PAHO Epidemiologic Bulletin*, Vol. 11, No. 2, 1990).

associated with the major outbreak of dengue and DHF/DSS in Cuba in 1981, dengue-1 and dengue-4 were the predominant circulating serotypes during the 1980s. In addition to the outbreaks in the five South American countries discussed above, dengue-1 also caused significant outbreaks in Aruba, Mexico, and Nicaragua. The introduction of dengue-4 into the Americas in 1981 was followed by dengue fever epidemics in the Caribbean, Central America, Mexico, and northern South America during 1981-1983, and it subsequently caused major epidemics with cases of DHF in Mexico (1984), Puerto Rico (1986), and El Salvador (1987). Dengue-4 virus is now endemic in the Region. The simultaneous circulation of serotypes 1, 2, and 4 over a period of several years has been observed in several countries, which puts these countries at high risk for epidemic DHF.

Molecular studies on the nucleotide sequences of dengue virus genomes allow classification of the agent into genotypes. One genotypic group of dengue-1 virus and two of dengue-2 virus are known to be circulating in the Americas. Another dengue-1 genotype was isolated in 1980, exclusively in Mexico. The clinical significance of the infection due to these genotypes in man is presently unknown, but they are useful for the understanding of the epidemiology of dengue viruses.

### Dengue Virus Transmission

In the Americas, the dengue virus persists through a man-*Aedes aegypti*-man transmission cycle. Following an infective blood meal, the mosquito can transmit the agent after a period of 8-12 days of extrinsic incubation. In addition, mechanical transmission can occur when feeding is interrupted and the mosquito immediately feeds on a nearby susceptible host. *Aedes albopictus*, now present in the Americas, is a maintenance vector of dengue in Asia, but so far it has not been associated with dengue transmission in the Americas. The epidemiologic significance of transovarial transmission of dengue virus in *A. aegypti* and other vectors in the Americas is presently unknown.

### Cost and Economic Impact

Few studies of the economic impact of dengue and DHF/DSS in the Americas have been conducted. A study in Puerto Rico during the 1977 dengue epidemic estimated that the costs in medi-

cal services and loss of work were between US\$ 6 million and US\$ 16 million; according to recent studies, the cost of the disease's epidemics in Puerto Rico since 1977 is estimated to be between US\$ 150 million and US\$ 200 million.

The cost of the DHF/DSS Cuban epidemic was estimated at about US\$ 103 million, a figure that includes the cost of control measures and medical services. Of this total, US\$ 41 million went for medical care; US\$ 5 million, for salaries paid to adult patients; US\$ 14 million, for lost production; and US\$ 43 million, for the direct initial cost of the *A. aegypti* control program. It should be mentioned that the cost of this epidemic would be considerably higher today due to inflation. It is conceivable that the disease has significantly affected tourism, particularly during epidemics; however, no estimates are available on the costs due to dengue.

### Clinical Manifestations and Diagnosis

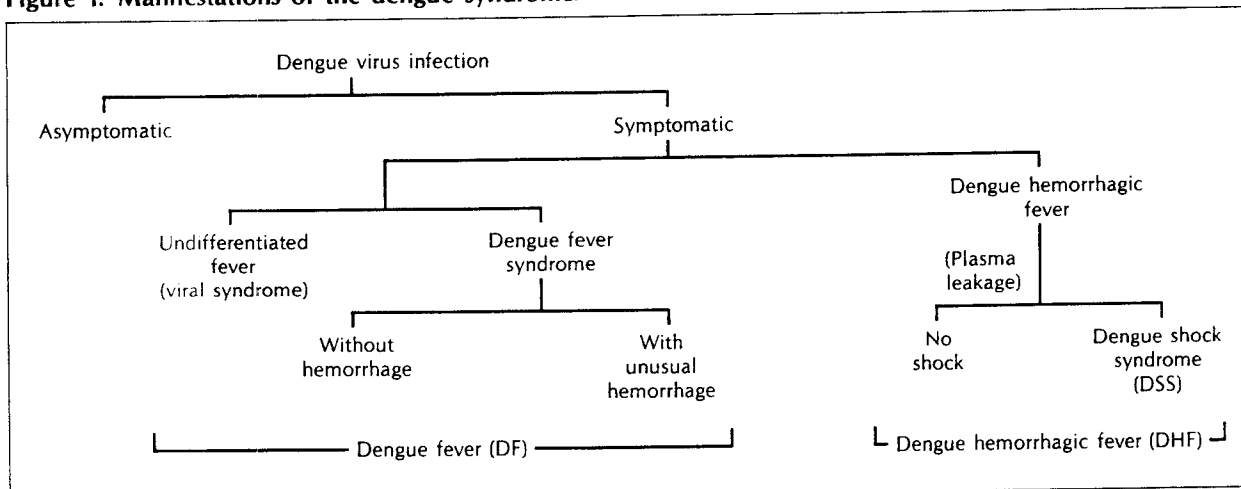
Dengue virus infections may be asymptomatic or may lead to undifferentiated fever, dengue fever, or dengue hemorrhagic fever (Figure 1). The incubation period lasts 4-6 days (minimum 3, maximum 14).

### Dengue Fever

The clinical features of dengue fever vary frequently, according to the age of the patient. Infants and young children may have an undifferentiated febrile disease with a maculopapular rash. Older children and adults may have either a mild febrile syndrome or the classical incapacitating disease with abrupt onset and high fever, severe headache, pain behind the eyes, muscle and joint pains, and rash. Skin hemorrhages (with a positive tourniquete test and/or petechiae) may be present. Leukopenia is usually found and thrombocytopenia may be observed. The case fatality rate is exceedingly low.

Many epidemics of dengue fever are accompanied by bleeding complications such as epistaxis, gingival bleeding, gastrointestinal bleeding, hematuria, and hypermenorrhea. Unusually severe bleeding has caused death in some of these cases. It is important to differentiate cases of DF with unusual hemorrhage from cases of dengue hemorrhagic fever. Table 3 shows the frequency of findings in classical dengue fever in adults and DHF in Thai children.

Figure 1. Manifestations of the dengue syndrome.



WHO 851632

### Dengue Hemorrhagic Fever

Typical cases of DHF, as seen in Asian countries, are characterized by four major clinical manifestations: high fever, hemorrhagic phenomena, hepatomegaly, and, often, circulatory failure (Table 4); moderate to marked thrombocytopenia with concurrent hemoconcentration is a distinctive clinical laboratory finding. The major pathophysiological change that determines the severity of disease in DHF and differentiates it from DF, is the leakage of plasma, as manifested by a rising hematocrit value and hemoconcentration. See Annex I for hospital record sheet for collecting this data.

Table 3. Observed frequency of findings in classical dengue fever in adults and dengue virus infections in Thai children diagnosed as hemorrhagic fever.<sup>a</sup>

Finding	Classical dengue in adults <sup>b</sup>	DHF in Thai children
Fever	++++	++++
Positive tourniquet test	++	++++
Petechiae or ecchymosis	+	++
Confluent petechial rash	0	+
Hepatomegaly	0	++++
Maculopapular rash	++	+
Myalgia/arthralgia	+++	+
Lymphadenopathy	++	++
Leukopenia	++++	++
Thrombocytopenia	++	++++
Shock	0	++
Gastrointestinal bleeding	0	+

<sup>a</sup>++ = 1%–25%; ++ = 26%–50%; +++ = 51%–75%; ++++ = 76%–100%

<sup>b</sup>The data have been taken from Halstead, S.B., et al. *Am J Trop Med Hyg*, 18:984–996 (1969) and refer mainly to Caucasian adults.

### Dengue Hemorrhagic Fever without Shock

The illness commonly begins with a sudden rise in temperature, which is accompanied by facial flush and other nonspecific constitutional symptoms resembling dengue fever, such as anorexia, vomiting, headache, and muscle or joint pains (Table 5). Some patients complain of sore throat, and a congested pharynx may be found upon examination. Epigastric discomfort, tenderness at the right costal margin, and generalized abdominal pain are common. The temperature is typically high and continues so for 2 to 7 days, and then falls to a normal or subnormal level. Occasionally, the temperature may be as high as 40°C–41°C, and febrile convulsions may occur.

The most common hemorrhagic phenomenon is

Table 4. Signs and symptoms observed in dengue hemorrhagic fever patients from Thailand.

Criteria	(%)
Duration of fever:	
2–4 days	23.6
5–7 days	59.0
>7 days	17.4
Hemorrhagic manifestations:	
positive tourniquet test	83.9
scattered petechiae	46.5
confluent petechial rash	10.1
epistaxis	18.9
gingival bleeding	1.5
melena/hematemesis	11.8
Hepatomegaly	90.0
Shock	35.2

Source: Based on Nimmannitya, S. et al. *Am J Trop Med Hyg* 18:954–971 (1969).

**Table 5. Non-specific constitutional symptoms observed in hemorrhagic fever patients with dengue in Thailand.**

Symptom	(%)
Injected pharynx	98.9
Vomiting	57.9
Constipation	53.3
Abdominal pain	50.0
Headache	44.6
Generalized lymphadenopathy	40.5
Conjunctival injection	32.8 <sup>a</sup>
Cough	21.5
Restlessness	21.5
Rhinitis	12.8
Maculopapular rash	12.1 <sup>a</sup>
Myalgia/arthralgia	12.0 <sup>a</sup>
Enanthema	8.3
Abnormal reflex	6.7
Diarrhea	6.4
Palpable spleen	6.3 <sup>b</sup>
Coma	3.0

**Source:** Based on Nimmannitya, S. et al. *Am J Trop Med Hyg* 18:954-971(1969).

<sup>a</sup>Statistically significant difference.

<sup>b</sup>Infants under 6 months.

a positive tourniquet test; easy bruising and bleeding at venipuncture sites are present in most cases. Fine petechiae scattered on the extremities, axillae, face, and soft palate may be seen during the early febrile phase. A confluent petechial rash with characteristic small round areas of normal skin is sometimes seen in convalescence, once the temperature has returned to normal. A maculopapular or rubella-type rash may be observed early or late in the disease. Epistaxis and gum bleeding are less common. Mild gastrointestinal hemorrhage is occasionally observed.

The liver is usually palpable early in the febrile phase. The size of the liver varies from just-palpable to 2-4 cm below the costal margin. Liver size is not correlated with disease severity, but hepatomegaly is more frequent in shock cases. The liver is tender, but jaundice is not usually observed even in patients with a large, tender liver. Splenomegaly is rarely observed in small infants; however, the spleen is sometimes prominent on X-ray examination.

In mild or moderate cases, all signs and symptoms abate after fever subsides. Fever lysis may be accompanied by profuse sweating and mild changes in pulse rate and blood pressure, together with coolness of extremities and skin congestion. These changes reflect mild and transient circulatory disturbances as a result of some degree of plasma leakage. Patients usually recover spontaneously or after fluid and electrolyte therapy.

## Dengue Shock Syndrome (DSS)

In severe cases, the patient's condition suddenly deteriorates after a few days of fever. At the time of or shortly after the temperature drop, between 3 and 7 days after onset, there are signs of circulatory failure: the skin becomes cool, blotchy, and congested; circumoral cyanosis is frequently observed; and the pulse becomes weak and rapid. Although some patients may appear lethargic, they become restless and then rapidly go into a critical stage of shock. Acute abdominal pain is a frequent complaint shortly before the onset of shock.

Shock is characterized by a rapid, weak pulse with narrowing of the pulse pressure (20 mmHg, or 2.7 kPa, or less, regardless of the pressure levels, e.g. 100/90 mmHg) or hypotension, with cold clammy skin and restlessness. Patients in shock are in danger of dying if they do not get appropriate treatment promptly. Patients may pass into a stage of profound shock with blood pressure and/or pulse becoming imperceptible. Most patients remain conscious almost to the terminal stage. Shock lasts a short time; the patient may die within 12-24 hours or recover rapidly following appropriate volume replacement therapy. Alternatively, uncorrected shock may give rise to a more complicated course with metabolic acidosis, severe bleeding from the gastrointestinal tract and from various other organs, and a poor prognosis. Patients with intracranial hemorrhage may have convulsions and go into coma. Encephalopathy may occur in association with metabolic and electrolyte disturbances.

Convalescence in DHF with or without shock is short and uneventful. Even in cases with profound shock, once the shock is overcome the surviving patients recover within 2-3 days. Return of appetite is a good prognostic sign. Common findings in convalescence include sinus bradycardia or arrhythmia and a characteristic dengue petechial rash.

## Laboratory Findings in DHF

Thrombocytopenia and hemoconcentration are constant findings in DHF. A drop in platelet count to below 100,000/mm<sup>3</sup> is usually found between the third and eighth days of illness. A rise in hematocrit level, indicating plasma leakage is always present, even in nonshock cases; it is always more remarkable, however, in shock cases. Hemocon-



centration with hematocrit increased by 20% or more is considered as an objective evidence of increased vascular permeability and leakage of plasma. It should be noted that the level of hematocrit may be affected by early volume replacement and by bleeding.

The white blood cell count is variable, ranging from leukopenia to mild leukocytosis. Lymphocytosis with atypical lymphocytes is a common finding near the end of the febrile phase. A transient mild albuminuria is sometimes observed. Occult blood is often found in the stool. In most cases, assays of coagulation and fibrinolytic factors show reductions in fibrinogen, prothrombin, factor VIII, factor XII, and antithrombin III. A reduction in  $\alpha$ -antiplasmin ( $\alpha$ -plasmin inhibitor) has been noted in some cases. In severe cases with marked liver dysfunction, reduction is observed in the vitamin-K-dependent prothrombin family, such as factors V, VII, IX, and X. Partial thromboplastin time and prothrombin time are prolonged in about one-half and one-third of DHF cases, respectively. Thrombin time is also prolonged in severe cases.

The other common findings are hypoproteinemia, hyponatremia, and mildly elevated serum aspartate aminotransferase levels. Metabolic acidosis is frequently found in cases with prolonged shock. Blood urea nitrogen is elevated at the terminal stage of cases with prolonged shock. Serum complement levels are reduced.

Chest X rays reveal pleural effusion, mostly on the right side, as a constant finding. The extent of pleural effusion is correlated with disease severity.

### Complications and Unusual Manifestations

Encephalitic signs such as convulsion and coma are not common in DHF. They may, however, occur as a complication in cases of prolonged shock with severe bleeding in various organs including the brain. Water intoxication as a result of inappropriate use of hypotonic solution to treat DHF patients with hyponatremias is not an uncommon iatrogenic complication that leads to encephalopathy.

A subtle form of seizure is occasionally observed in infants under 1 year old during the febrile phase, and some is considered to be febrile convulsions, as the cerebrospinal fluid is normal.

In recent years there has been an increasing number of reports of dengue, DF, or DHF with unusual manifestations. Although with low inci-

dence, the unusual central nervous system manifestations, including convulsions, spasticity, change in consciousness and transient paresis, have been observed and are of major concern. Some of these cases may have encephalopathy as a complication of DHF with severe disseminated intravascular coagulation that may lead to focal occlusion or hemorrhage. Reported fatal cases with encephalitic manifestations have been observed in Indonesia, Malaysia, Myanmar, India, and Puerto Rico; however, in most cases there have been no autopsy studies to rule out bleeding or occlusion of the blood vessels. Further studies are needed to identify the factors contributing to these unusual manifestations. Attention should be given to the study of underlying host factors such as convulsive disorder and concurrent diseases. Encephalopathy associated with acute liver failure is commonly observed and renal failure usually occurs at the terminal stage. Liver enzymes are markedly elevated in these cases, with serum aspartate aminotransferase about 2.5 times higher than serum alanine aminotransferase.

Other rarely observed, unusual manifestations include acute renal failure and hemolytic uremic syndrome. Some of these cases have been observed in patients with underlying host factors (e.g. G6PD deficiency and hemoglobinopathy) that lead to intravascular hemolysis. Dual infections with other endemic diseases, such as leptospirosis, viral hepatitis B, and melioidosis, have been reported in cases with unusual manifestations.

### Clinical Manifestations in Adults

Cuba's experience in 1981, with 130 adult cases (26 with fatal outcome), showed that the infection was usually manifested by the clinical symptoms of dengue fever (high fever, nausea/vomiting, retro-orbital headache, myalgia, and asthenia), regardless of whether the patient had a fatal outcome or not. Less frequently, patients demonstrated thrombocytopenia and hemorrhagic manifestations, the most common of which were skin hemorrhages, menorrhagia, and hematemesis. Overt shock in adults was less frequently observed than in children, but was severe when it did occur; it was found mostly in white adults with a history of bronchial asthma and other chronic diseases. In one series of 1,000 adult cases studied in Cuba, the persons who were severely ill usually showed thrombocytopenia and hemoconcentration. In the five cases with hypovolemic shock not associated

with hemorrhage, the disease responded, as in children, to vigorous fluid replacement.

In the 1986 Puerto Rico outbreak, DHF with overt shock in adults was not rare, but did occur less frequently than in children.

### Criteria for Clinical Diagnosis of Dengue Hemorrhagic Fever/Dengue Shock Syndrome

The following clinical manifestations and laboratory determinations have been selected as indicating a clinical diagnosis of DHF. *The use of these criteria may help prevent overdiagnosis of the disease.*

#### Clinical

- Fever: acute onset, high, continuous, and lasting 2–7 days.
- Any of the following hemorrhagic manifestations, including at least a positive tourniquet test:<sup>2</sup> petechiae, purpura, ecchymosis; epistaxis, and gum bleeding; and hematemesis and/or melena.
- Enlargement of liver (observed at some stage of the illness in 90%-96% of Thai children and 67% of Cuban children with DHF); frequency of hepatomegaly is, however, variable.
- Shock: manifested by rapid and weak pulse with narrowing of the pulse pressure (20mmHg, or 2.7kPa, or less) or hypotension, with the presence of cold, clammy skin and restlessness.

#### Laboratory

- Thrombocytopenia (100,000/mm<sup>3</sup> or less).<sup>3</sup>
- Hemoconcentration; hematocrit increased by 20% or more of recovery value.

The first two clinical criteria, plus thrombocytopenia and hemoconcentration or a rising hematocrit, are sufficient to establish a clinical diagnosis of DHF. When there is anemia or severe hemorrhage, pleural effusion (chest x-ray), and/or hypoalbuminemia provide supporting evidence of

<sup>2</sup>The tourniquet test is performed by inflating a blood pressure cuff to a point midway between the systolic and diastolic pressures for 5 minutes. A test is considered positive when 20 or more petechiae per 2.5 cm<sup>2</sup> (1 inch) are observed. The test may be negative or mildly positive during the phase of profound shock. It usually becomes positive, sometimes strongly positive, if the test is conducted after recovery from shock.

<sup>3</sup>Direct count using a phase-contrast microscope (normal 200,000–500,000/mm<sup>3</sup>). In practice, for outpatients, an approximate count from a peripheral blood smear is acceptable. In normal persons, 4–10 platelets per oil-immersion field (the average observed from 10 fields is recommended) indicates an adequate platelet count. An average of 2–3 per oil immersion field or less is considered low (i.e., < 100,000/mm<sup>3</sup>).

plasma leakage; this is particularly useful in those patients who experience anemia and/or severe hemorrhage.

Shock with a high hematocrit (except in patients with severe bleeding) and marked thrombocytopenia supports a diagnosis of DHF/DSS.

The relationship of clinical syndromes with physical and laboratory findings is shown in Figure 2.

### Case Definition for Dengue Fever

A case definition for dengue fever has been recommended. However, given the variability of the clinical illness associated with dengue infection, it is not appropriate to adopt a detailed clinical definition that specifies degrees of fever and number of criteria. Laboratory confirmation should be emphasized.

#### Clinical description

An acute febrile illness characterized by frontal headache, retro-ocular pain, muscle and joint pain, and rash.

#### Case classification

**Probable:** An acute febrile illness with two or more of the following manifestations:

- Headache
- Retro-orbital pain
- Myalgias
- Arthralgia
- Rash
- Hemorrhagic manifestations
- and supportive serology (a reciprocal HI antibody titer  $\geq$  1280 or an equivalent IgG ELISA titer, or a positive IgM antibody test on a single late acute or convalescent-phase serum specimen to one or more dengue antigens
  - or occurrence at the same location and time as other confirmed cases of dengue.

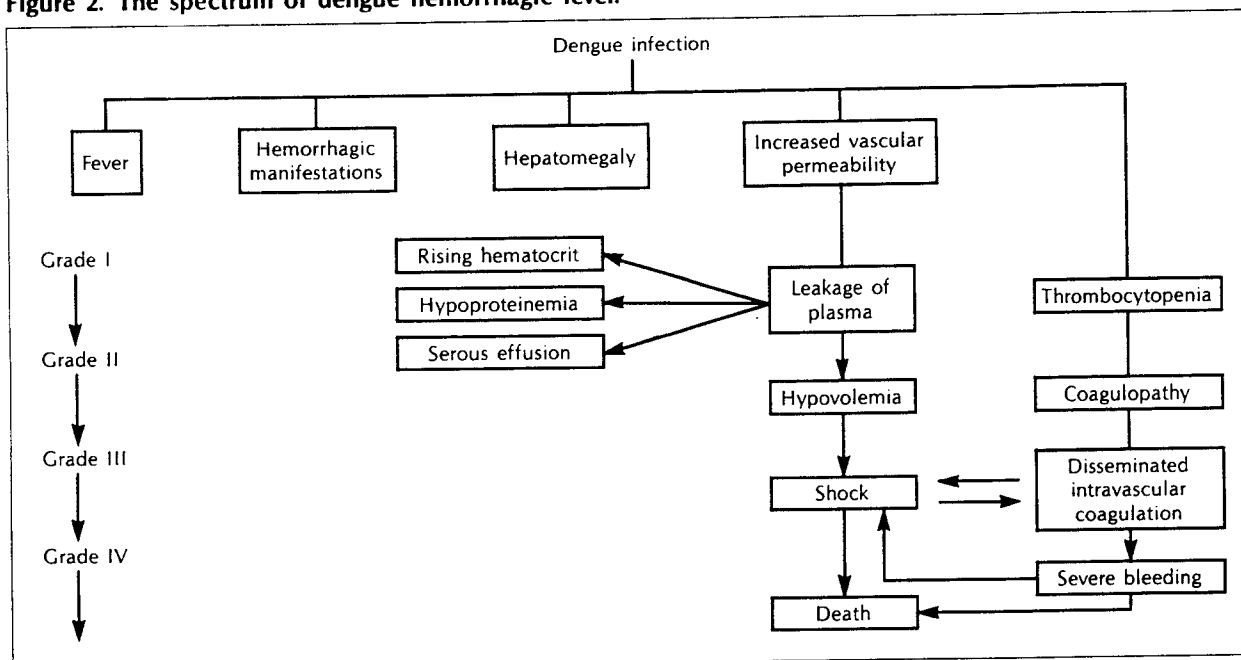
**Confirmed:** a case that is laboratory confirmed.

**Reportable:** all probable and confirmed cases should be reported as cases of dengue to local and national health authorities.

#### Laboratory criteria for confirmation

- Isolation of dengue virus from serum and/or autopsy samples, or

Figure 2. The spectrum of dengue hemorrhagic fever.



WHO 851633

- Demonstration of a fourfold or greater change in reciprocal IgG or IgM antibody titers in paired serum samples to one or more dengue virus antigens, or

- Demonstration of dengue virus antigen in autopsy tissue or serum samples by immunohistochemistry, by immunofluorescence or by viral nucleic acid detection.

#### Clinical Case Definition for Dengue Hemorrhagic Fever

The following must all be present:

- Fever, or recent history of acute fever.
- Hemorrhagic tendencies, as evidenced by at least one of the following: positive tourniquet test; petechiae, ecchymoses, or purpura; and bleeding from mucosa, gastrointestinal tract, injection sites, or others.
- Thrombocytopenia (100,000 mm<sup>3</sup> or less).
- Plasma leakage due to increased capillary permeability as manifested by at least one of the following: hematocrit on presentation that is  $\geq 20\%$  above average for that age, sex, and population;  $\geq 20\%$  drop in hematocrit following treatment; or commonly associated signs of plasma leakage—pleural effusion, ascites, and hypoproteinemia.

#### Clinical Case Definition for Dengue Shock Syndrome

All of the above-mentioned four criteria, 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;<sup>4</sup> and
- cold, clammy skin and altered mental status.

#### Reportable Cases of DHF or DSS

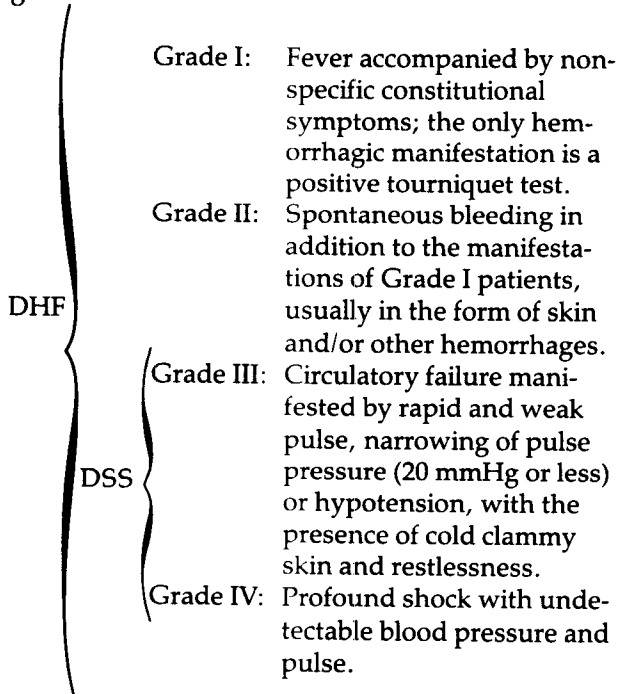
These cases will fit the above criteria, plus will have one of the following:

- Virological or serological evidence of acute dengue infection, or
- 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).

<sup>4</sup>Hypotension: < 5 years, 80mmHg;  $\geq 5$  years, < 90mmHg (systolic pressure). Note that narrow pulse pressure is observed earlier while hypotension is found later, or in cases with severe bleeding.

### Grading the Severity of Dengue Hemorrhagic Fever

The severity of DHF is classified into four grades:



The presence of thrombocytopenia with concurrent hemoconcentration differentiates Grades I and II DHF from dengue fever.

Grading the severity of the disease has been found clinically and epidemiologically useful in DHF epidemics in children in the Southeast Asian, Western Pacific, and American Regions. The experiences in Cuba, Puerto Rico, and Venezuela suggest that this classification also is useful for adults.

### Differential Diagnosis

Early in the febrile phase, the differential diagnosis includes a wide spectrum of viral, bacterial, and protozoal infections. In the Americas, diseases such as leptospirosis, malaria, infectious hepatitis, yellow fever, meningococemia, rubella, and influenza should be considered.

The presence of marked thrombocytopenia with concurrent hemoconcentration differentiates DHF/DSS from other diseases. In patients with severe bleeding, evidence of pleural effusion and/or hypoproteinemia may indicate plasma leakage. A normal erythro sedimentation rate in DHF/DSS helps to differentiate this disease from bacterial infection and septic shock.

**Table 6. Clinically diagnosed DHF cases in children in which secondary infection was proven, Cuba, 1981.**

Clinical and laboratory findings	Studied children	
	No. positive of 124 examined	(% positive)
Fever (> 37°C)	120 <sup>c</sup>	(97)
Vomiting	108	(87)
Thrombocytopenia <sup>a</sup>	97	(78)
Hepatomegaly	83	(67)
Abdominal pain	78	(63)
Hemoconcentration <sup>b</sup>	103	(83)
Ascites	38	(31)
Pleural effusion	70	(56)
Petechiae	62	(50)
Hematemesis	37	(30)
Melena	10	(8)
Ecchymoses	9	(7)
Epistaxis	11	(9)

Adapted from Guzmán et al. *Bull Pan Am Health Organ* 1987; 21(3):270-279.

<sup>a</sup>< 100,000/mm<sup>3</sup>

<sup>b</sup>Hematocrit increased > 20%

<sup>c</sup>Four cases had fever history at home

### Facts and Figures from the Americas

Findings from studies conducted in the Americas on the clinical presentation of laboratory confirmed DHF cases are shown on Tables 6 and 7.

In Tables 8 and 9 the clinical manifestations and the autopsy findings of 72 total cases in children are shown (Cuba, 1981). Not all the pathological findings are directly related to the pathology of DHF/DSS.

On the one hand, congestion and pulmonary edema could be due, in part, to excessive intravenous-fluid therapy. On the other, the pulmonary inflammatory reaction was associated with concurrent infections, and atelectasis was

**Table 7. Signs and symptoms in laboratory confirmed DHF cases, Puerto Rico, 1986.<sup>a</sup>**

Clinical and laboratory findings	Number	% positive
Fever	29/29	100
Thrombocytopenia <sup>b</sup>	29/29	100
Hemoconcentration <sup>b</sup>	29/29	100
Vomiting	18/29	62
Petechiae	14/29	48
Hepatomegaly	9/20	45
Hematemesis	11/29	38
Prolonged PTT	7/20	35
Hematuria	6/29	21
Melena	5/29	17
Purpura/ecchymoses	5/29	17
Epistaxis	5/29	17
Bleeding at venipuncture sites	3/20	15

<sup>a</sup>All cases met the WHO case definition; CDC unpublished data.

<sup>b</sup>Hematocrit increased > 20%.

**Table 8. Clinical manifestations among 72 children who died of DHF in Cuba, 1981.<sup>a</sup>**

Nonhemorrhagic manifestations	Number of cases	% positive
Fever	72	100
Nausea and vomiting	61	85
Shock	72	100
Hepatomegaly	56	78
Abdominal pain	41	57
Pleural effusion	22	31
Rash	16	22
Ascites	7	10
Splenomegaly	7	10
<b>Hemorrhagic manifestations</b>		
Hematemesis	43	60
Petechiae	28	39
Epistaxis	16	22
Melena	14	19
Hematoma	13	18
Hemoptysis	8	11
Gum bleeding	7	10
Ecchymoses	7	10
Enterohagia	6	8
Hematuria	5	7
Venipuncture bleeding	5	7

<sup>a</sup> Unpublished information: Bravo, J., Kouri, G., Guzmán, M.G., and Martínez, E., "Pedro Kouri" Institute of Tropical Medicine, Havana, Cuba. Note: Menorrhagia was present in 8% (3 out of 39) females.

generally due to assisted ventilation. Heart dilatation observed in 12% of cases could not be directly related to DHF/DSS.

## Vector Distribution and Biology

The most important, and perhaps only, vector of dengue in the Americas is *Aedes aegypti*. *Aedes albopictus*, a proven secondary vector in Asia and the Pacific, has recently invaded the New World, but, thus far, has not been implicated in transmission of dengue in this Region.

### *Aedes aegypti*

*A. aegypti*, a species of the subgenus *Stegomyia*, probably originated in Africa, where both sylvatic and domestic forms occur, whereas the Region of the Americas only has the domestic forms. It probably was first transported from the Old World to the New World in water barrels on ships during the early European explorations and colonizations. *A. aegypti* is commonly known as the "yellow fever mosquito," because for centuries this species

**Table 9. Autopsy findings among 72 children who died of DHF in Cuba, 1981.<sup>a</sup>**

Observation	% positive
Gastrointestinal hemorrhage	98
Ascites	88
Hepatic necrosis	70
Pleural effusion	70
Lung congestion and edema	70
Pulmonary hemorrhage	68
Intrahepatic hemorrhage	60
Brain congestion and edema	56
Intraventricular hemorrhage	52
Fatty liver	40
Hepatic and splenic congestion	40
Renal congestion	30
Atelectasis	26
Pericardial effusion	20
Hepatic inflammatory reaction	14
Lung inflammatory reaction	14
Heart dilatation	14
Acute gastric ulcer	12
Pericardial and/or epicardial hemorrhage	12
Tracheo-bronchial hemorrhage	12

<sup>a</sup> Unpublished information, Bravo et al., "Pedro Kouri" Institute of Tropical Medicine, Havana, Cuba.

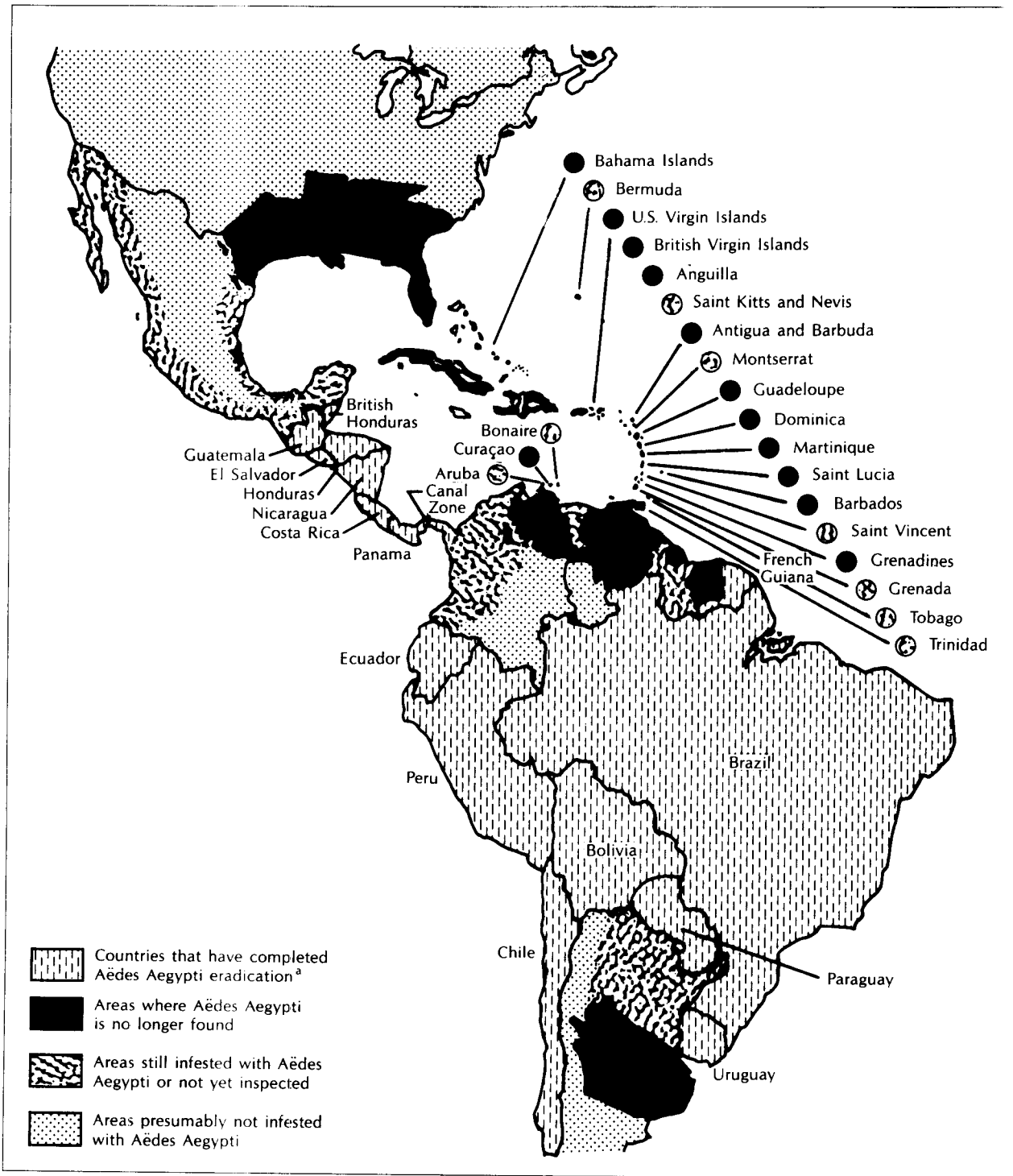
transmitted urban yellow fever, a serious public health problem in Africa and the Americas. Although sylvatic yellow fever cases transmitted by mosquitoes other than *A. aegypti*, are still reported every year from several South American countries, for unknown reasons there has been no documented urban transmission in four decades.

*A. aegypti* is a tropical and subtropical species found around the globe, usually within 35° N and 35° S latitudes, corresponding to a winter isotherm of 10°C. Although it has been found as far north as 45° N, these invasions occur during the warm season and the populations do not survive the winter.

Distribution of *A. aegypti* also is limited by altitude. Although it is usually not found above 1,000 meters, it has been reported at 2,121 meters in India and at 2,200 meters in Colombia where the mean annual temperature was 17°C.

At the beginning of this century, *A. aegypti* was found in all the American countries except Canada, from the southern United States to Buenos Aires, Argentina. The hemispheric eradication campaign, which began in earnest in 1947, succeeded in eliminating *A. aegypti* from 18 continental countries and several small Caribbean islands by 1962. Only the United States, Venezuela, Suriname, the Bahamas and several of the Caribbean islands remained infested (Figure 3). After 1962, three more countries eliminated this vector, but in the meantime reinfestation began to occur in countries that had previously eradicated it. As of 1991,

Figure 3. Status of the *A. aegypti* eradication campaign, April 1962.



<sup>a</sup>Eradication carried out according to the standards established by the Pan American Health Organization.

only four countries had not been permanently reinfested (Bermuda, Cayman Islands, Chile, and Uruguay). One by one, virtually all of the reinfested countries have had at least one dengue epidemic.

In the New World, *A. aegypti* is primarily a "domestic" species, infesting man-made or natural containers found in or near human dwellings. The female feeds mostly on human blood or on that of domestic animals. This mosquito is rarely

found farther than 100 meters from houses, although exceptions have been reported in the West Indies and the southern United States. Prior to eradication in Cayman Brac, *A. aegypti* larvae were found in roof catchment cattle cisterns more than 400 meters away from human dwellings; on the island of Anguilla, infestation occurred in fossilized coral rock holes (Karst solution holes), sometimes more than one kilometer away from dwellings. Both populations apparently had the coloration of the "domestic" form of *A. aegypti*. In southeast Texas, *A. aegypti* eggs were found in oviposition traps more than 8 km from the nearest human habitation, and larvae were collected from a tree hole 3.2 kilometers from human dwellings.

Because of its close association with man, *A. aegypti* is essentially an urban mosquito. However, Brazil, Mexico, and Colombia have all reported significant rural infestations, sometimes many kilometers from the nearest urban center and the nearest vehicular road; rural infestation is probably common in other countries as well. *A. aegypti* apparently invades rural areas as eggs or larvae. It is found in domestic containers that are transported to rural houses for water storage.

*A. aegypti* eggs are attached singly to the inside surface of containers in the damp area just above the water surface. Embryonic development is usually completed within 48 hours if the environment is humid and warm. Once embryonic development is complete, the eggs can withstand long periods of desiccation, sometimes for more than a year. When the eggs are eventually flooded, most hatch rapidly, though some may not respond until they have been inundated several times.

The capacity of the eggs to withstand drying is one of the greatest obstacles to the eradication of this vector. Eggs can be transported over great distances in dry containers. Elimination of adults and larvae from a locality during many months does not prevent reinfestation by emergence from recently flooded eggs that had been hidden in dry containers.

The larvae pass through four developmental "instars." Duration of larval development depends on temperature, availability of food, and larval density in the receptacle. Under optimal conditions, the time from hatching to pupation can be as short as 5 days; under harsh low temperature or food scarcity conditions, it may take several weeks.

Although food scarcity may interfere with the growth of *A. aegypti* larvae, flooding, rinsing, or premature draining and drying of containers prob-

ably accounts for much of the immature mortality. Many discarded containers that serve as production sites are small (e.g., tires, tin cans) and are found outdoors; these are vulnerable to drying from the sun and flooding and overflowing from the rain. Other containers used for domestic water storage are frequently emptied and washed or variable amounts of water are removed from them.

About 1-2 days after emergence, the mosquitoes mate and females take a blood meal. These activities often occur almost simultaneously because, although the males do not feed on blood, they are attracted to the same hosts as the females; this facilitates male-female encounters. Females will feed on most vertebrates but show a decided preference for humans. Blood feeding provides a source of protein for the development of the eggs and occurs primarily during daylight hours, except at midday.

Usually, a batch of eggs develops after each blood meal. However, *A. aegypti*, more than most other species of mosquitoes, will frequently feed more than once between ovipositions, especially if disturbed before full engorgement, a characteristic that increases the chances of ingesting and transmitting virus.

The interval between blood engorgement and oviposition can be as short as 3 days under optimal conditions of temperature and availability of hosts, and the female can feed again on the same day that she lays eggs. Most oviposition occurs in the late afternoon. The gravid female is attracted to dark or shaded containers with rough walls on which to deposit the eggs. Relatively clean, clear, uncolored water is preferred to turbid, polluted water of high organic content. Usually, the female distributes each batch of eggs among several different containers.

Flight dispersal of *A. aegypti* is very short when compared to that of most other mosquito species. The female often passes her entire lifetime close to the emergence site, provided that hosts, resting places and oviposition sites are available. Flight dispersal of over 100 meters is considered to be rare. It has been shown, however, that a gravid female can and will fly up to 3 km in search of a place to lay eggs if suitable containers are not present nearby. Males disperse less than females. Most dispersal of *A. aegypti* over great distances occurs via transport of eggs and larvae in containers.

When not mating, seeking a host, or dispersing, the mosquitoes seek dark, quiet places to rest. Resting *A. aegypti* are most commonly found inside

houses in bedrooms, bathrooms, and kitchens and only occasionally outdoors in garden vegetation. The preferred resting surfaces are walls, furniture, and hanging articles such as clothing, towels, curtains, and mosquito netting. Many of the resting sites are secluded, in bedroom closets, and under beds and other furniture.

*A. aegypti* adults can live for several months in the laboratory, but they usually live only a few days in nature. Despite their short average life span, some adults live long enough to transmit virus.

### *Aedes albopictus*

The "Asian tiger mosquito" is a close relative of *A. aegypti*, belongs to the same subgenus, *Stegomyia*, and has many of the same habits. It is widely distributed in Asia and the Pacific, ranging from temperate regions to the tropics, and has recently been found in Italy, South Africa, and Nigeria. Although several isolated introductions were found and eliminated in the continental United States as early as 1946, it was not until 1985 that it was found to be well-established in Texas, and subsequently in many other states and as far north as Illinois at 42° N latitude. Since 1986, *A. albopictus* has been found in five Brazilian states. In 1993, Santo Domingo (the Dominican Republic) and some northern border states of Mexico were found to be infested.

*A. albopictus* is mainly a forest-edge species that has adapted to rural, suburban and urban human environments. It oviposits and develops in tree holes, bamboo stumps, and leaf axils in the forest, and in artificial containers in urban areas. It is much less "domestic" than *A. aegypti*, feeding and ovipositing outdoors in the peridomestic environment or far from human habitation. It is a catholic feeder, biting animals other than humans much more frequently than *A. aegypti*. Its flight range appears to be somewhat greater than that of *A. aegypti*, up to 500 meters. Unlike *A. aegypti*, it is a cold-adapted species in northern Asia with eggs that spend the winter in diapause.

In areas where *A. albopictus* has become established in the United States, there is a tendency for the *A. aegypti* population to decrease or disappear altogether, apparently either through larval competition for food or adult male competition for mating with females. In the laboratory, female *A. aegypti* inseminated by *A. albopictus* males lay infer-

tile eggs and *vice versa*. There is still much controversy over the occurrence and mechanism of this phenomenon of "species displacement."

Recent electrophoretic studies have demonstrated that both the North American and Brazilian strains of *A. albopictus* are genetically similar to Japanese strains; Southeast Asian strains from different locations vary genetically, whereas North American strains are quite homogeneous. The genetic similarity between American and Japanese strains, coupled with the finding of *A. albopictus* in tire shipments from Japan, indicates that *A. albopictus* was introduced into the United States in tires transported in large cargo containers from that country. Further introduction of *A. albopictus* to other countries in the Americas seems likely.

Earlier conclusions that the Brazilian strains had a different origin than the North American strains because of their lack of adaptation to the cold, were apparently incorrect. The potential for diapause may be latent in these mosquitoes.

In Asia and the Pacific, *A. albopictus* has been shown to be a vector of dengue, although it is second in importance to *A. aegypti*. In Brazil, although *A. albopictus* occurs in areas with endemic dengue, *A. aegypti* is also present in those areas. No dengue transmission has yet been detected in areas of Brazil where *A. albopictus* occurs in the absence of *A. aegypti*.

In the laboratory, both species have been shown to transmit dengue virus vertically (transovarially), although *A. albopictus* does so more readily than *A. aegypti*. Hence, during periods when cases are not being detected in the human population, the virus may still be present in mosquito eggs, larvae, or adults. Vertical transmission apparently occurs too infrequently to contribute to the magnitude of human transmission.

In the laboratory, *A. albopictus* transmits yellow fever virus to monkeys, but it has not been incriminated as a vector in the field. There is little overlap between the distribution of yellow fever and *A. albopictus* in the Old World. There is no yellow fever in Asia, and *A. albopictus* has been found in Africa only recently. In the Americas, this mosquito may, in the future, bridge the gap between the sylvatic cycle of yellow fever and the susceptible urban human population.

Eastern equine encephalitis virus has recently been isolated from *A. albopictus* in Florida (U. S. A.) and various nonpathogenic arboviruses also have been isolated, findings that reflect the broad host-range of this mosquito species.



## Risk Factors for Dengue and Dengue Hemorrhagic Fever

“Risk” is a concept used to measure the probability of a future occurrence of a negative outcome such as dengue infection or a dengue outbreak. This probability depends on the presence of one or more characteristics or determinants of the event.

The transmission dynamics of dengue virus are determined by the interaction of the environment, the agent, the host population, and the vector that exist together in a specific habitat. The magnitude and intensity of that interaction will define the dengue transmission in a community, region, or country. These components may be divided into macro- and microdeterminants.

### Macro-determinants of Dengue Transmission: Environmental and Social Risk Factors.

Among the macro-determinants of transmission (see Table 10) are the geographical areas where the vector develops and contacts the host population. Dengue is mainly transmitted in the tropical and subtropical regions of the Americas that lie between 35° N and 35° S latitudes. Elevation is a limiting factor for vector and virus development. At lower elevations, mean annual temperature, humidity, and pluvial precipitation are the conditions that affect vector survival and reproduction, and temperature also affects viral replication in the vector. These geographical and climatological parameters may be used to stratify the areas where the expected transmission may be endemic, epidemic, or sporadic.

Several social determinants of dengue transmission are also recognized (see Table 10). In the Americas, dengue is primarily an urban disease. Moderate to high human population densities, unplanned urbanization, and high housing densities are associated with dengue transmission. Houses with inadequate screens or no screens at all allow mosquitoes to come in; rain gutters blocked with debris allow mosquito production. Water that is stored inside the home for more than a week and the use of uncovered water storage drums and tanks create foci. In many communities in the Americas, individual piped water supplies are scarce, and public standpipes provide water only intermittently; consequently, as people store drinking water in their homes, foci are created.

Inadequate systems for collecting and storing

**Table 10. Macro-determinants of dengue transmission: environmental and social risk factors.**

- Environmental
  - Latitude: 35°N to 35°S.
  - Elevation: < 2200 m.
  - Ambient temperature range: 15–40°C.
  - Relative humidity: moderate to high.
- Social
  - Population density: moderate to high
  - Settlement patterns: unplanned urbanization and high settlement density.
  - Housing: screening inadequate or lacking and rain gutters with debris.
  - Water supply: water stored in home > 7 days, no individual piped water supply, intermittent availability, and uncovered drums or tanks.
  - Solid waste collection: inadequate storage bins, collection inadequate or lacking, discarded small containers < 50 liters, discarded tires/tire piles, and junk autos.
  - Socioeconomic status
  - Inactive daytime periods in the home
  - Beliefs and knowledge about dengue

Key references: Christophers, 1960; Nelson, 1986; WHO, 1986; Koopman et al., 1991.

solid waste and failure to remove discarded bulky items such as junk cars, result in the proliferation of foci. Discarded tires and small discarded containers containing less than 50 liters of water have been associated with an increased risk of dengue transmission.

Socioeconomic status is another determinant of dengue transmission; however, in any one community either the wealthier or poorer neighborhoods may propagate large numbers of foci. Women and small children who spend long periods of time in the home, engaged in minimal activity during daylight hours, may experience longer exposures to potentially infected mosquitoes than those who are out of the house or active. Beliefs and knowledge held by families about dengue, the causes of the disease, and means to prevent or control it, affect the level of sanitation in the domestic environment, and ultimately govern the availability of larval production sites in the domestic setting.

In summary, the geographic distribution and density of human populations, beliefs concerning dengue, socioeconomic status, the availability of public services, and housing conditions all may influence the risk of transmission.

### Micro-determinants of Dengue Transmission: Host, Agent, and Vector Risk Factors.

The risk factors that influence transmission of dengue virus (Table 11) must be separated from

**Table 11. Microdeterminants of dengue transmission: host, agent, and vector risk factors.**


---

Individual host factors
Sex
Age
Immune status
Specific health conditions
Occupation
Disease agent factors
Level of viremia
Vector factors
Abundance and types of mosquito production sites
Density of adult females
Age of females
Frequency of feeding
Host preference
Host availability
Innate susceptibility to infection

---

those that influence the severity of the disease. Among the categories of recognized risk factors for transmission, are those of the host, the vector, and the agent. The *host factors* include sex, age, immune status, specific health conditions, and occupation. All humans are susceptible to infection but, as noted above, women and small children may be at greater risk because their activities put them in more prolonged contact with the infected mosquitoes in the domestic setting. The susceptibility of the human population determines whether any and how many indigenous cases of dengue will occur.

A *disease agent factor* that influences the transmission of dengue is the level of viremia. Persons with high viremia provide a higher infectious dose of virus to the biting mosquito vector. For example, a person with high viremia may infect 100% of the mosquitoes taking a blood meal, and even though mosquito density may be low, some mosquitoes may survive the extrinsic incubation period and transmit the virus. On the other hand, a person with low viremia may not infect any of the mosquitoes that take a blood meal, even though mosquito densities may be high.

Among the most important *vector risk factors* are the densities of adult female mosquitoes, and their age, frequency of feeding, and host preference and availability; the host's susceptibility to infection (a highly competent vector may become infected by feeding on a person with a low viremia); and the abundance and types of breeding sites. The last factor is conditioned by such climatological factors as rainfall, temperature, and humidity, as well as

by the supply of piped water, solid waste collection, and the behavior of the human population.

Few studies have been done to determine the relative importance of the risk factors for dengue. Two studies in Mexico showed that the most important risk factors at the household level were the number of potential *A. aegypti* breeding sites per premise; at the community level, the most significant risk factors were median temperature during the rainy season, proportion of houses with larvae, and proportion of houses with uncovered water containers.

### Risk Factors for the Appearance of DHF/DSS

---

The risk factors responsible for the development of severe dengue disease are not fully understood, and of the risk factors that have been postulated several are controversial.

Sequential infections with different dengue serotypes have been shown to be strongly associated with DHF/DSS in Thailand and Cuba, although in some outbreaks, severe hemorrhagic illness, sometimes followed by shock and death have occurred after a primary dengue infection. Laboratory investigations demonstrate that subneutralizing amounts of dengue antibody enhance dengue virus replication in mononuclear phagocytes. A similar phenomenon may occur during human infections, provided enough time (approximately from 6 months to 5 years) has elapsed between infections by different serotypes or when maternal derived antibodies in an infant reach a subneutralizing level.

Viral virulence may also have a significant role in the severity of dengue disease. Some strains of dengue virus may have the potential to cause hemorrhagic disease. It also has been suggested that viral virulence may increase after the agent has passed through several persons. Studies on the replication of dengue virus in peripheral blood leukocytes provide evidence on the different virulence of different strains; such studies demonstrate that dengue-2 strains associated with either grade II DHF or DSS grow to higher titers in peripheral blood leukocytes than those dengue-2 strains isolated either from uncomplicated dengue or grade I DHF.

Individual susceptibility also seems to influence the occurrence of DHF/DSS. Studies have shown

that severe disease was found more frequently among children than in adults, in females than in males, and in well-nourished children than in malnourished children. Other studies have shown that DHF/DSS was more common in whites than in blacks, and also among persons with certain chronic diseases (such as asthma, diabetes, and sickle cell anemia).

The intensity of dengue transmission and the simultaneous circulation of several serotypes also

has been considered as a risk factor for the occurrence of DHF/DSS. Therefore, hyperendemicity of dengue infection would expose a population to increased risk of appearance of DHF/DSS.

A combination of the above-mentioned risk factors and perhaps other unknown factors may play an important role in the appearance of DHF/DSS. More studies are needed to clarify the relative contributions of virus and host factors in triggering DHF/DSS.



## 3. SURVEILLANCE

### Disease Surveillance

---

In order to permit immediate actions to prevent or control epidemic dengue, a surveillance system must be *simple* in its structure and operation, *representative* of the population it serves, *acceptable* to the users, *flexible* to allow the incorporation of new information, and *opportune* in data collection and analysis. The system must have adequate *sensitivity* and *specificity* to correctly identify those individuals with the disease in question and to efficiently exclude those without it.

In the case of dengue/DHF, the surveillance system must address the disease from both a clinical and an entomological perspective. The clinical spectrum of illness associated with dengue infection may range from nonspecific viral syndrome to severe and fatal hemorrhagic disease. Because it often is impossible to clinically differentiate dengue from illnesses caused by other viruses, bacteria, or even some protozoa, surveillance for dengue/DHF must be laboratory-based.

Surveillance for dengue/DHF can be either active or passive. Active surveillance involves a proactive search for dengue infections, especially in situations where they might be attributed to other causes, such as influenza or rubella. Passive surveillance, on the other hand, depends on case reports from physicians who recognize dengue-like illness. In most countries where dengue transmission is reported, the surveillance system is of the passive type, with health authorities waiting until transmission is recognized by the medical services and detected through the routine reporting system. It is strongly recommended that dengue be made a reportable disease in every country at risk, so that dengue/DHF surveillance programs will have a statutory basis.

#### Passive (Reactive) Surveillance

Every dengue-endemic country should have a passive surveillance system, mandated by law,

that makes dengue/DHF a reportable disease. Passive surveillance should require case reports from every clinic, private physician, and health center that provides medical attention to the population at risk. The system should define trends in dengue transmission and detect any increase in dengue incidence.

A legal mandate for reporting dengue cases is essential for this type of surveillance. Even so, passive surveillance is insensitive because not all clinical cases are correctly diagnosed during periods of low transmission, when the level of suspicion among medical professionals is generally low. Moreover, many patients with mild, nonspecific viral syndrome treat themselves at home and do not seek medical treatment. By the time dengue cases are detected and reported by physicians in a passive surveillance system, substantial dengue transmission has already occurred and even may have peaked. In this case, it may be too late for control measures to significantly reduce transmission.

#### Active Surveillance

The objective of an active, laboratory-based surveillance system is to provide early and precise information to public health officials on four aspects of increased dengue activity: time, location, virus serotype, and disease severity. It should, therefore, be a proactive surveillance system that will allow for early detection of dengue cases and thus will improve the capacity of health officials to prevent and control the spread of dengue. Among the main characteristics of this type of surveillance is its predictive capability. Analysis of trends of reported cases, the establishment of sentinel clinics, the confirmation of dengue cases by the laboratory, and the rapid identification of the serotypes involved in transmission, provide the necessary information to predict dengue transmission and guide implementation of control measures well in advance of peak

transmission. Proactive clinical surveillance must be linked to entomologic surveillance, in order to identify dengue transmission in time and place.

Optimal clinical samples for specific tests must be accompanied by sufficient clinical information to allow the disease's severity to be identified (see sample form in Annex II). All clinical samples must be accompanied by a form stating the name, age, sex, and address of the patient; date of onset of symptoms; date of sample collection; symptoms (a short list of important manifestations); travel history for the two weeks before onset; place of hospitalization; and the name, address and telephone number of the attending physician.

A laboratory-based surveillance system of this type will provide information on the onset, location, infecting virus serotype, and severity of disease. It also will allow prompt reporting of results to submitting clinics and physicians, and the ability to obtain further information, if necessary, on cases of severe disease or of public health importance.

**Surveillance Systems Adapted to the Disease Situation**

There are three epidemiologic situations where different levels of surveillance are recommended (Table 12): 1) countries where no dengue transmission has been detected, but where *A. aegypti* is present; 2) countries where *A. aegypti* is present, dengue is endemic, and seasonal increases in transmission occur; and 3) areas where epidemic dengue is occurring. For maximum efficiency, the surveillance system must be adaptable to changes in disease incidence.

**Areas with *Aedes aegypti* Infestation and No Dengue Reported**

In areas where *A. aegypti* is present and no dengue illness has yet occurred, the population is at risk of a major dengue epidemic. In these areas, physicians and clinics will not suspect dengue until late in the outbreak. Dengue surveillance, therefore, should rely on searching for, and investigating, clusters of nonspecific febrile illness or viral syndrome by a method such as the "fever alert."

In a fever alert system, trends in rates of febrile illness are monitored as a crude indicator of possible dengue activity. Health centers should report to their respective health region, on a weekly basis, the total number of patients attending the center and the total number of febrile cases (temperature  $\geq 38^{\circ}\text{C}$ ). When weekly reporting by all centers is not feasible, a sentinel system of at least 30% of the region's health centers should be selected for participation on the basis of high clinic attendance, high vector densities in the catchment area, and efficient communications between the data processing center and the diagnostic laboratory. The data processing center will update health center and/or regional incidence summaries.

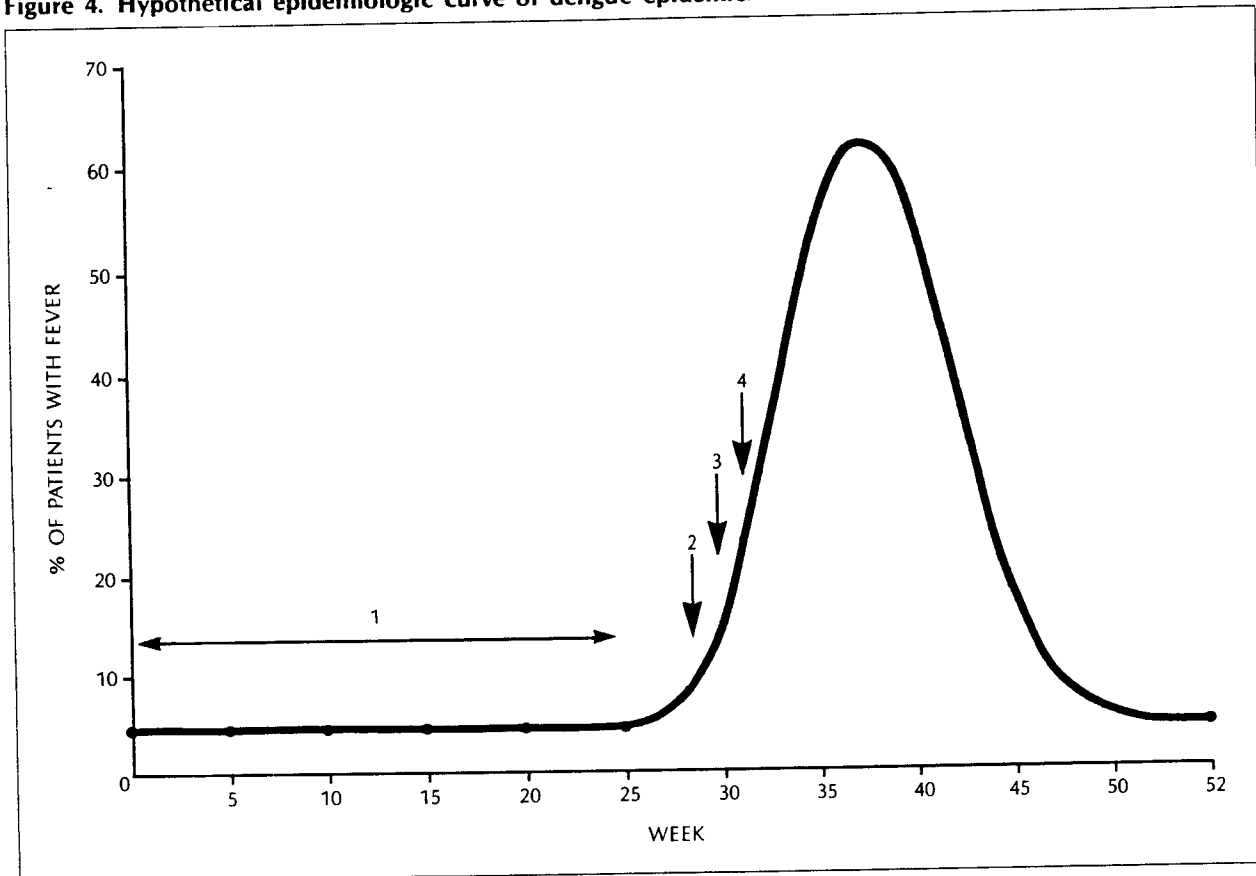
As soon as a significant increase in febrile illness or viral syndrome is noted with respect to previously obtained data, the data center should quickly inform the reporting clinic and responsible health authorities, and any cluster of febrile illnesses should be immediately investigated. Blood specimens should be drawn from a representative sample of febrile patients or, if appropriate, from patients with headache and any third symptom compatible with dengue.

**Table 12. Levels of dengue surveillance according to the epidemiologic situation of the disease.**

Disease status when <i>A. aegypti</i> is present	Surveillance					
	Reactive (passive)	Proactive (laboratory-based)				
		Fever alert	Clinical		Laboratory support	
			Dengue fever (DF)	Severe DF DHF, DSS	Serologic	Virologic
No dengue	+	+++	++	+++	+++	+
Endemic dengue	++	++	+++	+++	++++	++++
Epidemic dengue	++	+	+	++++	+++	+++

**Note:** The plus (+) signs indicate the relative importance to be given to components of the system in a given situation.

Figure 4. Hypothetical epidemiologic curve of dengue epidemic.



Data from a fever alert system, with recommended action: 1) routine surveillance, 2) alert phase; intensify surveillance, 3) begin control if increase is caused by dengue, and 4) increase hospital-based surveillance for severe disease (DHF/DSS).

Note: The percentage values in this graph do not represent rigid recommendations since the threshold values (percent of patients with fever) may be different in each geographic area.

Emergency rooms at pediatric and/or general hospitals may also be selected for monitoring, using similar criteria. A predetermined number of blood samples should be drawn daily for early dengue virus detection.

When virus isolation facilities are available at the central laboratory, isolation should be attempted, but in its absence, serologic testing by MAC-ELISA will provide a rapid laboratory result. For virus isolation and identification, a sample of acute serum appropriately packaged should be sent to a regional or a reference laboratory without delay.

Febrile illness surveillance that is supported by laboratory investigation provides information on early confirmation of dengue infections and early recognition of a new virus serotype circulating in the community (Figure 4). An increase in the rate of fever cases coupled with a higher than baseline rate of serologic response will serve to alert health officials before there is an increase in the number

of cases and severity of illness. The alert provided by febrile illness surveillance should trigger a switch to intensify active surveillance for cases of dengue-like illness. All health care providers and institutions should be reminded of the case definitions and the reporting requirements for dengue/DHF. During active surveillance, a public health official, such as an infection control officer, may be requested to review admissions to the hospital and outpatient clinics on a daily basis. Any admissions with fever and other symptoms suspicious of dengue/DHF would be followed up to ensure that probable dengue/DHF cases have been identified, appropriate investigations have been requested, and confirmed cases have been reported. In addition, vector control officers may hear about suspicious cases in the community, and can bring these to the attention of the district public health nurse for active follow-up; these persons may otherwise not have sought medical care.

## Dengue Endemic Areas

During interepidemic periods and during the months of the year with seasonally low disease incidence, there may be little or no case identification of dengue/DHF. Therefore, few samples are sent to the laboratory for dengue testing. In this situation, sentinel clinics and medical practices should be established. Criteria for taking blood samples must be expanded to include febrile cases with history of recent travel, and situations where dengue might be causing clusters of fever cases with rash. The clinical information provided with blood samples from these cases is usually sufficient to establish a profile of disease severity. Clinical surveillance can be as simple as maintaining frequent communications with key clinics or physicians who are likely to see ill travelers or cases of febrile illness (infectious disease specialists), rash illness (pediatricians), or interested physicians with large practices who are willing to obtain blood samples for dengue testing. In exchange for the results of a sophisticated laboratory test, physicians and clinics usually are happy to collaborate in a detailed evaluation of the patient's symptoms and clinical risk factors for infection.

If a new serotype is identified or increased dengue activity is confirmed, it should constitute an alert to intensify active surveillance for dengue/DHF and to coordinate activities with vector control units of the Ministry of Health.

## Areas with Epidemic Dengue

During epidemic periods, and in areas with high endemicity, (multiple virus serotypes circulating simultaneously), a surveillance system for clinical disease provides a comparison and supplements information provided with blood samples. Such a surveillance system might include a structured, hospital-based reporting system, in which infection control nurses (or similar hospital professionals) send written summaries by facsimile or courier, or report by telephone the number of cases admitted with a presumptive diagnosis of dengue or in which dengue is included in the differential diagnosis. The surveillance system must specify what type of case should be reported, if a blood sample should be sent, and what clinical information is necessary, but the reporting professional's work should be kept to a minimum, or the system will not function well.

For complete documentation of DHF cases,

patient information must include platelet count, lowest and highest hematocrit value (to measure hemoconcentration), results of tourniquet test, any hemorrhagic manifestation, chest x-ray (for pleural effusions), blood pressure, hepatomegaly, coagulation tests (prothrombin time and partial thromboplastin time), and liver enzymes (see Annex I). All patients hospitalized with hemorrhagic disease, viral encephalitis, aseptic meningitis, or experiencing a fatal outcome following a viral prodrome, regardless of diagnosis, should have blood and tissue samples submitted for dengue testing.

During an epidemic, when the clinical syndrome and the disease diagnosis are established and the infecting serotype(s) has/have been identified, it is a misuse of resources to attempt serologic or virologic confirmation of every suspected dengue case. Laboratory work should be focused on identifying new areas where the disease might be spreading, detecting new serotypes coming into already infected areas, and monitoring severe and fatal cases attributed to dengue.

Population-based community serosurveys, conducted in the area shortly after the peak of the epidemic, provide an estimate of true disease incidence. The serosurvey need not cover an entire country, province, or city, but may focus instead on a town, community, or neighborhood of particular interest. Records of clinic attendance and school or factory absenteeism may provide an index of disease activity to identify a severely affected suspect location. Care must be taken that the survey will obtain information that will be representative of the target population, so that the data will be useful to validate the accuracy and sensitivity of the surveillance system.

## Laboratory Support for Dengue Surveillance

Table 13 shows the type of specimens to be collected and the way they should be processed for the laboratory diagnosis of dengue. The following information should be collected with the blood sample:

- name of patient;
- address, age, and sex;
- summary clinical history;
- disease suspected;
- date of onset and specimen collection;
- travel history;
- name of physician; and
- name of hospital/clinic.



**Table 13. Collection and processing specimens for laboratory diagnosis of dengue.**

Specimen type	Time of collection	Clot retraction	Storage	Shipment
Acute blood	0–5 days	2–6 hours, 4°C	Serum –70°C	Dry ice
Convalescent blood	14–30 days	2–24 hours ambient	Serum –20°C	Frozen or ambient
Tissue	As soon as possible after death		–70°C or in formalin	Dry ice or ambient

There are several laboratory tests that can be used for routine serologic diagnosis of dengue viruses, including the hemagglutination-inhibition (HI), the complement fixation (CF), the neutralization (N), and the IgM-capture ELISA (MAC-ELISA) tests. The first three all require paired serum samples from suspected cases, and use of these tests, therefore, involves long delays before laboratory confirmation can be made. The MAC-ELISA, on the other hand, generally requires only one serum sample and is a simple, quick test that requires very little sophisticated equipment. It is, therefore, the most useful test for surveillance purposes, and has become widely used in recent years.

MAC-ELISA's diagnosis is based on detecting dengue-specific IgM antibodies in the test serum by capturing them out of solution using anti-human IgM antibody that was previously bound to the solid phase of a 96-well plate. If the patient's serum contains anti-dengue IgM antibody, it will bind the dengue antigen that is added in the next step and can be detected by subsequent addition of an enzyme-labeled anti-dengue antibody.

Anti-dengue IgM antibody develops rapidly, and by day 5 of illness, 80% of cases, both primary and secondary, have detectable IgM antibody; by day 6 to 10 of the illness, 93% to 99% of cases have detectable IgM antibody. In some primary infections that produce large amounts of antibody, detectable IgM may persist for over 90 days. On average, however, IgM antibody wanes to undetectable levels between 30 and 60 days after onset of illness. The major drawback of this test is its inability to detect dengue infection if the serum sample is drawn very early (< 5 days) after onset of illness.

Although the MAC-ELISA is slightly less sensitive than the HI test for diagnosis of dengue infections, it has the advantage of requiring only a single blood sample. In one series of 386 patients, comparing the MAC-ELISA on single acute serum

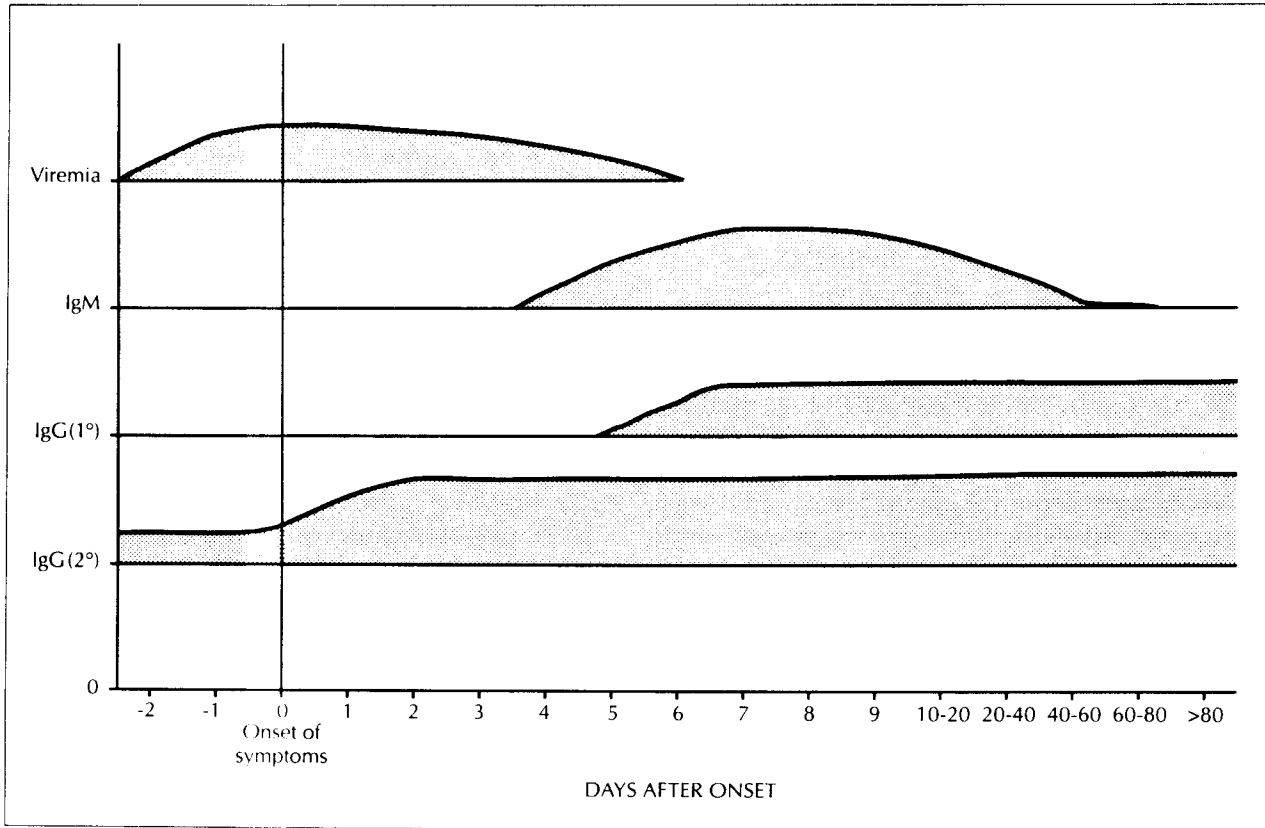
samples to paired samples from the same patients tested by HI, the false negative rate of the MAC-ELISA was 10% and the false positive rate was 1.7%. Considering the difficulty in obtaining second blood samples and the long delay in obtaining conclusive results by the HI test, this low error rate is acceptable in most surveillance systems. It must be emphasized, however, that because IgM antibody may persist for 60 to 90 days, MAC-ELISA positives on single serum samples are only provisional and do not necessarily mean that the dengue infection is current. It is reasonably certain, however, that the person had a dengue infection within the previous 2 to 3 months.

In summary, the MAC-ELISA has become an invaluable tool for surveillance of dengue/DHF, and is the serologic test of choice for most laboratories. It can be used for clinical surveillance and for estimating transmission rates from population-based serosurveys carried out shortly after epidemic transmission begins to wane. Reference laboratories should have the capability to do HI, CF and N tests, but further discussion of these tests is beyond the scope of this document.

Virologic surveillance complements serologic surveillance and is critical to developing an early warning, predictive capability for epidemic dengue. The method of choice for routine virus isolation is inoculation of the C6/36 mosquito cell line, which provides a relatively rapid, sensitive, and economical method that can be set up in most general laboratories. Human sera or blood are inoculated directly into the cell cultures, which are incubated for 5 to 10 days, depending on the clone of cells used, and virus infection is detected by direct or indirect fluorescent antibody test. Virus isolates are identified using an indirect fluorescent antibody test with serotype-specific monoclonal antibodies.

A more sensitive method of virus isolation is mosquito inoculation. Although this method is slow and labor intensive, dengue viruses often can

Figure 5. Representation of the temporal appearance of virus, IgM, and IgG antibodies in persons infected with dengue virus. Shaded areas represent approximate time periods when virus or antibody can be detected using current methods; 1° = primary infection; 2° = secondary infection.



be isolated from severe and fatal cases by mosquito inoculation when cell culture methods yield negative results. While it is not possible for all diagnostic laboratories to have this capability, it is important that reference laboratories provide the service for other laboratories in the Region. Reference laboratories also may use polymerase chain reaction or immunohistochemical methods for viral antigen detection from serum or tissue samples.

The recommendations for laboratory support for dengue/DHF surveillance in different epidemiologic situations are summarized in Table 12. It will be noted that both serologic and virologic support is highly recommended in most situations. While this may not be possible to achieve immediately, the ultimate goal should be to establish this capability in every dengue endemic country. In the interim, support should be provided to facilitate shipment of specimens to regional reference laboratories that can provide this service. Figure 5 shows the temporal appearance of virus, IgM, and IgG antibodies in persons infected with dengue virus.

It should be emphasized that effective surveillance is dependent upon an efficient information exchange. If published at least monthly, the PAHO "Dengue Newsletter for the Americas" could serve this function, provided that relevant information is promptly provided by Member Countries. This topic is discussed in detail below, but it should be noted here that timely exchange of information between laboratories and epidemiologists in the Region is critical to developing effective regional surveillance for dengue/DHF that can be used for prevention and control of epidemics. It is recommended that a central laboratory/office be responsible for collecting and disseminating information to participating countries.

### Vector Surveillance

Entomological surveillance is used to determine changes in geographic distribution of the vector, to obtain relative measurements of the vector population over time, and to facilitate appropriate and

timely decisions regarding interventions. It may serve to identify areas of high density infestation or periods of population increase. In areas where the vector is no longer present, entomological surveillance is critical in order to rapidly detect new introductions before they become widespread and difficult to eliminate. Monitoring of insecticide susceptibility of the vector population also should be an integral part of any program that uses insecticides.

There are available methods for detecting or monitoring larval and adult populations. The selection of appropriate sampling methods depends on the surveillance objectives, on the levels of infestation, and on the skills available for their implementation. Some guidance as to the choice of methods is given in Table 14.

### Sampling the Larval Population

For reasons of practicality and reproducibility, the most common survey methodologies employ larval sampling procedures rather than egg or adult collections. The basic sampling unit is the house or premises, which is systematically searched for water-holding containers. These containers are examined for the presence of mosquito larvae, pupae, and larval and pupal skins. Depending on the objectives of the survey, the search may be terminated as soon as aedine larvae are found, or it may be continued until all containers have been examined. Laboratory examination is usually necessary to confirm the species. The following three indices are commonly used to record *A. aegypti* infestation levels:

*House (premises) index:* percentage of houses infested with larvae and/or pupae.

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

*Container index:* percentage of water-holding containers infested with larvae or pupae.

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

*Breteau index:* number of positive containers per 100 houses inspected.

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

The house index has been used most widely for measuring population levels, but it does not take into account the number of positive containers nor the productivity of those containers. Similarly, the container index only provides information on the proportion of water-holding containers that are positive. The Breteau index establishes a relationship between positive containers and houses, and is considered to be the most informative, but again there is no accommodation of container productivity. Nevertheless, in the course of gathering the basic information for calculating the Breteau index, it is possible and highly desirable to obtain a profile of the larval habitat characteristics by simultaneously recording the relative abundance of the various container types either as potential or actual sites of mosquito production (e.g., number of positive drums per 100 houses, number of positive tires per 100 houses, etc.). These data are particularly relevant for focusing larval control efforts on the management or elimination of the most common habitats and for the orientation of educational messages for community-based initiatives.

For the selection of appropriate interventions for targeted container management or elimination, it is important to understand from the household resident's perspective, the significance of the container type. If a population considers a man-made habitat to be "useful" or "essential" (e.g., a rain-

**Table 14. *Aedes aegypti* surveillance methods.**

Objectives	Methods						
	Larval surveys	Human bait collections	Resting collections	Ovitrap	Tire larvitrap	Adult/larval bioassay	Susceptibility tests
Baseline infestation surveys	X						
Control program monitoring: levels > 5%	X						
Low infestation levels < 5%	X			X	X		
Surveillance against reinfestation	X			X	X		
Verification of eradication	X	X		X	X		
Evaluation of control methods <sup>a</sup>	X	X	X	X	X	X	X

<sup>a</sup>Choice depending on intervention used.

water drum or a house plant) the strategy employed will most probably be one of management or modification rather than destruction or removal. For a "useless" or "nonessential" category (e.g., a discarded tire or abandoned domestic appliance), the option of removal is open. Natural habitats (e.g., rock holes, tree holes, plant axils) constitute a third category that may be subject to either elimination or management.

It should be noted that larval indices are a poor indication of adult production. For example, adult emergence rates from rainwater drums are likely to differ markedly from those for discarded cans or house plants, yet the larval survey registers them only as positive or negative. The implication is that for localities with similar larval indices but different container profiles, adult densities, hence, transmission potentials, may be quite different.

The rates of recruitment of newly-emerged adults to the adult mosquito population from different container types can vary widely. Estimates of relative adult production may be based on pupal counts (i.e., the counting of all pupae found in each container). The corresponding index is:

*Pupal index*: number of pupae per 100 houses

$$PI = \frac{\text{Number of pupae}}{\text{Houses inspected}} \times 100$$

To compare the relative importance of the larval habitats, the pupal index in "useful" containers may be compared with the pupal index in "nonessential" containers and "natural" containers. If desired, this may be broken down further by container type, such as pupal index in tires, flower vases, etc.

Given the practical difficulties and effort entailed in obtaining accurate pupal counts, especially from large containers, this method need not be used in every survey, but may be reserved for special studies or used once in each locality during the wet season and once during the dry season.

### Sampling the Adult Population

Adult vector sampling procedures can provide valuable data for specific studies such as seasonal population trends, transmission dynamics, or evaluation of adulticiding interventions. However, results are less reproducible than those obtained from sampling of immature stages. The collection methods also tend to be labor intensive and

heavily dependent on the collector's proficiency and skill.

### Landing/Biting Collections

Landing/biting collections on humans are a sensitive means of detecting low level infestations, but are very labor intensive. Both male and female *A. aegypti* are attracted to humans. Because adults, especially males, have low dispersal rates, their presence can be a reliable indicator of close proximity to hidden larval habitats. Rates of capture, typically using hand nets or aspirators as mosquitoes approach or land on the collector, are usually expressed in terms of *landing-biting counts per hour*.

### Resting Collections

During periods of inactivity, the adult mosquitoes typically rest indoors, especially in bedrooms, and mostly in dark places such as clothes closets and other sequestered sites. Resting collections comprise the systematic searching of these sites with the aid of a flashlight, and the capture of adults using mouth or battery-powered aspirators and hand-held nets. Recent resting collection studies with backpack aspirators powered by automobile air conditioner motors and rechargeable 12v power packs have proven to be an efficient and effective means of evaluating adult densities.

Following a standardized collection routine, densities are recorded as the *number of adults per house* (females, males or both) or the *number of adults per man-hour* of effort. With low infestation levels the *percentage of houses positive* for adults is sometimes used.

### The Measurement of Oviposition Rates

#### Oviposition Traps

Also known as "ovitrap," these devices constitute a sensitive and economical method for detecting the presence of *A. aegypti* and *A. albopictus* in situations where infestations are light and larval surveys are generally unproductive (e.g., when the Breteau index is < 5). They have proven especially useful for the early detection of new infestations in areas from which the mosquito has been eliminated. For this reason, they are used extensively for surveillance at international ports of entry which, according to international sanitary codes, should be maintained free of vector breeding.

The standard ovitrap is a wide-mouth, pint-sized glass jar painted black on the outside, and equipped with a cardboard or wooden paddle clipped vertically to the inside with its rough side facing inwards. The jar is partially filled with water and is appropriately placed in the field.

Ovitrap are usually serviced on a weekly basis and the paddles are examined for the presence of *A. aegypti* eggs. The *percentage of positive ovitraps* provides the simplest index of infestation levels. In more detailed studies, all the eggs on each paddle are counted and the *mean number of eggs per ovitrap* is calculated. For accurate interpretation, field records must indicate the location of each ovitrap and its condition at the time of servicing; if it was flooded, dry, missing, or overturned, the data should be discarded.

A recently developed "enhanced CDC ovitrap" has yielded eight times more *A. aegypti* eggs than the original version. In this double ovitrap method, one jar contains an olfactory attractant made from a "standardized" 7-day-old hay infusion, while the other contains a 10% dilution of the same infusion. Unlike the original version, with which positivity rates and egg counts are seldom sufficiently high, the enhanced ovitrap has proven suitable for monitoring changes in adult female populations on a daily rather than a weekly basis, and has been successfully used for monitoring the impact of adulticidal space spraying on adult female populations.

#### *Tire Section Larvitrap*s

Tire section larvitrap of various designs have also been used for monitoring oviposition activity, the simplest being a water-filled radial section of the tire. A prerequisite for any design is that it either facilitate visual inspection of the water *in situ* or the ready transfer of the contents to another container for examination. Tire larvitrap differ functionally from ovitraps in that water level fluctuations brought about by rainfall induce hatching of eggs, and it is the larvae that are counted rather than the eggs deposited on the inner surfaces of the trap. Their usefulness as an alternative to the ovitrap for early detection of new infestations and for surveillance of low density vector populations has been well demonstrated.

#### **Insecticide Susceptibility Testing**

The initial and continued susceptibility of the vector to insecticides is of fundamental importance

for the success of larviciding or adulticiding operations. The development of resistance may lead to control failure unless it is carefully monitored and a timely decision is made to use alternative insecticides or control strategies.

Standard WHO bioassay procedures and kits are available for determining the susceptibility or resistance of mosquito larvae and adults to insecticides. Biochemical and immunologic techniques for testing individual mosquitoes also have been developed in recent years, but are not yet available for routine field use.

#### **Sampling Strategies**

There are only exceptional conditions where larval surveys of every house (i.e., census) are warranted. Such situations arise when the objective is one of vector eradication and there is a need to locate every larval focus after infestation levels have been reduced to very low levels ( $HI < 1.0\%$ ); or to verify that eradication has indeed been achieved or to ensure that reinfestation has not occurred. Otherwise, the number of houses to be inspected should be based on considerations of available resources, the desired level of precision of the results, and the total number of houses in the locality. This is contrary to the routine procedures employed in many vector control programs in which eradication campaign methodologies have persisted and entomologic data are collected from every house immediately prior to insecticide treatment, usually by the same individual administering treatment. Such practices, if used solely for measuring infestation levels, are a wasteful use of resources and are likely to result in poor quality of reporting due to conflicts of interest and the tedious nature of the routine work. Whenever possible, it is recommended that a different team or individual conduct the entomologic evaluation, or that the two tasks be performed separately. The sample size for routine surveys can be calculated using statistical methods based on the expected level of infestation and the desired level of confidence in the results. Annex III gives tables and examples for determining the number of houses to be inspected.

Several sampling procedures that eliminate or minimize bias can be applied equally well to the selection of houses for larval, adult, ovitrap, or knowledge-attitude-practice (KAP) surveys:

*Systematic sampling* of every 'n'th house throughout a community or along linear transects through

the community. For example, if a sample of 5% of the houses is to be inspected, every 20th house (= 100/5) would be inspected. This is a practical option for rapid assessment of infestation levels, especially in areas where there is no house numbering system. All areas of the locality are well represented.

*Simple random sampling*, whereby houses to be selected are obtained from a list of random numbers (either from tables of random numbers in a statistical text book or from a calculator or computer-generated list). This is a more laborious process, as detailed house maps or lists of street addresses are a prerequisite for identifying the selected houses. Many statistical tests require random sampling. Unfortunately, although every house has an equal chance of being selected, usually some areas of the locality are under-represented and others are over-represented.

*Stratified random sampling* minimizes the problem of under- and over-representation by subdividing the localities into sectors or "strata," usually based on identified risk factors, such as areas with houses without a piped water supply, areas not served by sanitation services, and densely-populated areas. A simple random sample is taken from each stratum, the number of houses inspected being in proportion to the number of houses in each stratum.

*Cluster sampling* may be conducted in large cities or geographic areas where it may be difficult or impossible to use random or systematic samplings because of limitations of time, money, and personnel or because of other logistical constraints. Under these circumstances, the sample can be selected in two stages, in order to minimize the resources needed for the survey. The first stage is obtained by simple or stratified random sampling of population groups or clusters (e.g., city blocks, villages, administrative districts). Having identified these clusters, simple or stratified random sampling procedures are again applied to identify the specific houses within each cluster for inclusion in the survey.

### Frequency of Sampling

The frequency of sampling depends on the frequency and expected duration of the control measures. For time-limited, insecticide eradication campaigns with cyclical rounds of treatment every

6–12 weeks, larval evaluation traditionally precedes each application. For control programs using integrated strategies, such frequent intervals for routine assessment of the impact of the applied measures often are unnecessary. This is especially true in those instances in which the effect of some of the alternative strategies being applied outlast residual insecticides (e.g., larvivorous fish in large potable water storage containers, source reduction or mosquito-proofing of containers). On the other hand, rapid feedback at monthly intervals is desirable to evaluate and guide community action activities and indicate the sectors that need more attention and activities that need reinforcement. For specific research studies, it may be necessary to sample on a weekly, daily or even on an hourly basis (e.g., to determine the diel pattern of biting activity).

### Non-entomological Surveillance

In addition to the evaluation of aspects directly pertaining to vector densities and distribution, community-oriented, integrated pest management strategies require that other parameters be measured or periodically monitored.

Distribution and density of the human population, settlement characteristics and conditions of land tenure, housing styles, education, and socio-economic status are all interrelated and of fundamental importance for planning purposes and for assessing dengue risk. Knowledge of and changes over time in the distribution of water supply services and their quality and reliability, as well as domestic water storage practices and solid waste disposal services are also of particular relevance. This type of information aids in the establishment of ecological profiles that can be of value for planning targeted source reduction or management activities and for organizing epidemic intervention measures.

Some of these data sets are generated by the health sector, while others are derived from external sources. In most cases, annual or even less frequent updates will suffice for program management purposes. However, in the case of meteorological data, especially rainfall patterns, a more frequent analysis is warranted, such as weekly or monthly, if it is to be of predictive value in determining seasonal trends and short-term fluctuations of the vector population.

## 4. PREVENTION AND CONTROL STRATEGIES

### The Success and Failure of the Hemispheric Eradication Program

The first *A. aegypti* programs were directed towards yellow fever. Great advances were made at the beginning of the century in Cuba and Panama to control this vector, chiefly through source reduction, oiling, and application of pyrethrins. In 1923, Brazil initiated an eradication campaign. The last urban epidemic of yellow fever in the Americas was reported in 1942, but the continued threat of the reappearance of this disease in urban areas and the increasing incidence of dengue led to continued support for vector control programs. The XI Conference of the Pan American Sanitary Bureau, held in 1942, urged infested countries to organize eradication projects based on strategies adopted by Brazil. With the discovery of the insecticidal properties of DDT, hemispheric eradication of *A. aegypti* seemed feasible.

Before the beginning of the eradication campaign, all Western Hemisphere countries, with the exception of Canada, were infested with *A. aegypti*. By 1962, 18 continental countries and several small Caribbean island countries had succeeded in eradication. The reasons for this spectacular success were the following:

- Adequate local and external funding, for well-trained personnel, equipment, and insecticides.
- Total coverage of the infested areas in time-limited programs.
- The use of DDT for perifocal spraying in and around all breeding sites.
- Streamlined, semiautonomous programs, separate from the national health programs.
- Centralized, vertically structured programs that had a military-type organization and clear lines of command, strict supervision, and a high level of discipline.

What went wrong with the eradication programs?

- Not all of the countries in the Hemisphere resolved to eradicate *A. aegypti*, and those countries that were still infested became sources of reinfestation for those countries free of the vector.

- In most of the countries that achieved eradication, *A. aegypti* programs lost political importance as the years went on, and surveillance against reinfestation gradually diminished until it was inadequate to detect small reinfestations.

- When a reinfestation was discovered, the response usually came too late, and the resources allocated to eliminate it before it became generalized and unmanageable usually were insufficient.

It is probably not feasible to attempt another hemispheric *A. aegypti* eradication campaign, for the following reasons:

- The *A. aegypti* problem is now several orders of magnitude greater than it was during the first eradication campaign. The human population in Latin America and the Caribbean is growing exponentially, with virtually all of this increase occurring in urban centers. There are now many more houses, there is more travel between urban centers within and among countries, and there are more disposable containers per household than ever before. The delivery of governmental services such as piped water and garbage collection often is inadequate in these exploding urban centers, and urban infrastructures are aging because of insufficient maintenance.

- Given the present economic crisis in Latin America and the Caribbean, very few countries have the resources to execute a vertical, paramilitary campaign with total insecticidal coverage.

- Many countries do not place high priority on *A. aegypti* programs or even on dengue control.

There are many other health problems that are considered more important and receive more resources.

- On the one hand, *A. aegypti* is now generally resistant to DDT throughout the Americas; on the other, organophosphate insecticides are more expensive and have shorter residual activity, and resistance to them is developing also.

- With time, even those well-funded and still semiautonomous programs often have become very inefficient: salaries and other monthly benefits are often not delivered to the workers on time, resulting in frequent strikes.

- Communities are less receptive to vertical disease control programs and often resist the delivery of services; there also is increasing public concern over the use of insecticides.

## Current Approaches for Surveillance and Control

After the ultimate failure of the hemispheric *A. aegypti* eradication campaign, many changes have been recommended and at least partially implemented in the vector control programs.

### The Change from Eradication Campaign to Control Programs

An important policy change was made in the XXXI Meeting of the Directing Council of PAHO in 1985. Where previous resolutions had insisted on the eradication of *A. aegypti* for all countries, resolution XXVI recognized, and for first time endorsed, the fact that some countries have programs to control *A. aegypti*.

This was an important step. The methodology used in an eradication campaign is very different from that used in control programs. Eradication involves complete and thorough coverage of the infested areas with frequent treatment cycles in order to eradicate the vector within a few years. Control is the cost-effective utilization of limited resources to reduce vector populations to levels at which they are no longer of significant public health importance.

Eradication is not merely "control done extremely well," because it is unnecessary to eliminate every breeding site in every area during a control program. For example, if treeholes, which are difficult to inspect and treat, are plentiful, but entomological surveys show they account for less than 1% of the actual mosquito production, and if

resources are limited, it is not cost-effective to attempt to fill every tree hole. Time and manpower can be better spent treating or eliminating those containers, such as tires or drums, that account for most mosquito production.

The following recommendations should be followed in order to implement long-term, sustainable control programs:

### *Integration of Vector Control Methods*

In pursuing vector control, instead of relying on a single control method, all of the potential vector control techniques are combined and integrated in the most compatible manner (see the section on "Integrated Control," beginning on page 58). Foremost in the armory of vector control methods is environmental management for the physical elimination or alteration of breeding sources (see the section on "Environmental Management," beginning on page 49). Chemical control with larvicides should be restricted to containers that cannot be controlled by any other means, and space sprays should be reserved for emergency situations (see the section on "Chemical Control," beginning on page 53). Biological and genetic control methods are mostly still experimental, or are used for application under certain special circumstances on a small scale (see the section on "Biological Control," beginning on page 56).

### *Integrating Aedes Control with Control of Other Pests*

Instead of targeting only one vector, several related vector species can be included in the same program. This broader approach, known as comprehensive vector control, not only addresses several public health problems simultaneously, but it also gains better public acceptance for the program. For instance, *Aedes* control can be combined with *Culex pipiens quinquefasciatus* control, the latter species being recognized as a much greater nuisance by the public. Collection of solid waste for *Aedes* programs need not be restricted to *Aedes* production sources, but can also include items that are associated with filth, flies, and rodents.

### *Integration with Other Sectors and with the Community*

The original eradication campaign was not sustainable, because of its costliness and isolation



from the rest of the health sector, other governmental sectors, the private sector, and the community.

**Local Health Care Systems.** Instead of isolating the control program from other health programs, it may be better and more efficient to integrate it with the local health care systems, by transferring responsibility, authority, resources, and knowledge from the central level to the local level (see the section on "Organization and Function of Control Activities," beginning on page 39).

**Intra- and Intersectorial Collaboration.** Contacts, liaisons, and cooperative activities should be promoted within the different divisions of the health sector (national malaria service, national health institute, epidemiology division, health education office, legal office), other governmental sectors (public works, water supply, sanitation, education), and the private sector (commercial enterprise, civic clubs). (See section on "Organization and Function of Control Activities," beginning on page 39).

**Social Participation and Health Education.** The public's involvement at the individual, family, and community levels can be promoted through the mass media, in the schools, at community meetings, and at fairs and contests (see the section on "Community Participation and Health Promotion," beginning on page 44).

#### *Enforcement of Sanitary Legislation*

Most countries have laws that prohibit unhealthy conditions in any public or private premise, but few enforce those laws regarding potential breeding sites of mosquito vectors, other insect pests, and rodents (see the section on "Legislative Support," beginning on page 47).

#### *Prioritization of High Risk Areas*

If resources are insufficient to cover all urban areas, the localities can be ranked in order of risk level by dengue incidence or *Aedes* infestation levels, so that greater attention is paid to the high risk areas. This is a dynamic process that should involve periodic revisions of the ranking.

#### *Stratification*

The important risk factors for transmission of dengue and DHF (see Tables 10 and 11) should be determined for each area, and the areas may be grouped according to common risk factors in order

to apply common, selective sets of treatment strategies instead of blanket use of one method everywhere (see the section on "Epidemiologic Stratification," beginning on page 37).

#### **Surveillance, Prevention, and Control Activities Established According to Different Epidemiologic Situations**

At any given time, each country in the Americas can experience a unique situation regarding the level of infestation with *A. aegypti* (from zero infestation to very high levels) and the level of dengue transmission (from no dengue to epidemic transmission). Although, no single, uniform strategy for surveillance and control is applicable to every situation, the diverse country situations can be grouped by vector and disease characteristics, and surveillance and control activities can be described for each group.

In Table 15 seven different situations of *A. aegypti* infestation (as measured by house index) and dengue activity are presented, starting with the most favorable situation where the vector is absent and progressing to the worst case where there is an epidemic under way.

Essentially, there are three kinds of long-term dengue programs: surveillance against reinfestation by the vector; eradication programs; and "routine" control programs. "Emergency" control is the short-term response to epidemic situations.

#### *Surveillance against Reinfestation*

A few countries (Bermuda, the Cayman Islands, Chile, and Uruguay) have not been permanently reinfested by *A. aegypti* after the initial successful eradication (see Table 15, situation 1), and some others (Brazil, Cuba) have large areas free of the vector. In these cases, surveillance against reinfestation is of paramount importance. Special attention should be given to seaports, airports, cemeteries, and tire recapping facilities.

**Seaports.** Maritime ports have been an introduction site for both *A. aegypti* and *A. albopictus* in Asia, the South Pacific, and North America. Ports receiving vessels from infested areas should have programs to inspect vessels, and to institute source reduction measures for shipboard foci and potential foci. Tires and tarps used to cover cargo and cargo containers, and water storage tanks and drums are some of the common shipboard foci for

**Table 15. Surveillance and control activities according to status of *Aedes aegypti* and dengue.**

<i>Aedes aegypti</i>	Situation		Program Status	Type of surveillance recommended		Type of control recommended	
	Dengue virus	Examples		Vector	Disease	Routine <sup>a</sup>	Emergency
Eradicated	Absent	Uruguay, 1993	Surveillance	++ (against reinfestation)		(+) (+)	
Low (<0.1%)	Absent	Cuba, 1993	Eradication	++ (against reinfestation)		+	
Medium (0.1–5%)	Absent	Panama, 1992	Control	++	++	+	
High (>5%)	Absent	Bolivia, 1986 Ecuador, 1987 Paraguay, 1988 Panama, 1989	Control	+ (only to evaluate control program)		++	+++
High (>5%)	Endemic	Puerto Rico, 1993 Ecuador, 1993 Guatemala, 1993 Venezuela, 1993 and most other countries	Control	+ (only to evaluate control program)		++	++
High (>5%)	Increasing	Puerto Rico, 1986	Alert	+ (only to evaluate control program)		++	+++ ++
High (>5%)	Epidemic	Brazil, 1986 Bolivia, 1987 Ecuador, 1988 Paraguay, 1989	Emergency	+ (only to evaluate control program)		++	+++ +++

(+): Optional ++: Necessary +++: Important ++++: Very important.

<sup>a</sup>Routine control: Long-term source reduction campaigns with some larviciding and perifocal treatment.

*A. aegypti*. Surveillance and source reduction also should be conducted at the entire port facility, its buildings and grounds, and the immediate surrounding area.

**Airports.** Airports also represent potentially important locales for the introduction of urban *Aedes* vectors, although it is usually the virus-infected human host entering a country at airports or seaports that represents the greater public health risk.

**Cemeteries.** Cemeteries act as important *Aedes* foci where flowers, live or artificial, are placed in vases and other containers.

**Tire Recapping Facilities.** Tire recapping facilities located at or near international seaports and airports are important potential key sites for the introduction of urban *Aedes* vectors. Periodic inspections for foci should be implemented at these facilities and include covering tire piles with tarp or placing tires under rain shelter.

The importance of maintaining a vector surveillance program in areas that are free of *A. aegypti* must be stressed. A good surveillance program designed to avoid reinfestation is much less costly than an eradication or control program set up after reinfestation has occurred.

### *Present-day Eradication Programs*

Eradication is still technically feasible in certain circumstances and areas in the Americas. For example, the present infestation in Cuba is limited to a small area of Havana, and intensified efforts should soon succeed (Table 15, situation 2). However, the benefits of success will only be realized if long-term vigilance against reinfestation is maintained, which has not been the case in most past programs.

Guidelines for the execution and verification of eradication are given in the "Guide for Reports on the *Aedes aegypti* Eradication Campaign in the Americas."

### *Routine Control*

The long-term activities aimed against the immature mosquito population are called *routine* control, and the principal method employed is source reduction. There is no need for space spraying, and larvicides need only be used in those containers that cannot be removed, destroyed, discarded, permanently drained, covered, or otherwise managed. To ensure sustainability, all sectors

of the community should be brought into the program. Table 15 shows the different epidemiologic scenarios where "routine" control is applicable.

As *Aedes* infestation increases (situation 3), vector surveillance becomes important for prioritizing and stratifying areas for intervention and for monitoring the effect of control efforts; disease surveillance now becomes necessary in order to detect the introduction and transmission of dengue virus.

When the *Aedes* infestation is high (shown in Table 15 as house index > 5%; however, this figure is arbitrary, because there is no known threshold level of house infestation below which it can be assured that there will be no outbreak of dengue) and if dengue is endemic (situation 5), routine control operations obviously are failing. Disease surveillance now gathers paramount importance in the effort to detect an increase in numbers of cases from the normal endemic level or the introduction of a new dengue serotype. Emergency preparations should be initiated: the medical community should be informed of dengue and DHF/DSS symptoms and the treatment of cases, a contingency hospitalization plan should be developed, and preparations for emergency vector control should be made.

### *Emergency Response*

*Emergency control* is the intense, short-term activity directed at a rapid reduction of the adult mosquito population, in order to suppress dengue transmission in an epidemic situation or when an epidemic appears to be imminent. Space sprays are the fastest available emergency method, but as epidemics may continue for several weeks, intensification of *routine* larval control measures such as source reduction and larviciding probably also helps to suppress them (see the chapter on "Emergency Preparation and Response," beginning on page 59).

### **Epidemiologic Stratification**

The traditional model of health intervention considered the study of the dynamics of dengue incidence and the understanding of risk factors for the disease as matters of minor importance, since it believed that single, "magic bullet" interventions were to be used for all situations and conditions of dengue outbreaks.

By using a nontraditional socioepidemiologic approach to dengue transmission, which is based on epidemiologic stratification, health professionals are better equipped to assess the short- and long-term impacts of various control strategies, including social participation and reduction/elimination of major dengue risk factors. This approach represents a substantial departure from traditional control interventions.

### **Epidemiologic Stratification of Dengue Risk**

The epidemiologic stratification of a disease such as dengue is a dynamic and ongoing process involving research, diagnosis, analysis, and the interpretation of information that serves as the basis for a comprehensive, methodological classification of geocological areas and population groups according to dengue *risk factors*.

A *risk stratum* is an aggregate of individuals and social groups that are located in well-defined geographical areas and that share a similar hierarchy of principal risk factors. Consequently, measures or interventions that are undertaken in order to modify these risk factors will be similar within each stratum. For example, for areas where the principal breeding sites are discarded containers, emphasis should be placed on the elimination of solid waste. In other areas where water storage containers provide most of the breeding sites, mosquito-proofing the water containers could be a short-term remedy, and provision of piped water supply might be the long-term solution.

The main feature of the socioepidemiologic approach is an epidemiologic study of the risk factors for specific individuals and social groups that are responsible for the incidence of dengue at the local level. The known risk factors for dengue transmission were discussed in the section on "Risk Factors for Dengue and Dengue Hemorrhagic Fever," beginning on page 19, (see also Tables 10 and 11), and use such critical parameters as socioeconomic conditions, vector biology, and the health program's ability to respond to prevention and control needs.

The establishment of risk profiles and ecological profiles for dengue transmission can be of great value for planning targeted source reduction and environmental management activities, as well as for organizing epidemic intervention measures.

The stratification process currently used in dengue programs in the Americas consists of classifying localities or neighborhoods according to a

set of *assumed* risk factors, usually without conducting previous studies to determine which are the most important factors and what each one's relative importance is. The assumed risk factors most commonly used by the country programs for their classification are: elevation, mean annual temperature, population density, history of infestation with *A. aegypti*, house index, breteau index, economic importance, proximity to positive localities, proximity to ports and international borders, and current dengue transmission.

Once the localities or neighborhoods have been classified, they are ranked according to level of risk. Number, intensity, and frequency of different control measures are greatest in the localities of highest risk. If resources are limited, higher-risk localities are treated first. For example, in Mexico localities are classified according to three ranges of elevation (0 to 600 m, > 600 to 1200 m, and > 1200 to 1800 m), three population sizes (> 2500 to 20,000, > 20,000 to 50,000, and > 50,000) and three mean annual temperatures (< 20°C, 20°C to

25°C, and > 25°C). Localities with the lowest elevation, highest population size, and highest temperatures receive the most frequent interventions and the most epidemiologic and entomological surveillance.

In summary, risk stratification and the socio-epidemiologic risk approach provides a rationale for dengue prevention and control activities at the local and regional levels. The purpose of this approach is to establish an epidemiologic hierarchy of possible specific measures or interventions that may be used to prevent dengue transmission by *eliminating or reducing the underlying risk factors* through primary prevention measures and appropriate vector control. Proposed specific interventions are based on the local epidemiologic situation and its principal risk factors. The approach is based on the study of epidemiologic, socioeconomic, and environmental parameters, including the managerial capability of local health care programs and the logistic and financial constraints of countries prone to dengue activity.

## 5. SUSTAINABLE PREVENTION AND CONTROL PROGRAMS

The failure of dengue control programs in the past was largely due to an inability to sustain costly, vertical, centralized, single-method strategies. The current trend is towards decentralization, both at the central and at local levels; increased cooperation with other health sectors; cooperation with other governmental sectors and nongovernmental organizations; and the community's involvement in the design, execution, and evaluation of surveillance, prevention, and control activities that rely on the safe, effective, and economical integration of all appropriate control methods (environmental, biological, and chemical).

### Organization and Function of Control Activities

---

The organization and function of sustainable control activities must involve the development of control programs (appointment of a national coordinator, information and resources review, integration and balancing disease control measures, financial considerations, and budget planning), cooperation within the health sector, cooperation between the health sector and other sectors of the economy, community participation and health promotion, and development and use of appropriate legislation. Each of these components is discussed, below.

#### Development of Control Programs

##### *National Coordinator*

Each country that is at risk of infestation or already infested with *A. aegypti* should appoint a national coordinator for the prevention and control of dengue and dengue hemorrhagic fever. This

person should be responsible for facilitating the implementation of intrasectorial and intersectorial surveillance and control measures at the national level and function as the liaison with international experts and technical assistance centers.

The coordinator must establish contacts with professionals from disciplines that are relevant to surveillance and control, including biologists, social scientists (anthropologists, sociologists), physicians, economists, engineers, and architects. The coordinator also will need to work with community leaders, municipal officers, and local politicians, as well as with chiefs of other central government ministries. The national coordinator should initiate and coordinate the program development steps outlined below.

##### *Preparatory Steps for Disease Control Strategy Development*

Regardless of the particular strategy that a country adopts, the development of a national strategy and a national program will depend on the following preparatory steps:

**Review of current data and information.** Data and information on the distribution of the virus, viral serotypes, vectors, populations at risk, and the national situation regarding water supply, sanitation and housing must be carefully reviewed. (See also the chapters on "Surveillance" beginning on page 23 and "Evaluation of Prevention and Control Programs" beginning on page 71.)

**Surveillance.** (See the chapter on "Surveillance," beginning on page 23.)

**Estimating disease control requirements.** The human resources, equipment, and supplies needed for disease diagnosis and treatment and for vector surveillance and control, should be based on existing data and information.

**A resources inventory.** An inventory should be conducted of health care facilities (primary and secondary care centers, etc.), laboratory and diag-

nostic facilities and related facilities in other programs and sectors, human resources, and major equipment.

**Additional resources.** Additional resources may be needed, including sharing human resources and funds in existing government programs in water supply, solid waste management, municipal sanitation, and slum renovation/urban renewal; support from local or international nongovernmental organizations and charitable foundations for community-based control measures such as environmental sanitation and management; and the identification of grants and loans from appropriate bilateral and multilateral development agencies for such activities as the construction of large water-treatment and delivery systems that require large capital investments.

### *Characteristics of a Successful Disease Control Strategy*

Whatever the strategies adopted by the dengue surveillance and control coordinator and the Ministry of Health, they should:

- be responsive to both felt and unfelt local needs,
- be efficacious and cost-effective,
- be economically sustainable,
- utilize appropriate technologies (small- or large-scale),
- be planned and evaluated with the community's direct assistance,
- be community-based in their implementation, and
- be socially and culturally acceptable to all affected populations.

### *Balance in Disease Control Strategies*

The strategies and tactics used in the integrated control program must consider the particular urban epidemiologic situation in the affected area (see also the section "Current Approaches for Surveillance and Control," beginning on page 34, for a description of typical epidemiologic situations faced by control personnel). Control measures also should be based on an analysis of the most vulnerable points in the local transmission cycle, and must reflect local epidemiologic circumstances (for epidemiologic stratification, see the section beginning on page 37) and socioeconomic and cultural conditions.

### *Financial Considerations in Disease Control Strategies*

In selecting the most cost-effective dengue control strategies (discussed further in the section on "Economics of Control Programs," beginning on page 74), administrators should carefully consider the following cost measures:

**Capital versus recurrent costs.** Medical surveillance and treatment and vector surveillance and control are typically long-term programs with recurrent costs, while improvement of water supplies and housing usually involve large initial capital costs with only a relative residual of recurrent costs for maintenance and upkeep.

**Foreign exchange substitution.** Many of the Region's countries that have dengue or dengue vector control programs purchase some diagnostic equipment and insecticides from abroad, using scarce foreign currency. In contrast, improvements in water supply, solid waste management, and housing can often utilize local capital resources and be paid with local currency, when locally available materials and labor are used.

**Opportunity costs.** Control program administrators should consider these and other typical dilemmas: If scarce foreign exchange is used to fund insecticide-based control programs with their marginal long-term benefits, what opportunities for investment of local capital and labor in improved water supply and sustainable, community-based environmental sanitation programs are lost? Given that local communities often have limited time and energy, is it better to utilize human resources in neighborhood clean-up campaigns once or twice a year, or to organize the community to make improvements in more permanent water works (e.g., installation of piped water supply, more reliable pumps, etc.)?

**Incidental benefits and disadvantages.** Dengue control program managers should recognize that in periods between epidemics, vector control programs based chiefly on chemicals have few benefits beyond the control of mosquito vectors, and can engender problems if careful, proper pesticide application is not achieved (e.g., community resistance to pesticide application). In contrast, control programs based on visible measures such as improved water supply, sanitation, and housing have concomitant, but often important, benefits by reducing the risk of communicable diseases and providing a universally-desired need, such as clean piped water.

### *Planning the Budget*

The budget for control programs should anticipate, wherever possible, all the short-term and long-term costs and benefits described above. Human resource needs should be estimated in person-months, while costs for land, capital (i.e., interest payments), transport and travel, equipment (with depreciation), supplies and labor (salaries, employment benefits, training), and community mobilization (health education, public health communication, household surveys, entomological control aides, local labor pools, prize monies, community grants, etc.) should all be specified in local currency and in a key international currency for imported goods or services. Enough margin for the implementation of emergency control measures (outbreak control) and for miscellaneous and contingency expenses should also be included in the control program budget.

### **Program Structure**

Traditional *A. aegypti* eradication programs were structured vertically. They were usually incorporated as a department of the National Malaria Eradication Service, which was a division of the Ministry of Health, but they had virtual autonomy from the Ministry's other divisions, with separate funds, administrative staff, equipment, supplies, and physical facilities. There was a clear chain of command, beginning with the National Malaria Eradication Service program director at the top of the pyramid at the central level, moving through various levels of area chiefs, field supervisors, and brigade chiefs, and finally ending with the sprayers. All decisions were taken at the central level, and all disbursements of funds, supplies, and equipment were made there. Because local-level personnel were only required to carry out orders, they were trained only to perform their specific tasks. The Service's area offices were separate from the regional health offices and there was very little contact between them. These vertical, centralized programs were highly effective, but not sustainable, mainly due to a lack of ongoing funds.

The current trend is to decentralize the control programs and to integrate them with the other health sectors at both the central and local levels. Most countries are committed to decentralizing dengue prevention and control, along with many

other health activities; however, some programs remain highly centralized, while others have transferred all activities to the local level. Decentralization has been a gradual process: first, contact and exchange between the National Malaria Eradication Service and other health personnel at the central and local levels are increased; next, funding and authority are transferred to the Area Offices. In the Ministry of Health's organizational chart, the Service stops being autonomous, becomes parallel to other divisions, and nearly always changes its name (such as to the Division for the Control of Vector-borne Diseases) or becomes a department in another division, such as the Division of Epidemiology.

In the final stage, dengue is no longer dealt with by one division, and there is no longer a division or department devoted solely to handling vector-borne diseases. For example, in this final scenario, the Division of Epidemiology is responsible for surveillance, the Division of Personal Health deals with diagnosis and treatment, and the Division of Environmental Health is charged with vector control. The area offices are totally integrated with the regional health centers and administrated by them. The central offices retain a technical and normative function, but not an administrative one.

Unfortunately, the responsibilities for dengue prevention and control is often passed on to the local level without funding and without proper training of local personnel. Along with decentralization of functions and responsibilities must come the decentralization of resources, knowledge, and managerial skills.

The central level itself should promote the decentralization process. Clear-cut definitions must be made of those functions that are under the responsibility of the central level (e.g., technical expertise and guidelines) and those that pertain to the local level (e.g., administration, operations). Occupational profiles must be prepared, and workers must be trained in technical and managerial skills.

### **Cooperation within the Health Sector**

The cooperation of other Ministry of Health departments and other health-related organizations with the dengue prevention and control department is necessary at both the central and local levels. At the central level, dengue prevention and control is not the responsibility of a single

department. Within the Ministry of Health, collaboration is essential among those departments responsible for vector control and surveillance, epidemiologic surveillance, clinical diagnosis and treatment, health education, community participation, and environmental health, as well as with the legal department. In addition, alliances may be formed among groups working with different diseases. For example, in Panama, the dengue and cholera education campaigns were combined: "Avoid cholera with personal hygiene; avoid dengue with environmental hygiene."

Other health entities, such as the national health institutes and the schools of public health also have an important role to play, and can sometimes carry out activities that the Ministry of Health cannot, such as research projects.

At the regional and local levels the dengue program becomes part of the local health systems, wherein lies the responsibility for the planning, execution, and evaluation of the dengue surveillance, prevention, and control program at the local level.

### **Intersectoral Cooperation**

Successful dengue surveillance and responsive dengue control are highly dependent on the careful coordination between the Ministry of Health and other ministries and government agencies and the private sector, nongovernmental organizations (NGOs), and local communities. In emergency situations, intersectoral cooperation becomes critical, as sparse or widely-dispersed human and material resources must be pooled and coordinated in a rapid effort to stem mortality and the spread of the disease.

Intersectoral cooperation involves at least two components, resource sharing and policy adjustment among the various ministries and nongovernmental sectors.

#### ***Resource Sharing.***

Resource sharing should be sought wherever the dengue control coordinator can make use of under-utilized human resources (e.g., prison labor to manufacture needed tools, seasonal government laborers for water supply improvement activities, or community or youth groups to clean up discarded tires and containers in neighborhoods); unused serviceable equipment (e.g., four-wheel drive vehicles, backpack sprayers), or stored sup-

plies with a limited shelf life (e.g., appropriate insecticides). (Also see the section "Development of Control Programs," beginning on page 39.)

#### ***Policy Adjustment.***

The dengue control coordinator and Ministry of Health should seek out a mutual accommodation or adjustment of existing policies and practices of other ministries, sectors, or municipal governments to include public health as a central part of the goals of those sectors and ministries. For instance, the public works sector could be encouraged to adjust its policies to give a first priority to water supply improvements for those communities at highest risk of dengue. In return, the Ministry of Health could authorize the use of some of its field staff to assist the Ministry Responsible for Public Works in repair of water supply and sewerage systems in other urban areas.

#### ***Opportunities and roles for other ministries and sectors in dengue control.***

The following examples show how several government ministries may contribute towards the dengue and dengue vector control efforts.

**Role of the Ministry Responsible for Public Works.** The Ministry Responsible for Public Works and its municipal counterparts should play a key role in dengue control, because they can carry out "proactive" source reduction by providing safe, dependable water supply, sanitation, and solid waste management systems to all planned communities. In addition, through the adoption and enforcement of housing and building codes, a municipality may mandate the provision of utilities such as individual household piped water supply or sewerage connections, and rainwater (stormwater) runoff control, for new housing developments, or forbid open surface wells.

Cities might emulate Singapore, where the modernization of decaying urban areas specifically incorporated an *A. aegypti* control goal. As long as all affected populations (e.g., displaced persons) in the urban renewal zone are reimbursed fairly and in a timely fashion for lost property and business opportunities and are provided with improved housing and related social services, the community can view urban renewal with great enthusiasm and can benefit from a reduced risk of dengue and of mosquito and other pest infestations.

**Role of the Ministry Responsible for Education.** Where dengue control and dengue vector control



programs involve a health education (health communication) component targeted to school children, the Ministry of Health should work closely with the Ministry Responsible for Education to devise and communicate appropriate health messages.

Health education models can be jointly developed, tested, implemented, and evaluated for various age groups. Research programs in universities and colleges can be encouraged to include components that produce information of direct importance (e.g., vector biology and control, case management) or indirect importance (e.g., improved water supplies, educational interventions to promote community sanitation, waste characterization studies) to dengue control programs. The section on "Community Participation and Health Promotion," beginning on page 44 discusses health education interventions in more detail.

**Role of the Ministry Responsible for Tourism.** The Ministry of Health should coordinate in advance with the Ministry Responsible for Tourism as to how to properly communicate outbreak or epidemic alert messages to tourists and the hotel industry in a timely manner. The Ministry Responsible for Tourism can work with the Ministry of Health and tourist industry to promote educational messages about dengue control among both tourists and the communities near the tourist resorts.

**Role of the Ministry Responsible for the Environment.** The Ministry of the Environment can help the Ministry of Health collect data and information on ecosystems and habitats that occur in or around cities at high risk of dengue. Data and information on local geology and climate, land forms, forest cover, surface waters, and human populations are useful in planning control measures for specific ecosystems and habitats. The Ministry Responsible for the Environment also may be helpful in determining the beneficial and adverse impacts of various *A. aegypti* control tactics (chemical, environmental, and biological).

**Cooperation with NGOs.** Nongovernmental organizations (NGOs) can play important roles in promoting and implementing environmental management for dengue vector control, most often involving health education, source reduction, and housing improvement related to vector control. Community NGOs may be informal neighborhood groups or formal organizations such as private voluntary organizations, service clubs, church and religious groups, and environmental and social action groups.

After proper training by Ministry of Health staff

in source reduction methods, NGOs can collect discarded containers (tires, bottles, tins, etc.), clean drains and culverts, fill depressions, remove abandoned cars and roadside junk, and distribute sand or cement to fill treeholes. NGOs also may play key roles in the development of recycling activities to remove discarded containers from the yards and streets.

These organizations also may be able to play a specific, but as yet unexplored, role in environmental management during epidemic control. Under guidance from the Ministry of Health, NGOs could concentrate on the physical control of locally identified, key breeding sites such as water drums, waste tire piles, and cemetery flower vases.

Service clubs such as the Rotary Clubs in Puerto Rico and Panama have provided money, advertisements, and political support to successful community-based source reduction campaigns; while women's clubs in Indonesia have contributed to *A. aegypti* control by conducting household inspections for foci and carrying out source reduction.

There are opportunities, mostly untapped, for environmental organizations and religious service groups to play similar roles in each *A. aegypti*-infested community.

**Cooperation with the Community-at-large.** The community's cooperation and direct participation provide a necessary counterpart to the government's efforts. (The community may consist of neighborhood groups or the formal organizations referred to previously.) The following are two examples of the community's cooperation with the Ministry of Health in dengue and dengue vector control:

**Clean-up Campaigns.** These are the most frequent form of voluntary cooperation between the community and the Ministry of Health. Some key factors for success of campaigns include extensive advertisement in the media, proper planning, pre-campaign evaluation of the number of foci, execution as promised to the community, and follow-up evaluations. Clean-up campaigns are discussed in more detail in the section on "Environmental Management," beginning on page 49.

**Novel Approaches to Cooperation with the Community.** In a unique case in China, the Government offered so-called "dengue insurance," whereby participants who bought the insurance from the Government were required to inspect their premises for foci and potential foci, and to destroy any larvae found. In turn, they were paid a set fee

towards medical care if they contracted dengue. The accumulated insurance funds also were used for vector control. Although this particular model has not been tried in the Region of the Americas, it should be noted that this type of cooperation, where both parties clearly benefit, can build mutual trust and respect between the general public and the Ministry responsible for dengue control.

### Community Participation and Health Promotion

Community-based health interventions can be effective environmental sanitation strategies for the reduction of vector densities. Material and information inputs, must be strategic tools, and must reflect the problems and priorities as defined by the community.

The following three conclusions can be drawn from previous experiences with community participation and health education in integrated *A. aegypti* control:

- Community participation in dengue prevention and control activities can enhance support for program activities, bring about behavioral changes, and lead to a reduction in larval indices. Although not a panacea, community participation and health communication should be well-developed components of all dengue control programs.

- Most community participation programs are built on one of two models—a *public health approach* or a *community development approach*—each with strengths and limitations that need to be explored.

- Communication programs also fall into two groups—*health education or health information approaches* and *health communication approaches*. The latter should complement traditional information-based programs.

Although four basic types of community participation may be considered—participation in decision-making, in implementation, in benefits, and in evaluation—traditionally, community participation in *A. aegypti* control programs has been actually limited to participation in implementation and benefits.

The community's participation in *A. aegypti* control almost always involves activities to control the vector's larval habitats; this may include the removal or destruction of cans, bottles, and other

sundry discarded items; storing containers so that they will not collect water; and covering potable water collections such as rainwater drums, wells, and cisterns to physically exclude mosquitoes. These source reduction efforts are frequently organized as periodic clean-up campaigns, and may be initiated through a process of social mobilization utilizing the mass media, community talks, school-based programs, legislative and policy reform, and various other strategies. Communities also can be encouraged to participate in searches for aquatic foci, by providing rewards or negative sanctions to households, and they can help to develop communication programs.

The following two approaches towards public participation in health programs have been described:

#### *The Public Health Approach*

With the public health approach, communities become involved primarily to assist in the control of *A. aegypti*. Experts such as vector control specialists, epidemiologists, and social scientists define, manage, and evaluate public participation in these activities. Advocates of this approach state that communities can best be mobilized by making them aware of the threat DHF poses to them and, especially, to their children, as well as by making them aware of how the infection is transmitted, of the vector's life cycle and main breeding sites, and how the threat of DHF can be reduced by having everyone take personal responsibility for eliminating mosquito production sites on their property. For adherents of the public health approach, knowledge is the key to behavior change, and great efforts are made to ensure that knowledge reaches people through such efforts as special classes in schools, community meetings, advertisements, television and radio programs, and pamphlets delivered door-to-door.

The perceptions that the general public and the medical profession have regarding "classical" dengue may confuse the disease with a variety of other diseases such as influenza and measles. Moreover, experiences with mild episodes of dengue fever lead many urban dwellers to conclude that, although it can cause great discomfort for a few days, it is in no way a life-threatening condition. For these reasons, the public health approach may be of limited use, except in those areas where dengue has become a health priority,

is well-known, and is recognized as potentially life-threatening.

### *The Community Development Approach*

In this approach, the community's involvement in *A. aegypti* control and other health activities ultimately aims at not just the control of dengue, but at the development of the community as a whole, with emphasis on self-reliance and planning in response to needs articulated by the community itself. Implicit in this approach is the idea that an awareness of the *A. aegypti* problem will lead to the recognition of or, at least, to a more constructive focus on other community problems such as deficient refuse collection and irregular potable water supply. Improving those services should result in the elimination of larval habitats, with a consequent reduction of *A. aegypti* infestation levels, but this is not always the case. For example, potable water storage vessels may not be eliminated or removed after a community water supply has been installed, especially in the absence of health education. In fact, the opposite may be true if community standpipes are installed instead of household connections, or if intermittent supplies result from periods of low pressure.

The suitability of the community development approach to vector control in a given community seems to depend on the community's various social, cultural, and political features. In small, well-organized, and culturally homogeneous rural settings it may work better than in rapidly changing, socially complex urban and periurban areas. Unfortunately, the latter are usually the areas at greatest risk of dengue transmission.

In *A. aegypti* control projects, a factor that significantly influences the suitability of the community development approach seems to be whether municipal services (refuse collection, wastewater disposal, provision of potable water, vehicle-dispensed spraying of insecticides) are not provided *at all* in the community, or whether they are present, but inadequate. When services are not provided at all, populations appear to be more willing to organize themselves to provide them. When services have been promised or are only partially delivered, populations appear less willing to provide the services themselves.

In summary, variations of the community development approach are appropriate in some situations where prerequisites for the approach are present, (e.g., viable, representative community

organizations, and favorable past experiences with community-based activities). Elsewhere, especially in urban areas, these prerequisites are seldom met.

### *Health Education and Health Communication*

Health education efforts have been successful in raising people's awareness and understanding of *A. aegypti* and dengue, but they have been generally unsuccessful in changing behavior to achieve meaningful reductions in vector densities without the complementary support of community participation strategies.

"Health education" has been a catchall term used to describe all kinds of public information or behavioral change programs. However, the term can mean many things, and it has been applied not only to efforts to communicate with the general public, but to efforts to educate health workers and professionals and to characterize the contents of school curricula and other professional didactic issues.

Given that, the term *public health communication* is preferable for describing health education activities that entail substantial formative research, the incorporation of local knowledge in program design that focuses on establishing a dialogue with the community in order to bring about behavioral change, and substantial monitoring of the program, including pretesting and modifying materials as the program progresses.

This approach, like the community development approach, does not necessarily focus on dengue or impart health information; instead, it may choose to promote other ways to engage a community in activities. A sanitation intervention, for example, might focus on aesthetic goals or simply on the need for organization and action, rather than on the particulars of disease transmission. A simply expressed idea might replace detailed descriptions of larval sites, or all mosquito species or all vermin might be targeted to raise support for the program. In fact, if a single-species sanitation approach to dengue prevention and control were to fail to address, for example, the concerns of a community that is pestered by *Culex pipiens quinquefasciatus*, the program's credibility and the prospects of that community's participation would be greatly diminished. In short, this approach does not assume that knowledge will lead to action, but allows other pathways to be explored.

During the past decade, international health programs in diarrheal disease control, immuniza-

tion, acute respiratory infection, and AIDS have been revolutionized by the move from traditional health education approaches to public health communication approaches. Communication efforts have become increasingly specialized and more professional, as market research and social marketing approaches have replaced information-based didactic approaches with their trademark flannel boards and flip charts. These contemporary efforts involve substantial audience research and extensive pretesting, and have introduced such methods as focus groups, ethnography, and rapid assessment procedures of the public health audience. They have emphasized a new model of communication that is interactive and that focuses on local knowledge and meaning, rather than one that is merely an academic monolog, and that focuses on information from other sources.

Formative research (i.e., basic, background research) that precedes and helps formulate the intervention is very important for interpreting the outcomes. Assessing pre-existing community knowledge and perceptions, significant community divisions and characteristics, and popular forms of participation are all aspects of program design. This information should be collected not only through questionnaires, but through open-ended interviews and other qualitative social survey methods. The elements of this research are:

- Basic, community-relevant information on the community's social and political characteristics and priority health concerns; understanding of dengue and other fevers and related illnesses; knowledge about mosquitoes, their life cycle and their disease threat; and previous experiences with health programs that is collected in an open-ended or semistructured fashion.
- Formative research to document the participation process and the development of the intervention.
- Formal evaluation studies that maximize the potential to learn about the intervention. Such interventions involve multiple sites and collect information about the process of implementation.
- Measures of exposure to the intervention and participation in the program, studied in a way that can be linked to outcome.

#### ***New Approaches to Community Participation in Vector Control***

Experience suggests that programs involving community participation and public health

communication can be effective, if changes are made in the ways both participation and communication are defined and if local governments further commit themselves to addressing community concerns.

#### ***How is Participation Defined?***

Urban and periurban neighborhoods where programs take place are not easily organized; few residents turn out for community meetings and to participate in programs. Instead of envisioning the neighborhood as the community, "action sets" should be used; these are voluntary associations of people who interact daily in work or institutional settings, or who come together for special purposes, such as school or church. Action sets have none of the geographic or cultural implications that the term community has. Rather, they are groups organized around shared purposes. For dengue, these shared purposes will undoubtedly involve an expansion of activities beyond *A. aegypti* control, perhaps to integrated mosquito control activities. School-based programs that target both parents and children have been reported in Puerto Rico, Panama, and elsewhere. Schools can be an effective starting point, but must interact with other community organizations and all households to guarantee coverage.

Limiting the community's participation in dengue control to labor-intensive and nontechnical activities, such as community clean-up campaigns, has greatly reduced the viability of participatory strategies. The fact that nontechnical activities traditionally used in participation programs are perceived by people as low-cost and poor-quality substitutes for services such as spraying with insecticides, have consequences that must be acknowledged. For example, if a ditch is filled in, there will not be an immediate decrease in the local adult mosquito population, whereas if adulticides are effectively sprayed, people will notice at least a temporary decrease in biting rates and may even find dead mosquitoes on their floors. Instead of organizing communities to conduct predefined activities associated with vertical programs, new programs need to incorporate local knowledge and encourage activities commonly found in communities.

#### ***How is Communication Defined?***

Providing information about the seriousness of DHF and its transmission by mosquitoes, as well

as information about the lifecycle and aquatic habitats of *A. aegypti* will remain important, but on its own it is not enough, at least in the short term, to bring about participation and behavioral changes. Information campaigns, even when implemented through community groups, may not be successful. Often, these programs provide little incentive for action, since dengue is not perceived as a significant health risk.

Although education about the mosquito lifecycle and other attributes of the vector is relevant, broader communication activities must be implemented. This communication must provide incentives to participate and must embrace issues related to rapid social change, urbanization, poverty and the environment, new relationships with the government, and individual responsibility. It must identify other incentives for participation in the program and understand the context of program activities.

Because urban environments are diverse, it may appear unrealistic to think about multiple communication activities. First, specific targeting of some audiences is unavoidable. However, by linking communication activities with participation, communities and groups can be involved in the development of their own programs. Group or "action set" development activities, combined with public health communications approaches can provide a powerful synthesis to help shape responses to dengue and *A. aegypti*.

To summarize:

- "Community" types and the social and political environment in which programs take place need to be taken into account when planning participation in dengue control programs.
- Public health communication approaches that incorporate local knowledge and concerns need to be used when developing program goals and plans.
- Programs must contemplate broadening the interventions to include other vectors (comprehensive control) or other problems locally defined as linked to dengue, in order to enlist participation.
- "Participation" must be defined in consultation with the communities themselves, so that control methods that are feasible and have a higher perceived efficacy are chosen.
- Monitoring the intervention, participation, and behavioral changes are essential to improving programs and impact.
- The relationship between the government, the communities, and individuals at risk needs to be clarified as part of the communication activities.

## Legislative Support

In Latin America, norms directed at the control of dengue and/or *Aedes aegypti* usually are part of sanitary codes, broad health laws, and regulations for international sanitary control that apply to any epidemiologic control program.<sup>1</sup> In most cases, these provisions were incorporated in the sanitary codes developed during the 1930s and 1940s, a period when many dengue/*A. aegypti* programs were being implemented. In general, these norms targeted entomological inspection of houses and vehicles, reduction of breeding sites by education, clean up campaigns, and the promotion of cooperation agreements among countries for vector reduction problems in border areas.

### *Characteristics of Dengue/Aedes aegypti Legislation*

Contemporary legislation regarding dengue and/or *A. aegypti* control is articulated through national norms and international agreements. At the national level, most health codes in Latin America include norms related to the control of transmissible diseases, even if they lack specific regulations for dengue. Most of these codes refer to the application of the principles contained in the Pan American Sanitary Code, the International Sanitary Regulations, and the international agreements signed by the country. Most of these provisions, however, fail to implement the principles they embody.

The above-mentioned national legislation deserves some criticism. First, these norms are not very explicit, because, for the most part, they are included in a general regulatory framework, which renders most of them declaratory, at best. In other cases, fines are not compulsory, and remain mostly as remnants of past practice. Furthermore, the enforcement of the regulatory network created by these norms would require well-developed administrative frameworks and human resources.

Even though legislation may lack specific provisions on dengue and/or *A. aegypti* control, sanitary codes contemplate the control of transmissible diseases in international airports, border cities, and ports; the control of vehicles; and the disinfection of areas, buildings, utensils, and other objects

<sup>1</sup>The legislation analyzed in this section was extracted from the LEYES database produced by Health Legislation (HLE), under the coordination of the Health Policies Program (HDD), Pan American Health Organization (PAHO).

exposed to contamination. These laws mandate that every person in the community allow inspectors to enter premises suspected of posing risks to health, and request compliance from individuals and institutions regarding the inspector's decisions. Most Latin American health codes include such provisions.

Legislation in the Caribbean is mainly concerned with eliminating, from any land or premises, conditions that cause or may cause breeding of mosquitoes in general, without referring specifically to dengue. As indicated above, this legislation contemplates the mandatory entry of health inspectors to premises to search for and destroy any larvae or adult mosquitoes, and to treat these premises with insecticides. However, the health officer is required to give a resident previous notice. This legislation also requires that any water containers be capable of being emptied and, in some cases, requires that aircraft and ships be disinfected upon arrival. Penalties are provided for non-adherence to these requirements.

Latin American legislation specifically related to dengue and/or *A. aegypti* control was structured mainly through regulations and ministerial resolutions aimed at modifying the strategic orientation of programs. In general, these norms envisioned the implementation of programs directed to that aim and the development of units specially charged with their implementation, requiring public and private companies working with huge amounts of water to take the necessary measures for avoiding mosquito breeding and to implement other prophylactic measures.

Other provisions require that *A. aegypti* eradication programs be implemented in ports and airports and that vessels and vehicles coming from abroad be inspected and fumigated, and prohibit introducing used tires into the country without previous fumigation, keeping used containers and recipients that are not properly cleaned, and storing materials that can generate breeding sites. There also are norms that require citizens to cooperate with health authorities in the implementation of prophylactic activities, and to allow access to sites and premises for the implementation of such measures.

Some of the above-mentioned provisions are accorded the status of norms of public order. Many others include in their text a variety of fines to individuals and institutions, or refer to sanctions contained in criminal codes, as is the case in Cuba, Nicaragua, Panama, and Singapore. However, use of sanctions may work as a deterrent to long-term

community cooperation, and carry the risk of corruption. Home visits or periodic household inspections combined with education, but without the use of fines, have proven to be effective in *Aedes* control in West Java, the Dominican Republic, and urban areas in Fiji.

Other enforcement methods that may be considered are:

- Ordinances that require the mosquito proofing of cisterns, water-storage tanks, wells, and septic tanks, as in Bombay.
- Ordinances that authorize the removal of junk cars and other scrap, after proper notification.
- Ordinances that authorize the posting of "No Dumping" and "No Littering" signs and civil penalties for violators.
- Ordinances that require homeowners to keep their yards free of junk, litter, and potential foci, under threat of civil penalty.
- Ordinances requiring mandatory household collection of solid waste for all neighborhoods.
- Statutes (i.e., laws) that require certification of imported tires as being dry and pest-free upon arrival in port.
- Laws that require disinfection and disinsection of aircraft arriving from infested countries.

#### ***Guidelines for the Formulation of Legislation on Dengue/Aedes aegypti Prevention and Control***

The following guidelines for the formulation of legislation on dengue/*A. aegypti* control are recommended:

1. Legislation should be a necessary counterpart of all the actions promoted and implemented by dengue/*A. aegypti* prevention and control programs.
2. All existing decrees and resolutions on dengue/*A. aegypti* prevention and control must be reviewed, and their effectiveness must be evaluated in terms of the structural, institutional, and administrative changes that have occurred in the last years and of the strategies proposed for program organization. It also is important to add dengue to the list of diseases that require mandatory notification in each country.
3. Regulations should be formulated on the basis of existing sanitary codes, a strategy that is most needed in those countries that lack legislation on the subject. For implementing this task, a small *ad hoc* group should be constituted to advise the Ministry of Health. In countries where sanitary regula-

tions are primarily the responsibility of agencies other than the Ministry of Health (e.g., municipal governments), a coordinated and cooperative line of action with the Ministry should be developed.

4. Legislation should incorporate the municipal authorities from the affected regions, in order to make them the central element for its implementation and enforcement. Where national legislation is weak or absent, municipal governments may consider the adoption of local ordinances for *A. aegypti* control.

5. Legislation should contemplate intersectoral coordination among the ministries involved in national development, in order to prevent the isolated implementation of their individual programs and harmful environmental changes that could create potentially hazardous public health conditions. These ministries should be advised on the best ways to encourage disease prevention.

6. Legislation should cover all aspects of environmental sanitation, in order to effectively contribute to the prevention of all transmissible diseases such as dengue, Chagas' disease, and cholera.

7. Laws should contemplate the existing judicial-administrative framework in the context of the national public administration. Importance also should be placed on norms aimed at developing human resources within the institutional framework.

8. In developing legislation, the social component must be considered. Legislation should seek support based on justice and justification: individuals and the community must be persuaded that the law is good and that it is intended to protect them and their families, and that compliance with it is one of the most important components for dengue control.

## Vector Control Methods

### Environmental Management

*Environmental management* is any change in the environment that prevents or minimizes vector propagation or man-vector-pathogen contact. The control of *A. aegypti* in Cuba and Panama in the early part of this century was based mainly on environmental management, and numerous programs in the Americas are returning to this basic tactic. Environmental management also is part of the set of control measures currently being applied against *A. albopictus* in the United States. Many of

these measures are applicable to regions in which dengue is endemic.

The World Health Organization has defined the three kinds of environmental management:

- Environmental modification: long-lasting physical transformations to vector habitat, such as improved delivery of potable water in the case of *A. aegypti* control.
- Environmental manipulation: temporary changes to vector habitat that involve the management (covering, protecting) of "essential" containers; proper storage, recycling, or disposal of "nonessential" containers; and management or removal of "natural" breeding sites.
- Changes to human habitation or behavior: efforts to reduce man-vector-pathogen contact, such as screening of windows and use of mosquito nets and repellents.

### Methods for Environmental Management

The main environmental methods used to control *A. aegypti* and *A. albopictus* and reduce man-vector contact are naturalistic methods, improvement of water supply, solid waste management, modification of man-made breeding sites, improved house design, and personal protection. Table 16 presents a summary of the major environmental management methods used for control of the immature stages of dengue vectors.

**Naturalistic Interventions.** Naturalistic methods involve changes to the natural environment designed to suppress the abundance of immature stages of vector mosquitoes. These measures may be either long-term, which are based on filling or draining of potential aquatic breeding sites for the vector, or short-term. On occasion, *A. aegypti* may breed in newly-constructed or abandoned septic tanks or latrines, and this may be prevented by draining or filling.

More temporary naturalistic measures may include landscaping efforts to remove the vegetation that provides shade, food, or water collection that might contribute to the abundance of these vector mosquitoes; vegetation near the home may influence the abundance of *A. aegypti*. Where possible, brush should be cut back or removed from the immediate vicinity of homes. Treeholes and other natural rainwater receptacles should be filled with concrete, sand, packed earth, gravel, or other suitable materials. Stumps and other vegetation near houses that could become foci should be removed, or at least cut back annually.

**Table 16. Environmental measures for the control of *Aedes aegypti* production sites.**

Production site	Clean	Cover	Store under roof	Modify design	Use EPS <sup>a</sup> beads	Fill (sand/soil)	Collect—recycle/dispose	Puncture or drain
Useful:								
Water storage tank/cistern	+	+		+	+			
Drum (40–55 gal)	+	+		+	+			
Flower vase with water	+					+		
Potted plants with saucers	+							
Ornamental pool/fountain	+							
Roof gutter	+							
Animal water container	+							
Nonessential:								
Used tires		+	+			+	+	
Discarded large appliances							+	
Discarded buckets (< 5 gal)			+				+	+
Tin cans							+	+
Natural:								
Treeholes						+		
Leaf axils								
Rock holes						+		

<sup>a</sup>Expanded polystyrene.

### Improvement of Water Supply and Storage.

One of the keys to the control of urban *Aedes* vectors, particularly *A. aegypti*, is improved domestic water supply. The mere *delivery* of potable water to neighborhoods or individual homes is not sufficient to reduce the use of the water storage containers that play such an important role in *A. aegypti* production in many cities. For example, piped water is supplied to the municipality of Phanus Nikhom in Thailand; yet, an average of 8.2 water storage jars are still kept by each household. Similar behavior has been reported in the Caribbean. Household water storage practices continue because city water supplies are problematic. With household water storage come concomitant problems such as improperly covered storage containers, which have been recognized as a measurable risk factor for dengue infection in Mexico.

The message is clear: potable water must be delivered in sufficient quantity, quality, and consistency year-round, in order to reduce the use of major breeding sites such as drums, overhead tanks, and jars. Individual household piped water supplies are the preferred alternative to the use of wells, communal standpipes, rooftop catchments, and other water delivery systems.

Water storage systems can be designed to prevent *A. aegypti* oviposition or adult emergence. In Sarawak, Malaysia, a mosquito-proof rainwater collection and storage container is made of high-density polyethylene plastic, with a fiberglass screen in the lid that allows rainwater to enter but prevents adult mosquitoes from emerging.

Storage tanks, drums, and jars should be covered with tight lids or screens, although this simple task is difficult to achieve, because most people fail to do it regularly and because existing lids and screens do not work well when misused by owners. Some scientists believe that the use of screens to protect stored water is a futile exercise, because the owners fail to inspect and maintain such devices, and because they tear and disintegrate with age and in harsh climates.

The use of expandable polystyrene beads in pit latrines for control of another mosquito, *Culex pipiens quinquefasciatus*, has been successful in several localities worldwide. Apart from their use in excreta disposal systems, it has been suggested that they may be effectively used in water tanks where the water is drawn off from below and not dipped out from above. Trials for control of *A. aegypti* using expandable polystyrene beads are being made in India, and are being considered for Latin America and the Caribbean. Expandable polystyrene beads have been successfully used in control of *A. albopictus* in septic tanks in Malaysia.

Educating the community in the importance of the proper use of water containers is essential. Competitions can be staged with prizes awarded for the best locally-designed lids and screens made of locally available and inexpensive materials for each of the various types of water storage containers used in the community.

**Solid Waste Management.** Vector control efforts employing solid waste management protect public health and conserve natural resources. Proper



storage, collection, and disposal of solid wastes protects the public health, while the reduction of the generation of wastes, reuse, and recycling conserve natural resources. Both approaches require community education and participation. Solid waste management for successful vector control consists of three aspects: waste reduction, recycling and re-use; collection; and appropriate disposal.

*Waste reduction, recycling, and reuse.* Solid waste reduction—the reduced generation of containers and other solid wastes—is achieved by encouraging manufacturers to package their products in smaller and in fewer packages, and by encouraging the consumer to buy the products with less packaging or to buy reusable products or products made from recycled materials. Waste reduction practices can be targeted against those discarded containers that have been identified as the most important mosquito production foci in the community.

In order to plan and target the recycling or reuse of containers that function as important foci, one should first characterize the waste stream of the target community by surveys of discarded items found in three general sites:

- residential yards and household compounds,
- streets and vacant lots,
- refuse bins, at curbside and office buildings, containing properly collected waste.

The waste characterization survey may be quantitative or qualitative. The survey may use data taken from the vector control program (Breteau index, container index), or consist of simple observations of the types and numbers of discarded containers seen in yards and streets. More formal tools to characterize wastes found in the waste stream and in landfills are given in the American Society for Testing Materials' "Method for Characterization of Municipal Solid Waste."

In order to encourage recycling, each type of discarded container targeted for control must have a real value in the marketplace, or an artificial value must be created for the containers (e.g., beverage container deposit laws). Once the value is created, the market for the containers will arise. Public health officers are often short-sighted about the potential to recycle such items as tires and discarded containers for vector control. However, recent studies in Africa have shown that strong local markets for waste materials have been found. For example, 142 plastic processing facilities alone are found in Nigeria, mostly in the large cities.

Informal economic markets (also known as parallel, underground, or black markets) have great economic importance for the lives of Latin America's urban masses. Many of the important, high-volume commodities in these underground markets are discarded items that are recycled or reused. The potential role of the informal market in urban *Aedes* control efforts is virtually unexplored. In one successful community-based clean-up and recycling campaign in Cali, Colombia, children collected discarded containers and other wastes from homes and streets, that were then sold to recyclers, and the funds generated were used to pave roads in the community. This type of activity may be well received in many neighborhoods. However, the encouragement of markets for recyclables should be accompanied by community education about the proper storage of recyclables (e.g., bottles) around the house, so as not to create more foci of vectors which would offset the gains made by promotion of recycling.

*Collection.* Containers should be easy to handle, easy to clean, and be equipped with tight-fitting lids. Solid waste should be placed in plastic bags, which are a widely available commodity in many Latin American and Caribbean cities today, and stored in proper refuse bins. This will reduce the dispersal of garbage into street gutters and drains, where urban *Culex* mosquitoes may be produced when such sites are blocked with refuse.

Frequency of collection is extremely important in urban mosquito vector management. Twice-weekly pickups are recommended for housefly and rodent control in warm climates. Collection services must cover all areas of the municipality, not only wealthy neighborhoods. Some detailed project manuals for proper environmental management of urban solid waste in developing countries are available for use by municipalities.

The use of ground or aerial surveillance photographs of neighborhoods should be explored as possible tools to evaluate the efficacy of collection programs and clean-up activities (e.g., one should take "before" and "after" photographs of clean-up campaign sites), general neighborhood sanitation, and to detect improper accumulations of discarded containers, tires, and other debris in residential yards and on rooftops, streets, and vacant lots.

Special collection days should be established for bulky items such as discarded refrigerators, stoves, junk cars, large tires, and other large scrap, which incidentally serve as *Aedes* breeding sites. These can be separate activities, or may be part of

park, beach, and neighborhood clean-up campaigns. If collection services are reliable, the development of "critical points" of refuse accumulation (i.e., clandestine dumping sites, such as vacant lots, street gutters, ravines, and stream and river margins) are reduced; otherwise, periodic clean-up campaigns and extensive community education will be necessary.

**Appropriate disposal.** Solid waste can be composted, shredded (e.g., junked cars), incinerated, or disposed of in sanitary landfills. All solid waste, especially tires and bulky waste, should be placed at the lowest point of the slope ("toe") of the daily cell in use at the landfill, and properly buried with at least 15 cm of compacted soil at the end of each day. In small communities, manually operated small landfills can be used. One can use construction/demolition wastes (e.g., broken concrete, asphalt, brick, and stone) as cost-effective material to fill earthen depressions. Because waste tires and used tires are such important production sites for dengue vectors, their management and disposal are discussed separately.

**Tire Management.** Waste tires are of critical importance to urban *Aedes* control, and there is no lack of waste tires in urban areas—200 million used tires enter the waste stream each year in the United States alone. Waste tire stockpiles are a significant public health (vectors) and safety (fire hazard) concern in cities, and imported used tires are believed responsible for the introduction of *A. albopictus* into the United States.

Tires may be treated with insecticides, salt, or soap for chemical control of immature mosquitoes. In Latin America, a certain percentage of the tires are reused (after recapping) or recycled into new rubber products, but many are simply illegally dumped or disposed of in landfills.

New technologies for tire reuse and disposal are continually coming into use, but most of them have proved to be of limited application or cost-effectiveness. Waste tires can be filled with earth or concrete and used for planters or traffic/crash barriers. They may be used as soil erosion barriers, or used to create artificial reefs and reduce beach erosion by wave action. Tires can be recycled into soles for sandals, floormats, industrial washers and gaskets, buckets and garbage pails, and carpet backing. Used truck tires have been made into durable, low-cost refuse containers.

Used tire rubber can be combined with virgin rubber or plastic chips to make injection-molded and extruded plastic products, such as rubber roof shingles, automobile fan belts, railroad crossing,

and truck bed liners. Crumb rubber is mixed with asphalt (asphalt rubber) to pave roads, seal road cracks and roofs, and line man-made ponds and lagoons, and tires are chipped or shredded for use as roadbase in road construction in flooded areas.

Tire disposal by incineration can take the common form of backyard or neighborhood tire pile burning, or proper incineration in waste transformation facilities (incinerators, cogeneration plants, cement kilns). Pyrolysis of tires (exposure to high heat in the absence of oxygen), an experimental technology, can generate oil that can be sold to be blended with fuel oils, and char that can be added to plastics.

If cut laterally into halves or chipped, tires can be mixed with other wastes and buried normally in a sanitary landfill. They may be safely disposed of in landfills by placing them at the toe of the daily cell and covering them with two m of soil, to avoid their "floating" upwards under compaction where they can disrupt soil cover. Waste tires may also be buried together in a separate place in the landfill (monofilling) under deep soil cover.

**Modification of Other Miscellaneous Man-made Production Sites.** Fences and fence posts made from hollow trees such as bamboo should be cut down to the node, and concrete blocks or broken glass bottles should be filled with packed sand, crushed glass, or concrete to remove potential *Aedes* foci. Tires and collections of other potential foci stored outside should be properly covered by a tarpaulin or placed in a shed. Buckets and other small containers should be inverted, if stored outdoors.

Flower pots for both live and artificial flowers should be punctured to produce drain holes. Alternatively, live flowers can be placed in a mixture of sand and water. Otherwise, all flowers should be removed and discarded weekly, and the vases scrubbed clean before reuse. Plants being propagated, should not be placed in water for rooting. A new commercial product with the trade name Water Crystal<sup>®</sup>, which is an acrylamide copolymer gel (not to be mistaken for unpolymerized acrylamide compounds, which are highly neurotoxic), is now used by gardeners in the United States for the rooting of plants, replacing open water in pots and flower containers. It may prove useful in the control of flower vase foci of *A. aegypti* in the house, but this has not been evaluated yet. Brass flower pots, which make poor larval habitats, can be used in cemeteries in place of traditional concrete or clay containers for live flowers.

Ant traps to protect food-storage cabinets can be

filled with oil or salty water, instead of fresh water. Condensation collection pans under refrigerators and air conditioning units should be inspected, drained, and cleaned regularly or, if made of plastic, have salt added. Floor drains and toilet flush tanks, should be inspected, cleaned or treated regularly, and kept covered at all times. Overflow pipes should be routinely inspected, and the pipe ends should be screened. Roof gutters and outdoor sinks, laundry basins, etc. should be inspected and cleaned of leaves and debris regularly. Ornamental pools and fountains can be regularly drained and scrubbed, chlorinated, or stocked with larvivorous fish.

**House Design.** Wherever possible, housing should be designed to minimize entry opportunities for mosquitoes. This measure would help reduce human-vector contact and, thereby, the risk of dengue. Housing design considerations include the construction of roofs without open eaves and the use of screened doors and windows.

**Personal Protection.** Personal protection measures have been used extensively in efforts to protect indigenous and rural people against malaria. Pyrethroid-impregnated bed-nets or curtains show real promise against the nocturnal vectors of this infection. In the case of the more diurnal *Aedes* vectors of dengue, however, such measures may have little relevance. Barriers may be erected to protect special groups of people such as the bed-ridden, infants, or night-workers.

Tourists or other temporary visitors to an endemic area may be protected by the use of repellents. Their clothing can be impregnated with DEET or other repellents and permethrin. In certain cases, repellent saturated anklets, wristlets, headbands, and detachable patches placed on exterior clothing may be useful. Where the traditional use of local herbs and plant oils as repellents is effective, such practices should be encouraged.

One common form of personal protection, the home use of insecticide sprays, apparently reduced the risk of dengue in Mexico.

### Conclusion

Environmental management should focus on those man-made containers and natural breeding sites that produce the greatest number of adult *Aedes* in each community. These foci can be targeted for destruction, alteration, disposal, or recycling. While working for the control of man-made and natural breeding sites of dengue vectors, one should simultaneously work to modify

human behavior through health education and public health communication, in order to reduce the number of breeding sites produced by the community.

The participation of the community in the planning, execution, and evaluation of container management programs (e.g., regular household sanitation and clean-up campaigns) is a necessary prerequisite for sustainable control of dengue vectors. The community also should participate in the evaluation of the results of the container management programs.

### Chemical Control

Chemicals have been used for the control of *A. aegypti* since the turn of the century. In the first campaign against yellow fever in Cuba and Panama, in addition to clean-up campaigns, breeding sites were oiled and houses were dusted with pyrethrin powders. When the insecticidal properties of DDT were discovered in the 1940s, this compound quickly became the method of choice for Hemisphere-wide *A. aegypti* eradication programs. When resistance to DDT began to appear in the 1960s, organophosphate insecticides had been developed and fenthion, malathion, fenitrothion and temephos came into use for *A. aegypti* control. The current trend is to restrict the use of chemicals for treatment of containers that cannot be otherwise eliminated or managed, and for emergency situations.

### Description of Methods

The methods for the application of insecticides for the control of *A. aegypti* are larviciding, perifocal treatment of containers, and space-spraying operations.

**Focal Control of Production Sites.** Larviciding or "focal" control of *A. aegypti* is usually limited to domestic-use containers that cannot be destroyed, eliminated, or otherwise managed. There are three insecticides that can be used for treating containers that hold drinking water:

- One percent temephos (Abate) sand granules applied to the containers using a calibrated plastic spoon to administer a dosage of 1 ppm. This dosage has been found to be effective for 8-12 weeks.
- The insect growth regulator methoprene (Altosid) is used in the form of briquets.
- BTI (*Bacillus thuringiensis* H-14).

All of these larvicides have extremely low mammalian toxicity and properly treated drinking water is safe for human consumption.

**Perifocal Treatment.** Hand or power sprayers are used to apply wettable powder or emulsifiable concentrate formulations of insecticides as peripheral sprays in and around containers. This will destroy existing and subsequent larval infestations, as well as adult mosquitos that frequent the sites. The method consists basically in the treatment of all containers of the type preferred by *A. aegypti*, whether they hold water or not, spraying the walls of the container both externally and internally so that they are completely covered by a residue of insecticide. In addition, spraying is extended to cover any wall within 60 cm of the container. The surface of nonpotable water in containers also is treated. The insecticides presently used are malathion, fenitrothion, fenthion, and some pyrethroids. Containers holding drinking water should be covered to prevent mosquito breeding or treated with insecticides considered safe for use in drinking water.

**Space Sprays.** Space spraying involves the application of small droplets of insecticide into the air in an attempt to kill adult mosquitoes. When space sprays are employed, it is important to follow the instructions on both the application equipment and the insecticide label. There also are several other factors that should be understood, if the equipment is to perform efficiently and be used safely. Droplets that are too small tend to drift beyond the target area, while large droplets fall out too fast and are not effective. Nozzles for ultra-low volume ground equipment should be capable of producing droplets in the 5 to 27 micron range and the mass median diameter should not exceed the droplet size recommended by the manufacturer. Generally, there are two forms of space-spray used for *A. aegypti* control.

**Thermal fogs** produced by special equipment in which the insecticide, usually mixed in an oil with a suitably high flashpoint, is vaporized by injection into a high-velocity stream of hot gas. When discharged into the atmosphere, the oil carrying the pesticide condenses in the form of a fog. Malathion, fenitrothion, fenthion, and some pyrethroids in diesel oil are commonly used in thermal fogging operations.

**Ultra-low volume (ULV) aerosols (cold fogs and mists,** involve the application of a small quantity of concentrated liquid insecticide. The use of less than 4.6 liters/ha (0.5 gal US per acre) of an insecticide concentrate is usually considered as ULV

**Table 17. Selected insecticides for use as cold fogs against *Aedes aegypti*.<sup>a</sup>**

Classes/Insecticide	Dosage (grams of active ingredient per hectare)
Organophosphates	
Malathion	100–500
Fenitrothion	200–400
Naled	56–280
Pirimiphos-methyl	230–330
Pyrethroids	
Deltamethrin	0.5–1.0
Resmethrin	7–16
Bioresmethrin	5–10
Permethrin	5–10
Cypermethrin	2– 8
Lambda-cyhalothrin	0.5–2.0

<sup>a</sup>Adapted from (PAHO 1982) and (WHO 1984).

application. Selected insecticides for use as cold fogs against *A. aegypti* are presented in Table 17. Aerosol mists and fogs may be applied by portable machines, vehicle-mounted generators or aircraft equipment.

**House-to-House Applications using Portable Equipment.** When the area to be treated is not very large, or in areas where vehicle-mounted equipment cannot be used, portable back-pack equipment can be used to apply insecticidal mists. Operators can treat an average of 80 houses per day, but the weight of the machine and the vibrations caused by the engine make it necessary to allow the operators to rest, so two or three operators are needed per machine.

**Street Applications using Vehicle-mounted Equipment.** Vehicle-mounted aerosol generators can be used in urban or suburban areas with a good road system. One machine can cover up to 1,500–2,000 houses (or approximately 80 ha) per day. It is necessary to calibrate the equipment, vehicle speed, and swath width to determine the coverage obtained by a single pass. A good map of the area showing all roads is of great help in carrying out operations. A major educational effort may be required to persuade the residents to cooperate by opening their doors and windows.

The speed and time of application are important factors to consider when insecticides are applied by ground vehicle. The vehicle should not travel faster than 16 kph (10 mph). When the wind speed is greater than 16 kph or when the ambient air temperature is greater than 28°C (82°F), the insecticide should not be applied. The best time for application is in early morning, (approximately 0600–0830 hours) or late afternoon (approximately 1700–1930 hours).

In most Latin American countries, the vehicle circles every block, to ensure that no blocks are missed and to achieve the greatest possible proximity of the spray machine to each house. Treatment in this manner with a vehicle speed of 10 kph and discharge rate of 127 ml per minute results in a dosage of 305 ml per ha, if the city blocks are 100 m on each side. Treatment by the "zig-zag" method in only one direction (e.g., north on the first street, south on the next, without treatment of the streets running east-west) results in only one-fourth as much insecticide being applied per ha. The effectiveness of ULV application for emergency control is discussed in the section on "Emergency Vector Control," beginning on page 69.

**Aerial Application.** Aerial spraying is often used in emergency situations when an extensive area must be treated in a short time. Although the equipment used (aircraft equipped with a spray system) may have a high initial cost, this form of application may be cost-effective since very large areas can be treated in a single morning.

The insecticides that can be used in aerial ultra-low volume applications are malathion, fenitrothion, naled, pirimiphos-methyl, resmethrin, cypermethrin, lambda-cyhalothrin and deltamethrin. Unless there is an indication of resistance, or unless other insecticides are more readily available, a ULV formulation of malathion at 220 ml/ha to 440 ml/ha (3 to 6 oz per acre) is recommended.

The treatment parameters for the aerial application of insecticides vary according to the types of aircraft, insecticide, and equipment used. The altitude of the aircraft should be between 30 to 65 m (90 to 150 ft) and aircraft speeds should be between 160 kph and 260 kph (100 mph and 162 mph). Swath widths will vary according to the altitude and wind. Early morning applications are preferable to application at any other times of day. Temperatures should be below 27°C (80°F) and wind velocity below 16 kph (10 mph).

**Aircraft Disinsection.** Freon-based aerosols are used for disinsection of aircraft to satisfy international regulations. Suitable aerosols are 2% formulations of the pyrethroids resmethrin, bioresmethrin, or phenothrin. Residual pyrethroids (e.g., permethrin) also may be used.

#### **Equipment for Insecticide Application**

**Equipment and Characteristics.** The following estimates have been made of the average coverage per day with certain aerosol and thermal-fog producers, from both the ground and the air:

Twin-engined aircraft or large helicopter:	6,000 ha
Light, fixed-wing aircraft or small helicopter:	2,000 ha
Vehicle-mounted cold-fog generator:	80 ha
Vehicle-mounted thermal fogger:	80 ha
Back-pack ULV mist blower:	5-30 ha
Hand-carried thermal fogger:	5 ha

**Calibration and Maintenance.** For reasons of efficiency and safety, the equipment used for the application of insecticides should be calibrated in order to assure the delivery of the appropriate droplet size and dosage as recommended by the manufacturer. Maintenance of the equipment is required for the same reasons mentioned above, and, particularly, to maintain operational readiness.

#### **Guidelines for Programs**

**When to Use Chemical Control.** The indiscriminate use of insecticides for dengue prevention and control should be discouraged. During periods of little or no dengue activity, routine source reduction measures described in the section on "Environmental Management," beginning on page 49, can be integrated with larvicide application in those containers that cannot be eliminated, covered, filled, or otherwise managed. In order for emergency control to suppress an ongoing dengue epidemic or to prevent an imminent one from occurring, the objective is the rapid and massive destruction of the *A. aegypti* population. This is the *only* situation where aerosol generators, either mounted on vehicles or aircraft, should be used, because reductions of *A. aegypti* populations from ULV applications are never 100% and usually last only 5-10 days.

**Safety Precautions.** All pesticides are toxic to some degree; consequently, several major safety precautions must be followed, including: care in handling pesticides, particularly regarding spraymen, and in carrying out applications in and around occupied residences.

A safety plan for insecticide application can be organized along the following lines:

- Spraymen should be provided with at least two uniforms to allow for frequent changes. Special safety gloves and masks should be used for machine calibration.
- Washing facilities with enough water and soap should be made available in appropriate locations.

- All working clothes must be removed at the end of each day's operations and a shower or bath taken.
- Working clothes must be washed regularly, the frequency depending on the toxicity of the formulation.
- Particular attention should be given to washing gloves. Wearing contaminated gloves may be more dangerous than wearing no gloves at all.
- Spray operators must wash before eating.
- Smoking during work hours must be strictly forbidden.
- Monitoring of blood cholinesterase levels should be undertaken if organophosphate insecticides are used.
- When work involves insecticides of relatively high toxicity, the hours of work must be arranged so that exposure to the material being used is not excessive. Transportation should be organized so that there is not a long delay between the end of the day's operations and the return to base for washing.
- Care must be taken for the safe disposal of used insecticide containers.

Specific guidelines on insecticides and safety procedures are found in the World Health Organization's "Chemical Methods for the Control of Arthropod Vectors and Pests of Public Health Importance" and "Safe Use of Pesticides, Fourteenth Report of the WHO Expert Committee on Vector Biology and Control."

**Insecticide Susceptibility Monitoring.** During the last 40 years, control of mosquitoes and other insects of public health importance has been achieved mainly by chemical methods. Insecticide pressure has resulted in widespread resistance in many vector species. Temephos and malathion resistance in *A. aegypti* is widespread throughout the Caribbean and in some countries of Central and South America. There also are reports that in a few countries the vector has already developed resistance to fenitrothion. Consequently, it is advisable, whenever possible, to obtain baseline data before control operations are started and to continue monitoring susceptibility levels on a periodic basis. WHO kits are available for testing insecticide susceptibility of adults and larvae of mosquitoes and other insect vectors. These can be obtained from the Division of Control of Tropical Diseases, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland, or through the PAHO/WHO Representation in each country.

Recent developments in biochemical methods

for determining the mechanisms of resistance in individual mosquitoes permit early detection of the presence of low levels of resistance. They also enable predictions to be made of the cross-resistance spectrum with other insecticides that have the same resistance mechanisms, allowing for resistance management by rotation of applied insecticides.

### Biological Control

Anti-dengue interventions based on the introduction of living organisms that will prey upon, parasitize, compete with, or otherwise reduce the abundance of *A. aegypti* or *A. albopictus* remain largely experimental, or are restricted to small-scale field operations that supplement other measures. Larvivorous fish and the biological insecticide *Bacillus thuringiensis* H-14 (BTI) are the two kinds of organisms most frequently employed, and some predaceous copepods appear promising.

The advantages of biological control measures include an absence of chemical contamination of the environment, specificity of activity against target organisms (the effect of BTI, for example, is limited to mosquitoes and related Diptera), and self-dispersion of certain of these agents into inaccessible sites that could not be easily treated through other means. The disadvantages of these measures include the expense of rearing the organisms, difficulty in their application and rearing, and limitation of utility in aquatic sites where temperature, pH, and organic pollution meet narrow specifications.

A disadvantage of biological agents employed against mosquitoes is that they are only employed against the immature stages. A reduction in larval numbers does not always result in a corresponding reduction of potential for disease transmission because if food is limited, lowering of larval densities may produce larger, healthier adults that can transmit virus over a longer period of time.

### Fish

Various fish can be used to eliminate mosquitoes from larger containers used to store potable water. These include *Gambusia affinis* and *Poecilia spp.* These and other fish may be potentially used where their introduction can be maintained and where the human population does not object to the presence of such obvious organisms in their domestic water-storage containers. Local, endemic

larvivorous fish species also may be evaluated for efficacy against *A. aegypti* larvae.

### *Toxorhynchites*

Although various larval mosquitoes feed on other mosquitoes, *Toxorhynchites* mosquitoes have two advantages as predators: they develop in the same kinds of containers as *A. aegypti*, and they do not feed on blood. Field trials have produced mixed results. On Union Island in Saint Vincent and the Grenadines, adult emergence was reduced when larval *Toxorhynchites* were introduced by hand, but the effect on adult abundance was not recorded.

In Indonesia, sustained release of first instar predatory larvae into virtually all household water storage basins failed to reduce the abundance of adult *A. aegypti*. This lack of effect may have been due to an inability of first instar *Toxorhynchites* larvae to survive in the absence of small prey.

### *Hormone Mimics*

Methoprene now promises to be the most environmentally acceptable larvicidal chemical usable against mosquitoes. The apparent absence of mammalian toxicity of this synthetic juvenile hormone mimic permits its use in potable water.

### *Cyclopoids*

Certain ubiquitous cyclopoid copepods ("water fleas") prey on newly hatched larvae. If the mosquitoes develop to the third instar, however, they are too large to be attacked by these minute predators. In Rongaroa (French Polynesia), *Mesocyclops* was used in larvicidal interventions against *A. aegypti* and *A. polynesiensis*. Crab-hole applications reduced the abundance of adult *A. polynesiensis* by about 76%. In Colombia, the abundance of copepods in natural settings inversely correlates with the abundance of larval anopheline mosquitoes. Cyclopoid copepods appear to limit naturally the abundance of certain kinds of mosquitoes. In a New Orleans (U. S. A.) trial, *Macrocyclus albidus* was most voracious killing virtually all freshly hatched, larval *A. albopictus* under all experimental conditions. Conditions have been standardized for the production of large masses of predatory copepods based on the use of protozoal infusions as food.

Not all copepods destroy mosquitoes. Predation efficacy of several different cyclopoids has been

tested in various kinds of containers, but no *Culex*, *Orthopodomyia*, or *Toxorhynchites* were killed. In order to select a suitable match of predator and prey, a routine was developed for comparing the efficacy of cyclopoids as predators of mosquitoes, based on predation efficacy and rate of increase at 30°C, the temperature of natural breeding sites.

Preliminary results from field trials of various species of copepods against either *A. aegypti* or *A. albopictus* in Australia, Brazil, China, Honduras, Tahiti, and the United States are encouraging. Suspensions of these organisms are applied as appropriate by means of a coarse-nozzled sprayer. The technology is "appropriate" and costs appear to be modest. Little environmental or toxicological risk is evident.

Certain drawbacks of a copepod release program have been identified. First, those cyclopoids that up to now have been used to this end do not resist desiccation. They must be reapplied frequently if the climate is arid or seasonal evaporation is high. Various *Macrocyclus* and *Acanthocyclops* species, however, can resist extended periods of drying. Second, because they kill only newly hatched larvae, BTI (discussed below) must be included in the formulation, unless the development and emergence of later instars is acceptable. Third, they are subject to human interference in certain target containers, (e.g., whole populations may be lost when water storage dams are cleared out or emptied). Finally, the main effect of a cyclopoid application effort is delayed, occurring only after some subsequent rainfall when a new lot of eggs hatch. In the event that the breeding site becomes too dry for the copepods to survive, the treatment will fail. Although highly promising, the practicality of these biological agents in anti-dengue interventions remains to be established.

### *Bacteria*

BTI, which was discovered in the 1970s, is a proven, environmentally nonintrusive mosquito larvicide that appears to be entirely safe for people. This fermentation product of *Bacillus thuringiensis* H-14 is the most acceptable material currently on hand for use against mosquitoes. It has become commercially available under such trade names as Teknar, Vectobac, and Bactimos, and can be purchased in lots of up to one-quarter of a million pounds. The large parasporal body that forms in this agent contains a toxin that degranulates solely in an alkaline environment, and only nematoceros Diptera have alkaline midguts. The

advantage of this material is that an application destroys larval mosquitoes but spares any entomophagous predators that may be present. However, BTI formulations tend to settle to the bottom of a water container soon after they have been applied. The toxin also is photolabile, and so is destroyed by sunlight. This forces frequent applications. Weekly visits to each breeding site may be required, thereby incurring unusual expense. Briquet formulations are particularly suitable for potable water.

*Bacillus sphaericus* is even more focused in its toxicity; larval *Culex* mosquitoes are highly sensitive to this material, but other kinds of mosquitoes that have been tested are not. This material is not suitable for use in a dengue campaign.

### Recommendations for Use of Biological Control

- The microbial pesticide *Bacillus thuringiensis* H-14 is a proven adjunct to a dengue control program. Preparations are commercially available and can be applied with confidence in drinking water. Briquet formulations can provide long-lasting protection.

- Copepods can be sprayed into small collections of water and may prove effective in destroying newly hatched dengue vectors. This method seems promising for dengue interventions.

- The use of small, omnivorous fish has a proven place in dengue programs in which the vector breeds in large, relatively permanent containers of water.

- Indiscriminate application of insecticide should be avoided, in order to preserve natural predators of adult and larval mosquitoes.

### Integrated Control

Integrated vector control is the rational combination of all available control methods in the most effective, economical, and safe manner to maintain vector populations at acceptable levels.

The 1981 *A. aegypti* eradication campaign in Cuba combined source reduction and modification

of drinking water storage tanks with a variety of other interventions, including sanctions, health education, biological control, and chemical control. This effort yielded remarkably low densities of this vector mosquito.

Control of *A. aegypti* can be combined with the control of other vectors, such as *Culex pipiens quinquefasciatus*, as it was done in urban Suva, Fiji Islands (1978–1979), urban Tanzania (1972), and Singapore (1978–1980s). The Suva program consisted of area clean-up campaigns, house inspections, ULV spray of malathion, threat of legal action, and health education. Monthly inspections were a major adjunct in reducing larval indices. The Tanzania program combined source reduction, public education, and clean-up campaigns, which led to reduced indices for both *A. aegypti* and *Culex pipiens quinquefasciatus*.

The joint *A. aegypti* and *A. albopictus* control program in Singapore consisted of slum clearance, resettlement of the displaced persons, source reduction by uniformed health officers, drain cleaning, mosquito-proofing of water tanks, health education, and strict enforcement, including large fines (US\$ 500) and/or 3-month jail sentences. As a result, the *Aedes* house index was reduced in the slums from 27.2% of houses infested during 1966–1968, to 5.4% in 1969 after slum clearance and resettlement, and to 1.6% citywide in 1981. The Singapore program cost US\$ 1–1.50 per person per year, and resulted in a reduced incidence of dengue, and lower densities of both *Aedes* and *Culex pipiens quinquefasciatus*.

Environmental management of dengue vectors can be successfully combined with health education and public health communication, where source reduction activities are promoted by local health care systems workers. For example, local health clinic workers trained primary school teachers and volunteers from women's clubs in Indonesia to recognize dengue cases and to implement source reduction of *A. aegypti*. The three main indices of *A. aegypti* infestation were reduced between 27% and 80%, within 6 months after implementation of the campaign.



## 6. EMERGENCY PREPARATION AND RESPONSE

Despite ongoing eradication or control programs, most countries in the Region that have been reinfested with *A. aegypti* have experienced at least one epidemic of dengue. Obviously, the programs are not achieving their purpose, and more outbreaks can be expected in the future, probably with ever-increasing frequency and with greater numbers of DHF cases. The objective of emergency control operations is to halt the epidemics altogether, or at least, to diminish their intensity.

Dengue outbreaks are frequently not recognized as such until cases reach into the thousands, and then the response is usually too little and too late to significantly alter the epidemic's course. For example, during the 1977-1979 dengue 1 pandemic in the Caribbean, northern South America, Central America, Mexico, and Texas (U. S. A.), most countries had many months of warning that this virus was moving from country to country, but were unable to prevent it from causing epidemics in their own; almost without exception, the emergency measures were begun too late and were insufficient to significantly reduce the numbers of cases. The same was true from 1986 to 1990 in Puerto Rico, Bolivia, Paraguay, Ecuador and Peru.

### Forming an Emergency Committee

The main reason that responses to a dengue outbreak fail is lack of preparedness. Obviously the best preparation is an effective, sustainable, routine program to keep mosquito infestations below levels that would permit epidemic transmission. If this is impossible, emergency preparations are necessary. Each country should establish an emergency committee charged with preparing an emergency plan (see Annex IV) and that meets periodically to revise the plan and to monitor the epidemiologic and entomological situation. Alternatively, a modified national cholera committee may be considered for the emergency control of and for monitoring dengue.

Before an outbreak occurs or during the inter-epidemic period, the emergency committee analyzes the dengue control program's capabilities in terms of personnel, equipment, insecticides, and rapid response. Maps should be prepared and periodically updated to show the areas considered to be at highest risk (see the section on "Risk Factors for Dengue and Dengue Hemorrhagic Fever," beginning on page 19). The insecticide susceptibility status of the potential vectors should be monitored; necessary supplies and equipment should be ordered, and a special fund should be designated for emergencies and reserved solely for that purpose; other national and international agencies that could assist during an emergency should be identified. "Contingency" contracts should be made with pest control and agricultural aerial spray companies in case their services are needed. Personnel with potentially important roles during an epidemic should be given special training through courses and simulation exercises. Pilot studies should be carried out to evaluate the control methodology under existing local conditions. Continuous epidemiologic surveillance for detection of introduced dengue, appearance of DHF, or an increase in cases is of paramount importance (see the section on "Disease Surveillance," beginning on page 23), as is educating the medical community to recognize and treat DHF/DSS cases and preparing a plan for hospitalization, both of which will be treated in more detail further in this chapter.

### The Alert Phase

An "alert" may be declared when an emergency appears imminent. Increased incidence, an epidemic in a neighboring country, or detection of a new dengue serotype are all criteria that can be used. At that juncture there is still time to implement more effective measures of source reduction and larviciding before the epidemic develops.

## Declaring an Emergency

The criteria for determining whether a given situation is an "emergency" varies from country to country and from one year to the next in each country. For example, in a country free of the vector, the discovery of an established infestation may be considered an emergency. In another country that has high infestation indices but without previous experience of dengue, the appearance of only a few cases could represent an emergency. In a country where dengue is endemic, a significant increase in incidence or the appearance of DHF or of a different virus serotype should be deemed an emergency. The appearance of a single case of urban yellow fever, which is also transmitted by *A. aegypti*, would be alarming and would result in declaring a public health emergency in most countries. It should be noted that the earlier the emergency is declared, the more effective the control measures will be in preventing epidemic transmission and severe disease.

## The Emergency Phase

Once the emergency has been officially declared, the activities foreseen in the emergency plan should be implemented. All concerned government agencies and the general public must be kept continually informed of the situation and requested to assist in the control activities. Human resources, equipment, and supplies must be mobilized. A map showing the location of known cases and areas considered to be at risk can be used to target areas to be treated with insecticide, but, in general, the high mobility of patients makes it necessary to treat very large areas, preferably an entire city.

## Education of the Medical Community

Because programs to prevent and control dengue/DHF will take several years to implement and refine, an epidemic of DHF may occur before the program is fully developed. It is necessary, therefore, to design and initiate a program to educate physicians on the clinical diagnosis and treatment of DHF as early as possible. Properly implemented, this will result in low case fatality rates, will improve the efficiency of the surveillance system, and will provide an important group of well-informed and highly-respected individuals who

can be instrumental in educating patients and their community about DHF prevention.

The medical community can be educated about dengue in several ways—through seminars and workshops on clinical diagnosis and treatment, as well as on epidemiology, surveillance, prevention and control of DHF. These seminars and workshops should be conducted at regular intervals in hospitals, clinics, and medical association meetings by dengue/DHF experts. An extension of this approach can use a process known as "peer education," whereby local, highly-respected physicians are recruited and trained in all aspects of the disease, and move on to become DHF experts. These local authorities then conduct seminars on DHF for peers in their communities or their professional associations.

For all seminars and workshops, high-quality visual aids should be produced and distributed to the speakers. In addition, handouts such as brochures, pamphlets, and booklets should be professionally prepared for distribution to participants. These should also include materials that physicians can give to their patients and/or family members (see Annex V).

A 30-minute video on the clinical diagnosis and treatment of DHF has been prepared and is available in both Spanish and English. This video is an excellent educational tool and should be made available to all hospitals and medical associations. Information about obtaining the video can be obtained from the Pan American Health Organization or the Centers for Disease Control and Prevention.<sup>1</sup>

In summary, the DHF prevention and control program will only be effective if the local medical community is knowledgeable about the disease and how to prevent it. It is recommended that a major effort be made early in the program development to educate and use this important segment of the community.

## Organization and Requirements for Medical Care

Within the above-mentioned emergency committee, a central organizing or coordinating committee, consisting of administrators, epidemiologists, clinicians, health educators, and laboratorians, should

<sup>1</sup>Requests should be addressed to PAHO, Division of Communicable Diseases, 525 Twenty-third St., N.W., Washington, D.C. 20037, U.S.A., or CDC, National Center for Infectious Diseases, San Juan Laboratories, 2 Calle Casia, San Juan, Puerto Rico 00921-3200.

be established to facilitate interdisciplinary and interagency communication; the responsibility for establishing this committee usually falls with the Ministry of Health. The committee should: 1) design and distribute appropriate protocols for the diagnosis and treatment of DHF/DSS; 2) compile and distribute appropriate literature on DHF/DSS; 3) prepare and circulate educational material directed towards both health workers and the public; 4) plan and implement training programs for health care workers and auxiliaries (e.g., hospital staff, medical students, nurses, and laboratory technicians); 5) assess the need for intravenous fluids, medications, blood products, intensive care equipment, teaching materials, and equipment for transporting patients; 6) supervise the use of supplies and the outcome of the clinical care program (on a daily basis, if required); and 7) coordinate clinical research on DHF/DSS during the outbreak.

It may be necessary to provide *additional beds* for observation at outpatient departments and at inpatient wards for the acute care of patients; initially, some of those beds assigned to nonessential care (e.g., elective surgery) may be taken over for this purpose. Moreover, it may be necessary to set up temporary care facilities in schools or other institutions, but this should be considered only if appropriate medical personnel and a laboratory capable of performing reliable hematocrits and platelet count determinations are available, since microhematocrit determinations are essential for monitoring therapy and its success. *It is recommended that all institutions that provide care for DHF patients have microhematocrit equipment and microscopes for platelet estimation.*

During an epidemic, outpatient and inpatient facilities may be overwhelmed with cases, and medical care staff can rapidly become exhausted. In these circumstances, it is essential that only persons who genuinely require hospital care be admitted. A fever and positive tourniquet test are sufficient for DHF to be suspected; a microhematocrit and platelet count should be done in the *outpatient department*. Patients with thrombocytopenia and elevated hematocrit should be sent to a specially-established *rehydration ward* or, if circulatory failure is suspected, they should be hospitalized. Patients who live far from the hospital and who have no accommodations nearby may have to be admitted for observation. Patients or their relatives should be carefully instructed that prompt return to hospital is necessary should restlessness, lethargy, acute abdominal pain, oliguria, or circumoral cyanosis be observed (see Annex V).

With proper training, paramedical workers can

triage patients. Competent laboratory assistance is desirable, but, even without a laboratory, patients can be evaluated by physical examination. Cool extremities, skin congestion, circumoral cyanosis, or a rapid pulse indicate that hospitalization is necessary. If possible, patients should be hospitalized for observation or warned that they should remain near the hospital until two days after the fever subsides.

### **Intensive Care/Special Care Unit**

Patients with similar severity of illness should be grouped together in a semi-intensive care/DHF special care unit, which should be well equipped and managed by DHF trained nurses and personnel. Those with shock require hospitalization and intensive care with 24-hour nursing and physician care. Paramedical workers, medical and nursing students, and even relatives can assist by administering oral fluid therapy or by monitoring the rate of intravenous fluid administration and the general status of rehydration ward patients.

### **Requirements for Inpatient Hospital Facilities**

In a worst-case scenario (e.g., Cuba in 1981), the incidence of seriously ill patients requiring hospitalization may approach 1 case per 100 inhabitants. An overall population of approximately 1 million persons translates into 10,000 persons hospitalized over a 3-month period, or approximately 3,000 hospitalized patients per month.

Even a moderate DHF outbreak, such as the epidemic that occurred in Venezuela in 1989–1990, may significantly affect the health care system, especially if an effective contingency plan is not available. Therefore, each country should evaluate the number of beds available in existing clinical facilities. Based on regional population estimates, contingency plans should be developed to convert school or public buildings to handle an excessive number of patients.

### **Supplies and Equipment**

*For outpatient department/rehydration treatment centers:*

**Diagnostic materials:** sphygmomanometer (adult and pediatric) and stethoscope; thermometers; hematocrit supplies (lancets, capillary tubes,

reader); microhematocrit centrifuge; compound microscope and materials for white blood cell and platelet counts; and vacutainers or syringes/needles for obtaining blood and other diagnostic test samples.

**Therapeutic materials:** Acetaminophen; WHO oral rehydration solution (see footnote 2 on page 66); intravenous fluids (physiological saline, Ringer's lactate,  $\frac{1}{6}$  mol/liter sodium bicarbonate)—Ringer acetate is now available and its use is recommended; and tubing and needles for intravenous therapy.

#### *For hospitals:*

**Diagnostic materials and patient monitoring:** same materials listed for outpatient department/rehydration treatment centers, plus, laboratory test equipment and supplies for blood typing and crossmatching, measuring arterial blood gases and pH, and measuring serum electrolytes; portable x-ray equipment; central venous pressure monitoring kits; arterial pressure and Swan-Ganz catheters and monitoring equipment, where available; and intake-output monitoring charts.

**Therapeutic materials:** same materials listed for outpatient department/rehydration treatment centers, plus colloidal fluids (one or more of the following, fresh frozen plasma, plasma, plasma

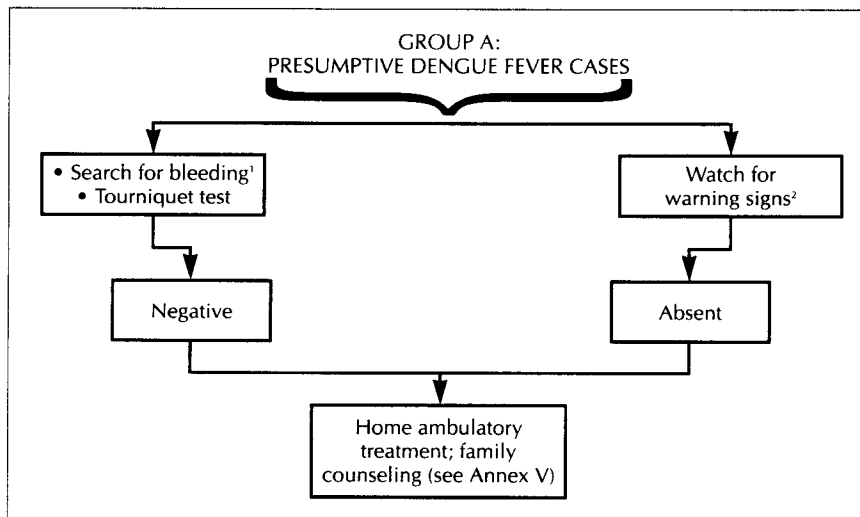
protein fraction [human 5%—Plasmanate], dextran-40, [medium relative molecular mass], whole blood, and platelet concentrate), analgesics (paracetamol), sedatives (chloral hydrate), diuretics (furosemide), and oxygen and delivery system.

Hospitalized patients will require some amount of intravenous fluid therapy with lactated Ringer's or glucose/normal saline. Approximately 20% of all hospitalized patients will require intravascular volume expanders such as dextran 40, plasmanate, or plasma; and about 10% will require the administration of whole blood. The volume of intravenous fluid needed in an individual case will depend on the weight of the patient and the severity of shock. However, assuming that 50% of the patients are children, the following estimate of the supplies required per 10,000 population (100 cases of DHF) in each region can be made: 200–300 liters of normal saline or lactated Ringer's, 200–300 liters of 5% glucose in water, 20 liters of volume expander, and 20 units of whole blood.

### **Case Management: Classification and Treatment of Patients**

The procedure to be followed when patients arrive at a health center is especially important in

**Figure 6. Classification of patients during epidemics of dengue hemorrhagic fever (DHF): Group A.**



<sup>1</sup>In facilities where such tests are routinely available, perform a platelet count and hematocrit, especially after the 3rd day of illness. If platelets are  $\leq 100,000$  mm<sup>3</sup> and hematocrit is high, admit patient to hospital outpatient room or to rehydration ward.

<sup>2</sup>Severe and continuous abdominal pain, persistent vomiting, restlessness or lethargy, sudden decrease in fever, hypothermia, prostration, or fainting.

cases of dengue and DHF. Adequate classification of the patient and adequate clinical observation, as well as timely, correct therapeutic action are essential to saving the patient's life.

This publication describes the different clinical syndromes that may be present in patients seeking medical attention. For each of these, the method for recognizing the case, the laboratory indications, the site for treatment (e.g., ambulatory treatment in the patient's home or in a treatment facility for observation and therapy), and the elements of therapy are presented.

Early recognition of an epidemic is vitally important for achieving timely decision-making and implementing measures directed toward the control of the disease. An epidemic of DHF/DSS should be suspected when an unusually high number of cases with fever and any type of hemorrhagic manifestations are observed. There may be unexplained deaths with or without the presence of hemorrhage and/or patients with nonspecific febrile illness, whose condition, instead of improving on the third or fourth day after onset and/or when fever subsided, deteriorates and results in bleeding or shock.

**Group A: Patients with fever and nonspecific constitutional symptoms.** In these patients, dengue should always be considered in the differential diagnosis (see Figure 6).

*Recognition:*

- Knowledge of the existence of dengue transmission; an increase in cases of fever in the community; presence of the mosquito vector; cases of dengue in the family, school, or work center.

- Clinical picture of dengue fever in adults—fever, joint pain, myalgia, rash, facial flushing, vomiting, abdominal pain, few or no respiratory manifestations.

- Perform a tourniquet test.

- Watch for warning signs (restlessness, lethargy, rapid/weak pulse, narrowing of pulse pressure, hypotension, cold and clammy skin, cyanosis, cold extremities, intense and continuous abdominal pain, persistent vomiting, oliguria).

*Laboratory:*

- White blood cell count (WBC), with complete blood count (CBC) (for differential diagnosis).

- Obtain blood sample for dengue tests (isolation of the virus or serological tests).

*Location of care:*

- Home: ambulatory treatment.

*Immediate treatment:*

- Analgesics and antipyretics (*no aspirin*).

Note: Inform the patient and his/her family of clinical signs that should be checked. Provide a copy of Annex V.

**Group B: Patients with fever, nonspecific constitutional symptoms, and hemorrhagic manifestations.** These patients may be cases of DHF with Grade I or II severity (see Figure 7).

*Recognition:*

- Febrile case with positive tourniquet test, or
- Febrile case with petechiae or other spontaneous bleeding (e.g., gingival bleeding, epistaxis, metrorrhagia, vomiting fresh blood, melena, or other hemorrhage).

*Laboratory:*

- Serial hematocrit to monitor status of hemoco-concentration (at least once daily).
- Serial platelet counts (at least once daily).
- Pleural effusion (verified by x ray).

*Location of care:*

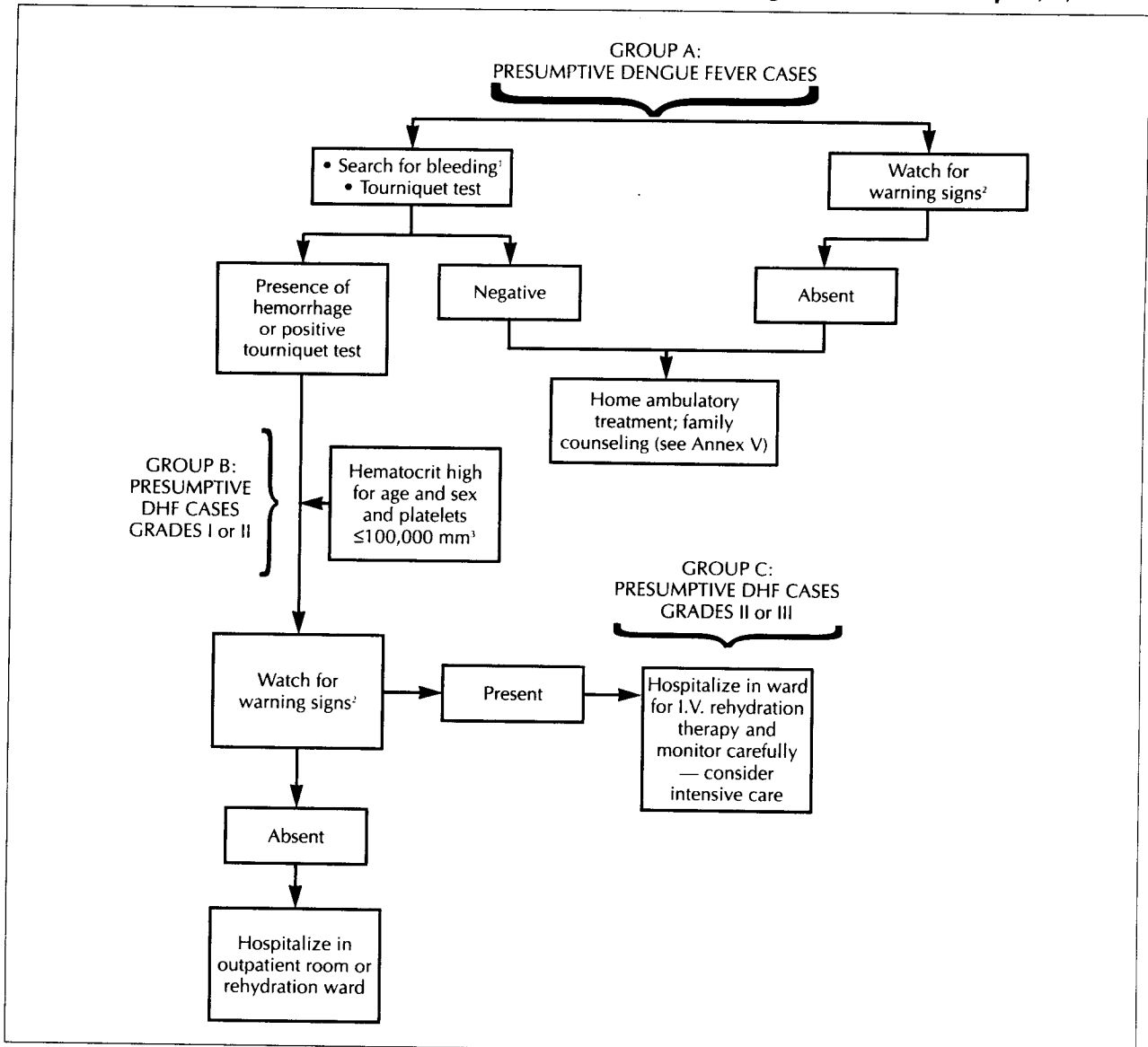
- Outpatient observation room in hospital or rehydration and observation center with conventional treatment (intravascular or oral rehydration solutions).

*Immediate treatment:*

- Comprehensive symptomatic treatment (see next section on the treatment of dengue and dengue hemorrhagic fever without shock beginning on page 66).

- Alert nursing staff to watch for and treat major bleeding and other warning signs: restlessness, lethargy, rapid and weak pulse, narrowing of pulse pressure, hypotension, cold extremities, congested skin, circumoral cyanosis, intense and continuous abdominal pain, persistent vomiting.

Figure 7. Classification of patients during epidemics of dengue hemorrhagic fever (DHF): Groups A, B, and C.



<sup>1</sup>In facilities where such tests are routinely available, perform a platelet count and hematocrit, especially after the 3rd day of illness. If platelets are  $\leq 100,000 \text{ mm}^3$  and hematocrit is high, admit patient to hospital outpatient room or to rehydration ward.

<sup>2</sup>Severe and continuous abdominal pain, persistent vomiting, restlessness or lethargy, sudden decrease in fever, hypothermia, prostration, or fainting.

**Group C: Patients with warning signs, without profound shock.** These patients could be cases of Grade II or III DHF/DSS (see Figure 8).

*Recognition:*

- Intense continuous abdominal pain.
- Persistent vomiting.
- Restlessness or lethargy.
- Sudden reduction in temperature associated with profuse perspiration, tachycardia, and faintness.
- Oliguria.

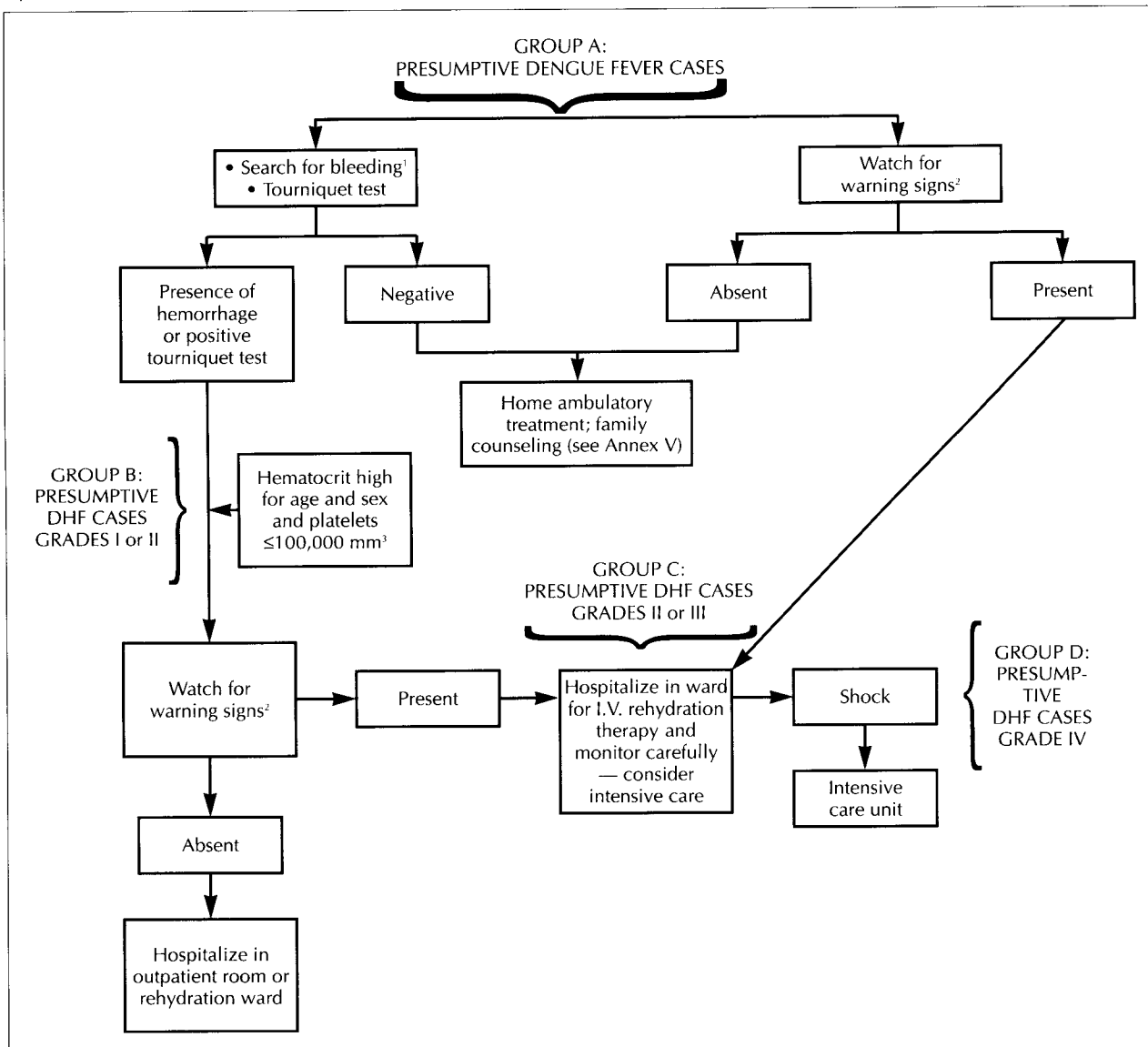
- Presence of cyanosis.
- Frailty and/or hypotension and/or narrowing of the pulse pressure (20 mmHg or less).
- Sudden increase in hematocrit.

Note: Not all signs need to be present. One or two of these warning signs are enough. Generally, but not always, patients have petechiae or other hemorrhagic manifestations upon arrival.

*Laboratory:*

- Serial hematocrit (at least once every 24 hours).

**Figure 8. Classification of patients during epidemics of dengue hemorrhagic fever (DHF): Groups A, B, C, and D.**



<sup>1</sup>In facilities where such tests are routinely available, perform a platelet count and hematocrit, especially after the 3rd day of illness. If platelets are  $\leq 100,000$  mm<sup>3</sup> and hematocrit is high, admit patient to hospital outpatient room or to rehydration ward.

<sup>2</sup>Severe and continuous abdominal pain, persistent vomiting, restlessness or lethargy, sudden decrease in fever, hypothermia, prostration, or fainting.

- Platelet count (at least once daily).
- Hypoalbuminemia or accumulation of fluids in serous cavities; clinical or radiologic signs of ascites or pleural effusion.

*Location of care:*

- Hospitalization for intravenous fluid treatment and close monitoring (rehydration therapy, preferably in an intermediate treatment room).

*Immediate treatment:*

- Intravenous infusions with saline-containing or albumin-containing solutions (see section on the treatment of dengue hemorrhagic fever without shock beginning on page 66).

- Clinical and laboratory monitoring.
- Monitoring for cyanosis.
- Monitoring for shock.
- Do not apply any invasive procedure.

Note: This patient is to be considered in imminent danger of shock. Early treatment for shock at this stage is decisive for the prognosis.

**Group D: Patients with shock.** These patients may be cases of Grade IV DHF/DSS (see Figure 8).

*Recognition:*

- Pulse pressure less than 20 mm Hg.
- Systolic pressure less than or equal to 80 mm Hg.
- Pallor, frailty, perspiration, cyanosis, tachycardia, oliguria.

*Laboratory:*

- Arterial blood gases and other essential studies for a patient in shock.
- Hypoalbuminemia or accumulation of fluids in serous cavities; clinical and/or radiological signs of ascites or pleural effusion.

*Location of care:*

- Immediate hospitalization in the intensive care unit.

*Immediate treatment:*

- Emergency access to one vein for fluid infusion.
- Intravenous infusions with saline-containing or albumin-containing solutions (see the section on the treatment of dengue shock syndrome beginning on page 67).
- Oxygen therapy.
- Monitoring for hematemesis or other massive bleeding.
- Monitoring for respiratory distress.
- Administer whole blood or components when needed.
- Prevention of pulmonary edema.
- Use of corticosteroids or heparin is contraindicated.
- Use of inotropic drugs (e.g., dopamine, dobutamine) is contraindicated while hypovolemia persists.

### Treatment of Dengue and Dengue Hemorrhagic Fever without Shock

High fever, anorexia, and vomiting lead to thirst and dehydration; therefore, copious amounts of

fluids should be ingested by mouth, to the extent tolerated. Solutions for oral electrolyte replacement, such as those employed in the treatment of diarrheal diseases,<sup>2</sup> and/or fruit juices are preferable to plain water.

During the febrile phase there is a risk of convulsions, and in patients with hyperpyrexia, antipyretic medication may be indicated. *Salicylates should be avoided*, since they may cause hemorrhage and acidosis. Paracetamol is preferable, in the following dosages: under 1 year old, 60 mg/dose; 1–3 years old, 60–120 mg/dose; 3–6 years old, 120 mg/dose; and 6–12 years old, 240 mg/dose.

Patients should be closely monitored for the initial signs of shock. The critical period is during the transition from the febrile to the afebrile phase, and usually occurs after the third day. Serial hematocrit determinations are an essential guide for treatment, since they reflect the degree of plasma leakage and the need for intravenous administration of fluids. Hemoconcentration usually precedes the blood pressure and pulse changes. Hematocrit should be determined daily, from the third day and until the temperature has remained normal for 1 or 2 days. If hematocrit determination is not possible, hemoglobin determination may be carried out as an alternative, but this is less sensitive.

Parenteral fluid therapy can be administered in an outpatient department rehydration unit in mild or moderate cases when vomiting produces or threatens to produce dehydration or acidosis or when hemoconcentration is present. The fluid to be administered to correct dehydration from high fever, anorexia, and vomiting is calculated according to the degree of dehydration and electrolyte loss and should have the following composition: 5% glucose in one-half or one-third physiological saline solution (PSS). In case of acidosis one-fourth of the total fluids should consist of 0.167 mol/liter of sodium bicarbonate (i.e. three-quarters PSS plus glucose plus one-quarter sodium bicarbonate).

When there is significant hemoconcentration, i.e., rising hematocrit of > 20% of the baseline value (alternatively, the normal hematocrit value of children in the same age group in the general population may be used to estimate the degree of

<sup>2</sup>If the WHO oral rehydration solution (ORS) (90 mmol of Na per liter) is to be used in children under 2 years old, additional fruit juice or water should be given in the proportion of one volume of fruit juice (or water) for each two volumes of ORS. The WHO oral rehydration solution consists of: 3.5 g sodium chloride, 2.9 g trisodium citrate dihydrate, 1.5 g potassium chloride, and 20.0 g glucose, dissolved in 1 liter of potable water.



**Table 18. Fluid for moderate dehydration (intravenous).<sup>a</sup>**

ml/lb body weight per day	Weight on admission		ml/kg body weight per day
	lbs	kgs	
100	< 15	< 7	220
75	16–25	7–11	165
60	26–40	12–18	132
40	> 40	> 18	88

<sup>a</sup>Adapted from *Pediatr Clin North Am* 11:1093 (1964).

hemoconcentration), the fluids to be used for replacement therapy should have a composition similar to plasma. The volume and composition are similar to those used in the treatment of diarrhea with mild to moderate isotonic dehydration (5–8% deficit).

The solutions used for volume replacement in DHF are the following: Ringer lactate (RL), Ringer acetate (RA); 5% glucose in RL and RA; 5% glucose in PSS, 5% glucose in  $\frac{1}{2}$  PSS, 5% glucose in  $\frac{1}{3}$  PSS; 5% glucose in  $\frac{1}{2}$  RL and  $\frac{1}{2}$  RA; and plasma, plasma substitutes, Dextran 40 (10% Dextran in PSS).

The choice and volume of fluids needed depend on the age and weight of the patient and the degree of plasma loss as reflected by the degree of hemoconcentration.

The schedule shown in Table 18 is recommended as a guideline. It is calculated for moderate dehydration of about 6% deficit (plus maintenance).

In older children who weigh more than 40 kgs, the volume needed for 24 hours should be calculated as twice that required for maintenance (using the Holliday and Segar formula).

The maintenance fluid should be calculated as follows:

Body weight (kgs)	Maintenance volume (in ml)
10	100 kg
10–20	1000 + 50 × kgs (excess 10)
> 20	1500 + 20 × kgs (excess 20)

For a child weighing 40 kgs, the maintenance is:  $1500 + (20 \times 20) = 1900$  ml.

The fluids as listed are calculated for administration over a 24-hour period. Since the rate of plasma leakage is not constant (it is more rapid around the time the temperature drops), the volume of intravenous fluid therapy must be adjusted accordingly to the rate and extent of plasma loss as reflected by hematocrit levels.

Patients should be hospitalized and treated immediately if there are any of the following signs and symptoms of shock: restlessness/lethargy;

cold extremities and circumoral cyanosis; oliguria; rapid and weak pulse; narrowing pulse pressure (20 mm Hg or less) or hypotension; and sudden rise of hematocrit to a high level or continuously elevated hematocrit levels despite administration of intravenous fluids.

## Dengue Shock Syndrome

Shock is a medical emergency. Volume replacement is the most important measure; the immediate administration of intravenous fluid to expand plasma volume, is essential. Children may go into and out of shock during a 48-hour period. Close observation with good nursing care 24 hours a day, is imperative.

### Immediate Replacement of Plasma Loss

Start initial intravenous-fluid therapy with Ringer's acetate or 5% glucose in PSS at the rate of 10–20 ml/kg body weight. Run fluid as rapidly as possible. Positive pressure may be necessary in case of profound shock. If shock persisted after initial fluid resuscitation with 20–30 ml/kg body weight, colloidal solution plasma or plasma expander (10% Dextran of medium relative molecular mass in PSS), should be administered at the rate of 10–20 ml/kg per hour. In most cases no more than 20–30 ml per kg of body weight of plasma or Dextran 40 is needed. In cases of persistent shock after adequate initial resuscitation with crystalloid and colloidal solutions, despite a decline in hematocrit level, significant internal bleeding should be suspected, and fresh whole blood transfusion is indicated. If hematocrit level is still above 40%, a small volume of blood (10 ml/kg body weight per hour), is recommended.

When improvement in vital signs is apparent, the intravenous infusion rate should be reduced; thereafter, it should be adjusted according to hematocrit levels and vital signs.

### Continued Replacement of Further Plasma Loss, Based on Frequent Microhematocrit Determinations

Intravenous administration of fluids (e.g., 5% Dextran, Ringer's lactate diluted 1:2, or PSS diluted 1:2) should be continued even when there is a definite improvement in vital signs and the hematocrit has decreased. The rate of fluid replacement should be decreased to 10 ml per kilogram

per hour, and readjusted thereafter to the rate of plasma loss, which may continue for 24 or 48 hours. The determination of central venous pressure may also be necessary in the treatment of severe cases of shock that are not easily reversible.

Intravenous administration of fluids *should be discontinued* when the hematocrit decreases to a stable level, around 40%, and the patient's appetite returns. Good urinary flow indicates that there is sufficient fluid circulating. In general, there is no need to administer liquids for more than 48 hours after the termination of shock. Reabsorption of extravasated plasma occurs (manifested by a further drop in hematocrit after the intravenous administration of fluid has been terminated), and may cause hypervolemia, pulmonary edema, or heart failure if more fluid is given. It is of the utmost importance that a decrease in the hematocrit in this phase not be interpreted as a sign of internal hemorrhage. Strong pulse and blood pressure (with wide pulse pressure) and diuresis are good vital signs during this reabsorption phase. They rule out the likelihood of gastrointestinal hemorrhage, which is found primarily in the shock phase.

#### ***Other Electrolyte and Metabolic Disturbances That May Require Specific Correction***

Hyponatremia occurs commonly and metabolic acidosis occurs occasionally in DHF patients. Electrolyte levels and blood gases should be determined periodically in severely affected patients and in patients who do not respond as quickly as expected. This will provide an estimate of the magnitude of the electrolyte (sodium) deficit and help determine the presence and degree of acidosis. Acidosis in particular, if unresolved, may lead to disseminated intravascular clotting and to a more complicated course of recovery for the patient. The use of heparin may be indicated in some of these cases, but *extreme caution* should be exercised when it is administered. In general, early volume replacement and early correction of acidosis with sodium bicarbonate results in a favorable outcome and precludes the need to use heparin.

#### ***Sedatives***

In some cases, treatment with sedatives is necessary to calm an agitated child. Hepatotoxic drugs should be avoided. Chloral hydrate, administered orally or rectally, is highly recommended at a dosage of 12.5–50 mg per kilogram of body weight

(but no more than 1 g) *as a single hypnotic dose*. Agitation/restlessness that results from poor tissue perfusion often subsides when adequate liquid volume replacement is given.

#### ***Oxygen Therapy***

Oxygen therapy should be provided for all patients in shock, but it must be remembered that an oxygen mask or tent may lead to increased patient anxiety.

#### ***Blood Transfusion***

Blood grouping and crossmatching should be carried out as a systematic precaution on every patient in shock, particularly in cases with prolonged shock. Blood transfusion is indicated in cases with significant hemorrhagic manifestations.

It may be difficult to recognize internal hemorrhage if there is hemoconcentration. A decrease in the hematocrit—e.g., from 0.5 (50%) to 0.4 (40%)—without clinical improvement, despite the administration of sufficient fluids, indicates significant internal hemorrhage. Fresh whole blood is preferable and the quantity of blood administered should not raise the red blood cell concentration above normal. Fresh frozen plasma and/or concentrated platelets may be indicated in some cases when disseminated intravascular coagulation causes massive bleeding. Disseminated intravascular coagulation is common in severe shock, and may play an important role in the development of massive bleeding and lethal shock. The results of the hematological tests (e.g., prothrombin time, partial thromboplastin time, and fibrinogen degradation products) should be studied in all cases of shock to determine the onset and severity of the disseminated intravascular coagulation. Results of these tests will determine the prognosis.

#### ***Essential Laboratory Tests***

To evaluate the patient's status the following tests are recommended: studies of the serum electrolytes and blood gases; platelet count, prothrombin time, partial thromboplastin time, and thrombin time; and liver function tests—serum aspartate aminotransferase (previously known as serum glutamic oxaloacetic transaminase, [SGOT]), serum alanine aminotransferase (previously known as serum glutamic pyruvic transaminase [SGPT]), and serum proteins.

### Monitoring Anti-shock Therapy

Frequent recording of vital signs and hematocrit determination are important in evaluating the treatment results. If the patient presents some indication of secondary shock, vigorous antishock therapy should be instituted promptly. These patients should be under constant and careful observation until there is reasonable assurance that the danger has passed. In practice:

- The pulse, blood pressure, respiration, and temperature should be recorded every 15 to 30 minutes or more frequently, until the shock has been overcome.
- The hematocrit and hemoglobin levels should be determined every 2 hours during the first 6 hours and later every 4 hours until stable.
- A fluid balance sheet should be kept, recording the type, rate, and quantity of fluid administered, to determine whether there has been sufficient replacement and correction of fluids and electrolytes. The frequency and volume of urine excreted also should be recorded.

### Criteria for Discharging Patients Hospitalized with Dengue/DHF

All of the following six criteria must be met before a patient is discharged.

- 1) Absence of fever for 24 hours without the use of anti-fever therapy (cryotherapy or antipyretics) and a return of appetite.
- 2) Visible improvement in clinical picture.
- 3) Stable hematocrit.
- 4) Three days after recovery from shock.
- 5) Platelet count greater than 50,000/mm<sup>3</sup>.
- 6) No respiratory distress from pleural effusion/ascites.

### Emergency Vector Control

The immediate goal for emergency control of *Aedes aegypti* is to reduce the number of infective mosquitoes as quickly as possible over the affected area. Space spraying by portable mist blowers or thermal foggers, by vehicle-mounted aerosol generators or foggers, or by aircraft-mounted generators are methods that result in rapid coverage of the area and attack the adult mosquito populations.

Although routine antilarval measures do not give immediate control of adult mosquitoes, it should be pointed out that most dengue epidemics last for many weeks. If space spraying is employed early in the epidemic, thereby delaying some portion of the transmission, this will give time for larviciding and community-based source reduction to have an effect. *Therefore, at the same time that the emergency space-spraying is initiated, source reduction measures should be intensified.* During an epidemic, the public is generally more responsive to calls for help in eliminating larval habitats and to using household aerosol cans.

There has been considerable controversy concerning the efficacy of vehicle and aircraft ultra low volume (ULV) applications for control of dengue emergencies. Recent studies have reconfirmed that ULV application of malathion at the standard dosages of 220–440 ml/ha (3–6 oz/acre), as described in the section on chemical control, beginning on page 53, results in a partial and temporary reduction of the adult female and male populations of *Aedes aegypti*. Depending on local conditions and the number of cycles, this reduction may be minimal or substantial (e.g., 30%–90%), but it never reaches 100%, and complete recovery of the vector population is usually observed within 1 or 2 weeks.

It is difficult to determine if emergency measures have had an impact on the course of an epidemic, because we do not know what would have happened had there been no ULV intervention. There is no well-documented example of interruption of an epidemic in the Americas. However, any control method that reduces the number of infective mosquito adults, even for a short period of time, should reduce virus transmission during that time. Annex IV presents considerations for emergency vector control.

### Misconceptions Concerning Natural Disasters

Natural disasters, such as earthquakes, hurricanes, floods, and volcanic eruptions, usually do *not* constitute an immediate emergency for vector-borne disease, but they should be considered an “alert” situation. The initial effect of these disasters is to *reduce* vector densities by wind action and flooding of the breeding places. Many human dwellings also are eliminated, which reduces the physical protection and eliminates many surfaces that had been sprayed with residual insecticide. Regular, routine vector control programs are generally in chaos from the effect of the disaster, and

their health personnel may be required to serve on more urgent activities, such as rescuing and caring for injured persons. The first priority in vector control is to reestablish the regular program as soon as possible and to evaluate the entomological and epidemiologic situation. When floodwaters recede, ground pools become production sites for anophelines and culicines, and containers strewn

about the landscape become breeding sites for *Aedes*. Until the interrupted piped water supply is reestablished, people will store water in containers and *Aedes* indices will gradually increase. These are problems that can be best resolved by reestablishing a safe, dependable piped water supply and the routine control program, not with emergency measures.

## 7. EVALUATION OF PREVENTION AND CONTROL PROGRAMS

### Epidemiologic Evaluation

The purpose of epidemiologic evaluation is to ensure that valid and useful evaluation results are readily available to influence policy and program decision-making. The strategy should be designed to help identify those programs to be evaluated, and, when this should occur, what methods should be used and how the evaluation results should be used.

Evaluation planning should be forward-looking and systematic rather than *ad hoc*. To anticipate future information needs, action must be taken to ensure the production of timely information specifically useful for measuring program performance. As programs are evaluated at different stages of their development, program effectiveness data can be incorporated into planning and budget proposals. Evaluations should be designed so as to produce information that can assess the program's contribution.

### Evaluation Planning

One way to approach program evaluation is to subject each program (or project) to a set of questions that describe the program in evaluation terms, determine its evaluation history, and identify additional information for evaluation needs. The following questions suggest information that could be collected to plan for future evaluations.

- 1) Are goals/objectives clearly stated?
- 2) Do goals/objectives directly relate to the program's mission?
- 3) Does the program's design set forth sound reasons to expect success?
- 4) Is the program being correctly implemented? What is the cost of implementation?

5) Are there significant changes in program direction or policy that influence the effectiveness of the program or components?

6) What evaluations have been completed?

7) What is the nature and quality of the data and/or information on the program's success?

8) Is there evidence of the relative cost-effectiveness of specific programmatic activities?

9) What evidence is there that evaluation information is used in managing the program?

10) What do evaluations reveal about the effectiveness of the overall program or specific activities?

11) What additional evaluation information is needed at this time?

12) What are the future plans for evaluating the program?

The answers to these questions will suggest the types of evaluations that should be planned. Overall, evaluation studies are either formative—which focus on the structure and process of a program—or summative—which focus on the outcomes of a program. Within these general categories, there are many types of studies and methods, but four basic types are of most importance.

▪ **Evaluability assessment**—designed to examine the readiness of the program, particularly new programs, for process and/or outcome evaluation. Programmatic inputs are examined, and an assessment is made of the links between program activities and outcomes. The evaluability assessment provides an understanding of the mechanics of the program, identifies the stakeholders, examines the program objectives and indicators for success, and results in immediate feedback for program improvement.

▪ **Process evaluation**—carried out at some time in the program's life to determine how and how

well the delivery goals are being met. The basic questions are: "Is the program reaching the appropriate targets/clients?" and "Is program implementation consistent with program design?" This type of evaluation may involve surveys, record keeping, or direct observation.

- **Outcome evaluation**—conducted at intervals during an ongoing program to identify program consequences and to establish that the consequences are attributable to the program. It is important to document whether or not the program makes a difference or what program activities work better. Outcome evaluations usually involve randomized designs and experimental methods.

- **Economic evaluations**—consist of comparative analyses of various courses of action, in terms of their costs and their consequences. The important question to answer is "What is the value of the outcome in comparison with the resources required?" The basic types of economic evaluations are cost-minimization analysis, cost-benefit analysis, cost-effectiveness analysis, and cost-utility analysis.

The use of evaluation results must be part of the evaluation's design and implementation. Several suggestions for increasing the relevance of an evaluation include:

- 1) Involve program managers and decision-makers during the design's planning stages, to make sure that the questions asked satisfy their information needs and that planned approaches will yield usable results.
- 2) Make sure that the evaluation results are timely, in other words, that they are available when needed for policy and program decision-making.
- 3) Present the final report and recommendations in a style and a format that are compatible with the experience, skills, and interests of users.
- 4) Provide clear-cut recommendations that can be implemented in the near future, not several years later.
- 5) Insure that the evaluation and recommendations are feasible and credible.
- 6) Make the final report and recommendations acceptable (i.e., avoid criticism and remain sensitive).

Dengue/DHF is a disease in which prevention of human infection depends on controlling the mos-

quito vector. Consequently, there must be epidemiologic evaluation of the control program, including several components such as proactive surveillance, educational activities, and mosquito control. Entomological evaluation is covered in the section beginning on page 73, and will not be discussed here. Evaluation of educational materials and/or programs is complicated and involves the use of social scientists. Only surveillance evaluation will be briefly discussed here.

Evaluation of the surveillance system should concentrate on defining the sensitivity of the surveillance system and its flexibility during periods of high and low transmission. The evaluation itself should enhance the surveillance system's use, promote its expansion within the health services to make it representative of the population being monitored, and make it more acceptable to its users.

Evaluation of a dengue surveillance program involves a close working relationship between epidemiologists and the diagnostic laboratory, which determines whether the cases reported as dengue are, in fact, dengue cases or cases of another clinically related illness. Evaluation, based on laboratory testing, should continue during both inter-epidemic and epidemic periods, and, when properly used, will generally document under-reporting during periods when no apparent dengue transmission is occurring, and over-reporting during periods of epidemic activity. The laboratory confirmation rate of reported cases can provide extremely useful feedback to the physicians and health officials responsible for the case reporting system. It is probably the most important type of information needed to increase the sensitivity of the surveillance system. Specifically, case reporting systems must be closely monitored, in order to insure that lack of interest or a low "index of suspicion" from participating physicians, clinics, and hospitals do not result in such gross under-reporting that the epidemic reaches almost peak transmission before it is recognized.

Seroepidemiologic surveys can be an important component of epidemiologic evaluation of surveillance systems. Following a period of increased or epidemic transmission, properly planned and conducted surveys can provide valuable information on age stratified and geographic transmission rates. Both blood samples for serology and questionnaire data should be collected. Such estimates of incidence and prevalence provide the data needed to make decisions on the future direction of control programs.

## Entomological Evaluation

Entomological evaluation is especially appropriate for assessing vector control programs in areas with high infestation levels (see Table 15, in the section "Current Approaches for Surveillance and Control," beginning on page 34.) Evaluation will determine the efficacy of an intervention and will provide information for making decisions on the appropriateness of the methodology, the timing and frequency of the activities, and other control aspects. It not only provides assurance of effectiveness, but it also can help identify reasons for failure. When failures occur, carefully designed and executed evaluation measures will provide data for selecting and planning alternative interventions in the future.

The techniques used in most entomological evaluation procedures, will be the same as those used for surveillance purposes (see the section on vector surveillance, beginning on page 28). The entomological techniques themselves, as well as the interventions to be applied and, where appropriate, the equipment and product to be used, should be evaluated, especially when new procedures are introduced.

For evaluating preventive measures (e.g., source reduction and management of container breeding sites within an integrated program), the traditional entomological parameters (e.g., house, container, and Breteau indices) will give some indication of the program's overall impact. However, they will not detect changes in the relative adult vector abundance. The relative importance of different container types in a given locality may be determined by computing the Breteau index for each type. An assessment of the extent to which discarded, non-essential containers have been eliminated or removed and the extent to which useful or essential containers have been appropriately managed or modified, should be considered for inclusion in program evaluation, especially when community-based strategies are being applied.

With respect to evaluation of larviciding and biocontrol measures, the efficacy and duration of control can be directly measured using standard larval survey and bioassay techniques.

For evaluating space sprays used for emergency suppression of adult vector populations, bioassay cages and droplet collection devices can be used to ascertain the penetration of spray droplets into exposed and sequestered sites in and around houses. However, the impact of sprays on caged mosquitoes does not necessarily reflect mortality

in the natural mosquito population. If resources permit, the effect of treatment on the wild mosquito population should be carefully assessed. This can be achieved by directly measuring changes in adult density, using either landing/biting or indoor resting collection techniques or indirectly by measuring oviposition rates. The latter approach, using the enhanced CDC ovitrap, has proven both practical and sensitive, and is less demanding of skills, personnel, and resources than are adult collection methods.

## Information Systems for *Aedes aegypti* Control Programs

The information needs of ongoing control programs based on primary health care strategies differ widely from those of time-limited eradication campaigns. In addition to the use of insecticides, contemporary programs incorporate other strategic approaches for the management of vector populations, including biocontrol methods such as larvivorous fish, and source reduction that, in turn, incorporates several options such as the destruction or removal of containers or their proper storage, mosquito proofing, and cleaning. Because eradication campaigns historically relied almost exclusively on the application of insecticides to all potential larval habitats, little importance was given to differences in larval ecology from locality to locality. In the context of the primary health care approach to vector control, a clear understanding of larval ecology and human behavior is required at the community level, so that health education and health promotion efforts can be focused on priority habitats, using the most appropriate strategies for container management, modification, or elimination. Moreover, the concept of "species sanitation" must be broadened to include mosquito species other than *A. aegypti* (e.g., *Culex pipiens quinquefasciatus*) and rodents, cockroaches, flies etc. which are perceived as nuisances and health problems by the community.

Priorities for operational coverage should be determined according to risk factors that only partially deal with vector densities traditionally measured using the house and/or Breteau and/or container indices. Other risk indicators include human population density, water supply adequacy, and availability and quality of solid waste disposal services. These indices are not part of the conventional data-gathering process.

In modifying and adjusting an information system for contemporary program delivery the following points should be considered:

- In addition to gathering data, the system should support the process of program development, planning, and decision-making.
- In keeping with more dynamic epidemiological control approaches, the system should be readily adaptable to local demographic, geographic, and ecological situations in accordance with the demands of the program.
- The system should provide information that facilitates the identification of new combinations of control tactics that could be implemented as integrated strategies.
- Databases should include community demography; knowledge, attitude, and practice (KAP) survey results; and other external data sets needed for planning and development of social participation strategies; the system should readily exchange information to and from other elements of the primary health care program.
- The entomological monitoring and surveillance system should be closely linked to the disease surveillance system.

### Data Categories

Two major categories of data can be identified: internal, those that are generated by the program itself, and external, those that are generated from other sources.

#### *Types of Internal Data*

In terms of internal data, the basic unit of data collection is the house, premise, or building. For program delivery (i.e., applying control measures), data are required from every premise visited; details should include whether or not the control measures were actually applied, or partially applied, and the reasons for any difficulties encountered. While this data set warrants routine collection, other parameters, such as mosquito population changes or larval habitat characteristics, can be measured on a sampling basis (see the section on vector surveillance, beginning on page 28) or by targeted research.

#### *Types of External Data*

Demographic data on the distribution and density of the human population, settlement charac-

teristics, and conditions of land tenure (e.g., squatter, owner/occupier, house styles, education, and socioeconomic status) are all interrelated, and are of fundamental importance for planning purposes and for assessing the risk of acquiring dengue. Knowledge of the water distribution system, its quality and reliability, as well as domestic water storage practices also are considered vital.

Of the other basic services, solid waste disposal ranks high in importance, since geographic coverage and the frequency and quality of collection may directly affect the density of vector habitats in a given locality. Sewerage and excreta disposal methods can be of particular significance in terms of the breeding of *Culex pipiens quinquefasciatus* and the proliferation of other insect and rodent pests.

To a greater or lesser extent, the delivery of these basic services are factors in determining the infestation characteristics of peridomestic mosquitos, rodents, and other pests. Knowledge of their quality and coverage provides insight into vector ecology in any given locality, and can be utilized to plan targeted source reduction or other management strategies or to organize epidemic intervention measures.

Meteorological variables, especially rainfall, directly influence vector populations by inundating outdoor container habitats. In addition, in some areas or during periods of limited rainfall, more extensive potable water storage may be needed. Unlike other external data types for which only periodic, perhaps annual, updates are required, meteorological data may warrant frequent monthly or weekly collection reviews, if it is to be of value in determining seasonal trends of the vector population and human behavior as it relates to peridomestic water storage.

The more a particular program promotes intersectorial strategies and social participation in vector control, the more relevant that data on community organizations such as non-governmental and private voluntary organizations, schools, youth organizations, and churches will be. Other government agencies with which collaboration can be sought should be identified. Local patterns of communication, language, and literacy skills will be especially important for developing health education strategies and community mobilization.

### Economics of Control Programs

In most countries of the Americas, it is difficult to estimate how much dengue prevention and/or



control programs spend annually. Often, dengue (or *Aedes*) control programs function as branches of malaria control programs and/or operate sporadically in response to real or perceived emergencies. Supplies, equipment, and personnel are not continuously available. In emergencies, or under public pressure, expenditures of national funds or donations can be very high, especially for insecticides, while little money is available for routine operations at other times.

As a result, substantial funds are spent on unstructured activities, the results of which are difficult or impossible to evaluate. It is important, therefore, that economic factors be considered during the reorganization or strengthening of dengue control programs recommended in this document.

Information of this nature is essential for planning, evaluation of the cost-effectiveness of individual control measures, comparison of different control measures, and evaluation of new methods.

Examples of the types of cost estimates that should be obtained include the following:

### **Vector Control Costs**

#### *Chemical*

It is not enough merely to estimate the quantities of insecticide required. Costing should begin with the size of the population to be protected and the number of premises or the area to be treated, as well as the personnel requirements (at all levels) based on the frequency of application. Personnel costs include expenditures on training, safety equipment, and per diem or overtime when applicable. Initial capital costs for equipment, depreciation, and/or shared usage with other programs must be considered. Operational costs, especially for ULV space spraying, should include machinery and vehicle maintenance, and frequent calibration of pumps, as well as the costs of monitoring vector populations, penetration of droplets, and the level of compliance by the local population, depending on the control measures employed. The compilation and analysis of data also involve real costs.

#### *Environmental management*

Source reduction programs are often thought to be less expensive alternatives to chemical control measures. However, this may only be true for short-term ("clean-up") campaigns. Long-term success in environmental management requires

health education, public health communication, and development of community cooperation. Educational materials, promotion through the media, introduction of sanitary concepts into school curricula, training teachers, etc., may involve considerable costs. Some of these costs can be covered by other sectors, (such as educational, municipal, or private), and such collaboration should be encouraged.

Environmental management campaigns, especially clean-up campaigns, may fail from a lack of trucks and facilities for solid waste disposal. Communities, especially cities, need either to invest in such equipment or must make arrangements to rent or borrow it from other sources.

As with chemical control, environmental management programs must be evaluated and the vector and disease data organized and analyzed; all of these activities will involve costs.

#### *Laboratories (surveillance)*

Most national laboratories that perform serodiagnosis or virus identification for dengue will also be responsible for other diagnostic services (measles, polio, etc.). The cost of the dengue component must be adequately funded based on an analysis of the number of samples processed, the reagents, and the equipment required. Long-term investment must be made, and accounted for, in the training of professionals and technicians. Refresher training sessions need to be routinely scheduled.

#### *Coordination with hospitals and medical supplies*

In addition to coordination among its component parts, the program requires coordination between the curative and preventive services and these expenses should be recognized. An information exchange network is required, and depending on the endemic status of dengue/DHF, and the potential for epidemic situations, hospital supplies and equipment must be readily available and be replaced and/or updated regularly. A list of such materials is provided in the section on "Organization and Requirements for Medical Care," beginning on page 60.

Each country should estimate the costs associated with individual case management and with cooperation and information from neighboring countries and international organizations, and estimate requirements on an annual or biennial basis.

### *Surveillance*

Guidelines for entomological, epidemiological, and viral surveillance methods are given in the chapter on "Surveillance," beginning on page 23. These can be used as a framework for estimating the size of the required surveillance system in a given city, state, province, or country, as well as the cost of the surveillance that, in addition to laboratory costs and information exchange, will include expenditures for collecting and processing samples in the field.

### **Community Participation, Health Education, and Communication Costs**

In addition to the costs that have already been mentioned, liaisons must be established with community groups, in order to provide technical assistance where required and to determine how the health authorities can assist those groups with their individual and collective efforts.

Health education and social communication activities will play significant roles in community participation efforts; consequently, it is extremely important to estimate their cost. The recording of actual costs of health education, communication, and community participation should also be made on an annual basis.

### **Other Costs**

Each national program will have additional cost elements, depending on the governmental structure and the requirements of their accounting systems. These may include depreciating capital investments (vehicles, pumps, etc.); shared use of facilities (warehouses, administrative services, etc.), and in-country purchase and delivery of supplies (insecticides).

In summary, once the costs of the components of individual dengue control projects have been determined, it will not only be possible to estimate total costs, but also to identify where savings may be gained through intersectorial collaboration with other government agencies and the private sector. The cost data collected, along with the epidemiological and entomological data, provide an initial framework for conducting cost-effectiveness studies of different interventions used in the national program. New methods and improvements of existing methods can be more effectively evaluated for operational use when their economic benefits or limitations are fully understood. The benefits of dengue control programs should be considered in light of the economic as well as the health impact of epidemics, as detailed in the chapter on "Dengue and Dengue Hemorrhagic Fever," beginning on page 3.

## 8. OPERATIONAL RESEARCH

New, practical, inexpensive, and easily applied methods and combinations of methods of control need to be developed. Moreover, many old methods that still are being used in combination with other measures that may mask their effect, need to be re-evaluated individually.

The following are some suggested topics for operational research:

- For each geographic area, determine which container types produce the most adult *A. aegypti*, their abundance and seasonal variations, and the duration of their presence.
- Identify people at high risk of dengue infection and develop methods to protect them.
- Conduct biological studies of the relationship between larval density and adult production and longevity.

- Evaluate methods for achieving greater social participation in dengue prevention.
- Evaluate the community's potential role for rapid response to an epidemic alert through source reduction.
  - Develop insect-proof water drums and other containers or covers that are easily constructed and used and that are appropriate for local conditions.
  - Determine the optimal dosages, droplet spectrum, and modes of application of aerosol insecticides.
  - Study the effect of insecticide applications on the predators of adult *A. aegypti*.
  - Develop a long-lasting, non-sedimentary formulation of the *Bacillus thuringiensis* H-14 for use in potable water.
  - Study the use of native desiccation-resistant cyclopoid copepods for the biological control of *A. aegypti*.



## 9. TRAINING IN DENGUE PROGRAMS

Bringing national dengue programs in line with an integrated, community-based prevention and control approach will require training personnel in new methods; conducting scientific congresses and seminars to exchange new information; holding meetings to promote new strategies; and presenting workshops to develop country plans of action and norms for dengue programs. These activities may be national or international in scope and should be appropriately directed toward field personnel, program directors, or research scientists.

For these activities, care must be taken to select candidates that are actively involved in the corresponding aspect of dengue control. Every event should be evaluated in order to identify those aspects that need improvement.

Training is recommended in the fields detailed below.

### **Clinical and Laboratory-based Surveillance, Diagnosis, and Case Management**

Because the success of laboratory techniques depends on mastering scientific knowledge and specific practices, training sessions should not attempt to cover all techniques in a short time, but should focus on one technique and allow sufficient practice time before the trainee learns additional techniques.

- There should be training in the following techniques: MAC-ELISA (IgM), hemagglutination-inhibition (HI), virus isolation in cell culture, and plaque reduction neutralization test.

- Training courses for the Region's scientists and laboratory technologists should be organized whenever new methods for rapid laboratory diagnosis become available.

- Local, regional, and central level personnel will need training on completing forms, identifying reportable cases, and collecting and submitting blood samples.

- Local, regional, and central level personnel will need training on dengue, its transmission, signs/symptoms, and vector's characteristics.

- Training should be given to physicians and nurses on the clinical aspects of dengue and on the appropriate management of patients.

### **Vector Surveillance**

- Statistical sampling methods for larval mosquito populations should be taught and used to optimize resource utilization.

- Nontraditional entomological evaluation techniques, including use of the enhanced CDC ovi-trap and backpack aspirator, should be incorporated.

### **Decentralization**

- Workshops on redistributing responsibility and disseminating knowledge to the local level should be held at the central and regional levels.

- Courses emphasizing managerial skills should be presented at the regional level.

- Prevention and control methods using appropriate technology should be emphasized at all levels.

- Workshops emphasizing training skills should be presented at all levels to facilitate replication of courses.

### **Environmental Management**

- Techniques in nonchemical source reduction of containers (e.g., draining, filling, puncturing, burial, and burning) should be demonstrated.

- Inspection techniques for foci amenable to source reduction (e.g., containers, tires, flower vases, rain gutters, septic tanks, junk cars) should be demonstrated.

- Design, use, and repair of individual and community potable water supply systems (e.g., individual and communal standpipes, cisterns, and drums) using appropriate technologies to insure water availability and quality, consistency of delivery, storage, and water supply protection and treatment should be covered.

- Economic theory and local practice of recycling should be discussed and reviewed. Markets for recyclable discarded containers should be developed and evaluated.

- Integrated solid waste management, including proper solid waste storage; waste collection frequency and community coverage; clean-up campaigns vs. regular solid waste pickups; and special waste collection (e.g., tires, junk cars, auto batteries) should be presented.

- Innovative sampling methods for containers (e.g., essential, nonessential, natural) should be taught.

- Environmental management at important nonresidential sites, such as seaports, airports, used tire facilities, schools, and hospitals, should be stressed.

- House design and personal protection measures to reduce mosquito biting should be reviewed.

### **Chemical Control**

- Techniques and dosage of insecticide application should be discussed.

- Larviciding (focal) and residual (perifocal) treatment procedures should be taught and practiced.

- Space spraying techniques should be presented and evaluated.

- Safe handling of pesticides and recognition of pesticide intoxication should be emphasized.

- The importance of monitoring blood cholinesterase levels in employees working with insecticides should be stressed.

- Procedures for determining vector susceptibility to insecticides should be taught.

### **Emergency Control**

- Training courses on the proper use and operation of space spray equipment should be conducted.

- Simulation exercises should be presented.

- International workshops should be held to evaluate emergency strategies.

### **Information Management**

- Manual-based information (data) collection and management systems should be presented for program incorporation.

- Theory and practice of computer-based information (data) management should be provided.

- Training in the use of database and spreadsheet computer software programs (e.g., Epi Info, Excel, Lotus 1-2-3) should be provided.

## 10. RECOMMENDATIONS FOR DENGUE PROGRAMS

Except in those few countries where *A. aegypti* eradication is still truly achievable, the program strategy should be changed from one of eradication to one of control that is based on the actions outlined below.

- Generating political support for the program at the highest national-government levels.
- Generating legislative support for the program, to ensure that adequate funds are available to run it, and, where applicable, levy and collect fines.
- Integrating the program within the health sector, other sectors of the economy, and other pertinent nongovernmental organizations to enhance its sustainability.
- Emphasizing environmental management as the main vector control tool; the prudent use of insecticides should only be undertaken when physical methods are impractical, and biological control methods should only be pursued if appropriate.
- Encouraging and incorporating the community's full participation in the design, execution, and evaluation of prevention and control activities.
- Continuing to monitor the vector population through appropriate statistical sampling procedures, in order to target control efforts and evaluate control interventions.
- Intensifying surveillance programs to prevent the spread of *A. albopictus*.
- Expanding the passive surveillance of dengue cases to a proactive program where fever alert, clinics, disease trend analysis, and early laboratory confirmation are used to detect early transmission.
- Developing laboratory capability utilizing the IgM-capture ELISA as the standard technique to support a laboratory-based surveillance network within individual countries or among neighboring countries; viral isolation capability also should be developed where possible.
- Promoting the medical education of physicians and medical care personnel in the recognition, management, and treatment of DHF.
- Conducting clinical, hematological, immunological, genetic, and virological studies of laboratory confirmed cases of severe dengue/DHF.
- Determining the important geographical, epidemiologic, and sociodemographic risk factors for dengue, and stratifying the infested areas by level of risk, in order to efficiently utilize available resources.
- Developing plans for emergency preparedness and response consisting of: actions to be conducted during the preparation, alert, and emergency phases; hospitalization plan; case management; and vector control, including both space spraying for rapid/temporary reduction of infected adult mosquitoes and source reduction for permanent control, plus monitoring vector susceptibility to the insecticides to be used during these periods.
- Utilizing information systems that integrate all pertinent data on the vector, disease, and risk factors, to aid in decision-making, improve the program, and provide future direction for the program.
- Initiating operational research projects of alternative methods and strategies of vector control.
- Periodically evaluating the cost-efficiency, effectiveness, and efficacy of prevention and control programs as a basis for adjusting program strategies.
- Providing continuing-education opportunities for program personnel.

## SELECTED BIBLIOGRAPHY

Note: Bibliography is not all-inclusive. Although in this list they appear only once under a single chapter heading, many references relate to more than one chapter.

### DENGUE AND DENGUE HEMORRHAGIC FEVER

---

- Christophers SR. *Aedes aegypti* the yellow fever mosquito: its life history, bionomics and structure. Cambridge University Press; 1960.
- Diaz AG, Kouri MG, Guzmán L, et al. Description of the clinical picture of dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS) in adults. *Bull Pan Am Health Organ*. 1988;22(2):133-44.
- Dietz VJ, Gubler DJ, Ortíz S, et al. The 1986 dengue fever outbreak in Puerto Rico: assessment of risk factors for severe dengue disease and observations on clinical illness. *Am J Trop Med Hyg*. 1992.
- Focks DA, Haile DG, Daniels E, Mount GA. Dynamic life table model for *Aedes aegypti* (Diptera: Culicidae): Analysis of the literature and model development. *J Med Entomol*. 1993;30(6):1003-1017.
- Focks DA, Haile DG, Daniels E, Mount GA. Dynamic life table model for *Aedes aegypti* (Diptera: Culicidae): Simulation results and validation. *J Med Entomol*. 1993;30(6):1018-1028.
- Gubler DJ, Dietz VJ, Kuno G, et al. The 1986 dengue fever outbreak in Puerto Rico: epidemiologic observations. *Am J Trop Med Hyg*. 1992.
- Gubler DJ, Kuno G, Waterman SH. Neurologic disorders associated with dengue infections. *Proc Intl Conf on dengue/dengue haemorrhagic fever*. Kuala Lumpur, Malaysia. 1983;290-301.
- Guzmán MG, Kouri GP, Bravo J, et al. Dengue haemorrhagic fever in Cuba: clinical investigation. *Trans R Soc Trop Med Hyg*. 1984;78:239-41.
- Guzmán MG, Kouri GP, Martínez E, et al. Clinical and serologic study of Cuban children with dengue haemorrhagic fever: DHF/DSS. *Bull Pan Am Health Organ*. 1987;21(3):270-79.
- Guzmán MG, Kouri GP, Bravo J, et al. Dengue haemorrhagic fever in Cuba, 1981: a retrospective seroepidemiologic study. *Am J Trop Med Hyg*. 1990;42(2):179-84.
- Kaplan JE, Eliason DA, Moore M, et al. Epidemiological investigations of dengue infection in Mexico-1980. *Am J Epidemiol*. 1983;117(3):335-34.
- Knudsen AB. *Aedes aegypti* and dengue in the Caribbean. *Mosq News*. 1983;43(3):269-75.
- Koopman JS, Prevots DR, Vaca Marín MA, et al. Determinants and predictors of dengue infection in Mexico. *Am J Epidemiol*. 1991;133:1168-178.



- Kouri GP, Guzmán MG, Bravo JR. Why dengue haemorrhagic fever in Cuba?: an integral analysis. *Trans Soc Trop Med Hyg.* 1987;81:821-23.
- Kouri GP, Guzmán MG, Bravo JR, Trujillo C. Dengue haemorrhagic fever/dengue shock syndrome: lessons from the Cuban epidemic—1981. *Bull World Health Organ.* 1989;67(4):375-80.
- Martínez E. *Dengue hemorrágico en niños.* Bogotá, Colombia: Instituto Nacional de Salud; 1990.
- Nelson MJ. *Aedes aegypti: biology and ecology.* Washington, DC: Pan American Health Organization; 1986; (PNSP/86-63).
- Pan American Health Organization. *Dengue in the Caribbean.* Washington, DC:PAHO/WHO; 1979. (Scientific Publication No. 375).
- Pan American Health Organization. *Aedes albopictus in the Americas.* In: Proceedings of the 99th meeting of the Executive Committee of the Directing Council of PAHO. Washington, DC: PAHO; 1987. (CE99-15).
- Pinheiro, FP. Dengue in the Americas. *Epidemiol Bull.* 1989;10(1):1-8.
- Rai KS. *Aedes albopictus in the Americas.* *Annu Rev Entomol.* 1991;36:459-84.
- World Health Organization. *Dengue haemorrhagic fever: diagnosis, treatment and control.* Geneva: WHO; 1986.

## SURVEILLANCE

- Brown TM, Brogdon WG. Improved detection of insecticide resistance through conventional and molecular techniques. *Annu Rev Entomol.* 1987;32:145-62
- Centers for Disease Control and Prevention. Case definitions for public health surveillance. *MMWR.* 1990;39(RR-13):10-11.
- Chan KL. Methods and indices used in the surveillance of dengue vectors. *Mosq Borne Dis Bull.* 1985;1(4):79-88.
- Cochran WG. *Sampling techniques.* 3rd ed. New York: John Wiley; 1977.
- Dietz VJ, Nieburg P, Gubler DJ, Gomez I. Diagnosis of measles by clinical case definition in dengue-endemic areas: Implications for measles surveillance and control. *Bull World Health Organ.* 1992; 70(6): 745-750.
- Gubler DJ. Dengue. In: Monath TP, ed. *Epidemiology of arthropod-borne viral diseases.* Boca Raton, FL: CRC Press; 1989.
- Gubler DJ. Surveillance for dengue and dengue haemorrhagic fever. *Bull Pan Am Health Organ.* 1989;23(4):397-404.
- Gubler DJ, Sather GE. *Laboratory diagnosis of dengue and dengue haemorrhagic fever.* Proceedings of the International Symposium on Yellow Fever and Dengue. Río de Janeiro, Brazil; 1988.
- Reiter P, Amador MA, Colon N. Enhancement of the CDC ovitrap with hay infusions for daily monitoring of *Aedes aegypti* populations. *J Am Mosq Control Assoc.* 1991;7(1):52-55.
- Service MW. *Mosquito ecology: field sampling methods.* Essex, United Kingdom: Applied Science; 1976.
- Sokal RR, Rohlf FJ. *Biometry: the principles and practices of statistics in biological research.* San Francisco: WH Freeman; 1981.
- Southwood TRE. *Ecological methods with particular reference to the study of insect populations.* 2nd ed. London: Chapman & Hall; 1978.
- Tinker M. Measurement of *Aedes aegypti* populations. *J Econ Entomol.* 1974;60(3):634-37.
- World Health Organization. *Instructions for determining the susceptibility or resistance of adult mosquitoes to organochlorine, organophosphate and carbamate insecticides.* Geneva: 1981. (no WHO/VBC/81.805,807).

World Health Organization. Resistance of vectors and reservoirs of disease to pesticides. *10th report of the WHO Expert Committee on Vector Biology and Control*. Geneva: WHO; 1986. (technical report no. 737).

## STRATEGIES FOR PREVENTION AND CONTROL

---

- Castillo-Salgado C. *Malaria stratification in the Americas: a socio-epidemiological risk approach*. Proceedings of the First Latin American Conference of Social Science Medicine. Santiago, Chile; 1991.
- Castillo-Salgado C, Bayona-Celis M. *Módulos de estratificación epidemiológica de la malaria*. Washington, DC: Pan American Health Organization; 1990.
- Gubler DJ, Casta-Vélez A. A program for prevention and control of epidemic dengue and dengue haemorrhagic fever in Puerto Rico and the U.S. Virgin Islands. *Bull Pan Am Health Organ*. 1991;25(3):237-47.
- Halstead SB. *Aedes aegypti*: why can't we control it? *Bull Soc Vector Ecol*. 1988;13(2):304-11.
- Kouznetsov RL, Molineau L, Beales PF. *Stratification of malaria situations in tropical Africa for the development of malaria control within the primary health care strategy*. Geneva: WHO; 1985. (no WHO/MAL/86/1028).
- Orlov VS, Semashko IN. *Malaria stratification as a tool in developing the strategy and tactics for modern long-term malaria control programmes*. Geneva: WHO; 1986. (no WHO/MAL/86/1029).
- Pan American Health Organization/World Health Organization. *Manual de normas técnicas y administrativas de la campaña de erradicación del Aedes aegypti*. Washington, DC: PAHO; 1956.
- Pan American Health Organization. *Manual of operations for an Aedes aegypti eradication service*. Washington, DC: PAHO; 1957.
- Pan American Health Organization. *Guía para los informes de la campaña de erradicación del Aedes aegypti en las Americas*. Washington, DC: PAHO; 1971;(Scientific Publication no 228).
- Soper FL. *Hacia la conquista de la salud*. Washington, DC: Pan American Health Organization; 1972.
- Soper FL, Wilson DB, Lima S, Antunes WS. *The organization of permanent nationwide anti-Aedes aegypti measures in Brazil*. New York: Rockefeller Foundation; 1943.

## SUSTAINABLE PREVENTION AND CONTROL PROGRAMS

---

- Annis B, Nalim S, Hadisuwono, Widiarti, Boewono DT. *Toxorhynchites amboinensis* larvae released in domestic containers fail to control dengue vectors in domestic container in a rural village in central Java. *J Am Mosq Control Assoc*. 1990;6:75-78.
- Armada-Gessa JA, Figueredo-González R. Application of environmental management principles in the programme for eradication of *Aedes* (*Stegomyia*) *aegypti* (Linnaeus-1762) in the Republic of Cuba—1984. *Bull Pan Am Health Organ*. 1986;20(2):186-93.
- Center for International Community-based Health Research. *Dengue control: the challenge to the social sciences*. Baltimore, MD: Johns Hopkins University School of Hygiene and Public Health; 1988.

- Cointreau SJ. *Environmental management of urban solid wastes in developing countries: a project guide*. Washington, DC: World Bank; 1982. (urban development technical paper no 5).
- Curtis CF, ed. *Appropriate technology in vector control*. Boca Ratón, FL: CRC Press; 1990.
- Flintoff F. *Management of solid wastes in developing countries*. New Delhi: WHO; 1984. (SEARO series no 1).
- Gordon AJ. Mixed strategies in health education and community participation: an evaluation of dengue control in the Dominican Republic. *Health Educ Rep*. 1988;3(4):399-419.
- Gordon, AJ. Cultural factors in *Aedes aegypti* and dengue control in Latin America: a case study from the Dominican Republic. *Int Q Community Health Educ*. 1990;10(3):193-211.
- Gubler DJ. *Aedes aegypti* and *Aedes aegypti*-borne disease control in the 1990's: top down or bottom up. *Am J Trop Med Hyg*. 1989;40(6):571-78.
- Kendall C, Hudelson P, Leontsini E, Winch P, Lloyd L, Cruz F. Urbanization, dengue and the health transition: anthropological contributions to international health. *Med Anthropol Q*. 1991;5(3):257-68.
- Marten GG. Elimination of *Aedes albopictus* from tire piles by introducing *Macrocyclus albidus* (Copepoda, Cyclopoidae). *J Am Mosq Control Assoc*. 1990;6:689-93.
- Morens DM, Rigau-Pérez JG, López-Correa RH, et al. Dengue in Puerto Rico-1977: public health responses to characterize and control an epidemic of multiple serotypes. *Am J Trop Med Hyg*. 1986;35(1):249-57.
- Nathan MB, Knudsen AB. *Aedes aegypti* infestation characteristics in several Caribbean countries and implications for integrated community-based control. *J Am Mosq Control Assoc*; 1991;7:400-04.
- Nathan MB. Critical review of *Aedes aegypti* control programs in the Caribbean and neighboring countries. *J Am Mosq Control Assoc*. 1993;9(1):1-7.
- Pan American Health Organization. *Emergency vector control after natural disaster*. Washington, DC: PAHO; 1982. (Scientific Publication no 419).
- Rawlins SC. Biological control of insect pests affecting man and animals in the tropics. *CRC Crit Rev Microbiol*. 1989;16:235-52.
- Rifkin SB. The role of the public in the planning, management, and evaluation of health activities and programmes, including self-care. *Soc Sci Med*. 1981;15A:377-386.
- Roberts J. *Community development: learning and action*. Toronto: University of Toronto Press; 1979.
- Service MW. Biological control of mosquitoes—has it a future? *Mosq News*. 1983;43:113-20.
- United Nations Centre for Human Settlements. *Refuse collection vehicles for developing countries*. Nairobi: UNCHS; 1988.
- Winch P, Lloyd L, Daltabuit-Godas M, Kendall C. Beliefs about the prevention of dengue and other febrile illnesses in Mérida, Mexico. *J Trop Med Hyg*. 1991;94:377-87.
- World Health Organization. *Environmental management for vector control*. 3rd report of the WHO Expert Committee on Vector Biology and Control. Geneva: WHO; 1980. (technical report no 649).
- World Health Organization. *Manual on environmental management for mosquito control*. Geneva: WHO; 1982. (offset publication no 66).
- World Health Organization. *Reglamento Sanitario Internacional-1969*. 3rd ed. Geneva: WHO; 1983.
- World Health Organization. *Chemical methods for the control of arthropod vectors and pests of public health importance*. Geneva: WHO; 1984.

- World Health Organization. Recommendations on the disinsecting of aircraft. *Wkly Epidemiol Rec.* 1985;60(7):45-47.
- World Health Organization. *Dengue haemorrhagic fever control program in Singapore: a case study on the successful control of Aedes aegypti and Aedes albopictus using mainly environmental measures as part of integrated vector control.* Geneva: WHO; 1986. (no WHO/VBC/86/928).
- World Health Organization. *Equipment for vector control.* 3rd ed. Geneva: WHO; 1990.
- World Health Organization. Safe use of pesticides. 14th report of the WHO Expert Committee on Vector Biology and Control. Geneva: WHO;1991. (technical report serial no 813).

## **EMERGENCY PREPARATION AND RESPONSE**

---

- Bres P. *Public health action in emergencies caused by epidemics.* Geneva: WHO; 1986.
- Chow CY, Gratz NG, Tonn RJ, Self LS, Pant C. *The control of Aedes aegypti-borne epidemics.* Geneva: WHO; 1977. (no WHO/VBC/77/660).
- Gratz NG. Emergency control of *Aedes aegypti* as a disease vector in urban areas. *J Am Mosq Control Assoc.* 1991;7(3):353-65.
- Pan American Health Organization. The emergency control of Aedes-borne epidemics. Proceedings of a workshop. Bridgetown, Barbados: PAHO; 1987.

## ANNEX I. DENGUE HEMORRHAGIC FEVER RECORD SHEET

Name \_\_\_\_\_ Age \_\_\_\_\_ Sex \_\_\_\_\_ Hospital Name \_\_\_\_\_  
 Race \_\_\_\_\_ Weight \_\_\_\_\_ Date of hospitalization \_\_\_\_\_ Patient No. \_\_\_\_\_  
 Address \_\_\_\_\_

Day of illness (circle day)	1	2	3	4	5	6	7	8	9	10	11	12
Maximum temp., °C or °F (circle)												
Pulse/BP												
Headache												
Tourniquet test (positive, negative, or not done)												
Petechiae												
Purpura/ecchymoses												
Epistaxis												
Hematemesis/melena												
Other hemorrhage												
Hepatomegaly (size)												
<u>Shock</u> Cold extremities Cold, clammy sweat												
Restlessness												
Lethargy												
Pleural effusions												
Ascites												
Rash (describe)												
Lymph nodes Other signs/symptoms												
Hematocrit (%) Platelets ( $\times 10^3$ ) Hemoglobin (Hb) WBC Neutrophils segments/stabs Lymphocytes/monocytes Serum albumin Serum ALT Serum AST Serum bilirubin Hematuria												
<u>Blood for virology/serology</u> Acute Convalescent												
<u>Treatment</u> LR/NSS Plasma Blood Others												

Notes:

# ANNEX II. SAMPLE DENGUE CASE INVESTIGATION FORM

## DENGUE CASE INVESTIGATION

HOSPITALIZED:

Yes \_\_\_\_\_ No \_\_\_\_\_

Name of hospital \_\_\_\_\_

Please complete all sections:

Country \_\_\_\_\_ ID (1-6)

Study  (7)  
Source  (8)  
Species  (9)

Name \_\_\_\_\_  
Last name First name Middle name

**HOME ADDRESS**

Number & Street: \_\_\_\_\_  
City, Town or Post Office: \_\_\_\_\_  
State & Zip or/  
Province, County or Parish: \_\_\_\_\_

Doctor who referred  
the case: \_\_\_\_\_

Office address: \_\_\_\_\_

Phone no: \_\_\_\_\_

Hospital & address: \_\_\_\_\_

Work Address: \_\_\_\_\_ Telephone: \_\_\_\_\_

Sex: Male \_\_\_\_\_ Female \_\_\_\_\_

Age: \_\_\_\_\_ years Date of birth: \_\_\_\_\_  
Month Day Year

Place of birth: \_\_\_\_\_

**CLINICAL DATA**

	Month	Day	Year
Date of first symptom	_____	_____	_____
Date specimen taken:			
first specimen	_____	_____	_____
second specimen	_____	_____	_____
third specimen	_____	_____	_____
Other (specify): _____	_____	_____	_____

**For San Juan Laboratories Use Only**

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
(11)	(61)	(60)
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
(12-13)	(14-15)	(78)
Onset Date		
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	(22-25)	Date of
Kind	Lab No.	Collection
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
(10)	(16-21)	(26-29)
		Days after Onset
		(30)

	Don't Know			
	Yes	No		
Fever				(19)
Headache				(20)
Eye pain				(21)
Body pain				(22)
Joint pain				(23)
Rash				(24)
Nausea or vomiting				(25)
Diarrhea				(26)
Chills				(27)
Cough				(28)
Petechiae				(29)
Purpura/Ecchymoses				(30)
Hemetamiasis				(31)
Melena				(32)
Epistaxis				(33)
Bleeding gums				(34)
Hematuria				(35)
Vaginal bleeding				(36)
Nasal congestion				(37)
Sore throat				(38)
Jaundice				(39)

Tourniquet Test \_\_\_\_\_ (19)  
Blood pressure \_\_\_\_\_ (20)  
Immunizations: \_\_\_\_\_ (21)  
  Yellow fever: \_\_\_\_\_ (22)  
  Others \_\_\_\_\_ (23-25)  
Pregnant? \_\_\_\_\_ (26)  
  Yes \_\_\_\_\_ Month of pregnancy \_\_\_\_\_ (27-29)

COMMENTS: \_\_\_\_\_ (30-39)

**LABORATORY DATA:**  
CBC: WBC \_\_\_\_\_  
  Hct \_\_\_\_\_  
  Hb \_\_\_\_\_  
Platelets \_\_\_\_\_  
Other: \_\_\_\_\_

**EPIDEMIOLOGIC DATA:**  
1. Have you had dengue before (with fever, body pain, and rash)?  
  Yes \_\_\_\_\_ No \_\_\_\_\_ Don't know \_\_\_\_\_ (62)  
2. When? \_\_\_\_\_/\_\_\_\_\_/\_\_\_\_\_  
  Month Year (63-65)  
3. How long have you lived in this location? \_\_\_\_\_ (66)  
4. During the 10 days before onset of illness have you traveled in other locations?  
  Yes \_\_\_\_\_ No \_\_\_\_\_ (67)  
5. Where did you travel? \_\_\_\_\_

(Courtesy: Dengue Branch, DVVID, NCID, Centers for Disease Control, San Juan, Puerto Rico).

Form CDC 56.31A. This questionnaire is authorized by law (Public Health Service Act, 42 USC 241). Although response to the questions asked is voluntary, the cooperation of the patient is necessary for the study and control of the disease.  
REV. 10-85

### ANNEX III. SAMPLE SIZE IN *Aedes* LARVAL SURVEYS

For *Aedes* larval surveys, the number of houses to inspect in each locality depends on the level of precision required, level of infestation, and available resources. Although the more houses inspected, the greater the precision, it is usually impractical to inspect a large percentage of the houses because of limited human resources.

Table 1 shows the numbers of houses that should be inspected to detect presence or absence of infestation. For example, in a locality with 5,000 houses, in order to detect an infestation of > 1%, it is necessary to inspect at least 290 houses. There is still a 5% chance of not finding any positive houses when the true house index = 1%.

**Table 1. Number of houses that should be inspected to detect *Aedes* larval infestation.**

Number of houses in the locality	True house index		
	> 1%	> 2%	> 5%
100	95	78	45
200	155	105	51
300	189	117	54
400	211	124	55
500	225	129	56
1,000	258	138	57
2,000	277	143	58
<b>5,000</b>	<b>290</b>	147	59
10,000	294	148	59
Infinite	299	149	59

Table 2 shows the number of houses that should be inspected in a large (> 5,000 houses), positive locality, as determined by the expected house index and the degree of precision desired. For example, if preliminary sampling has indicated that the expected house index is approximately 10%, and a 95% confidence interval of 8%–12% is desired, then 1,000 houses should be inspected. If there are only sufficient resources to inspect 200 houses, the 95% confidence limits will be 6%–14%. In other words, there is only a 5% chance that the true house index is less than 6% or greater than 14%.

**Table 2. Precision of the *Aedes* house index in large localities (> 5,000 houses), 95% confidence interval of the house index.**

House index (%)	Number of houses inspected			
	100	200	300	<b>1,000</b>
2	0.2–7.0	0.5–5.0	0.7–4.3	1.2–3.1
5	2–11	2–9	3–8	4–7
<b>10</b>	5–18	6–14	7–14	<b>8–12</b>
20	13–29	16–26	16–25	18–23
50	40–60	43–57	44–56	47–53
70	60–79	62–76	64–75	67–73

In small localities, the same precision may be obtained by inspecting fewer houses. For example, if the expected house index is 50% and a 95% confidence interval of 44%–56% is acceptable, then in a *large* locality it would be necessary to inspect 300 houses (Table 2). However, as seen in Table 3, if the locality consists of only 1,000 houses the same precision will be obtained by inspecting 231 houses.

**Table 3. Number of houses to inspect in small localities.**

Total number of houses in the locality	Number of houses to be inspected for desired precision if this were a large locality (from Table 2)			
	100	200	300	1,000
50	33	40	50	50
100	50	66	75	100
200	67	100	120	170
300	77	122	150	230
400	80	134	171	290
500	83	142	189	330
<b>1,000</b>	91	166	<b>231</b>	500
5,000	100	200	285	830
10,000	100	200	300	910
20,000	100	200	300	950
30,000	100	200	300	1,000
40,000	100	200	300	1,000
100,000		200	300	1,000



## ANNEX IV. EMERGENCY PLAN GUIDE

- I. The Emergency Committee (appointed by the Minister of Health)
  - A. Membership
    1. Chairman and Dengue Control Coordinator (from Ministry of Health)
    2. National epidemiologist
    3. Press officer (Ministry of Health)
    4. Chief of the national public health laboratory
    5. Chief medical officer
    6. Chief public health inspector
    7. Chief of vector or *Aedes aegypti* control program
    8. Sentinel physician representative
    9. Representatives from other governmental agencies and NGOs.
      - a. Agriculture
      - b. Tourism/Chamber of Commerce
      - c. Defense
      - d. Public works
      - e. Housing
      - f. Civil aviation authority
    10. PAHO Representation
  - B. Duties
    1. Writing the plan
    2. Declaring an emergency
    3. Coordinating emergency activities
    4. Designating responsibilities during an emergency
    5. Procuring necessary resources
  - C. Center of Operations
    1. Location
    2. Requirements
      - a. Space
      - b. Telephones and communications equipment
  - D. Meetings
    1. Frequency
    2. Purpose
- II. The Emergency Plan
  - A. Preparatory Phase
    1. Analysis of risk (i.e., preparation of tables, figures, maps, aerial photographs)
      - a. Vector
        - 1) Distribution
        - 2) Indices
        - 3) Susceptibility to insecticide
      - b. Disease
        - 1) Historical and present occurrence of dengue, DHF/DSS, and yellow fever in the country and neighboring countries
        - 2) Populations at risk

- 3) Number and distribution of cases
    - a) House surveys
    - b) Notification from health posts/clinics.
  2. Analysis of Current Vector Control Programs
    - a. Institutions
      - 1) National (National Malaria Eradication Service, Vector Control Division)
      - 2) Local (General Health Service; public works, solid waste management, potable water, etc.)
    - b. Inventory of Resources
      - 1) Human resources
      - 2) Space spray equipment and spare parts (number, condition, etc.)
      - 3) Vehicles (number, condition)
      - 4) Insecticides (quantity, age, storage, and location)
      - 5) Source reduction tools and implements.
  3. Emergency Requirements (based on an estimate of the area and population at risk and the treatment strategy)
    - a. Items now available
    - b. Items to be stockpiled
    - c. Items to be obtained locally or internationally upon entering into an "alert phase" or an "emergency phase."
  4. Procurement of Equipment and Supplies
    - a. Emergency budget
      - 1) Standing emergency reserve funds
      - 2) Provision for allotment of funds upon declaring an emergency.
    - b. Sources of equipment
      - 1) Local (Ministry of Health, Ministry Responsible for Agriculture, Ministry Responsible for Tourism, Ministry of Defense, hotels/private industry, pest control agencies, and private enterprise)
      - 2) Imported (For a list of sources, see *Emergency Vector Control After Natural Disaster* [PAHO Scientific Publication No. 419, pp. 90-93]; also consider bilateral agreements for possible provision of insecticide and equipment)
    - c. Sources of human resources
    - d. Funding agencies
    - e. Contingency contracts for consultants or equipment
  5. Special training in preparation for an emergency
    - a. Courses
    - b. Field training simulation exercises to test the Emergency Plan
    - c. Evaluation of current and new methodologies
- B. The Alert Phase:**
1. Dengue, DHF/DSS, or yellow fever in the country
    - a. Criteria
    - b. Plan of Action
  2. Dengue, DHF/DSS, or yellow fever in a neighboring country
    - a. Criteria
    - b. Plan of Action
  3. After a natural disaster
    - a. Criteria
    - b. Plan of Action
- C. The Emergency Phase:**
1. Criteria for determination of an emergency
    - a. Epidemiologic
      - 1) Dengue, DHF/DSS, or yellow fever

- 2) Clinical cases
- 3) Laboratory confirmation
- 4) Determining whether isolation is necessary
- 5) Populations at risk
- 6) Probability of epidemic
- b. Entomologic
  - 1) Adult vector indices
  - 2) Larval indices
2. Declaring an emergency
3. Responsibilities
  - a. Coordination
  - b. Vector control and surveillance
  - c. Disease treatment and surveillance
  - d. Setting up rehydration wards in hospitals and clinics
4. Dissemination of information
  - a. Other government agencies
  - b. General public
  - c. Bee keepers
  - d. NGOs, service clubs, tourist resorts
5. Procurement and organization of necessary human resources, equipment, and supplies
6. Determination of areas to be treated
  - a. If area is large and located in a heavily populated urban area, consider aerial ULV.
  - b. If cases are in a small city, or in a confined area, consider using vehicle mounted machines.
    - 1) On a map, divide affected area into zones, each zone corresponding to an area that a vehicle mounted fogger could cover in one day of operation.
    - 2) Use a color scheme with corresponding color to designate type of application.
    - 3) Color the zone treated with a particular machine and include date of treatment, thereby visually following the progress of what has been treated, what has not been treated, where individual machines are spraying, zones that still require treatment or retreatment, and smaller zones for which back pack or combination treatment can be designated.
  - c. If cases occur in slums or are scattered in areas with no roads, consider using portable back pack mistblowers or foggers.
  - d. Many areas will require the use of both vehicle mounted and back pack portable equipment.
7. Vector control
  - a. Adult control
    - 1) Ground application
      - a) Type of machines
        - (1) Vehicle mounted
        - (2) Back pack
      - b) Insecticides (based on susceptibility and previous trials)
      - c) Dosage as determine by:
        - (1) Discharge rate
        - (2) Swath width
        - (3) Speed of vehicle
    - 2) Aircraft application
      - a) Type and source of aircraft and spray equipment

- (1) Single engine aircraft
- (2) Twin engine aircraft
- (3) Helicopter
- b) Time required to formalize contract
- c) Configuration time and steps for installation of spray equipment
- d) Federal aviation restrictions over urban areas
- e) Center of operations at airport
- f) Calibrations
- g) Reconnaissance flights
- h) Special staff
  - (1) Pilot
  - (2) Ground crew
- i) Swath markers
- j) Insecticide, dosage, droplet size, and climatological limitations
- k) Height of flights during spraying
- b. Larval control
  - 1) Focal
  - 2) Elimination of breeding containers
    - a) Source reduction
    - b) Destruction and removal
- 8. Evaluation of the emergency control measures (tables, graphs, and maps)
  - a. Type
    - 1) Operational
    - 2) Entomological
      - a) Adult mosquito bioassays
      - b) Ovitrap
      - c) Resting adults
    - 3) Epidemiologic: serological surveys; house surveys
  - b. Frequency

## ANNEX V. HANDOUT FOR PATIENTS WITH DENGUE FEVER

### Important information to be given to the parents or family members of outpatients suspected of having dengue fever

Your child or family member probably has dengue fever.

Since this disease can *rapidly* become very serious and lead to a medical emergency, it is important for you to carefully watch your child or relative for the next few days. The complications associated with dengue fever usually appear between the third and fifth day of illness, and, therefore, you should watch the patient for two days after the fever disappears.

#### **“What should you do?”**

1) In order to lower the fever, bathe the patient in tepid water and then place ice (in a pack or bag) or cold water on the head and abdomen.

Give the patient: \_\_\_\_\_.

*DO NOT GIVE THE PATIENT ASPIRIN.*

2) Give large amounts of fluids (water, soups, milk, juices, and sodas) along with the patient’s normal diet.

3) See that the patient gets plenty of bed rest.

4) *Immediately consult your physician if any of the following manifestations appear:* red spots or points on the skin; bleeding from the nose or gums; frequent vomiting; vomiting with blood; black stools; sleepiness; constant crying; abdominal pain; excessive thirst (dry mouth); pale, cold, or clammy skin; or difficulty breathing.

*Do not wait. Immediately consult your physician. It is critical to quickly treat anyone with these complications.*

## ANNEX VI. PARTICIPANTS AT THE DENGUE GUIDELINES MEETING, 16–20 DECEMBER 1991, WASHINGTON, D.C.<sup>1</sup>

### **Brazil**

Rogério Valls de Souza, Fundação Oswaldo Cruz  
Carlos J. Mangabeira da Silva, Fundação Nacional da Saúde

### **Cuba**

Rafael Figueredo, Ministerio de Salud Pública  
Gustavo Kouri, Instituto de Medicina Tropical "Pedro Kouri," Chairman

### **Honduras**

José Gómez, División de Enfermedades Transmitidas por Vectores, Ministerio de Salud Pública  
Enrique Gil-Bellorín, Ministerio de Salud Pública

### **Mexico**

Jorge Méndez Galván, Dirección de Promoción de Salud, Chiapas  
Héctor Gómez Dantés, Dirección General de Epidemiología

### **Panama**

Bedsy Dutary, Laboratorio Conmemorativo Gorgas

### **United States**

Andrew Arata, USAID Vector Biology and Control Project  
Steven Ault, California Environmental Protection Agency and Environmental Health Consultants International, Rapporteur  
Gary G. Clark, Centers for Disease Control and Prevention  
Duane J. Gubler, Centers for Disease Control and Prevention  
Carl Kendall, The Johns Hopkins School  
José G. Rigau, Centers for Disease Control and Prevention  
Andrew Spielman, Harvard School of Health

### **Venezuela**

Iris V. de Chacón, Hospital Central de Maracay  
Diógenes Coello, Ministerio de Salud

### **Pan American Health Organization**

Antonio Benítez, Haiti  
Mónica Bolis, HSP, Washington, D.C.  
Roberto Capote, HSD, Washington, D.C.  
Carlos Castillo-Salgado, HPT, Washington, D.C.  
Francisco López Antuñaño, HPD, Washington, D.C.  
Michael Nathan, Caribbean Program Coordination, Barbados  
Michael Nelson, HPT, Panama  
Ramón Ocegüera, HPT, Panama  
Francisco P. Pinheiro, HPT, Washington, D.C.  
Rodolfo Sáenz, HPE, Washington, D.C.  
Gabriel Schmunis, HPT, Washington, D.C.

<sup>1</sup>Subsequent to the meeting, Erick Martínez of Hospital William Soler in Havana, Cuba, and Suchitra Nimmannitya of Children's Hospital in Bangkok, Thailand, also contributed invaluable to these guidelines.